Al-Mustaqbal University

Pathophysiology

3rd stage

Diabetes Mellitus Part II

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Type 1 Diabetes Mellitus

Type 1 diabetes is most commonly seen in:

- Non-obese individuals less than 30 years old.
- Slightly higher proportion of males than females.

It is autoimmune antibody directed against β cells. Destruction of beta cells is related to genetic susceptibility and environmental factors.

By the time, more than 80% of the pancreatic beta cells have been destroyed, type 1 diabetes is diagnosed.

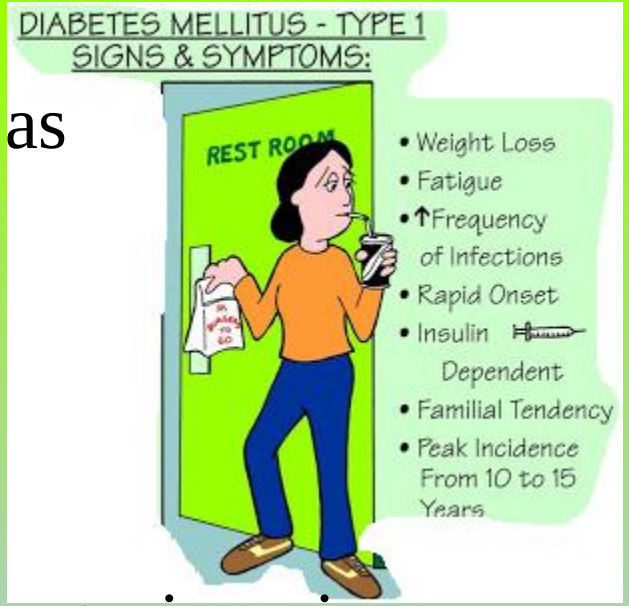
Clinical Manifestations and Mechanisms for Type 1 Diabetes Mellitus

1- Polydipsia : Intracellular dehydration and stimulation of thirst in hypothalamus.

2- Polyuria: Hyperglycemia acts as an osmotic diuretic.

3- Polyphagia: Depletion of cellular stores increase in hunger.

4- Weight loss: Because of fluid loss in osmotic diuresis and loss of body tissue as fats and proteins are used for energy.



5- Fatigue: Poor use of food products, contributing to lethargy and fatigue.

6- Recurrent infections: Growth of microorganisms is stimulated by increased glucose levels.

7- Prolonged wound healing: Impaired blood supply hinders healing.

8- **Genital pruritus:** Hyperglycemia and glycosuria favor fungal growth; candidal infections, resulting in pruritus, are a common presenting symptom in women.

9- **Blurred vision:** occurs as water balance in eye fluctuates because of elevated blood glucose levels; diabetic retinopathy may ensue

10- **Paresthesias:** Paresthesias are common manifestations of diabetic neuropathies.

11- Some individuals with type 1 diabetes are obese and may have manifestations of metabolic syndrome, including dyslipidemia, and hypertension.

12- **Nausea** or vomiting: due to dehydration and Ketones production.

Diagnostic Criteria for Diabetes Mellitus

In most cases, the suspicion of type 1 diabetes arises clearly with a history of polyuria, polydipsia, polyphagia, and weight loss. The individual may experience repeated vomiting and appear very sick.

1. HbA1C (hemoglobin A1C or glycosylated hemoglobin) ≥6.5%

OR 2. fasting plasma glucose ≥126 mg/dl (7.0 mmol/L); fasting is defined as no caloric intake for at least 8 hr.

OR 3- 2 hr plasma glucose ≥200 mg/dl during oral glucose tolerance testing.

