MEDICINE

432 Team

37

Type Two Diabetes Mellitus

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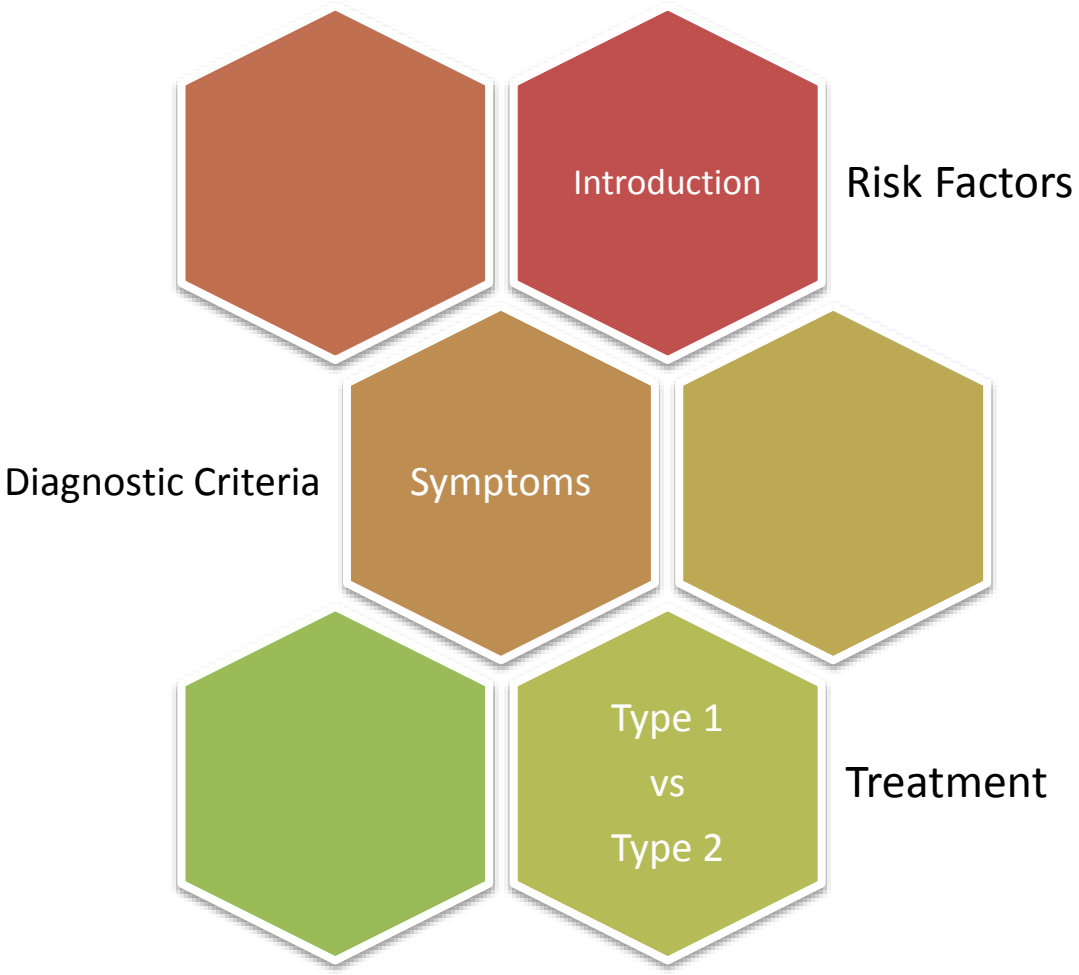
COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives


Introduction
Risk Factors
Diagnostic Criteria
Symptoms
Type 1
vs
Type 2
Treatment

Introduction

Diabetes mellitus is a clinical syndrome characterized by an increase in plasma blood glucose "**hyperglycemia**" [1]. 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 [2].

Patients with type two diabetes have associated disorders including hypertension, dyslipidemia, non-alcoholic fatty liver, and in women, polycystic ovarian syndrome [1].

Risk Factors of Type Two Diabetes

1. Genetics: Having a family member with either type two diabetes or other medical problems associated with diabetes, such as high cholesterol levels, high blood pressure, or **obesity** [3].

