

Diabetes mellitus (DM)

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General information

- First reports – ancient times
 - ‘diabetes’ – excessive urination
 - ‘mellitus’ –honey.
- 1922 – insulin discovery
- Severe complications
- The greatest number of diabetic patients are between 40 and 59 years of age
- The most common endocrine disorder

DM statistics (IDF)

- 382 millions diabetic patients worldwide (8,3%)
- 46% undiagnosed (in Sub-Saharan Africa up to 90%)
- 80% patients in low- and middle income countries
- India – 65,1 millions of patients (8.5%) -2nd position in the world
- Nigeria – 3,9 millions (5%)
- Ukraine – 1 million (3%)

Insulin effects

Carbohydrate Metabolism


- **Insulin dependent tissues** – muscles, adipose tissue, liver - can uptake glucose ONLY in the presence of insulin.
- **Insulin non-dependent tissues** - nervous tissue, kidneys, endothelium cells, cells of intestines, beta-cells of pancreas – free glucose uptake

Insulin effects

Carbohydrate Metabolism

- Increases glycogen synthesis in the liver.
- ↓ blood glucose concentration.

In the absence of insulin, insulin-dependent tissues switch to alternative sources of energy (fatty acids).



Insulin effects

Lipid metabolism

- □ **synthesis of fatty acids** in the liver.
- □ **lipolysis** in adipose tissue.
- □ **synthesis of glycerol** in adipocytes □
□ **synthesis of triglycerides** □ **fats storage**

Protein metabolism


- □ **proteins synthesis** and □ **proteolysis**

Biological effects of insulin

- **Very fast** effect – □ glucose and ions transport into the cells.
- **Fast effects** - □ glycogen, fat acids, glycerol and protein synthesis.
- **Slow effects** - □ enzymes synthesis that regulate anabolic processes; □ catabolic enzymes.
- **Very slow effects** - □ cells division.

DIABETES -

is a complex metabolic disorder
resulting from
absolute or relative
insulin deficiency



The types of diabetes mellitus

Characteristic	Type 1	Type 2
% in population	10	90
Age at onset	< 30 years	> 30 years
Associated obesity	No	Very common
Propensity to ketoacidosis	Yes	No

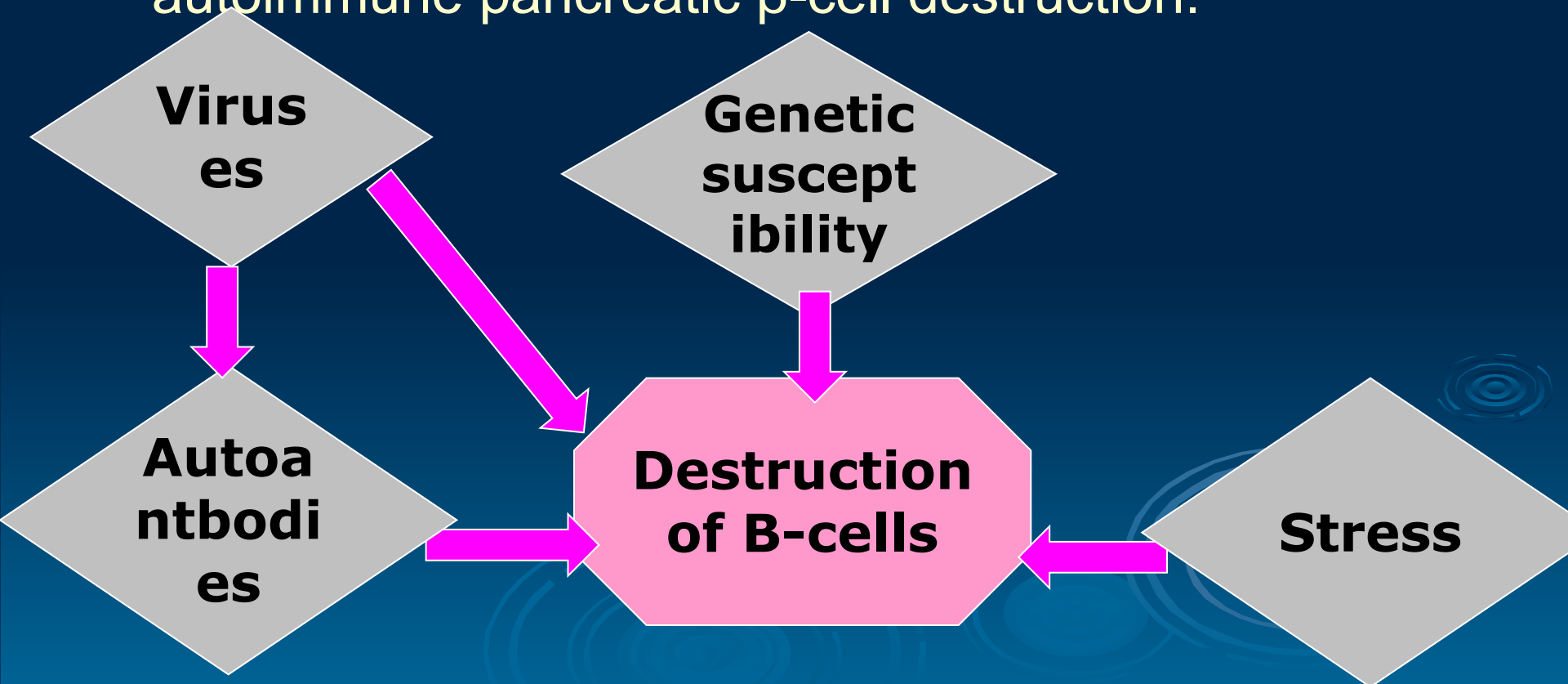
The types of diabetes mellitus

Characteristic	Type 1	Type 2
Plasma levels of endogenous insulin	Extremely low to undetectable	Variable
Islet cell antibodies	Yes	No
Islet pathology	Insulinitis, loss of most β cells	Normal-appearing
Treatment	Insulin injections	Oral antihyperglycemic drugs

