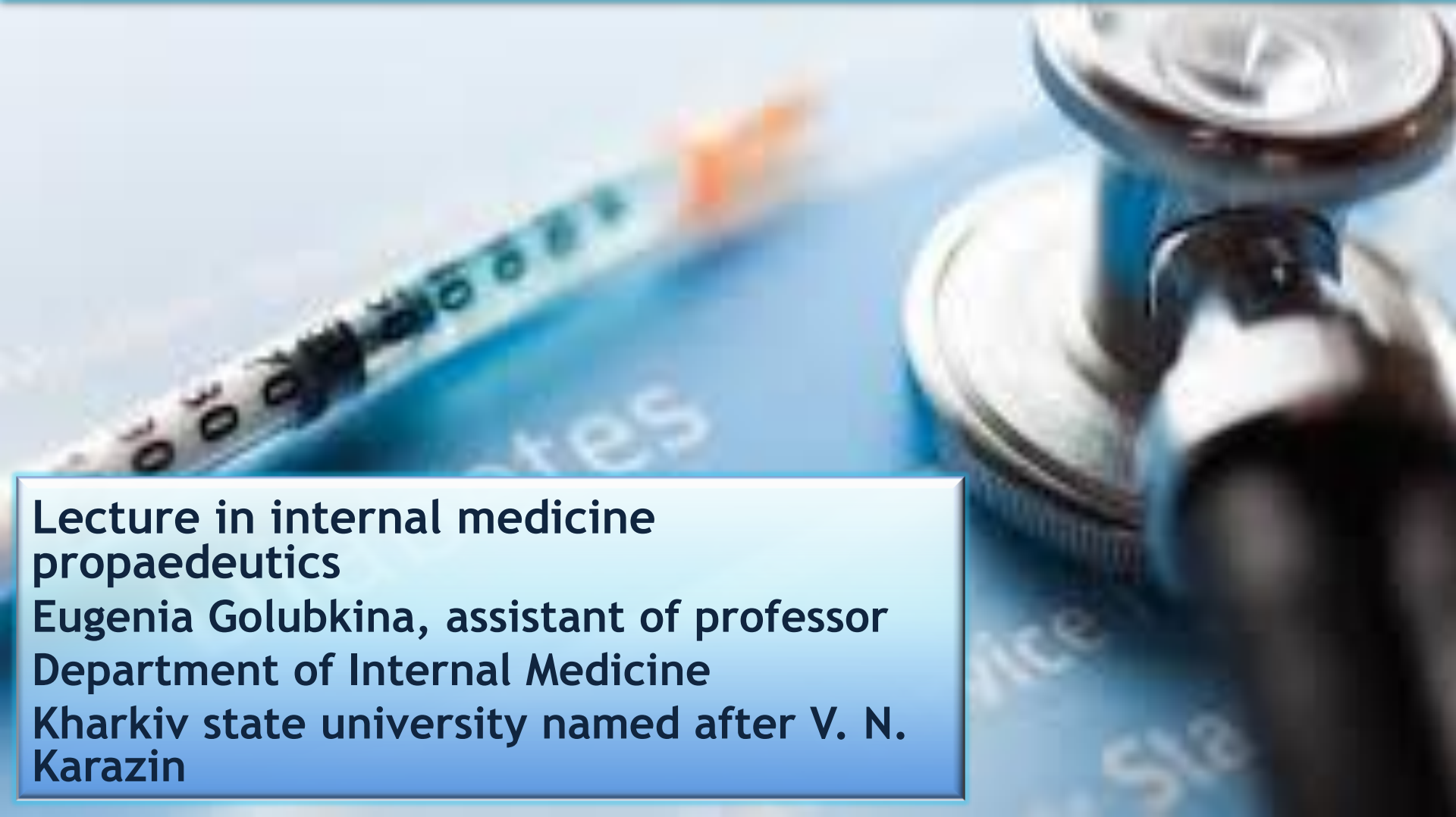
Signs and symptoms of endocrine organ diseases and metabolic disorders. (diseases of pancreas and thyroid gland)



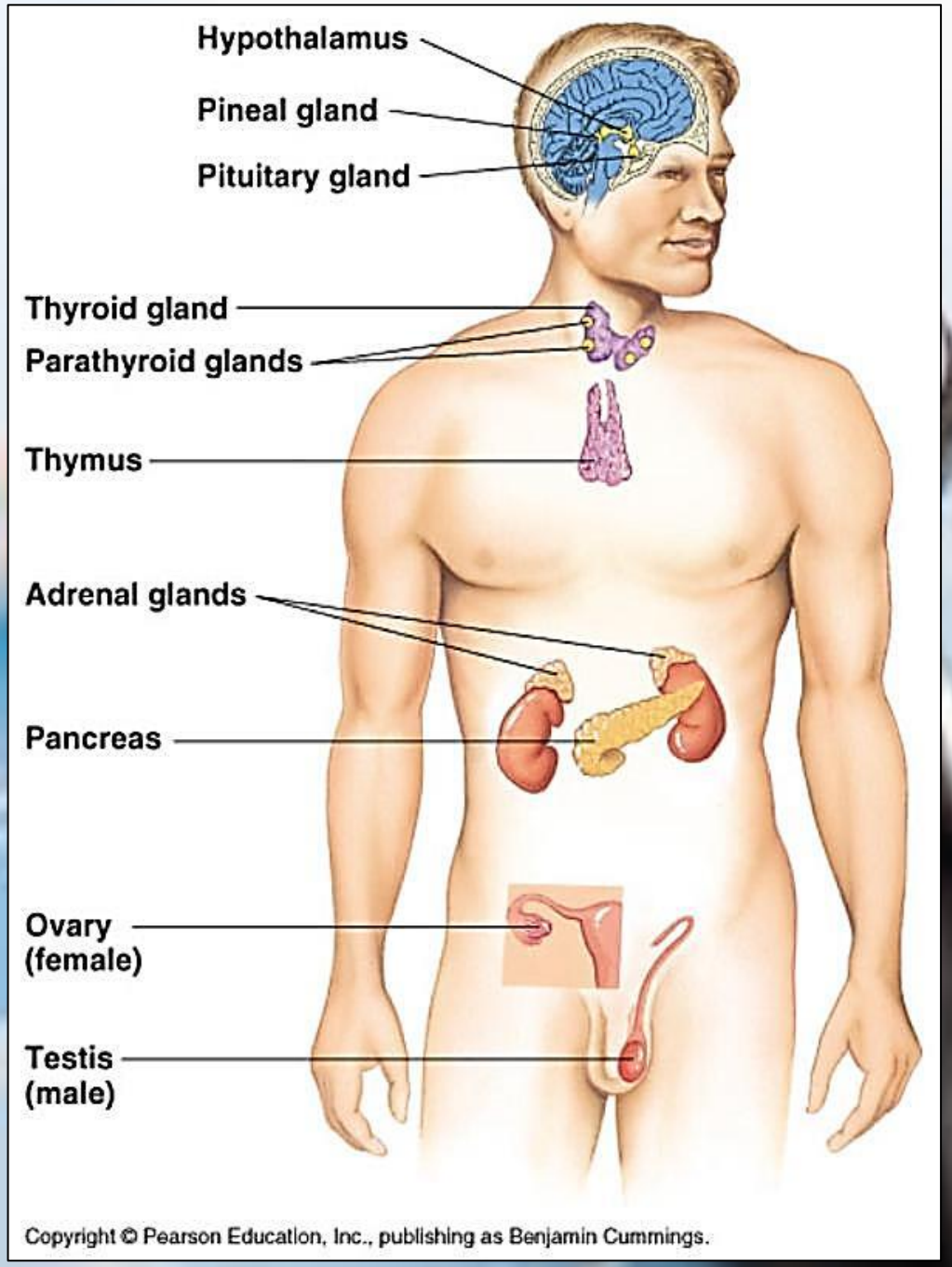
Lecture in internal medicine propaedeutics
Eugenia Golubkina, assistant of professor
Department of Internal Medicine
Kharkiv state university named after V. N. Karazin

INTRODUCTION

Endocrine gland - a gland of the body that produces hormones and secretes them directly into the bloodstream.

Hormone-a chemical substance secreted by an endocrine gland or group of endocrine cells that acts to control or regulate specific physiological processes, including growth, metabolism, and reproduction.

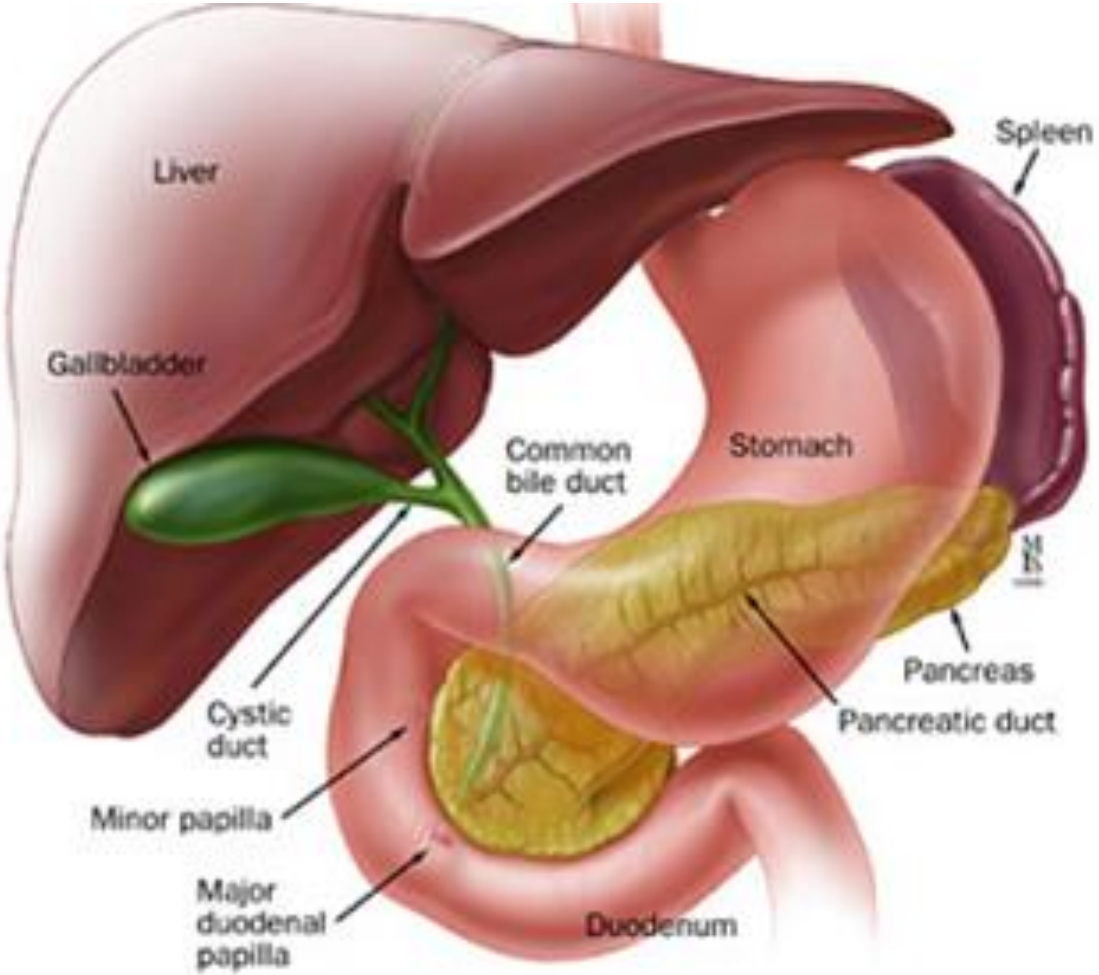
The American Heritage® Science Dictionary



PANCREAS

Location :
in the retroperitoneal space of the upper part of the abdomen.

Features:
almost completely covered by the stomach and duodenum.
Has lobe-like structure.



http://www.hopkinsmedicine.org/gastroenterology_hepatology/_pdfs/pancreas_biliary_tract/chronic_pancreatitis.pdf

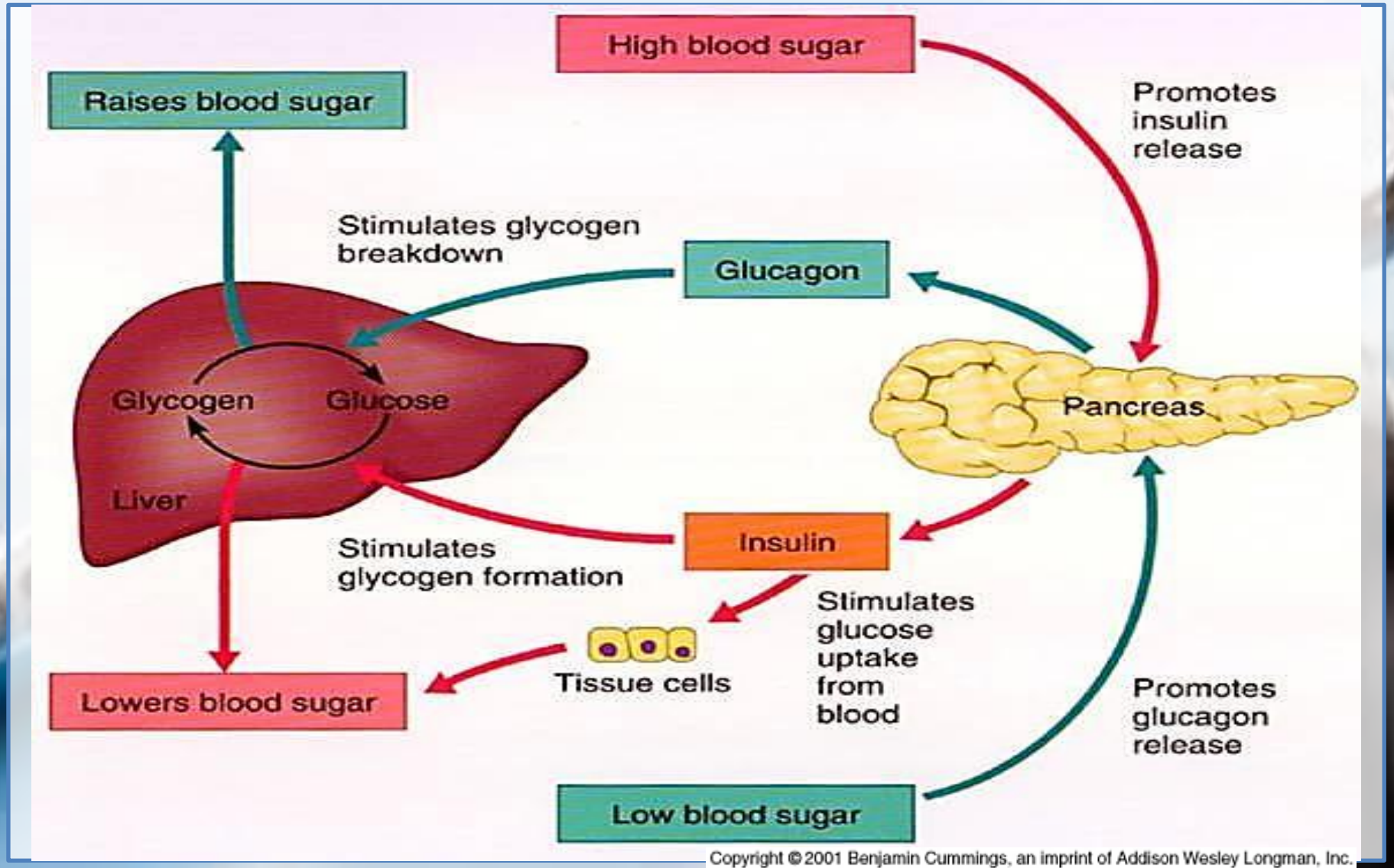
FUNCTIONS OF THE PANCREAS

Pancreas has two main functions:

1. **Exocrine:** the acini of the pancreas secrete pancreatic juice to complete the digestion of chyme in the duodenum. Pancreatic juice is a mixture of water, salts, bicarbonate, and many different digestive enzymes.