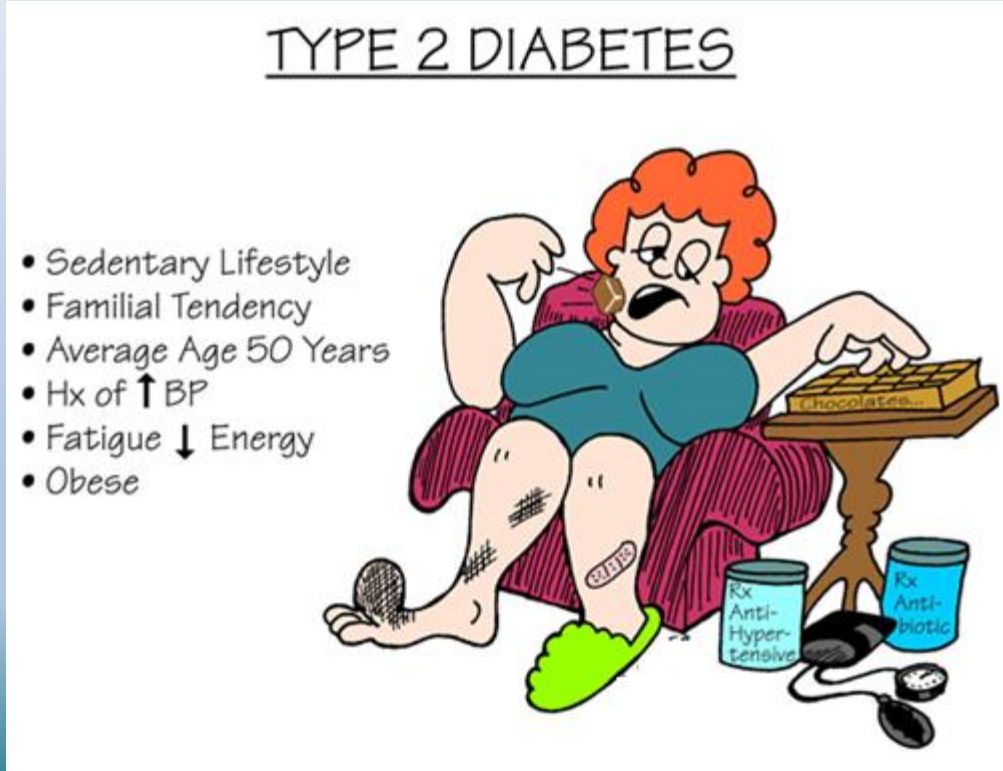
OR 4- In an individual with classic symptoms of hyperglycemia or hyperglycemic
crisis, a random plasma glucose ≥200 mg/dl

Patient with classical symptoms and single reading > 200 or $HbA_{1c} \geq 6.5$ consider as DM .

Type 2 Diabetes Mellitus

Hyperglycemia caused by cellular insensitivity to insulin is called type 2 diabetes mellitus.

In type 2 diabetes mellitus, women are over-represented compared with men.



The most well-recognized risk factors are:

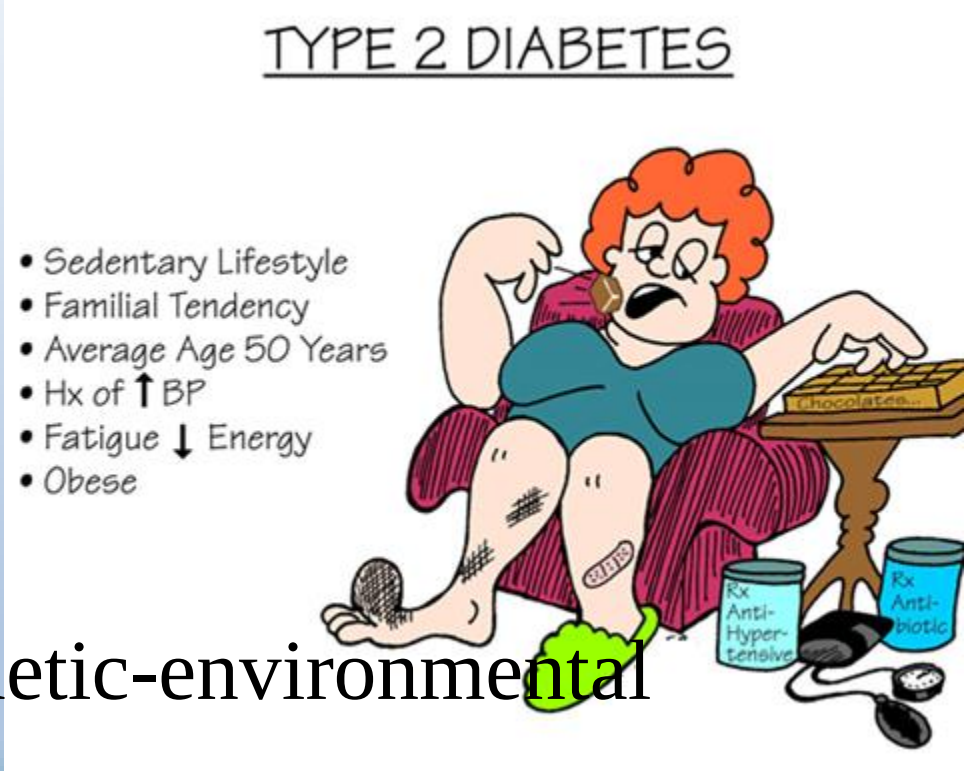
age,

obesity,

hypertension,

physical inactivity,

and family history (a genetic-environmental interaction).



