

NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF PATHOLOGICAL PHYSIOLOGY

***Pathophysiology of the
carbohydrate metabolism.
Diabetes mellitus.***

***PLAN OF LECTURE**

1. Types of carbohydrate metabolism disorders:
hyper- and hypoglycemia.
2. Definition, classification of diabetes mellitus.
3. Type 1 diabetes: etiology, pathogenesis.
4. Type 2 diabetes: etiology, pathogenesis.
5. Clinical manifestations of diabetes mellitus.
6. Complications of diabetes mellitus.

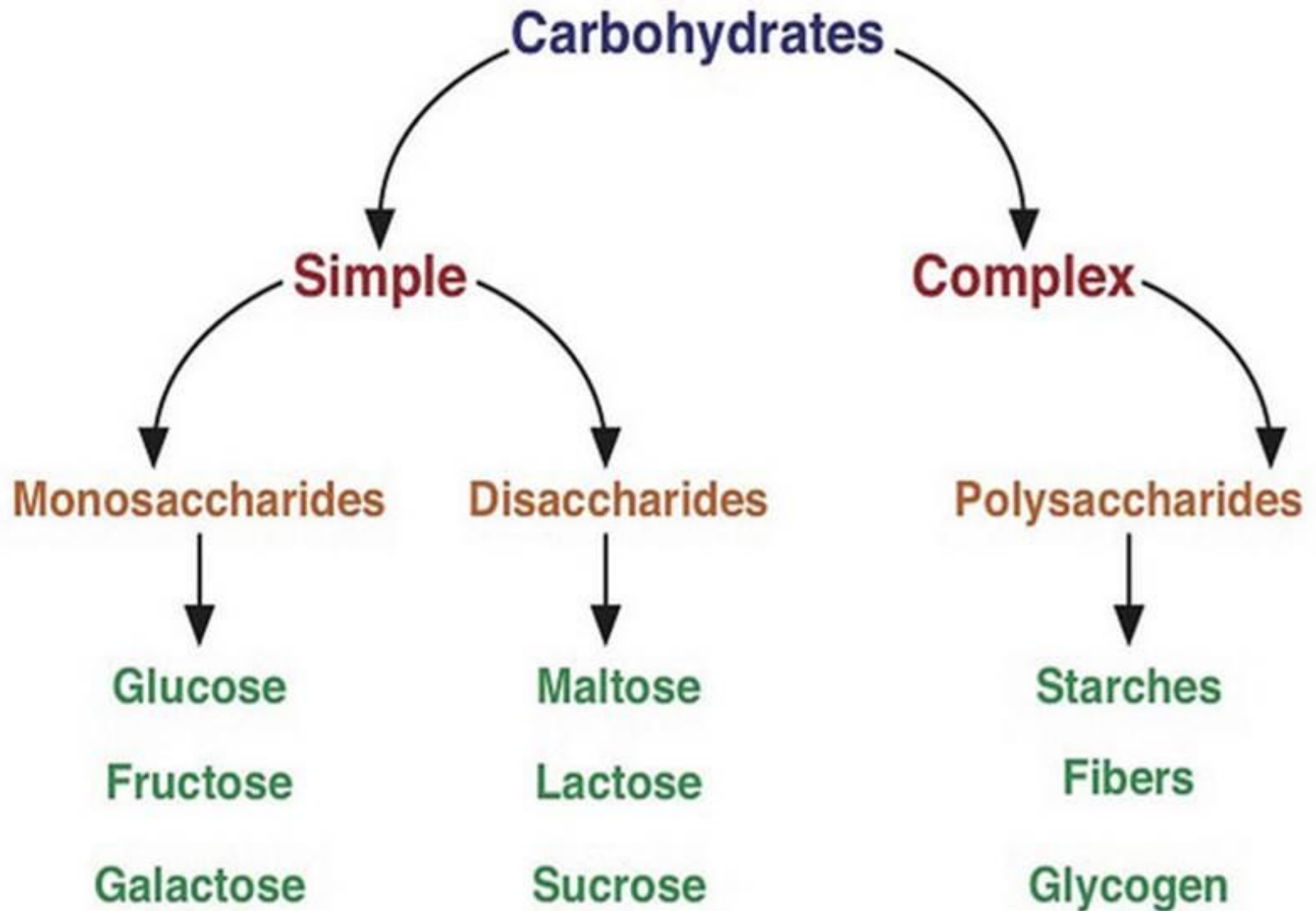
*Suggested Reading

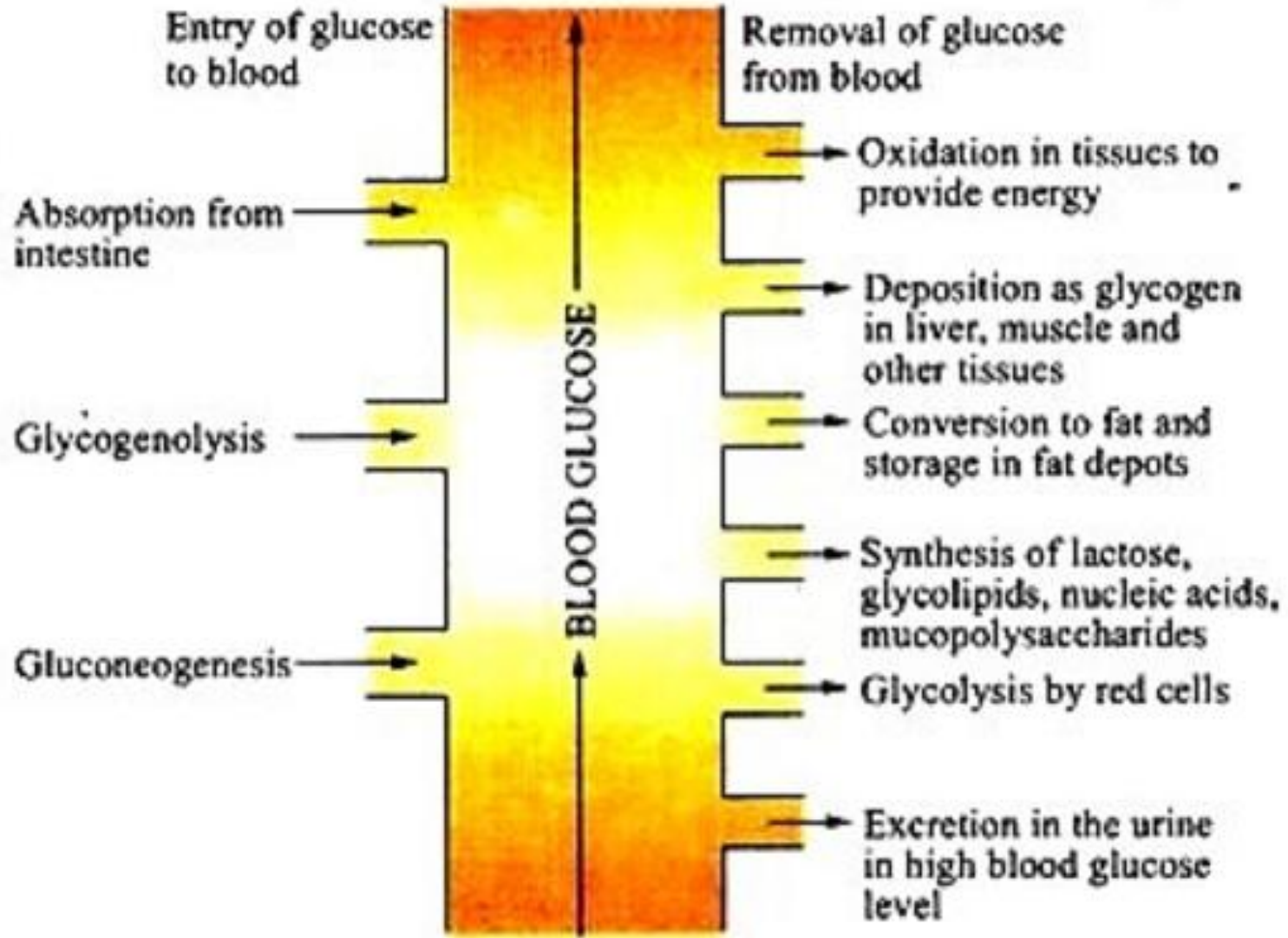
Basic

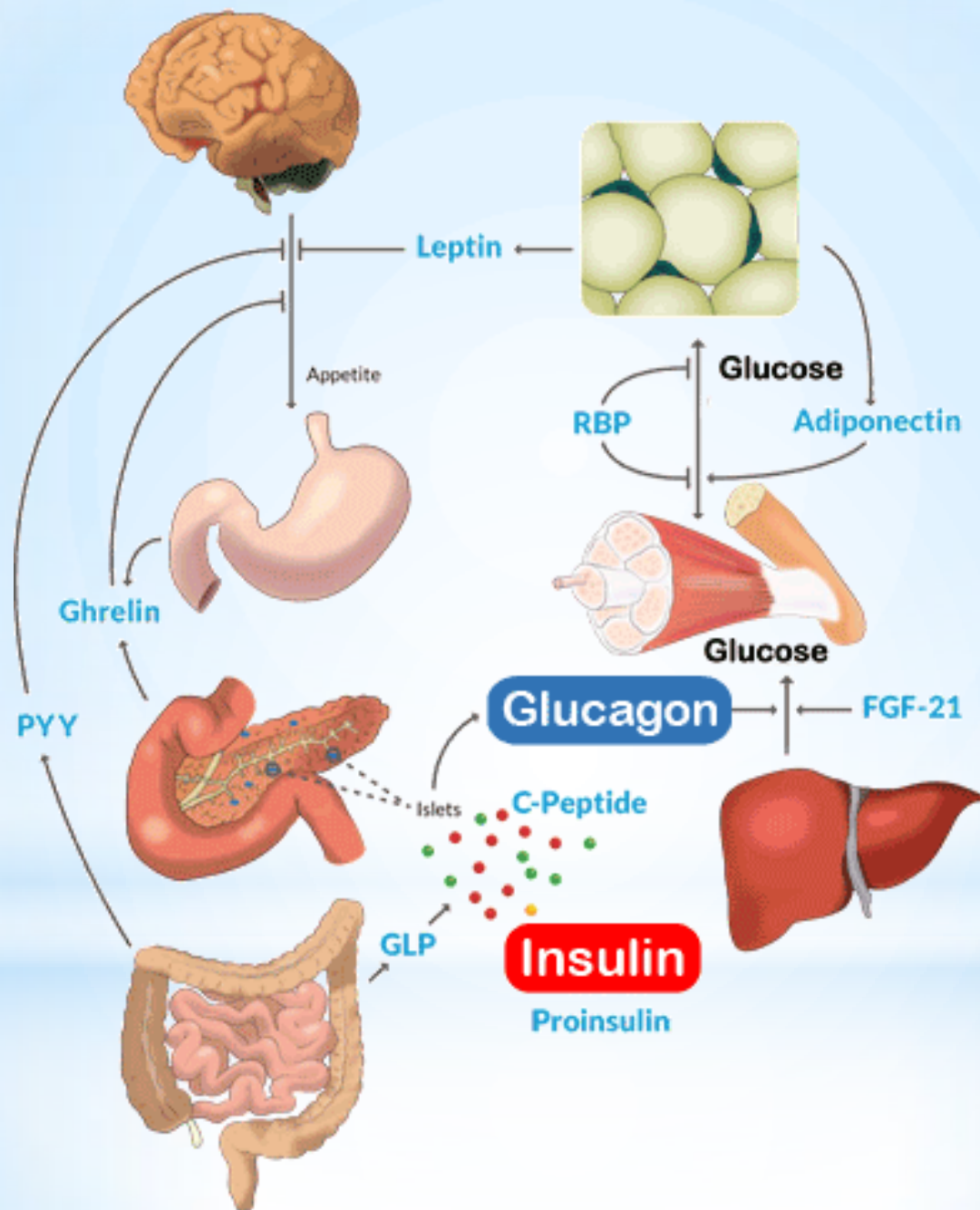
1. General and clinical pathophysiology/ Editor by Anatoliy V. Kubyshkin. - Vinnytsa : Nova Knyha Publishers, 2016. - 656 p.
2. Lecture notebook pathological physiology. Manual for working in lectures / N.M. Kononenko, S.I. Kryzhna, V.A. Volkovoy et al.; Kh.: NPhaU, 2013. - 99 p.
3. Pathological Physiology: The textbook for the students of higher pharmaceutical educational institutions and pharmaceutical faculties of higher medical educational institutions III-IV levels of accreditation / S.I. Kryzhna, N.M. Kononenko, I.Yu. Tishenko et al.: under edition of the professor A.I. Berezhnyakova. - Kharkiv: NphaU, 2006. - 416 p.

