Session 7 , Lecture 1

Duration : 1 hr.

Metabolism

Diabetes Mellitus

Module staff

Dr. Amani Naama.
Dr. Zainab Almnaseer
Dr. Hamid Jaddoa
Dr. Zainab Muzahim
Dr. Maida Abdulaa Adnan
Dr. Ahmed Jaffar Hendi
Dr. Dhaighum Al-Mahfoodh
Dr. Ammar Mohammed Saeed
Dr. Sara Mohammed
Ass. Lecturer Eatidal Akram

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2. Lehninger Principles of Biochemistry Sixth Edition (6th Edition)
3. Marks Essentials of Medical Biochemistry.

Learning outcomes(LO)

- Describe Diabetes Mellitus (DM). **LO 1**
- The main differences between Type 1 diabetes (T 1 D) and Type 2 diabetes (T 2 D) **LO 2**
- The typical pattern of presentation of T 1 D and T 2 D. **LO 3**
- The sequence of events leading to ketoacidosis. **LO 4**
- The causes and consequences of hypoglycemia. **LO 5**
- The consequences hyperglycemia ,the common long-term side effects of DM. **LO 6**
- The principles of management of DM. **LO 7**
- The principle and practice of measuring glycosylation of hemoglobin as an index of blood glucose control in the diabetic. **LO 8**

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2. Lehninger Principles of Biochemistry Sixth Edition (6th Edition)
3. Marks Essentials of Medical Biochemistry.

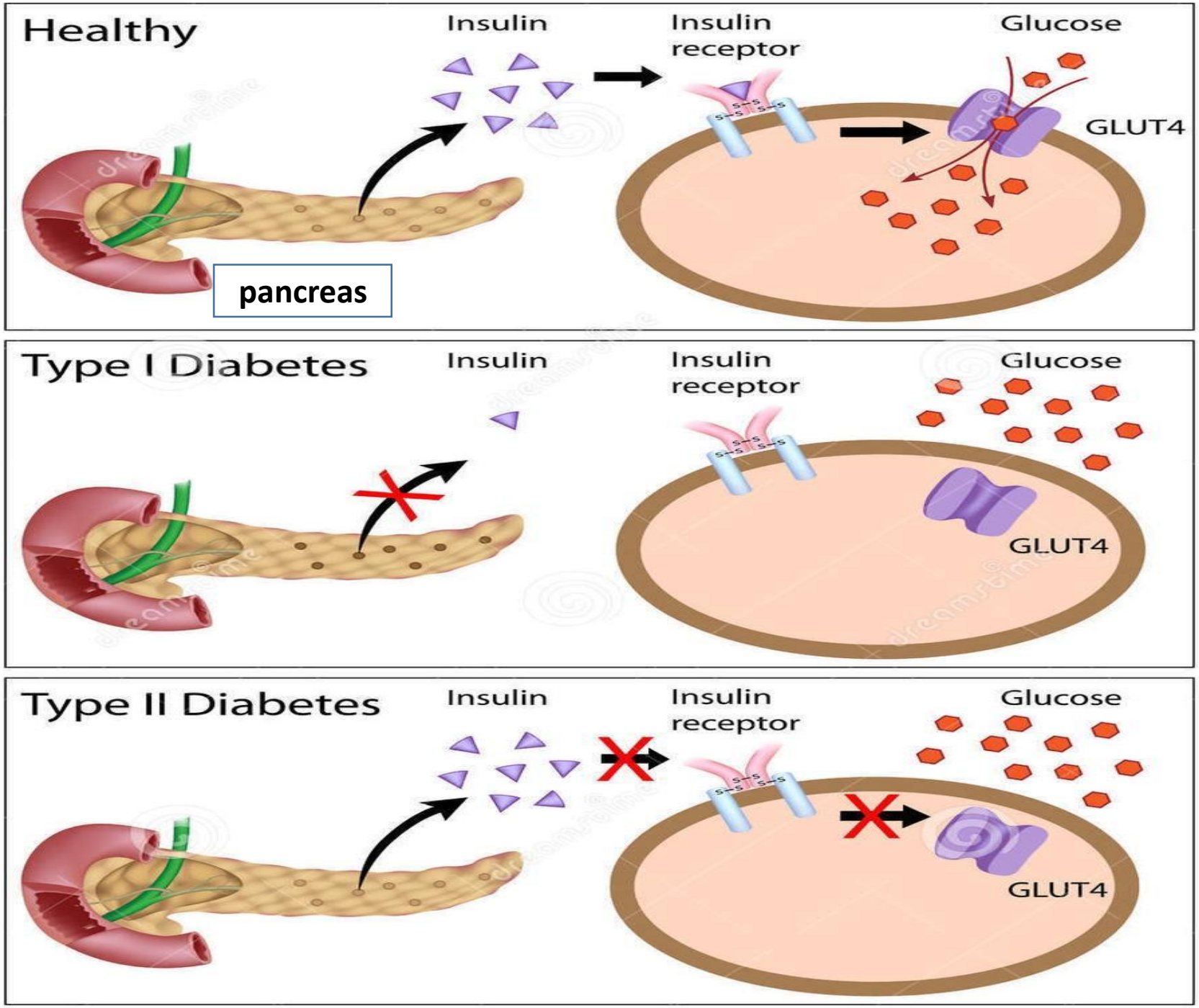
LO1

Diabetes Mellitus (DM) definition

A group of metabolic disorders characterized by chronic hyperglycemia (high blood glucose) due to insulin deficiency, insulin resistance, or both.

