Endocrine pathology-1. Diabetes mellitus

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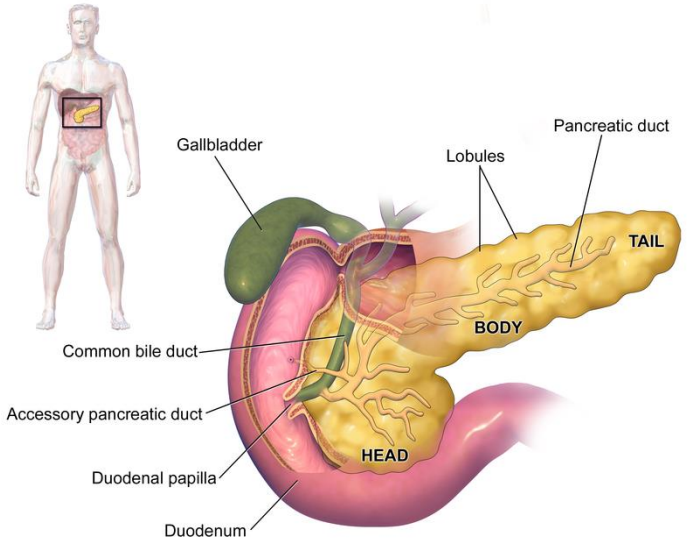
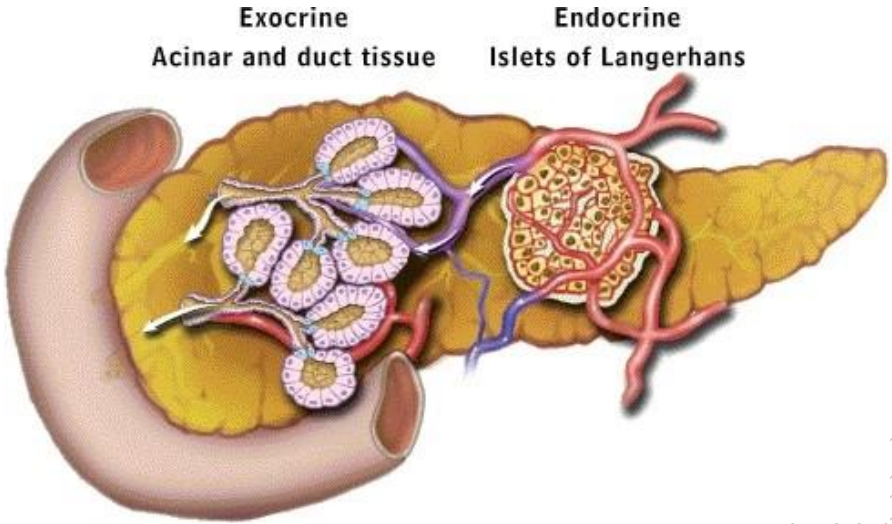
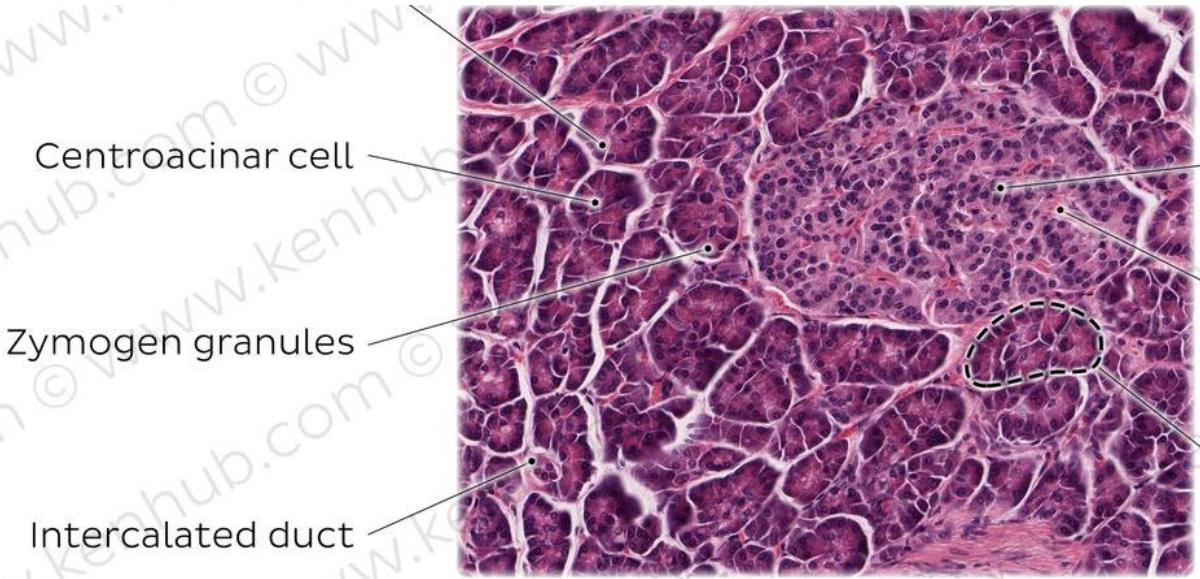
13-5-2024.