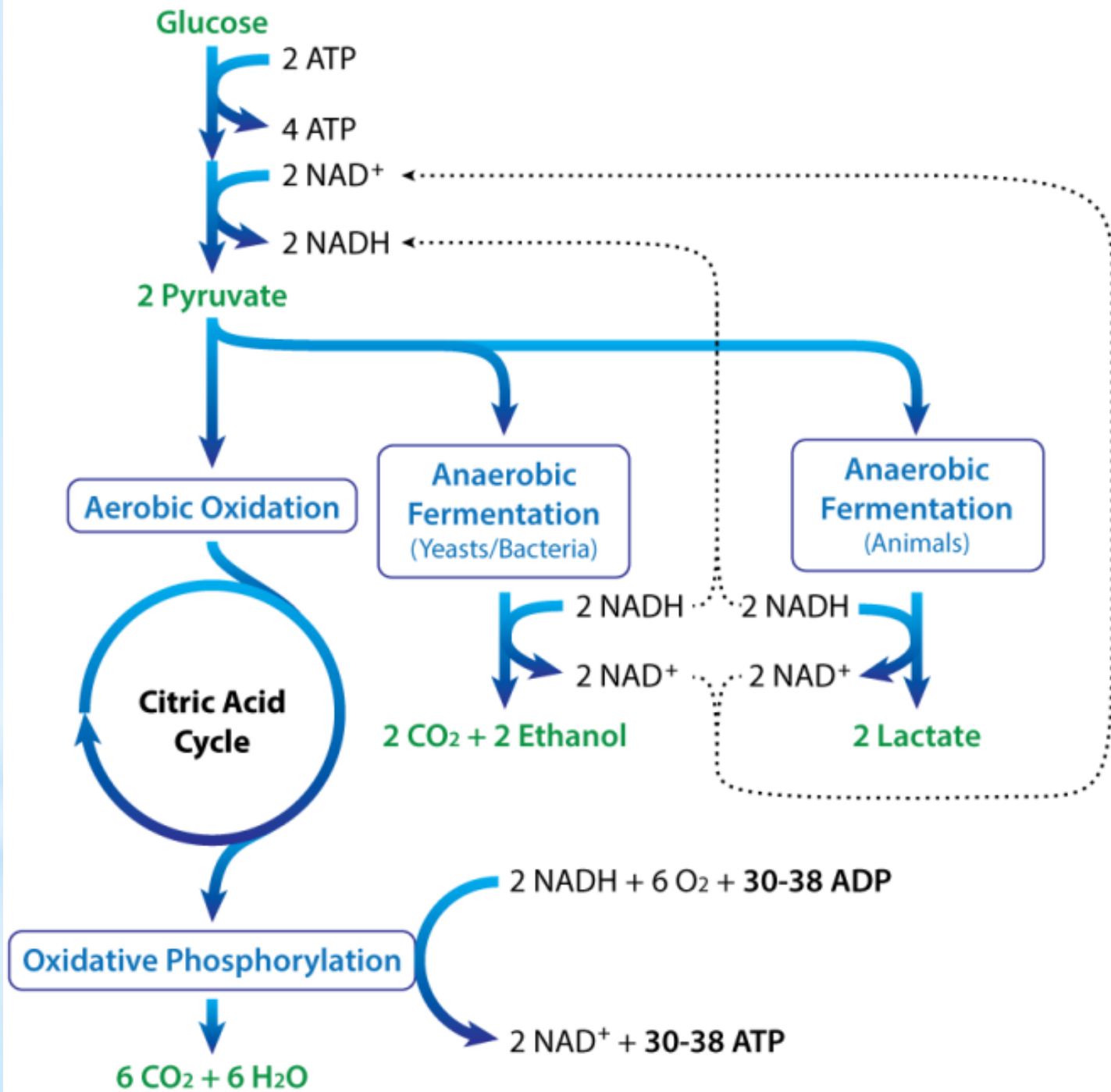
Auxiliary

1. Professional guide to Pathophysiology / M.H. Birney, C. L. Brady, K.T. Bruchak et al. - Lippincott Williams and Wilkins. - 2002. - 696 p.
2. Crowley L.V. An introduction to human disease: pathology and pathophysiology correlations / L.V. Crowley . - London : Lones and Bartlett Publishers International Bard House. 2001. - 790 p.



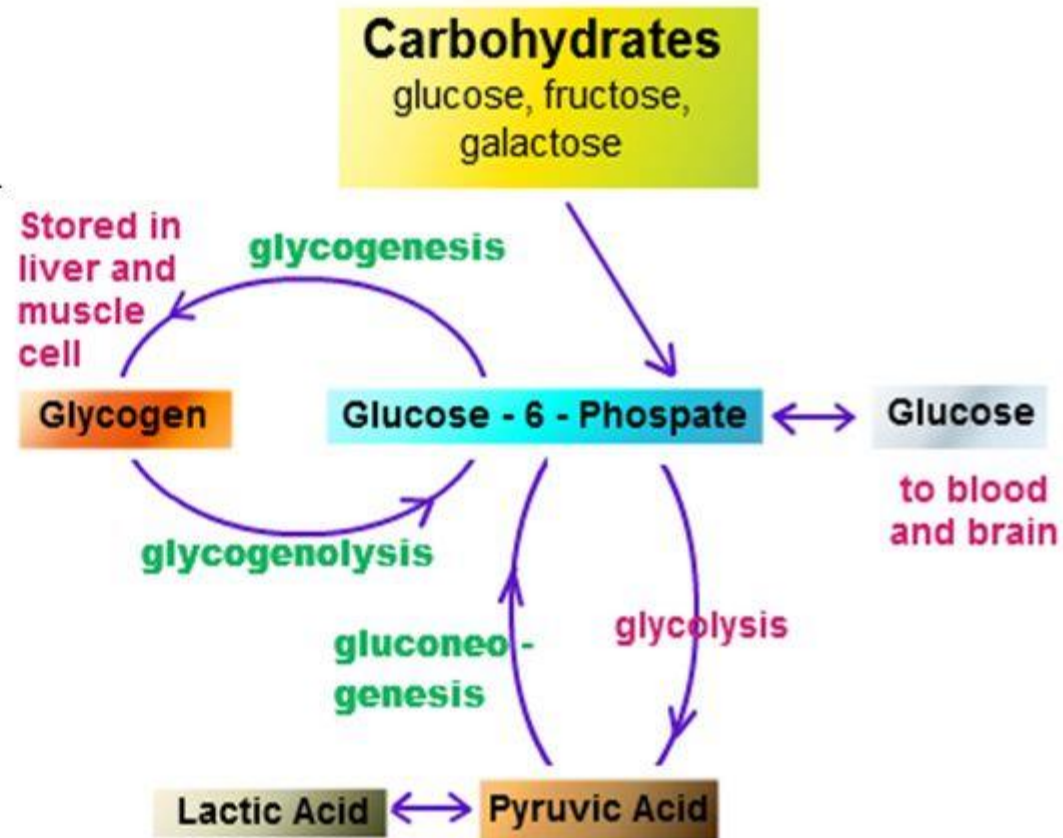




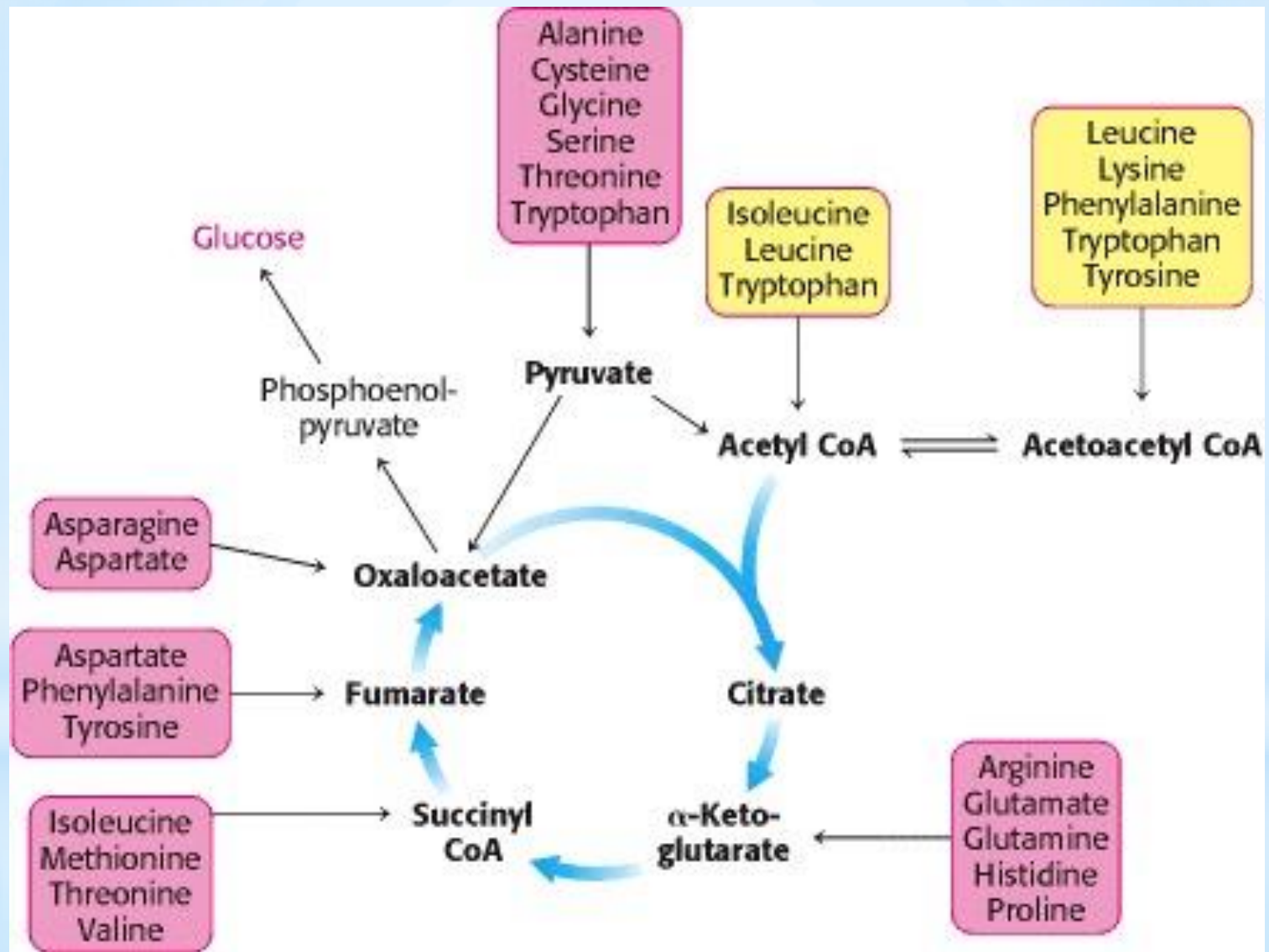


Glycogenesis

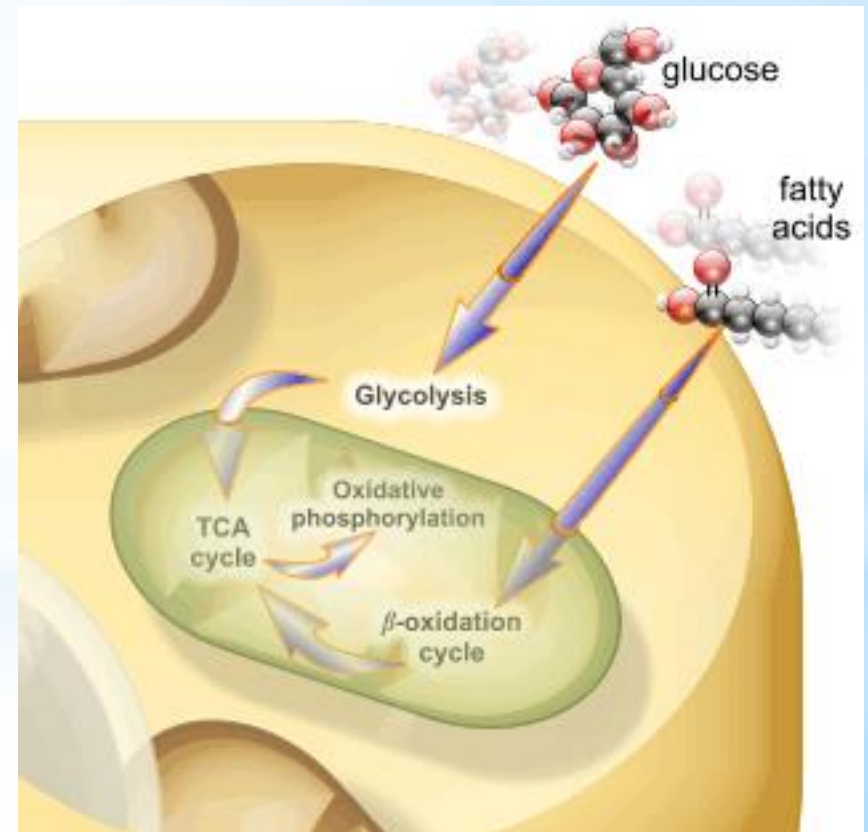
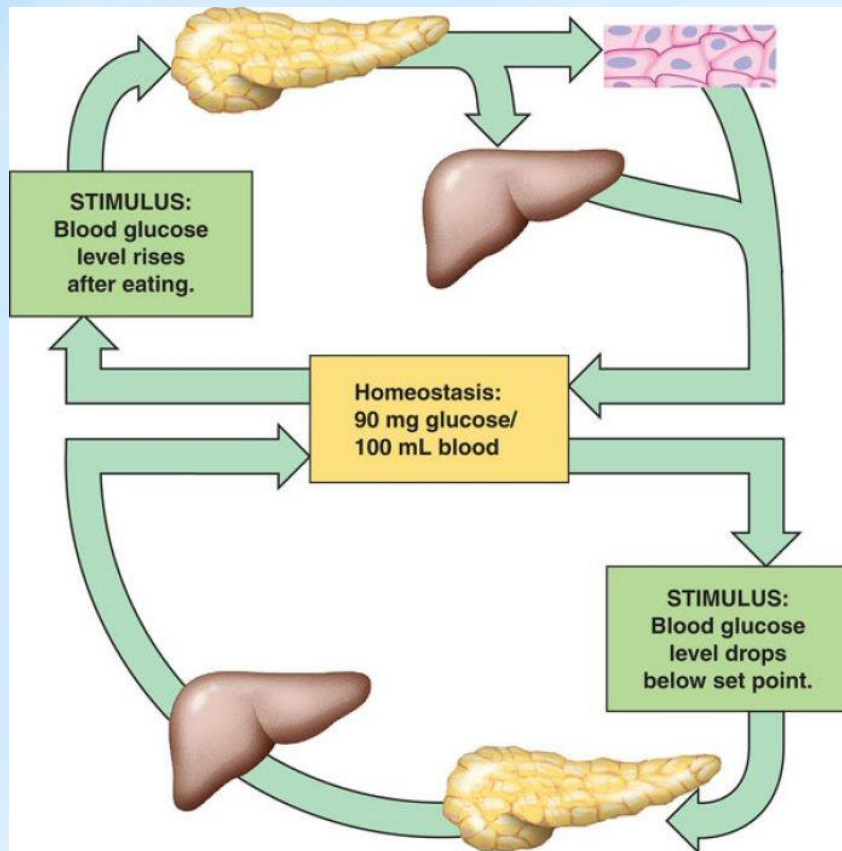
- The process of converting glucose to glycogen is called **glycogenesis**
- This process is stimulated by the hormone **insulin**
- Glycogen itself cannot be used by cells so it must be converted back to glucose for use