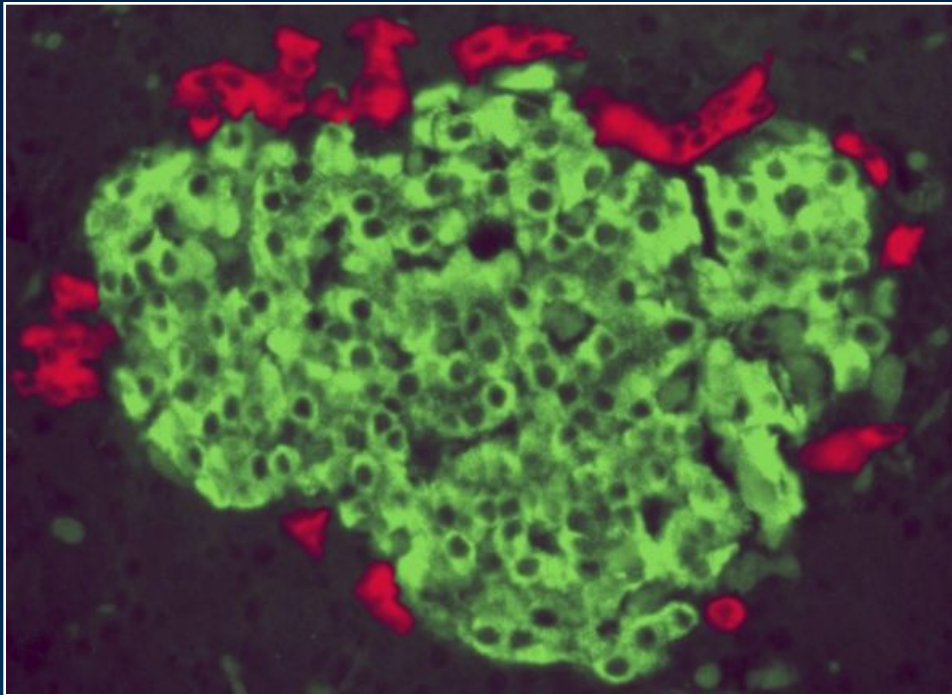
Diabetes Mellitus type 1

Type 1 DM was previously named insulin-dependent.

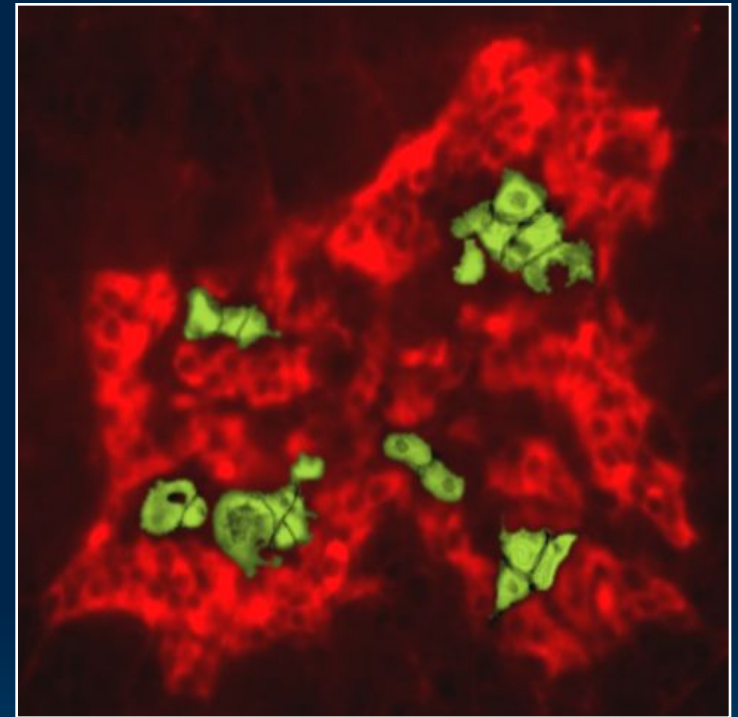
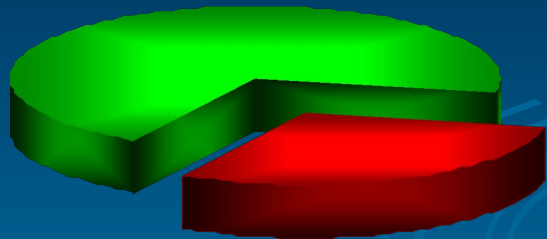
- Insulin production is **low** or **absent** because of autoimmune pancreatic β -cell destruction.



