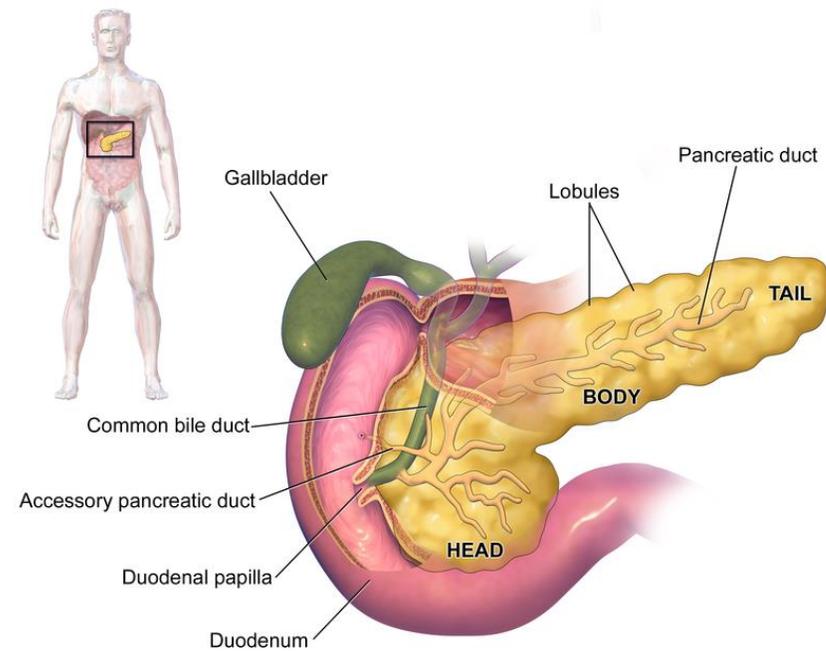


Endocrine pathology-3. Diabetes mellitus

Dr.Eman Krieshan, M.D.

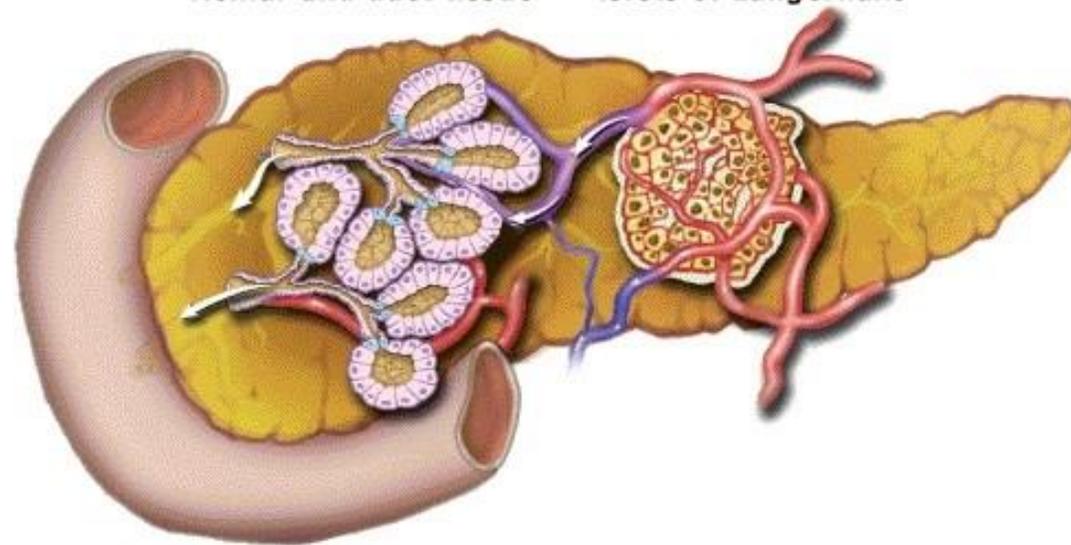
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Pancreas. anatomy.

