Propedeutics in Diabetology

Eva Papežová, Jana Hartlová

Diabetes Center
Department of Internal Medicine and Gastroenterology
University Hospital Brno and Masaryk University

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Diabetes mellitus (DM)

- metabolic disease characterized by a high blood sugar level
- **Type 1 DM** – caused by gradual loss of beta cells in pancreas leading to absolute insulin deficiency (autoimmune or idiopathic), including LADA
- **Type 2 DM** – a heterogeneous group of diseases caused by relative insulin deficiency in the body (combination of insulin secretion disorder and some degree of insulin resistance)
- **other types of DM** – MODY (a rare monogenic inherited form of DM, autosomal dominant), DM in patients with chronic diseases of the pancreas, under immunosuppression, in endocrinopathies, and other
- **gestational DM** – insulin resistance typically increases in the 2nd half of pregnancy

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- **prediabetes** – pre-stage of DM, consists of Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT), or a combination of both

Medical History and Clinical Examination

- **symptoms of high blood sugar level:**
  - **thirst, polydipsia, polyuria**, nycturia, dehydration, blurred vision, irritability, fatigue, sleepiness to lethargy, weight loss
  - when the disruption of the internal homeostasis in type 1 DM is severe, so-called **diabetic ketoacidosis** can occur – characterized by fatigue, anorexia, vomiting, abdominal pain, headache, fruity-smelling breath, and later rapid deep (Kussmaul) breathing
- **symptoms of hypoglycemia (blood sugar below 3,9 mmol/l):**
  - **adrenergic symptoms** (tremor, sweating, tachycardia) and **glucose CNS deficiency symptoms** (cognitive disorders, confusion, nausea, aggression, convulsions, unconsciousness to coma)
- at the onset of type 2 DM, the individual is often asymptomatic
- while taking **medical history** of the patient, we should ask for symptoms of hyperglycemia, frequent urogenital infections, incidence of DM in the family, gestational DM in pregnancies, autoimmune diseases (thyroid disease, celiac disease), dyslipidemia, hypertension, cardiovascular diseases (risk factors for atherosclerosis)
- in patients with DM the **standard physical examination** should be accompanied by detail examination of the lower limbs and evaluation of patient‘s height, weight, BMI, waist circumference (in cm), blood pressure and heart rate

Laboratory Tests

Glycemia (blood sugar level)

- sample of venous blood (in the laboratory), or capillary blood sample (glucose meter)
- fasting blood sugar test is performed after at least 8-hour overnight fasting

Fasting Blood Glucose	Interpretation
< 5,6 mmol/l	No DM
5,6 – 6,9 mmol/l	Impaired Fasting Glucose (IFG)
≥ 7,0 mmol/l	DM

Glycated hemoglobin (HbA1c)

- product of non-enzymatic reaction between hemoglobin and blood glucose
- monitoring of long-term DM compensation – shows an average glycemia over past 4-8 weeks
- results are unreliable for example in anemia and hemoglobinopathies
- in patients with DM, HbA1c < 45 mmol/mol is considered an excellent DM compensation, HbA1c < 53 mmol/mol is an acceptable DM compensation

C-peptide (connecting peptide of insulin chains in insulin precursor - proinsulin)

- allows us to evaluate endogenous insulin secretion – C-peptide is produced in equimolar amount to endogenous insulin while it is not so quickly metabolized
- helpful in initiation of insulin therapy in type 2 DM patients

Laboratory Tests

Urinalysis in DM

- **glucose in urine** - glucosuria is present in patients with decompensated DM and high blood sugar levels (CAVE: use of antidiabetics that cause glucosuria - SGLT2 inhibitors)
- **ketones in urine** - ketonuria may occur during diabetic ketoacidosis, it is recommended to test for ketones in the urine in patients with hyperglycemia and clinical symptoms of diabetic ketoacidosis
- **albumin in urine** - albuminuria is pathologically increased urinary excretion of albumin, it indicates presence of renal impairment in DM (mainly the albumin / creatinine - ACR - concentration in the first morning urine sample is monitored, normal albuminuria is usually defined by ACR up to 3 mg/mmol creatinine), results above the upper limits for albuminuria are referred to as proteinuria