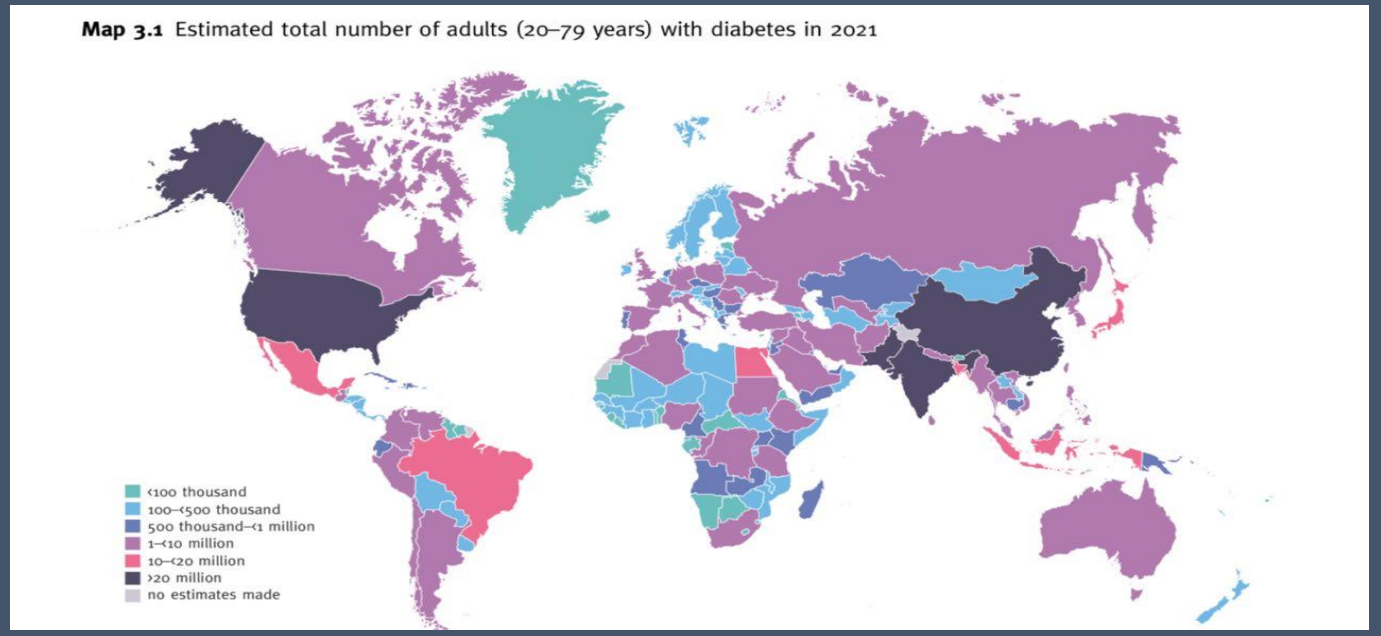
- Insulin resistance is defined as “a decreased biological response to normal concentrations of circulating insulin”

LO1


Healthy
Insulin
Insulin receptor
Glucose
GLUT4
pancreas
Type I Diabetes
Insulin
Insulin receptor
Glucose
GLUT4
Type II Diabetes
Insulin
Insulin receptor
Glucose
GLUT4

Diabetes by Numbers

- 537 million adults (20– 79years) are diabetics . This represents 10.5% of the world's population in this age group
- The number is predicted to rise to 643 million (11.3%) by 2030
- Over 1.2 million children and adolescents have type1 Diabetes.

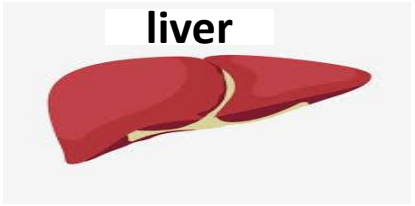


IDF Diabetes Atlas 2021 – 10th edition

Metabolic changes in DM

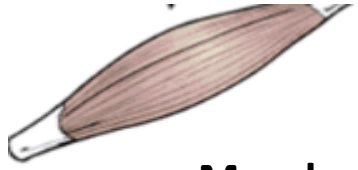
LO1

Insulin deficiency and /or resistance



Increase hepatic glucose output: gluconeogenesis ,glycogenolysis

Decrease glucose uptake



Muscle

Decrease glucose uptake

hyperglycemia

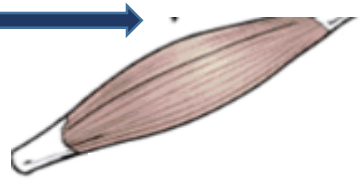
Metabolic changes in DM

LO1

Insulin deficiency

Adipose tissue

lipolysis



Muscle

protein degradation

liver

Increase gluconeogenesis

Increase Ketogenesis

Classification of Diabetes Mellitus

LO1

- Type 1 diabetes (T1DM)
- Type 2 diabetes (T2DM) (about 90% of diabetic)
- Gestational diabetes mellitus (GDM)
- Other specific types (secondary) :-

1. Genetic defects in insulin action , β-cell function
2. Endocrinopathies : Cushing syndrome
3. Drug : steroid
4. Infections : cytomegalo virus