2. Environmental Conditions [1][4][5]:

1. **Obesity** and underactivity.
2. Having a waist measuring more than 31.5 inches (80 cm) if you are a woman or more than 37 inches (94 cm) if you are a man.
3. Previous gestational diabetes.
4. Age (insulin production decreases with age).

Step-up to Medicine 3rd Edition

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.
In the liver, free fatty acids increase the production of glucose, too.

Note:

The majority of obese people are able to increase insulin secretion to compensate for the increased demand, so those who develop diabetes are genetically susceptible [1].
*The more **obesity** you have, the more **likely** you will have Type Two Diabetes.*
It is a "correlation" (likelihood) not "causation" relation.

Symptoms of Type Two Diabetes (1)(3)(5)(6)

- The disease develops slowly over months to years.
- *Most people have no symptoms at all.* Those who have symptoms mostly they will be: **Chronic fatigue and malaise.**
- Symptoms of **thirst, polyuria, nocturia, and rapid weight lost** are more prominent in type-one diabetes.
- In general, the classical symptoms of hyperglycemia are:
  (Hyperglycemia => Microvascular injury)
  - ✓ **Dry mouth**
  - ✓ **Polyuria** (glucose in renal tubules causes osmotic retention of water causing a diuresis)
  - ✓ **Thirst "polydipsia"** (physiologic response to diuresis to maintain plasma volume)
  - ✓ **Nocturia**
  - ✓ **Tiredness and fatigue** (body can't utilize glucose efficiently)
  - ✓ **Weight loss** (due to loss of anabolic effect of insulin)
  - ✓ **Blurred vision** (swelling of lenses due to osmosis caused by increased glucose)
  - ✓ **Nausea and headache**
  - ✓ **Hyperphagia; predilection to sweet food**
  - ✓ **Mood changes; irritability and difficulty in concentrating**
  - ✓ **Fungal infections with Candida Albicans especially with uncontrolled diabetes.**
  - ✓ **Slow healing**

Note:

In general, symptoms of hyperglycemia are triggered by insulin deficiency. That's why they are more prominent in type-one diabetes, since they have absolute deficiency of insulin.
Advanced cases of type-two diabetes might present with weight loss and diabetic ketoacidosis (DKA).

Diagnostic Criteria (1)(3)(6)

1. Normal

Fasting blood glucose less than **100 mg/dl (5.55 mmol/L)**

2. Pre-diabetes

- Impaired fasting glucose "IFG": fasting plasma glucose ≥ **6.0 mmol/L and < 7.0 mmol/L**

- Impaired glucose tolerance "IGT": fasting plasma glucose **< 7.0 mmol/L** and 2-hours postprandial glucose = **7.8-11.1 mmol/L**

- HbA1c: **5.7-6.4 %**

3. Diabetes

Fasting plasma glucose **≥ 7.0 mmol/L (126 mg/dl)**

Random plasma glucose or 2-hours postprandial glucose **> 11.1 mmol/L (200 mg/dl)**

HbA1c **> 48 mmol/mol (6.5 %)**

Repeat the tests to confirm the diagnosis.

Note (1):

- Pregnant women with abnormal glucose tolerance should be fully investigated when the diagnosis of diabetes is confirmed. The investigations include plasma urea, Creatinine and electrolytes, lipids, liver and thyroid function tests, and urine testing for ketones, protein or microalbuminuria.
- Venous plasma values are more reliable for diagnostic purpose.

Note:

- Glucose Loading test used only for research purposes or in diagnosing Gestational Diabetes (Used to know if we challenged a person would he have diabetes or not).

Type one Vs. Type two Diabetes (1)(5)

	Type 1	Type 2
Onset	Sudden	Gradual
Duration of symptoms	Weeks	Months to years
Age	Any age (typically young)	Mostly adults
Body habitus	Usually thin	Obese
Ketosis	Common	Rare
Rapid death without insulin	Yes	No
Diabetic complications at diagnosis	No	25%
Autoantibodies	Present	Absent
Endogenous insulin	Low or absent	Normal, low and increased
HLA association	Yes (HLA –DQ/DR)	No
Genetic factors	Concordance rate between identical twins is 50%	Concordance rate between identical twins is 90%
Family history	Uncommon	Common
Other autoimmune diseases	Common	Uncommon

Treatment of Type Two Diabetes (1)(5)

Diet and exercise should ideally be the only interventions in most type-two diabetics**.** It is especially effective in obese and sedentary patients.
Oral hypoglycemic drugs used when conservative therapy (diet and exercise) fails**.** (Step-Up to Medicine 3rd Edition)

Hypoglycemic drugs:

(Start with lifestyle modification)

Remember: Exercised muscle is an insulin-sensitive muscle!

