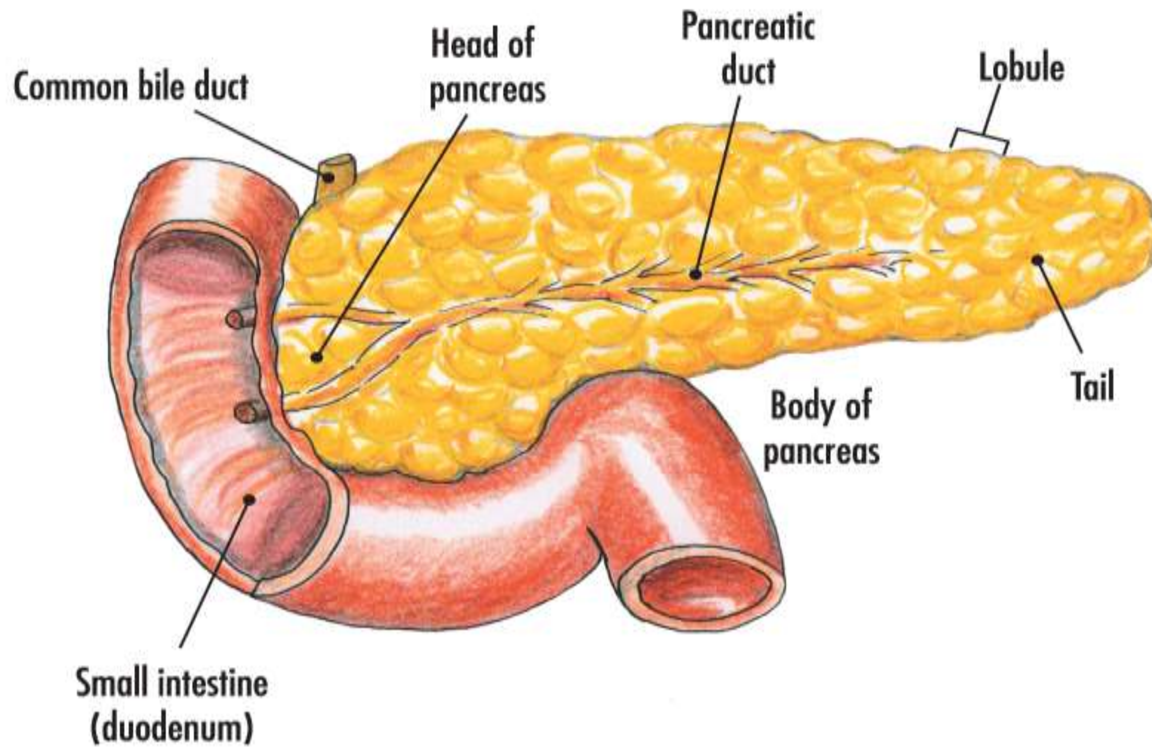
Endocrine pancreas and Diabetes Mellitus