Pathophysiology

Many organs contribute to insulin resistance, chronic hyperglycemia, and the consequences of type 2 diabetes.

Insulin resistance is defined as a suboptimal response of insulin-sensitive tissues (especially liver, muscle, and adipose tissue) to insulin and is associated with obesity.

Several mechanisms are involved in abnormalities of the insulin signaling pathway and contribute to insulin resistance.

These include:

- An abnormality of the insulin molecule,
- High amounts of insulin antagonists,
- Down-regulation of the insulin receptor,
- Alteration of glucose transporter (GLUT) proteins.

Q- Choose more appropriate one.

- Regarding type 2 diabetes mellitus all of the following mechanisms may cause insulin resistance except …….. .

a- An abnormality of the insulin molecule,

b- High amounts of insulin antagonists,

c- Autoimmune antibody against β cells.

d- Down-regulation of the insulin receptor,

e- Alteration of glucose transporter (GLUT) proteins.

Clinical manifestations Type 2 Diabetes Mellitus

The affected individual is often:

1- Overweight.

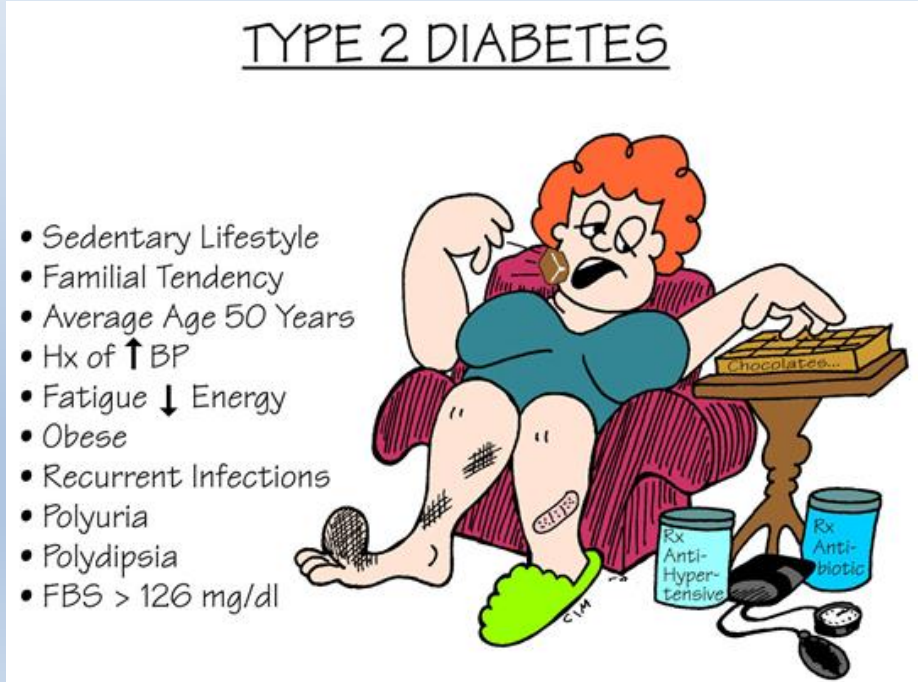
2- Dyslipidemic.

3- Hyperinsulinemic.

4- Hypertensive.

5- Polyuria and

6- Polydipsia.