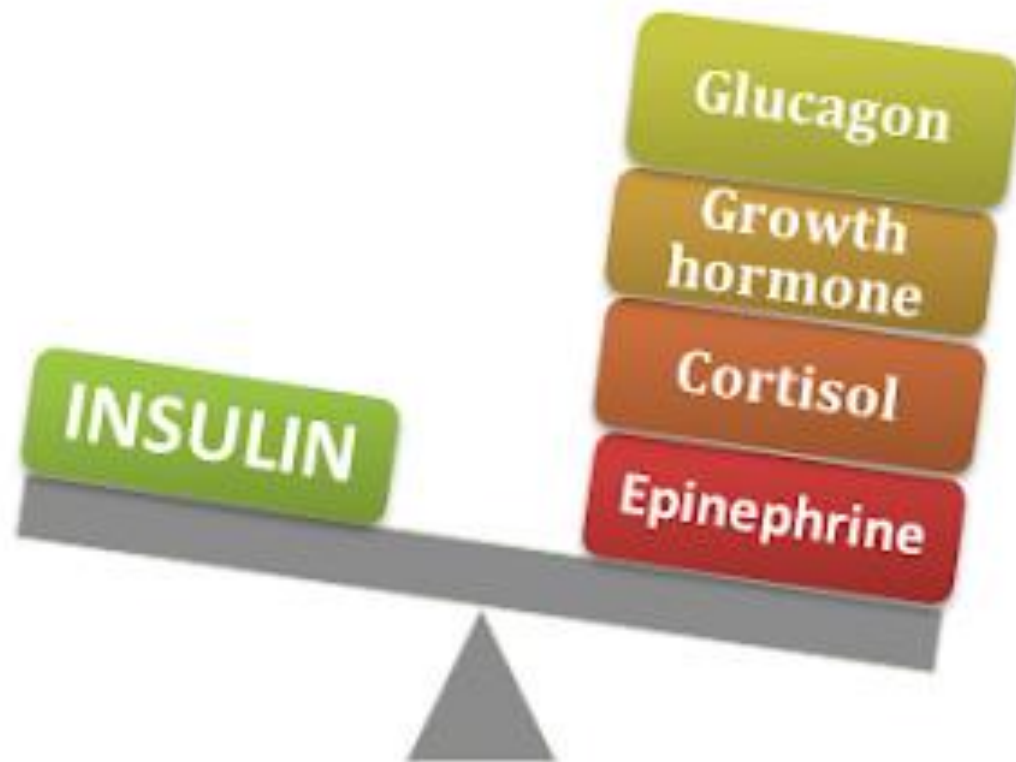
GLUCONEOGENESIS



Normal level of glucose is
3,3-5,5 mmol/l



Anti Insulin / Counter regulatory hormones



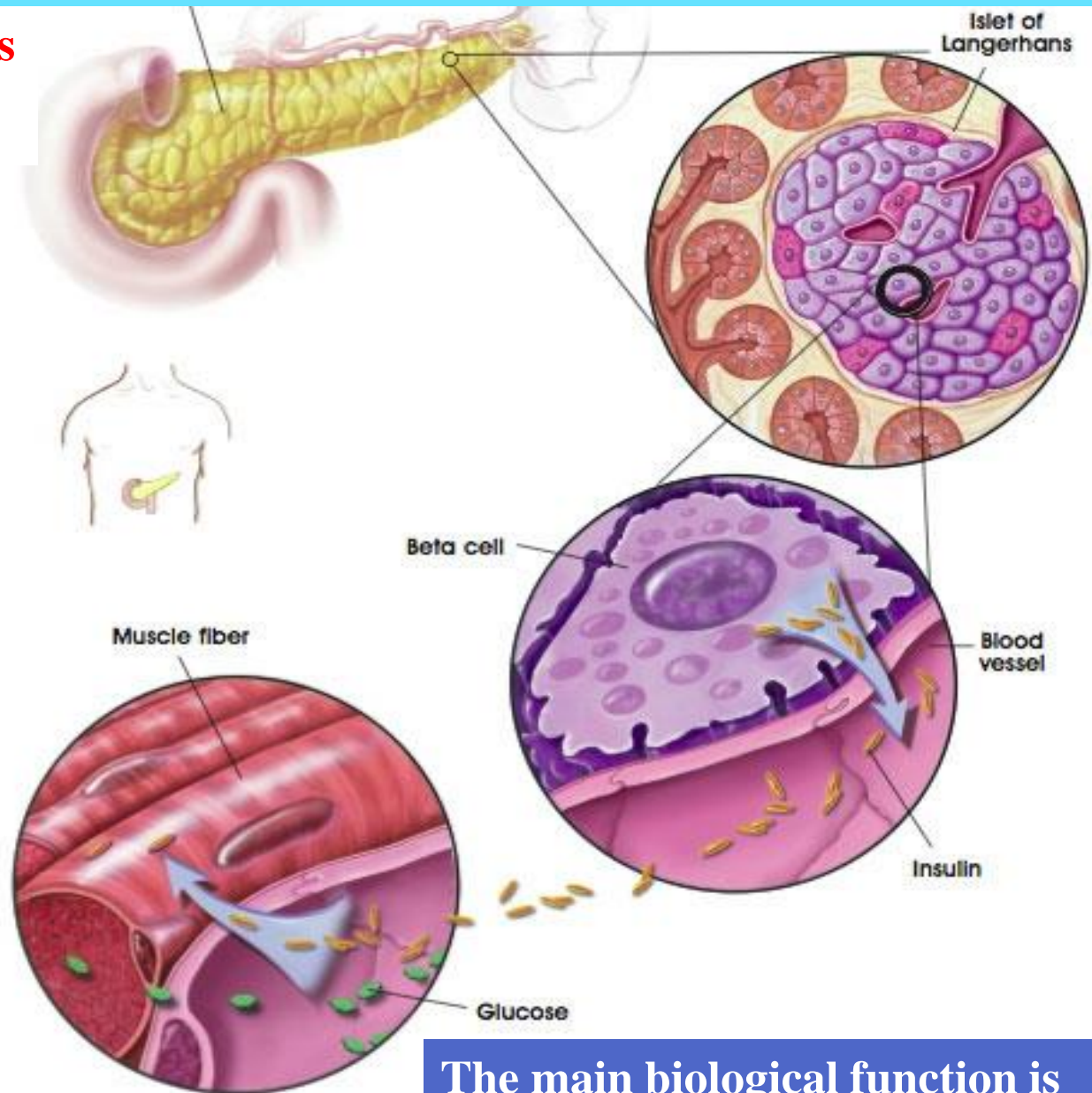
Insulin is produced by β -cells islets of Langerhans

Normal level of glucose is

3,3-5,5 mmol/l

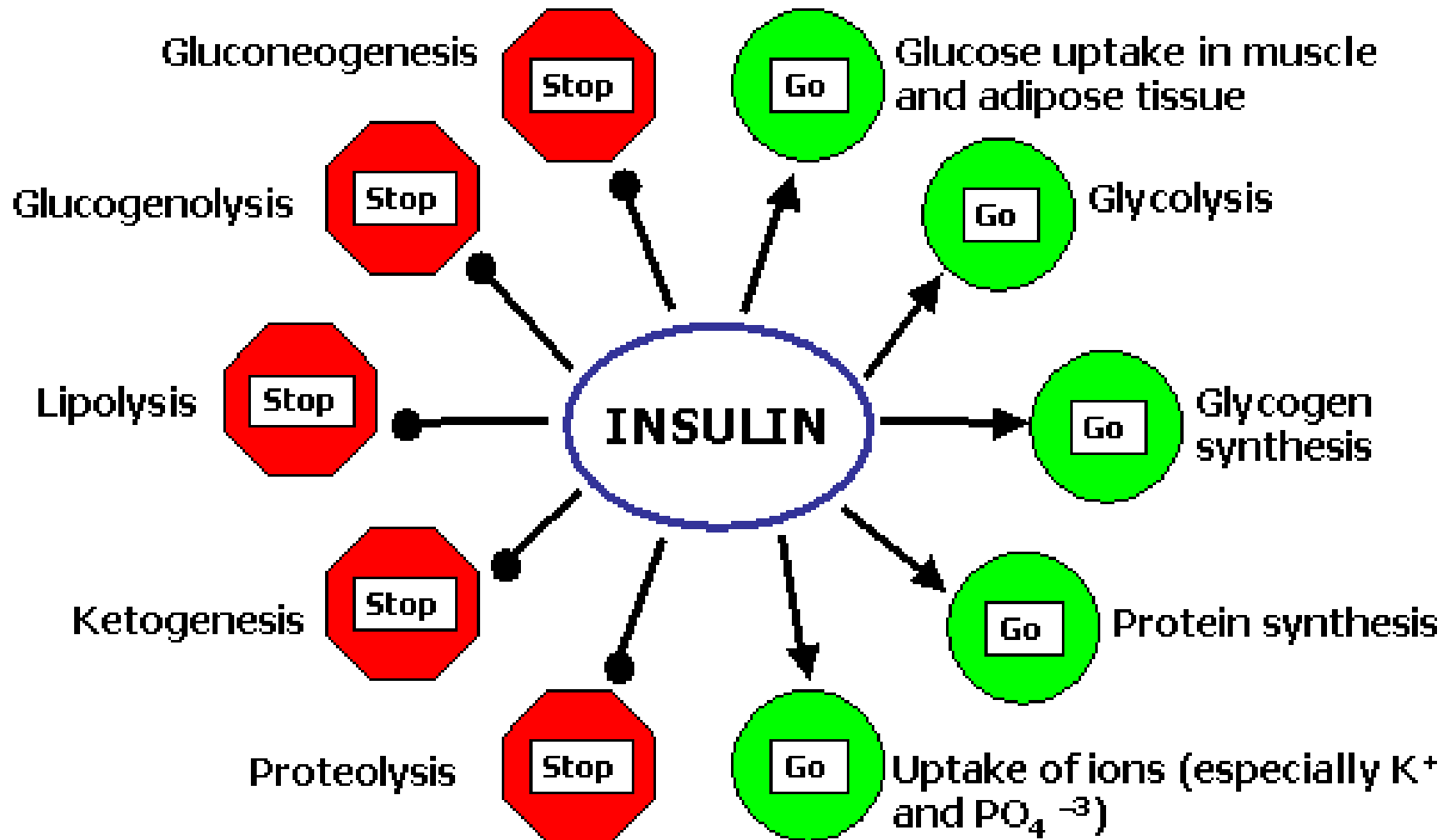
Contrinsulin hormones:

- somatotropic hormone (STH),
- thyroxin,
- epinephrine,
- glucocorticoids;
- glucagon



The main biological function is decreasing of glucose in the blood

Effects of insulin



The main biological effects of insulin

❖ Hypoglycemic effect:

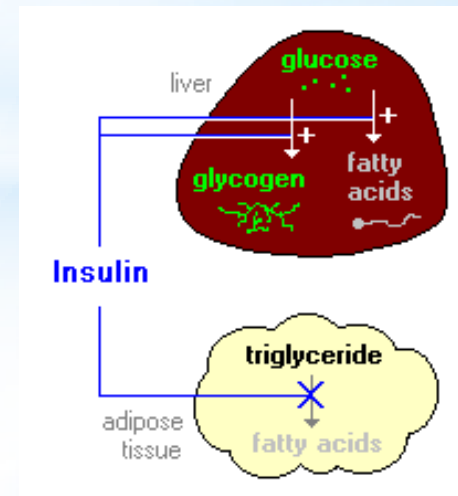
- ✓ Insulin facilitates entry of glucose into muscle, adipose and several other tissues.
- ✓ Insulin stimulates the liver to store glucose in the form of glycogen – the process of **glycogenesis**

❖ Anabolic action:

- ✓ Synthesis glycogen in liver
- ✓ Insulin promotes synthesis of fatty acids in the liver and proteins in muscles

❖ Mitogenic effect:

- ✓ insulin stimulates cell division



INSULIN SENSITIVITY OF ORGANS AND TISSUES

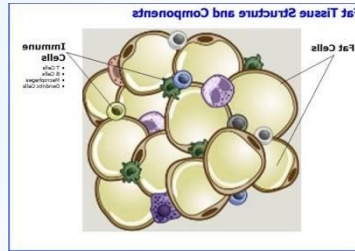
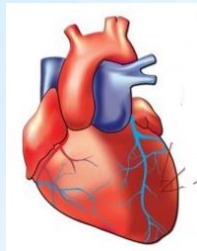
Insulin-dependent tissue and organ

Skeletal muscle

Myocardium

Liver

Fat tissue



Insulin-independent tissue and organ

Brain

Red blood cells

Kidney medulla

Lens

Adrenal gland



Relativ Insulin-dependent tissue and organ

Lung

Kydney

GTI and other

Pathology of carbohydrate metabolism

- 1. Disorders of digestion and absorption of carbohydrate**
- 2. Disorder of synthesis and splitting of glycogen**
- 3. Disorders of intermediate carbohydrate metabolism**
- 4. Disorder change of the nervous hormonal regulation**



