Team Medicine

Lecture 9 :

Diabetes Mellitus Type 2

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■ Medicine Teamwork 430 ■ Doctors notes

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431 Teams

Diabetes Mellitus Type 2

Definition:

Relative insulin deficiency due to impaired beta cells function. Also, resistance to the actions of the insulin in the liver and muscle tissues occurs later in life, it takes months to years to develop the symptoms. Patients usually present with complications.

Insulin resistance appears to come first, and leads to elevated insulin secretion in order to maintain normal blood glucose levels. However, in susceptible individuals the pancreatic β cells are unable to sustain the increased demand for insulin and a slowly progressive insulin deficiency develops.

If the patient is not treated, he/she will end up with a complete picture of DM, meaning they'll have hyperglycemia & hypoinsulinima.
Patients with this type don't develop DKA. It is a familial disease.

Davidson

Normal glucose and fat metabolism:

Blood glucose is tightly regulated and maintained within a narrow range. A balance is preserved between the entry of glucose into the circulation from the liver, supplemented by intestinal absorption after meals, and glucose uptake by peripheral tissues, particularly skeletal muscle. A continuous supply of glucose is essential for the brain, which cannot oxidize free fatty acids and relies upon glucose as its principal metabolic fuel.

When intestinal glucose absorption declines between meals, hepatic glucose output is increased in response to low insulin levels and increased levels of the counterregulatory hormones, glucagon and epinephrine (adrenaline).

The liver produces glucose by gluconeogenesis and glycogen breakdown. The main substrates for gluconeogenesis are glycerol and amino acids. After meals, blood insulin levels rise. Insulin is an
anabolic hormone with profound effects on the metabolism of carbohydrate, fat and protein . Insulin is secreted from pancreatic Beta cells into the portal circulation, with a brisk increase in response to a rise in blood glucose. A number of other factors can augment insulin release, including amino acids and hormones, such as glucagon-like peptide 1 (GLP-1), released from the gut following food intake .

Doctor: How gut contributes to the development of Diabetes?
GLP-1 or Glucagon like peptide is produced by the gut after food intake. It increases insulin secretion and decreases glucagon secretion. People with Diabetes type 2 have a deficiency in production of this peptide. This is how the gut contributes to the development of diabetes. Treatment: give them GLP-1.

Insulin lowers blood glucose by suppressing hepatic glucose production and stimulating glucose uptake in skeletal muscle and fat, mediated by the glucose transporter, GLUT 4.

Adipocytes (and the liver) synthesize triglyceride from non-esterified ('free') fatty acids (FFAs) and glycerol. Insulin stimulates lipogenesis and inhibits lipolysis, promoting triglyceride accumulation. Lipolysis is stimulated by catecholamines and liberates FFAs which can be oxidized by many tissues. Their partial oxidation in the liver provides energy to drive gluconeogenesis and also produces ketone bodies (acetoacetate, which can be reduced to 3-hydroxybutyrate or decarboxylated to acetone) which are generated in hepatocyte mitochondria. Ketone bodies are organic acids which, when formed in small amounts, are oxidized and utilized as metabolic fuel. However, the rate of utilization of ketone bodies by peripheral tissues is limited, and when the rate of production by the liver exceeds their removal, hyperketonaemia results. This occurs physiologically during starvation, when low insulin levels and high catecholamine levels increase lipolysis and delivery of FFAs to the live.

Pathophysiology: Insulin resistance and Beta cells failure:

- It is when the body's own sensitivity to insulin is reduced.
- It is often associated with other disorders such as hypertension, dyslipidemia and central obesity.

Type 2 diabetes, or its antecedent impaired glucose tolerance, is often associated with other disorders, particularly central (visceral) obesity, hypertension and dyslipidaemia (characterised by elevated levels of small dense low-density lipoprotein (LDL) cholesterol and triglycerides, and a low level of high-density lipoprotein (HDL) cholesterol).

It has been suggested that coexistence of this cluster of conditions, all of which predispose to cardiovascular disease, is a specific entity **(the 'insulin resistance syndrome' or 'metabolic syndrome'),** with insulin resistance being the primary defect and the presence of obesity being a powerful amplifier of the insulin resistance.

Davidson

What is the cause of insulin resistance?

The primary cause of insulin resistance remains unclear.

Intra-abdominal 'central' adipose tissue is metabolically active, and releases large quantities of FFAs which may induce insulin resistance because they compete with glucose as a fuel supply for oxidation in peripheral tissues such as muscle. In addition, adipose tissue releases a number of hormones (including a variety of peptides, called 'adipokines' because they are structurally similar to immunological 'cytokines') which act on specific receptors to influence sensitivity to insulin in other tissues. Because visceral adipose tissue drains into the portal vein, central obesity may have a particularly potent influence on insulin sensitivity in the liver, and thereby adversely affect gluconeogenesis and hepatic lipid metabolism.