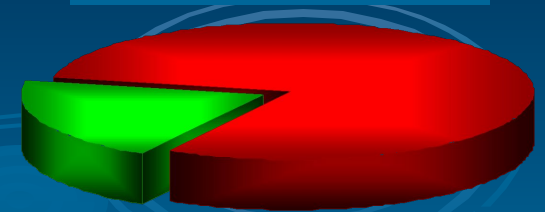
Diabetes Mellitus Type 1 Pathogenesis



NORMAL ISLET

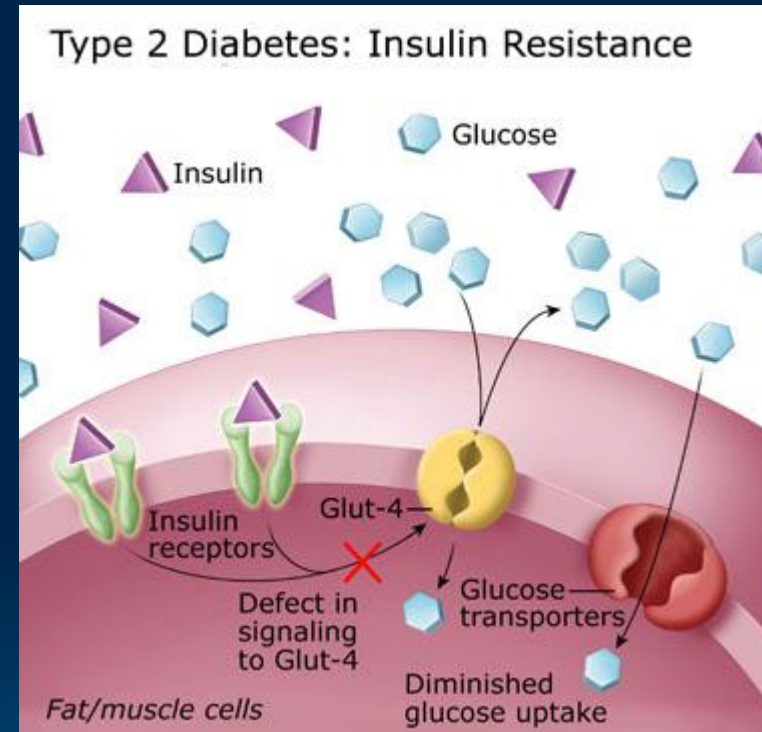


DIABETIC ISLET

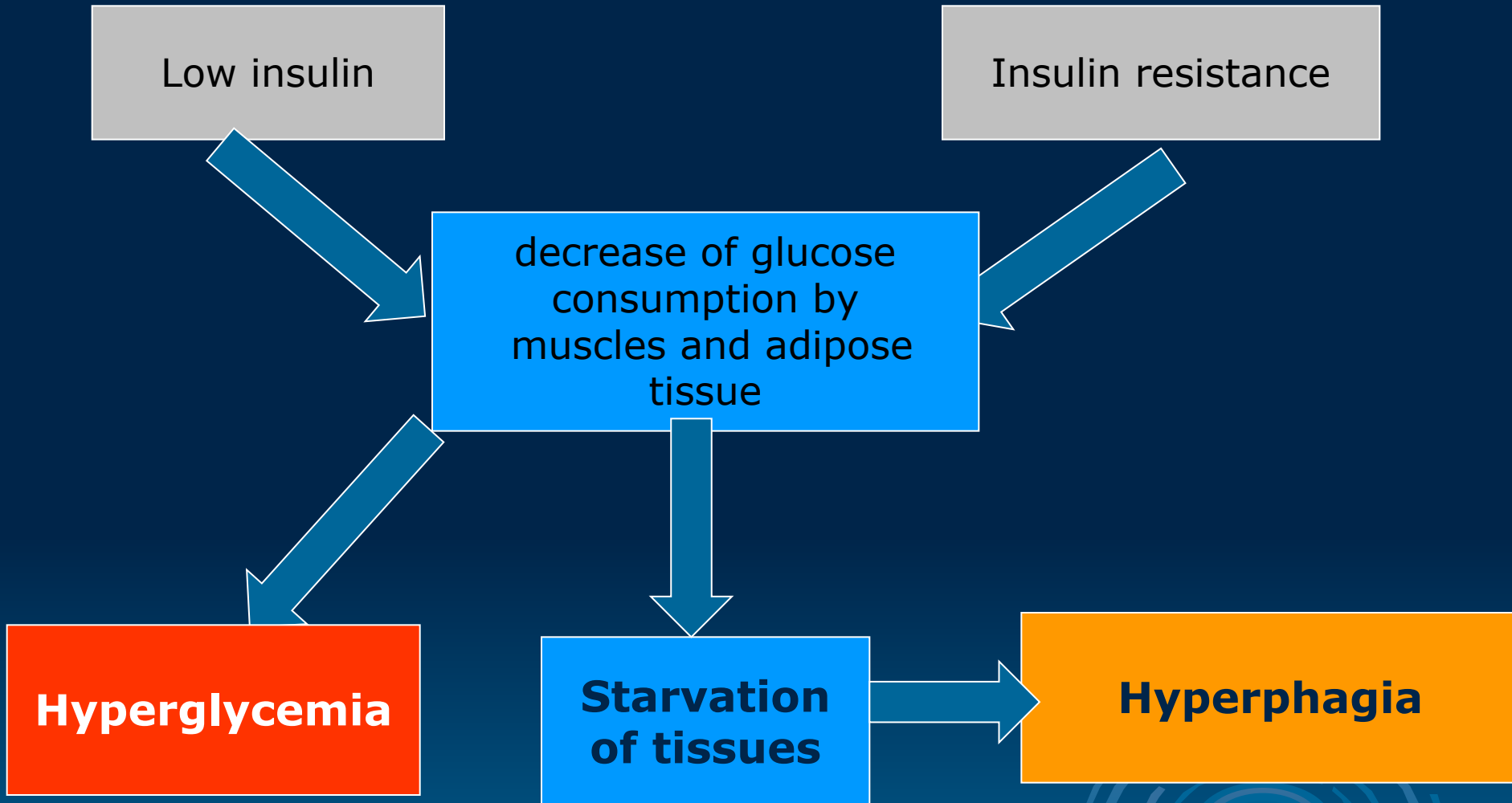


Diabetes Mellitus Type 2

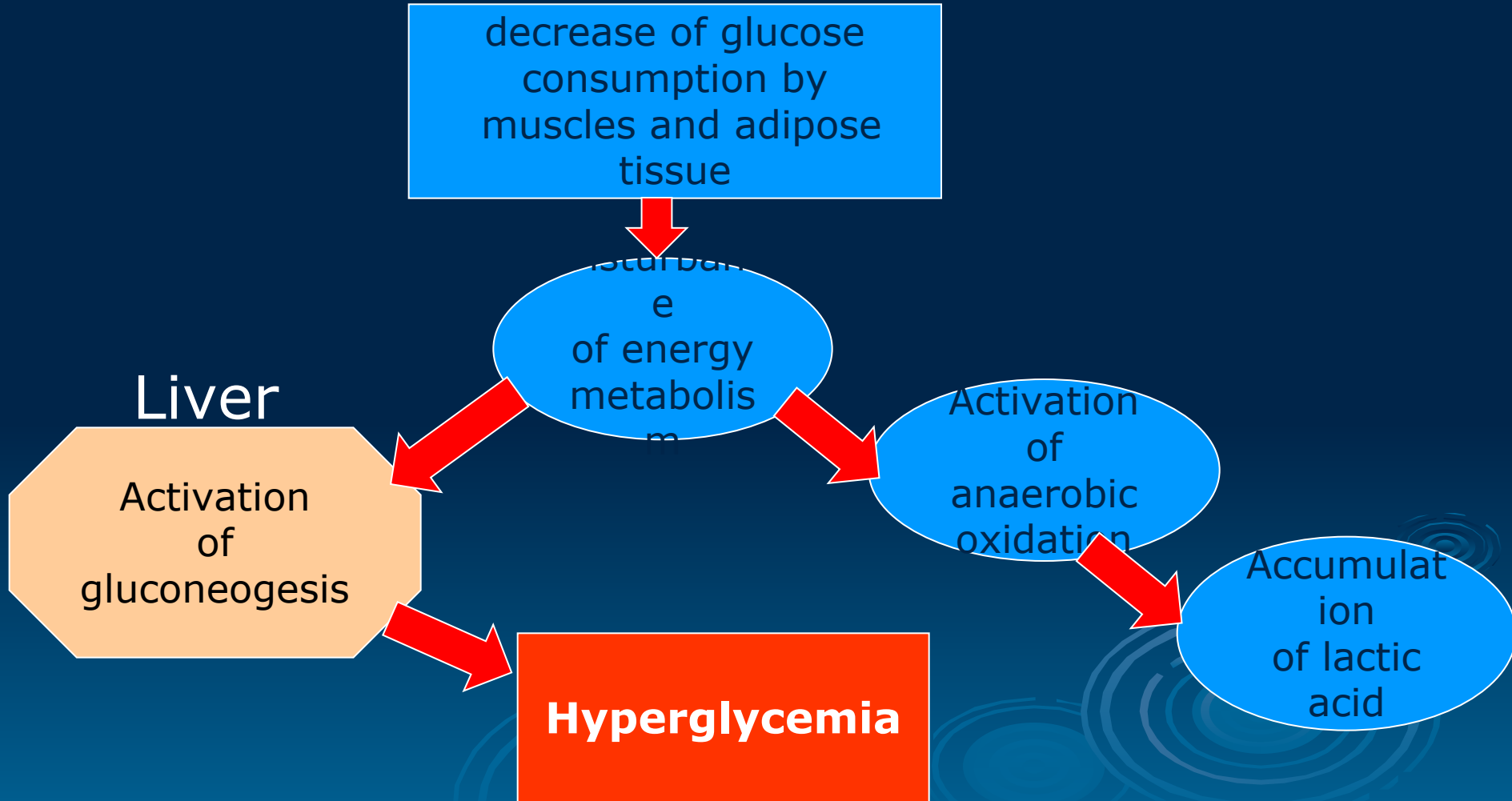
- 90% of adults with DM
- Key pathogenic factor is insulin resistance
- In early stages of disease insulin level is high
- When insulin secretion can no longer compensate for insulin resistance - hyperglycemia develops.
- Obesity and weight gain may increase insulin resistance



