Lecture 4 & 5

Diabetes Mellitus

*432 **Pathology** Team*

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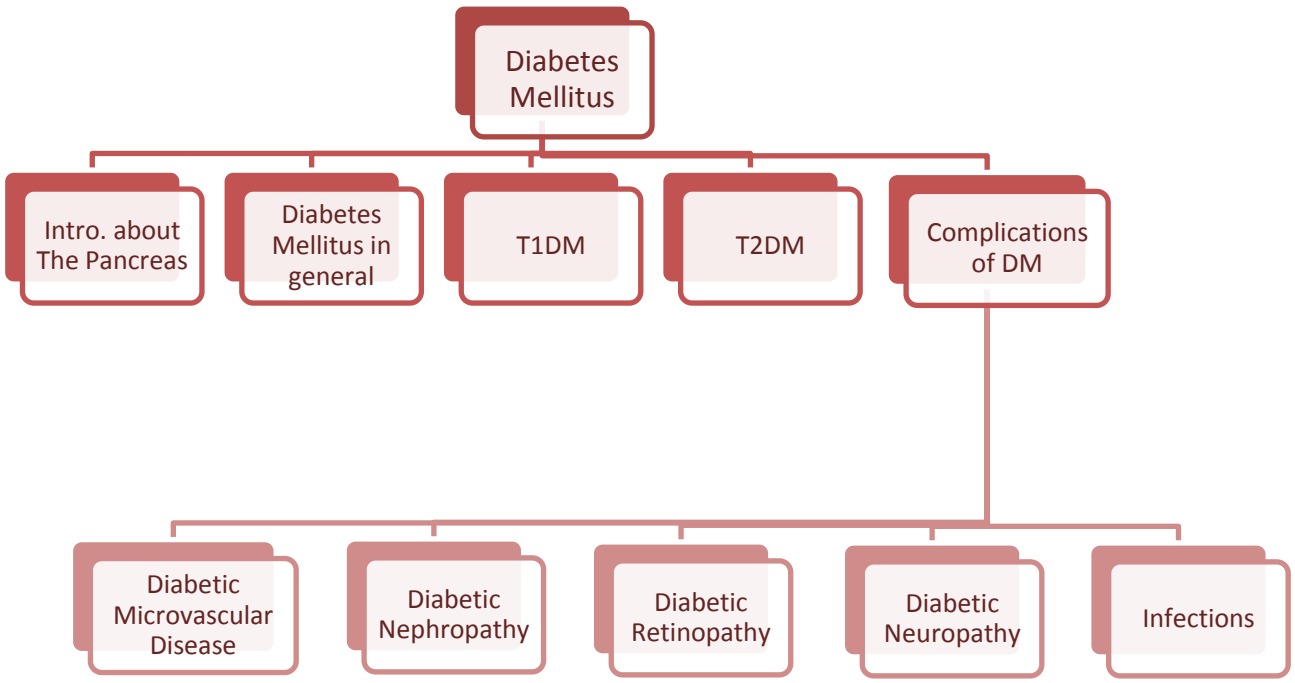
Endocrine Block

Color Index: Female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Diabetes Mellitus

Mind Map:



THE ENDOCRINE PANCREAS

- Pancreas has endocrine and exocrine components.
- The endocrine pancreas composed of 1 million clusters of cells, the islets of Langerhans, which contain four major and two minor cell types .
- The four main types are β, α, δ, and PP (pancreatic polypeptide) cells .
- The β cell produces insulin, as will be detailed in the discussion of diabetes .
- The α cell secretes glucagon.
- δ cells contain somatostatin, which suppresses both insulin and glucagon release.
- PP cells contain a unique pancreatic polypeptide.
- The two rare cell types are D1 cells and enterochromaffin cells.
- PP cells exert several gastrointestinal effects, such as stimulation of secretion of gastric and intestinal enzymes and inhibition of intestinal motility.
- D1 cells elaborate vasoactive intestinal polypeptide (VIP), a hormone that induces glycogenolysis and hyperglycemia; it also stimulates gastrointestinal fluid secretion and causes secretory diarrhea.
- Enterochromaffin cells synthesize serotonin and are the source of pancreatic tumors that cause the carcinoid syndrome.