Doctor: One of the contributing factors to insulin resistance is **Tumor necrosis factor alpha(TNF-alpha),** and you get this factor from fat. This is one of the reasons how fat can lead to insulin resistance.

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More on this:

The potential Role of Tumor necrosis factor alpha (TNF-alpha) in the pathogenesis of T2DM:

Tumor necrosis factor alpha (TNF-alpha) has well-described effects on lipid metabolism in the context of acute inflammation, as in sepsis. Recently, increased TNF-alpha production has been observed in adipose tissue derived from obese rodents or human subjects and *TNF-alpha has been implicated as a causative factor in obesity-associated insulin resistance and the pathogenesis of type 2 diabetes*. Thus, current evidence suggests that administration of exogenous TNF-alpha to animals can induce insulin resistance, whereas neutralization of TNF-alpha can improve insulin sensitivity. Importantly, results from knockout mice deficient in TNF-alpha or its receptors have suggested that TNF-alpha has a role in regulating in vivo insulin sensitivity.

Read more : http://www.ncbi.nlm.nih.gov/pubmed/10878750

In the early stages of type 2 diabetes, reduction in the total mass of pancreatic islet tissue is modest. At the time of diagnosis, around 50% of beta -cell function has been lost and this declines progressively with time.

Some pathological changes are typical of type 2 diabetes, the most consistent of which is deposition of amyloid. In addition, elevated plasma glucose and FFAs exert toxic effects on pancreatic beta cells to impair insulin secretion. *However*, while beta-cell numbers are reduced, a-cell mass is unchanged and glucagon secretion is increased, which may contribute to the hyperglycaemia.

Risk factors:

Many risk factors contribute in developing type 2 diabetes, such as:

- **Genetic predisposition:**

  Genetic factors are important in type 2 diabetes, as shown by marked differences in susceptibility in different ethnic groups and by studies in monozygotic twins where concordance rates for type 2 diabetes approach 100%.

  However, many genes are involved and the chance of developing diabetes is also influenced very powerfully by environmental factors. Genome-wide association studies have identified over 20 genes or gene regions that are associated with type 2 diabetes, each exerting a small effect. The largest effect is seen with variation in TCF7L2; the 10% of the population with two copies of the risk variant for this gene have a nearly twofold increase in risk of developing type 2 diabetes. Most of the genes known to contribute to risk of type 2 diabetes are involved in b-cell function or in regulation of cell cycling and turnover, suggesting that altered regulation of b-cell mass is a primary predisposing factor .

- **Age :** More common in middle aged and elderly people.
- **Diet :** High fat foods and food rich with carbohydrates.

- **Obesity:** It increases the risk of developing diabetes in genetically predisposed people. Around 70% of type 2 diabetics are obese. The risk of developing type 2 diabetes increases tenfold in people with a body mass index (BMI) > 30 kg/m2 .

- **Sedentary lifestyle**

Physical activity is another important determinant of insulin sensitivity. Inactivity is associated with downregulation of insulin-sensitive kinases and may promote accumulation of FFAs within skeletal muscle. Sedentary people are therefore more insulin-resistant than active people with the same degree of obesity**. Moreover***, physical activity allows non-insulin-dependent glucose uptake into muscle, reducing the 'demand' on the pancreatic beta cells to produce insulin.*

Signs and symptoms:

The severity of the classical 'osmotic' symptoms of polyuria and polydipsia is related to the degree of glycosuria. In type 2 diabetes, hyperglycaemia develops slowly over months or years and there is a rise in the renal threshold for glucose (the capacity of renal tubules to reabsorb glucose from the glomerular filtrate), so that glycosuria is limited and osmotic symptoms are usually mild. This is one reason that many cases of type 2 diabetes are discovered coincidentally and a large number are undetected. Thus, patients are often asymptomatic and usually present with a long history (typically many months) of fatigue, with or without osmotic symptoms.

In some patients with type 2 diabetes, presentation is late and pancreatic b-cell failure has reached an advanced stage of insulin deficiency. These patients may present with weight loss.

Microvascular and Macrovascular complication of Diabetes:

Diabetes complications are divided into **microvascular** (due to damage to small blood vessels) and **macrovascular** (due to damage to larger blood vessels).

Microvascular complications include damage to eyes (retinopathy) leading to blindness, to kidneys (nephropathy) leading to renal failure and to nerves (neuropathy) leading to impotence and diabetic foot disorders (which include severe infections leading to amputation).