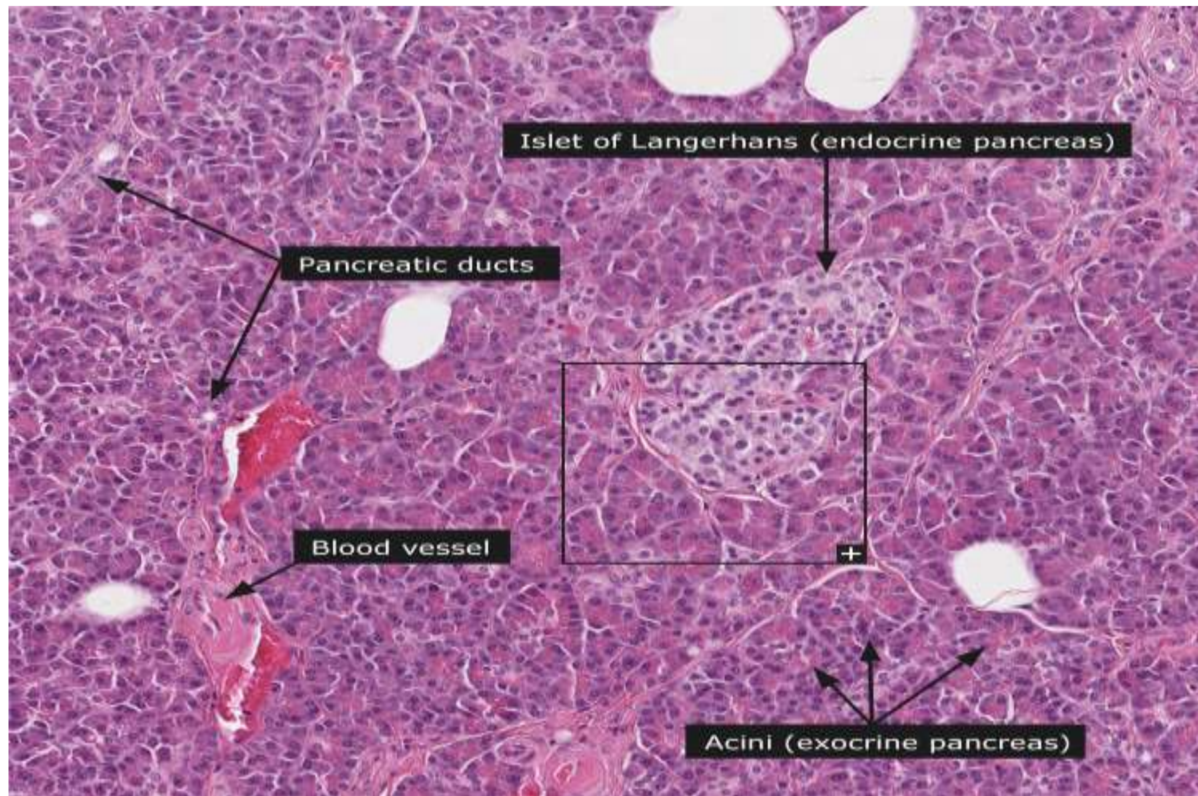
Dr Heyam Awad
FRCPath

The pancreas

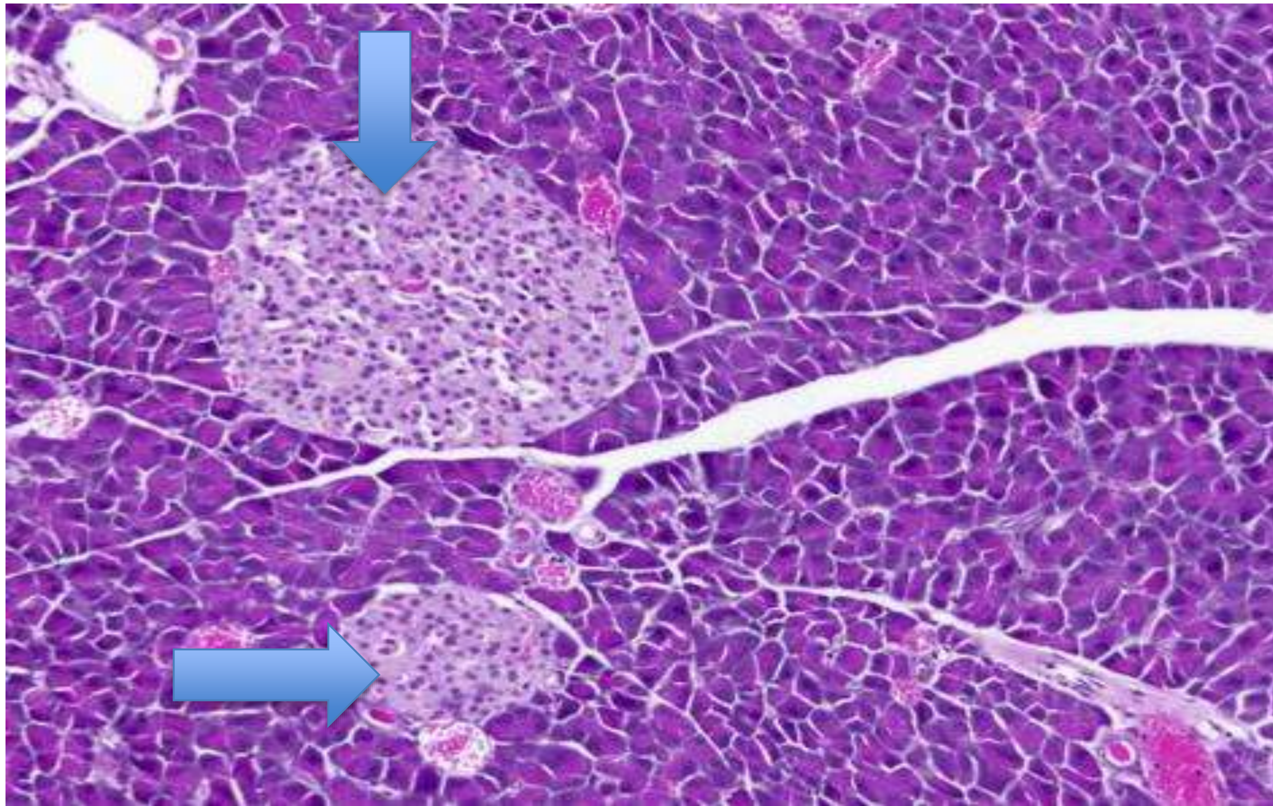


Exocrine pancreas= glands and ducts that secrete enzymes, mainly for digestion.

Endocrine pancreas= Islets of Langerhans (clusters of endocrine cells)that secrete hormones.