Diabetes Mellitus

Intro + Epidemiology:

- Sir William Osler defined diabetes mellitus as “a syndrome due to a disturbance in carbohydrate metabolism from various causes, in which sugar appears in the urine, associated with thirst, polyuria, wasting and imperfect oxidation of fats.”
- Major health problem that affects increasing numbers of persons in the developed world.
- Group of metabolic disorders sharing the common underlying feature of **hyperglycemia.**
- According to the American Diabetes Association, diabetes affects over 20 million children and adults, or **7%** of the population, in the United States.
- Approximately 1.5 million new cases of diabetes are diagnosed each year in the United States.
- Diabetes is the leading cause of end-stage renal disease, adult-onset blindness, and non-traumatic lower extremity amputations.
- Two major forms of diabetes mellitus are recognized, distinguished by their underlying pathophysiology.
- In Saudi, 40% of the population are diagnosed with diabetes.

Diagnosis of DM:

Any one of three criteria:

1. A random glucose concentration greater than **200 mg/dL**, with classical signs and symptoms.
2. A fasting glucose concentration greater than **126 mg/dL** on more than one occasion.
3. An abnormal oral glucose tolerance test (OGTT), in which the glucose concentration is greater than **200 mg/dL** 2 hours after a standard carbohydrate load.
4. HBA_1C is now used to diagnose DM as well. And it has half-life (120 days).

- Those with fasting glucose concentrations greater than 100 mg/dL but less than 126 mg/dL, or OGTT values greater than 140 mg/dL but less than 200 mg/dL, are considered to have impaired glucose tolerance, also known as "pre-diabetes."
- Pre-diabetic individuals have a significant risk of progressing to overt diabetes over time, with as many as 5% to 10% advancing to diabetes mellitus per year. In addition, pre-diabetics are at risk for cardiovascular disease.

Classification of DM:

1. Type 1 diabetes (formerly known as **insulin-dependent (IDDM)** or **juvenile-onset diabetes**, is caused by **autoimmune destruction of the insulin-producing B-cells** in the pancreatic islets of Langerhans, and affects less than 10% of all patients with diabetes. Cause: β-cell destruction, usually leading to absolute insulin deficiency)

2. Type 2 diabetes (formerly known as **non–insulin-dependendent (NIDDM)** or **maturity onset diabetes**, is typically associated with **obesity** and results from a complex interrelationship between resistance to the metabolic action of insulin in its target tissues and inadequate secretion of insulin from the pancreas). (Combination of insulin resistance and β-cell dysfunction)

3. Genetic defects of β-cell function: (There are genetic defects, but it will not appear until some environmental factors (diet, obesity, and physical activity) play around. That explains why we didn't have MODY in the past 40-50 years)

- Maturity-onset diabetes of the young (MODY) (Explained later) caused by mutations in:
- Hepatocyte nuclear factor 4α (HNF4A), MODY1
- Glucokinase (GCK), MODY2
- Hepatocyte nuclear factor 1α (HNF1A), MODY3
- Pancreatic and duodenal homeobox 1 (PDX1), MODY4
- Hepatocyte nuclear factor 1β (HNF1B), MODY5
- Neurogenic differentiation factor 1 (NEUROD1), MODY6

4. Genetic defects in insulin action
Type A insulin resistance, Lipoatrophic diabetes, including mutations in PPARG

5. Exocrine pancreatic defects: Chronic pancreatitis, Neoplasia, Cystic fibrosis. (destruction of the pancreas)

6. Infections: CMV, **Coxsackie B virus**, Congenital rubella

7. Drugs: Glucocorticoids, Thyroid hormone, Interferon-α, β-adrenergic agonists…

8. Genetic syndromes associated with diabetes: Down's, Kleinfelter syndrome, Turner syndrome, Prader-Willi syndrome (remember that some syndrome can show diabetes).

9. Gestational diabetes mellitus: develops in a few percent of pregnant women, owing to the insulin resistance of pregnancy combined with a B-cell defect, but almost always abates following parturition.

NOTE: Abates: becomes less active,

Parturition: Giving birth… so it means that it almost always disappears after giving birth

Gestational diabetes mellitus: the baby will be larger (macrosomia) due to high hyperglycemia in the mother triggers the baby's pancreas to produce insulin (anabolic hormone) that's why her baby has excess weight , and that's why the doctor used to use C section during labor.

10. Diabetes can also occur secondary to other endocrine conditions or drug therapy, especially in patients with Cushing's syndrome or during treatment with glucocorticoids.