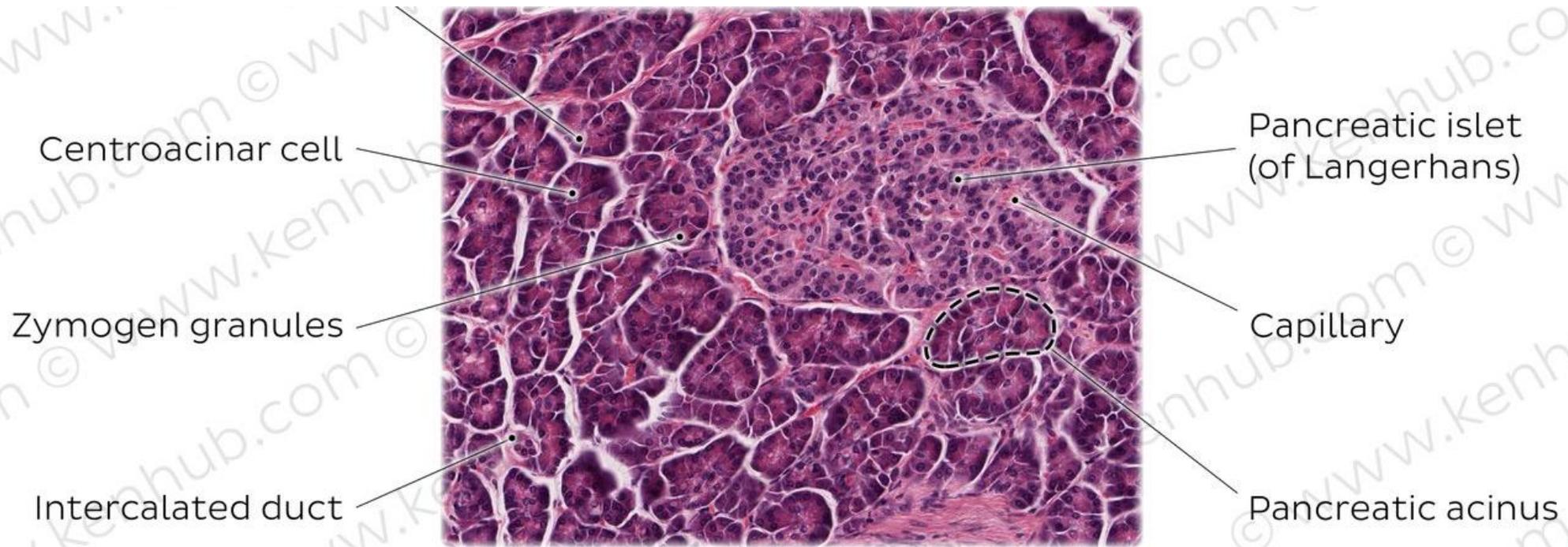


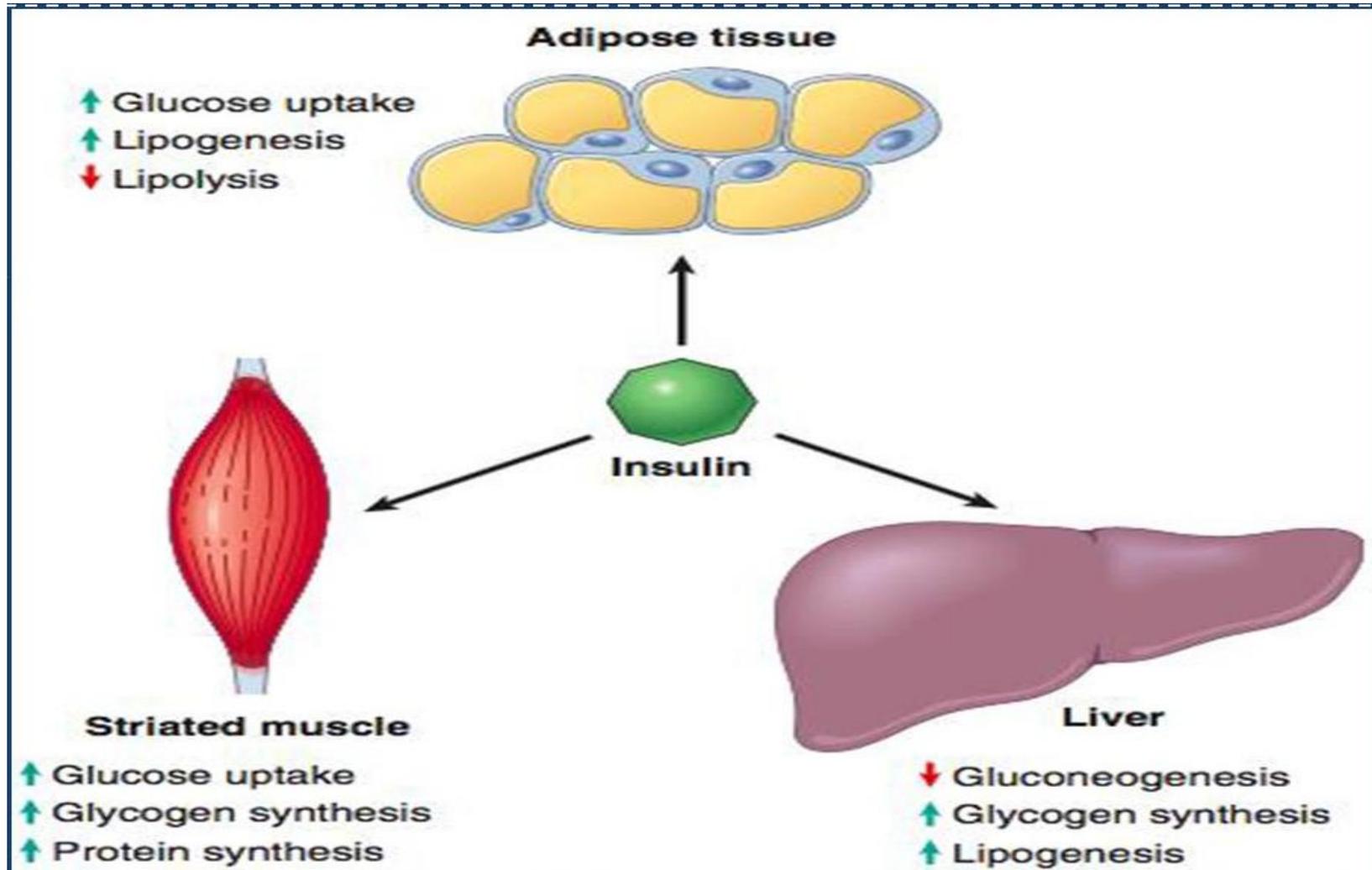
Exocrine
Acinar and duct tissue

Endocrine
Islets of Langerhans



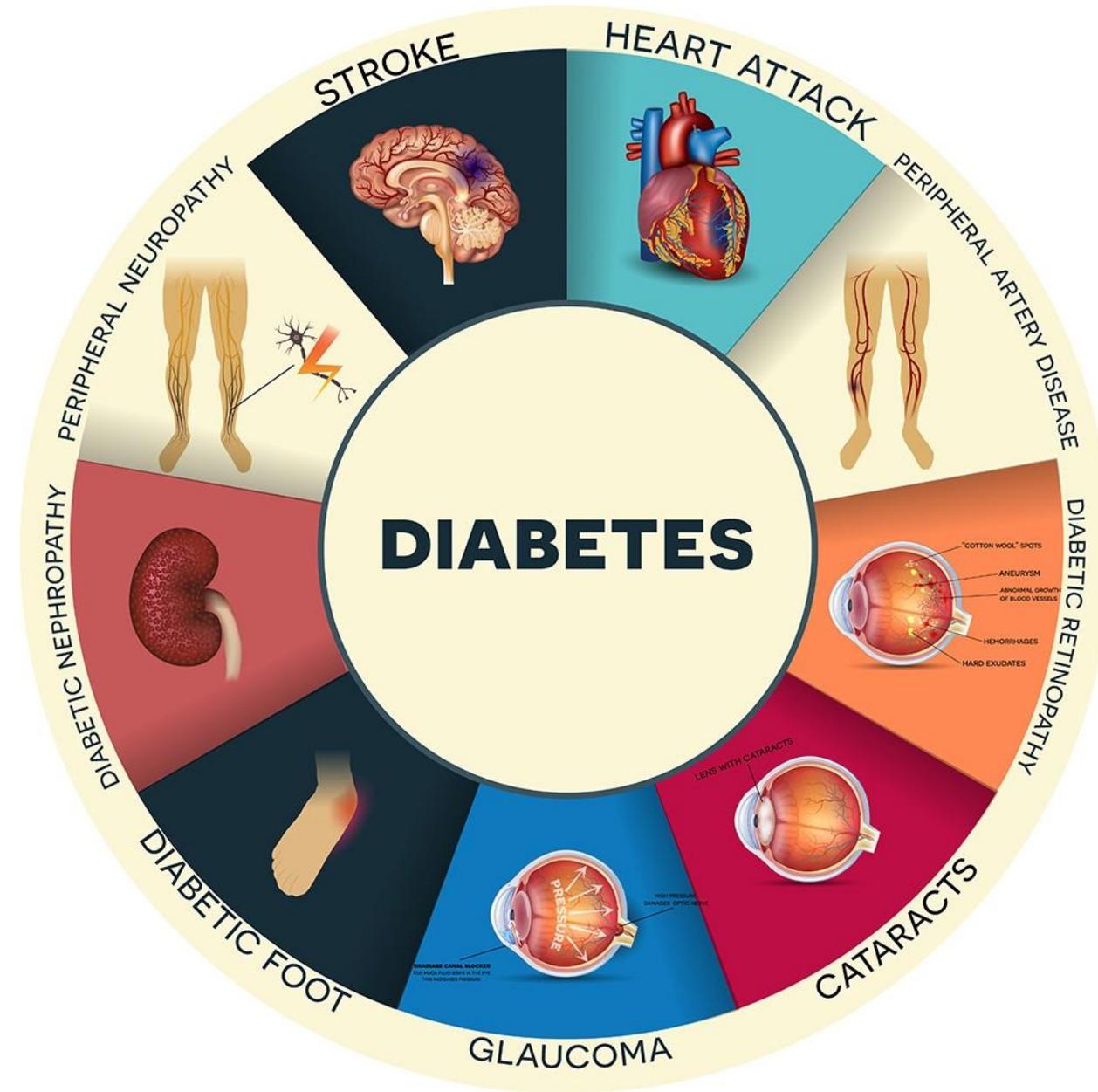
Histology





Diabetes mellitus (DM) is a global health issue affecting children, adolescents, and adults.

- ❖ The WHO estimates that diabetes resulted in :
 - ✓ 1.5 million deaths in 2012.
 - ✓ making it the 8th leading cause of death.