Pancreas. anatomy.



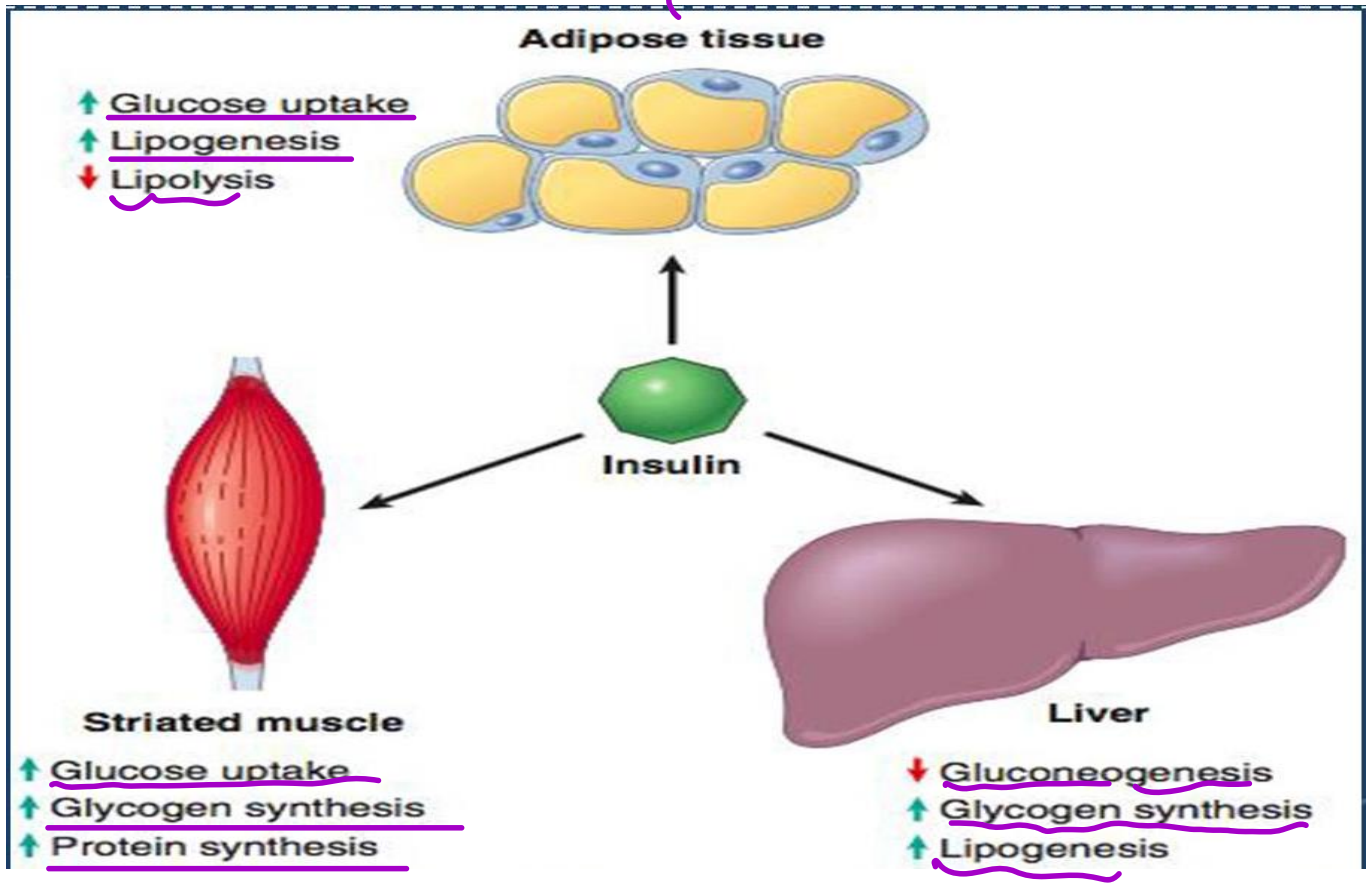


Histology

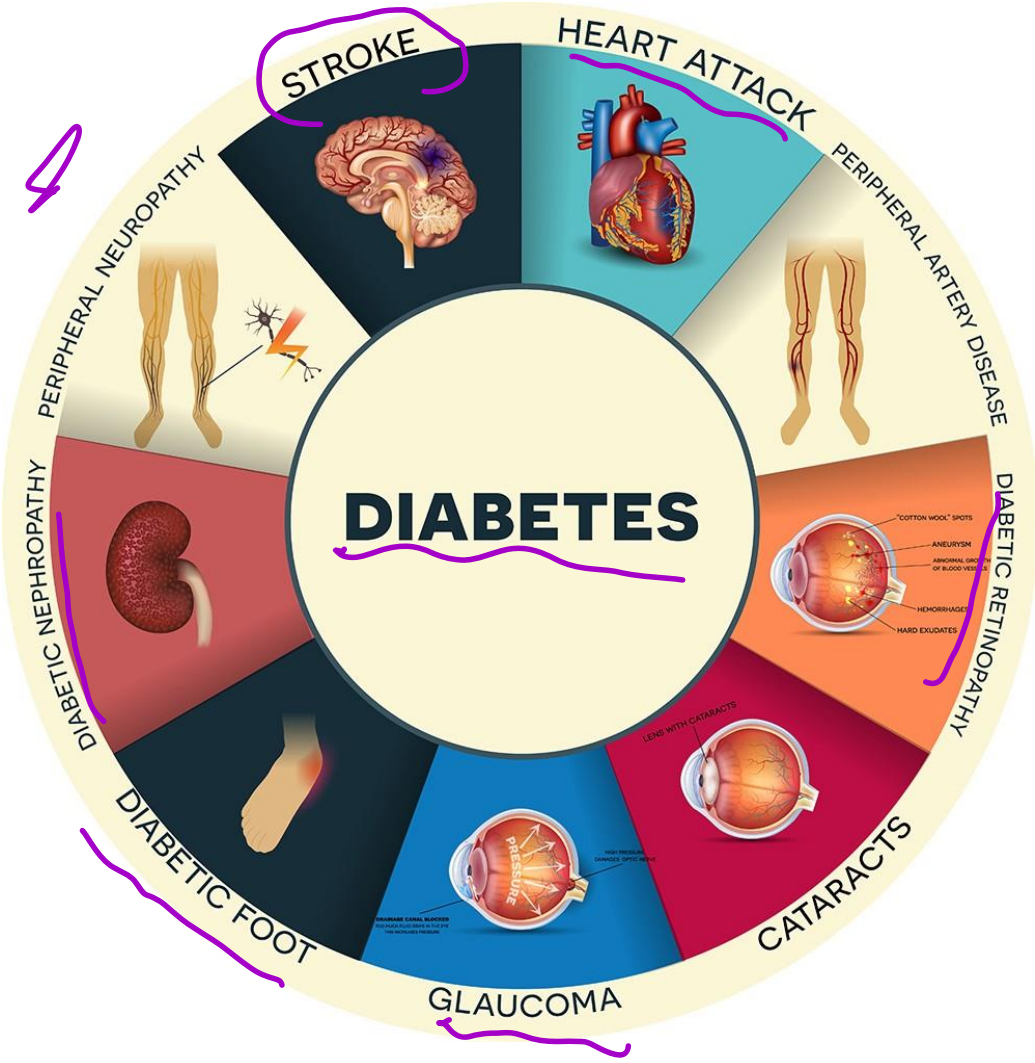


Endocrine

Exocrine


Adipose tissue
Glucose uptake
Lipogenesis
Lipolysis
Insulin
Striated muscle
Glucose uptake
Glycogen synthesis
Protein synthesis
Liver
Gluconeogenesis
Glycogen synthesis
Lipogenesis