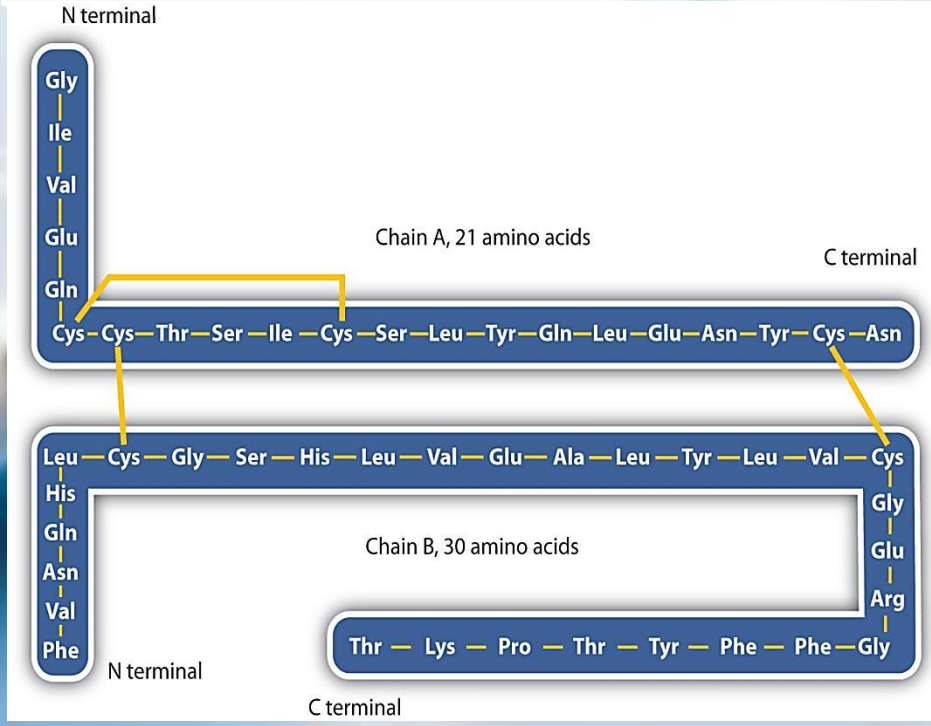
2. **Endocrine:** the endocrine cells form the Islets of Langerhans, consisting of B (ß) cells secreting insulin, A (α) cells secreting glucagon, D (δ) cells secreting somatostatin, and F cells secreting pancreatic polypeptide. These hormones are secreted into the portal circulation.

INSULIN AND GLUCAGON



MAIN FUNCTIONS OF INSULIN

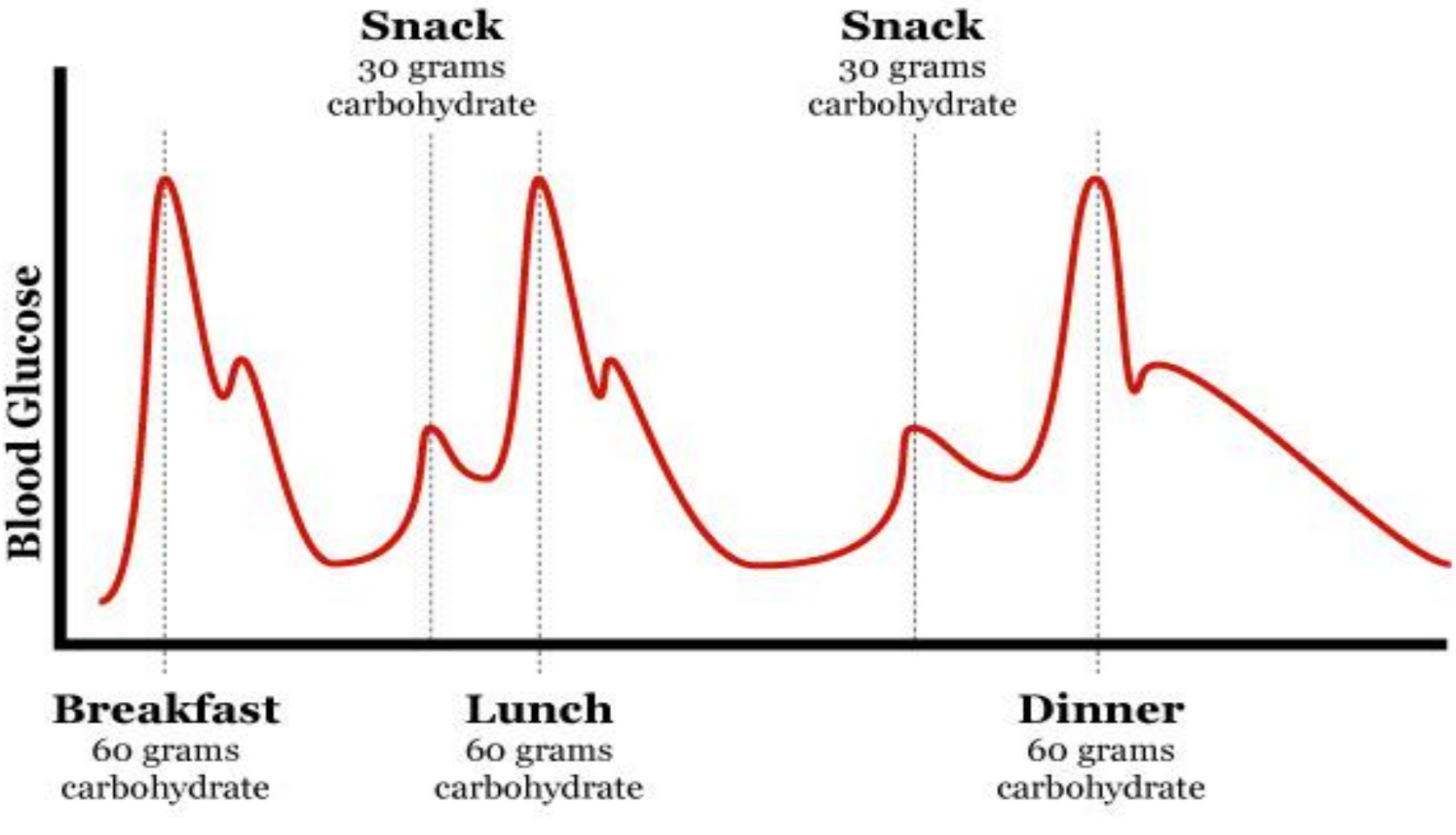
Insulin is a polypeptide hormone, composed of two chains (A and B), derived from proinsulin



Activates +	Inhibits -
Glucose uptake in muscles and adipose tissue	Ketogenesis
Glycolysis	Gluconeogenesis
Glycogen synthesis	Glycogenolysis
Protein synthesis	Proteolysis
Amino acid transport	

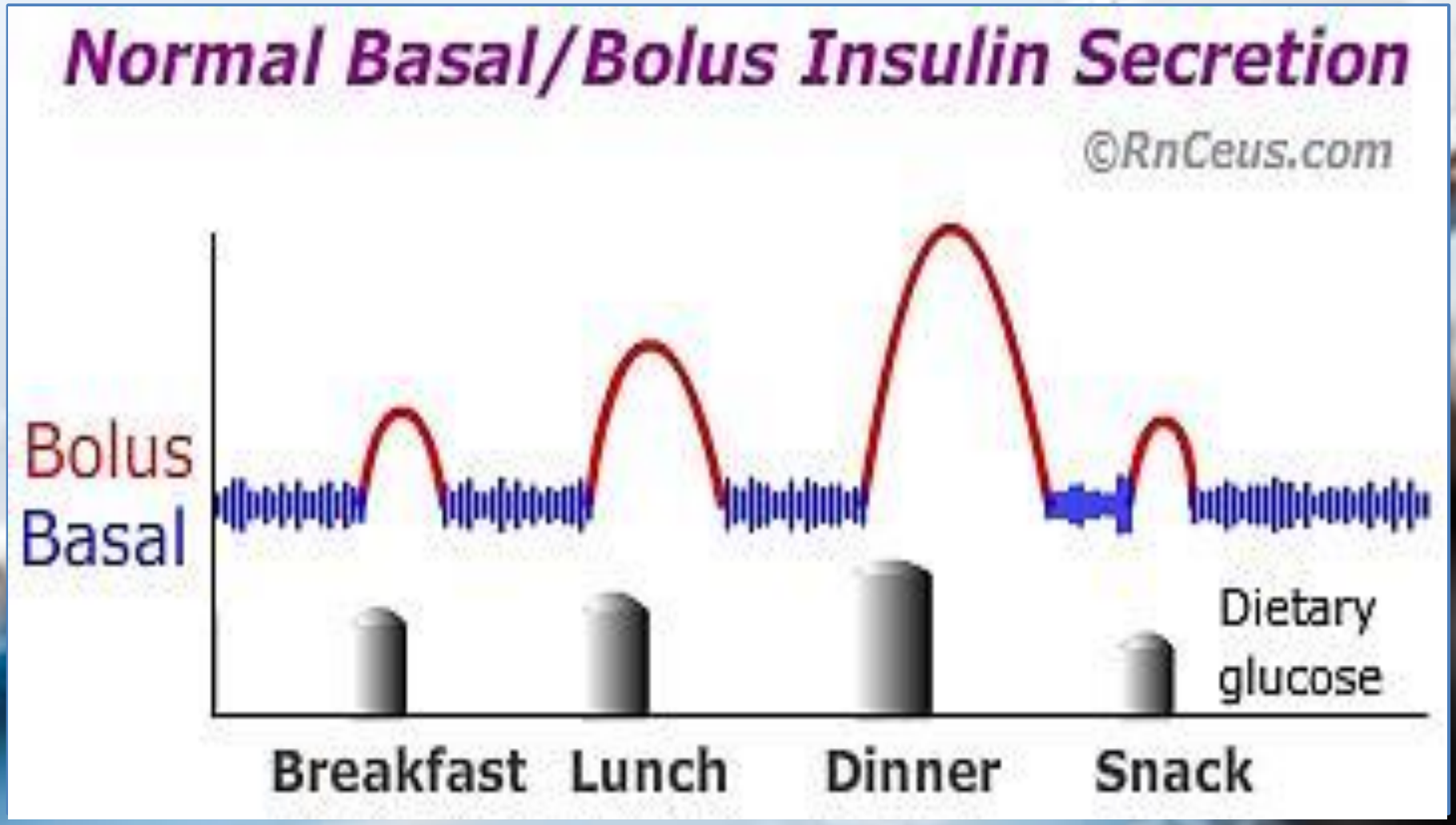
https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcR_jf1lerjdCqUhJBhZ8R97nVT4czJ4I3LOAi7fouMPM0D-10AM6A

BASAL AND POSTPRANDIAL LEVELS OF GLUCOSE



http://www.rnceus.com/dmeds/images/secretion.jpg

BASAL AND POSTPRANDIAL LEVELS OF INSULIN SECRETION



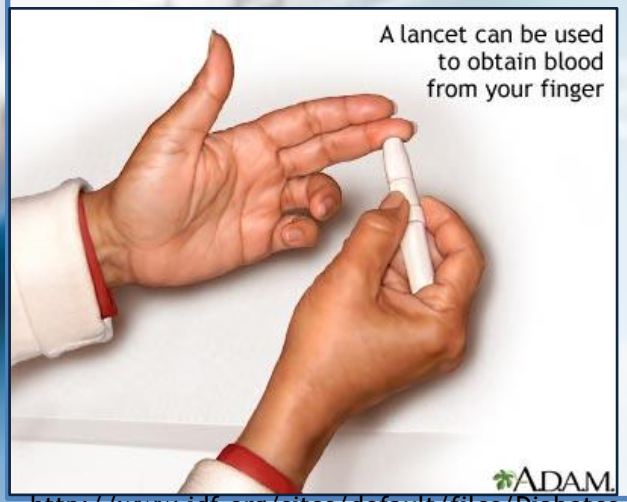
http://www.rnceus.com/dmeds/images/secretion.jpg

NORMAL AND PATHOLOGICAL VALUES OF BLOOD GLUCOSE

Euglycaemia – a normal blood glucose concentration; 3.9-5.5 mmol/l (70-99 mg/dl)

Hyperglycaemia – high blood glucose concentration; >5.5 mmol/l (>70 mg/dl)

Hypoglycaemia – low blood glucose concentration; Starts with 3.3-3.9 mmol/l (60-70 mg/dl)



http://www.idf.org/sites/default/files/Diabetes-in-Childhood-and-Adolescence-Guidelines.pdf

HYPERGLYCAEMIC SYNDROME

Symptom	Characteristic features	Pathogenesis
Polydipsia (“poly” - much, many; “dipsia”- thirst)	Amount of fluid intake is over 2 liters per day.	Increased osmolality of blood due to hyperglycaemia leads to cellular dehydratation and activation of thirst center
Polyuria	Amount of excreted urine is over 2,5-3 liters per day	Due to polydipsia and glucoseuria (osmotic diuresis)
Polyphagia	Increased appetite (hunger)	Compensatory reaction to decrease prevalence of catabolic state

CAUSES OF HYPERGLYCAEMIA

- Diabetes mellitus type1
- Diabetes mellitus type2
- Another types of diabetes mellitus
- Severe stress
- Critical illness (ex. MI, stroke, trauma, infections)
- Surgery
- Drugs (corticosteroids, thiazide diuretics, epinephrine, etc.)
- Diet with high amounts of carbohydrates

HYPOGLYCAEMIC SYNDROME

Autonomic symptoms	Neurological (neuroglycopenic) symptoms	General symptoms
Trembling	Drowsiness	Headache
Palpitations	Discoordination of speech and movements	Dizziness
Sweating	Abnormal behavior, Irritability, anger	Weakness
Anxiety	Confusion	
Hunger	Seizures	
Nausea	Dyplopia	

CAUSES OF HYPOGLYCAEMIA

- Inadequate insulinotherapy
- Strenuous exercise
- Starvation
- Alcohol abuse
- Diseases such as hypothyroidism, tumors (insulinoma)

healthline.com

WHAT IS DIABETES MELLITUS?

Diabetes mellitus is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin production, insulin action, or both.