But more often will have nonspecific symptoms such as:

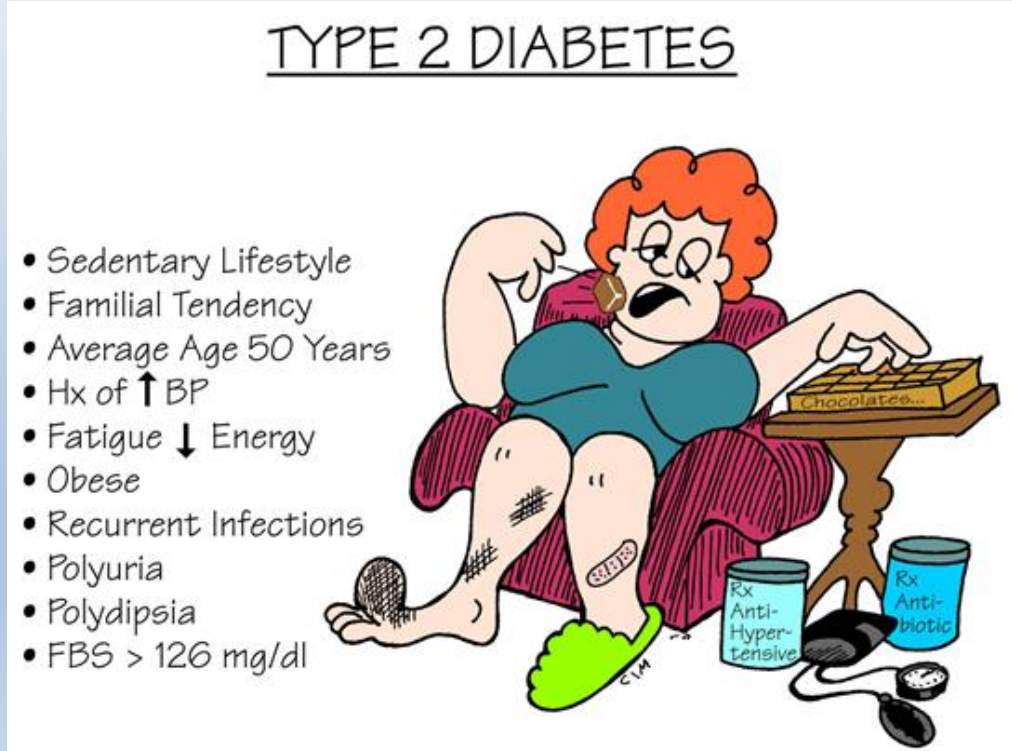
7- Fatigue.

8- Pruritus.

9- Recurrent infections.

10- Visual changes.

11- Paresthesias or weakness.



Other Specific Types of Diabetes Mellitus

The best-described of these other specific types of diabetes is termed **maturity-onset diabetes of youth (MODY)**.

MODY includes six specific autosomal dominant mutations that affect critical enzymes involved in beta-cell function or insulin action.

Diagnosis and management are similar to those techniques used for type 2 diabetes.

Gestational diabetes mellitus (GDM) has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy.

GDM complicates approximately 7% of all pregnancies.
Screening for GDM is recommended in asymptomatic, pregnant women after 24 weeks of gestation. An OGTT is used to confirm the diagnosis.

Careful glucose control prenatally, during pregnancy, and after delivery is essential to the short- and long-term health of both mother and baby.

Women who have GDM have a greatly increased subsequent diabetes risk, making consistent follow-up important

Acute Complications of Diabetes Mellitus

1- **Hypoglycemia:** is a blood glucose level less than **50 mg/l00 mL** of blood.

can be caused by fasting or, especially, fasting coupled with exercise, because exercise increases the usage of glucose by skeletal muscle.

Hypoglycemia in diabetes is sometimes called insulin shock or insulin reaction.

It most common in Individuals with type 1 diabetes

Hypoglycemia does occur in type 2 diabetes when treatment involves insulin secretogogues (e.g., sulfonylureas) or exogenous insulin.

Symptoms include:

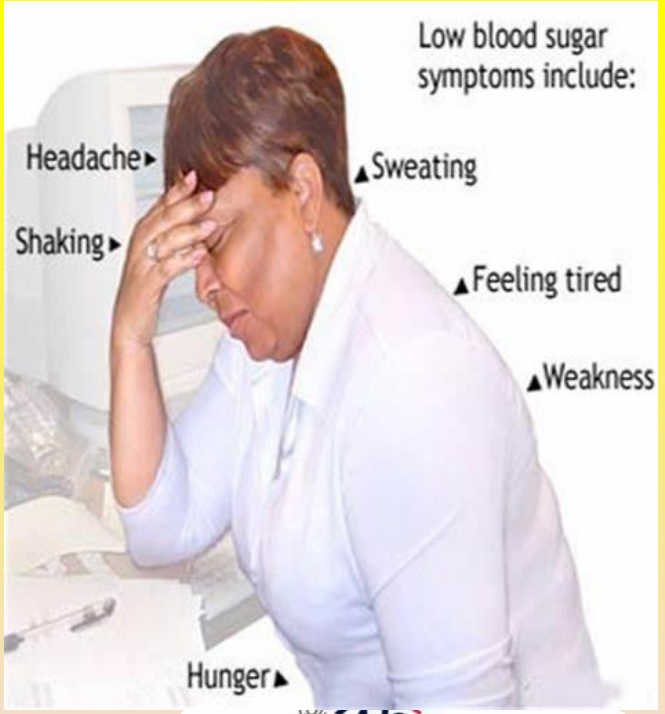
Because the brain relies on blood glucose as its main energy source, hypoglycemia results in many symptoms of altered central nervous system (CNS) functioning, including
confusion,
irritability,
anxiety,
seizure,
and coma.

headache, as a result of alteration of cerebral blood flow, and changes in water balance.

hypoglycemia causes activation of the sympathetic nervous system.
Tremor , pallor
stimulating hunger,
nervousness,
sweating,
and tachycardia.

Treatment requires immediate replacement of glucose either orally or intravenously.

Glucagon for home use can be prescribed for individuals who are at high risk



Diabetic ketoacidosis (DKA) is a serious complication related to a deficiency of insulin and an increase in the levels of insulin counterregulatory hormones
(catecholamines, cortisol, glucagon, growth hormone)

It is characterized by hyperglycemia, acidosis, and ketonuria.

insulin deficiency causes lipolysis and increased glyconeogenesis which contributing to hyperglycemia and production of ketone bodies at a rate that exceeds peripheral use.

Accumulation of ketone bodies causes a drop in pH, resulting in metabolic acidosis.

Q- Choose more appropriate one.

- Diabetic ketoacidosis is characterized by all the following except …….

A- hyperglycemia,

B- alkalosis.

C- deficiency of insulin .

B- acidosis,

C- ketonuria.

Symptoms of diabetic ketoacidosis include

Hyperventilation in an attempt to compensate for the acidosis,
postural dizziness,
central nervous system depression,
ketonuria,
anorexia,
nausea,
abdominal pain,
thirst, and polyuria.

Microvascular Disease

Diabetic microvascular complications (disease in capillaries) are a leading cause of blindness, end-stage kidney failure, and various neuropathies.

Hypoxia and ischemia accompany microvascular disease, especially in the eye, kidney, and nerves.

Many individuals with type 2 diabetes will present with microvascular complications because of the long duration of asymptomatic hyperglycemia that generally precedes diagnosis.

Diabetic retinopathy

Diabetic retinopathy results from relative hypoxemia, damage to retinal blood vessels, red blood cell (RBC) aggregation, and hypertension

The three stages of retinopathy that lead to loss of vision are:
1- nonproliferative (stage I), characterized by an increase in retinal capillary permeability, vein dilation, microaneurysm formation, and superficial and deep hemorrhages.

2- preproliferative (stage II), a progression of retinal ischemia with areas of poor perfusion that culminate in infarcts; and

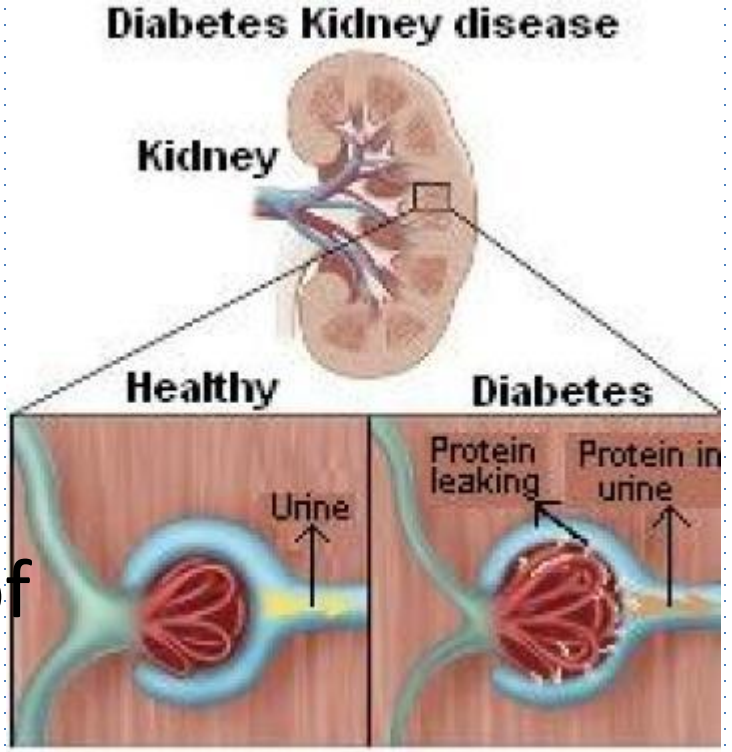
3- proliferative (stage III), the result of angiogenesis and fibrous tissue formation within the retina or optic disc.

