433 Teams

MEDICINE

5 | Type II Diabetes

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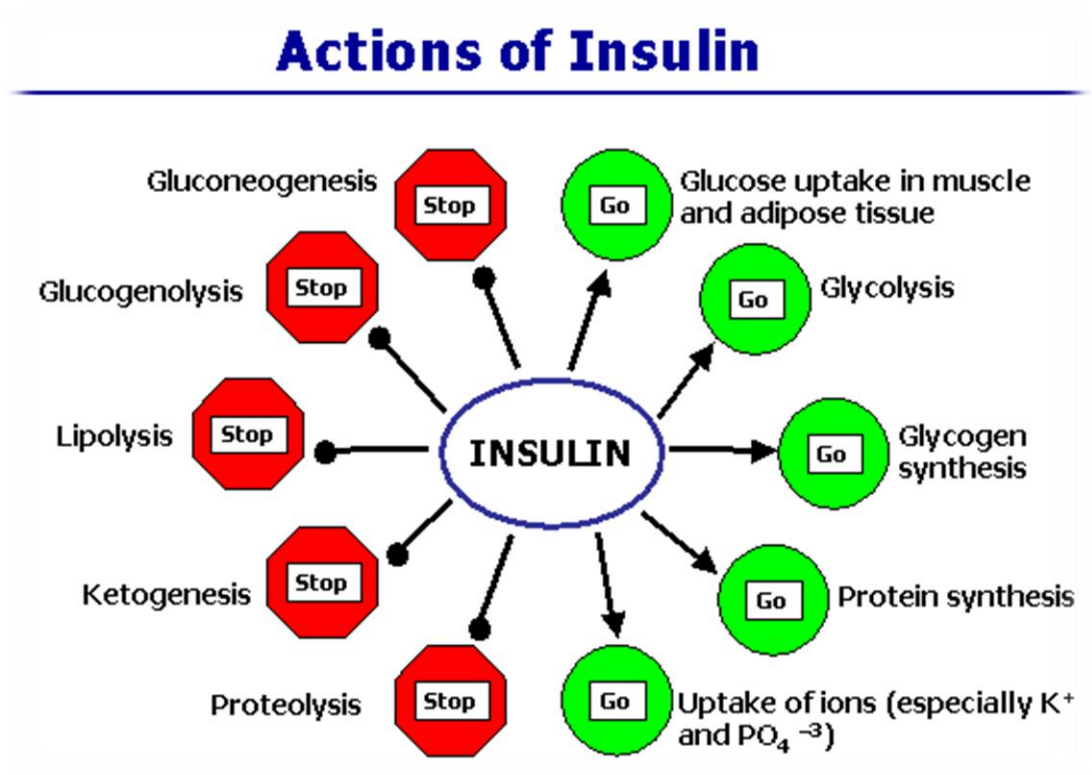
Objectives:

1. Explain the nature of type 2 diabetes mellitus
2. Know how to make the diagnosis in adults and pregnant
3-Gain knowledge in the pathophysiology
4- Gain knowledge in epidemiology and prevention

Introduction:

Type 2 diabetes, which accounts for ~90–95% of those with diabetes, is a clinical syndrome characterized by an increase in plasma blood glucose "**hyperglycemia**". Type two diabetes, once known as **adult-onset or noninsulin-dependent diabetes**, is a chronic condition that affects the way of glucose mobilization inside the body. The body either resists the effects of insulin or doesn't produce enough insulin to maintain a normal glucose level.

Patients with type two diabetes usually have associated disorders including hypertension, dyslipidemia, non-alcoholic fatty liver, and in women, polycystic ovarian syndrome. This cluster has been termed the 'insulin resistance syndrome' or '***metabolic syndrome***', and is much more common in patients who are ***obese***.