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

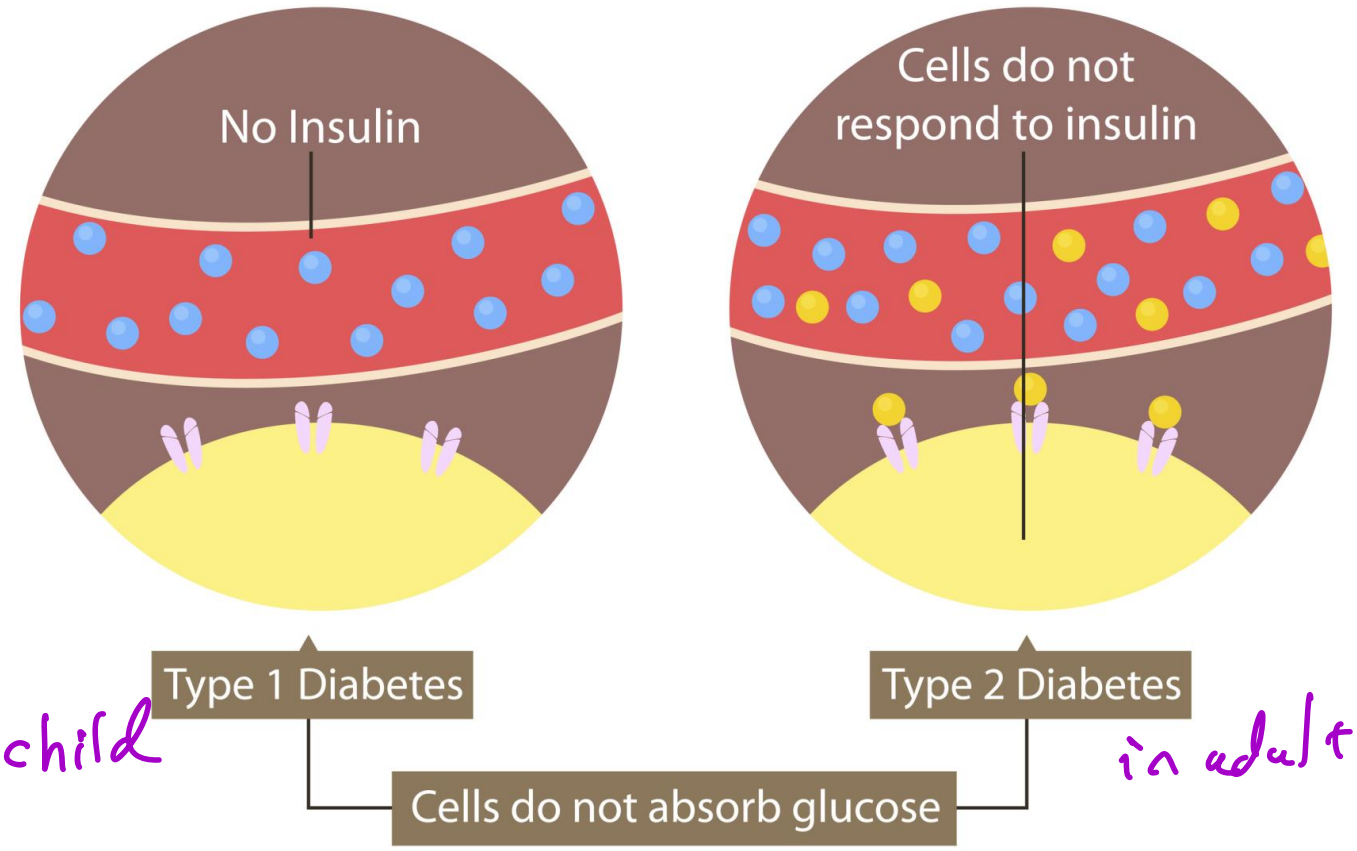
- Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia

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



in child

in adult

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

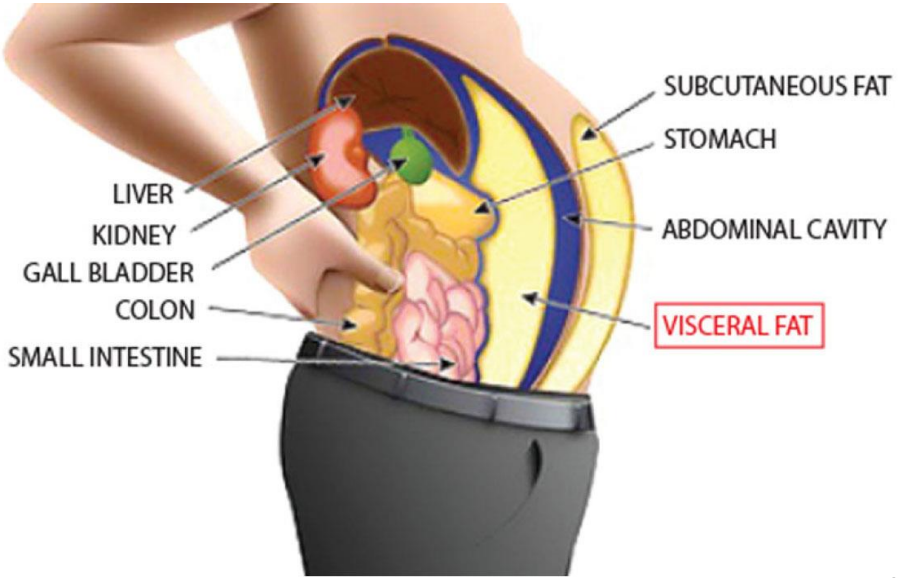
Insulin resistance

- 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

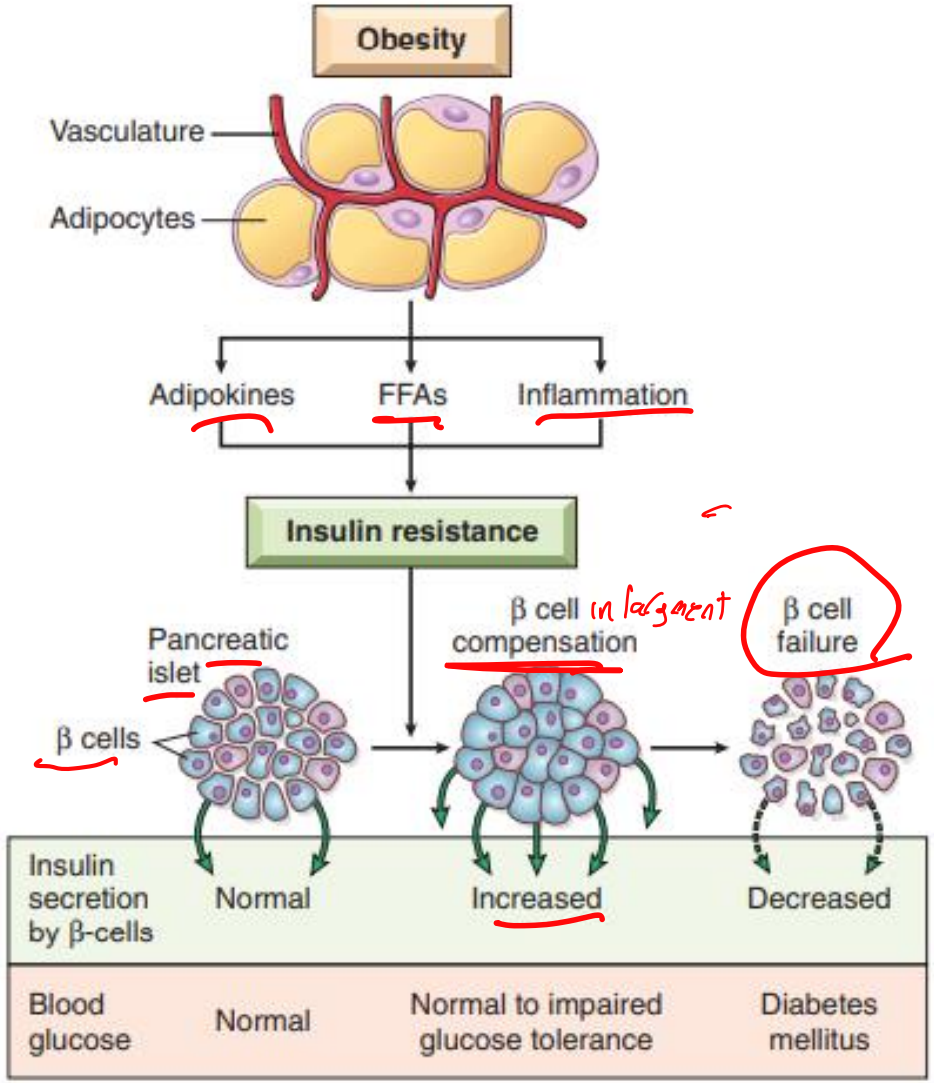
Obesity and Insulin Resistance

insulin resistant

- 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

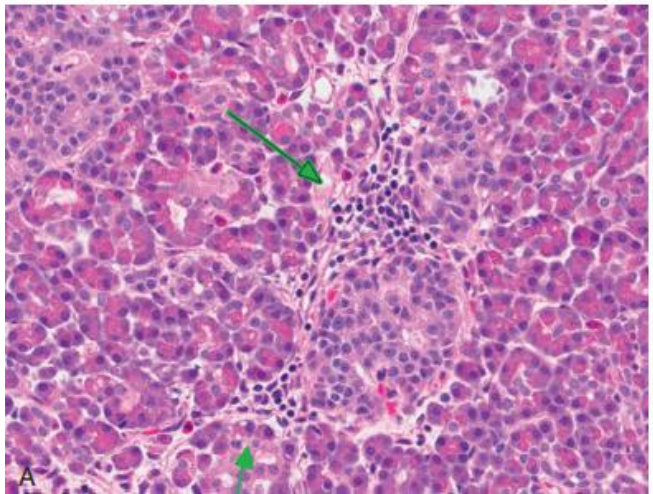
- 1. Excess FFAs. Free fatty acid.
- 2. Adipokines.
- 3. Inflammation:
- inflammatory milieu (mediated by proinflammatory cytokines that are secreted in response to excess nutrients such as FFAs) results in both peripheral insulin resistance and beta cell dysfunction

