

Type 1 diabetes mellitus (endocrinology)

Pathogenesis

The cause is an absolute lack of insulin caused by inflammation - **insulinitis**. It affects the β -cells of the islets of Langerhans pancreas. Their destruction leads to insulin deficiency. **Type 1 DM** is characterized by onset in childhood. Currently, the so-called **LADA** (latent autoimmune diabetes of adults) variant of type 1 DM is also described, which manifests itself at any age and usually progresses slowly.

According to the cause of the destruction of β -cells, we distinguish two types of type 1 diabetes:

- **autoimmune condition** - autoantibodies against β -cells of the pancreas;
- **idiopathic**.

According to Eisenberg, DM is divided into six stages:

1. genetic susceptibility,
2. trigger mechanism,
3. insulinitis without insulin secretion disorder,
4. insulinitis with gradually decreasing insulin secretion,
5. manifestation of diabetes,
6. full dependence on insulin replacement.

Viral infections are likely the trigger. HLA class II molecules will be expressed on the cell surface. T-cells can recognize β -cell antigens. This can trigger **autoimmune insulinitis**. A genetic predisposition at the level of the HLA system is always necessary for the development of type 1 DM. As the pancreas has a large secretory reserve, the manifestation of diabetes only occurs when approximately 90% *destruction occurs*^[1] of all β -cells. *Manifestations can be facilitated by greater physical, or psychological stress, infection, virus, trauma (situations with an increased need for insulin, or current insulin resistance).*

Clinical picture

It involves the movement of glucose from the extra- to the intracellular fluid of cells, mainly in **muscle** and **fat tissue**. An increased concentration of glucose in the extracellular fluid leads to a rise in osmolality, which leads to an increase in the supply of osmotically active substances in the kidney and osmotic diuresis and polyuria. Polyuria leads to loss of extracellular fluid and clinical signs of dehydration:

- reduction of skin turgor,
- dryness of the mucous membranes of the tongue and oral cavity,
- reduced tone of the eyeballs.

Greater loss of extracellular fluid leads to hypotension, extreme up to the development of shock state with renal hypoperfusion, oliguria to anuria, with severe decompensation to somnolence to sopor. The hyperosmolality of the extracellular fluid leads to osmotic dehydration of cells and to a disruption in the transport of substances through the cell membrane.

An absolute lack of insulin and an absolute or relative increase in the concentration of glucagon lead to an increased formation of ketobody in hepatocytes, the plasma concentration of acetoacetate and β -hydroxybutyrate increases, which leads to a decrease in pH to values of 6.8. A ketoacidotic coma develops. Acidosis also leads to irritation of the respiratory center in the medulla oblongata and deep Kussmaul breathing. Exhaled ketone bodies smell of acetone, we are talking about the so-called *foetor acetonaemicus* (reminiscent of the smell of overripe apples).



Laboratory finding

- **hyperglycemia** > 5.6 mmol/l^[2]
- drop **pH down to 6.8**
- reduced K^+ in polyuria
- increase in K^+ in oliguria or severe catabolism
- reduction of Na^+ and depletion of phosphates
- urea increases in oliguria or anuria

Diagnosis

- hyperglycemia, disorder ABR,
- zero concentration of C-peptide (in fully developed diabetes),
- mostly autoantibodies against glutamate decarboxylase (anti-GAD),

- antibodies against islet cells (ICA),
- islet cell surface antibodies (ICSA).

Therapy

The most common is insulin substitution. It is necessary to imitate both basal secretion (= 15-20 j per day) and stimulated secretion (= 15-20 j after main meals). Basal secretion is imitated using long-acting insulins (basal insulins, acting for 24-30 hours) – 20-28 I per day usually divided into morning and evening doses.

Stimulated secretion is imitated using short-acting insulins (acts for 5-6 hours, e.g. Insulin-mono N®, Humulin R®, Actrapid®), morning dose 8-12 units, noon 8-10 units, evening 6-8 units.

Necessary measures

- **diabetic diet** - with higher energy content, 275g carbohydrates and 325g carbohydrates, for obese 225g carbohydrates, 1 exchange unit = 10g carbohydrates,
- **self-control** (selfmonitoring (https://www.wikiskripta.eu/w/Selfmonitoring_glykemie)) – glucometers, once a week the patient should perform a so-called big profile: measure glycemia one hour before meals, after each large meal and at 10:00 p.m., 01:00 a.m. and 04:00 a.m. in the morning. Currently, no non-invasive glucometers
- **continuous blood glucose measurement** (CGM) - a sensor in the subcutaneous tissue measures the concentration of glucose in the interstitial fluid, high financial demand.

Therapy options

- **basal bolus system** - the patient administers 1-2 doses of long-acting insulin (6.00 in the morning, 6.00 in the evening, 18 and 28 days), with each meal a small dose of short-acting insulin = insulin bolus (6-12 j s.c.),
- at night we apply medium-acting insulin (around 10-12 o'clock, e.g. Insulin-mono D®, Semilente®): 8-12 j at 10 p.m.; in the morning, at noon and in the evening, short-acting insulin before meals,
- **continuous subcutaneous insulin infusion** (KSII) with an *insulin pump* - continuous s.c. insulin at a basal rate, in the period before a meal, the pump delivers a bolus of insulin that can be set in advance. Risk: uncontrolled hypoglycemia with pump failure → onset of ketoacidosis, often without significant hyperglycemia,
- **transplantation of a segment of the pancreas and pancreatic islets** - in the Czech Republic, those diabetics who need a kidney transplant due to chronic renal insufficiency have the external pancreatic duct sealed, or leads to the bladder, then life-long immunosuppression. The islets are transplanted under the capsule of the kidney or into the portal basin.



Insulin pump



Insulin pen

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 named 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 (biochemistry)
- Type 2 diabetes mellitus (endocrinology) • Type 2 diabetes mellitus (biochemistry) • Type 2 diabetes mellitus (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
- Diabetes mellitus treatment history
- Psychological aspects in patients with diabetes mellitus
- Effect of physical activity on diabetes mellitus

References

1. BUREŠ, Jan. *Internal Medicine 2*. Second, Revised and Enlarged edition. Galen, 2014. pp. 1017. ISBN 978-80-7492-145-2.
2. KLENER, Paul. *Internal Medicine*. 3. edition. Karolinum, Galen, 2006. pp. 880. ISBN 80-246-1253-4 (Carolinum).

Source

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