LO2

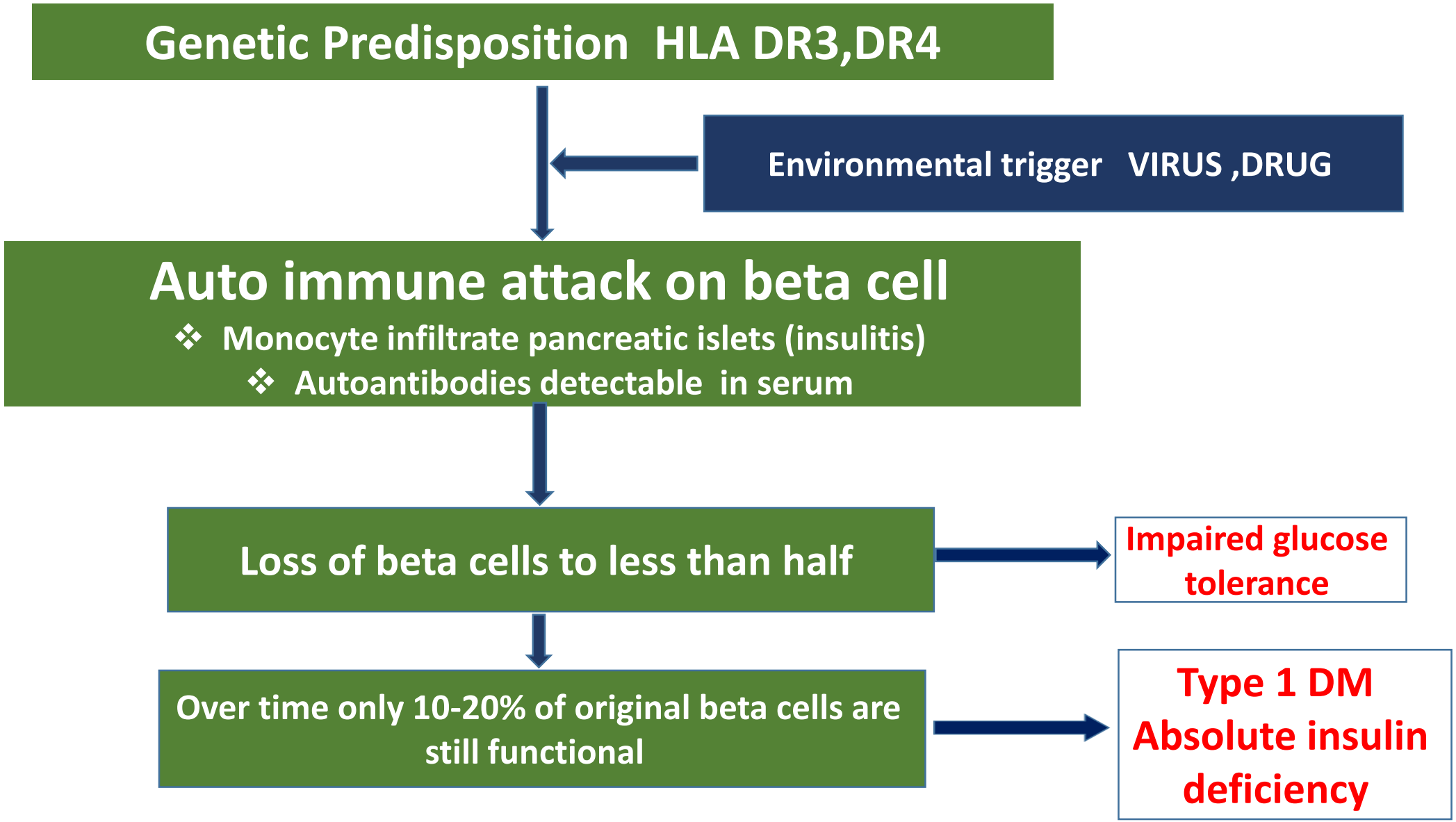
T1DM		T2DM
Auto- immune destruction of insulin producing cell of pancreas causing insulin deficiency		Insulin resistance with progressive B-cell dysfunction
Most frequent among children and adolescent		Most frequent in adult
Autoantibodies		No Autoantibodies

LO2

T1DM	T2DM
Insulin therapy required immediately	Life style ,oral drug ,may require insulin eventually
Rapid onset and rapidly fatal if not treated	Gradual onset (many years), no rapid fatality
Ketoacidosis common	Ketoacidosis very rare