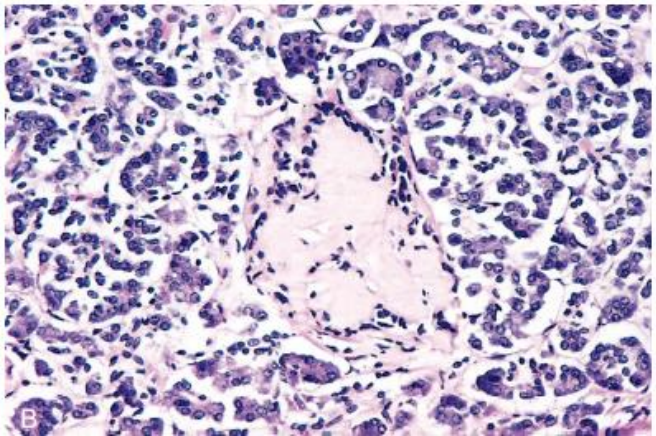
Beta Cell Dysfunction

- 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.

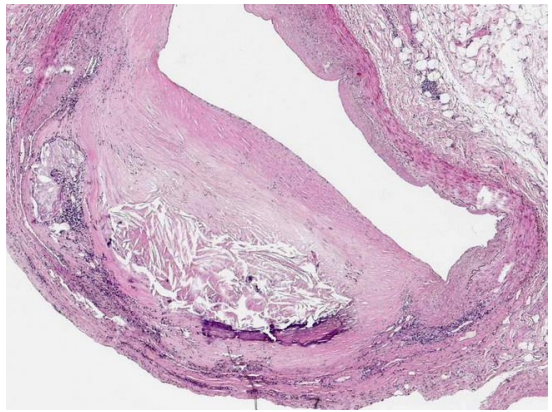


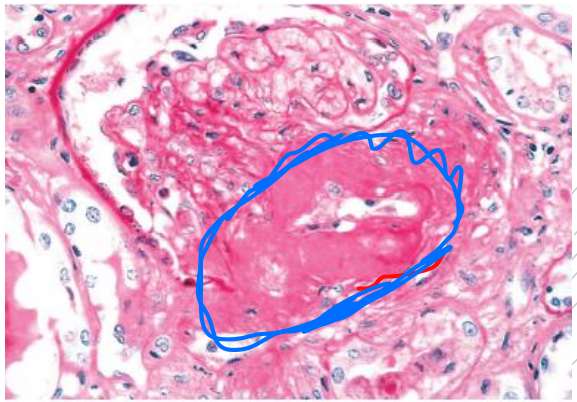


micro vascular: in retina
in hart

Morphology cont.