DM pathogenesis

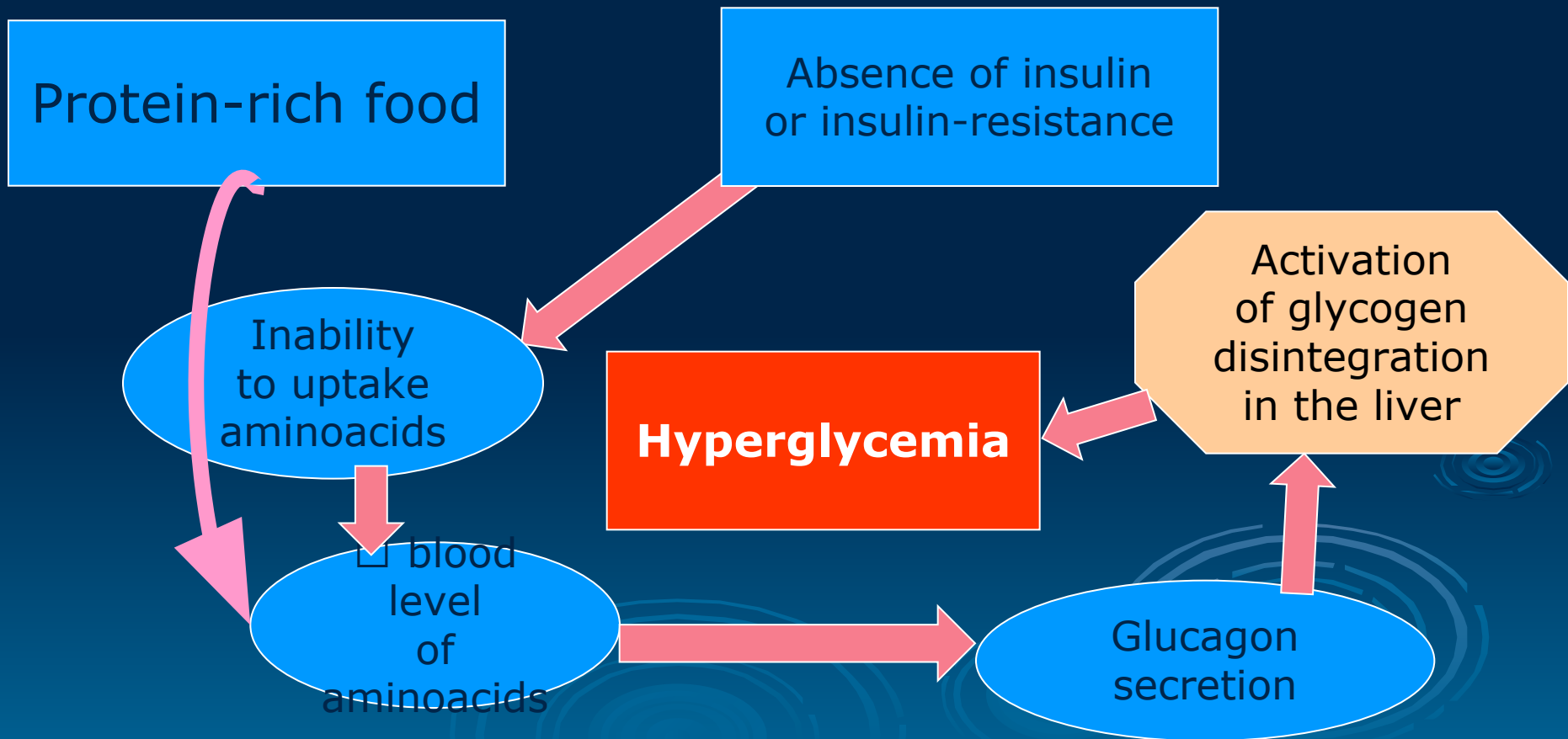


DM pathogenesis



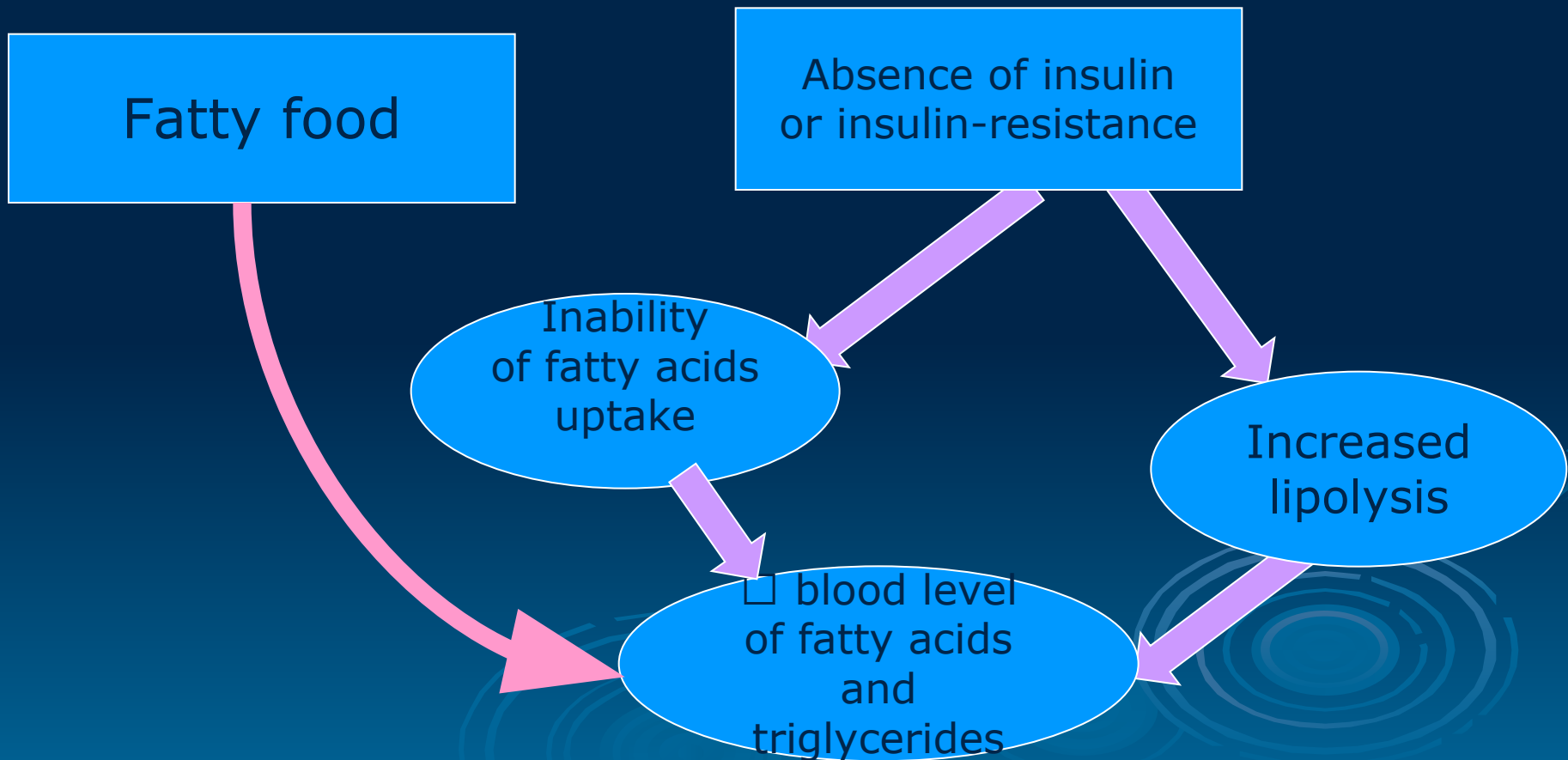
DM pathogenesis

Disturbance of protein metabolism

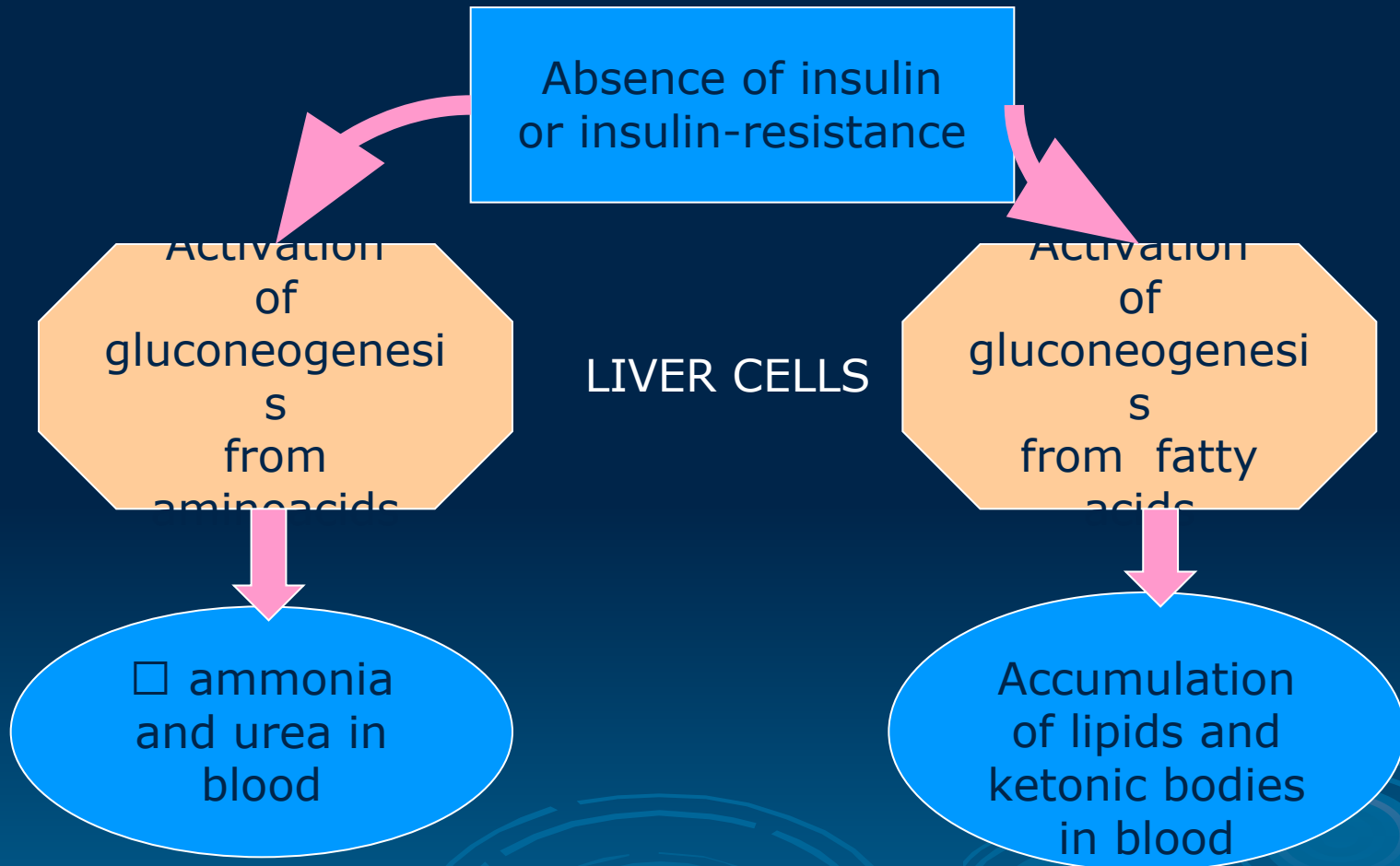


DM pathogenesis

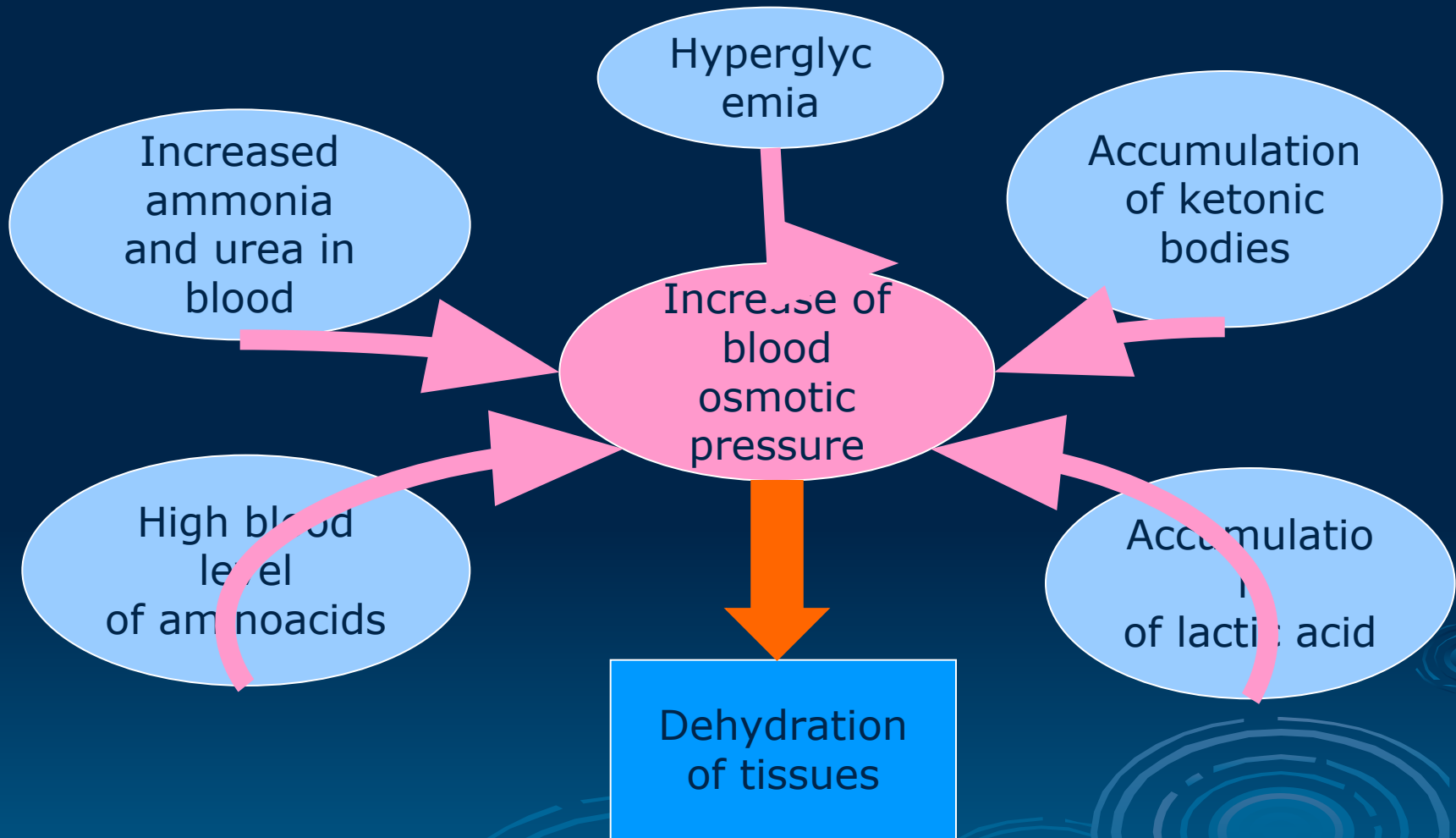
Disturbance of lipid metabolism