Macrovascular complications include cardiovascular diseases such as heart attacks, strokes and insufficiency in blood flow to legs. There is evidence from large randomized-controlled trials that good metabolic control in both type 1 and 2 diabetes can delay the onset and progression of these complications. *" WHO"*

Read More: http://www.who.int/diabetes/action_online/basics/en/index3.html

- **Type 2 diabetics** will present with vascular complications once they're diagnosed because the disease has been quiet for years.

Doctor: When undiagnosed diabetic patient goes to the ophthalmologist, during fundoscopic examination the doctors can know immediately that this patient is diabetic. Doctor can see **a macular retinal dots**. Only diabetes give you that appearance.

Type 2 diabetics patients might complain of early microvascular diseases (the disease has been there for more than 5 to 10 years). Once a patient is diagnosed with type 2 diabetes, he should be screened right away for **micro**vascular complications.

The Risk to develop DM Type II:

- **If** there is no DM in the family your chance to be diabetic is 5%.
- **If** either your mother or father have DM your chance to be DM will be 15%
- **If** your mother & father have DM your chance to be DM will be 45%.
- **If** either your mother or father & one of the brother or sister have DM your chance to be DM will be 70%.

Can we reduce this percentage?

- Yes, you can reduce it by exercising 20 min. a day, 3 times a week.
- This will reduce 2/3 of the risk.
- If you maintain the normal body weight, you will reduce half of the risk.
- If you eat healthy foods, you will reduce 1/3 of the risk.

How familial diseases differ from genetic ones?

Familial disease are caused by an expression of **multiple genes** together, that's why it's called a polygenic disease, because there are many genes working together, like the obesity gene, insulin resistant gene and beat gene dysfunction. However in Genetic disease we have just **one gene**. Type 2 DM is preventable while Type 1 is not.

IGT (impaired glucose tolerance):

This is the stage before the person gets type II diabetes.

Note: if you catch the patient in that golden phase you can prevent type II up to 80%.

What can we do for them? Give them synthesizer or we ask them to lose weight & to exercise It is a phase to type II diabetes.

Secondary DM:

Rare, usually secondary to trauma to the pancreas which lead to its surgical removal, recurrent pancreatitis, Cushing syndrome, glucagonoma, excess growth hormone secretion, acromigaly or very rare genetic diseases.

Doctor: DM could be secondary to steroid use. Once you stop them, diabetes disappears.

Steroid diabetes (also "steroid-induced diabetes") is a medical term referring to prolonged hyperglycemia due to glucocorticoid therapy for another medical condition. It is usually, but not always, a transient condition. *"Wikipedia".*

Gestational DM (temporary DM):

This is due to placenta secrete human lactogens . This human lactogens (like growth hormone) induce insulin resistance. It is a temporary DM, meaning that when the pregnancy is over, the diabetes will disappear, but there is a chance it continues after pregnancy.

First pregnancy has a 7-8% chance of Diabetes, **second pregnancy** has a 30% chance (if she developed Diabetes in the first one) and **the third** has a 70% chance (If she developed Diabetes in both the first and second）.
The effect (danger) of gestational diabetes will be on the baby not on the mother because it can cause congenital malformations and intrauterine death. When a person has sedentary life, the insulin resistance will begin, and when their calorie intake increases she will become obese, when those two occur (insulin resistance + obesity) she will develop type II DM. Repeated pregnancy increases the likelihood of developing irreversible diabetes, particularly in obese women; 80% of women with gestational diabetes ultimately develop permanent diabetes.

Davidson

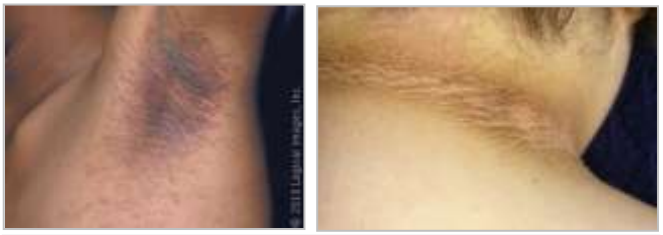
Implications for the fetus:
A clear relationship exists between maternal blood glucose and perinatal morbidity for the baby. Maternal glucose crosses the placenta and is an important fuel for the developing fetus. An elevated maternal blood glucose promotes fetal insulin production and hence stimulates fetal growth (macrosomia), which may complicate labour and delivery, resulting in a higher caesarean section rate. Fetal hyperinsulinaemia may also result in neonatal hypoglycaemia. Reduction of maternal blood glucose by insulin therapy can reduce fetal growth.

Investigations and Diagnoses:

Diabetes is defined as: a fasting blood glucose level equal to or more than 126 mg on two different occasions on one to two weeks apart. Once these patients have that, they have diabetes and they carry the diagnoses for the rest of their lives.