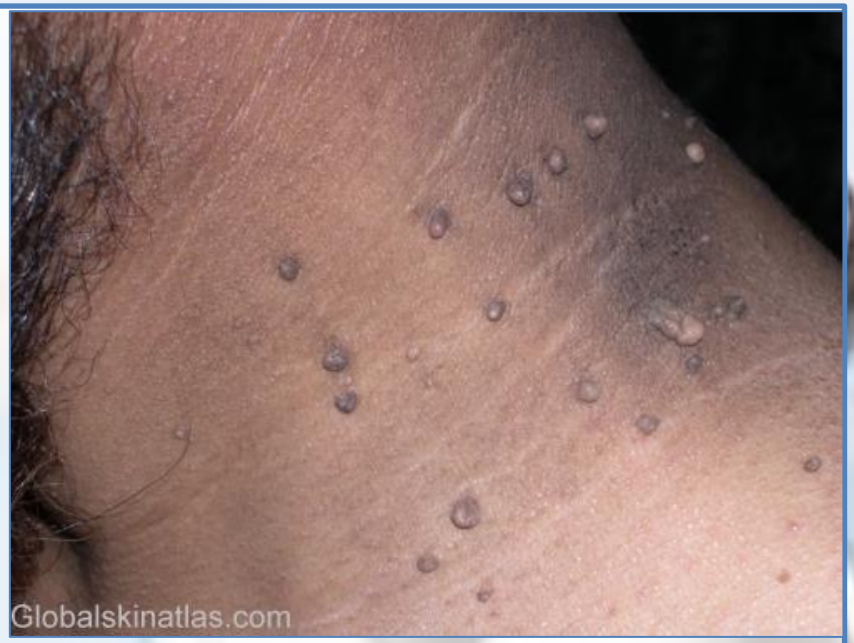
Diabetes - greek for “siphon” or “fountain” for the characteristic frequent urination;

Mellitus - latin for “sweet as honey”

Diabetes Care Volume 38, Supplement 1, January 2015 http://www.diapedia.org/introduction-to-diabetes-mellitus/1104085113

RISK FACTORS FOR DIABETES

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity
- Women who delivered a baby >9 lb or were diagnosed with GDM



- Atherosclerosis
- Arterial Hypertension
- Conditions associated with insulin resistance: severe obesity, acanthosis nigricans, PCOS (polycystic ovary syndrome)
- CVD history

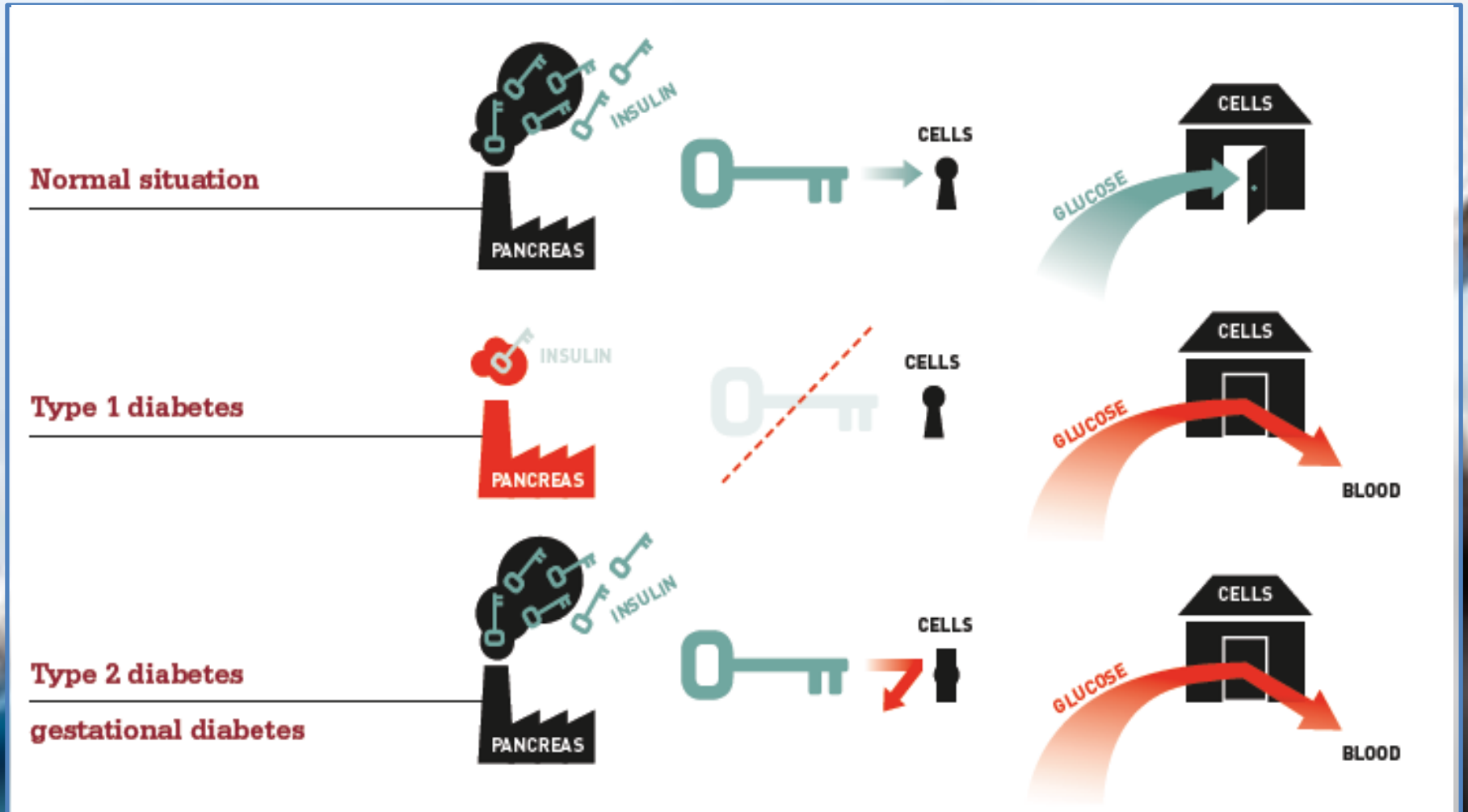
2015 American Diabetes Association (ADA) Diabetes Guidelines - modified

CLASSIFICATION OF DIABETES MELLITUS

1. Type 1 diabetes (due to b-cell destruction, usually leading to absolute insulin deficiency)
2. Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance)
3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes)
4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes

Diabetes Care Volume 38, Supplement 1, January 2015

MAIN TYPES OF DIABETES MELLITUS



Insulin acts as a key that lets the body's cells take in glucose and use it as energy.

Diabetes Care Volume 38, January 2015

Diabetes mellitus 1 type	Diabetes mellitus 2 type
Autoimmune disease: Islet cell autoantibodies, insulitis, Association with other autoimmune diseases	No immune disturbance Insulin resistance Is related to obesity, decreased physical activity and unhealthy diets
Absolute deficiency of the insulin	Partial (relative) insulin deficiency initially
Usually lean (↑ lypolysis)	Often overweight (↑ lypogenesis)
Younger (usually < 30 years of age)	Usually (but not always) older (usually > 30 years of age)
Always need lifelong insulin for survival	usually do not require insulin (can control glycaemia with diet and exercise, or with oral medications, or with the addition of insulin)
Onset is mostly acute; Ketoacidosis is common	Variable; from slow (often insidious) to severe

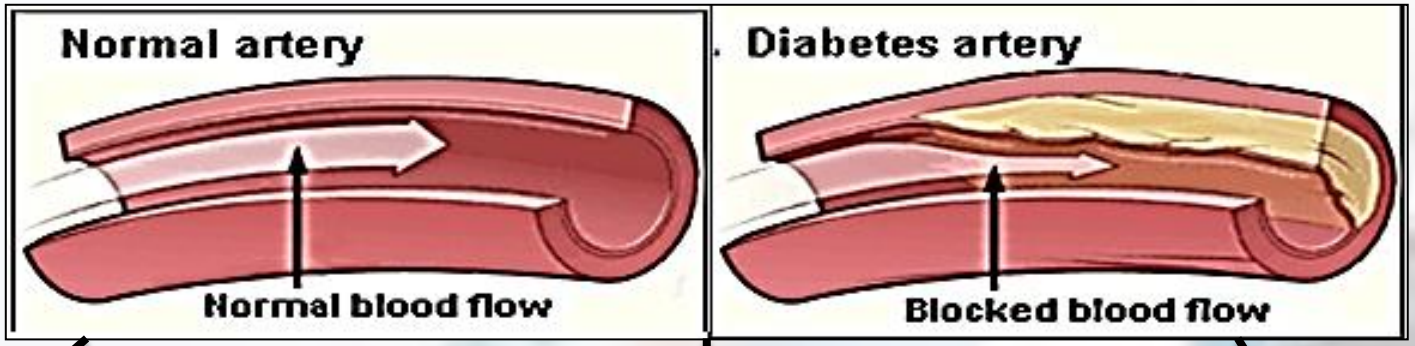
SOME FACTS ABOUT DIABETES

- Without insulin, a person with type 1 diabetes will die.
- People with type 2 diabetes mellitus can stay undiagnosed for many years unaware of the long term damage being caused by the disease.
- Poorly controlled diabetes leads to serious complications and early death.
- Gestational diabetes can result in birth complications that can affect both mother and child and increase the risk for developing type 2 diabetes later in life.

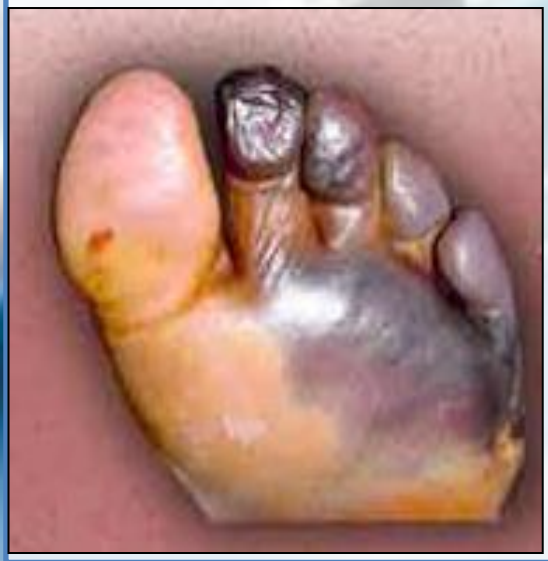
Diabetes Care Volume 38, January 2015

MACROVASCULAR COMPLICATIONS OF DIABETES

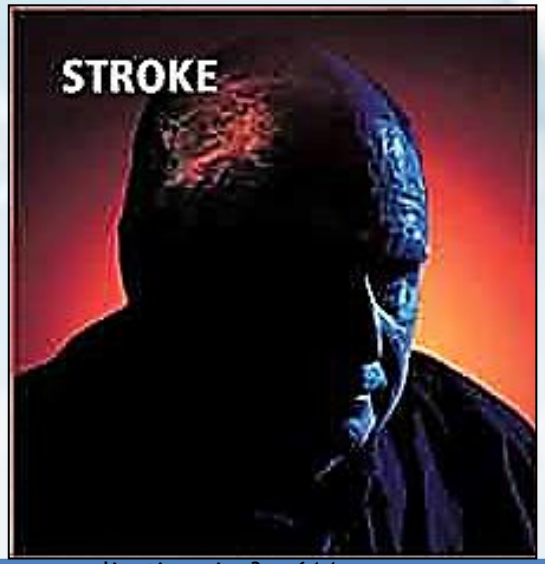
Macrovascular complications - affection of large vessels:



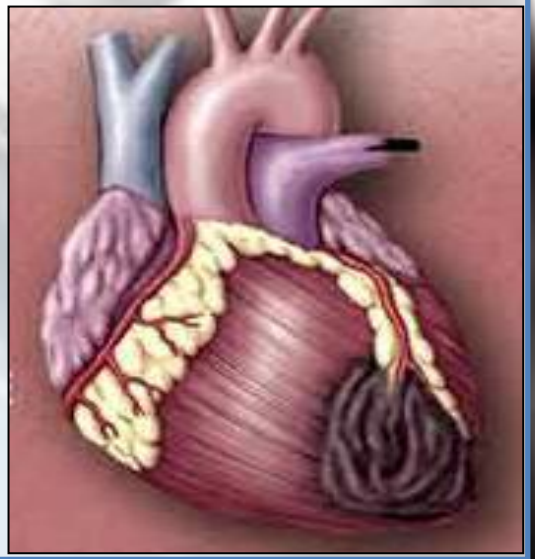
Peripheral vascular disease



Cerebrovascular disease



Coronary artery disease



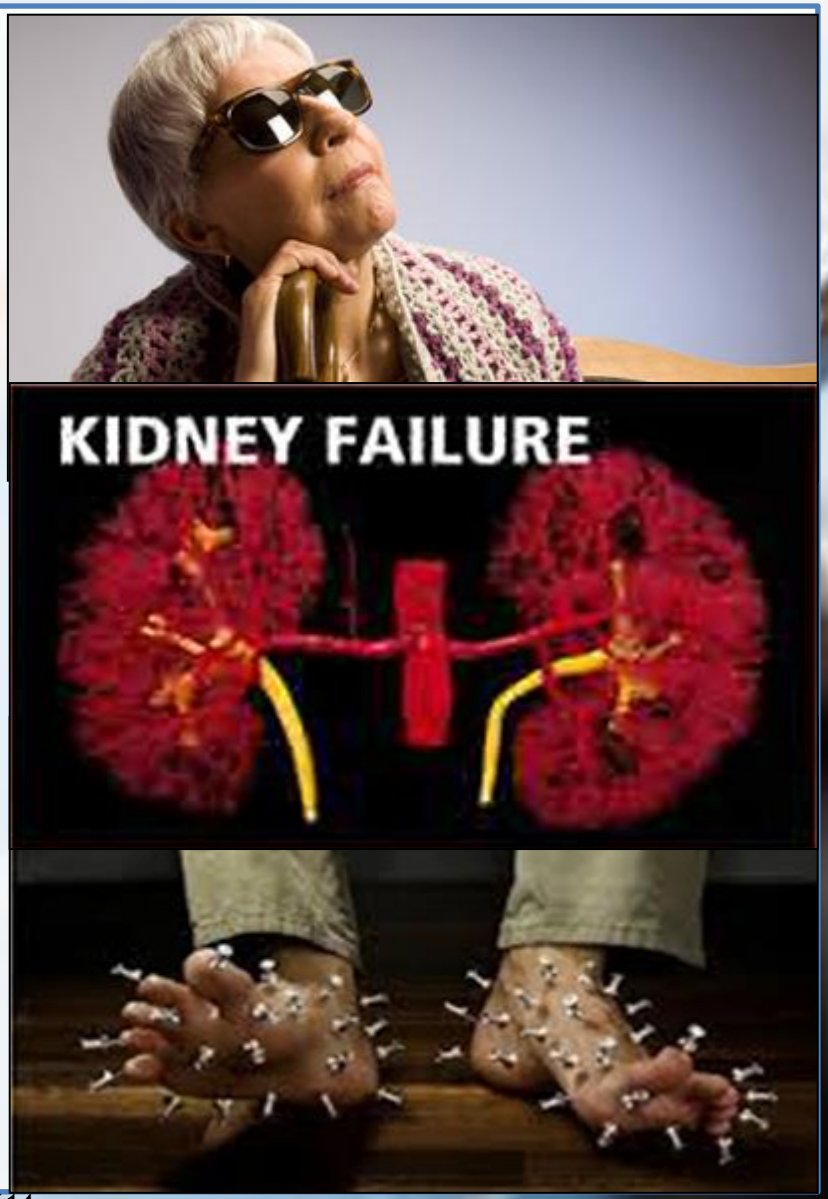
https://anu4bindu.files.wordpress.com/2013/03/diabetes-complications.jpg?w=614

http://healthy-ojas.com/diabetes/heart-disease.html

MICROVASCULAR COMPLICATIONS OF DIABETES

Microvascular complications - affection of small vessels:

- Retinopathy- damaged blood vessels in retina, may cause blindness;
- Nephropathy – may lead to kidney failure and death
- Neuropathy – "Walking on pins and needles"



https://anu4bindu.files.wordpress.com/2013/03/diabetes-complications.jpg?w=614

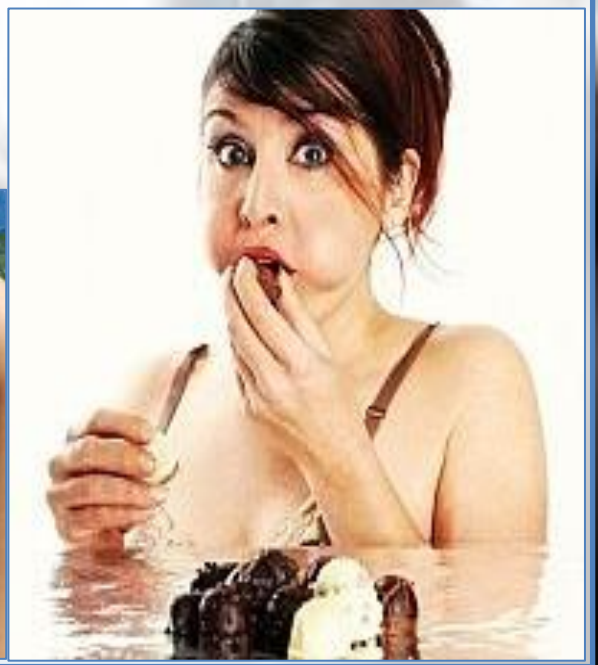
DIABETES MELLITUS: MAIN COMPLAINTS

Classic triple P:

Poliuria - increased urinary frequency ;

