

# Type 2 diabetes mellitus (endocrinology)

Template:Infobox - onemocnění Diabetes mellitus is a complex metabolic disorder in which the body is unable to process glucose as under physiological conditions due to an absolute or relative lack of insulin and concomitant peripheral insulin resistance. In type 2 DM, it is a relative deficiency, but in later stages, depletion of  $\beta$  pancreatic cells and the emergence of an absolute lack of insulin.

## Risk factors

- Diabetes mellitus in the family history;
- obesity;
- arterial hypertension;
- hyperlipoproteinemia;
- age over 40 years;
- impaired glucose tolerance ((so-called prediabetes);
- history of gestational diabetes mellitus.

## Pathogenesis

The development of type 2 DM is conditioned by a combination of insulin resistance and relatively or later absolutely reduced insulin secretion<sup>[1]</sup>. The development of type 2 DM is conditioned by a combination of insulin resistance and relatively or later absolutely reduced insulin secretion [1]. Insulin resistance is compensated by an increase in insulin secretion. Hyperglycemia develops after this compensation fails. Type 2 DM is largely associated with the presence of obesity (visceral), arterial hypertension, dyslipidemia, hyperuricemia. It is therefore a metabolic syndrome. An additional risk is an increase in the waist/hip ratio - it signals central deposition of fat (in the omentum and in the subcutaneous tissue of the abdomen); Insulin resistance + obesity → increase in insulin secretion → gradual depletion of  $\beta$ -cells. Hyperglycemia alone leads to increased insulin resistance = glucose toxicity, but obesity, lack of exercise, dietary and genetic factors also contribute. The central type of obesity is associated with insulin resistance, hyperlipoproteinemia, type 2 DM and premature mortality (CVD diseases). Peripheral (gynoid) type of obesity is not associated with risk. Insulin resistance is associated with a decrease in the number of insulin receptors on the cell membrane and subsequent post-receptor defects

## Clinical picture

The clinical picture of diabetes is an acute or long-term consequence of hyperglycemia. We can divide them into:

1. Classic symptoms of diabetes - **thirst** , **polydipsia** and **polyuria** , which are a direct result of hyperglycemia, weight loss , **fatigue** and vision problems.
2. Hyperglycemic states with impaired consciousness - this can also be a consequence of hypoglycemia during therapy.
3. Susceptibility to infections
4. Macrovascular and microvascular complications - during long-term decompensation<sup>[1]</sup>

Type 2 DM with fully expressed symptoms is almost never encountered in clinical practice. Vague symptoms of fatigue, thirst and frequent urination are the most common symptoms. DM is a progressive disease, and despite treatment, microvascular or macrovascular changes occur in most patients, which fundamentally determine the prognosis. The risk of cardiovascular complications is 2-3 times higher and is the most common cause of death in diabetics. Vascular damage leads to renal insufficiency on the basis of diabetic nephropathy. Other complications of diabetes are diabetic neuropathy, diabetic retinopathy and the development of lower limb defects - the development of diabetic foot. thumb|Diabetic retinopathy



Defect on DK's thumb in diabetic foot syndrome

## Diagnosis and differential diagnosis

The diagnosis of type 2 DM is based on evidence of hyperglycemia and does not differ from other diabetes. Determining the response to insulin - euglycemic hyperinsulin lock (clamp) - cannulas into both cubital veins, insulin is administered once at a constant rate, blood glucose is determined every 5 minutes, in the 2nd infusion there is a 20% glucose solution, its rate is adjusted so that blood glucose was in the range of 4.8–5.2 mmol/l, in people with higher insulin sensitivity, glucose consumption is higher to maintain euglycemia, in people with lower sensitivity or resistance to insulin, glucose consumption is lower. A typical finding is a postprandial increase in blood glucose (the ability of  $\beta$ -cells to respond to an increase in plasma glucose is impaired).

Differential diagnosis is based on differentiating type 2 DM from other types of diabetes. It includes differentiation from slowly progressive type 1 DM, MODY diabetes and secondary diabetes.

# Non-pharmacological therapy

## Diet

Low energy (reduction) diet (type 9A) - basis of therapy (175 g carbohydrates, less than 300 mg cholesterol, less than 30% fat, salt less than 3 g/day) + regular exercise (at least 8 weeks before starting therapy after PAD) . Another useful dietary approach may be intermittent fasting.

## Physical activity

Regular aerobic physical activity 4 times a week for 30 minutes also affects diabetes compensation and body weight. Studies show that weight loss of at least 5-10% leads to a significant reduction in cardiovascular complications.

## Bariatric treatment

It is undoubtedly a promising treatment modality in diabetology. In obese diabetics who are difficult to compensate with standard treatment, it brings success in 70-90% depending on the type of surgery used. There is either a significant improvement in compensation or even complete disappearance of diabetes. According to current criteria, a diabetic with a BMI over 35 kg/m<sup>2</sup> is indicated for bariatric surgery.