Kumar

Physical examination at diagnosis:
Evidence of weight loss and dehydration may be present, and the breath may smell of ketones. Older patients may present with established complications, and the *presence of the characteristic retinopathy is diagnostic of diabetes*. In occasional patients there will be physical signs of an illness causing secondary diabetes. Patients with severe insulin resistance may have **acanthosis nigricans**, which is characterized by blackish pigmentation at the nape of the neck and in the axillae.



acanthosis nigricans

Diagnostic Criteria:

If the patient is symptomatic, then diagnosis is confirmed by:

- Random plasma glucose concentration equal to or more than 200 mg
- Or fasting plasma glucose concentration equal to or more than 126 mg.
- If patient is asymptomatic two samples are required.

Box 19.1 WHO diagnostic criteria – 1999

WHO criteria for the diagnosis of diabetes are:

- Fasting plasma glucose >7.0 mmol/L (126 mg/dL)
- Random plasma glucose >11.1 mmol/L (200 mg/dL)
- One abnormal laboratory value is diagnostic in symptomatic individuals; two values are needed in asymptomatic people.

The glucose tolerance test is only required for borderline cases and for diagnosis of gestational diabetes.

The glucose tolerance test – WHO criteria

	Normal	Impaired glucose tolerance	Diabetes mellitus
Fasting	<7.0 mmol/L	<7.0 mmol/L	>7.0 mmol/L
2 h after glucose	<7.8 mmol/L	7.8–11.0 mmol/L	≥11.1 mmol/L

- Adult: 75 g glucose in 300 mL water
- Child: 1.75 g glucose/kg body weight
- Only a fasting and a 120-min sample are needed
- Results are for venous plasma – whole blood values are lower.

Note: There is no such thing as mild diabetes. All patients who meet the criteria for diabetes are liable to disabling long-term complications.

Oral glucose tolerance test :

glucose tolerance test is hardly ever necessary for clinical purposes. is indicated when plasma glucose levels are elevated but not diagnostic of diabetes:

- Random plasma glucose concentration between 140-199 mg
- Fasting plasma glucose concentration between 110- 126 mg.

Urine dipstick : For glycosuria, ketonuria , albuminuria.

Davidson's	Testing the urine for glucose with dipsticks is a common screening procedure for detecting diabetes. If possible, testing should be performed on urine passed 1–2 hours after a meal to maximise sensitivity .Glycosuria is **NOT diagnostic** of diabetes but indicates the need for further investigations. About 1% of the population has renal glycosuria. This is an inherited low renal threshold for glucose.
Kumar	**The greatest disadvantage** of urinary glucose measurement is the individual variation in renal threshold for glucose. The most common cause of glycosuria is a low renal threshold, which is common during pregnancy and in young people; 'renal glycosuria' is a benign condition unrelated to diabetes. Some drugs may interfere with urine glucose tests.

Hemoglobin A1C:

It is the best test to follow response to therapy over the last several months.

(HbA1c) refers to HbA that has been modified by attachment of glucose to the N-terminal amino acid of the beta globin chain. Hemoglobin A1C is the part of hemoglobin that has glucose residues. If the patients' glycoselated hemoglobin is known, their mean sugar during the last several months will be detected. Normal hemoglobin A1C = 6.5 and its equal to mean sugar of 125 mg. This allows assessment of glycaemic control by repeated measurements every few months in patients with known diabetes, **but current assays may not be sufficiently sensitive to make a diagnosis of diabetes and are usually within the normal.**

Other investigations: No further tests are needed to diagnose diabetes. Other routine investigations include screening the urine for protein, a full blood count, urea and electrolytes, liver biochemistry and random lipids.

Management: Lifestyle modifications:

- Exercising regularly: When type 2 diabetics lose weight, their cells become less insulin resistant.
- Healthy diet: restricted carbohydrates, fat, and salt diet.
- No smoking or alcohol consumption (alcohol suppresses gluconeogenesis so it can cause hypoglycemia in patients who are on insulin or oral hypoglycemic drugs.
- Oral hypoglycemic agents: Physician can give one oral hypoglycemic agent a combination of hypoglycemic agents. It is only used in type 2 diabetes.

Beta cell implants: Very good modality of treatment. The beta cells are separated off the exocrine cells (cadavers/donors). Pure beta cells are put in the liver.