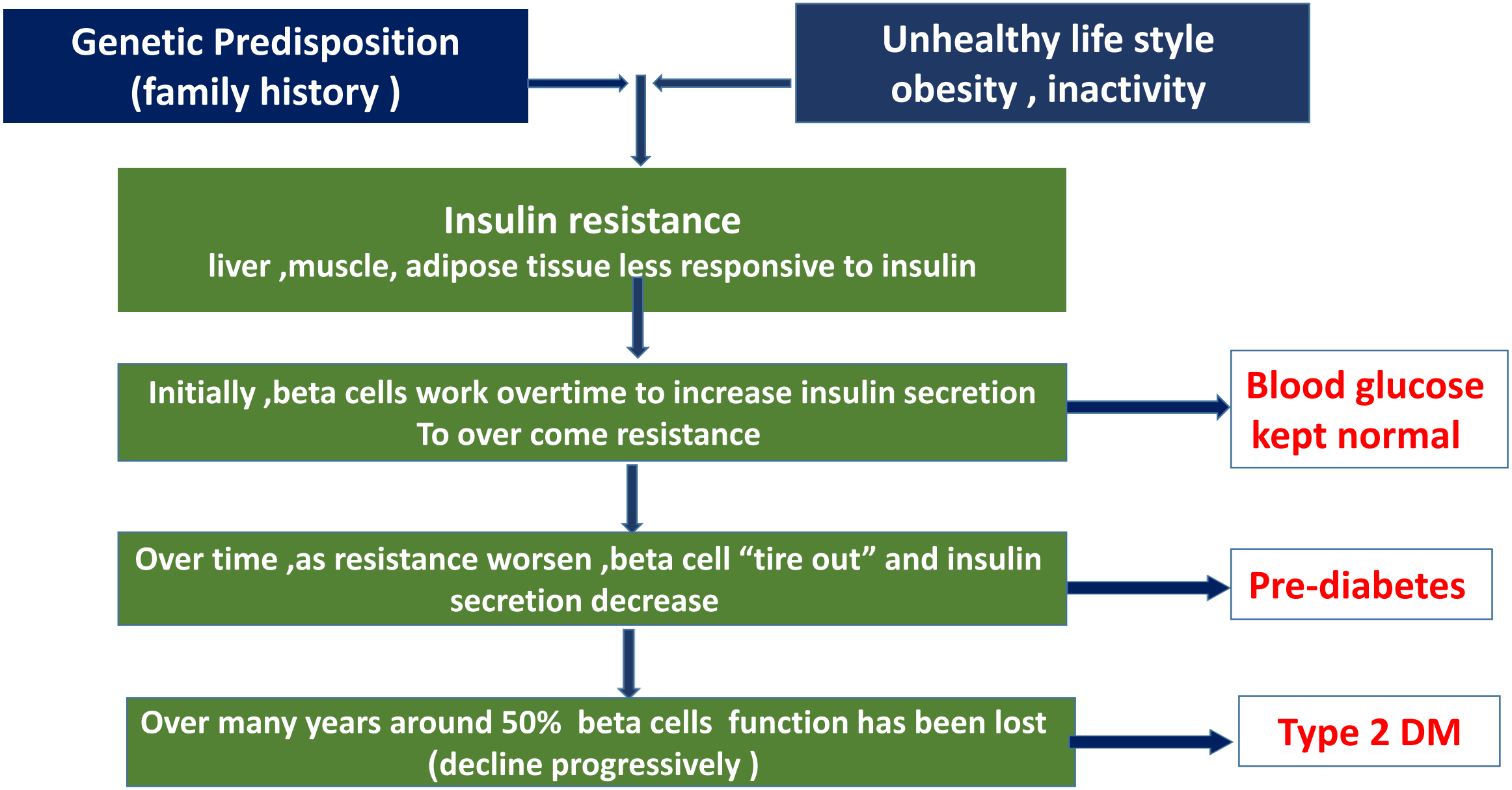
Pathophysiology of T1DM

LO2



Pathophysiology of T2DM

LO2

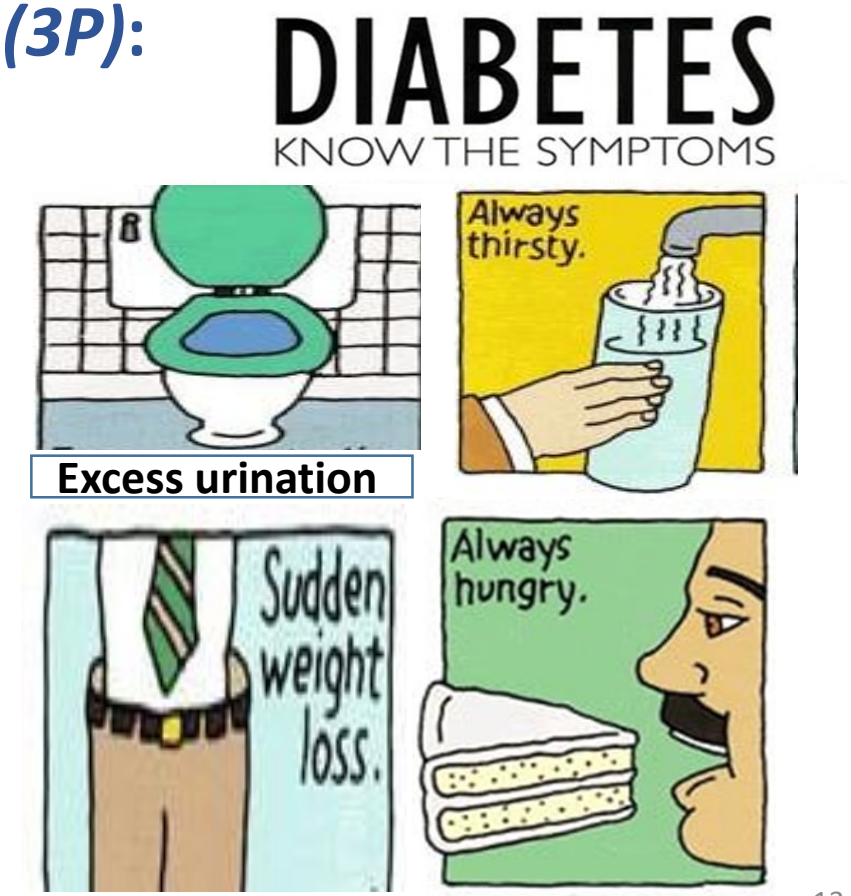


LO3

Typical pattern of presentation of T1DM

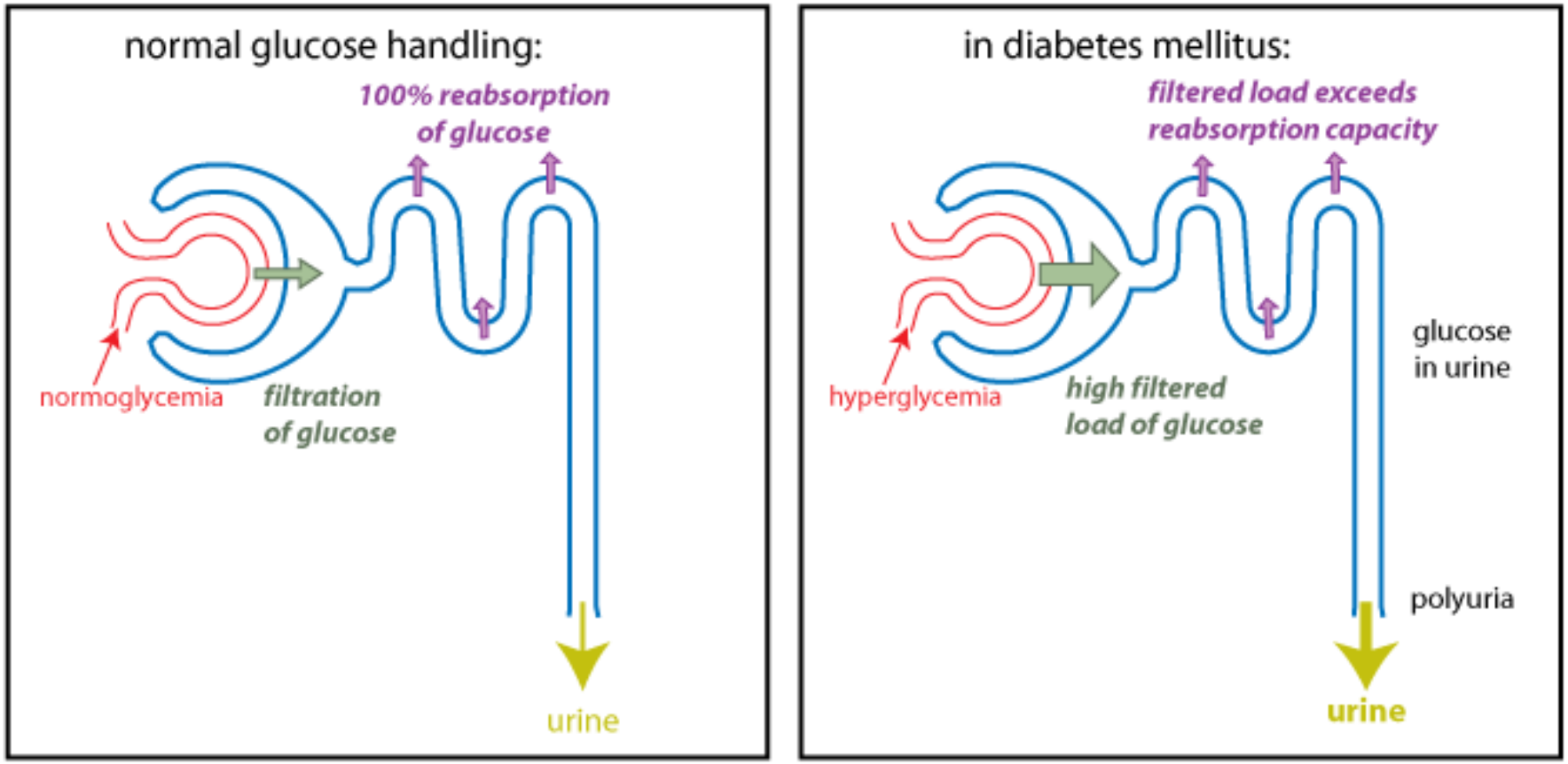
Young + lean + recent viral infection + *TRIAD (3P)*:

Polyuria (excess urine volume)
Polydipsia (thirst)
Polyphagia (excessive hunger)
weight loss



LO3

Polyuria.



LO3

Polydipsia : caused by excessive water loss and the osmotic effects of glucose on the thirst center.