> One theory is centered around the adipocyte; this is particularly appealing, as obesity is a major cause of increased insulin resistance. Intra-abdominal 'central' adipose tissue is metabolically active, and releases large quantities of FFAs (free fatty acids), which may induce insulin resistance because they compete with glucose as a fuel supply for oxidation in peripheral tissues such as muscle. (Davidson)

Pathophysiology of type IIDM: (insulin resistance of target tissues)

It's also called non-insulin dependent DM. it's often associated with obesity and caused by down regulation of insulin receptor in target tissues and insulin resistance .Insulin IS SECRETED NORMALLY by beta cells but at normal concentration , it can't activate its receptors on muscle, liver and adipose tissue thus insulin is unable to produce its usual metabolic effects . Typically, the blood glucose is elevated in both fasting and postprandial

Risk factors of type II Diabetes mellitus (DM):

Diabetes Risk Factors	
Obesity (Greatest Risk Factor)	Obesity is associated with increased plasma levels of free fatty acids, which make muscles more insulin resistant, reducing glucose uptake. Therefore, **obesity exacerbates insulin resistance**. About 90% of patients who develop type 2 diabetes mellitus are obese! In the liver, free fatty acids increase the production of glucose.
Genetics	Multi-factorial. Constitutional factors such as obesity (which itself has strong genetic determinants), hypertension, and the amount of exercise influence the phenotypic expression of the disorder.
Age	Insulin production decreases with age

Symptoms of type II DM:

a.The disease develops **slowly** over months to years .This is usually discovered on screening urinalysis or blood sugar measurement.

Sometimes the diagnosis is made during evaluation for other diseases (e.g.,heart, kidney, neurologic, infection).

b. Symptomatic patients may present with polyuria, polydipsia, polyphagia, fatigue, blurred vision, weight loss, and/or candidal vaginitis.

c. Patients who have not routinely sought medical attention may present with complications such as myocardial ischemia, stroke, intermittent claudication, impotence, peripheral neuropathy, proteinuria, or retinopathy

- In general, the classical symptoms of hyperglycemia are:

TABLE 4-5 Symptoms of Diabetes Mellitus

Symptom	Cause
Polyuria	Glucose in renal tubule causes osmotic retention of water, causing a diuresis
Polydipsia	A physiologic response to diuresis to maintain plasma volume
Fatigue	Mechanism unknown, but probably due to increased glucose in plasma
Weight loss	Due to loss of anabolic effects of insulin
Blurred vision	Swelling of lens due to osmosis (caused by increased glucose)
Fungal infections	Fungal infections of mouth and vagina common—*Candida albicans* thrives under increased glucose conditions
Numbness, tingling of hands and feet	Neuropathy Mononeuropathy: due to microscopic vasculitis leading to axonal ischemia Polyneuropathy: etiology is probably multifactorial

Extra Explanation

Polyphagia is one of the symptoms that can be seen in diabetic patients. They feel hungry a lot because they lose blood glucose in the urine, which will affect their satiety center. (Glucose is lost in urine = less glucose in blood = Feeling hungry.)

Diagnostic Criteria: Diabetes is defined/diagnosed as:

- ✓ Two fasting blood glucose >7.0 mmol/L (126 mg/dL)
- ✓ Random plasma glucose >11.1 mmol/L (200 mg/dL)
- ✓ Increased glucose level on oral glucose tolerance testing
- ✓ Hemoglobin A1c >6.5% is a diagnostic criterion and is the best test to follow response to therapy over the last several months.

TABLE 4-4 Diagnostic Criteria for Diabetes Mellitus

Glucose Test	Impaired Glucose Tolerance (mg/dL)	Diabetes Mellitus (mg/dL)
Random plasma	—	>200 with diabetic symptoms
Fasting	110–126	>126 on two occasions
2-hr postprandial	140–200	>200
Hemoglobin A1c (%)	5.7–6.4	>6.5

Diagnosing in pregnancy:

21.23 Identifying patients with gestational diabetes

Women at high risk of gestational diabetes

- BMI > 30 kg/m^2
- A previous macrosomic baby weighing ≥ 4.5 kg at birth
- Previous gestational diabetes
- A first-degree relative with diabetes
- A high-risk ethnicity – South Asian, black Caribbean or Middle Eastern