 - ✓ 2.2 million deaths worldwide were attributable to high blood glucose and the increased risks of cardiovascular disease and other associated complications (e.g. kidney failure),



Diabetes mellitus

- Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia

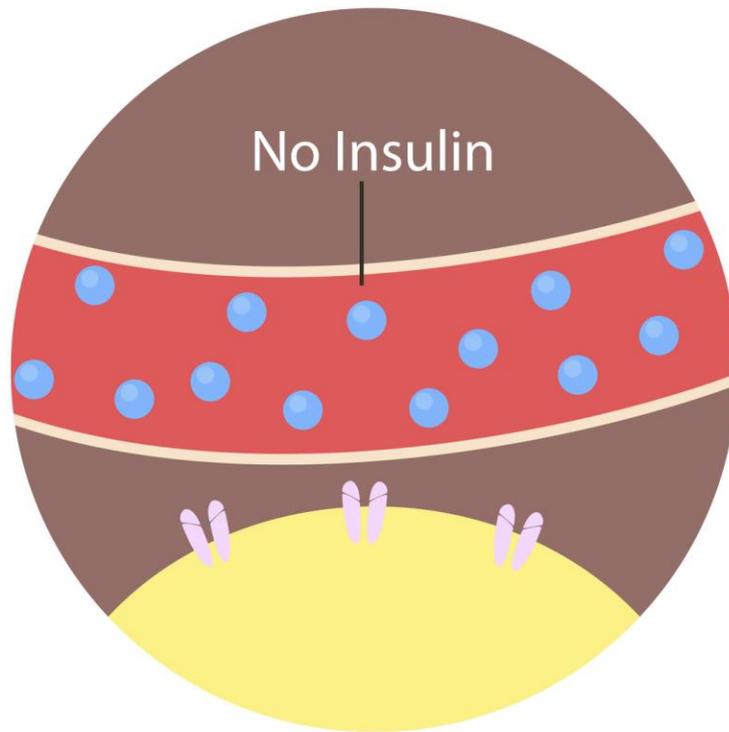


Types

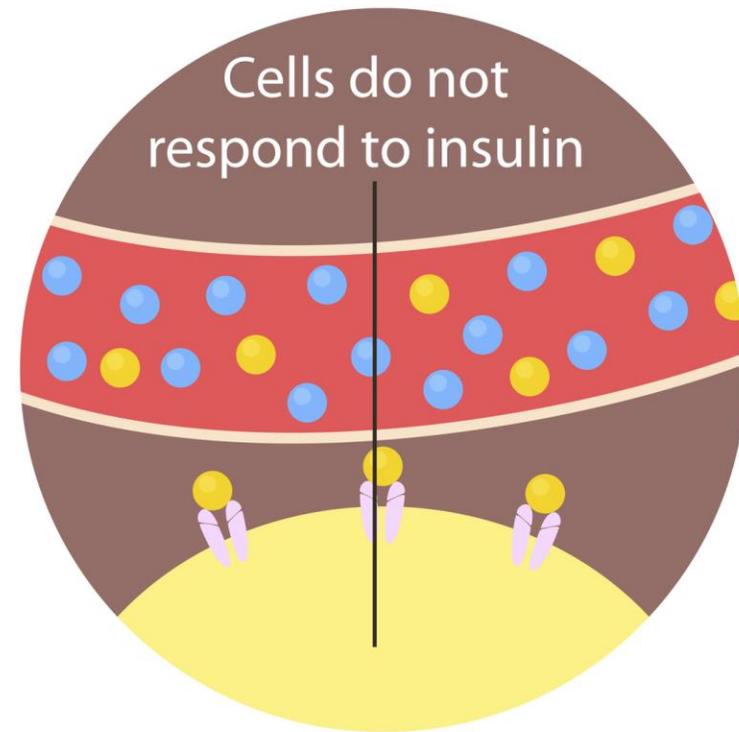
Table 20.5 Simplified Classification of Diabetes