NOTE:

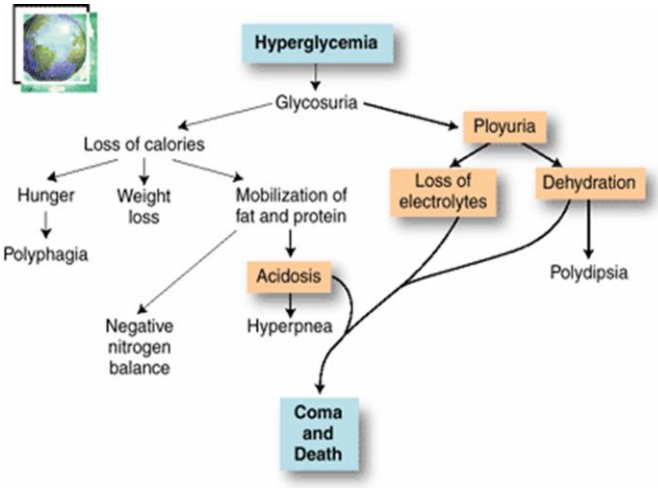
MODY: Maturity-onset diabetes of the young (MODY):

- Rare **autosomal dominant** form of inherited diabetes.
- Associated with a variety of gene defects that affect B-cell function, including **glucokinase**, an important sensor for glucose metabolism within the B-cell, and several mutations in genes that control the development and function of the B-cells.
- Mutations in these genes, however, do not account for the typical prevalent forms of T2DM.

Management:

- **Type 1:** Insulin absolutely required.
- **Type 2:** lifestyle modification; diet, exercise, oral drugs, often insulin supplement needed.

Type 1 Diabetes Mellitus



- Type 1 diabetes mellitus (T1DM), formerly known as insulin-dependent (IDDM)or juvenile-onset diabetes
- Autoimmune destruction of the B cells in the islets of Langerhans.
- The disease is characterized by:
  - few if any functional B cells in the islets of Langerhans and
  - Extremely limited or nonexistent insulin secretion.
- As a result, body fat rather than glucose is preferentially metabolized as a source of energy; those people in many times are thin people.
- In turn, oxidation of fat overproduces ketone bodies (acetoacetic acid and B-hydroxybutyric acid), which are released into the blood from the liver and lead to metabolic ketoacidosis, ketone bodies differentiate clinically between T1DM and T2DM.
- Hyperglycemia results from unsuppressed hepatic glucose out-put and reduced glucose disposal in skeletal muscle and adipose tissue and leads to glucosuria and dehydration from loss of body water into the urine.
- Always glucose urea induces polydipsia, dehydration, loss of calories, polyphagia, negative nitrogen balance and polyuria.
- If uncorrected, the progressive acidosis and dehydration ultimately lead to coma and death.

EPIDEMIOLOGY:

- T1DM is most common among northern Europeans and their descendants and is **not seen** as frequently among Asians, African-Americans, or Native Americans.
- Can develop at any age, the peak age of onset coincides with puberty.
- Some older patients may present with autoimmune B-cell destruction that has developed slowly over many years.
- An increased incidence in late fall and early winter has been documented in many geographical areas.

PATHOGENESIS:

Represents interplay of genetic susceptibility, autoimmunity and environmental factors.

Genetic Factors:

- Genome-wide association studies have identified multiple genetic susceptibility loci for type 1 diabetes, as well as for type 2 diabetes.
- For type 1 diabetes the most important is the **HLA locus on chromosome 6p21.**
- 90% to 95% of Caucasians with this disease have either a **HLA-DR3 or HLA-DR4** haplotype (N: 30-40%).
- 40% to 50% of type 1 diabetics are combined DR3/DR4 heterozygotes (Normal 5%).
- Several *non-HLA genes* also confer susceptibility to type 1 diabetes.
- Fewer than 20% of those with T1DM have a parent or sibling with the disease.
- Monozygotic twins: 50% concordant.
- The children of fathers withT1DM are three times more likely to develop the disease than are children of diabetic mothers.

Autoimmunity:

There is always autoimmune destruction of B-cells and we can prove that by pathologic examinations. Patients who die shortly after the onset of the disease often exhibit an infiltrate of mononuclear cells, lymphocytes and plasma cells, in and around the islets of Langerhans, termed Insulitis. (Inflammation of the pancreas in the early stage of diabetes).