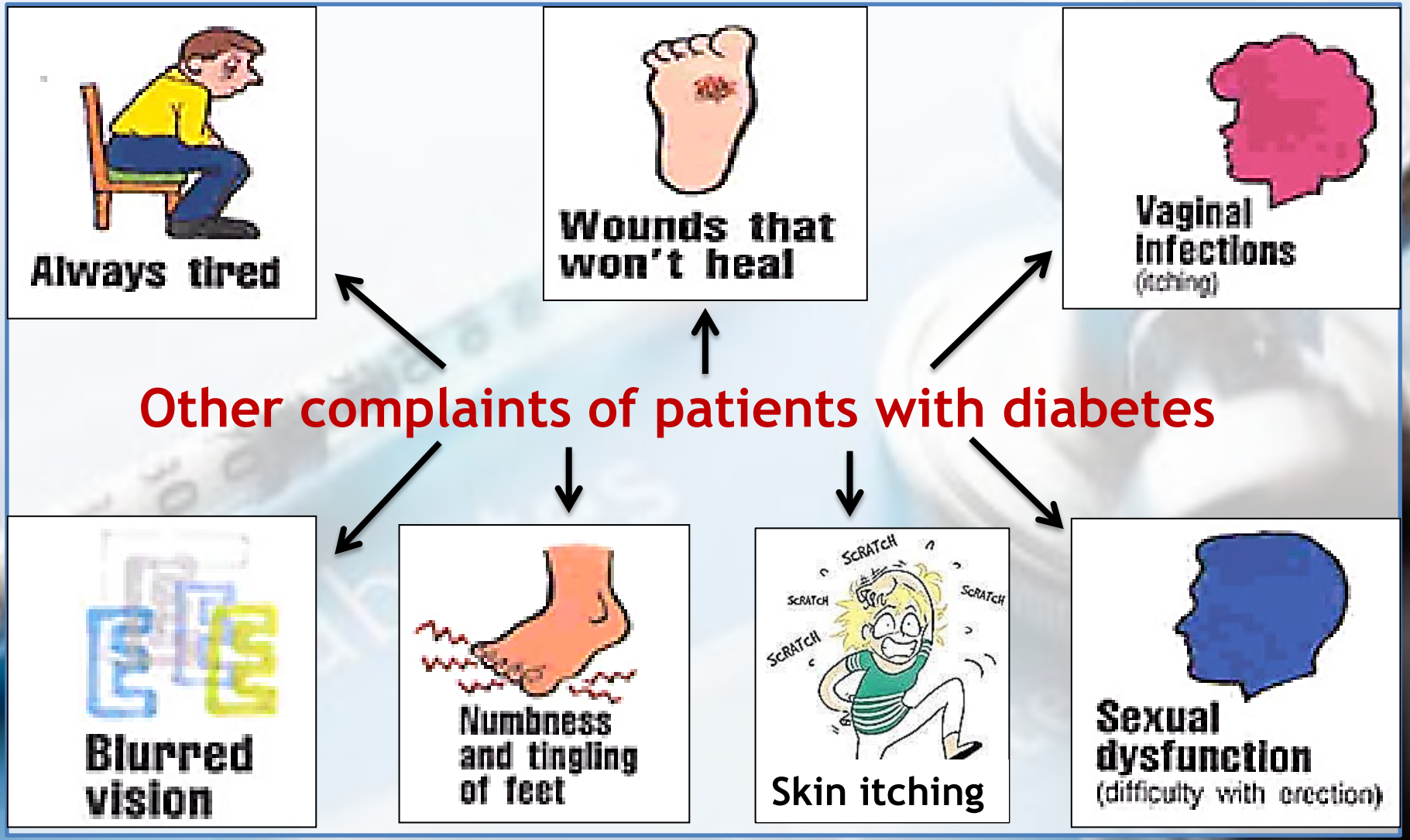
Polydipsia – increased thirst;

Polyphagia – increased hunger



http://dhrcindia.com/diabetes_e_6.html

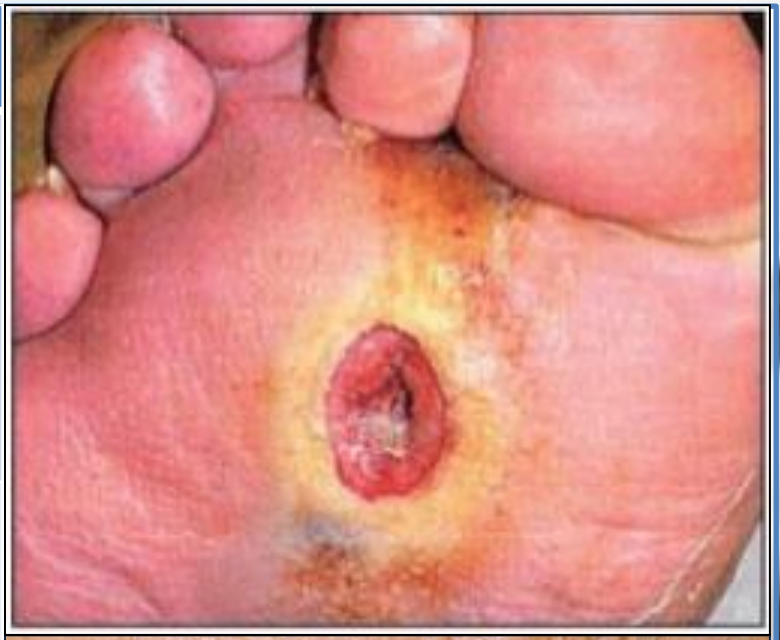
DIABETES MELLITUS: COMPLAINTS

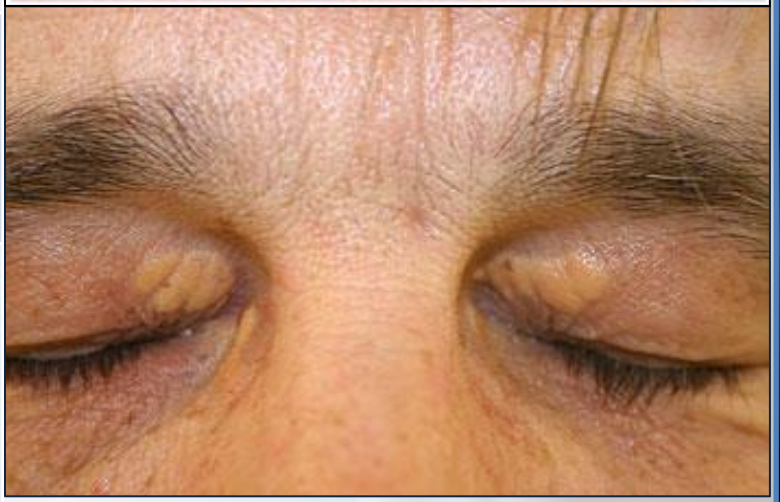


http://www.planetayurveda.com/blog/natural-herbal-remedies-diabetes-ayurvedic-treatment/

DIABETES: INSPECTION

Symptom	Pathogenesis
Dry peeling (flaking) skin with trophic changes, ulcers	As a result of dehydratation and affection of small vessels
Xanteplasma palpebrarum	Disbalance of lipids
Furunculosis, mycosis	Impaired immunological defense
Rubeosis (redness of forehead, cheeks)	Dilatation of capillaries



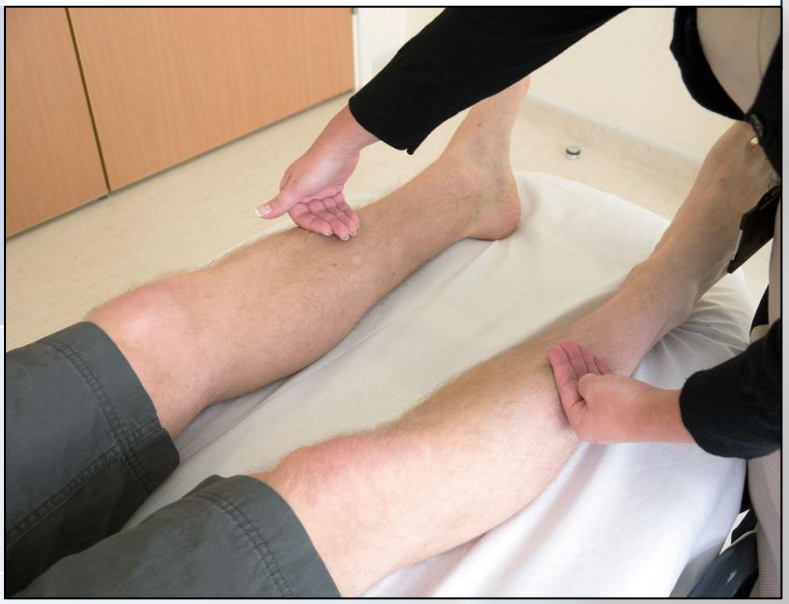


http://www.skinsight.com/adult/xanthelasmaPalpebrarum.htm

http://www.slideshare.net/ChamplainDRCC/foot-care-training-presentation-dec-6-2012-on-final

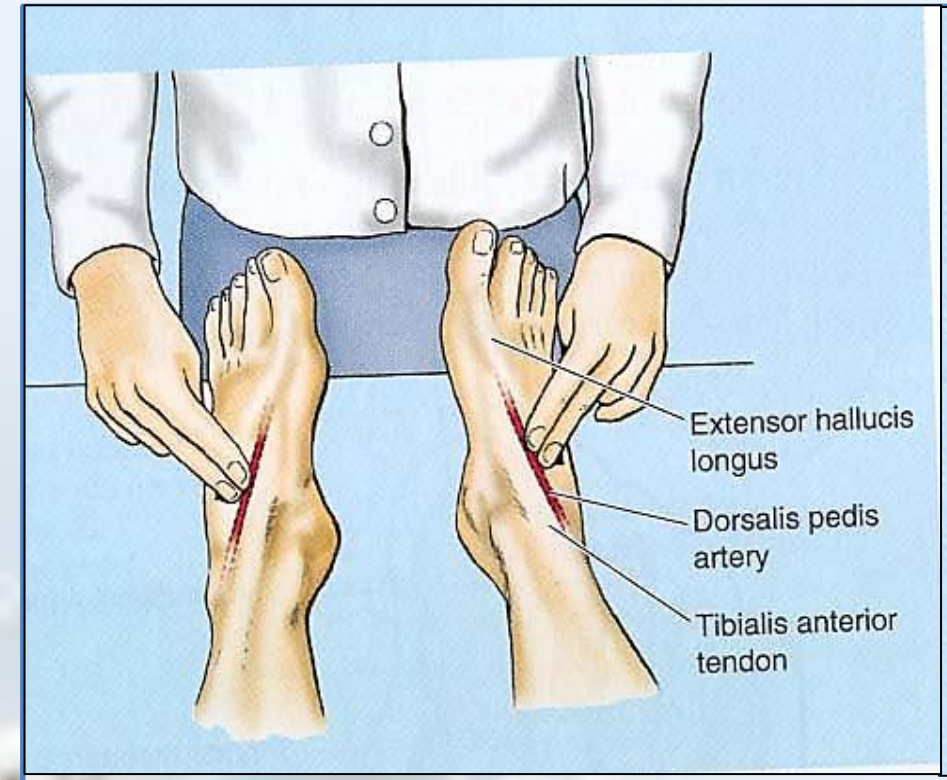
DIABETES: PALPATION

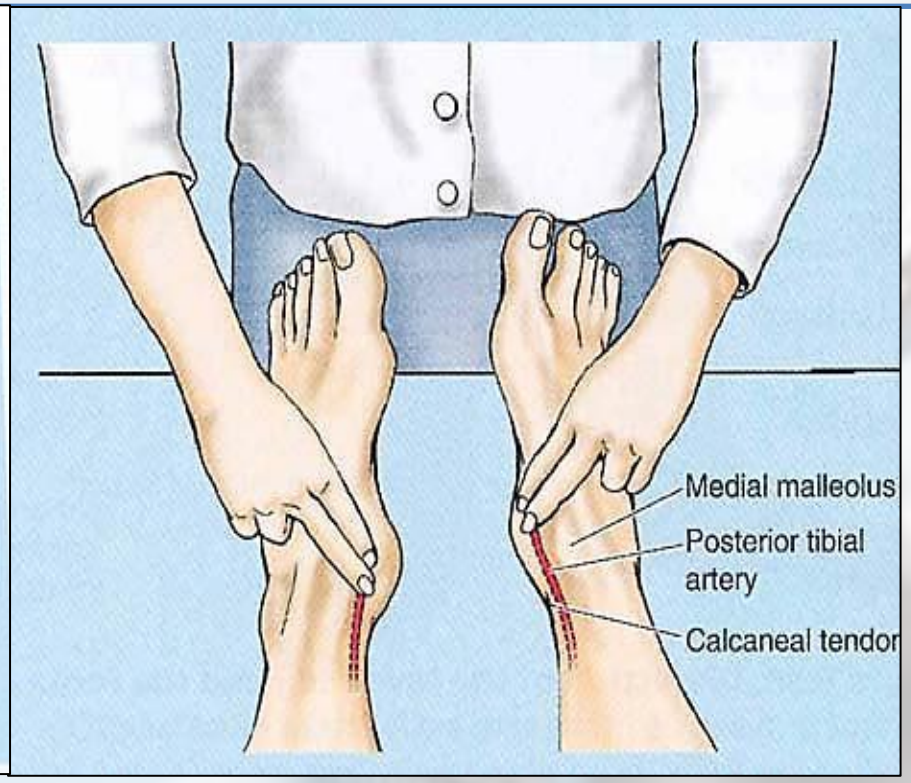
Assessment of humidity of skin	Dry skin with decreased turgor
Assessment of pedal pulse	Pulse is diminished or absent
Assessment of skin temperature	Decreased temperature of lower extremities
Palpation of liver	Hepatomegaly as a result of steatosis



http://www.osceskills.com/e-learning/subjects/peripheral-vascular-examination/

ASSESSMENT OF PEDAL PULSE





The dorsalis pedis pulse is felt on the dorsal surface of the foot, just lateral to the extensor hallucis longus tendon.

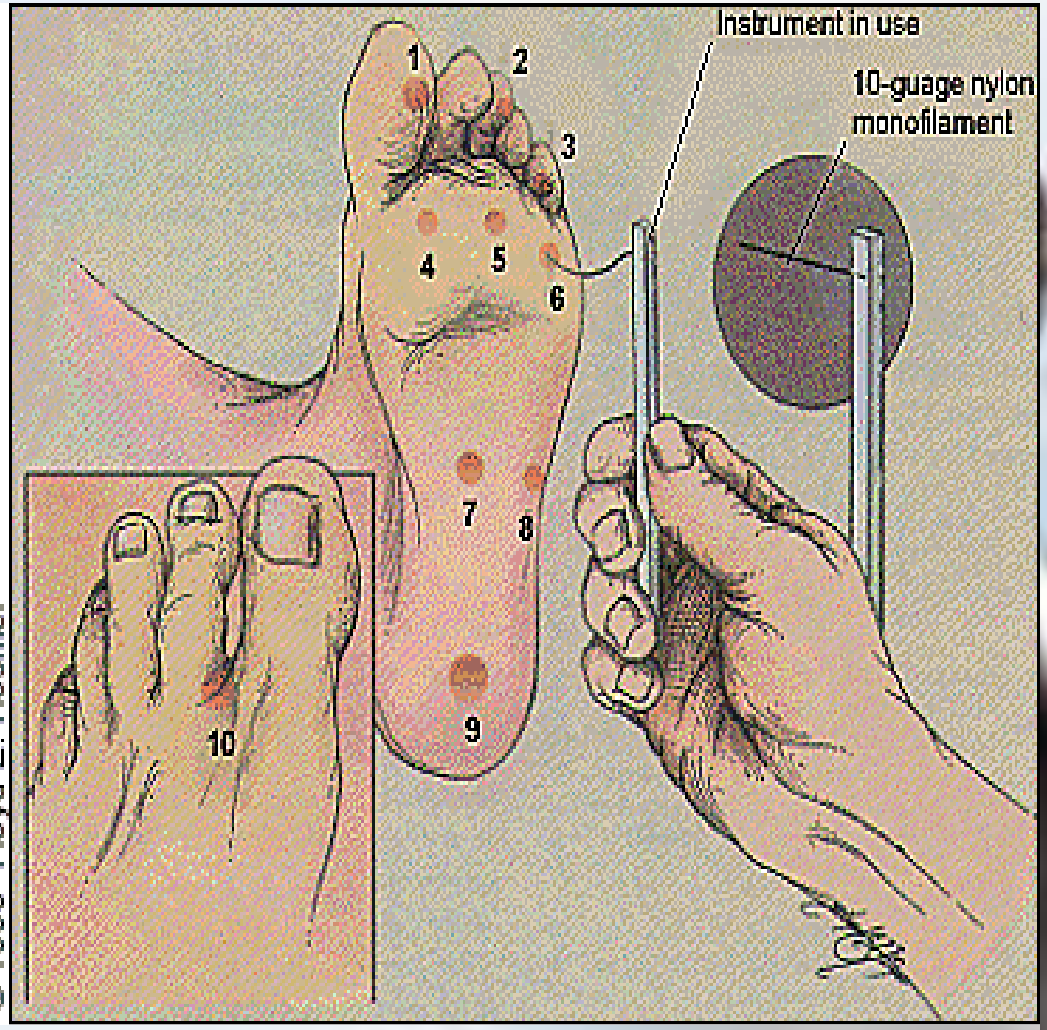
The posterior tibial pulse is felt on the posterior surface of the medial malleolus, between it and the medial border of the calcaneal tendon.

https://academic.amc.edu/martino/grossanatomy/site/Medical/CASES/Lower%20limb/POP_UPS/popliteal%20anspop_up4.htm

ASSESSMENT OF SENSITIVITY

Nylon monofilament test.