1. *Type 1 Diabetes*
Beta cell destruction, usually leading to absolute insulin deficiency
2. *Type 2 Diabetes*
Combination of insulin resistance and beta cell dysfunction
3. *Genetic Defects of Beta Cell Function*
Maturity-onset diabetes of the young (MODY) (see text)
Insulin gene mutations
4. *Genetic Defects in Insulin Action*
Insulin receptor mutations
5. *Exocrine Pancreatic Defects*
Chronic pancreatitis
Pancreatectomy
Cystic fibrosis
Hemochromatosis
6. *Endocrinopathies*
Growth hormone excess (acromegaly)
Cushing syndrome
Hyperthyroidism
Pheochromocytoma
7. *Infections*
Cytomegalovirus infection
Coxsackievirus B infection
Congenital rubella
8. *Drugs*
Glucocorticoids
Thyroid hormone
 β -Adrenergic agonists
9. *Gestational Diabetes*
Diabetes associated with pregnancy

Types of Diabetes



Type 1 Diabetes



Type 2 Diabetes

Cells do not absorb glucose

Type 1 diabetes (T1D).

- Autoimmune disease in which islet destruction is caused primarily by immune effector cells reacting against endogenous beta cell antigens.
- formerly known as juvenile diabetes.
- Most patients with type 1 diabetes depend on exogenous insulin for survival; without insulin they develop serious metabolic complications such as ketoacidosis and coma.

Pathogenesis

- the pathogenesis of type 1 diabetes involves:
 - ✓ genetic susceptibility: HLA-DR3, or DR4, failure of self-tolerance in T cells specific for beta cell antigens.
 - ✓ environmental factors: infection?
- ✓ All lead to :
- ✓ production of autoantibodies against a variety of beta cell antigens, including insulin and the beta cell enzyme glutamic acid decarboxylase.

Type 2 diabetes (T2D)

- heterogeneous and multifactorial complex disease that involves interactions of genetics, environmental risk factors, and inflammation.
- Unlike type 1 diabetes, however, there is no evidence of an autoimmune basis.
- The two defects that characterize type 2 diabetes are:
 - ✓ (1) a decreased ability of peripheral tissues to respond to insulin (insulin resistance).
 - ✓ (2) beta cell dysfunction that is manifested as inadequate insulin secretion in the face of insulin resistance and hyperglycemia