- Cell-mediated immune mechanisms are fundamental to the pathogenesis of T1DM, **CD8+T lymphocytes** pre-dominate, although some CD4+cells are also present .
- The infiltrating inflammatory cells also elaborate cytokines, for example, IL-1, IL-6, interferon-alpha, and nitric oxide, which may further contribute to B cell injury.
- An autoimmune origin for T1DM was initially suggested by the demonstration of circulating antibodies against components of the B cells (including insulin itself) in most newly diagnosed children with diabetes. The autoimmunity in some T1DM can be predictable by measuring these antibodies in the peripheral blood.
- Many patients develop islet cell antibodies months or years before insulin production decreases and clinical symptoms appear.
- Detection of serum antibodies to islet cells and certain islet antigens remains a useful clinical tool for differentiating between type 1 and type 2 diabetes.
- The destruction of B-cells in T1DM generally develops slowly over years.

REMEMBER:

- CD4 are the T-cell helper.
- CD8 are the T-cell suppressor or CYTOTOXIC
- CD4/CD8 → 2/1
- Most common cells in the peripheral blood are CD4.

Environmental Factors:

- Viruses and chemicals, CMV, Mumps and **group B Coxsackie**, Rubella viruses.
- Geographical and seasonal differences in the incidence of T1DM further suggest that environmental factors are important in its pathogenesis.
- Lymphocytic infiltrate in the islets (insulitis), sometimes accompanied by a few macrophages and neutrophils. The major inflammatory cells infiltrate are lymphoplasma cells.

As the disease becomes chronic, the B cells of the islets are progressively depleted of Beta cells.
Fibrosis of the islets is **uncommon.**
In contrast to T2DM, deposition of amyloid in the islets of Langerhans **is absent** in T1DM.
The exocrine pancreas in chronic T1DM often exhibits diffuse interlobular and interacinar fibrosis, accompanied by atrophy of the acinar cells.

There is no cure of DM1, Except (Transplantation) of pancreas, and if this choice is taken, the doctor used to do kidney transplantation as well (pancreatic kidney transplantation (PKT))).
Combined transplantation of the kidney and pancreas is performed for those who have kidney failure as a complication of insulin-dependent diabetes mellitus (also called Type I diabetes). Kidney and pancreas transplant candidates might be currently on dialysis or might require dialysis in the near future.

After combined transplantation of the kidney and pancreas, the kidney will be able to filter and excrete wastes so dialysis will not be needed. The transplanted pancreas will produce insulin to control the diabetes.

For further reading:
http://my.clevelandclinic.org/services/kidney_transplantation/hic_what_is_a_kidney_pancreas_transplant.aspx

Type 2 Diabetes mellitus

Introduction:

Formerly known as non–insulin-dependent (NIDDM) or maturity-onset diabetes is typically associated with obesity and results from a complex interrelationship **(Heterogeneous disorder)** between:

1. Resistance to the metabolic action of insulin in its target tissues.
2. Inadequate secretion of insulin from the pancreas.

Overt diabetes (the symptoms appear) usually in patient with both of these defects.

Epidemiology:

Almost 10%of persons older than 65 years of age are affected, and 80% of patients with T2DM are overweight. The disease usually develops in adults, with an increased prevalence in obese persons and in the elderly.

Recently, T2DM has been appearing in increasing numbers in younger adults and adolescents, owing to worsening obesity and lack of exercise in this age group.

Hyperglycemia in T2DM is a failure of the B-cells to meet an increased demand for insulin in the body.

Pathogenesis:

- Complex interplay between underlying resistance to the action of insulin in its metabolic target tissues and reduction in glucose-stimulated insulin secretion **(peripheral resistance and not enough insulin from beta cell).**
- Progression to overt diabetes in susceptible populations occurs most commonly in patients exhibiting both of these defects.

1- GENETIC FACTORS:

- Multi-factorial.
- Family history of diabetic: 60% of patients have either a parent or a sibling with the disease. Among monozygotic twins, both are almost always affected.
- No association with genes of the major histocompatibility complex (MHC), as seen in T1DM.
- The inheritance pattern is complex and thought to be due to multiple interacting susceptibility genes.
- Constitutional factors such as obesity (which itself has strong genetic determinants), hypertension, and the amount of exercise influence the phenotypic expression of the disorder.

2- GLUCOSE METABOLISM:

In a normal person, the extracellular concentration of glucose in fed and fasting states is maintained in a tightly limited range. This rigid control is mediated by the opposing actions of insulin and glucagon.

Following a carbohydrate-rich meal, absorption of glucose from the gut leads to an increase in blood glucose, which stimulates insulin secretion by the pancreatic B-cells and the consequent insulin-mediated increase in glucose uptake by skeletal muscle and adipose tissue.