There is a risk of ulcer formation if the patient is unable to feel the monofilament when it is pressed against the foot with just enough pressure to bend the filament. The patient is asked to say “yes” each time he or she feels the filament. Failure to feel the filament at four of 10 sites is 97 percent sensitive and 83 percent specific for identifying loss of protective sensation.



http://www.aafp.org/afp/1998/0315/p1325.html

DIAGNOSTICS OF DIABETES

- Complaints (polyuria, polyphagia, polydipsia, weight loss, etc.)
- Anamnesis vitae (i.e. family history of diabetes)
- Anamnesis morbi (abrupt or slow onset, etc.)
- Objective examination (signs of dehydratation, ketoacidosis, etc.)
- Fasting plasma glucose (FPG)
- Oral glucose tolerance test (OGTT)
- Random plasma glucose
- Urine analysis
- Glycated haemoglobin (HbA1c)
- C-peptide
- Islet-autoantibodies

CRITERIA FOR DIABETES

	Normal	Prediabetes	Diabetes
Fasting plasma glucose (FPG)	3.8-5.5mmol/l or 70-99 mg/dl	5.6-6.9mmol/L or 100-125 mg/dL	7.0 mmol/L or 126 mg/dL
Oral glucose tolerance test (OGTT)	<7.8 mmol/L or <140 mg/dl	7.8-11.0 mmol/L or 140-199 mg/dl	≥11.1 mmol/L or >200mg/dl
*HbA1c	<5.7%	5.7-6.4%	≥6,5%

Symptoms of diabetes plus random plasma glucose concentration ≥ 11.1 mmol/l (200 mg/dl).

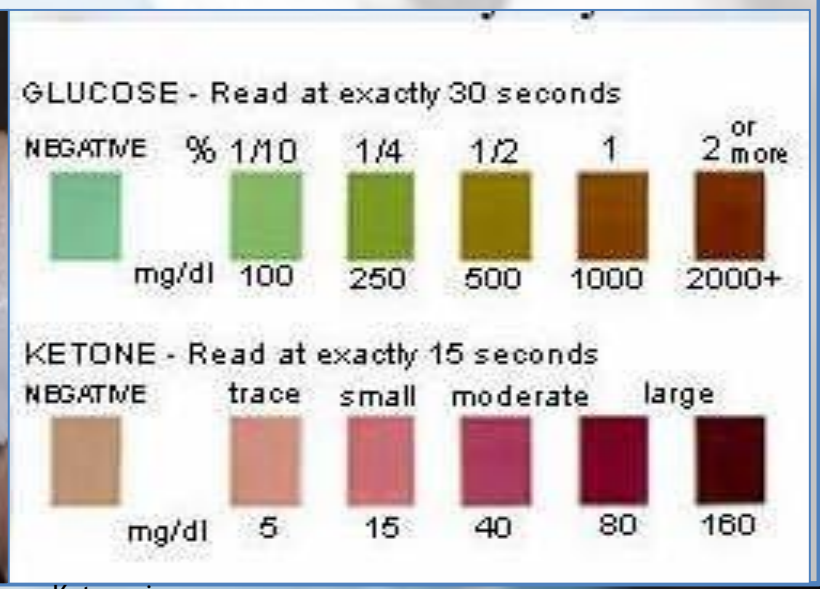
*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

DIAGNOSTIC TESTS FOR DIABETES

Urine analysis – findings:

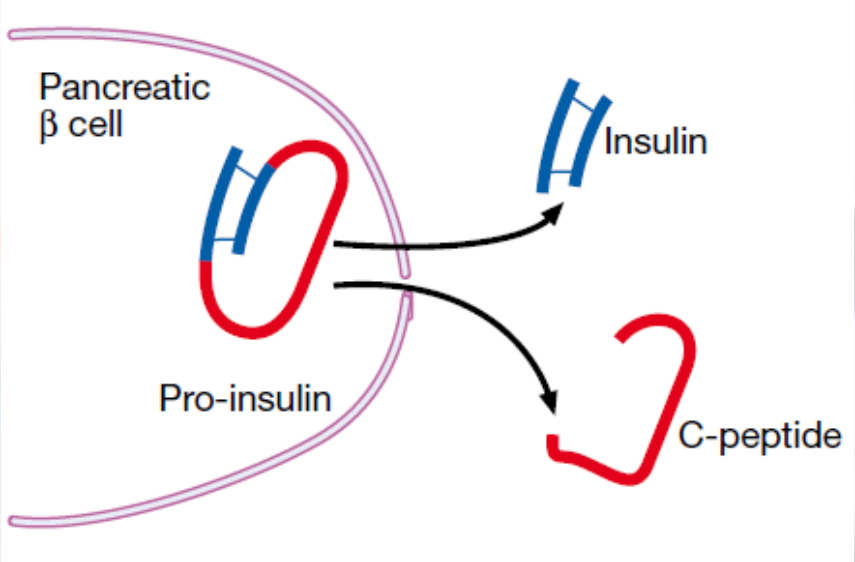
Glucosuria – presence of glucose in urine; can be detected if level of blood glucose exceeds more than 10-12 mmol/l (diabetes mellitus, renal tubular dysfunction – glucose is not being reabsorbed in tubules)

Ketonuria - presence of ketones in urine (in case of ketoacidosis);



ADDITIONAL TESTS

C-peptide is a peptide composed of 31 amino acids. It is released from the pancreatic beta-cells during cleavage of insulin from proinsulin.
The reference range is 0.8-3.1 ng/mL or 0.26-1.03 nmol/L (SI).



Is decreased in 1 type DM, increased in insulin resistance.

Islet autoantibodies: presence of ICA (islet cell antibodies), IAA (antibodies to insulin) and GADA (antibodies against the enzyme glutamic acid decarboxylase) can confirm 1type diabetes mellitus or LADA (Latent autoimmune diabetes in adults)

Davidson's Principles and Practice of Medicine, 21th edition, p.800

EMERGENCY STATES IN DIABETES: KETOACIDOSIS

Diabetic ketoacidosis (DKA) is a complex disordered metabolic state characterized by hyperglycaemia, acidosis, and ketonaemia.

Precipitating factors:

- Infection, stress;
- Discontinuation of or inadequate insulin therapy;
- Intercurrent illness (i.e. MI, cerebrovascular accident)
- new-onset type 1 diabetes or discontinuation of insulin in established type 1 diabetes
- In young patients with type 1 diabetes, psychological problems complicated by eating disorders

https://www.bsped.org.uk/clinical/docs/DKAManagementOfDKAinAdultsMarch20101.pdf

http://care.diabetesjournals.org/content/32/7/1335.full.pdf+html

PATHOGENESIS OF KETOACIDOSIS

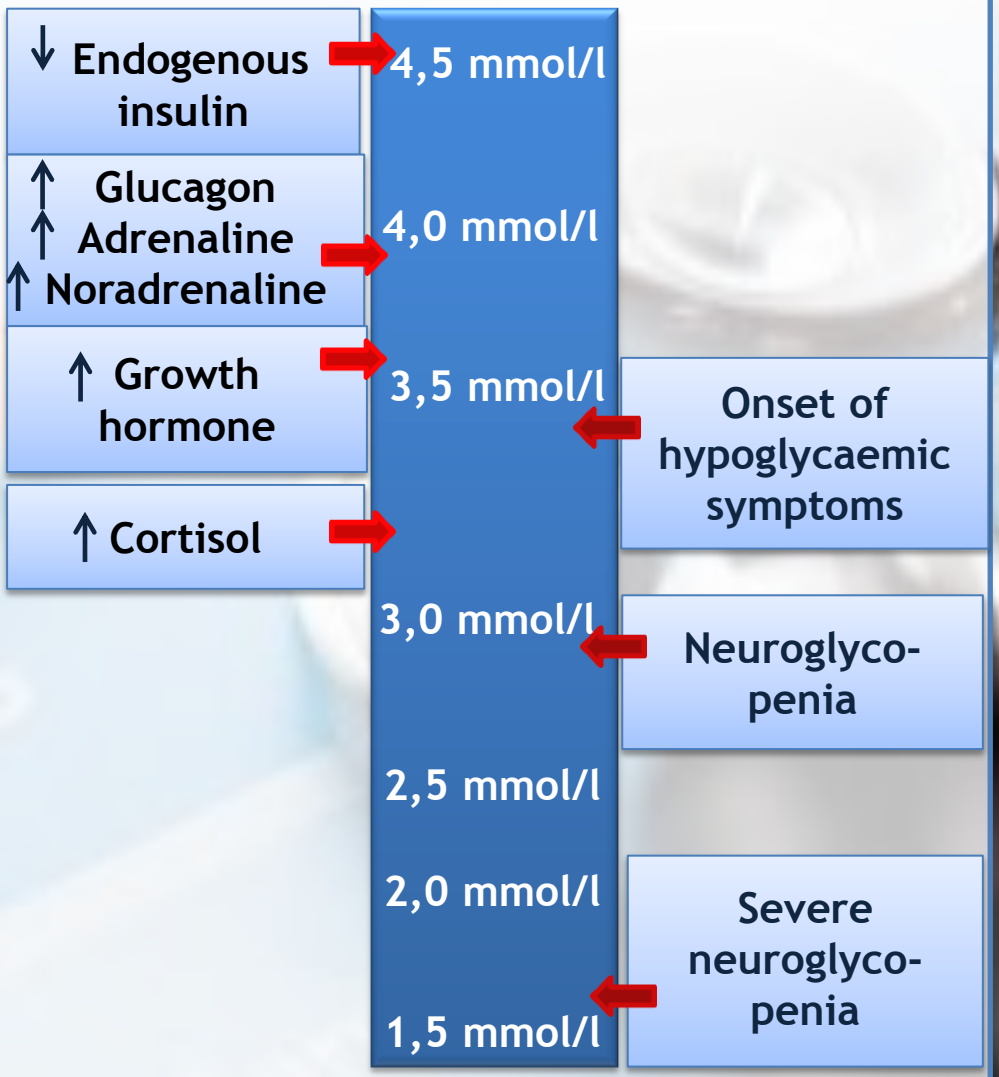
- In diabetic ketoacidosis, the insulin level is inappropriately low, leading to hyperglycaemia and inappropriately high rates of lipolysis. This state is accompanied by an increase in counterregulatory hormones (ie, glucagon, cortisol, growth hormone, epinephrine).
- The excess of free fatty acids is oxidized to ketoacids (acetone, 3-beta-hydroxybutyrate, and acetoacetate), which are the hallmark of DKA. Accumulation of large quantities of ketone bodies leads to subsequent metabolic acidosis.
- Since lipolysis is easily inhibited at low levels of insulin, ketoacidosis only develops in the presence of severe insulin deficiency, and is therefore more common for type 1 diabetes.

http://www.diapedia.org/acute-and-chronic-complications-of-diabetes/71040851425/diabetic-ketoacidosis-and-hyperglycaemic-hyperosmolar-state

EMERGENCY STATES IN DIABETES: HYPOGLYCAEMIA

Hypoglycemia is defined by:

- the development of autonomic or neuro-glycopenic symptoms;
- a low plasma glucose level (<4.0 mmol/L for patients treated with insulin or an insulin secretagogue);
- symptoms responding to the administration of carbohydrate



Canadian Diabetes Association Clinical Practice Guidelines Expert Committee

http://www.emconsulte.com/en/module/displayarticle/article/278561/iconosup/fig0005

EMERGENCY STATES IN DIABETES: HYPOGLYCAEMIA

Precipitating factors:

- Inappropriate dose of insulin
- Impaired awareness of hypoglycemia
- Autonomic neuropathy
- Skipping meals
- Strenuous exercise
- Alcohol

Impaired awareness of hypoglycaemia (IAH) is an acquired complication of insulin therapy, which affects people with type 1 and insulin-treated type 2 diabetes mellitus, whereby the ability to perceive the onset of hypoglycaemia becomes diminished or absent.

http://www.ncbi.nlm.nih.gov/pubmed/21211739

Symptoms	Diabetic ketoacidotic coma	Hypoglycaemic coma
Early signs	Weakness, vomiting, dry mouth, polyuria	Hunger, trembling (tremor), sweating
Onset of coma	Slow	Rapid
Features of precoma	Progressive loss of conciousness	Excitation → sopor → coma
Breathing	Kussmaul respiration	normal
Skin	Dry with decreased turgor	Wet with normal turgor
Tongue	Dry with	Wet
Tone of eyeballs	Decreased	Normal or increased
Glycaemia, glucoseuria	High	Low
Ketonaemia, ketonuria	present	absent

EMERGENCY STATES IN DIABETES: HHS

Hyperosmolar hyperglycaemic state (HHS) is caused by blood hyperosmolality and pronounced intracellular dehydration without ketosis and can be characterized by:

- Hypovolaemia
- Marked hyperglycaemia without significant hyperketonaemia or acidosis
- High Osmolality

Features:

It usually affects elderly patients, many with previously undiagnosed type 2 diabetes.

Hyperosmolar coma develops gradually over several days, rarely - overnight.