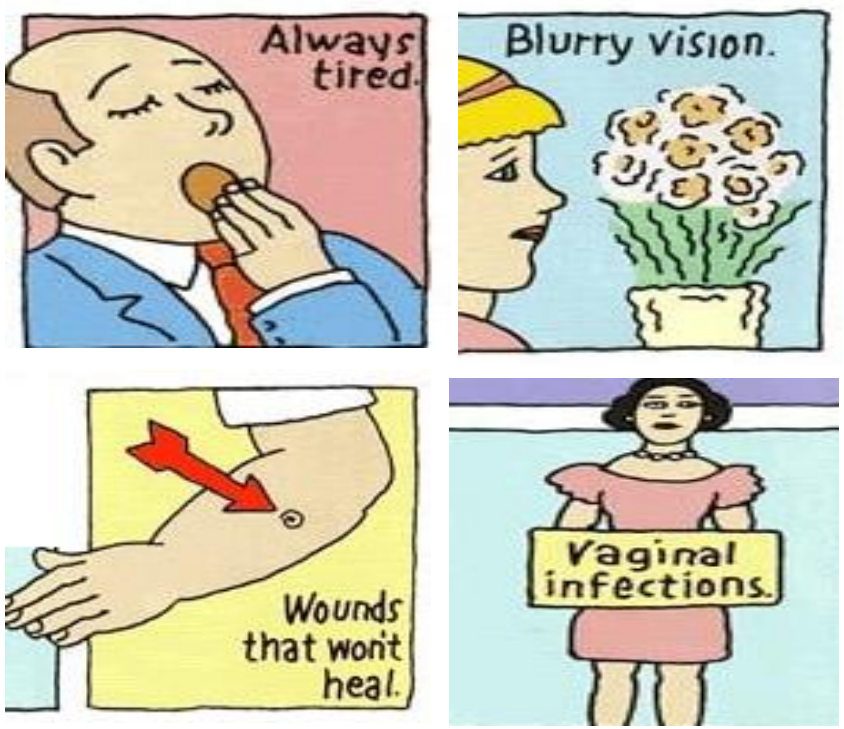
Polyphagia : excessive hunger and food consumption ,that is although high amount of glucose is available ,it cannot be utilized and the cells are starving

Weight loss : as adipose tissue fats and muscle proteins are catabolized.

LO3

Typical pattern of presentation of T2DM

- Lack of energy.
- Persistent infection (genital thrush).
- Feet infection.
- Slow wound healing.
- Visual problems.