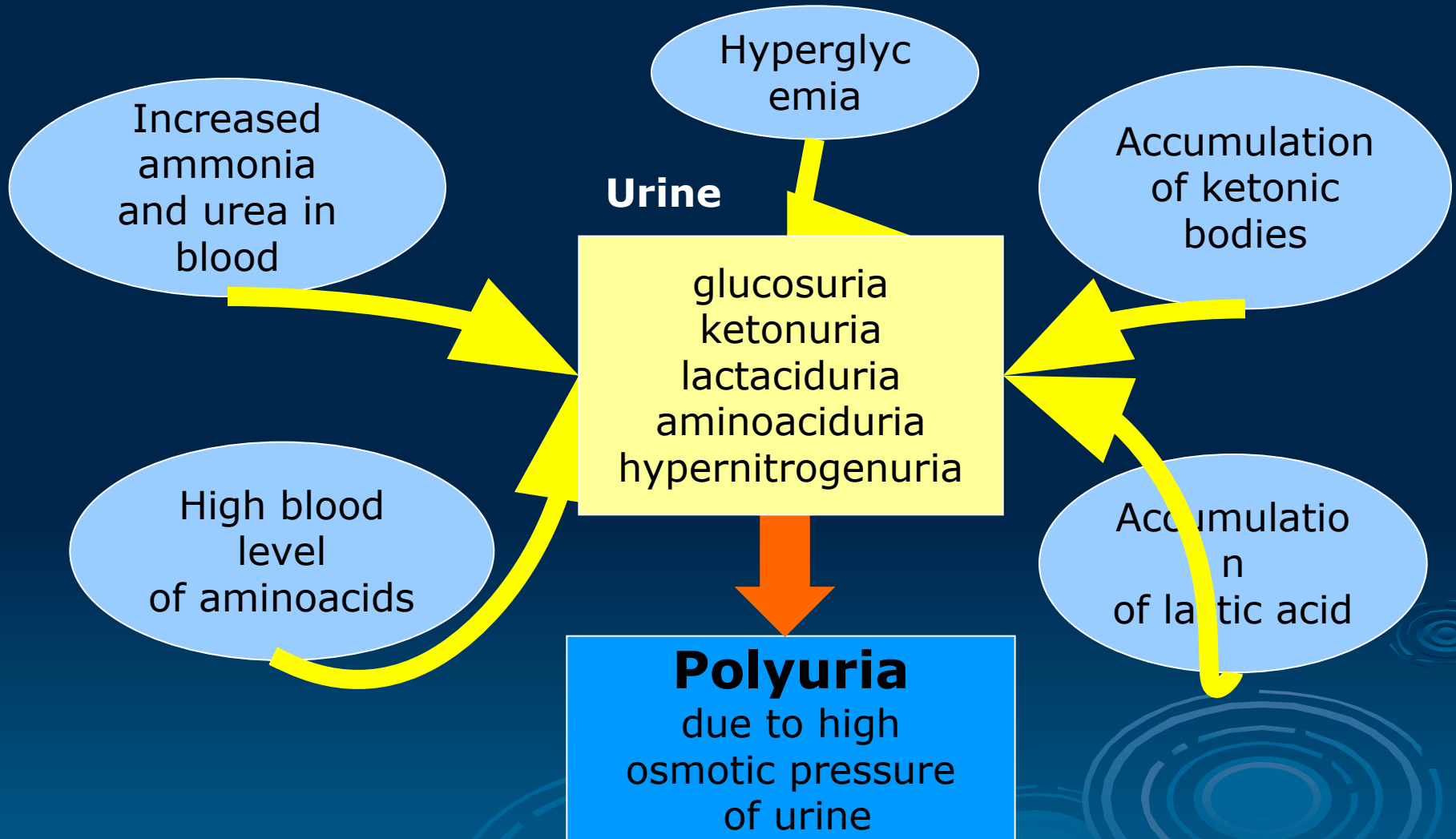
DM pathogenesis



DM pathogenesis



DM pathogenesis



Diagnosis of Diabetes Mellitus

▣ ***Fasting Blood Glucose Test.***

- $\leq 6,1$ mmol/L - normal.
- 6,1 mmol/L - 6,9 mmol/L - impaired
- $\geq 7,0$ mmol/L on two occasions = diabetes

▣ ***Casual Blood Glucose Test.***