Type of disorders of carbohydrate metabolism

Hyperglycemia -

increase of glucose in
the blood higher

5,6 mmol/l

Hypoglycemia -

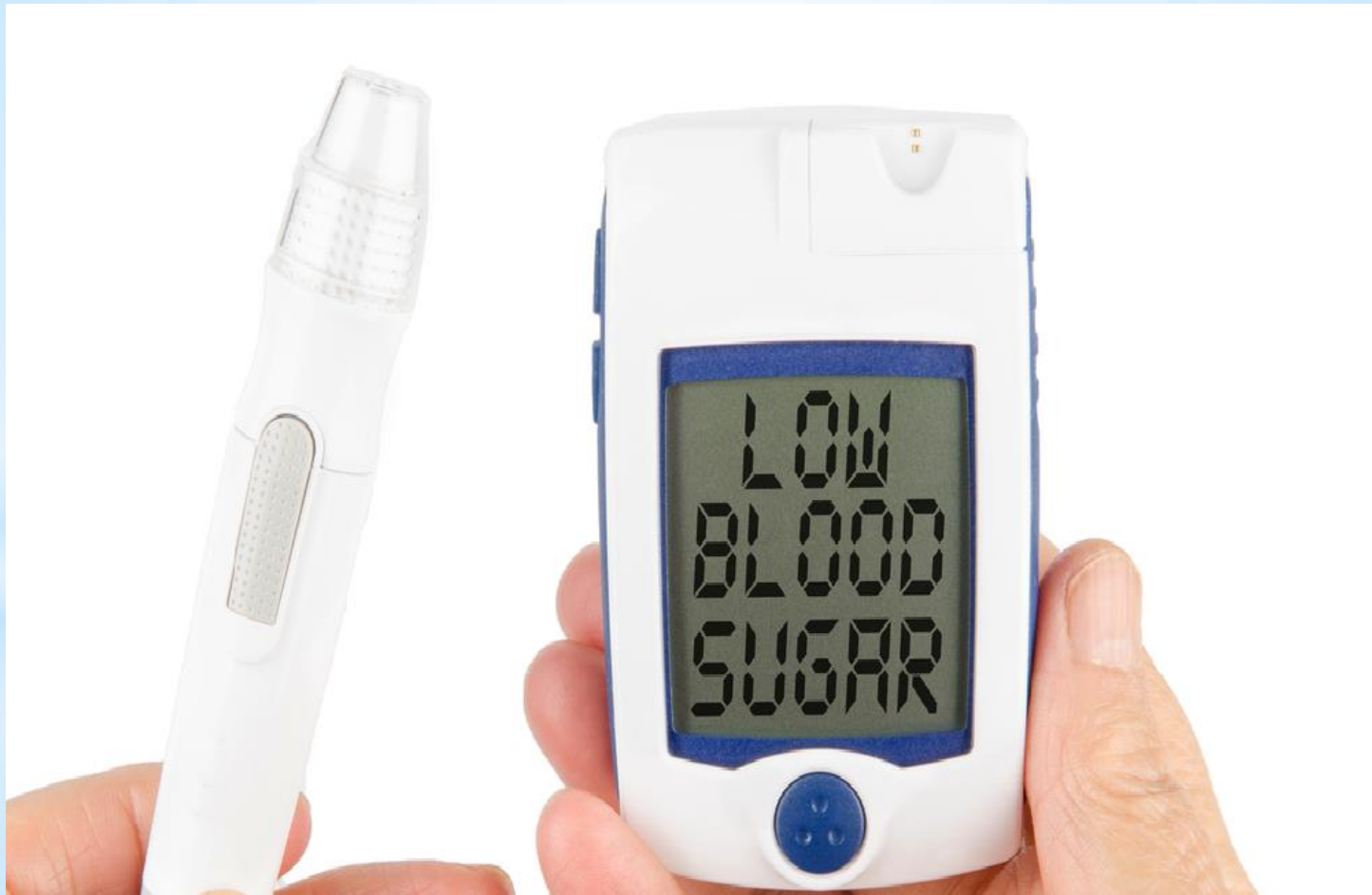
decrease of glucose in
the blood below

3,2 mmol/l

HYPOGLYCEMIA

←
Physiological

→
Pathological



PHYSIOLOGICAL HYPOGLYCEMIA

- heavy and prolonged physical or mental activity
- in women during lactation
- develops after alimentary hyperglycemia due to compensatory release of insulin into the blood



PATHOLOGICAL HYPOGLYCEMIA

- overdose of insulin in treatment of diabetes mellitus;
- increased production of insulin due to hyperfunction of the insular apparatus of the pancreas (insulinoma)
- insufficient production of hormones promoting catabolism of carbohydrates: thyroxin, adrenalin, glucocorticoids;
- damage of the hepatic cells (hepatitis);
- carbohydrate malabsorption;
- renal diabetes in intoxication by poisons blocking hexokinase



HYPOGLYCEMIA



SLEEPINESS



SWEATING



PALLOR



**LACK OF
COORDINATION**



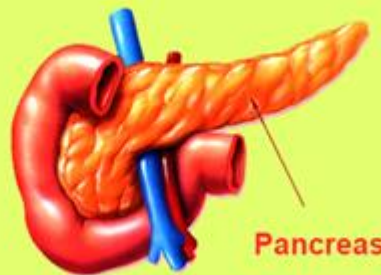
IRRITABILITY



HUNGER

Hyperglycemia

- **Alimentary** – as a result large intake of easily digested carbohydrates
- **Neurogenic** – developing during stress, narcosis, pain
- **Endocrine** - disease of endocrine glands (thyroid gland, adrenal gland)



HYPERGLYCEMIA

SYMPTOMS



DRY MOUTH



**INCREASED
THIRST**



WEAKNESS



HEADACHE



**BLURRED
VISION**



**FREQUENT
URINATION**

Diabetes mellitus is a disease resulting from the absolute or relative insufficiency of insulin in the organism and accompanying by disorder of all kinds of metabolism, mainly the carbohydrate one.



Risk Factors for Pre-Diabetes



Poor nutrition



Tobacco, Alcohol, Drugs



Sedentary



Emotional Health:
Stress, Anger, Depression



Abdominal fat



High BG, Blood Pressure,
High Triglycerides, LDL, Homocysteine,
CRP, TNF- α , IL-6



Age (>45)



Family Background

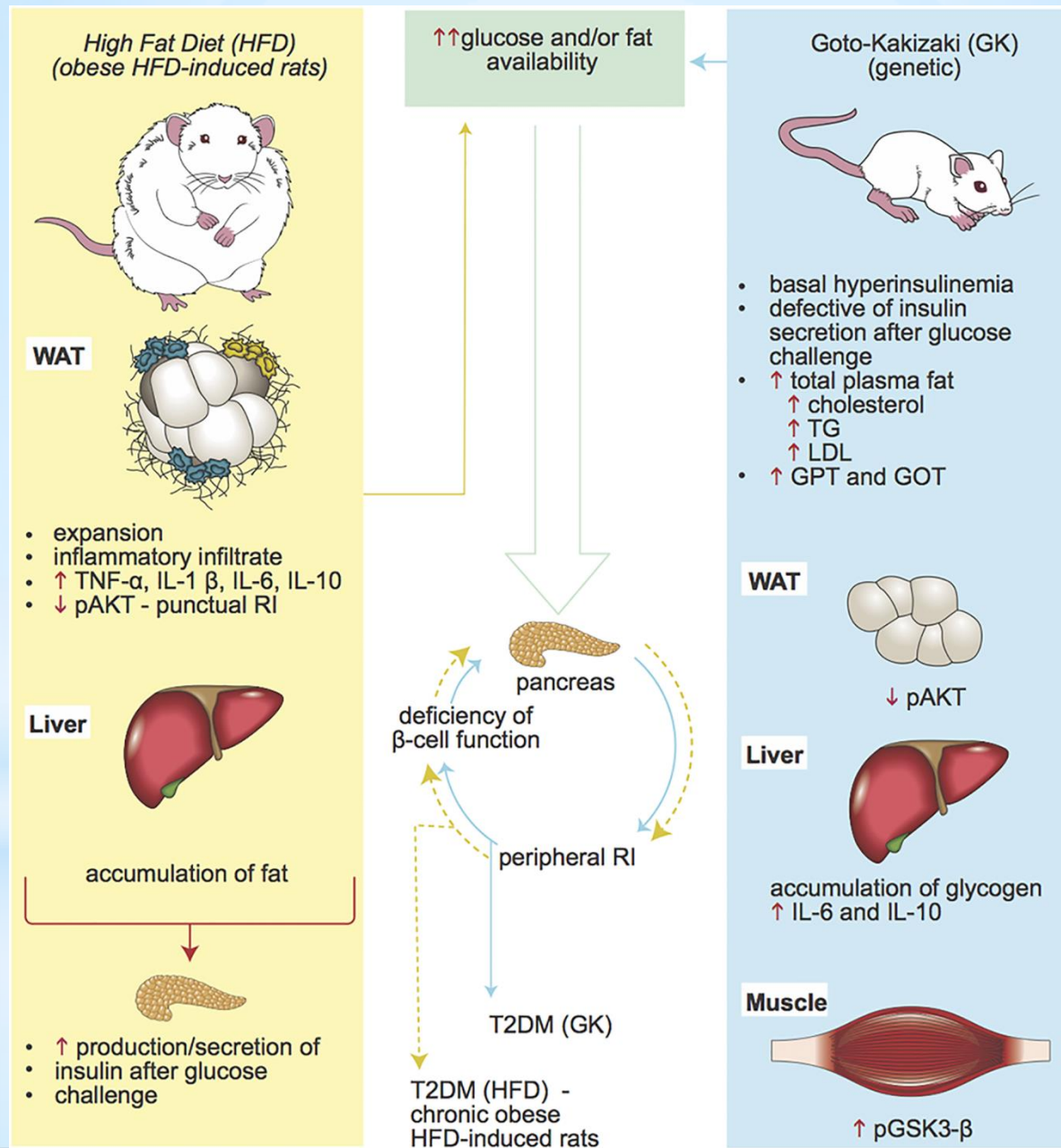


Ethnic Background



Gestational
Diabetes

Animals Models in Diabetes Research



Etiology

The cause of diabetes mellitus is absolute or relative insufficiency of insulin in the organism.

The absolute insufficiency of insulin (pancreatic)

The damage of beta-cells of the Langerhans' islets of the pancreas by inflammation (virus infection, syphilis), hypoxia, tumor

The relative insufficiency of insulin (extrapancreatic)

Insulin resistance or reduced insulin sensitivity (defective responsiveness of tissues to insulin) as a result:

- * of disorder the insulin receptor sensitivity in cell membranes;
- * decreased number of receptors to insulin;
- * excess fatty acids in the blood (obesity);
- * excess connection with transport proteins

Types of diabetes mellitus:



1st Type Diabetes mellitus
called as
insulin-dependent diabetes
mellitus [IDDM]

or juvenile-onset diabetes.

1st Type diabetes usually occurs
in children and young adults
(before age 30) which won't
survive without daily injections
of insulin. This type has a
hereditary predisposition.

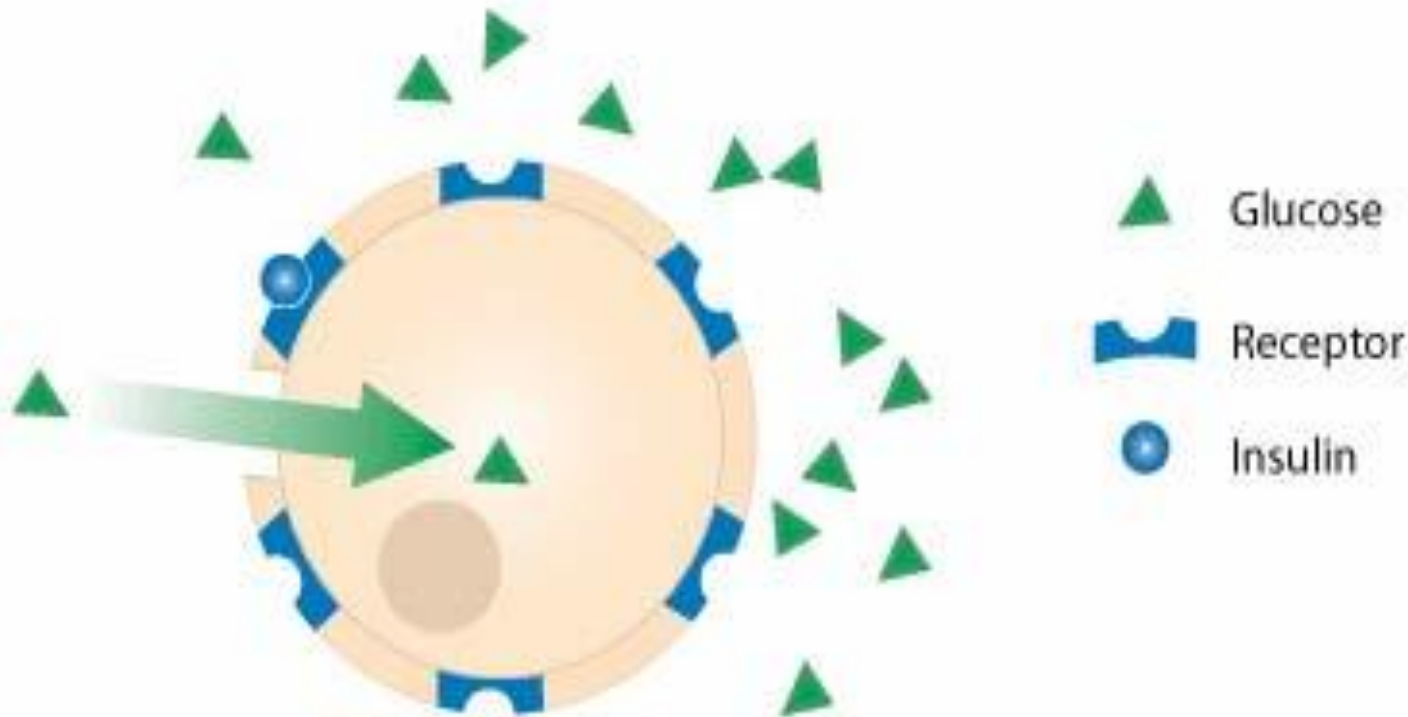
2nd Type Diabetes mellitus
called as
noninsulin-dependent diabetes
mellitus [NIDDM]
or adult-onset diabetes.






2nd Type manifested after age
40 and is treated with diet and
oral antidiabetic drugs.