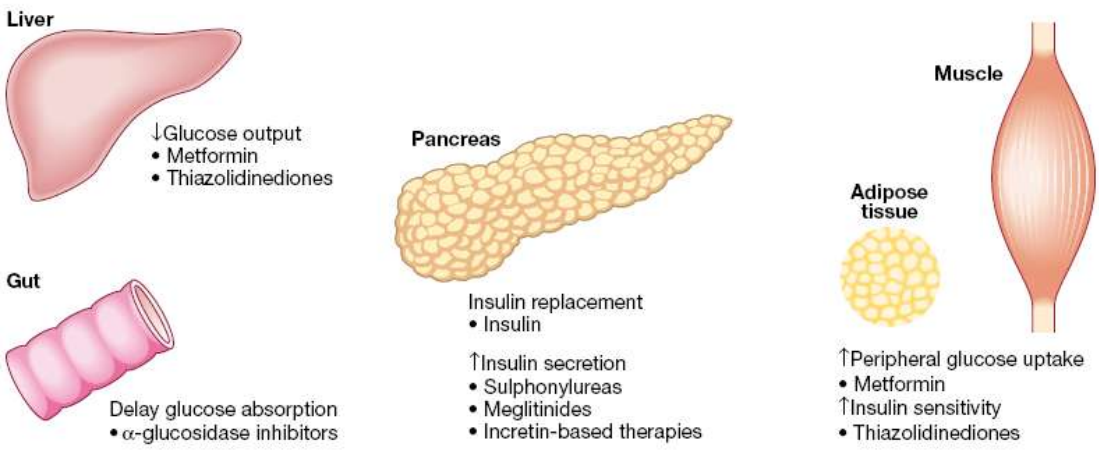
Problems: Patients must be continuously given immunotherapy.

The half-life of beta cells is 5 years > Must be done every 5 yrs.

To give 1 dose of beta cells, 2 donors must be available in order to concentrate the beta cell

Only used in very complicated patients.

Treatment- Oral Anti-diabetic drugs:



1- Sulphonylureas: (chloropropamide / tolbutamide / glipizide):

Mechanism of action:

- They act on the beta cells to increase the secretion of insulin.
- All these drugs are excreted renally except tolbutamide; it is metabolized by the liver.

Side effects:

- *Hypoglycemia:* it is a common side effect especially in older patients who they forget to eat after taking the drug or overdose.
- *Weight gain:* It is not preferred to use it in obese patients because it causes weight gain. (more insulin resistance, more medications needed)

Indications/Contraindications:

- Indicated in non obese patients with type 2 diabetes who didn't respond to dietary measures alone.
- Contraindicated in patients with renal failure. Not preferred in obese patients.

Additional:

Davidson

- **Tolbutamide**, the mildest of the first-generation sulphonylureas, is very well tolerated. Its duration of action is relatively short, it is usually administered 8- or 12-hourly, and it is a useful drug in the elderly in whom the risk and the consequences of inducing hypoglycaemia are greater.
- **Chlorpropamide** has a biological half-life of about 36 hours and is taken once daily, but may cause severe and prolonged hypoglycaemia and is rarely used.
- Of the second-generation sulphonylureas**, gliclazide and glipizide** cause few side-effects, but **glibenclamide** is prone to induce severe hypoglycaemia and should be avoided in the elderly.
- Newer long-acting preparations such **as glimepiride** and a modified-release form of gliclazide can be administered once daily with no apparent increased risk of hypoglycaemia.

2- Biguanides: metaformin – Glucophage:

- It's the **drug of choice** and it's the first line drug.
- It's the most important drug you can use for type 2 diabetes; **they don't cause hypoglycemia or weight gain.**

Mechanism of action:

- It blocks gluconeogensis and production of glucose by the liver
- It suppresses the reabsorption of glucose from the GIT
- Facilitates glucose into the muscle.

Side effect:

- **GIT symptoms** such as diarrhea, nausea and abdominal cramps. (start low doses then increase it, patient will get used to it)
- Lactic acidosis: it's very uncommon but it is the most feared side effect. **It occurs in patients with renal failure.**

Contraindications:

- Contraindicated in patients with renal failure or impaired hepatic function.
- Preferred in obese patient.

Metformin proved unexpectedly beneficial in reducing cardiovascular risk, an effect that could not be fully explained by its glucose-lowering actions. **Metformin is currently the only oral agent** to have demonstrated unequivocal cardiovascular protection within a randomized controlled trial.

3- Thiazolidinediones : Glitazone (pioglitazone / rosiglitazone) :

- Used as a 2nd line treatment in combination with metformin or with insulin.

Mechanism of action:

They sensitize the cells to insulin. TZDs enhance the actions of endogenous insulin, partly directly (in the adipose cells) and partly indirectly (by altering release of 'adipokines' such as adiponectin and resistin which alter insulin sensitivity in the liver). **Plasma insulin concentrations are not increased and hypoglycaemia does not occur.**

Side effects: hepatotoxicity, sodium and water retention.