- If $\geq 11,0$ mmol/L + classic symptoms = diabetes

▣ ***Glucose Tolerance Test*** (oral intake 75 g of concentrated glucose solution)

- Normally blood glucose levels return to normal within 2 to 3 hours after ingestion of a glucose load.

Diagnosis of Diabetes Mellitus

- ▣ ***Glycated Hemoglobin Testing (hemoglobin A1C)*** provides an index of blood glucose levels over the previous 6 to 12 weeks
 - Hemoglobin normally doesn't contain glucose
 - If blood glucose level is high the level of A1C is ▣
 - Glycosylation is essentially irreversible

Urine Tests

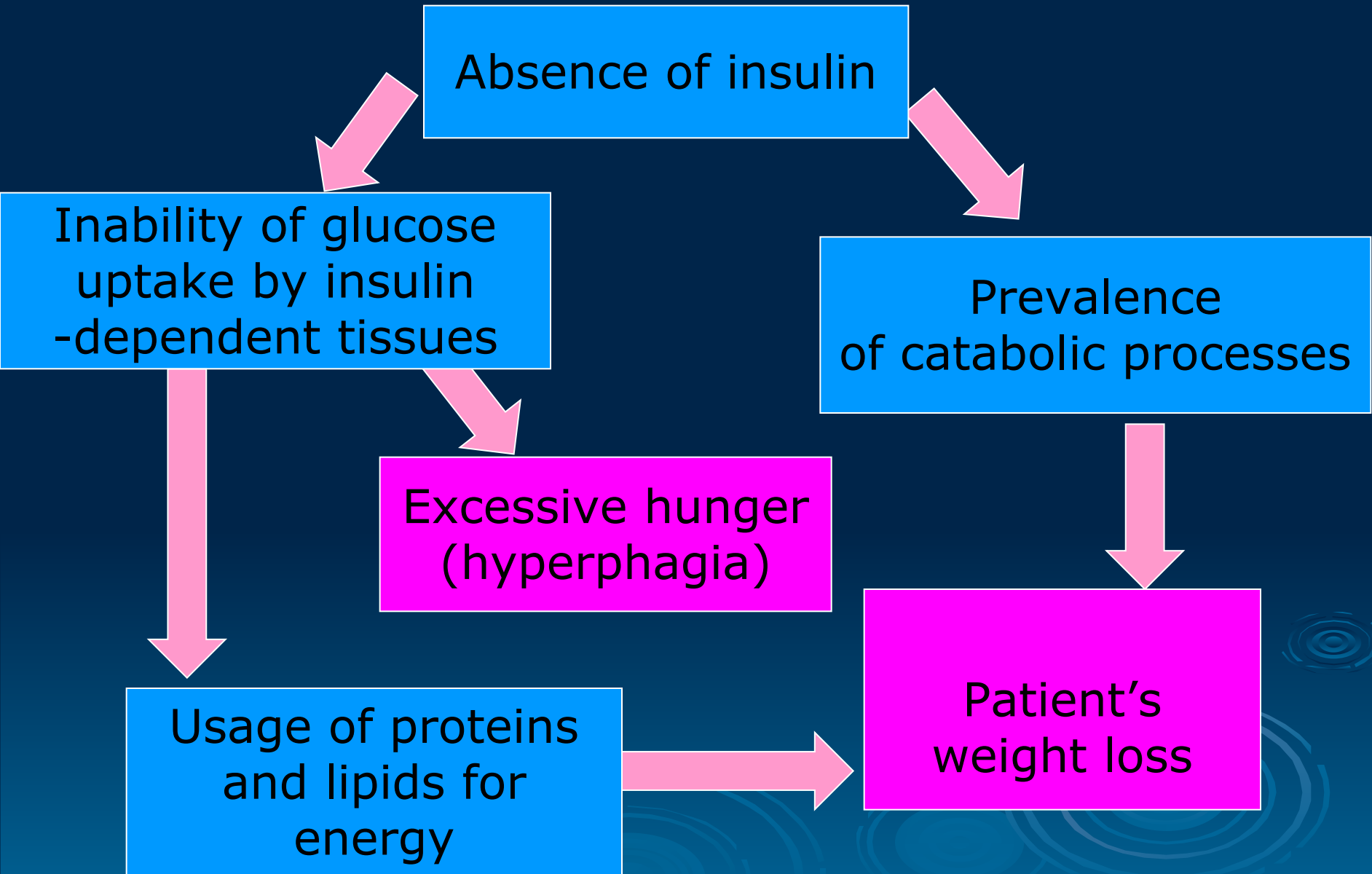
- ▣ Presence of glucose
- ▣ Presence of ketone bodies