SYMPTOMS OF TYPE 1 DIABETES



Abnormal thirst and dry mouth



Frequent urination



Lack of energy, fatigue



Blurred vision



Constant hunger



Sudden weight loss



Bed-wetting

SYMPTOMS OF TYPE 2 DIABETES



Excessive thirst and dry mouth



Frequent and abundant urination



Lack of energy, extreme tiredness



Blurred vision



Recurrent fungal infections of the skin



Slow healing wounds



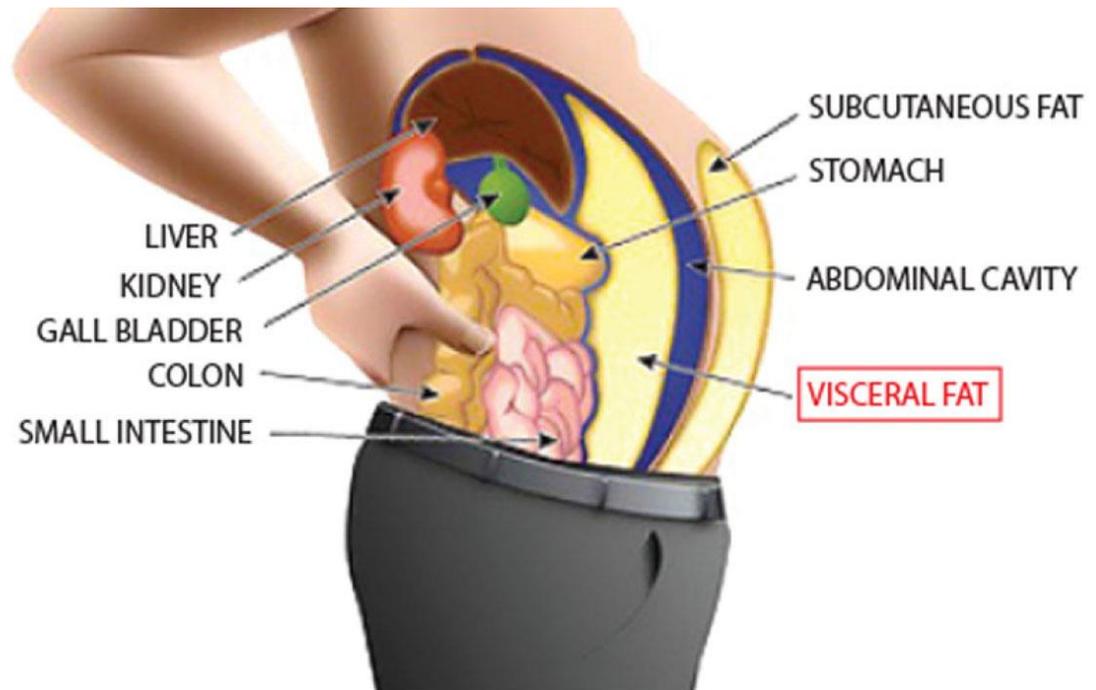
Tingling or numbness in hands and feet

Insulin resistance

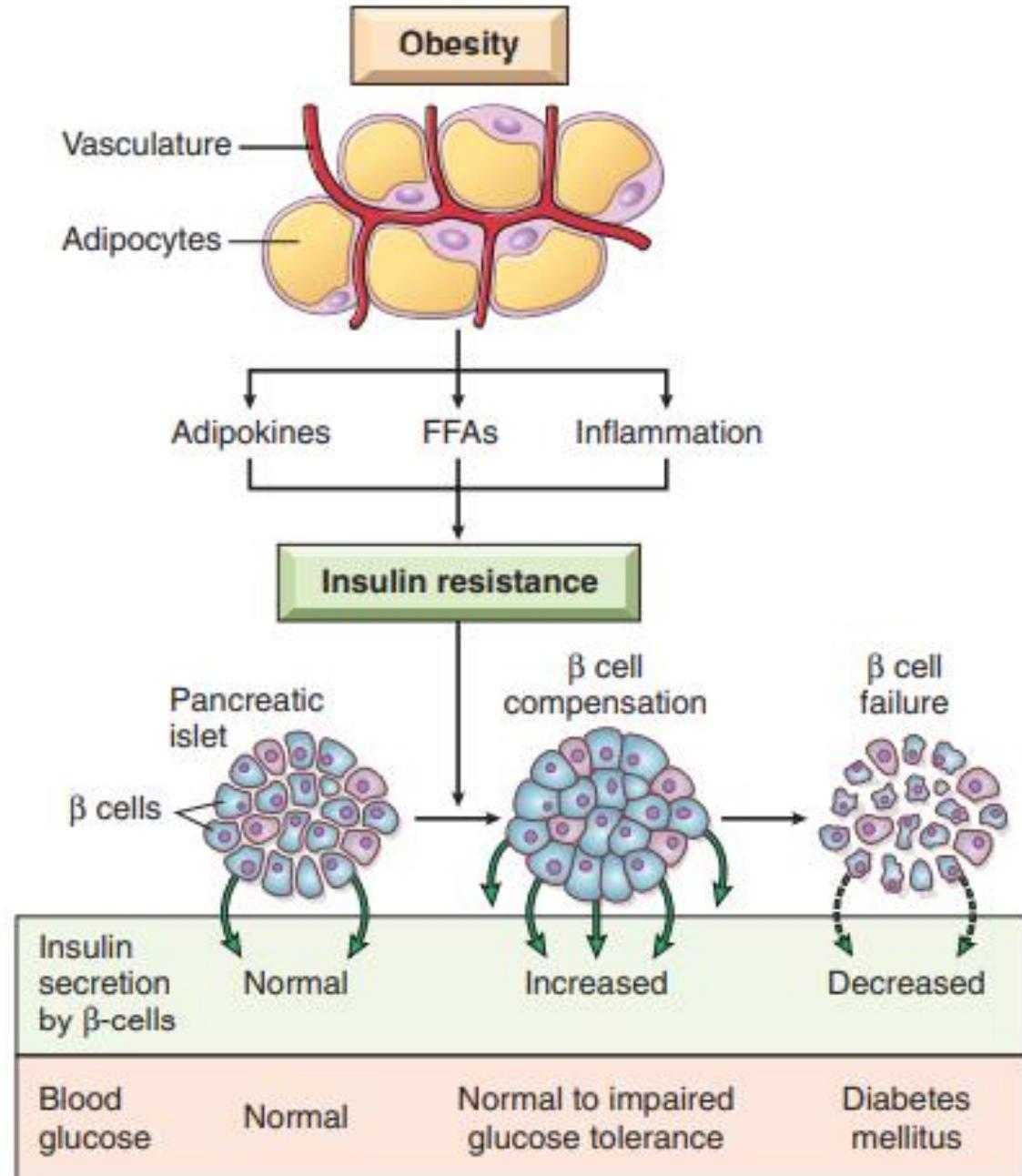
- Insulin resistance is defined as the failure of target tissues to respond normally to insulin.
- The liver, skeletal muscle, and adipose tissue are the major tissues where insulin resistance manifests as follows:
- Failure to inhibit endogenous glucose production (gluconeogenesis) in the liver, which contributes to high fasting blood glucose levels .
- Abnormally low glucose uptake and glycogen synthesis in skeletal muscle following a meal, which contributes to a high postprandial blood glucose level.
- Failure to inhibit hormone-sensitive lipase in adipose tissue, leading to excess circulating free fatty acids (FFAs), which, exacerbates the state of insulin resistance

Obesity and Insulin Resistance

- The association of obesity with type 2 diabetes has been recognized for decades, with visceral obesity being common in a majority of affected patients.



Pathogenesis



Obesity can adversely impact insulin sensitivity in numerous ways

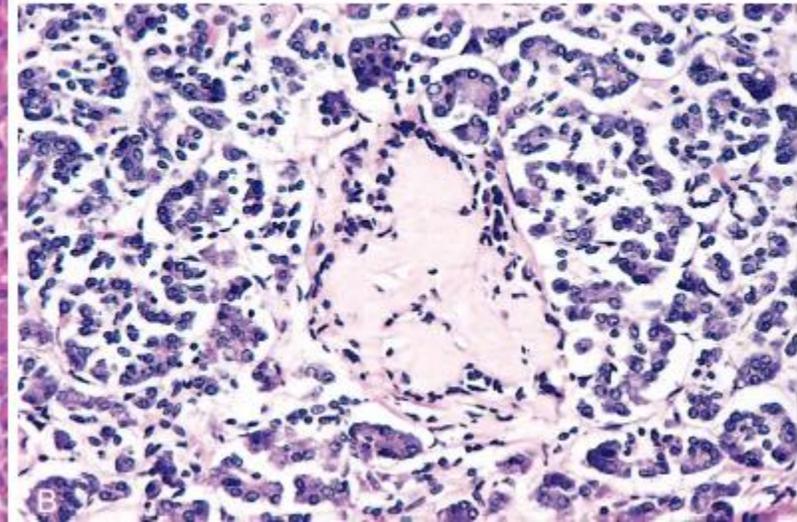
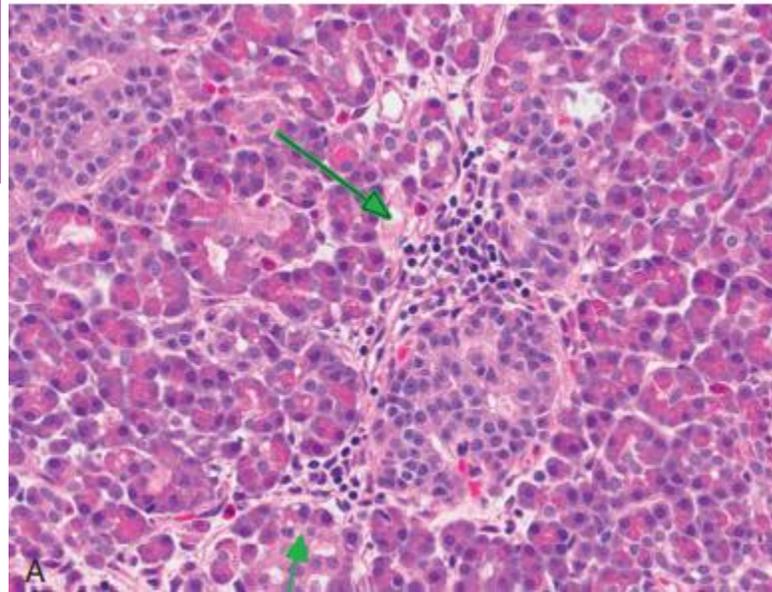
- 1. Excess FFAs.
- 2. Adipokines.
- 3. Inflammation:
 - inflammatory milieu (mediated by proinflammatory cytokines that are secreted in response to excess nutrients such as FFAs) results in both peripheral insulin resistance and beta cell dysfunction