At the same time, **insulin suppresses hepatic glucose production.**

3- B-CELL FUNCTION:

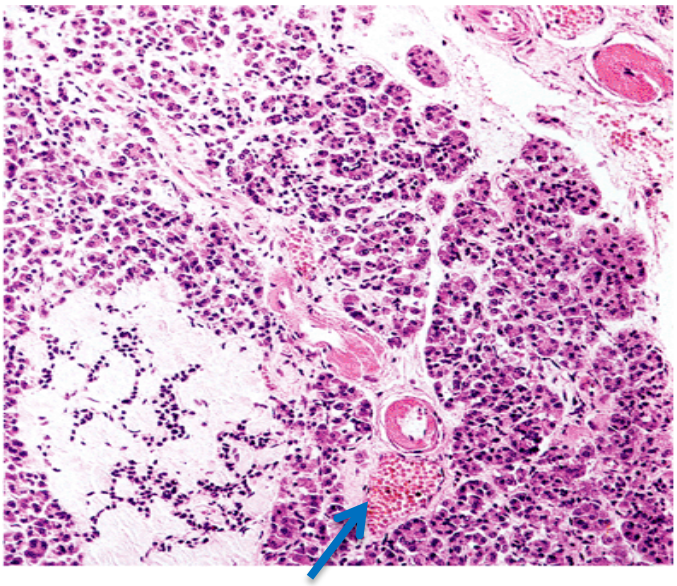
Persons with T2DM exhibit impaired B-cell insulin release in response to glucose stimulation. This functional abnormality is specific for glucose, since the B-cells retain the ability to respond to other stimulants, such as amino acids.

B-cell function may also be affected by the chronically elevated plasma levels of free fatty acids that occur in obese persons. "The free fatty acids work against the action of insulin which explain why obesity is a predisposing factor in T2DM" **(that's why they should monitor food)**.

Histopathology:

Neither morphologic changes nor reduction in number of B-cells are seen here. (Absent)

In some islets, fibrous tissue accumulates, sometimes to such a degree that they are obliterated. Fibrous tissue accumulation.



Amyloid deposition (amyloidosis) around capillaries (arrow) and between cells is often present particularly in patients over 60 years of age. Very important

REMEMBER:

- T2DM is a heterogeneous disorder, resulting from insulin resistance by target tissues + an inadequate insulin secretion.
- Usually affect old and obese people, some life styles are causes.
- Fibrosis and amyloidosis are important characteristics.

For more details:

http://www.youtube.com/watch?v=OXAe3eOjqCk

http://education-portal.com/academy/lesson/type-2-diabetes-risk-factors-signs-treatment.html#lesson

Table for comparison between the two types

Type1 DM	Type2 DM
- Diabetes Usually before 20	-Usually after 30
- Abrupt; symptomatic (polyuria, polydipsia, dehydration); often sever with ketoacidosis	-Gradual; usually subtle
-Normal weight ; recent weight loss is common	- Overweight
-Genetics <20%	->60%
-Monozygotic Twins 50% concordant	-90% concordant
-HLA Association , ABS to islet cell AG +	-No
-Histopatholog . Early—inflammation . Late—atrophy and fibrosis	-Histopathology: Late-Fibrosis, amyloid
B-cell mass: Markedly reduced	- Normal or slightly reduced
-Insulin levels :Markedly reduced	- Elevated or normal

NOTE:

- Ketoacidosis is typical for type 1 diabetes.
- Amyloid deposition is typical for type 2 diabetes.
- Number of β cells in type 2 diabetes most of the time almost normal.
- Insulin levels in type 2 diabetes always normal or elevated.

Complications of Diabetes

1- Diabetic Microvascular Disease (microangiopathy)

- Responsible for many of the complications of diabetes, Including renal failure and blindness.
- Arteriolosclerosis and capillary basement membrane thickening (eye, kidney) are characteristic vascular changes in diabetes.
- The frequent occurrence of Hypertension contributes to the development of the arteriolar lesions. In addition, deposition of basement membrane proteins, which may also become glycosylated, increases in diabetes.
- Aggregation of platelets in smaller blood vessels and impaired fibrinolytic mechanisms **(hypercoagulable state > fibrinotic mechanism not working properly > clot)** have also been suggested as playing a role in the pathogenesis of diabetic microvascular disease that would effect:
- Tissue perfusion, wound and chronic ulcers healing.
- Reduce the blood flow to the heart (which is already compromised by coronary atherosclerosis).