Indications/contraindications:

- Used in patients with renal insufficiency.
- Contraindicated in patients with liver dysfunction.
- Contraindicated in patients with cardiac failure

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4- Meglitinides

These insulin secretagogues are called **prandial glucose regulators**.
Repaglinide directly stimulates endogenous insulin secretion through the sulphonylurea receptor and is taken immediately before food. It is less likely to cause hypoglycaemia than sulphonylureas. Nateglinide has a similar mode of action, restores first-phase insulin secretion, and can be prescribed with metformin.

5- Alpha- glucosidase inhibitors :

The α-glucosidase inhibitors delay carbohydrate absorption in the gut by selectively inhibiting disaccharidases. Acarbose and miglitol are available and are taken with each meal. Both lower post-prandial blood glucose and modestly improve overall glycaemic control.

The main side-effects are flatulence, abdominal bloating and diarrhoea.

Doctor: 6- New drug is **DPP-4 inhibitors** , that prevent the break down of GLP Glucagon-like-peptide 1 (which is deficient is patient with T2DM and it increases insulin and decrease glucagon) .

> Inhibitors of dipeptidyl peptidase 4, or gliptins, are a class of oral hypoglycemics that blockDPP-4. They can be used to treat diabetes mellitus type 2. The first agent of the class - sitagliptin - was approved by the FDA in 2006.
>
> Glucagon increases blood glucose levels, and DPP-4 inhibitors reduce glucagon and blood glucose levels. The mechanism of DPP-4 inhibitors is to increase incretin levels (GLP-1 and GIP), which inhibit glucagon release, which in turn increases insulin secretion, decreases gastric emptying, and decreases blood glucose levels. *" Wikipedia"*

7-Insulin:

Added if the patient is not controlled with oral hypoglycemic agents.

There are four types:

1. **Ultra short acting insulin** (insulin lispro/aspart): taken right after meals.
2. **Regular insulin**.
3. **intermediate insulin** (NPH)
4. **Long acting** (Glargine): It provides a steady state of insulin for the entire day. Long acting dose of insulin is combined with insulin lispro after meals. This is the best way to control diabetes.

Table from step up to medicine:

TABLE 4-7 Types of Insulin

Type	Onset	Duration	Comments
Human insulin lispro	15 min	4 hr	
Regular insulin	30–60 min	4–6 hr	Only type that can be given intravenously
NPH insulin/lente insulin	2–4 hr	10–18 hr	Most widely used form of insulin
Ultralente insulin (long-lasting)	6–10 hr	18–24 hr	
70/30 mixture	30 min	10–16 hr	70% NPH, 30% regular
Glargine (lantus)	3–4 hr	24 hr	given at bedtime

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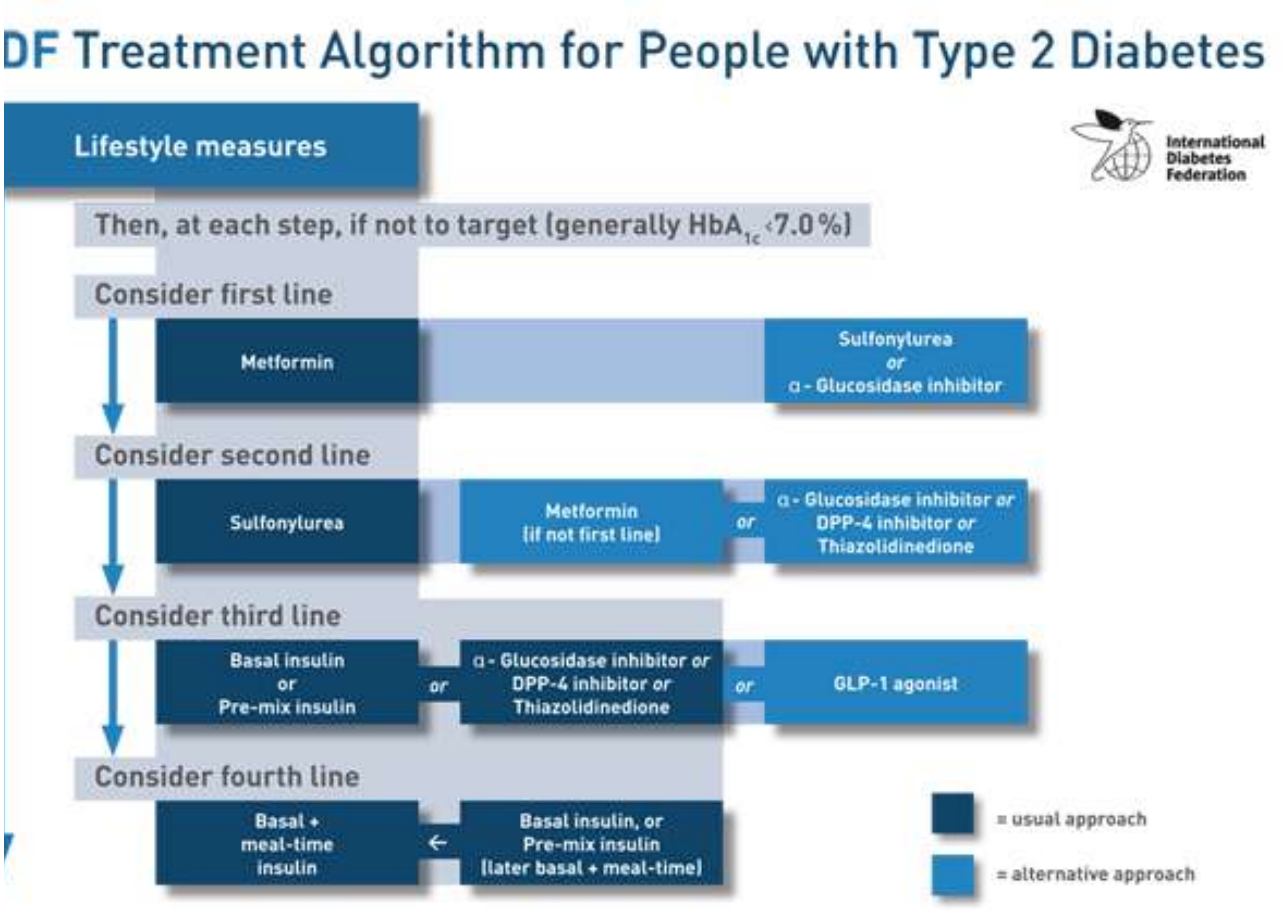