Diagnosis

- High-risk women should have a 75 g oral glucose tolerance test before 28 weeks' gestation
- Gestational diabetes is diagnosed when:
  Fasting plasma glucose ≥ 5.1 mmol/L (92 mg/dL) *or*
  1-hr plasma glucose (after glucose load) ≥ 10 mmol/L (180 mg/dL) *or*
  2-hr plasma glucose (after glucose load) ≥ 8 mmol/L (144 mg/dL)
- Consider testing high-risk women at first booking visit with an HbA_{1c} or fasting blood glucose

Management of type 2 DM:

Management of type 2 DM:		
Diet, Exercise, and Weight Loss Weight loss can control as much as 25% of cases of Type 2 DM without the need for medications, since decreasing the amount of adipose tissue helps to decrease insulin resistance. Exercising muscle does not need insulin	**Hypoglycemics drugs**	**Insulin** Added if the patient is not controlled with oral hypoglycemic agents. Insulin glargine gives a steady state of insulin for the entire day. Dosing is not tested. Glargine provides much more steady blood levels than NPH insulin, which is dosed twice a day. Long-acting insulin is combined with a short-acting insulin such as lispro, aspart, or glulisine. Regular insulin is sometimes used as the short-acting insulin.

The goal of therapy is HgA1c <7%.

Doctor's Notes:

Advise the patient to lose 5% to 10% weight for example, don't go from 120 kg to 70 kg, go from 120 kg to 100, because at the beginning you will lose visceral fat which causes damage.

Hypoglycemics:

Drug	Notes
Metformin (Biguanide)	• The best initial drug. • Works by blocking gluconeogenesis., and by increasing insulin sensitivity. (Does not affect insulin secretion) • Does NOT cause hypoglycemia (the safest drug to start with) • Contraindicated in those with renal dysfunction because it can accumulate and cause metabolic acidosis.
Sulfonylureas	• NOT used as first line therapy because they increase insulin release from the pancreas, thereby driving the glucose intra-cellulary and increasing obesity.
Thiazoladinediones (Glitazones)	• No clear benefit over the other hypoglycemic • medications. They are relatively contraindicated in CHF because they increase fluid overload.
Nateglinide and Repaglinide	• Similar to sulfonylureas (increase insulin release) but do not contain sulfa.
Alpha glucosidase inhibitors (Acarbose, Miglitol)	• Block glucose absorption in the bowel. They add about half a point decrease in HgA1c. • Can be used with renal insufficiency. • Side effects: Flatus, diarrhea, and abdominal pain.
Incretins (exenatide, sitagliptin, saxagliptin, linagliptin)	• Incretins are a group of metabolic hormones that stimulate a decrease in blood glucose levels by suppression of glucagon and increase insulin secretion by pancreases. • They also decrease gastric motility and help in weight loss, decreasing Type 2 diabetes. • Exenatide may cause pancreatitis.
Pramlintide	• An analong of Amylin (a protein that is secreted normally with insulin). • Amylin decreases gastric emptying, decreases glucagon levels, and decreases appetite.

Insulin:

Pharmacokinetics of Insulin Formulations			
Insulin formulation	**Onset**	**Peak action**	**Duration**
Lispro, aspart, and glulisine	5–15 minutes	1 hour	3–4 hours
Regular	30–60 minutes	2 hours	6–8 hours
NPH	2–4 hours	6–7 hours	10–20 hours
Glargine	1–2 hours	1–2 hours	24 hours

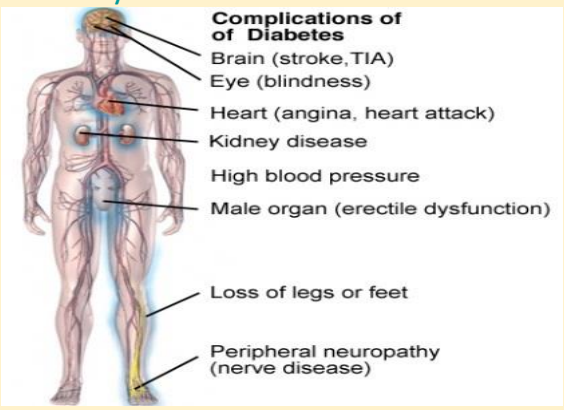
Doctor's Notes:

- **Management divided to 2 schools:**
  1. **Try till fail: give them 1 till it fails then give them 1 till it fail and so on.**
  2. **Big bang from the beginning: give them all from the beginning**

Type 1 VS Type 2 DM:

	Type 1	Type 2
Onset	Sudden	Gradual
Age at onset	Any age (Typically young)	Mostly in adult
Body habitus	Usually thin	Frequently obese
Ketosis	Common	Rare
Autoantibodies	Present in most cases	Absent
Endogenous insulin	Low or absent	Can be normal, decreased or increased.
HLA Association	Yes (HLA- DQ/DR)	No
Genetic factors	Concordance rate between identical twins is 50%	Concordance rate between identical twins is 90% Therefore, type II demonstrates a much stronger genetic component than type I
Family history	Uncommon	Common

Chronic Complications of Diabetes Mellitus:

Macrovascular complications	Microvascular complications
The main problem is accelerated atherosclerosis, which puts patients at increased risk of stroke, MI, and CHF. Risk of CAD is two to four times greater in •diabetic than in nondiabetic persons. • Most common cause of death in diabetic patients • Silent myocardial infarctions are common.  	**Diabetic nephropathy—**most important cause of end-stage renal disease (ESRD) **Diabetic retinopathy** Funduscopic examination shows hemorrhages, exudates, microaneurysms, and venous dilatation. **Diabetic neuropathy** Loss of sensation leads to the following: ulcer formation (patients do not shift their weight) with subsequent ischemia of pressure point areas; Charcot's joints **Diabetic foot** Caused by a combination of artery disease (ischemia) and nerve disease (neuropathy)— can lead to ulcers/infections and may require amputation **Increased susceptibility to infection**

MCQs

Question1:

A 50-year-old female is 5 feet 7 inches and weighs 165 pounds. There is a family history of diabetes mellitus. Fasting blood glucose is 150 mg/dL on two occasions. She is asymptomatic, and physical exam shows no abnormalities. The treatment of choice is:
a. Observe
b. Diet and weight reduction
c. Insulin
d. Oral hypoglycemic agent

Question2:

A diabetic patient asks for clarification about dietary management. Which of the following is good advice?
a. Restrict carbohydrates and eat a high-protein diet
b. Avoid artificial sweetners
c. Less than 10% of caloric intake should be saturated fat
d. Caloric intake should be very consistent from one day to another

Question3:

What is the best advice to give a middle-aged diabetic male about exercise?
a. Exercise should be avoided because it may cause foot trauma
b. Active lifestyle helps prevent the long-term complications of diabetes
c. Vigorous exercise cannot precipitate hypoglycemia
d. A stress test is a necessity for all diabeticsprior to beginning an exercise program

Answer 1-B .2-C .3-B

Answer1 :

The answer is b. The primary treatment for type 2 diabetes is dietary. About half of all patients can maintain a normal blood sugar with weight reduction. If weight reduction fails, a number of oral hypoglycemics are available as the next step.

Answer2 :

The answer is c. In order to reduce plasma cholesterol and decrease the risk of vascular disease, fat intake should be moderated, with less than 10% of total caloric intake being saturated fat. Caloric distribution does not restrict or decrease carbohydrates. Dietary protein should be moderated, and in patients with diabetic nephropathy, reducing dietary protein is often recommended. Patients with diabetes are usually advised to use artificial sweetners rather than concentrated sweets.

Answer3 :

The answer is b. An active lifestyle and good exercise program can prevent the complications of diabetes. However, there are pitfalls to such a program. Some forms of exercise might jeopardize adequate foot care. Exercise can potentiate hypoglycemia by potentiating insulin action. Diabetics who have other risk factors for cardiovascular disease such as hypertension and hyperlipidemia should have an exercise stress test prior to engaging in a rigorous exercise program.

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