Beta Cell Dysfunction

- beta cell dysfunction is an essential component in the development of overt diabetes.
- Several mechanisms have been implicated:
 - Excess free fatty acids that compromise beta cell function and attenuate insulin release (lipotoxicity).
 - Chronic hyperglycemia (glucotoxicity).

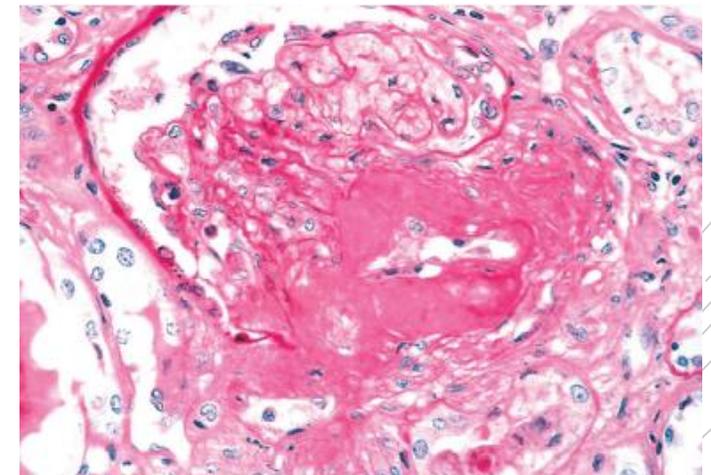
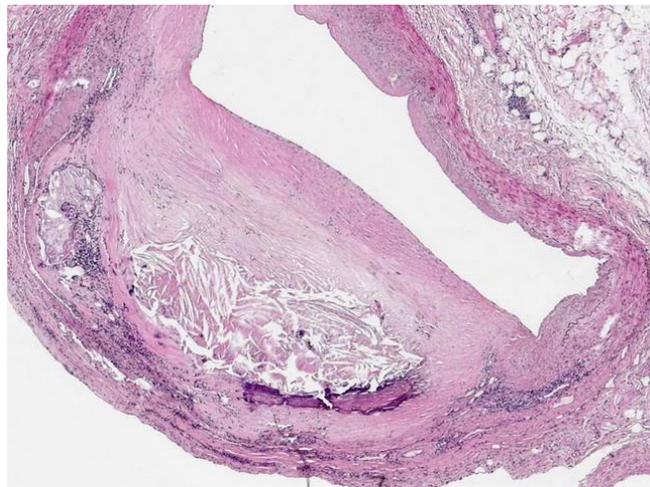
MORPHOLOGY

- Reduction in the number and size of islets.
- Leukocytic infiltrates in the islets.
- Amyloid deposition within islets in type 2 diabetes.



Morphology cont.

- Diabetic macrovascular disease. The hallmark of diabetic macrovascular disease is accelerated atherosclerosis.
- Hyaline arteriolosclerosis.