NOTE:

In the periphery it can lead to a unique type of necrosis, gangrenous necrosis (dry gangrene) which is the clinical term for the coagulative necrosis resulting from ischemia + superimposed bacterial infection.
The capillaries' basal lamina will markedly be thickened by concentric layers of hyaline materials composed predominantly of type IV collagen.

When they have myocardial infarction (MI) they don't feel the pain because of the neuropathy.

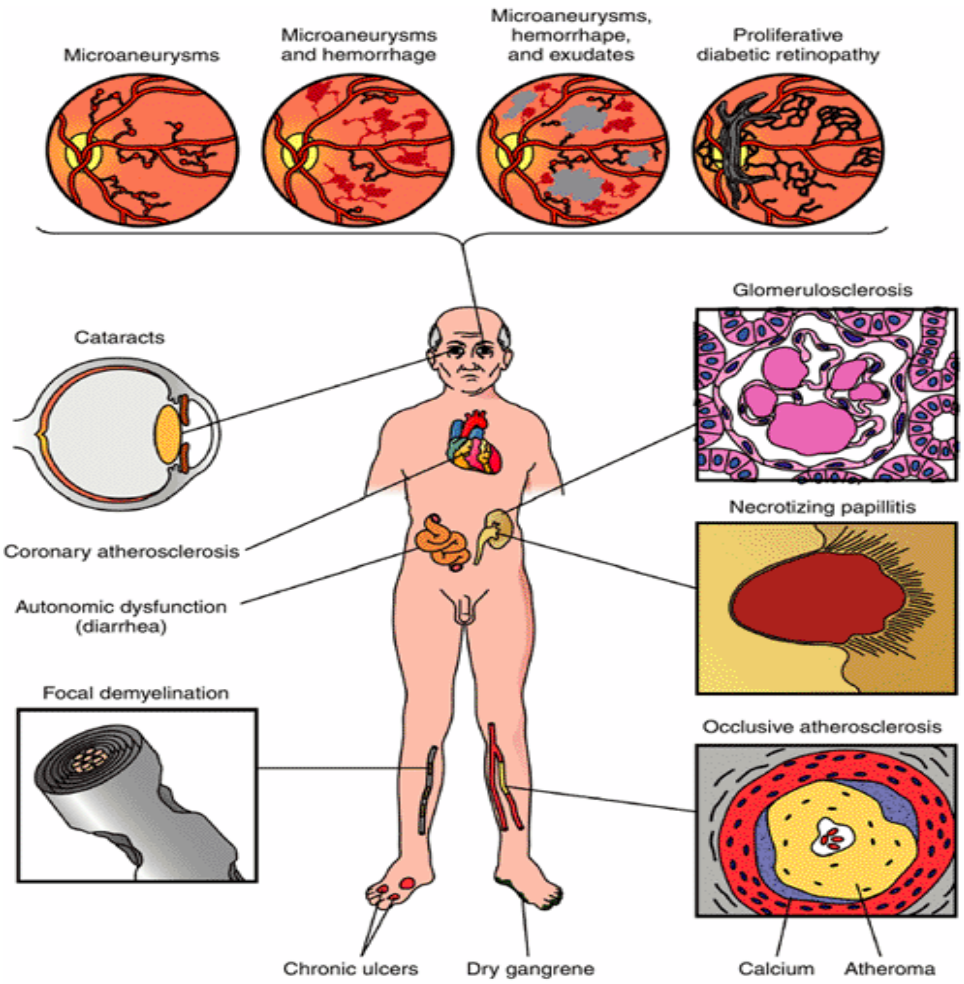
The effects of microvascular disease on tissue perfusion and wound healing are profound.

↓

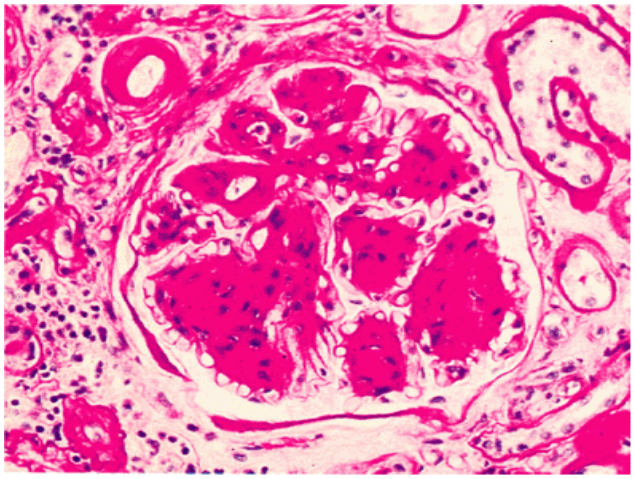
Reduce blood flow to the heart, which is already compromised by coronary atherosclerosis.