1. **Metformin:** **First line therapy for type-two diabetes.**

   Reduces hepatic glucose production, increase insulin-mediated glucose uptake, affects gut glucose uptake and utilization, and enhances insulin sensitivity.

   Weight-natural and doesn't cause **hypoglycemia.**

   Used with caution in renal impairment, contraindicated in impaired hepatic function.

Side effects: Diarrhea, abdominal cramps, bloating, and nausea.

2. **Sulphonylureas:** E.g. Glyburide, Glipizide, Glimepiride

   Promotes pancreatic secretion of insulin.

   Used as add-on therapy to Metformin, if glycaemia were inadequately controlled with Metformin only.

Main side effects: Weight gain and hypoglycemia.

3. **Alpha-glucosidase inhibitors:** E.g. Acarbose, Miglitol

   Reduce postprandial hyperglycemia and improve overall glycemic control.

Side effects: Bloating and diarrhea.

4. Thiazolidinediones: E.g. Pioglitazone

Enhance the action of endogenous insulin (reduce insulin resistance).

Increase fat mass and body weight by acting directly on adipose tissue.

Side effects: Hepatotoxicity, and if combined with insulin could increase fluid retention and the risk of heart failure.

5. DPP-4 (Dyspeptidyl Peptidase 4) inhibitors: E.g. Sitagliptin, Vildagliptin, Saxagliptin, Linagliptin

Prevent the breakdown of incretin hormones GLP-1 **(Glucagon-like peptide 1)** and GIP **(Gastric Inhibitory Polypeptide)** by the enzyme GPP-4.

6. GLP-1 agonists: E.g. Exenatide, Liraglutide

Not orally effective so they are used as subcutaneous injections.

Delay gastric emptying at the level of hypothalamus, so they reduce appetite, and eventually reduce body weight.

Both DPP-4 inhibitors and GLP-1 agonists promote insulin release only when triggered, so they don't cause hypoglycemia.

Note:

Only 1% reduction in HbA1C = 40% reduction in microvascular complications!

SUMMARY

1. In Diabetes Mellitus type II there is insulin resistant which will lead to hyperglycemia (the thing causing complications!)
2. At first, Insulin insensitivity (resistant) alone will not cause any problems since the pancreas will compensate by secreting more insulin until it can't make enough insulin.
3. Diabetics are fatigued because they can't utilize the glucose.
4. Risk Factors include: **OBESITY**, genetics and age.
5. Diet and exercise (lifestyle modifications) is the first line treatment in DM type II.
6. Oral Hypoglycemic agent (Metformin) is the best initial drug therapy.
7. Use Metformin with caution in renal impairment, contraindicated in impaired hepatic function.

IMPORTANT NOTES FROM EXTERNAL RESOURCES

	Notes
(1)	Davidson's Principles and Practice of Medicine 22th Edition, Chapter 21
(2)	http://www.mayoclinic.org/diseases-conditions/type-2-diabetes/basics/definition/con-20031902
(3)	http://www.uptodate.com/contents/diabetes-mellitus-type-2-overview-beyond-the-basics
(4)	http://www.patient.co.uk/health/type-2-diabetes
(5)	Step-Up to Medicine 3rd Edition, Chapter 4
(6)	http://www.nhs.uk/Conditions/Diabetes-type2/Pages/Symptoms.aspx

For approach please go back for Lecture 36-Type I Diabetes Mellitus

Questions

1) Which of the following is a true regarding DM type II?
   a. Absent endogenous insulin
   b. Ketosis is common
   c. Has HLA –DQ/DR association
   d. Patients usually obese

2) Which of the following drugs doesn't cause weight gain?
   a. Metformin
   b. Sulphonylurea
   c. Thiazolidinedione
   d. Insulin

3) The most important risk factor for Diabetes Mellitus type-two is?
   a. Smoking
   b. Male Gender
   c. Obesity
   d. High sugar diet

432 Medicine Team Leaders

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Answers:

1st Questions: D

2nd Questions: A

3rd Questions: C