Gestational diabetes,
which emerges during pregnancy

IDDM Type1

NIDDM Type 2

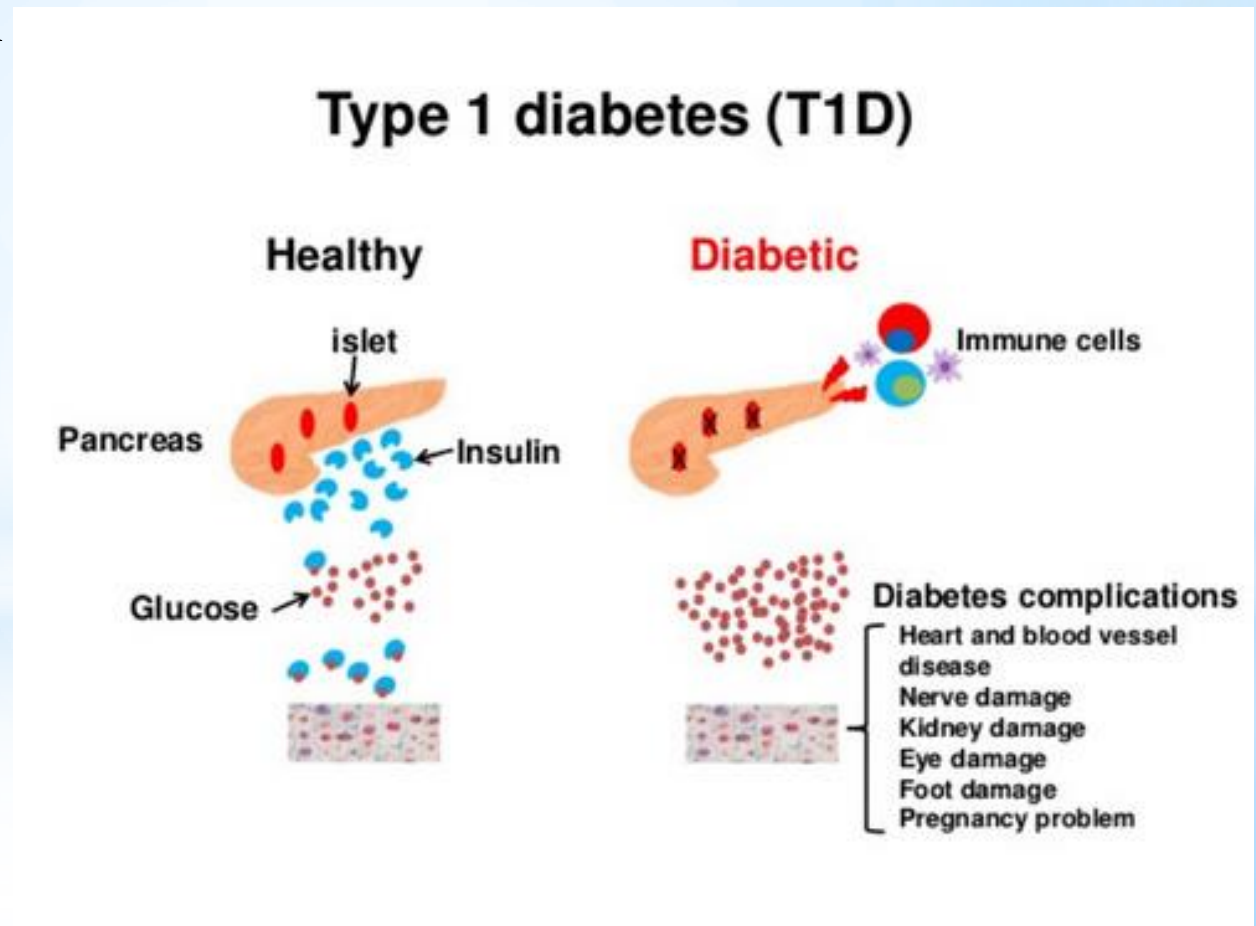


In the human cell, insulin  must bind with receptors  before glucose  can enter the cell. Without enough Insulin , very little glucose  is transported to the cell.

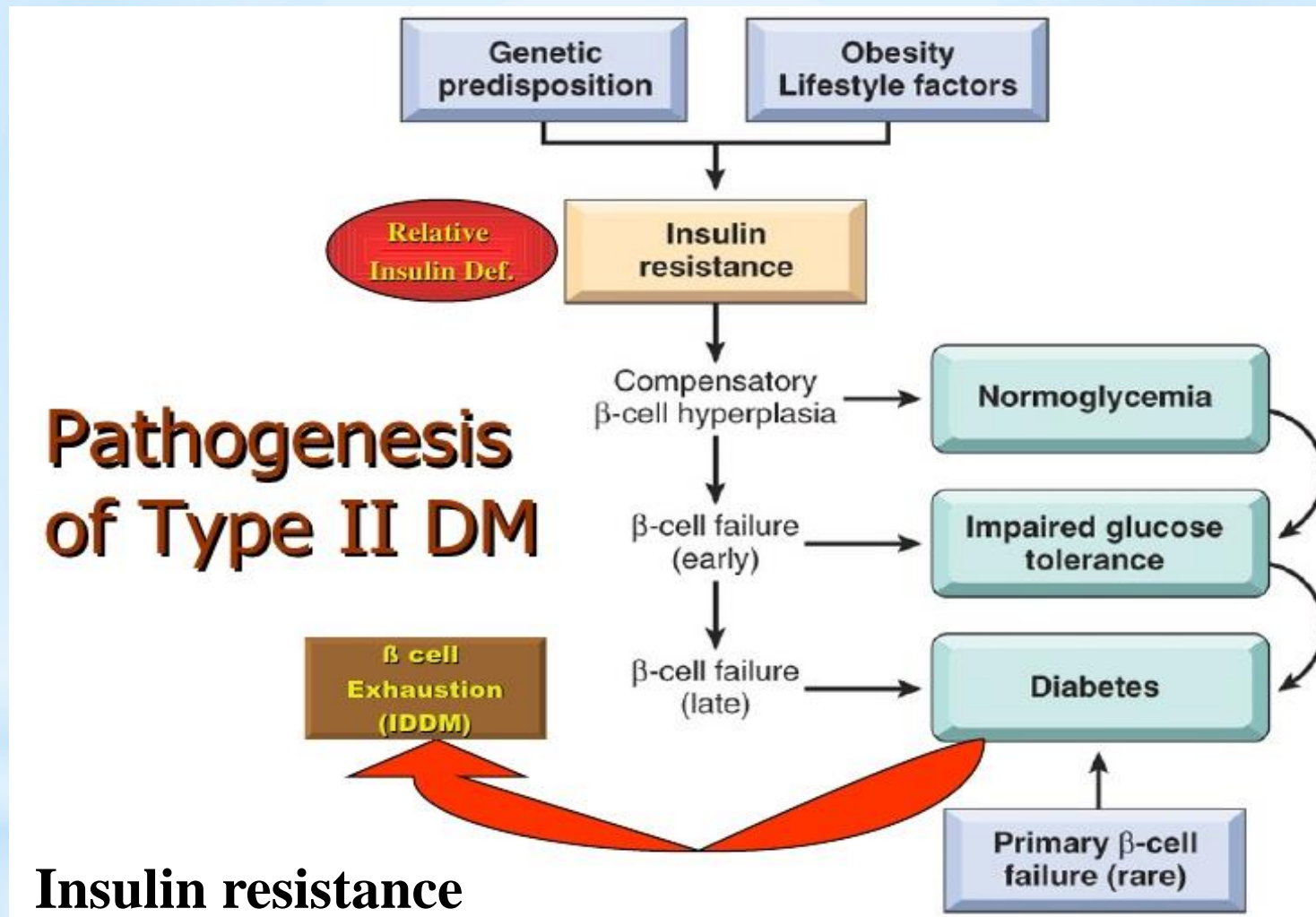
Most people with Type 2 have more than enough insulin but the receptors are resistant to insulin.

Pathogenesis of Insulin-dependent diabetes mellitus

Autoimmune process is started damage of beta-cells of the Langerhans' islets of the pancreas that leads by absolute reduced secretion of insulin



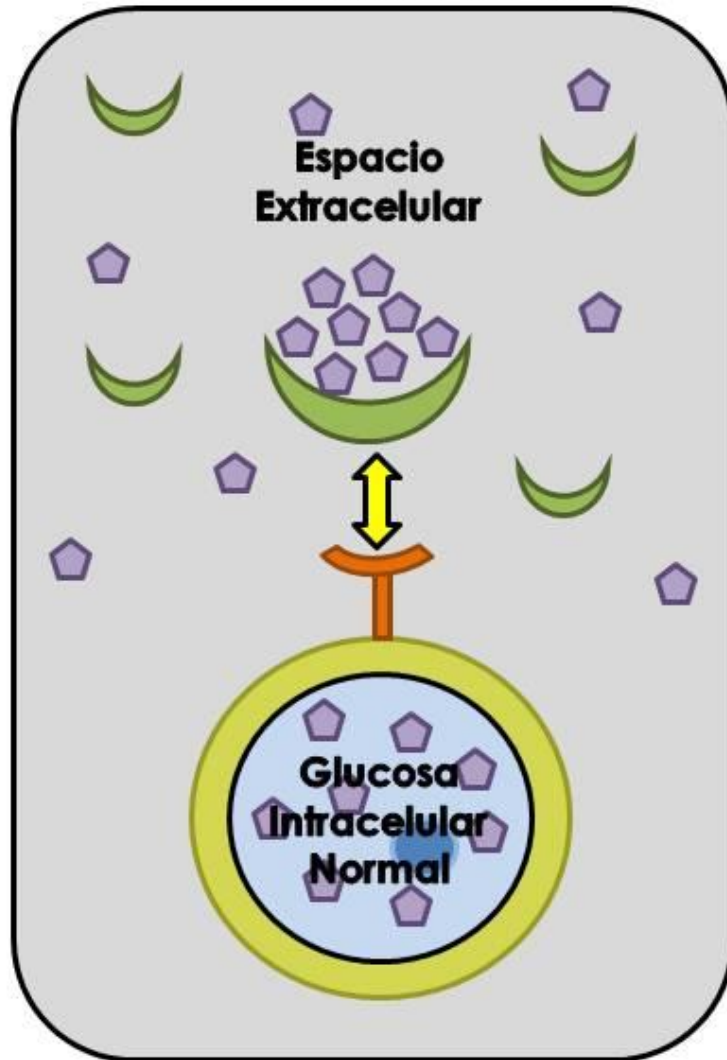
Pathogenesis of non-Insulin-dependent diabetes mellitus