↓

Healing of chronic ulcers that develop from trauma and infection of the feet in diabetic patients is commonly defective.



2- Diabetic Nephropathy



- Up to 40% of T1DM develop renal failure, while the percentage is 20% in T2DM.
- Diabetic nephropathy accounts for one third of all new cases of renal failure.
- The prevalence of diabetic nephropathy increases with the severity and duration of the hyperglycemia.
- **Kidney disease due to diabetes is the most common reason for renal transplantation in adults**.
- The glomeruli in the diabetic kidney exhibit a unique lesion termed:
  Kimmelstiel-Wilson disease = nodular glomerulosclerosis

Kimmelstiel-Wilsonm

This is nodular glomerulosclerosis (the Kimmelstiel-Wilson lesion) of diabetes mellitus. Nodules of pink hyaline material , in regions of glomerular capillary loops in the glomerulus. This is due to a marked increase in mesangial matrix from damage as a result of non-enzymatic glycosylation of proteins. This is one form of chronic kidney disease (CKD) with loss of renal function over time. ,

Microaneurysm > adhesion is week between capillary + mesentery > aneurysm dilatation > try to fill it by producing mesential matrix > nodular appearance.

3-Diabetic Retinopathy:

- It is the most devastating ophthalmic complication of diabetes.
- The most important cause of blindness in the United States in persons under the age of 60 years.
- The risk is higher in T1DM than in T2DM.
- 10% of patients with T1DM of 30 years' duration become legally blind. There are many more patients with T2DM, so these are the most numerous patients with diabetic retinopathy. They should check every 6 months.

Ocular involvement can take other forms like: Non-proliferative retinopathy, cataract formation or glaucoma. Some changes can be diagnostic for DM.

Stages of proliferative retinopathy:
Microaneurysms
↓
Microaneurysms
+ hemorrhage
↓
Microaneurysms and hemorrhage
+ Exudate
↓
Proliferative diabetic retinopathy
(can't be treated)

4-Diabetic Neuropathy: (both nerve and the blood supply of the nerve are affected)

- Characterized by pain and abnormal sensations in the extremities.
- The most common and distressing complications of diabetes.
- Microvasculopathy involving the small blood vessels of nerves contributes to the disorder.
- Affects Sensory and Autonomic Innervations, Peripheral sensory impairment, and autonomic nerve dysfunction. (diarrhea)
- Changes are complex, and abnormalities in axons, the myelin sheath, and Schwann cells have all been found.
- Peripheral neuropathy can leads to foot ulcers.
- Plays a role in the painless destructive joint disease that occasionally occurs.

5-Infections:

- Bacterial and Fungal Infections Occur in Diabetic Hyperglycemia if Poorly Controlled
- Renal papillary necrosis may be a devastating complication of bladder infection.
- Mucormycosis: A dangerous infectious complication of poorly controlled diabetes is often fatal fungal infection tends to originate in the nasopharynx or paranasal sinuses and spreads rapidly to the orbit and brain.(Diabetic patient have flu that is not healing send for ENT may have **Mucormycosis (zygomycosis) : calture ny GMS , PSD > broad, non-septate hyphae)**.

Gestational diabetes

- Diabetes occurring during pregnancy.
- May put both the mother and the fetus at risk.
- Develops in only a few percent of seemingly healthy women during pregnancy.
- It may continue after parturition in a small proportion of these patients.
- Pregnancy is a state of insulin resistance.
- These women highly susceptible to overt T2DM later in life.

Diabetes & Associated Complications

http://www.youtube.com/watch?v=DpdlJ79ACCo

SUMMARY FROM ROBBINS

Type 1 diabetes is an autoimmune disease characterized by a progressive destruction of islet beta cells, leading to absolute insulin deficiency. Both autoreactive T cell and autoantibodies are involved.

Type 2 diabetes is caused by insulin resistance and beta cell dysfunction, resulting in relative insulin deficiency autoimmunity is not involved.