# Pharmacological treatment

## Oral antidiabetic drugs (PAD)

Oral antidiabetics

### Biguanides

Template:HVLP is the drug of first choice in the treatment of type 2 diabetes. It works on the principle of suppression of hepatic gluconeogenesis and reduction of insulin resistance, thus contributing to the reduction of fasting blood glucose. It is used in a wide range of doses from 500 to 3000 mg. daily. Does not cause hypoglycemia. Contraindication to its use is renal insufficiency GFR <30 ml/min) with a rise in serum creatinine concentration above 135 µg/l and conditions with severe tissue hypoperfusion (e.g. heart failure), where the risk of lactic acidosis increases. It can be used in monotherapy or in combination with other PADs, insulin. **Metformin must also be discontinued 48 hours before surgery and the use of iodine contrast!**

**Metformin XR** is a form of the drug with a prolonged effect, it has a lower incidence of side effects such as dyspeptic syndrome. It is preferred in patients who poorly tolerate classic metformin.

### Sulfonylureas

They stimulate the secretion of insulin and thus primarily reduce postprandial glycemia. Their disadvantage is the risk of hypoglycemia and weight gain. They are therefore not the drug of first choice for obese diabetics, but are suitable in combination with metformin. The most commonly used Template:HVLP and Template:HVLP can also be used in patients with milder renal failure when the doses are reduced.

### Glitazones

They increase insulin sensitivity by acting on nuclear receptors. Again, they are used in combination with metformin. An adverse effect is an increased incidence of heart failure and weight gain. Currently, only pioglitazone is available Template:HVLP.

### Incretins

They are the most modern of PADs. They work on the principle of increasing insulin secretion, but only in Hyperglycemia. In normoglycemia, their effect does not apply, so unlike sulfonylurea derivatives, they do not cause hypoglycemia. This group of drugs includes GLP-1 analogues (injection administration) such as Template:HVLP and oral dipeptidyl peptidase-4 (DPP4) inhibitors Template:HVLP such as Template:HVLP. They can be used in monotherapy or in combination with other PADs, insulin.

**GLP-1 analogues** support the production and secretion of GLP-1 and have a positive effect on reducing CVD risk, they also have an effect on weight reduction, which is why they are suitable for obese patients.

**DPP4 inhibitors (gliptins)** prevent inactivation and increase the concentration of GLP-1 and modulate glucagon secretion. They have a neutral effect on weight.

## Insulin treatment

Insulin treatmentTemplate:HVLP in type 2 diabetics has its own specifics. Due to the presence of insulin resistance, the need for insulin can be expected to increase several times, so 40IU is often not enough. At the same time, it is necessary to take into account the anabolic effect of insulin, which leads to weight gain, which is especially inappropriate in DM type 2. We combine insulin therapy with treatment with metformin, which we therefore do not discontinue for patients.

### Administration of basal insulin

It is the simplest regimen, which consists of the application of long-acting insulin once a day in the evening. The goal is to reduce fasting hyperglycemia.

### Application of premixed insulins

It is advantageous because, in addition to fasting hyperglycemia, it also affects postprandial hyperglycemia. Premixed insulin is applied twice a day before breakfast and before dinner.

### Intensified insulin therapy

As with type 1 DM, the basal-bolus system is used. We approach this mode only after exhausting other options.

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## History

One of the less important events that went down in the history of diabetes treatment belongs to the year 1921, when the doctor Frederick Grant Banting and his assistant, a medical student, Charles Herbert Best, discovered a substance in the pancreas of animals, after which the blood sugar level of dogs dropped. They called this substance insulin. Later, they repeated the experiment on a thirteen-year-old diabetic boy, Leonard Thompson, who thus became the first successfully treated diabetic in the world and survived another 13 years.

## Links

### Related articles

- Diabetes mellitus • Diabetes mellitus (pediatrics) • Gestational diabetes mellitus • Newborn of a diabetic mother
- Diabetes mellitus type 1 (endocrinology) • Diabetes mellitus type 1 (biochemistry)
- Diabetes mellitus type 2 (biochemistry) • Diabetes mellitus type 2 (pediatrics)
- Complications of diabetes mellitus
- Diabetes and tumors • Transplantation in diabetology • Pancreas transplantation
- Metabolic syndrome and insulin resistance
- Diabetic ketoacidosis/case report
- Diabetic education • Selfmonitoring blood glucose
- Defective counterregulation syndrome
- Formation of AGEs
- Incretin analog
- Diabetes mellitus treatment history
- Psychological aspects in patients with diabetes mellitus

### References

- ČESKA, Richard, et al. *Internal* 1st edition. Prague: Triton, 2010. 855 pp. ISBN 978-80-7387-423-0 .
- Recommended diagnostic and therapeutic procedures for VPL. *Diabetes Mellitus* . Prague: Center of recommended procedures for PL. 2020. Amendment 2020. pp. 12-14. Also available from the URL < <https://www.svl.cz/files/files/Doporucene-postupy/2020/DIABETES-MELLITUS-2020.pdf> >

### References

1. CZECH REPUBLIC, Richard, et al. *Internal* 1st edition. Prague: Triton, 2010. 855 pp. ISBN 978-80-7387-423-0 .
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