The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes Joint British Diabetes Societies

EMERGENCY STATES IN DIABETES: HHS

Precipitating factors:

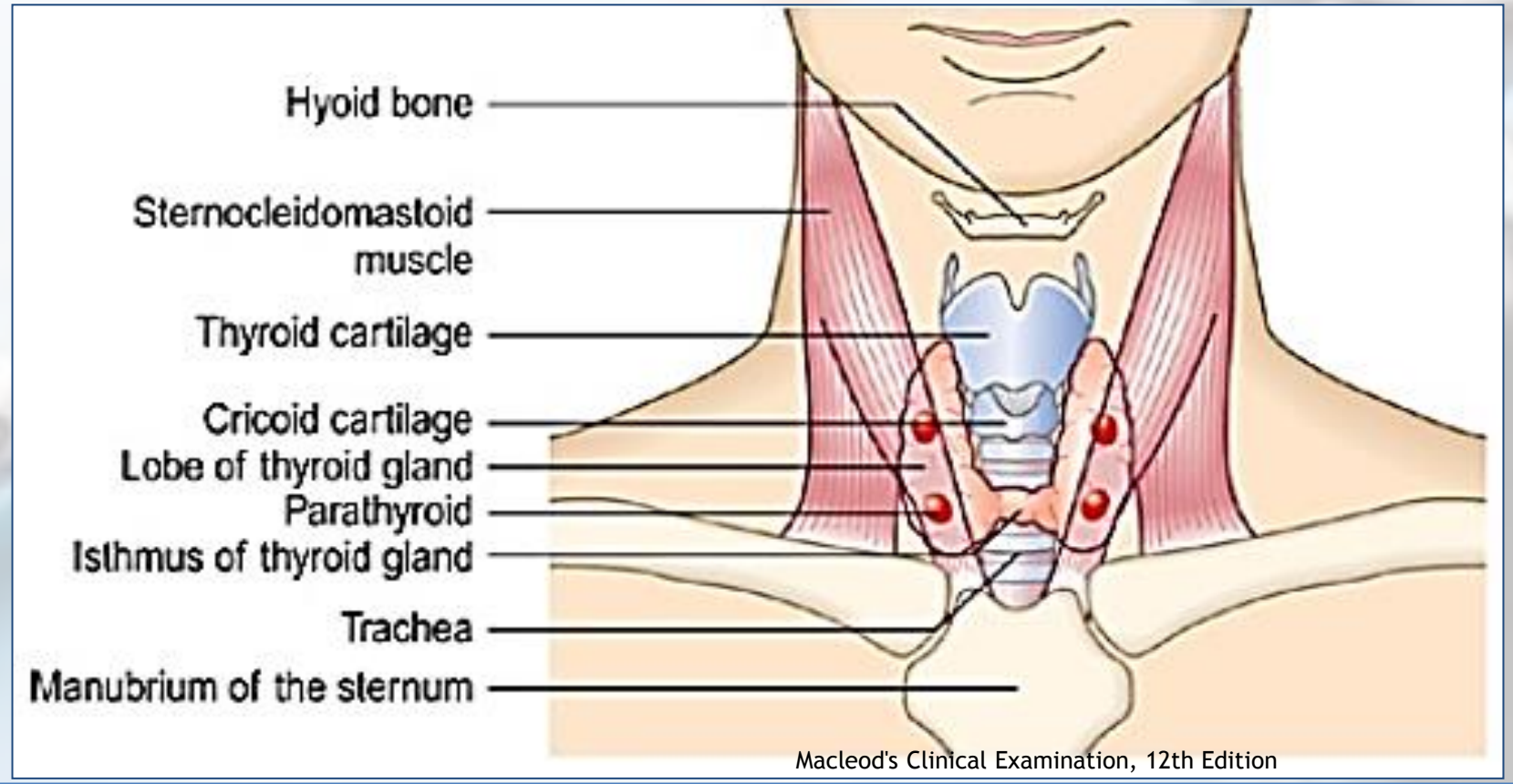
- Severe dehydration - vomiting, diarrhea, blood loss, increased urine output, burns, frostbite;
- Excessive injection of solutions of glucose and saline solutions;
- Intercurrent infectious diseases;
- Surgery;
- Prolonged treatment with diuretics, massive doses of corticosteroids, immunosuppressants.

The predecessors of HHS are: polyuria, polydipsia, sometimes polyphagia. Then develops fatigue, signs of dehydration, drowsiness, confusion.

Blood hyperosmolality is accompanied by a pronounced tendency to thrombosis, severely impaired microcirculation in different tissues - especially in the brain and kidneys.

THYROID GLAND

Location and anatomy : The thyroid gland is made up of the isthmus and 2 lateral lobes. The isthmus overlies the 2nd and 3rd rings of the trachea whilst the lobes extend from either side of the thyroid cartilage downward.



Macleod's Clinical Examination, 12th Edition

Oxford Handbook of Clinical Examination and Practical Skills, 1st Edition

FUNCTIONS OF THYROID GLAND

The thyroid synthesizes two hormones, **L-thyroxine (T4)** and **triiodothyronine (T3)**, of which T3 acts at the cellular level and T4 is the prohormone.

Main functions of thyroid hormones are:

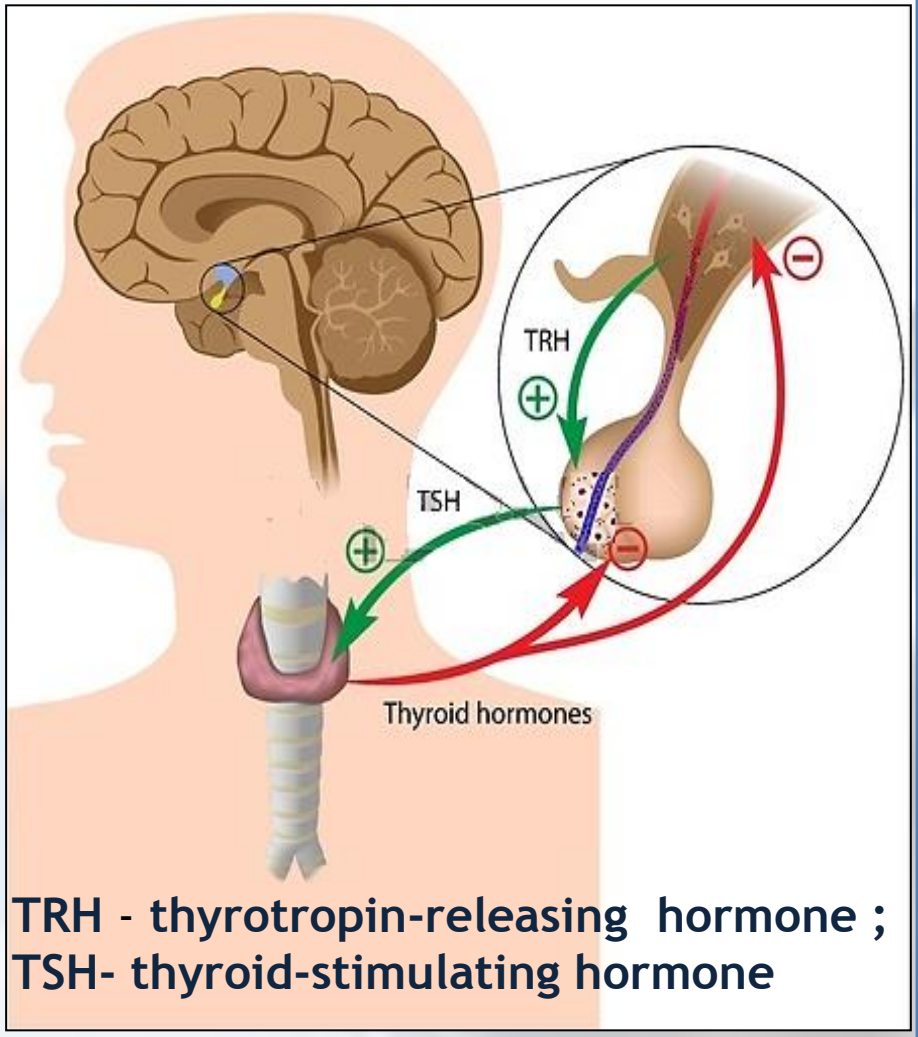
- accelerated rate of utilization of foods for energy;
- increased protein synthesis and the rate of protein catabolism;
- increase the rate and depth of respiration;
- increased heart rate and cardiac output;
- increased bone turnover and resorption;
- increases gut motility;
- stimulation of erythrogenesis

FUNCTIONS OF THYROID HORMONES CONT.

- increased speed of muscle contraction and relaxation and muscle protein turnover.
- increased hepatic gluconeogenesis/glycolysis and intestinal glucose absorption.
- increased lipolysis and cholesterol synthesis and degradation
- increased catecholamine sensitivity and ß-adrenergic receptor numbers in heart, skeletal muscle, adipose cells and lymphocytes.
- Decreases cardiac α-adrenergic receptors.

HYPOTHALAMUS-PITUITARY-THYROID AXIS

- **TRH** (synthesized by the hypothalamus) is transported to the pituitary gland, where it binds to receptors on thyrotrophic cells, stimulating the synthesis and secretion of TSH.
- **TSH** is transported in the circulation to the thyroid gland, where it binds to the TSH receptor on thyrocytes. This stimulates iodide transport, organification,hydrolysis of thyroglobulin, and secretion of thyroid hormone.



TRH - thyrotropin-releasing hormone ;
TSH- thyroid-stimulating hormone

- Circulating **T4** and **T3** exert negative feedback at the levels of both the hypothalamus and the pituitary gland, inhibiting the synthesis and secretion of TRH and TSH, respectively.

FUNCTIONAL STATE OF THYROID GLAND

Euthyreosis – normal levels of thyroid hormones T3 and T4

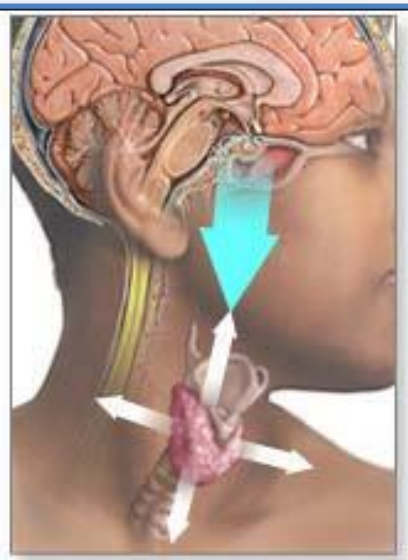
Hyperthyroidism – syndrome caused by persistently elevated level of thyroid hormones T3 and T4 in blood, which occurs with various diseases or excessive exogenous entry of thyroid hormones.

Hypothyroidism - syndrome characterized by prolonged persistent lack of thyroid hormones in the body or reducing their effect at the tissue level.

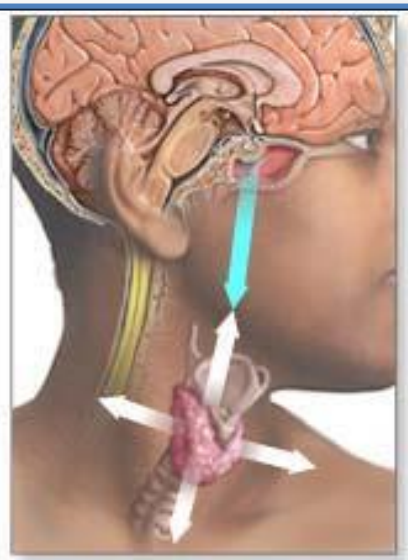
PATHOLOGICAL STATES OF THYROID GLAND

Hyper- and hypothyroidism can be:

- primary (lesions in thyroid gland) and
- secondary or central (lesions in pituitary or hypothalamus).



Primary hypothyroidism: thyroid can't produce amount of hormones pituitary calls for

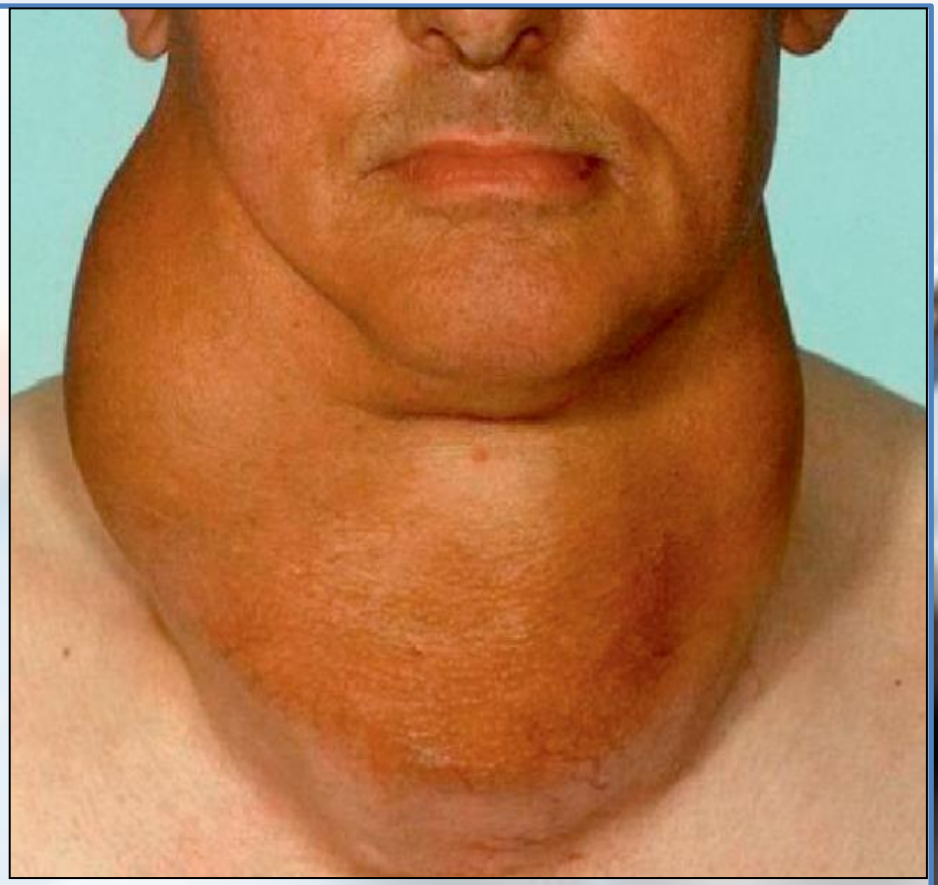


Secondary hypothyroidism: thyroid isn't being stimulated by pituitary to produce hormones

Euthyreosis	TSH (0.4-4.2 mIU/L)	Free T4 (10-25 pmol/L)	Free T3 (3.5-7.5 pmol/L)
Primary/Secondary Hyperthyroidism	Suppressed/Increased (< 0.05 mU/L)	Increased	Increased
Primary/Secondary hypothyroidism	Increased (> 10 mU/L)/Normal	Low	low

CAUSES OF HYPERTHYROIDISM

- Diffuse toxic goitre (Grave's disease, Bazedow's disease)
- Nodular (multinodular) goitre
- Thyroiditis (acute, subacute, etc.)
- Solitary thyroid adenoma
- Drugs (e.g. amiodarone, l-thyroxine)
- Struma ovarii (ovarian teratoma containing thyroid tissue)
- TSH-secreting pituitary adenoma



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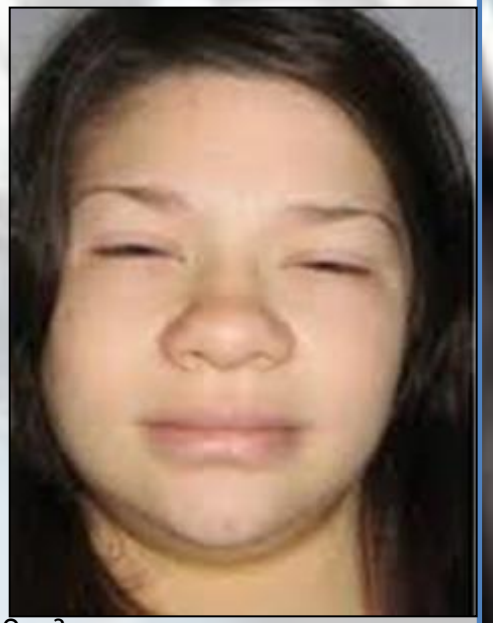
CAUSES OF HYPOTHYROIDISM

Primary hypothyroidism:

- Congenital absence of thyroid tissue
- Autoimmune diseases and autoimmune thyroiditis (Hashimoto's thyroiditis)
- Surgical removal of thyroid tissue, radioablation of thyroid tissue by radioactive iodine or external beam radiation
- Impaired thyroid hormone synthesis, iodine deficiency
- Congenital enzymatic defects that disrupt thyroid hormone synthesis
- Drug-mediated inhibition of thyroid hormone
- production and release (eg. amiodarone)

Secondary hypothyroidism:

- Insufficient secretion of TRH or TSH
- Tumor (lymphoma, germinoma, glioma)
- Hypopituitarism
- Pituitary surgery and radiation



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SYNDROME OF HYPERTHYROIDISM : COMPLAINTS