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



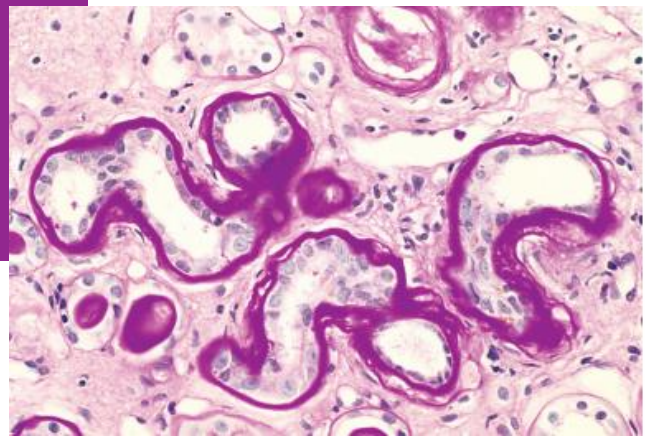


Mechanisms for vascular disease in diabetes

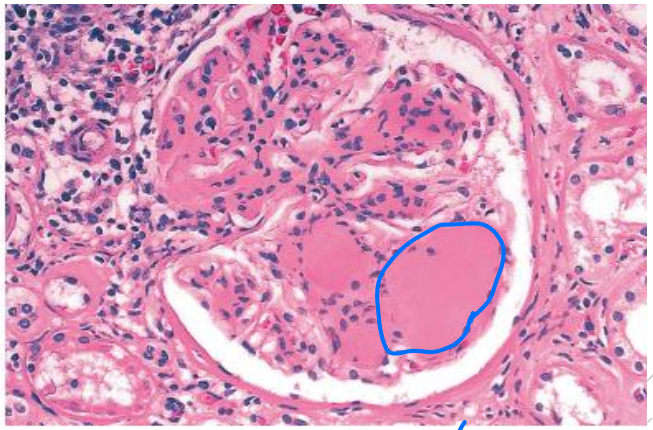
- pathologic effects of advanced glycation end product accumulation.
- impaired vasodilatory response attributable to nitric oxide inhibition,.
- smooth muscle cell dysfunction.
- overproduction of endothelial growth factors.
- chronic inflammation

Diabetic nephropathy.

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



Renal cortex showing thickening of tubular basement membranes .



Nodular glomerulosclerosis (Fibrosis)

No Function unit in the place
(Fibrosis)

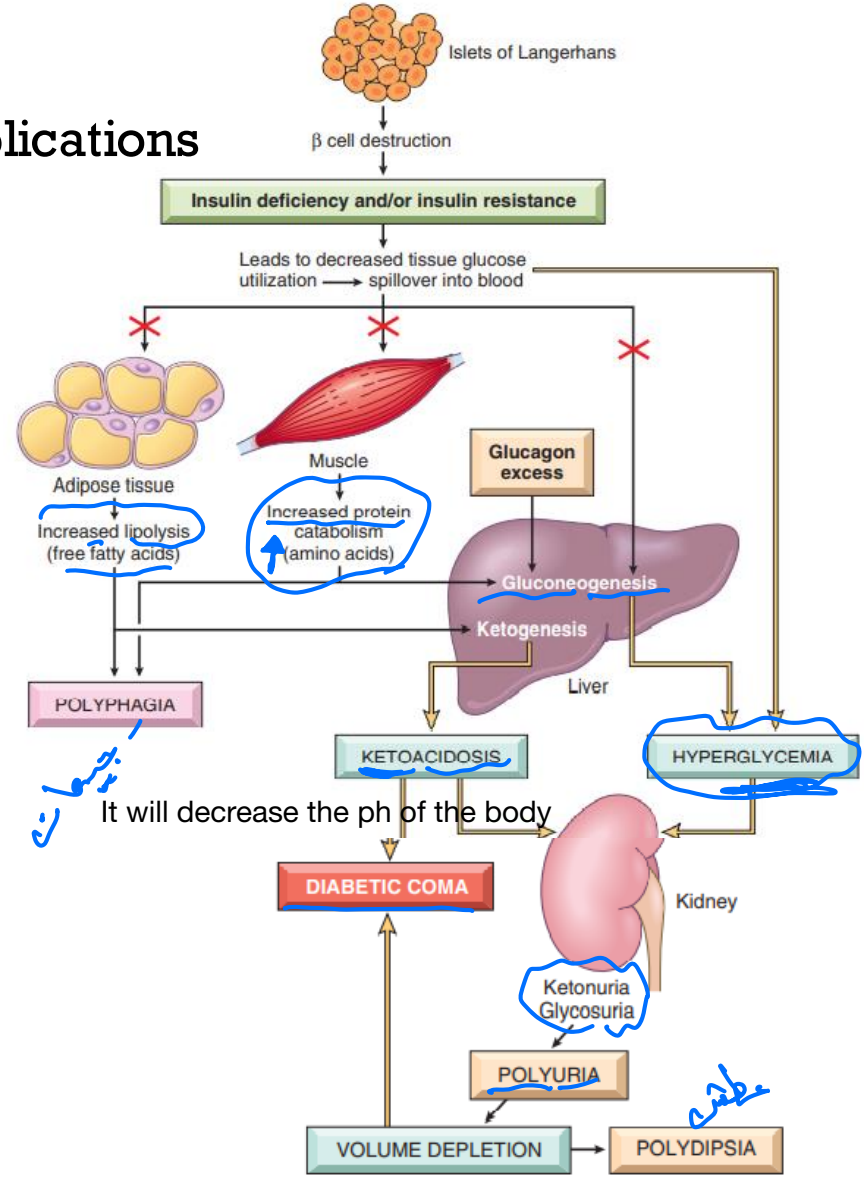
Metabolic Complications.