Macular edema is the leading cause of blurred vision among persons with diabetes.

nephropathy start with microalbumineurea after glomerular hyperfilteration (enlarged kidney followed by glomerular sclerosis) in which protienurea < 300 micg. (macroprotienurea > 300 micg./ 24h).

DM is the most common cause of Renal failure.

Diabetic nephropathy

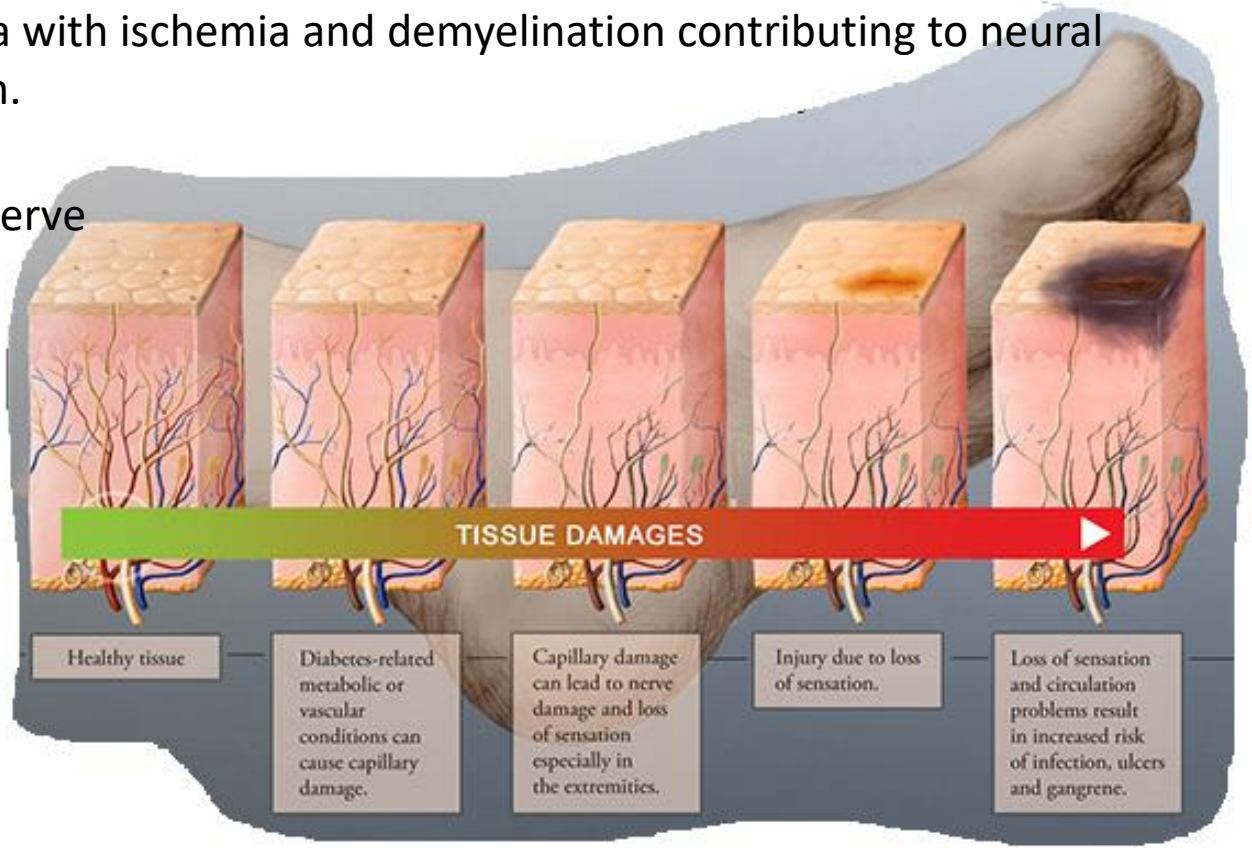


Diabetic neuropathies

The underlying pathologic mechanism includes both metabolic and vascular factors related to chronic hyperglycemia with ischemia and demyelination contributing to neural changes and delayed conduction.