Summery:

-Type 2 diabetes is the most common form of diabetes. It occurs when there is Insulin resistance and relative insulin deficiency; it takes months to years to develop the symptoms.

-The most consistent pathological changes of DMT2 are the deposition of amyloid. In addition, elevated plasma glucose and FFAs exert toxic effects on pancreatic beta cells to impair insulin secretion.

-The gut's contribution to Diabetes type 2 is by having a deficiency in production of GLP-1.

-TNF-alpha is a contributing factor to insulin resistance.

-Type 2 diabetes is often associated with other disorders, particularly central (visceral) obesity, hypertension and dyslipidaemia.

-Risk factors: Genetic predisposition, Age, Diet, Obesity and Sedentary lifestyle.

-Complication of Diabetes:

1)Microvascular →a. Eye (retinopathy)→macular retinal dots→blindness.

b. Kidneys (nephropathy) →renal failure.

c. Nerves (neuropathy) →impotence and diabetic foot disorders.

2)Macrovascular → e.g. heart attack, stroke and insufficient blood flow to legs.

-Patients should be screened for Microvascular complications as soon as they are diagnosed with DMT2.

-**Familial diseases** are caused by an expression of multiple genes together, while **Genetic diseases** are caused by just one gene.

-Impaired glucose tolerance→ golden phase → prevent type II up to 80%.

-Gestational DM is due to placenta secrete human lactogens.

-Testing the urine for glucose with dipsticks is a common screening procedure for detecting diabetes ***but*** it's NOT diagnostic.

-The best test for follow up after therapy is Hemoglobin A1Cn.

-Management: Exercise, Healthy diet, No smoking or alcohol consumption, Oral hypoglycemic agents and Beta cell implants (used in very complicated patients.)

-Treatment→Oral Anti-diabetic drugs: Sulphonylureas: (chloropropamide)/ Biguanides: (metaformin)/ Thiazolidinediones: (Glitazone)/ Meglitinides/ Alpha- glucosidase inhibitors/ DPP-4 inhibitors/ Insulin.

Questions:

1-A50-year-old female is 5ft 7in tall and weighs 185lb.There is a family history of diabetes mellitus. Fasting blood glucose (FBG) is 160 mg/dL and 155 mg/dL on two occasions. HgA1c is 7.8%. You educate the patient on medical nutrition therapy. She returns for reevaluation in 8 weeks. She states she has followed diet and exercise recommendations but her FBG remains between 130 and 140 and HgA1C is 7.3%. She is asymptomatic, and physical examination shows no abnormalities. Which of the following is the treatment of choice?

a. Thiazolidinediones
b.Encourage compliance with medical nutrition therapy
c. Insulin
d. Metformin
e.Observation with repeat HgA1C in 6 weeks.

2-A55-year-old type-2 diabetic patient has lost weight and has had good control of his blood glucose on oral metformin, with HgA1c of 6.4%. He has a history of mild hypertension and hyperlipidemia. Which of the following statements is correct regarding routine testing for diabetic patients?