- 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:

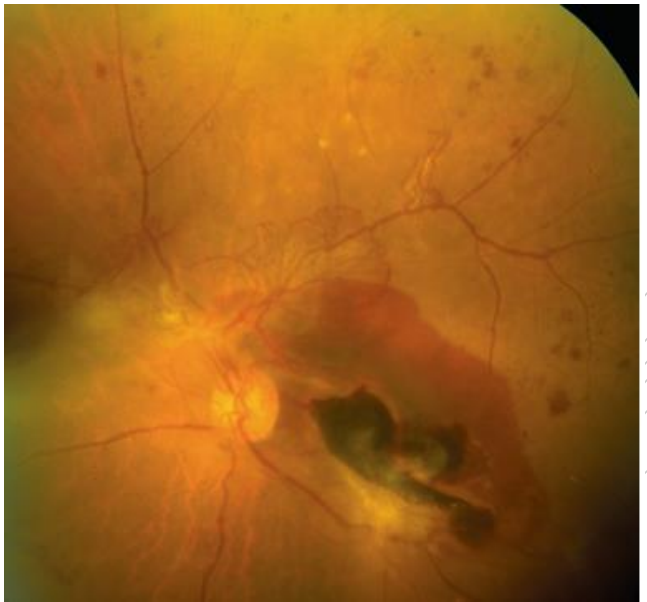
✓ advanced proliferative retinopathy.

✓ retinal hemorrhages.

✓ Exudates.

✓ neovascularization.

✓ tractional retinal detachment



Chronic Complications of Diabetes

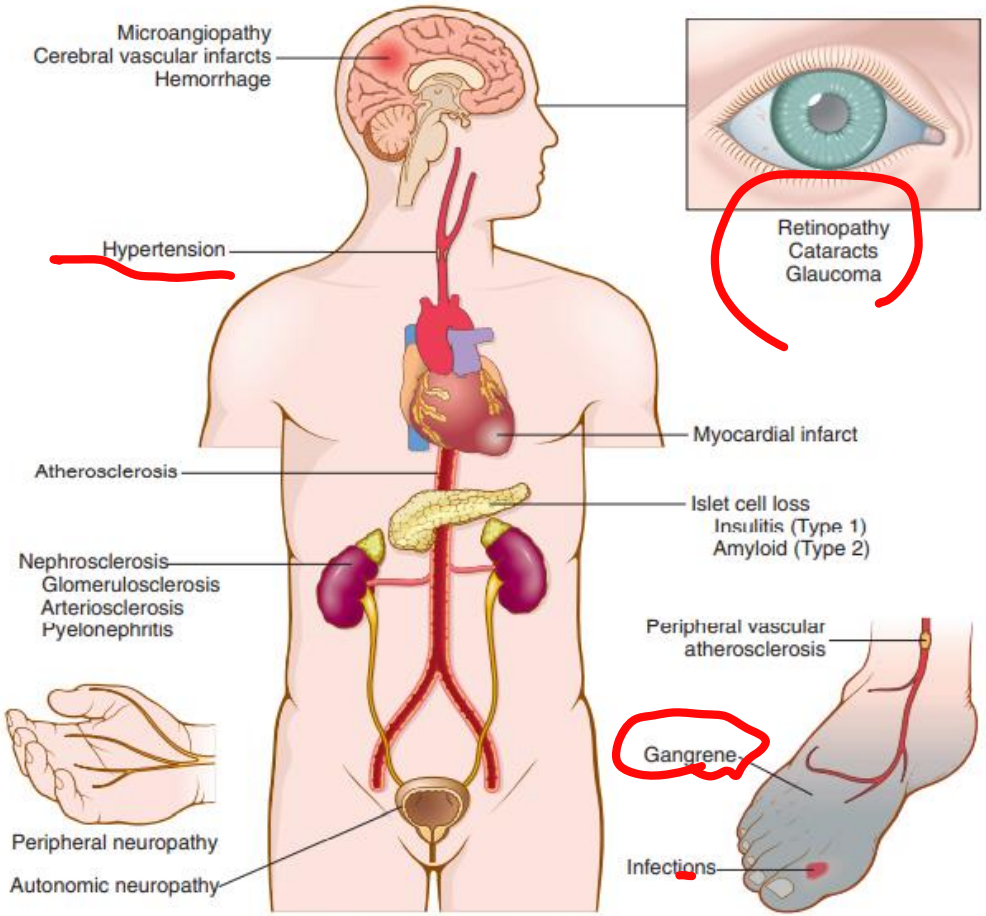


Fig. 20.25 Long-term complications of diabetes.


Thank You