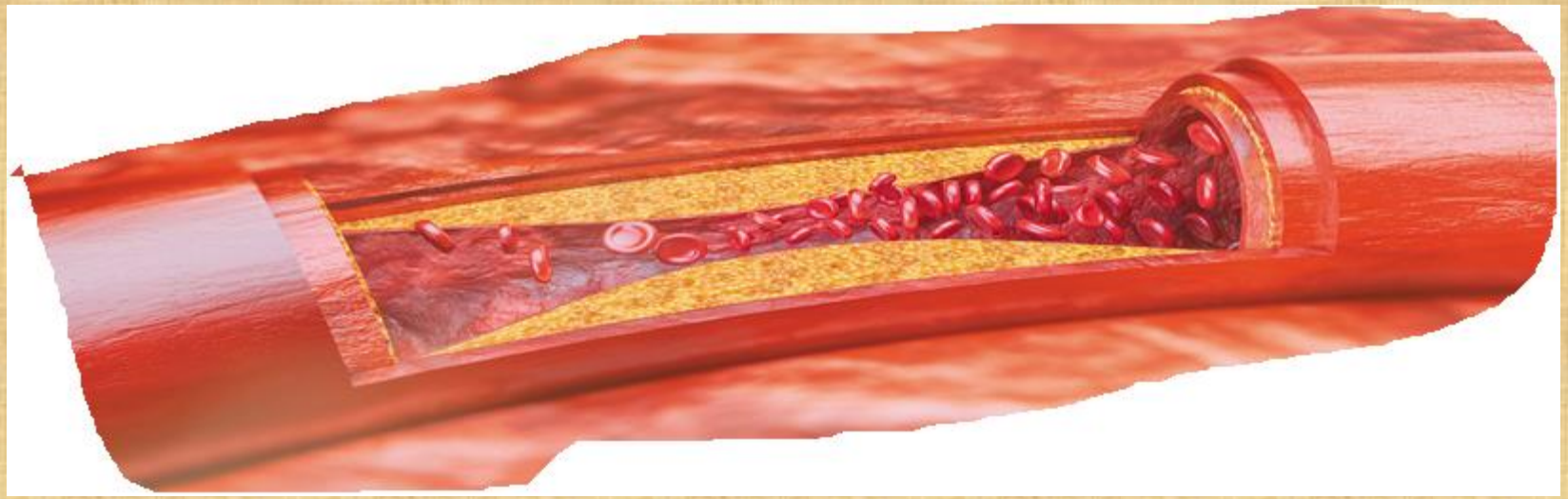
Both somatic and peripheral nerve cells show diffuse or focal damage, resulting in polyneuropathy.

Loss of pain, temperature, and vibration sensation is more common than motor involvement and often involves the extremities first in the hands and feet.



Macrovascular Disease

Macrovascular disease (lesions in large- and medium-sized arteries) increases morbidity and mortality and increases risk for hypertension, accelerated atherosclerosis, cardiovascular disease, stroke, and peripheral vascular disease, particularly among individuals with type 2 diabetes mellitus.



Cardiovascular disease.

Cardiovascular disease is the ultimate cause of death in up to 68% of people with diabetes, with higher risk for women

Mechanisms of disease include:

vessel injury related to insulin resistance and hyperglycemia oxidative stress, accelerated atherosclerosis associated with high levels of triglycerides, high levels of small low-density lipoproteins (LDLs), and low levels of high-density lipoproteins (HDLs); platelet activation and prothrombosis; and endothelial cell dysfunction.

In general, the prevalence of Coronary artery disease increases with the duration but not the severity of diabetes and the onset can be silent.

Reference: Corwin , Pathophysiology, 3rd Edition