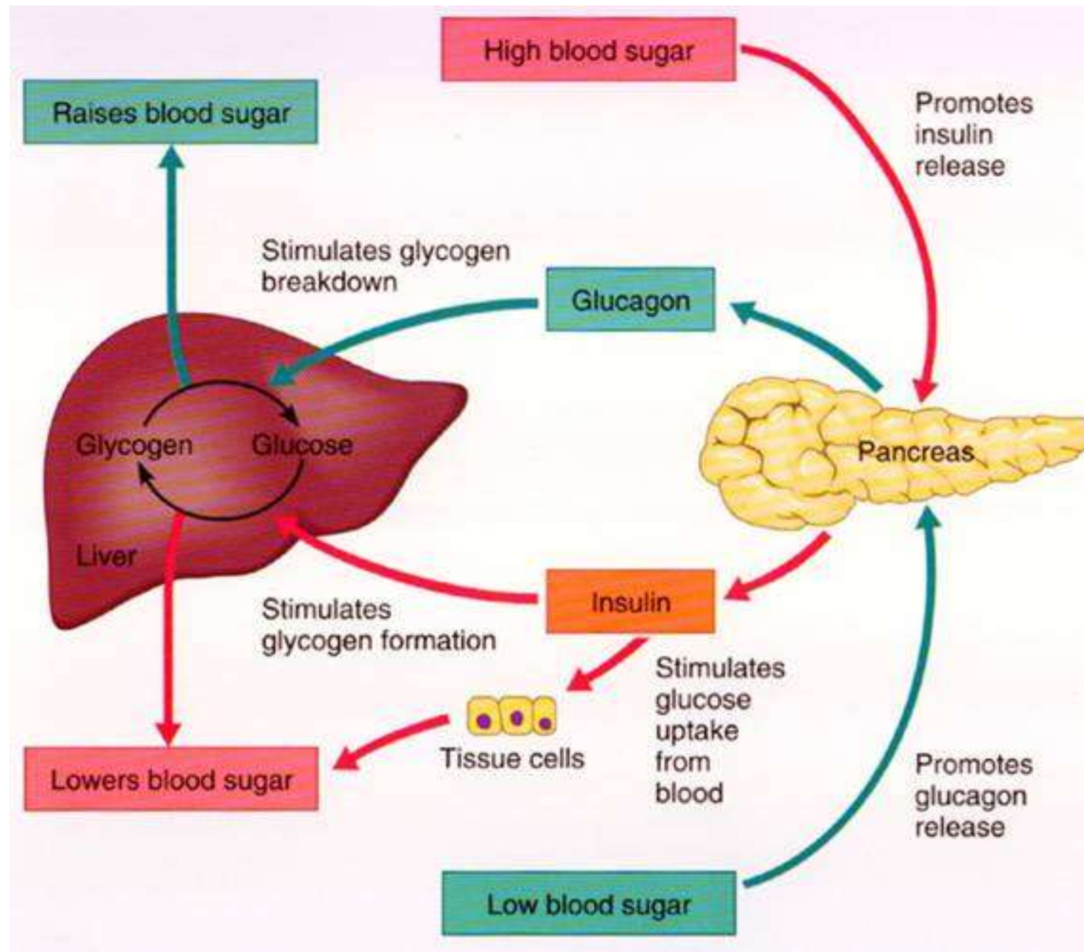


There are around one million Islets (arrows) in the pancreas!



- Islets of Langerhans contain several types of cells, the most important are alpha and beta
- Alpha cells secrete glucagon
- Beta cells secrete insulin
- Delta cells secrete somatostatin, which suppresses both insulin and glucagon.