Insulin resistance

decreased sensitivity of body tissues to the action of insulin

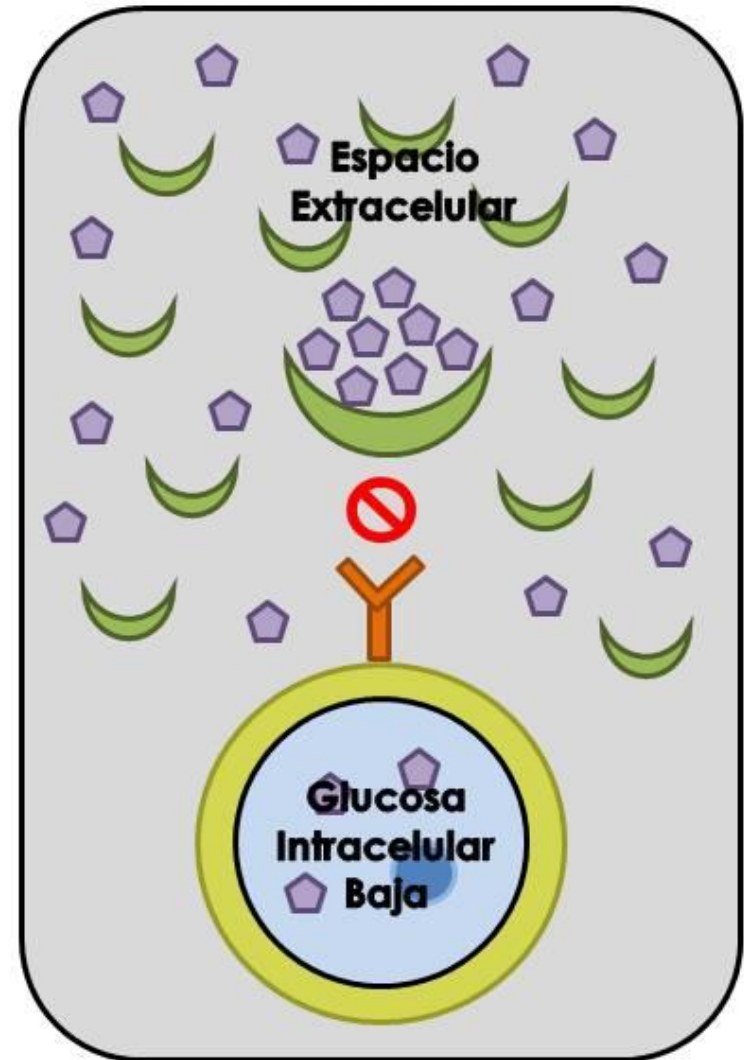
Metabolismo Normal



Insulina

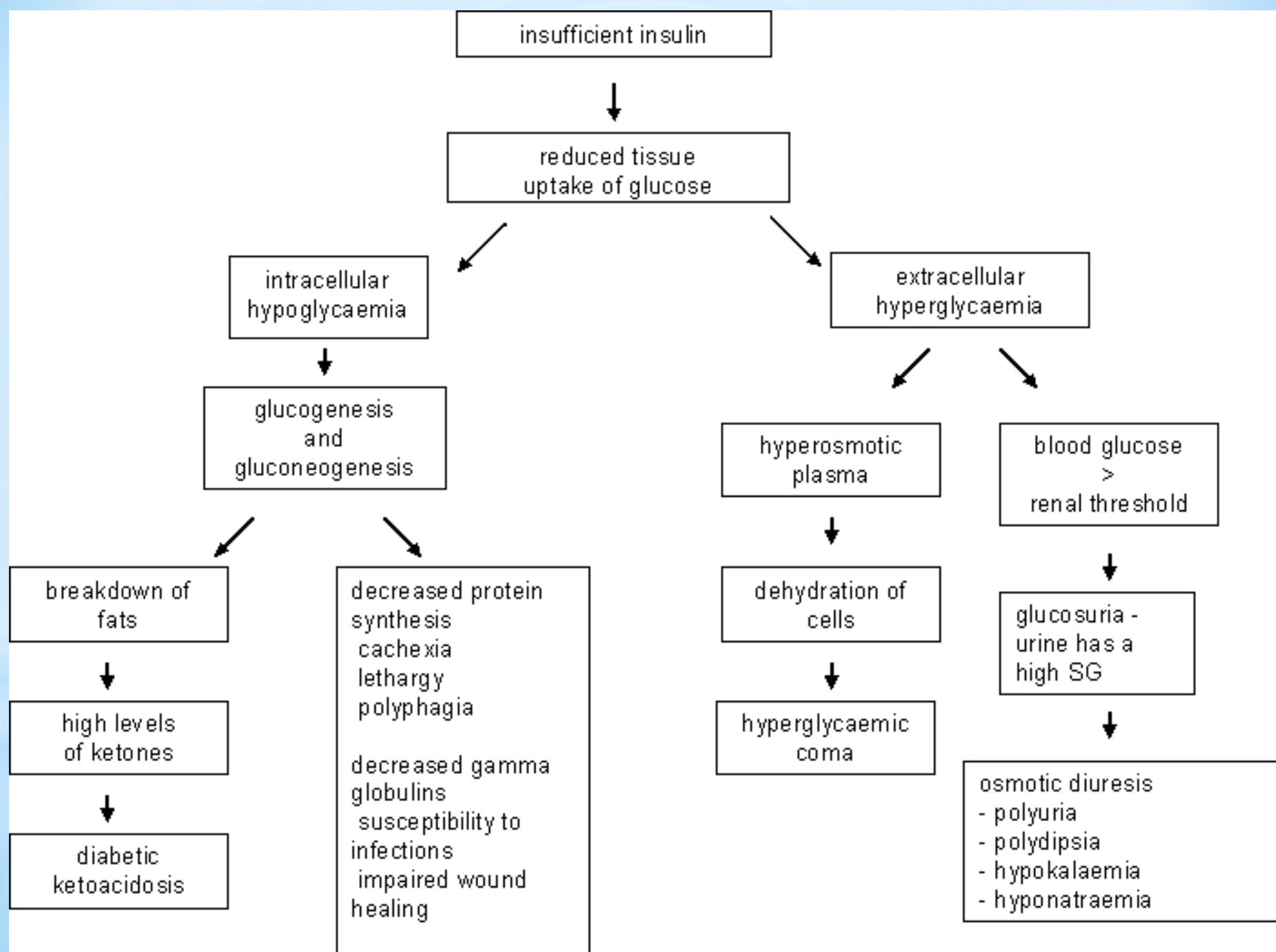
Receptor de Insulina Funcional

Resistencia Insulínica

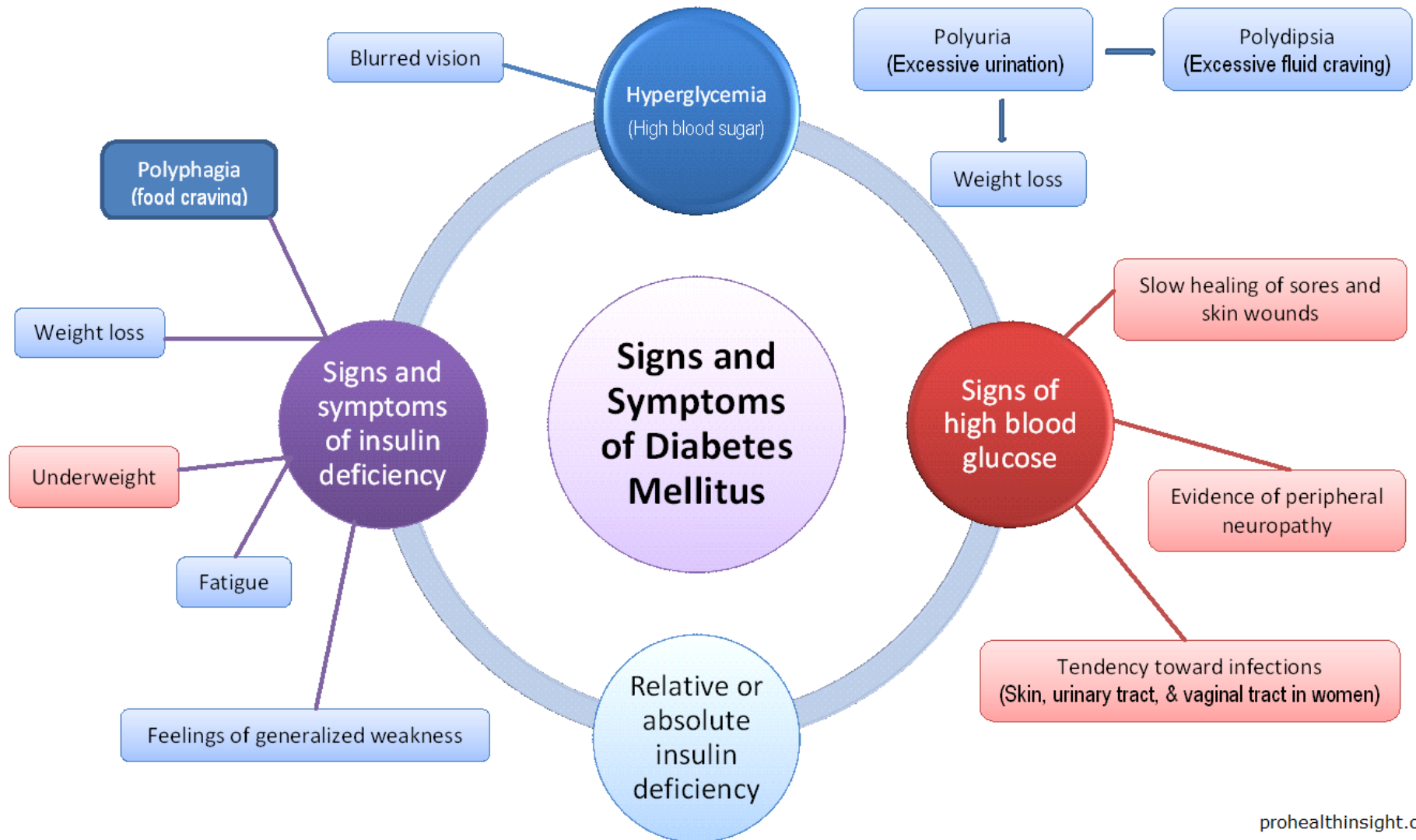


Glucosa

Receptor de Insulina No Funcional



Signs and Symptoms of Diabetes Mellitus



Clinical signs:

Hyperglycemia - the result of disorders uptake glucose by cells

Glucosuria - glucose in the urine - when the glucose level in the blood exceeds 10 mmol/l, it appears in the secondary urine as the result of inhibition enzyme hexokinase and disturbed reabsorption glucose in the nephritic ducts.

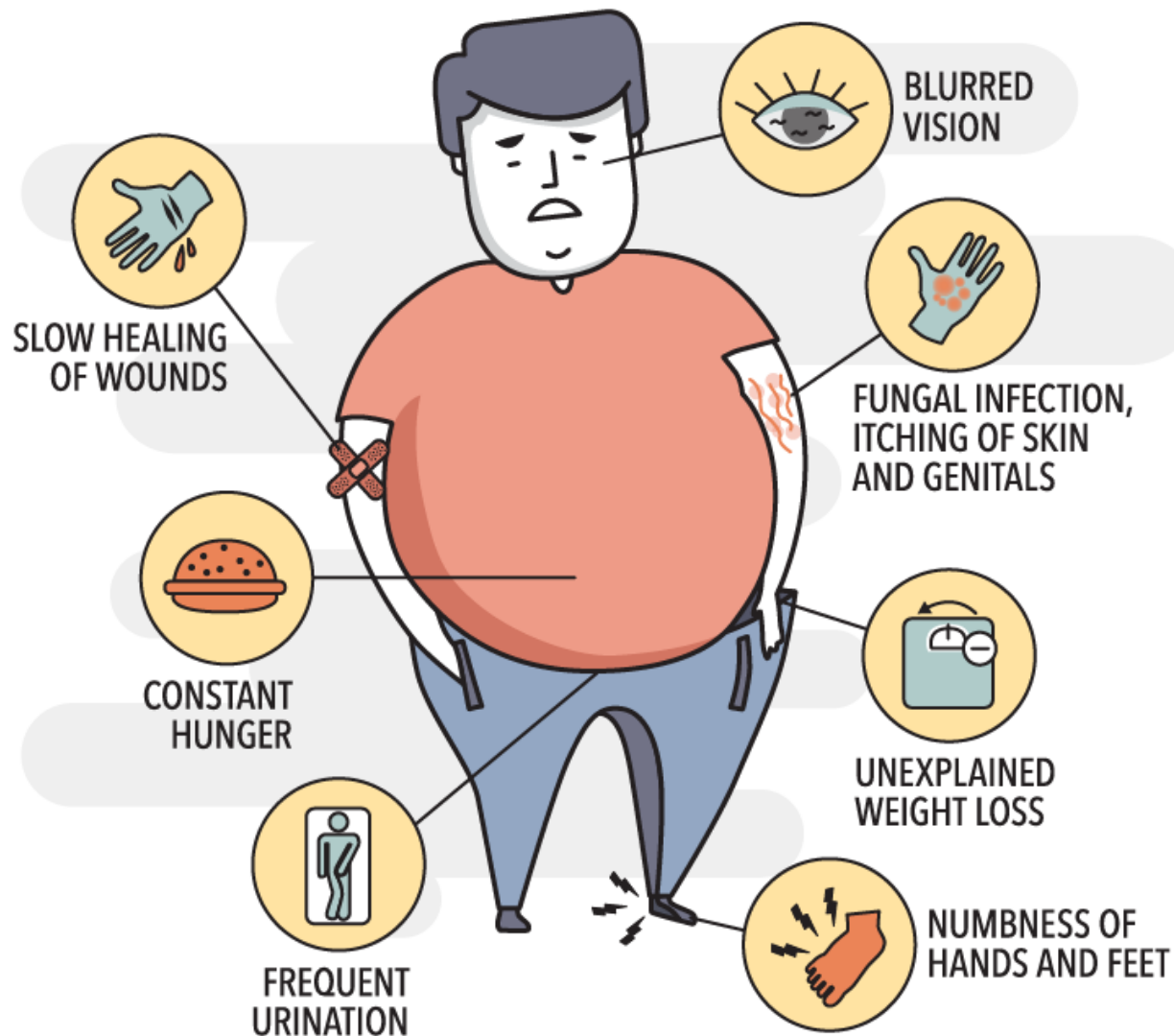
Polyuria – increase in daily diuresis –high the osmotic pressure of the primary urine leads to the disturbance water's reabsorption in the tubules, dehydration develops. Daily diuresis may be 5 -10 liters

Polydipsia - thirst - as the result of the dehydration

Polyphagia - increase in the appetite – deficiency of energy in the cells

Ketonemia and ketonyria - increase content of ketonic bodies in the blood and the urine – as the result disorder fat metabolism

7 COMMON SYMPTOMS OF TYPE 2 DIABETES



Differences between insulin-dependent and non-insulin-dependent diabetes mellitus

Sign	Diabetes mellitus type I	Diabetes mellitus type II
Insulin deficiency	pancreatic (absolute)	extrapancreatic (relative)
Age of onset	20-30 years old	After 40
Onset of the disease	quickly	slowly
Role of seasons fluctuations	Autumn-winter	no
Association with the HLA antigens (Antibodies to pancreatic cells)	determined from the first days of the disease	usually not defined
The frequency of diabetes in relatives of the 1st line	Less 10%	More 20%
Body weight	Loss of the weight	Obesity
Condition of the pancreas	Reduce the number of insulin producing cells	The number insulin producing cells are normal
Treatment	Insulin	Antidiabetic medicines

Complications of diabetes mellitus

I. Acute complications:

- *diabetic ketoacidosis*
- *hypoglycemia*
- *diabetic nonketotic hyperosmolar coma*

II. Chronic complications:

a. Microvascular

- *retinopathy*
- *nephropathy*
- *neuropathy*
- *diabetic foot*
- *dermopathy*

b. Macrovascular

- *Cerebrovascular.*
- *Cardiovascular.*
- *peripheral vascular disease.*

Complications of Diabetes Mellitus

Cerebrovascular
disease



Retinopathy
and Blindness



Permanent
kidney damage



Heart attack



Diabetic Foot
Infections

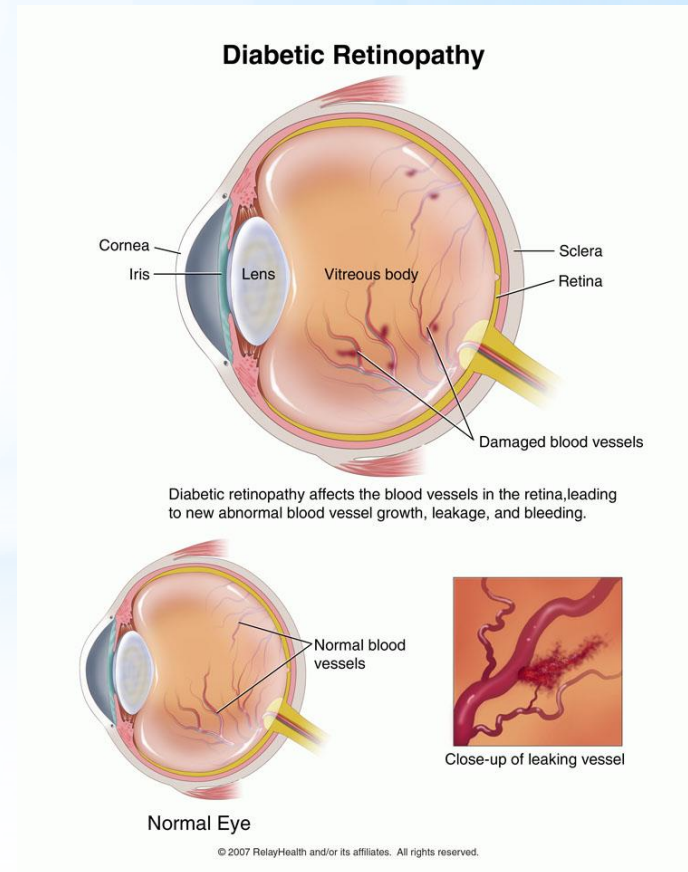
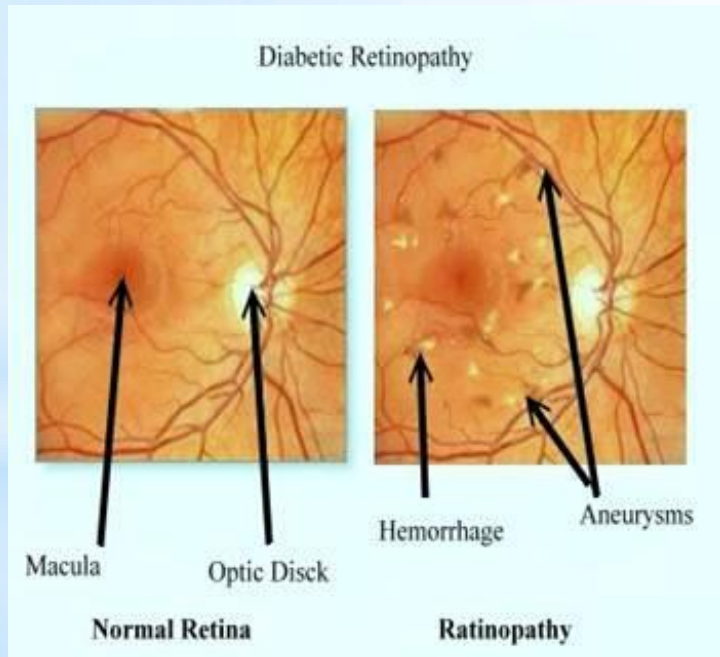