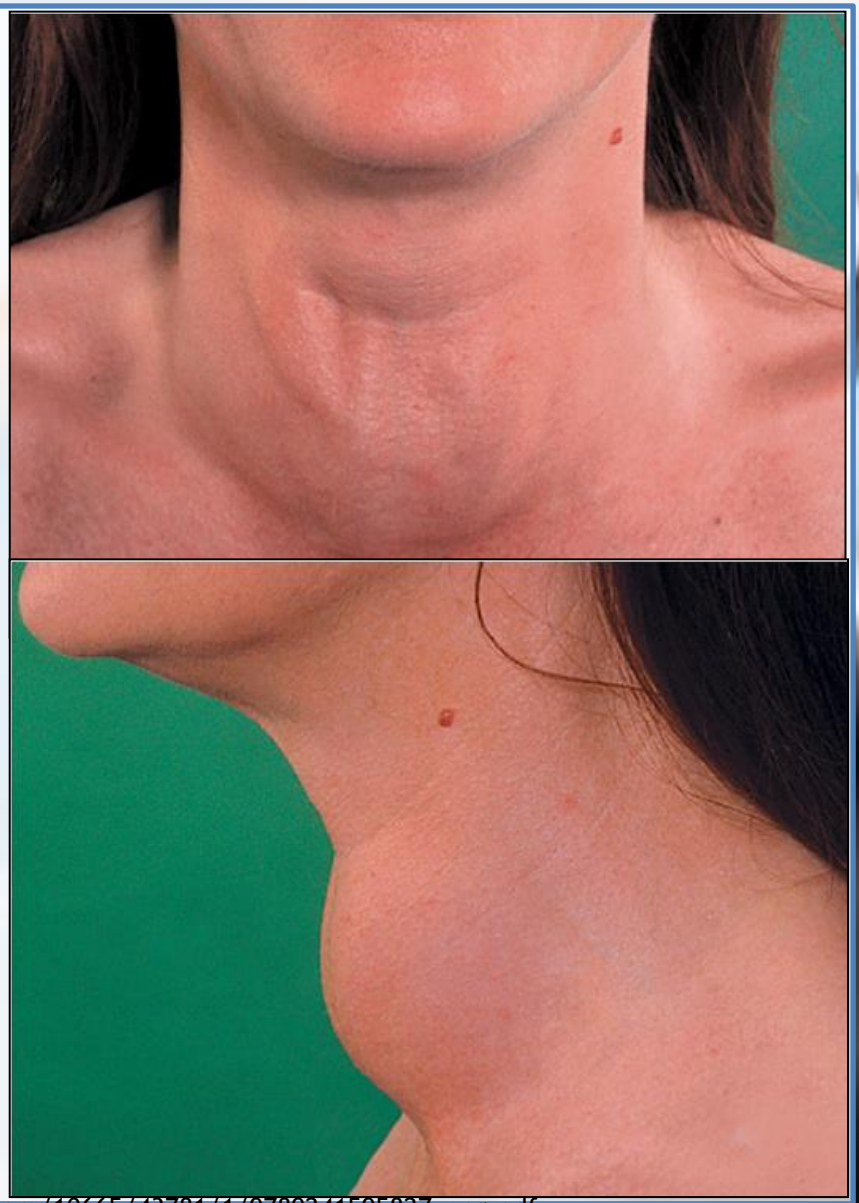
Symptom	Pathogenesis
Weight loss (>10%)	↑ thyroid hormones → activation of metabolic processes
Weakness	Toxic myopathy
Sweatiness, increased temperature	↑ baseline metabolism
Irritability, fast mood changes	Toxic encephalopathy
Palpitations, intermissions in the work of the heart	Sympaticotonia
Diffuse neck swelling	Presence of goitre (enlargement of thyroid gland)

HYPERTHYROIDISM: INSPECTION, PALPATION

Symptom	Features	Pathogenesis
Warm skin	Increased temperature of skin	Hypermetabolic state
Hyperhydrosis	Wet palms, increased sweating	Autonomic dysfunction and increased temperature
Enlargement of thyroid gland	Due to WHO classification	Hyperplasia of folliculi, of thyroid gland
Eye symptoms	Positive Shtelwag's, Moebius's, Gref's, Dalrymple symptoms	autoimmune-mediated inflammatory process of the orbital tissues, predominantly affecting the fat and the extraocular muscles

WHO CLASSIFICATION OF GOITRE

- **Grade 0** - no palpable or visible goitre
- **Grade 1** - A goitre that is palpable but not visible when the neck is in the normal position (i.e., the thyroid is not visibly enlarged)
- ***thyroid nodules in a thyroid which is otherwise not enlarged fall into this category
- **Grade 2** - A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated



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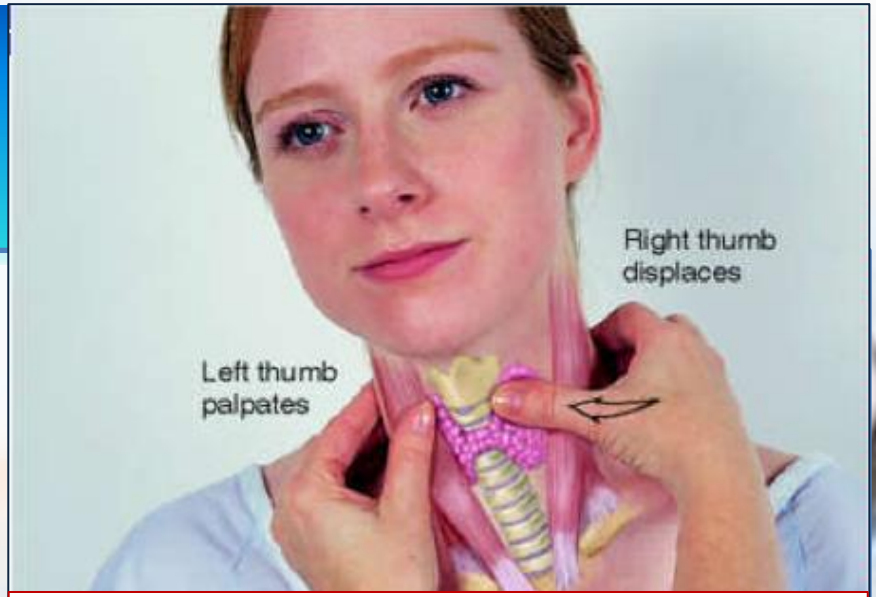
http://apps.who.int/iris/bitstream/10665/43781/1/9789241595827_eng.pdf

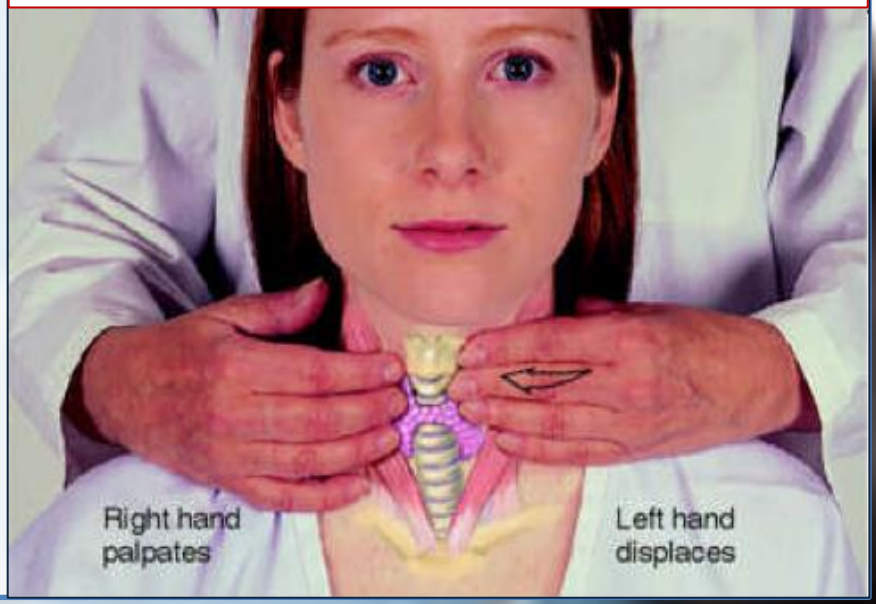
PALPATION OF THYROID GLAND

Pay attention on:

- Shape and surface (smooth, diffuse, symmetric or not);
- Mobility (moves with swallowing or not);
- Consistency (nodules);
- Tenderness (diffuse or localized);
- Thyroid bruit;



Anterior approach
Posterior approach

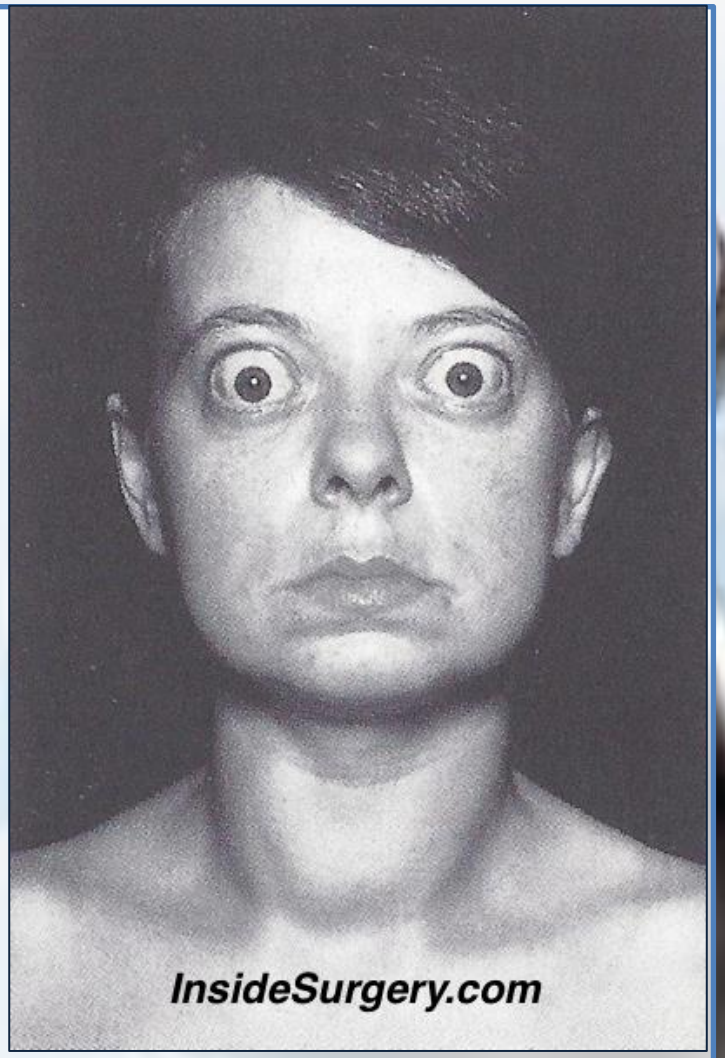


HYPERTHYROIDISM : LESIONS OF SYSTEMS

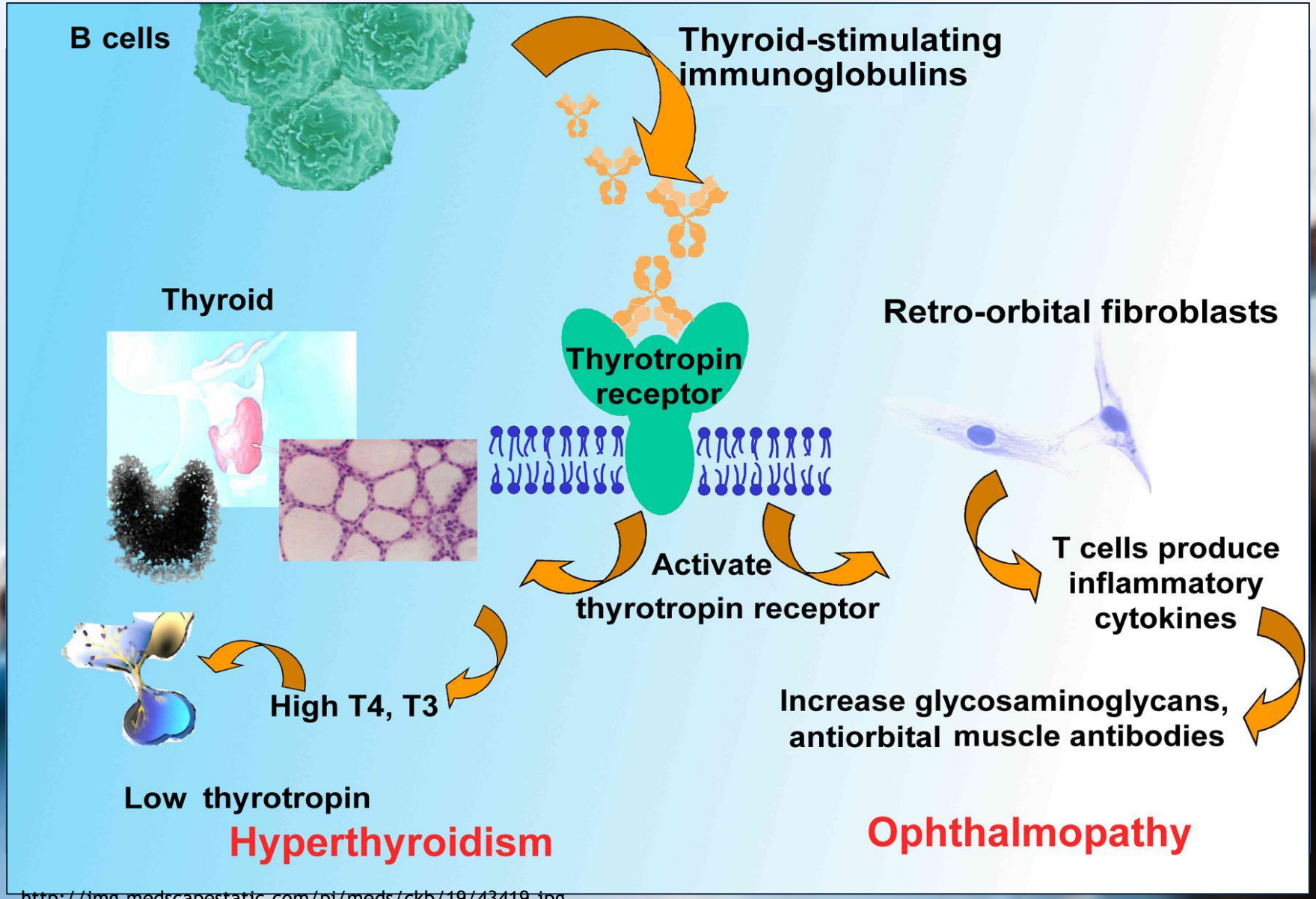
System	Lesion
Respiratory	↑RR>18/min
Cardio-vascular	Tachycardia HR>100/min (palpitations) Arterial systolic hypertension Rhythm disturbances (Atrial fibrillation) Cardiac failure
Gastro-intestinal	Diarrhoea Vomiting
Nervous	Irritability, tearfulness, behavior change Tremor Fatigue Restlessness

GRAVE'S DISEASE

- Synonims: diffuse toxic goitre, Basedow's disease (Germany), Grave's disease (Britain), Flajani`s disease (Italy).
- Definition: it is autoimmune thyroid disease, which manifests with diffuse thyroid enlargement and hyperthyroidism.
- Cause of hyperthyroidism in Graves' disease is the production of thyroid-stimulating immunoglobulins (autoantibodies) that bind to and activate the TSH receptor, promoting thyroid hormone secretion and growth of the thyroid gland (they behave like TSH).