Insulin effect



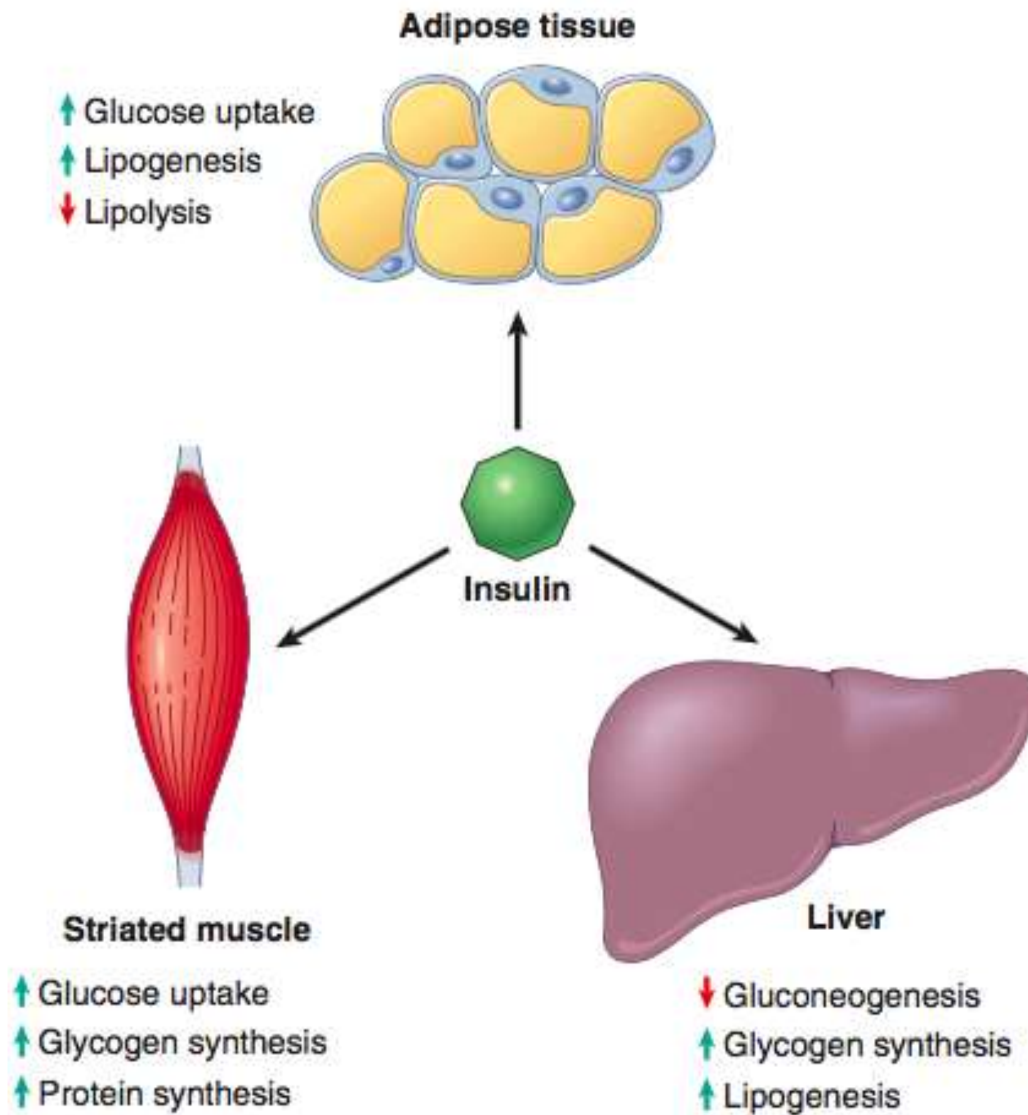


Fig. 20.21 Metabolic actions of insulin in striated muscle, adipose tissue, and liver.

Insulin effect

- Increase uptake of glucose by striated muscle and adipocytes.
- Insulin has anabolic effect on lipid, protein and glycogen.
- Insulin reduces production of glucose from liver.

Diabetes Mellitus (DM)

- DM IS A GROUP OF METABOLIC DISORDERS SHARING HYPERGLYCEMIA.

- Blood glucose levels normally are maintained in a very narrow range, usually 70 to 120 mg/dL.
- This is maintained by the balance between insulin and glucagon

NOTE

Many acute stresses, such as severe infections, burns or trauma, can lead to transient hyperglycemia due to secretion of hormones like catecholamine and cortisol that oppose the action of insulin. **The diagnosis of diabetes requires persistence of hyperglycemia following resolution of the acute stress.**

Classification of DM

- Type 1… absolute insulin deficiency due to destruction of the islets by autoimmune mechanisms
- Type 2.. Relative insulin deficiency …. Peripheral resistance to insulin and inadequate compensatory response of insulin secretion.

TYPE 1 Diabetes :-

- It accounts for 10% of all cases .
- Is an autoimmune disease destructing Pancreatic B cells leading to an absolute deficiency of insulin
- Most commonly develops in childhood, becomes manifest at puberty, and patients depend on exogenous insulin for survival; without insulin they develop complications
- The classic manifestations of the disease occur late in its course, after 90% of the beta cells have been destroyed.

-genetic predisposition.

Pathogenesis:- autoimmune:

a. Defective deletion of self-reactive T cells in the thymus,
b. defects in the functions of regulatory T cells
c. Autoantibodies against B cell antigens, including insulin and enzyme glutamic acid decarboxylase, are detected in the blood of 70% to 80% of patients

??? Effects of viral infections.

Type 2 diabetes :

Accounts for 80% to 90% of cases

- Caused by a combination of

a. Peripheral resistance to insulin action and
b. An inadequate compensatory response of insulin

Insulin resistance: :

- Is defined as the failure of target tissues to respond normally to insulin
- It leads to decreased uptake of glucose in muscle, reduced glycolysis in the liver.

Obesity and Insulin Resistance :Visceral obesity is common in majority of affected patients and insulin resistance is present even with simple obesity un-accompanied by hyperglycemia, indicating a fundamental abnormality of insulin signaling in states of fatty excess.