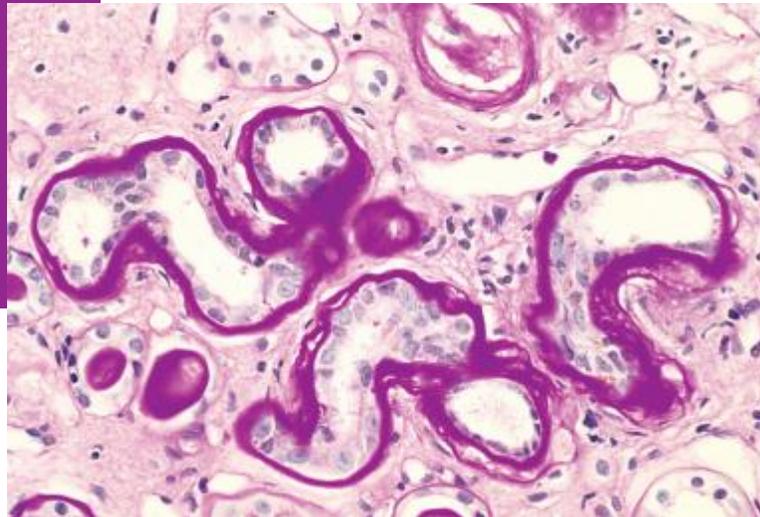


Mechanisms for vascular disease in diabetes

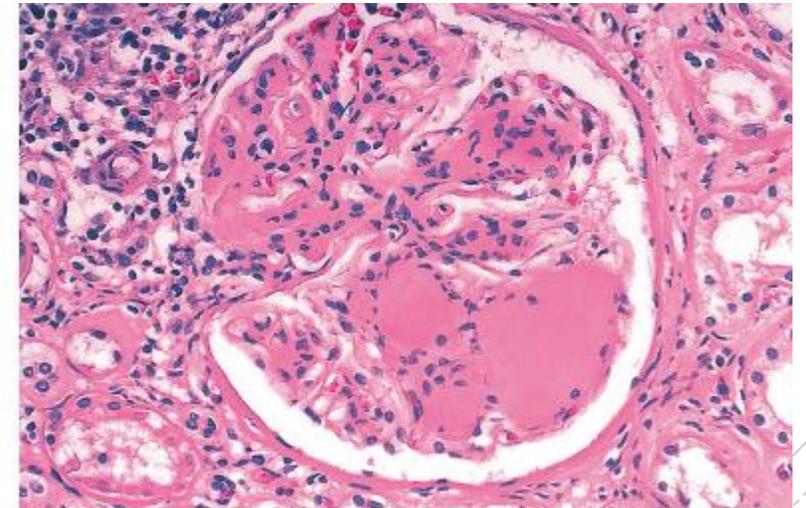
- pathologic effects of advanced glycation end product accumulation.
- impaired vasodilatory response attributable to nitric oxide inhibition,
- smooth muscle cell dysfunction.
- overproduction of endothelial growth factors.
- chronic inflammation

Diabetic nephropathy.

- glomerular lesions.
- renal vascular lesions, principally arteriosclerosis.



Renal cortex showing thickening of tubular basement membranes .



Nodular glomerulosclerosis

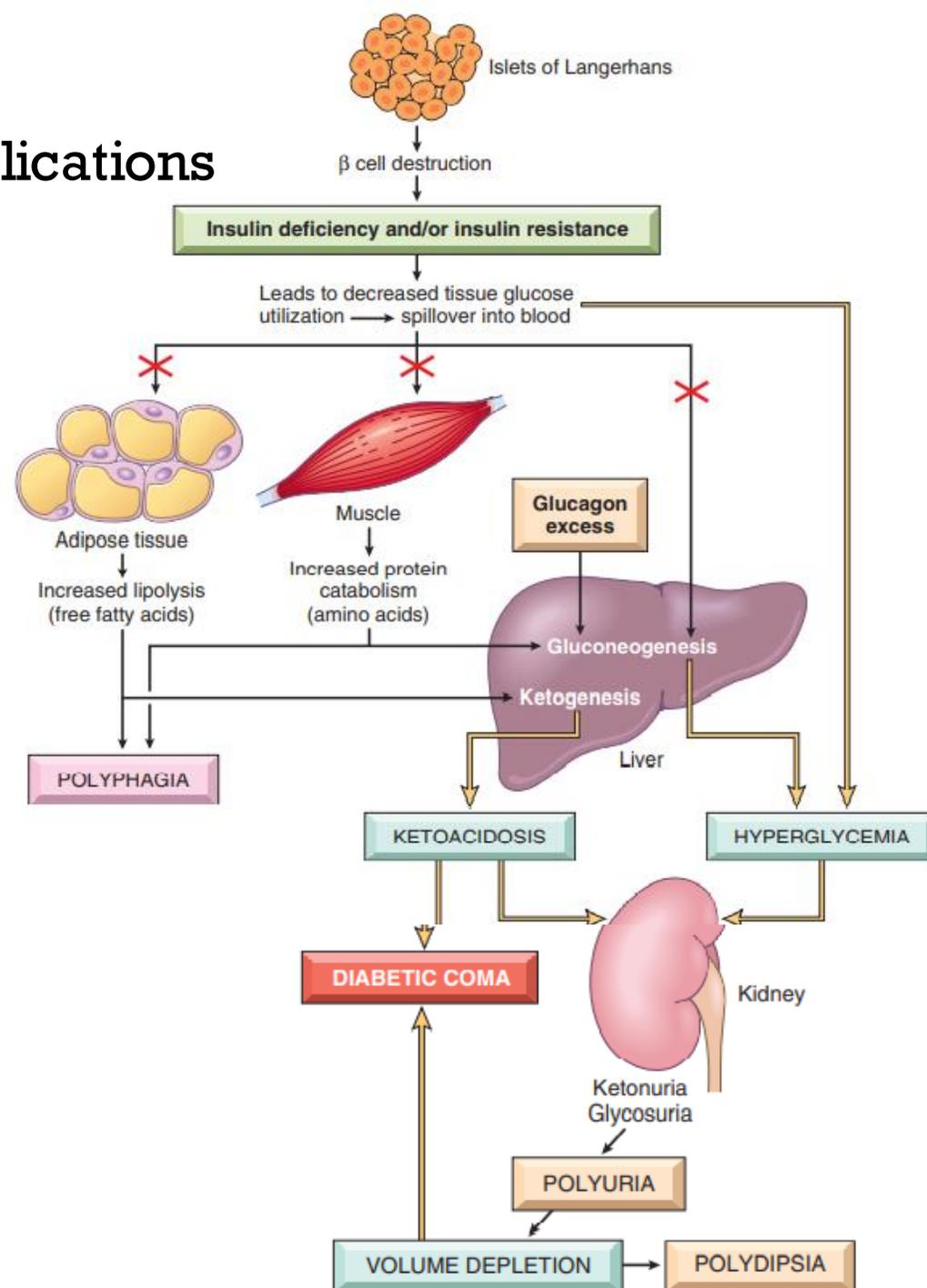
Metabolic Complications.

- **Acute Metabolic Complications of Diabetes.**
- **Chronic Complications of Diabetes.**

Acute Metabolic Complications

classic triad of diabetes:

- Polyuria.
- polydipsia.
- Polyphagia.