LO3

Criteria for the Diagnosis of Diabetes Mellitus

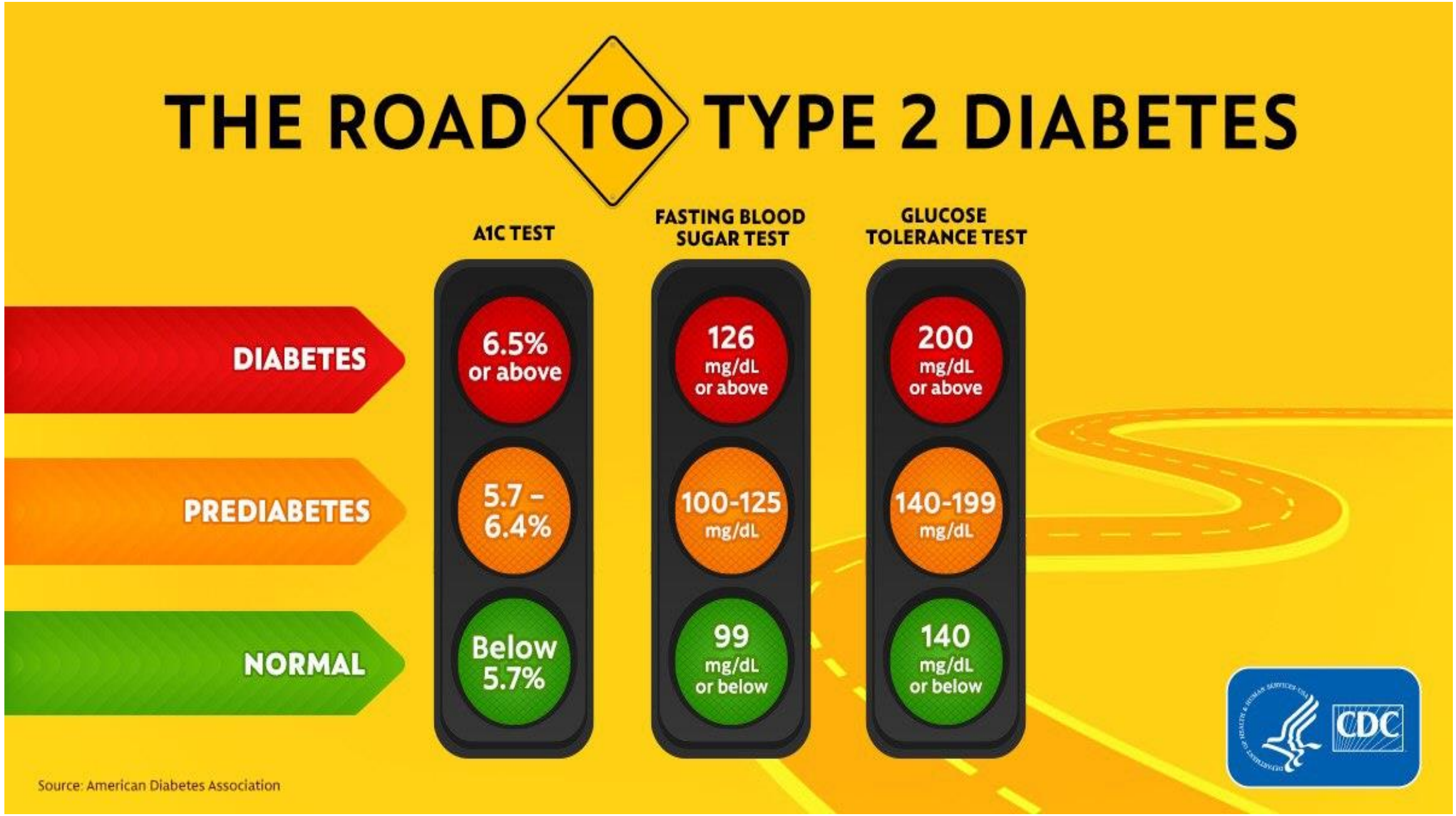
Symptoms plus one of the following:

- Fasting blood glucose (FBG) ≥ 126 mg/dl (7.0 mmol/L.)
- Random blood glucose (RBG) ≥ 200 mg/dl (11.1 mmol/L).
- 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test (OGTT)
- Hemoglobin A1c (HbA1c) ≥ 6.5%

If no symptoms → repeat the test.

Diagnosis of Diabetes Mellitus

- ✓ Fasting is defined as no calorie intake for at least 8 hours.
- ✓ Random is defined as any time of day without regard to time since the last meal.
- ✓ The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss.


THE ROAD TO TYPE 2 DIABETES
A1C TEST
FASTING BLOOD SUGAR TEST
GLUCOSE TOLERANCE TEST
DIABETES
PREDIABETES
NORMAL
6.5% or above
5.7 – 6.4%
Below 5.7%
126 mg/dL or above
100-125 mg/dL
99 mg/dL or below
200 mg/dL or above
140-199 mg/dL
140 mg/dL or below
CDC
Source: American Diabetes Association

LO4

Complications of Diabetes

Acute

- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmolar non ketotic coma

Chronic

Microvascular:

Retinopathy
Nephropathy
Neuropathy
Diabetic foot

Macrovascular

Myocardial infarction
Stroke
Peripheral vascular disease

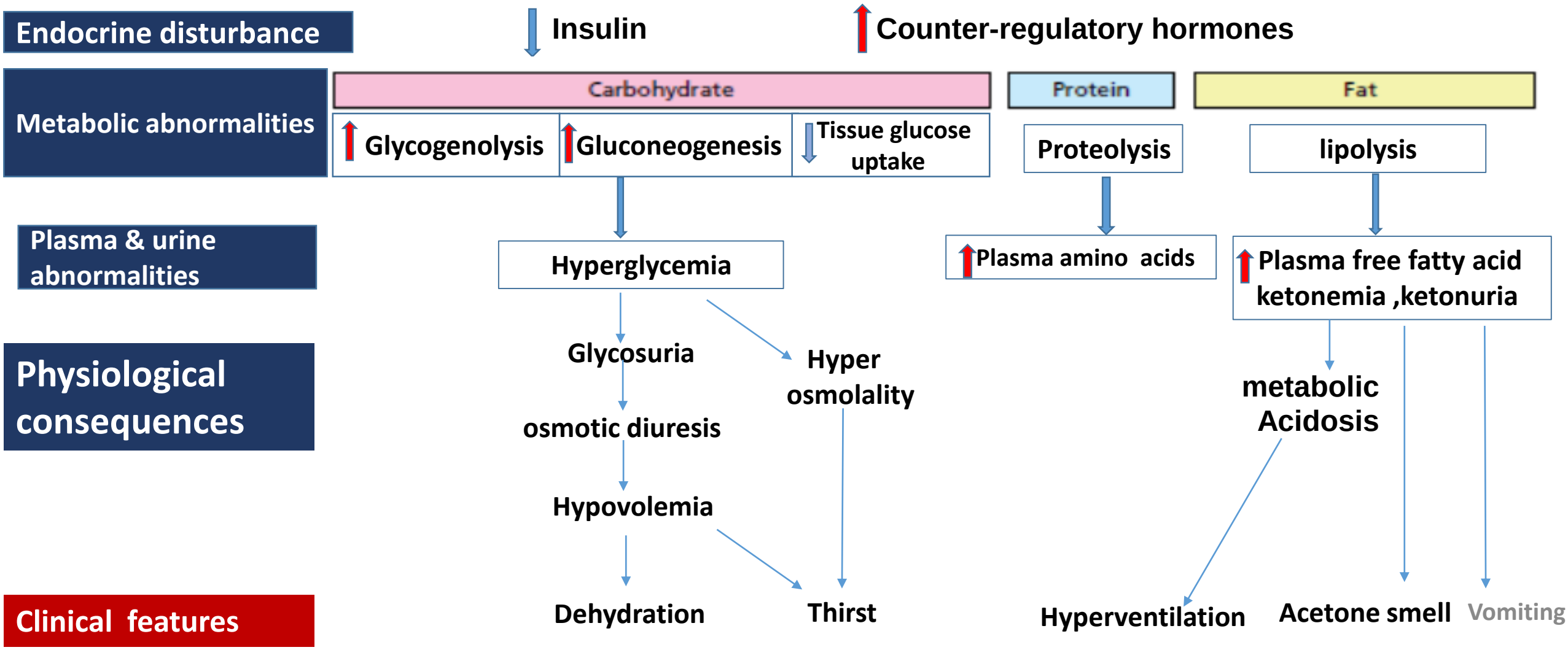
LO4

Diabetic ketoacidosis (DKA)

- DKA is a medical emergency and a serious cause of morbidity, principally in people with type 1
- DKA may be the **presenting feature** in previously undiagnosed patient .
- Precipitated by **omitting** insulin doses, or the insulin dose becoming **inadequate** because of an increase in hormones with opposing action, due to intercurrent infection, trauma, or stress.

Metabolic and clinical abnormalities in DKA

LO4



❖DKA is less common in type 2 compared to type 1 diabetics

Explain why ?

Hypoglycemia

LO5

- This is probably the most common cause of coma seen in diabetic patients.

Precipitating causes :

1. High a dose of insulin or hypoglycemic drug (most common)
2. The patient may have missed a meal or taken excessive exercise after the usual dose of insulin or oral hypoglycemic drugs.

Symptoms :

- Sweating, tachycardia and agitation **(adrenaline secretion is stimulated)**
- **Decrease cerebral glucose supply** result in dizziness, lethargy, may progress rapidly to coma and, if untreated, permanent cerebral damage or death may occur.