Clinical signs of DM

hyperglycemia **hyperketonemia**
glucosuria **ketonuria**
polyuria **hyperlipidemia**
polydipsia (thirst) **hyperazotemia**
hyperphagia (hunger) **hyperazoturia**
hyperlactacidemia



Clinical signs of DM



□ Choose the characteristic feature of type 1 diabetes mellitus

- Middle age at onset
- Associated obesity
- Low plasma levels of endogenous insulin
- Insulin resistance

→ Presence of antibodies to islet cells



□ A patient with constant thirst and increased urination was done oral glucose tolerance test that proved diabetes mellitus diagnosis. Which sign of diabetes is typical only to type 1 diabetes mellitus?

- hyperglycemia
- hypoglycemia
- relative insulin deficiency
- obesity

→ absolute insulin deficiency

□ One of the diabetes mellitus clinical symptoms is hyperphagia. It is developed due to...

→ Lack of energy in the organism

- lack of fatty acids in the blood
- lack of insulin
- excess of glucose in the blood
- affection of appetite controlling centers

□ Patient with diabetes mellitus has hyperglycemia 19 mmol/ l, which is clinically developed as glucosuria, polyuria, polydipsia. What mechanism is responsible for polydipsia development?

- low osmotic pressure of blood plasma
- lack of insulin

→ tissues dehydration

- glucosuria
- hyperglycemia

Acute complications of DM


Diabetic comas

- hyperglycemic
- hypoglycemic
- hyperosmolar
- hyperlactatacidemic



Acute complications of DM

Hyperglycemic coma

- expressed **hyperglycemia** (>20 mmol/l);
 - progressive **dehydration** of the organism;
 - **ketoacidosis** (metabolic acidosis) with a typical acetone smell from the breath;
 - increased blood level of catecholamines and glucocorticoids;
 - **inhibition of CNS activity**;
 - **Kussmaul's** respiration;
 - decreased arterial pressure;
 - tachycardia accompanied by extrasystolia.
- 

Acute complications of DM

Hypoglycemic coma may develop if the glucose intake does not match the insulin treatment .

- The patient become agitated, sweaty, activation of sympathetic nervous system
- Consciousness can be altered.
- Treatment: sweet drinks /food; in severe cases, an injection of glucagon or an intravenous infusion of glucoset.

Acute complications of DM

Hyperosmolar coma high concentration of glucose, Na, Cl, bicarbonates, urea, ammonia in blood; the level of ketonic bodies is usually normal.

- the disturbance of consciousness;
- the absence of acetone smell from the mouth;
- frequent superficial breath, short breath;
- tachycardia and heart rate disturbances.

Hyperlactatacidemic coma - rare complication of DM

- is observed in elderly people suffering severe accompanying diseases.

Chronic complications of DM

Microvascular disturbances

- **Diabetic retinopathy** - severe vision loss or blindness.
- **Diabetic neuropathy** – usually in stocking distribution starting at the feet but potentially in other nerves.
 - When combined with damaged blood vessels this can lead to diabetic foot .
- **Diabetic nephropathy** - renal failure.

Chronic complications of DM

Macrovascular disease

- **Coronary artery disease**, leading to myocardial infarction ("heart attack") or angina;
- **Stroke** (mainly ischemic type)
- **Peripheral vascular disease**, which contributes to diabetic foot;
 - Diabetic foot may cause necrosis, infection and gangrene.

Chronic complications of DM

Diabetic cardiomyopathy results from many factors (atherosclerosis, hypertension, microvascular disease, endothelial and autonomic dysfunction, metabolic disturbances).

Infection: Diabetics are prone to bacterial and fungal infections (hyperglycemia impairs phagocyte and T-cell function).

Principles of treatment

Control of hyperglycemia.

- Type 1 diabetics require insulin.
- Type 2 diabetics should be prescribed a trial of diet and exercise followed by a oral antihyperglycemic drugs.

Prevention of DM

- Early type 1 DM in some patients may be prevented by suppression of autoimmune β -cell destruction.
- Type 2 DM usually can be prevented with lifestyle modification.

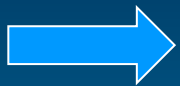
Patients with impaired glucose regulation should be monitored closely for development of DM symptoms or elevated plasma glucose.

□ Which coma often occurs in the patients with diabetes mellitus type 1 when diet is not balanced with insulin injections?

- hyperglycemic
- hyperlactatacidemic
- hyperosmolar
- ketonemic
- hypoglycemic



- Patient R., 46 years old, has diabetic neuropathy. What is the main mechanism in nervous fibers damage under diabetes?
- glucose toxic action
 - ketones toxic action
 - nervous fibers dehydration
 - metabolic acidosis development
 - glucose accumulation in nervous tissue



□ A patient was delivered to the hospital by an emergency. Patient is unconscious, the skin dry, face is cyanotic. Heart rate is 132 bpm. There is acetone smell from the mouth. Blood glucose level – 20.1 mmol/L, urine glucose – 3,5 g/L. What is the probable diagnosis?

- hypoglycemic coma
- acute infectious intoxication
- anaphylactic shock
- acute heart failure

 hyperglycemic coma