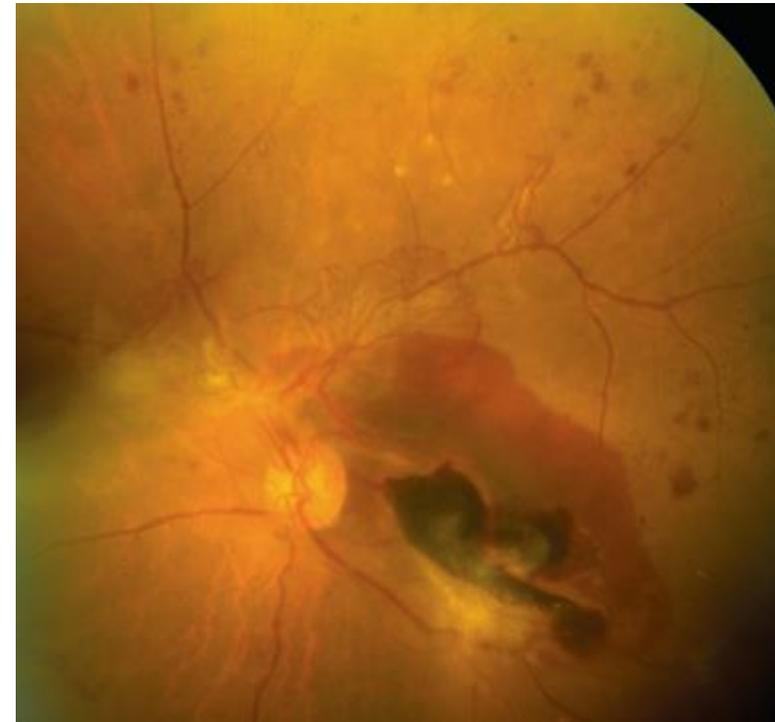


Chronic Complications of Diabetes

- damage induced in :
 - ❖ large- and medium-sized muscular arteries (diabetic macrovascular disease).
- causes accelerated atherosclerosis among diabetics, resulting in increased myocardial infarction, stroke, and lower-extremity ischemia
 - ❖ small-vessels (diabetic microvascular disease)
- The effects of microvascular disease are most profound in the retina, kidneys, and peripheral nerves, resulting in:
 - ✓ diabetic retinopathy.
 - ✓ nephropathy.
 - ✓ neuropathy.

diabetic retinopathy

- Features include:
 - ✓ advanced proliferative retinopathy.
 - ✓ retinal hemorrhages.
 - ✓ Exudates.
 - ✓ neovascularization.
 - ✓ tractional retinal detachment



Chronic Complications of Diabetes

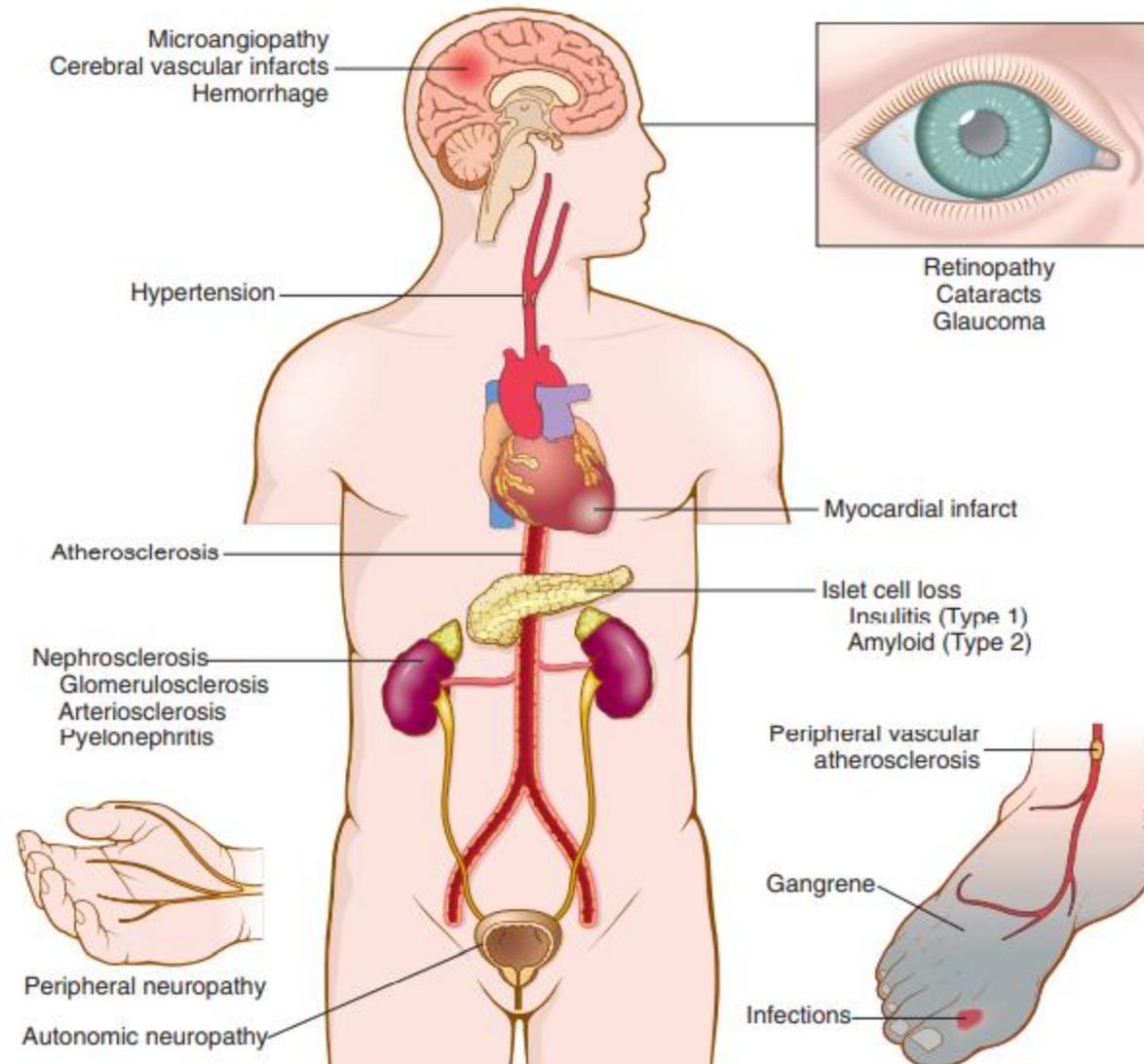


Fig. 20.25 Long-term complications of diabetes.



Thank You