PATHOGENESIS OF GRAVE'S DISEASE



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GRAVE'S OPHTHALMOPATHY

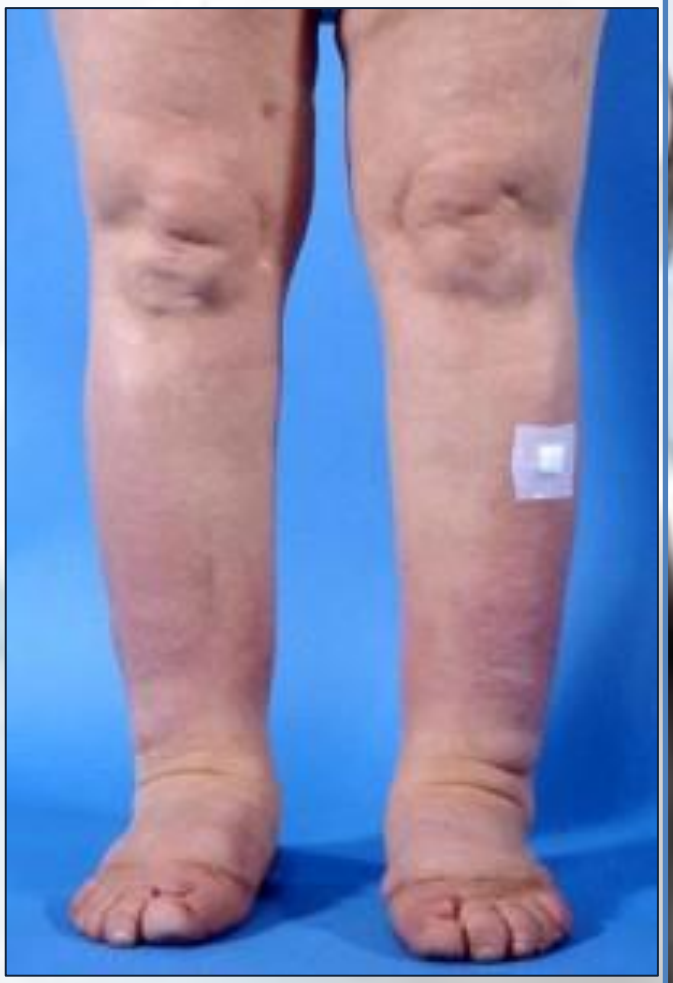
Exophtalmos (proptosis) - abnormal protrusion of the eyeball
Stellwag sign (stare)- incomplete and infrequent blinking
Möbius sign - poor convergence
Dalrymple sign - retraction of the upper and/or lower lid due to hyperstimulation of the sympathetically innervated muscles in the upper and lower lids;
von Graefe sign (Lid lag on downgaze) - while slowly moving the fixation object from upward to downward, the eyelid lags behind the globe on downgaze.

Seidel H: Mosby's guide to physical examination, 4th ed 4, St. Louis, 1999, Mosby, Macleod's Clinical Examination, 12th Edition

THYROID DERMOPATHY

Synonyms: pretibial myxedema (PTM), localized myxedema

- It can be described as localized lesions of the skin resulting from the deposition of hyaluronic acid in the dermis and subcutis.
- The precise cause of PTM remains uncertain but it is nearly always associated with autoimmune thyroid disease
- Although PTM is most often confined to the pretibial area, it may occur anywhere on the skin, especially the ankle, dorsum of the foot, knees, shoulders, elbows, upper back, pinnae, nose, neck.



Thyroid dermopathy. Courtesy of Dr. Vahab Fatourechi, Mayo Clinic

THYROID STORM

Thyroid storm, also referred to as thyrotoxic crisis, is an acute, life-threatening, hypermetabolic state induced by excessive release of thyroid hormones in individuals with thyrotoxicosis.

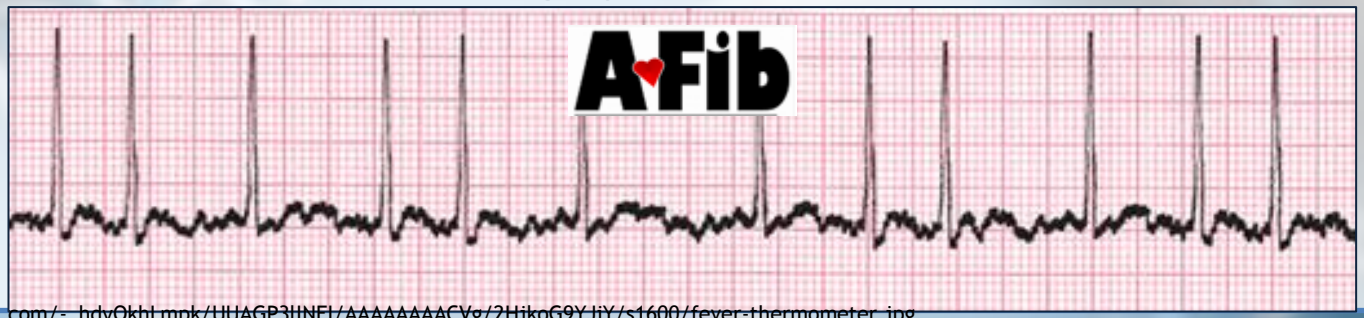
Predisposing factors:

- Sepsis,
- Surgery, anesthesia induction
- Radioactive iodine (RAI) therapy
- Drugs (anticholinergic and adrenergic drugs, eg, pseudoephedrine; salicylates; NSAIDs; chemotherapy)
- Excessive thyroid hormone (TH) ingestion
- Withdrawal of or noncompliance with antithyroid medications
- Direct trauma to the thyroid gland
- Vigorous palpation of an enlarged thyroid

http://emedicine.medscape.com/article/925147-overview#showall

THYROID STORM: CLINICAL PRESENTATION

- Fever (38.5°C - 41°C)
- Excessive sweating
- CVS: accelerated tachycardia, hypertension with wide pulse pressure, high-output cardiac failure, cardiac arrhythmias (supraventricular arrhythmias are more common, [eg, atrial flutter and fibrillation], but ventricular tachycardia may also occur).
- NS: severe agitation, altered behavior, delirium, seizures, and coma.
- GIT: diarrhea, vomiting, jaundice, and abdominal pain.



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GRAVE'S DISEASE: INVESTIGATIONS

Thyroid function tests:

- Thyroid hormones - T3, T4

NB! In most patients serum T3 and T4 are both elevated but T4 is in the upper part of the normal range and T3 raised (T3 toxicosis) in about 5%.

- TSH

NB! Serum TSH is undetectable in primary thyrotoxicosis but values can be raised in the very rare syndrome of secondary thyrotoxicosis caused by a TSH-producing pituitary adenoma.

Antithyroid antibodies:

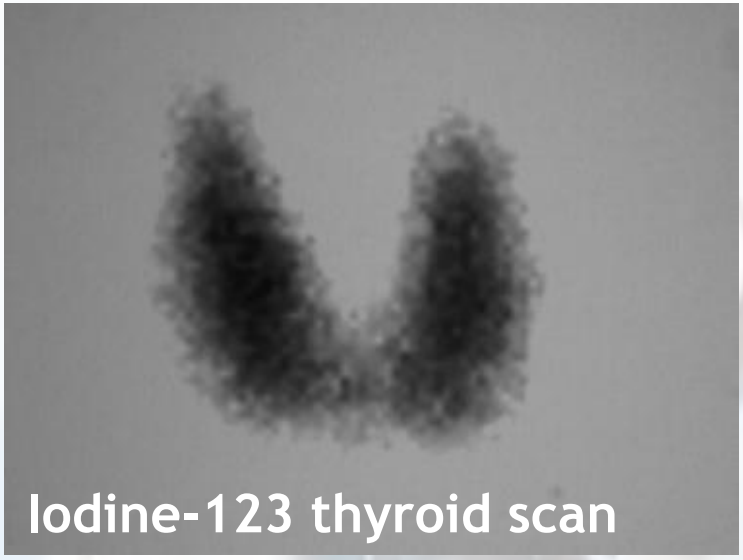
- TSH receptor IgG antibodies (TRAb);
- TPO (thyroid peroxidase) antibodies;
- Thyroglobulin antibodies;

These antibodies are elevated in most patients with Grave's disease.

GRAVE'S DISEASE: INVESTIGATIONS

- **Radioactive iodine scanning and measurements of iodine uptake**

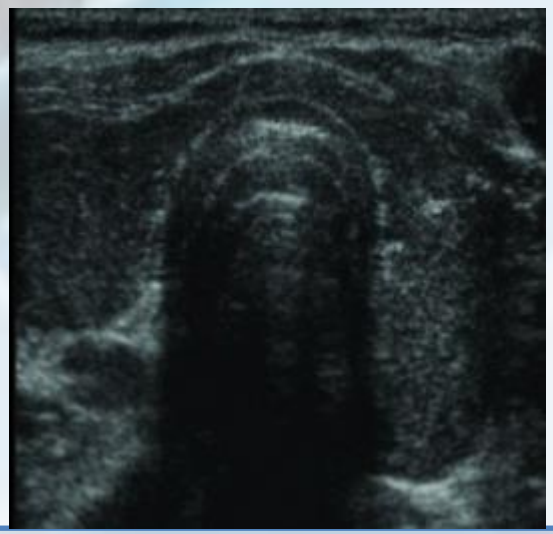
NB! In Graves disease, the radioactive iodine uptake is increased and the uptake is diffusely distributed over the entire gland.



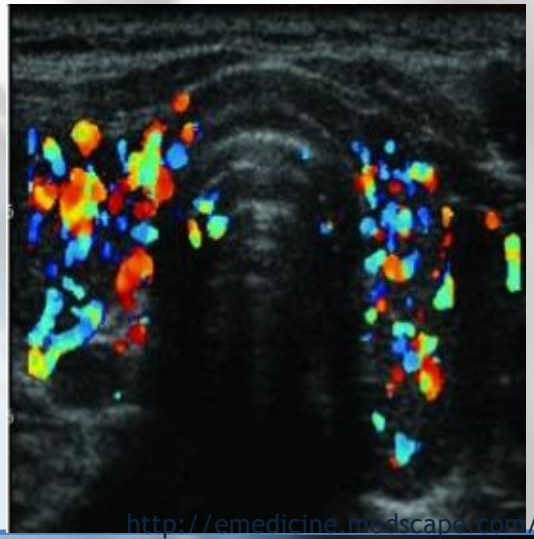
Iodine-123 thyroid scan

- **Ultrasound of thyroid gland with color-Doppler evaluation**

A Grey-scale image with increased echogenicity



Color flow Doppler image with increased vascularisation



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http://emedicine.medscape.com/article/383062-overview

GRAVE'S DISEASE: INVESTIGATIONS

- Computed tomography scanning or magnetic resonance imaging (of the orbits) may be necessary in the evaluation of proptosis. If routinely performed, most patients have evidence of orbitopathy, such as an increased volume of extraocular muscles and/or retrobulbar connective tissue.
- Biopsy rarely to exclude other reasons for hyperthyroidism (eg. cancer)

Also can be done:

- A CBC count to check for development of fever or symptoms of infection and hematological side effects of antithyroid medications;
- Liver function test results should be obtained to monitor for liver toxicity caused by antithyroid medications.

SYNDROME OF HYPOTHYROIDISM : COMPLAINTS

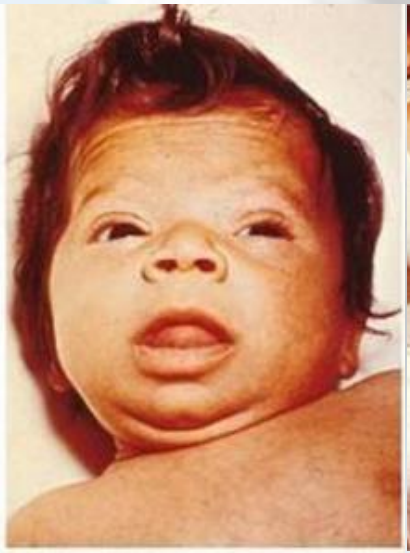
Symptom	Pathogenesis
Weight gain (>10%)	↓thyroid hormones → inhibition of metabolic processes
Chilliness, cold intolerance, decreased temperature	↓baseline metabolism
Constipation	↓motility of GIT
Facial puffiness	The deposition of mucopolysaccharides in the subcutaneous fat tissue
Dysmenorrhoea	
Poor memory	Dyshormonal encephalopathy
Diffuse neck Swelling	Presence of goitre - goitrous hypothyroidism may occur in endemic goiter in iodine deficiency regions

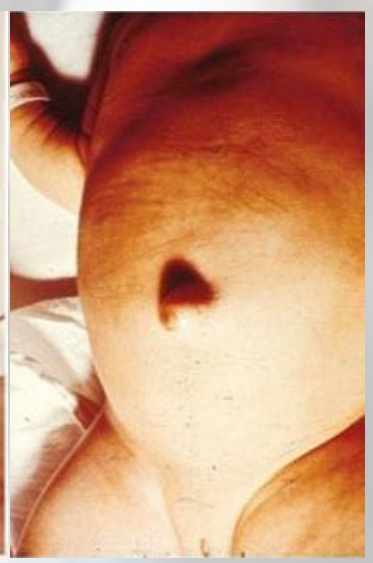
HYPOTHYROIDISM: INSPECTION, PALPATION

Symptom	Features	Pathogenesis
Dry skin, hyperkeratosis, dry brittle unmanageable hair, brittle nails	decreased temperature of skin	❖ Hypometabolic state: ↓metabolism of proteins, lipids, carbohydrates, vitamins; ❖ Autonomic dysfunction
Edemas, periorbital edemas	Non-pitting edemas	The deposition of mucopolysaccharides in the subcutaneous fat
Hoarse voice, enlarged tongue		Edema of tongue, swelling of vocal cords

HYPOTHYROIDISM : LESIONS OF SYSTEMS

System	Lesion
Cardio-vascular	Bradycardia HR<60/min, hypotension, ischemic coronary disease due to atherosclerosis (hyperlipidemia)
Gastro-intestinal	Decreased appetite, flatulence, constipation
Nervous	Sleepiness, poor memory, dementia, depression
Congenital hypothyroidism may lead to cretinism (mental retardation)	





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MYXEDEMA COMA

- Mixedema coma a rare, life-threatening condition, occurs late in the progression of hypothyroidism. The condition is seen typically in elderly women and is often precipitated by infection, medication, environmental exposure, or other metabolic-related stresses.
- Its characteristics include coma with extreme hypothermia (temperature 24° to 32.2 °C), areflexia, respiratory depression with CO2 retention, convulsions are not uncommon and cerebrospinal fluid (CSF) pressure and protein content are raised.

HYPOTHYROIDISM: INVESTIGATIONS

- Elevated TSH with decreased T4
- Elevated TSH (usually 4.5-10.0 mIU/L) with normal free T4 is considered mild or subclinical hypothyroidism
- Assays for anti-thyroid peroxidase (anti-TPO) and antithyroglobulin (anti-Tg) antibodies may be helpful in determining the etiology of hypothyroidism or in predicting future hypothyroidism.
- In patients with hypothalamic or pituitary dysfunction, TSH levels do not increase in appropriate relation to the low free T4 levels.
- Ultrasonography of the neck and thyroid can be used to detect nodules and infiltrative disease.
- The use of color flow Doppler scanning allows assessment of vascularity, which can help to distinguish thyroiditis (decreased flow) from Graves disease (increased flow).

http://emedicine.medscape.com/article/122393-workup#c6

HYPOTHYROIDISM: INVESTIGATIONS

Other abnormalities include the following:

- anaemia, which is usually normochromic and normocytic in type but may be macrocytic (sometimes this is due to associated pernicious anaemia) or microcytic (in women, due to menorrhagia)
- increased serum aspartate transferase levels, from muscle and/or liver
- increased serum creatine kinase levels, with associated myopathy
- hypercholesterolaemia and hypertriglyceridaemia
- hyponatraemia due to an increase in ADH and impaired free water clearance.

HYPOTHYROIDISM: SCREENING

No universal screening recommendations exist for thyroid disease for adults. The American Thyroid Association recommends screening at age 35 years and every 5 years thereafter, with closer attention to patients who are at high risk, such as the following:

- Pregnant women
- Women older than 60 years
- Patients with type 1 diabetes or other autoimmune disease
- Patients with a history of neck irradiation

http://emedicine.medscape.com/article/122393-workup#c7

Thank you for your attention!