LO6

Major Complications of Diabetes

Microvascular

Eye

Kidney

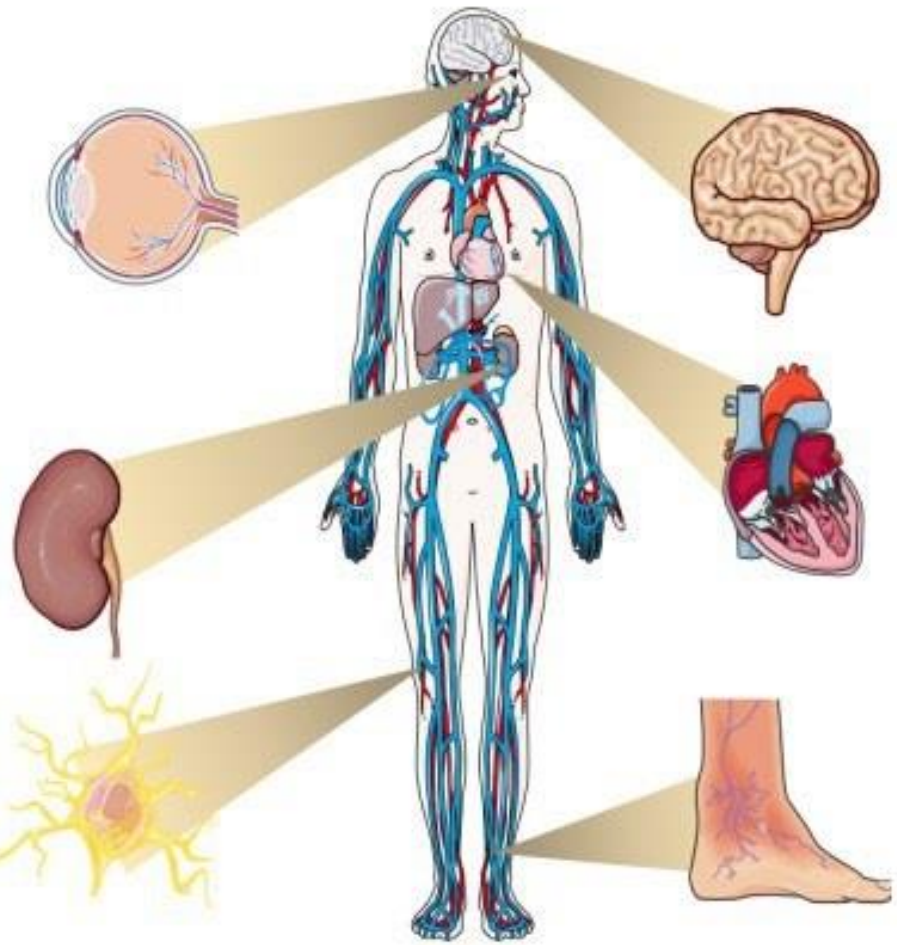
Neuropathy

Macrovascular

Brain

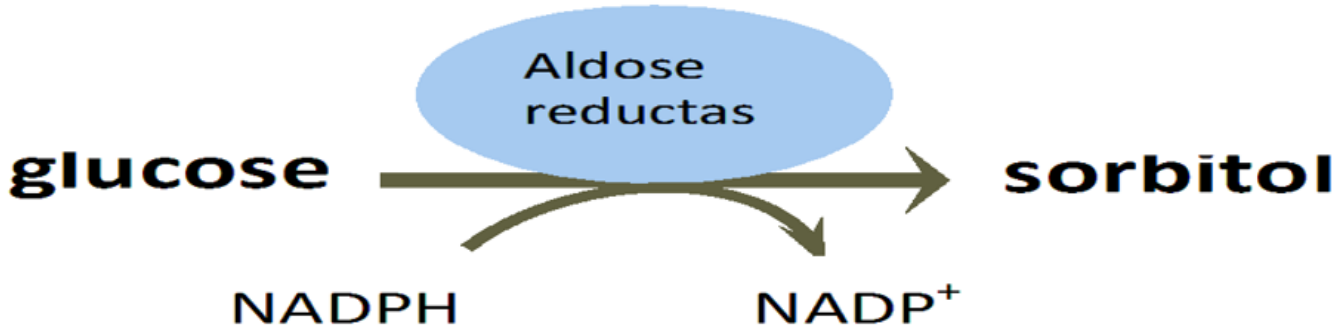
Heart

Extremities



Pathophysiology of microvascular complications :

1. The uptake of glucose into cells of tissues such as **peripheral nerves, the eye and the kidney** **does not require insulin** Thus, during hyperglycemia the intracellular concentration of glucose in these tissues increases and glucose is metabolized via the **enzyme aldose reductase** :



➢ This reaction result in :

- Depletion of cellular NADPH leading to increased disulphide bond formation in cellular proteins, altering their structure and function.
- Accumulation of sorbitol causing osmotic damage to cells.

2. Persistent hyperglycemia also increases the glycation of proteins affecting their function.

❖ **Pathophysiology of macrovascular complications :**

Diabetes is associated with enhanced **atherosclerosis ,** involving cardiac, cerebral, and peripheral large vessels.

Management

LO7

Exercise

Lifestyle

Diet modification

Pharmacotherapy

Oral antidiabetic

insulin

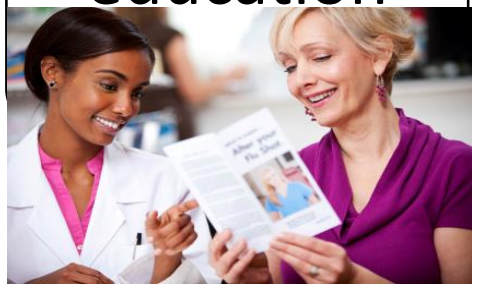
Aims

improve symptoms

Reduce risk of complications

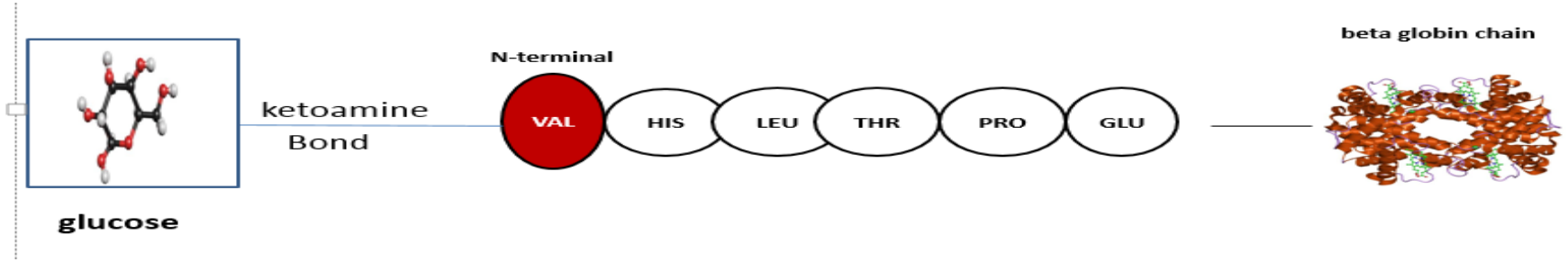
Self monitoring

Patient education



Glycated Hemoglobin (HbA1c)

Glucose in the blood will react with the N- terminal valine of the hemoglobin molecule to produce glycated hemoglobin (HbA1c).



- This expressed as a percentage of total blood hemoglobin concentration
- HbA1c is an indicator of **glycemic control**. As red blood cells normally spend about 3 months in the circulation the % HbA1c is related to **the average blood glucose concentration over the last 2-3 months.**
- In normal healthy individuals HbA1C = 4- 6% , in poorly controlled diabetics this value can increase above 10%.
- HbA1c also included in **diagnostic criteria** for DM

THANK YOU
I WISH YOU GOOD HEALTH