Peripheral
Neuropathy

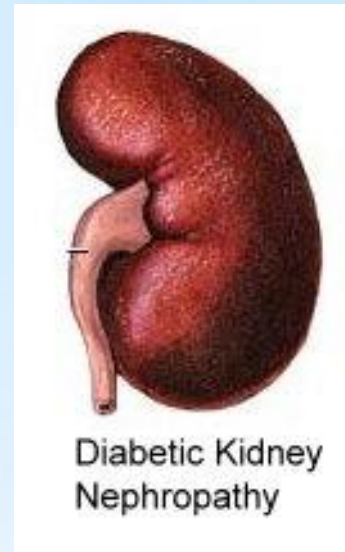
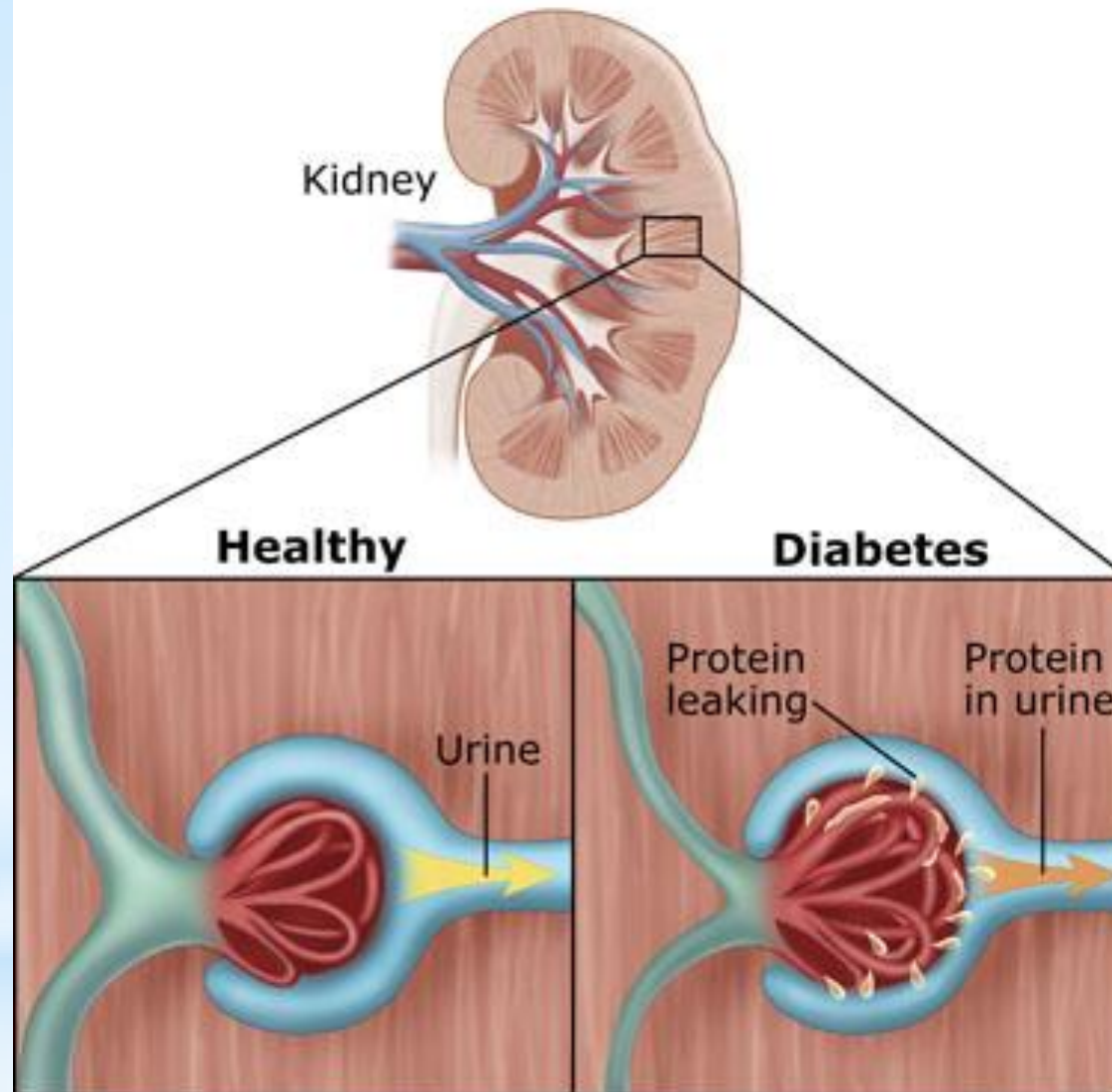
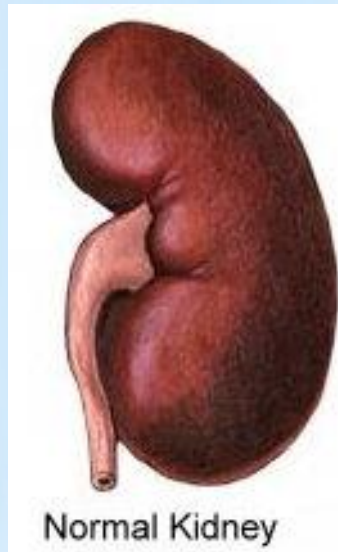


Complications of Diabetes mellitus

- **Microangiopathy** – accumulation glucoproteins in internal wall of vessels (insulin-dependent tissue) leads to thicker and weaker. As a result, some organs and tissues do not get enough blood and are damaged, for example, the **retina (diabetic retinopathy)** or **kidney (diabetic nephropathy)**.

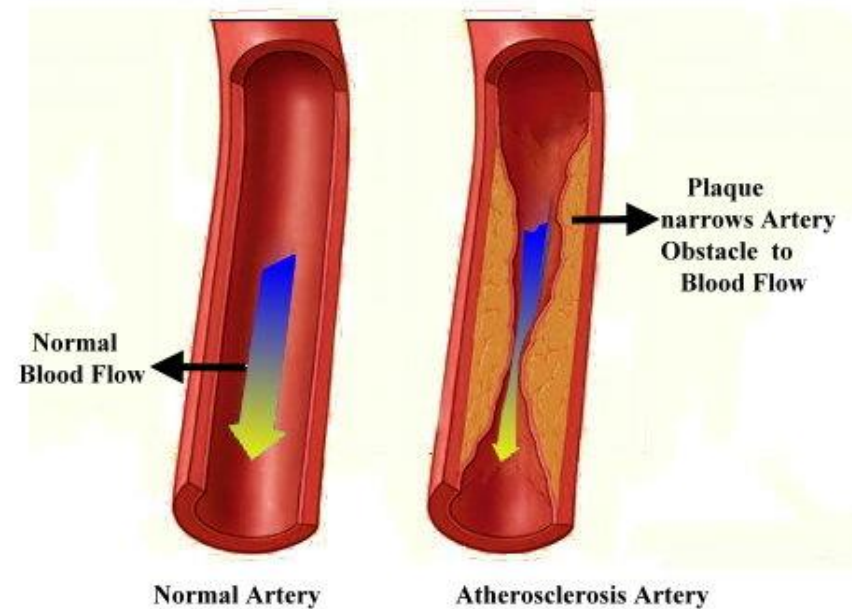
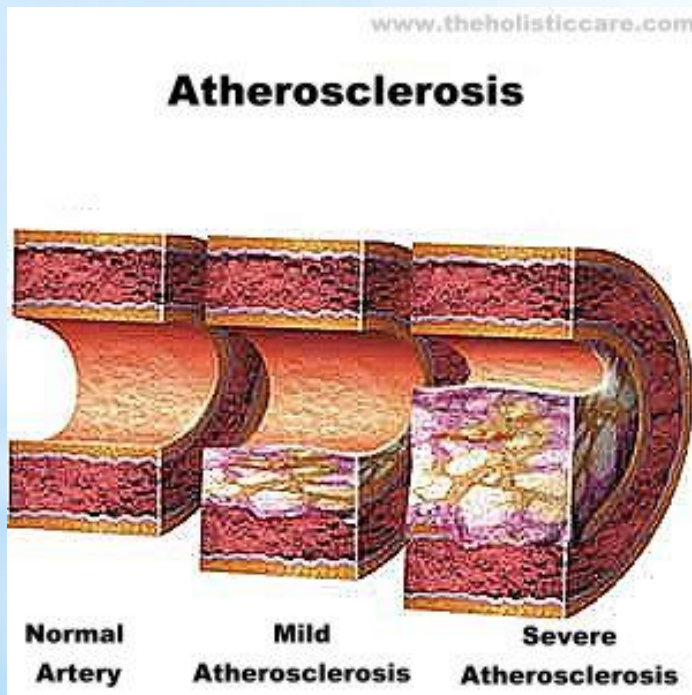


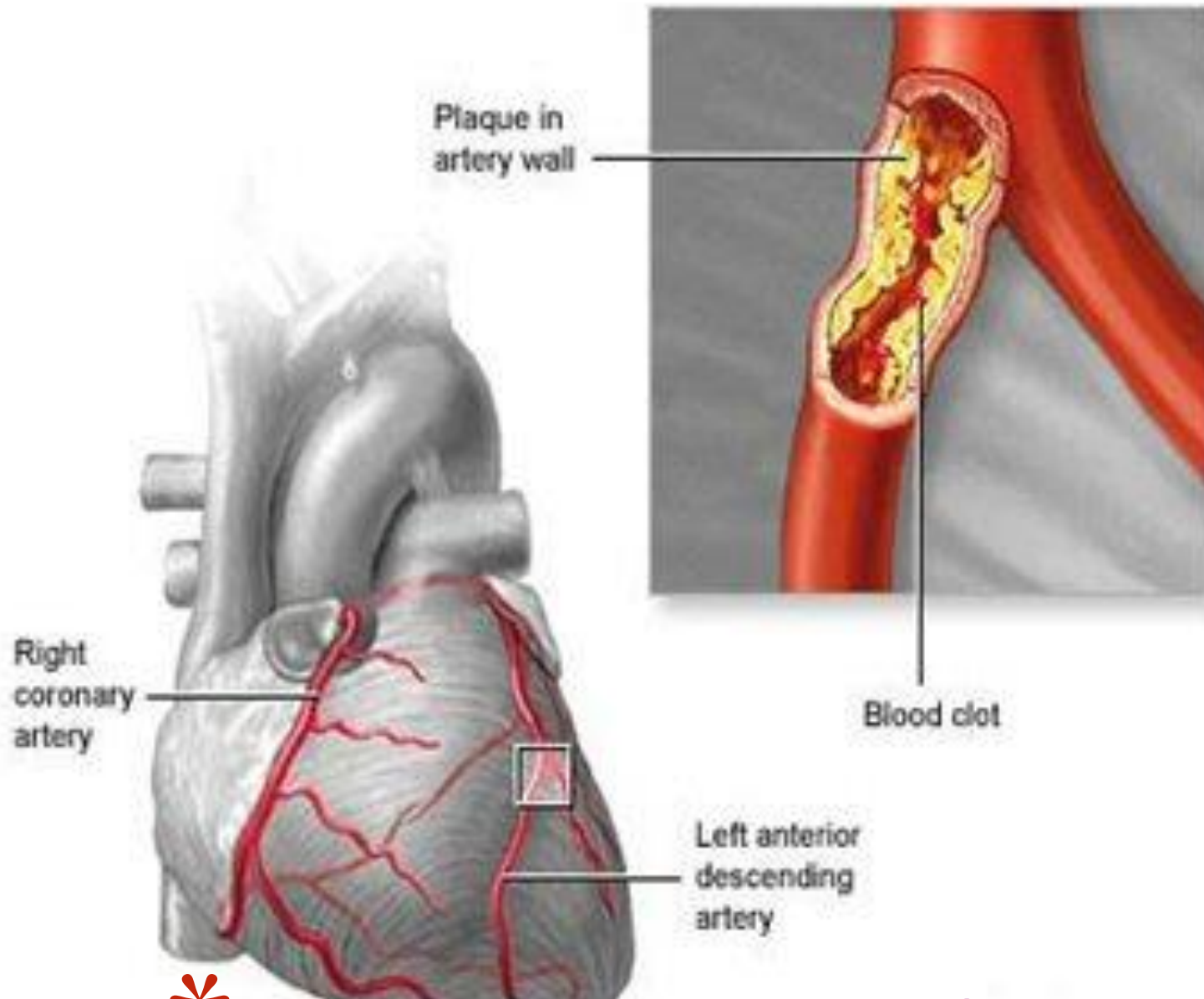
Diabetes Affects the Kidney



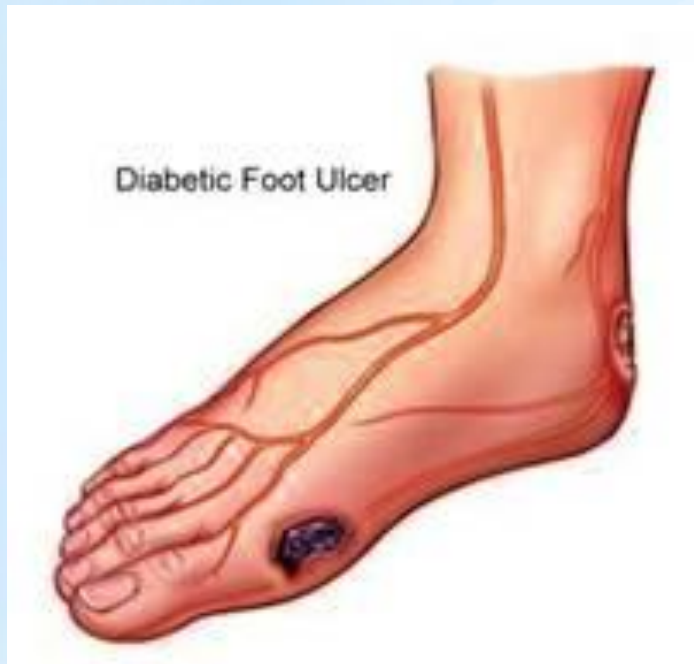
* *Complications of Diabetes*

- **Macroangiopathy** – the disturbances of fat and protein metabolism led to development of atherosclerosis and a resultant blood plaque and clot forms on the large blood vessels and blocks the flow of blood. Macroangiopathy may cause other complications, such as **ischemic heart disease, stroke and peripheral vascular disease** which contributes to the diabetic foot ulcers and the risk of amputation.