Obesity has an important relationship with insulin resistance (T2DM), probably mediated by cytokines released from adipose tissues (adipocytokines).Other players in the *adipo-insulin axis* include FFAs (which may cause lipotoxicity) and the PPARγ receptor, which modulate adipocytokines levels.

Monogenic forms of diabetes (caused by a single-gene defect) are uncommon. In contrast, genetically complex forms (like type 1,2) are the most common.

The long-term complications are similar in both types, affecting mainly blood vessels, and the kidneys, nerves and eyes. The development of these complications is attributed to three underlying mechanisms: formation of advanced glycation end products (AGEs), activation of PKC and disturbance in polyol pathways leading to oxidative stress.

Questions

1/ A 14-year-old boy presents for a pre-summer camp physical examination. Routine urinalysis discloses 3+ glucosuria. He admits to thirst and frequent urination, accompanied by a 4-kg weight loss over the past few months. His parents note that he had a flu-like illness 5 months ago. His blood glucose is 220 mg/dL. Which of the following best explains the pathogenesis of hyperglycemia in this patient?

(A) Excess dietary glucose

(B) Increased peripheral insulin uptake

(C) Irregular insulin secretion

(D) Islet cell destruction

2/ A 10-year-old boy with a recent onset of diabetes mellitus dies following an automobile accident. Injury to pancreatic islet cells in this patient was most likely mediated by which of the following mechanisms of disease?

(A) Antibody-mediated islet cell destruction
(B) Cell-mediated immunity
(C) Direct viral cytopathic effects
(D) Hypovolemic shock

3/ A 56-year-old man with a 14-year history of diabetes mellitus presents with poor vision, peripheral vascular disease, and mild proteinuria. Which of the following is the best monitor of the control of blood sugar levels in this patient?

(A) Glycosylated hemoglobin
(B) Islet cell autoantibody
(C) Serum myoinositol
(D) Serum sorbitol

4/ A 55-year-old obese woman (body mass index = 33 kg/m2) complains of declining visual acuity. Funduscopic examination shows peripheral retinal microaneurysms. Urinalysis reveals 3+ proteinuria and 3+ glucosuria. Serum albumin is 3 g/dL, and serum cholesterol is 350 mg/dL. These clinicopathologic findings are best explained by which of the following mechanisms of disease?

(A) Anti-insulinantibodies
(B) Increased peripheral insulin uptake
(C) Irregular insulin secretion
(D) Peripheral insulin resistance

5/ A 60-year-old man with diabetes mellitus complains of deep burning pain and sensitivity to touch over his hands and fingers. Nerve conduction studies show slow transmission of impulses and diminished muscle stretch reflexes in the ankles and knees. Sensations to vibrations and light touch are also markedly diminished. The development of polyneuropathy in this patient correlates **best** with which of the following conditions?

(A) Anti-insulin antibody titer
(B) Hyperglycemia
(C) Insulin deficiency
(D) Intermittent hypoglycemia

6/ A 65-year-old obese man (body mass index = 32 kg/m2) presents with a 2-year history of difficulty walking. Physical examination reveals chronic ulcers in the lower extremities. Funduscopic examination reveals proliferative retinopathy. Which of the following best describes the pathogenesis of chronic ulcers on the legs of this patient?

(A) Abnormal glycosylation of hemoglobin
(B) Inadequate leukocytic response to infection
(C) Low concentrations of insulin in tissues
(D) Microvascular disease

7/ A 58-year-old man with a long-standing history of type 2 diabetes mellitus suffers a massive hemorrhagic stroke and expires. Examination of the pancreas shows hyalinization of many islets of Langerhans. Which of the following characterizes the material within the islets of Langerhans?

(A) Amyloid
(B) Collagen type IV
(C) Fibrin
(D) Fibronectin

8/ A 50-year-old man with diabetes mellitus develops swelling in his lower extremities. Urinalysis shows 3+ proteinuria and 3+ glucosuria. Serum albumin is 3 g/dL and serum cholesterol is 350 mg/ dL. A kidney biopsy is done. Which of the following glomerular changes is evident in this biopsy specimen?

(A) Amyloidosis
(B) Deposition of basement membrane like material
(C) Endothelial cell hyperplasia
(D) Fibrinoid necrosis
(E) Mesangial hyperplasia

Answers:

- 1- D
- 2- B
- 3- A
- 4- D
- 5- B
- 6- D
- 7- A
- 8- B

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us on: 432PathologyTeam@gmail.com