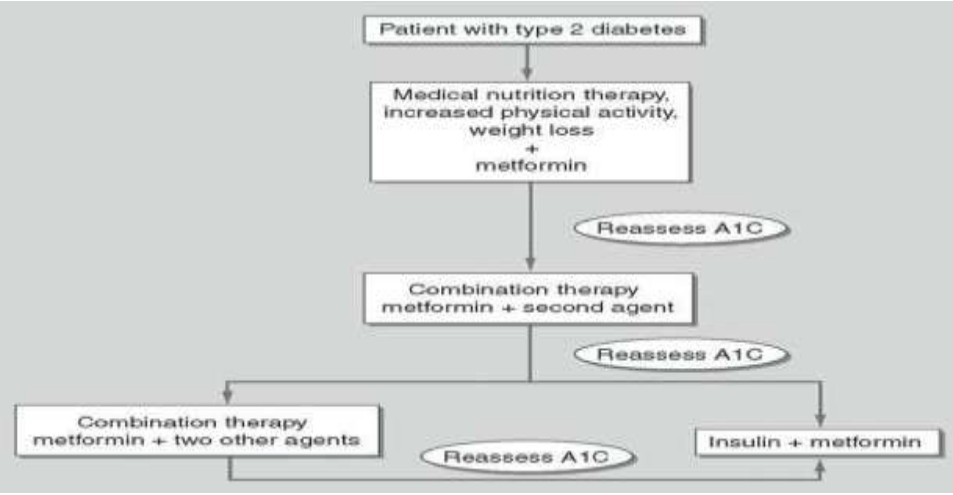
a.Dilated eye examination twice yearly
b.24-hour urine protein annually
c.Home fasting blood glucose measurement at least once per week
d.Urine microalbumin annually
e.Referral to neurologist for peripheral neuropathy evaluation

3-A57-year old male had a fasting plasma glucose level of 160mg/dL 1 month ago. Today, his fasting glucose level is 140 mg/dL. He has a history of HTN that is controlled with an ACE inhibitor. He has no other medical problems. He is 521122 and weighs 215 lb. His deceased father had DM, but the family history is otherwise noncontributory. This patient is asymptomatic, and his physical examination is unremarkable. What's your initial step in management?

a.Start oral hypoglycemic
b.Order 24-hour urine protein
c.Diet and exercise
d.Order Oral glucose tolerance test

Answers: Q1-d/ Q2-d/ Q3-c

A1- ***The answer is d***. The classification of diabetes mellitus has changed to emphasize the process that leads to hyperglycemia.



Type 2 DM is a group of heterogeneous disorders characterized by insulin resistance, impaired secretion of insulin, and increased glucose production. In this type 2 patient, the first intervention, medical nutrition therapy, failed to achieve the goal HgA1c of < 7.0%. Medical nutrition therapy (MNT) is a term now used to describe the best possible coordination of calorie intake, weight loss, and exercise. It emphasizes modification of risk factors for hypertension and hyperlipidemia, not just weight loss and calorie restriction. Blood glucose control should be evaluated after 4 to 6 weeks and additional therapy should be added; therefore, continued observation is not the best option. Metformin is considered first-line therapy in that it promotes mild weight loss, has known efficacy and side effect profile, and is available as a generic with very low cost. Thiazolidinediones ("glitazones"), sulfonylureas, and insulin are considered second line or add-on therapy for most patients with type 2 DM.

A2-***The answer is d.*** Guidelines for ongoing medical care in diabetic patients recommend that the following screenings or interventions be performed annually: dilated eye examination, lipid profile, and medical nutrition therapy and education. Annual screening for diabetic nephropathy begins with dipstick assessment of urine protein and, if negative, testing of a single voided specimen for albumin/creatinine ratio. Twenty-four-hour urine testing is not recommended. A foot examination should be performed yearly by the physician and daily by the patient. Peripheral neuropathy is first suggested by distal loss of sensation on clinical exam. HgA1c testing should be performed 2 to 4 times a year depending on patient's diabetes control (if patient HgA1c at goal, twice yearly is adequate). Blood pressure should be measured quarterly. Home glucose measurements are usually performed once daily in well-controlled type 2 diabetics.

A3- ***the answer is c.*** Given two blood glucose measurements of 126 mg/dL, this patient has diabetes. Diet and exercise should be the initial measures taken. If conservative therapy fails, an oral hypoglycemic agent may be initiated (metformin or glipizide). Order an Hb A1c test to get an idea of his average blood glucose over the past few months. Perform a thorough examination (with attention to the feet). Provide teaching on self-monitoring
of glucose as well as dietary and exercise education. Screen for microalbuminuria, and refer the patient to an ophthalmologist.