The risk of diabetes increases as the body mass index increases, suggesting a dose-response relationship between body fat and insulin resistance.

MORPHOLOGY of DM : Pancreas

a. Reduction in the number and size of islets, most often in type 1 particularly with rapidly advancing disease.

b. Leukocytic infiltration of the islets: seen in both type 1 and type 2 DM although it is more severe in type 1

- In both types inflammation is often absent by the time the disease is clinically evident

c. Amyloid replacement of islets in long-standing type 2 diabetes, appear as deposition of pink, amorphous material beginning in capillaries between cells

d. At advanced stages the islets may undergo fibrosis .

Clinical features of DM

(Frequent Urination)

(Excessive Thirst)

Polyphagia (Excessive Hunger/Increased Appetite)

Involuntary Weight Loss

clinical features

a. The hyperglycemia exceeds the renal threshold for reabsorption, and glycosuria induces an osmotic diuresis and *polyuria,*

b. The obligatory renal water loss combined with the hyperosmolarity tends to deplete intracellular water, triggering the thirst centers of the brain and this generates intense thirst (*polydipsia*).

c. Deficiency of insulin leads to catabolism of proteins and fats which tends to induce a negative energy balance, which in turn leads to increasing appetite (*polyphagia)*

COMPLICATIONS OF DM

- Blood vessels: atherosclerosis, hyaline arteriosclerosis, microangiopathy
- Nephropathy : Glomerular lesions, arteriosclerosis, pyelonephritis.
- Ocular complications
- neuropathy

Morphology and clinical manifesations of complications

1. Diabetic Macrovascular Disease.:

- The hallmark is accelerated atherosclerosis affecting the aorta , large and medium-sized arteries and it is more severe with early onset in diabetics than in nondiabetics
- Myocardial infarction due to Coronary artery athero-sclerosis is the most common cause of death in diabetics and is as common in diabetic women as in diabetic men
- Gangrene of the lower extremities is 100 times more common in diabetics than in the general population ..

A Normal artery

Artery wall

Normal blood flow

Artery cross-section

B Narrowing of artery

Abnormal blood flow

Plaque

Narrowed

Plaque

2. Hyaline arteriolosclerosis,

- Is the vascular lesion associated with hypertension
- It takes the form of hyaline thickening of the wall of the arterioles, which causes narrowing of the lumen

Hyaline arteriolosclerosis

3. Diabetic Microangiopathy. :

Diffuse thickening of basement membranes, is most evident in the capillaries of the skin, skeletal muscle, retina and , renal glomeruli,

- It may be seen in renal tubules, nerves, and placenta.
- It underlies the development of diabetic nephropathy, retinopathy , and some forms of neuropathy

4. Diabetic Nephropathy.:

- The kidneys are prime targets of diabetes and renal failure is second only to myocardial infarction as a cause of death from this disease

lesions encountered are:

A. **Glomerular lesions, several forms of glomerulonephritis occur.**
B. **Renal atherosclerosis and arteriolosclerosis** .
C. **Pyelonephritis**,: inflammation in the interstitial tissue and involve the tubules and it has both acute and chronic forms

5. Ocular Complications of Diabetes:

- Visual impairment, and blindness, is one of the more feared consequences of long-standing DM.
- Retinopathy, the most common pattern, consists of changes that are considered by many ophthalmologists to be virtually diagnostic of the disease

Note:

- DM currently is the fourth leading cause of acquired blindness in the United States.
- About 60% to 80% of patients develop a form of diabetic retinopathy approximately 15 to 20 years after diagnosis

6. **Diabetic Neuropathy.:**

a. The most frequent pattern of involvement is that of a peripheral, symmetric neuropathy of the lower extremities affecting motor and sensory nerves

b. Autonomic neuropathy produces disturbances in bowel and bladder function

- The neurologic changes may be the result of microangiopathy and increased permeability of capillaries that supply the nerves, as well as direct axonal damage

Thank you

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