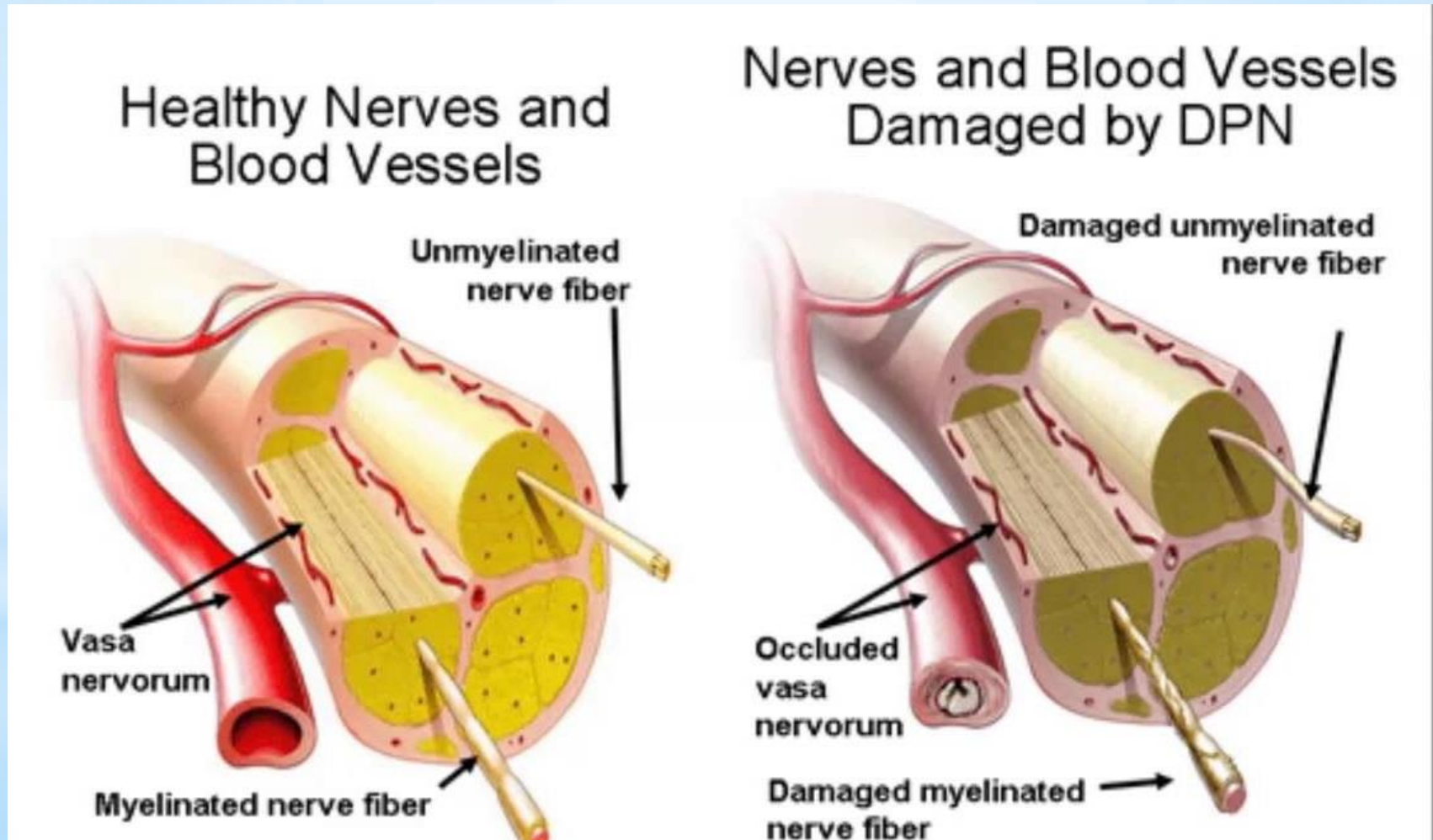


Complications of Diabetes

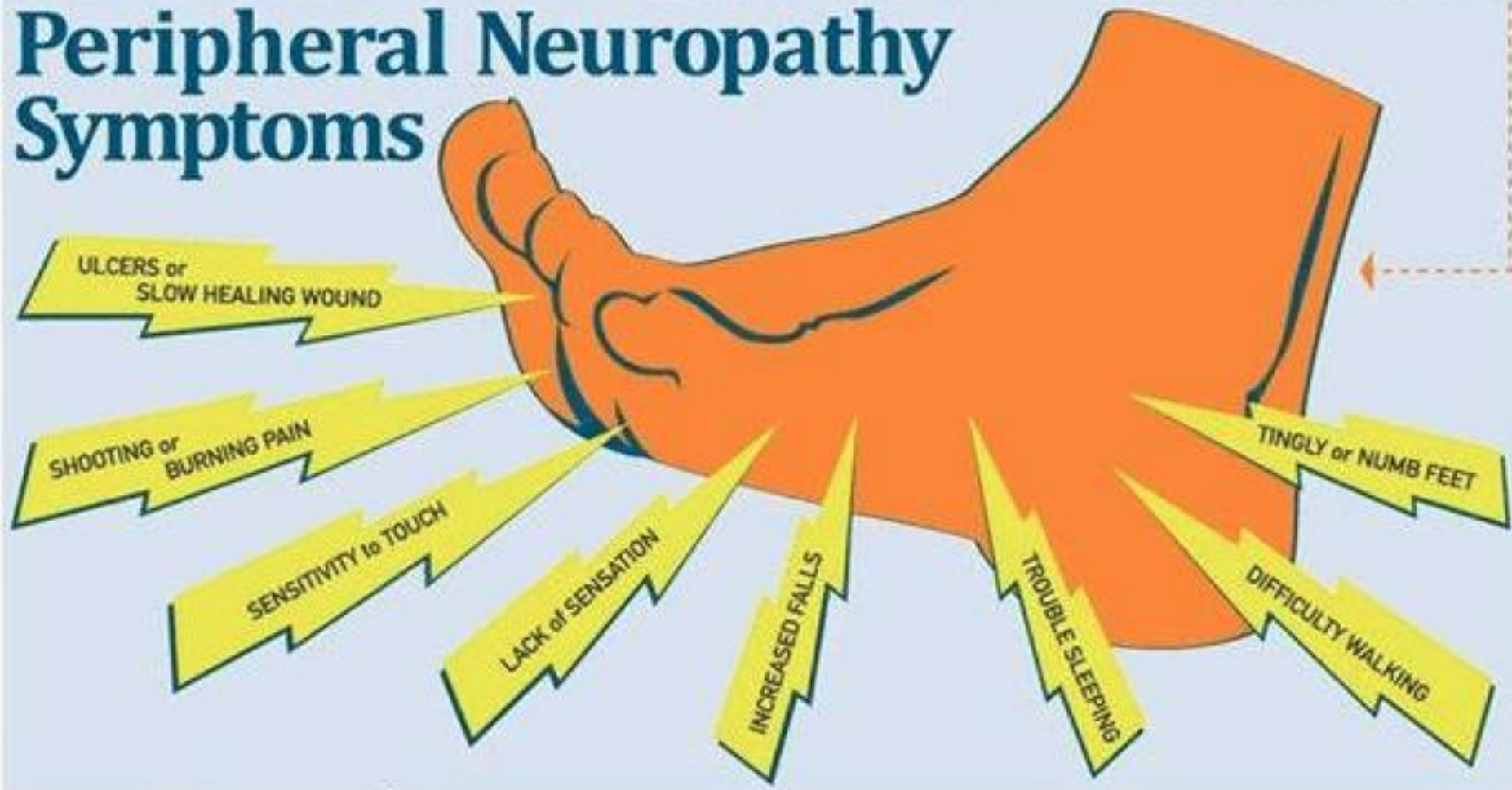


Diabetic foot ulcer

Neuropathy – nerves and neurons are also damaged which leads to loss of function (diabetic neuropathy, especially peripheral neuropathy).



Peripheral Neuropathy Symptoms



Hyperglycemic coma and Hypoglycemic coma: etiology, clinical signs, emergency care

Type of coma	Diabetic (Hyperglycemic or Hyperketonemic)	Hypoglycemic
<i>Etiology</i>	Disturbance of the diet, deficiency of the insulin, alcohol intake, heart accident, infectious disease	Overdose of insulin, stress, physical work, untimely eating
<i>Pathogenesis</i>	High concentration of ketonic bodies in the blood (hyperketonemia), development of non-gas acidosis, inhibits the central nervous system	Acute decrease of the level of the glucose in the blood, development of the hypoxia, loss of consciences
<i>Development</i>	slowly	quickly

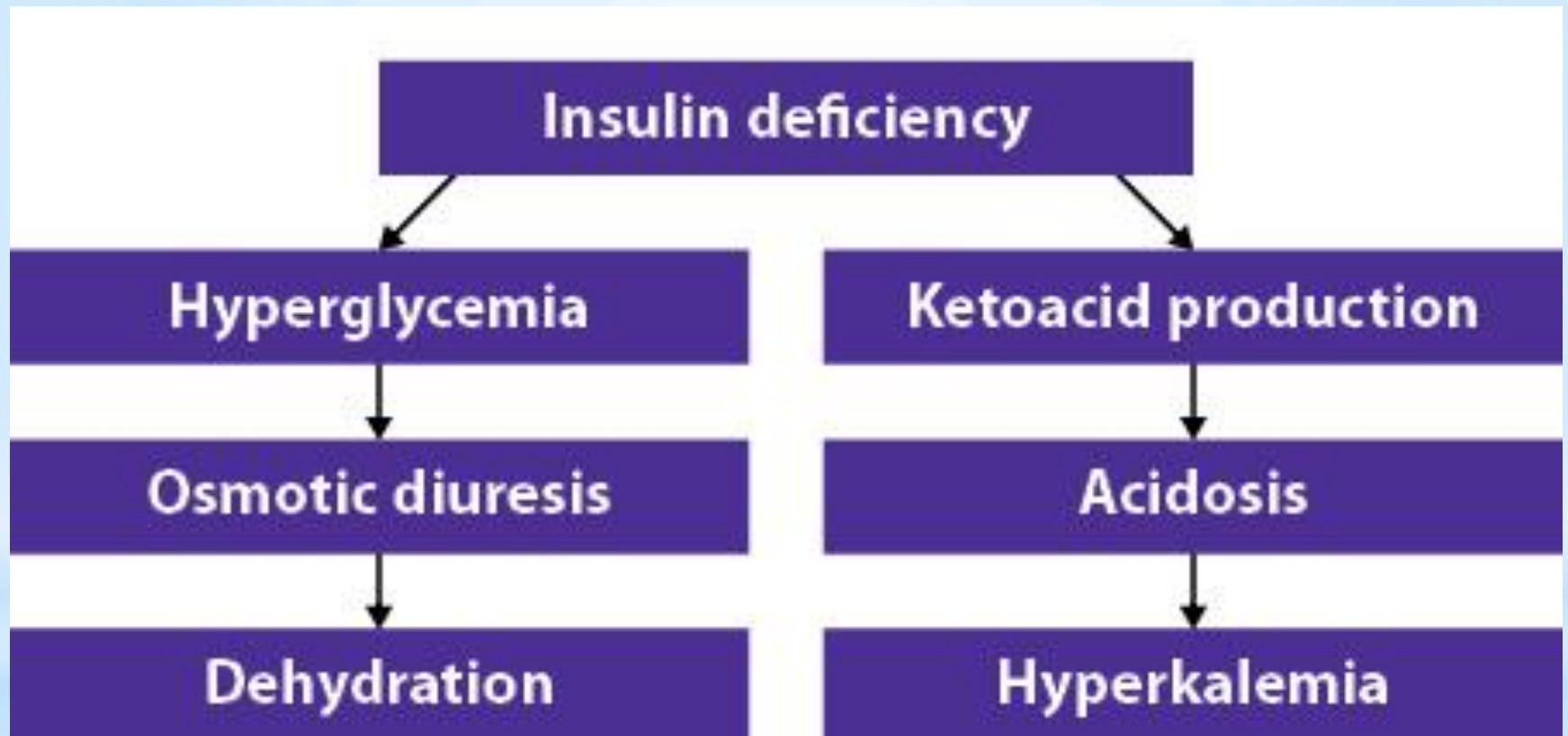
Hyperglycemic coma and Hypoglycemic coma: etiology, clinical signs, emergency care

Type of coma	Diabetic (Hyperglycemic or Hyperketonemic)	Hypoglycemic
<i>Clinical signs</i>	<ul style="list-style-type: none"> * loss of consciousness * dryness of the skin and the mucous membranes * respiration noisy and need (Kussmaul's type) * the smell of acetone in exhaled air * the tone of eyeballs is lower * frequent weak pulse * decrease of the arterial pressure * disappearance of reflexes * muscular hypotonia * pain in the abdominal, nausea, vomiting 	<ul style="list-style-type: none"> * loss of consciousness * the skin pale and moist * diplopia (double vision) * respiration normal * exhaled air doesn't have smell of the acetone * the tone of eyeballs is normal * pulse is normal * arterial pressure has normal level * convulsions presents

Hyperglycemic coma and Hypoglycemic coma: etiology, clinical signs, emergency care

Type of coma	Diabetic (Hyperglycemic or Hyperketonemic)	Hypoglycemic
<i>Changes in blood</i>	*Hyperglycemia *Hyperketonemia	*hypoglycemia
<i>Changes in urine</i>	*glucosuria *Ketonuria	
<i>Emergency care</i>	Injection of insulin 40-100 AUs	Injection of 40% solution 20-100ml glucoses

Pathogenesis of Diabetic coma



Treatment of diabetic ketoacidosis

Adequate correction of :

- **Hyperglycemia** (*insulin*)
- **Dehydration** (*fluid therapy*)
- **Electrolyte deficits** (*potassium therapy*)
- **Ketoacidosis** (*bicarbonate therapy*)

TREATMENT OF HYPOGLYCEMIC COMA

- Intravenous bolus introduction of 20-50 ml of **40 % glucose (dextrose) solution**.
- If the condition doesn't improve, after 10-20 minutes the injection should be repeated.
- In case of absence of effect intravenous dropping infusion of **5 % glucose solution** should be started.
- Correction of blood pressure and stimulation of glycogenolysis – **adrenalin** hydrochloride.
- Prophylaxis and treatment of brain edema – **mannit, glucocorticosteroids**.



Thanks for attention