Autoantibodies (anti-ICA, anti-GAD, anti-IA-2A, anit-IAA, anti-ZnT8)

- appropriate to recognize autoimmune origin of DM

Molecular Genetic Testing (PCR)

- useful in classification of monogenic types of diabetes – e.g. MODY

Specific Testing in Diabetology

Oral Glucose Tolerance Test (oGTT)

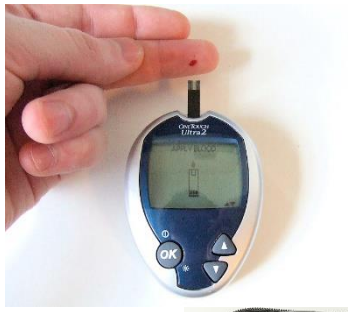
- **procedure:** 10-14 hours of fasting is necessary prior to the test; the tested person is asked to drink a solution of 75 g of glucose within 3-5 minutes, fasting blood glucose level and glucose level 2 hours after the load are measured
- most frequently used to confirm the diagnosis of DM in patients with fasting glycemia 5,6 – 6,9 mmol/l and also in the diagnosis of gestational DM

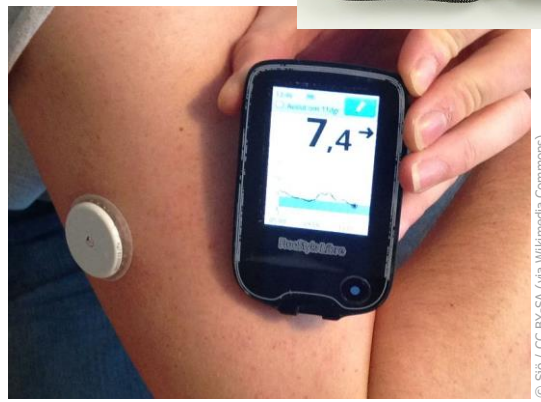
Glycemia 2 hours after the load	Interpretation
< 7,8 mmol/l	No DM
7,8 – 11,0 mmol/l	Impaired Glucose Tolerance (IGT)
≥ 11,1 mmol/l	DM

Diagnosis of DM - Three Different Situations:
Fasting blood glucose level ≥ 7 mmol/l
Blood glucose at 120 minutes on oGTT ≥ 11,1 mmol/l
Random blood glucose ≥ 11,1 mmol/l together with typical clinical signs of DM

Self-monitoring of Blood Glucose

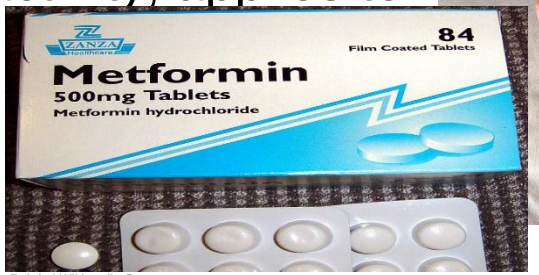
- patients with DM measure their blood sugar themselves at home using a glycemic reader (glucose meter)
- there are two types of 24 hour **glycemic profile**: standard glycemic profile (includes 4 daily glucose checks - 3 before each meal and 1 at bedtime) and an extended prandial glycemic profile (glucose checks before each meal and 1,5-2 hours after meals, at bedtime and usually also at night at 3:00 a.m.)
- subcutaneous sensors are also available for continuous monitoring of blood sugar level in interstitial fluid - readings can be made using a specialized reader or a mobile phone; some sensors offer the possibility of alarm setting (warning for too low/high glycemia)





DM Therapy

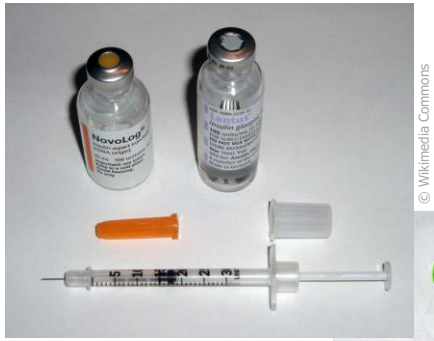
- normalization of blood glucose is the treatment goal in DM – optimal is keeping blood sugar in the normal range while minimizing glycemic fluctuations and occurrence of hypoglycemia
- **non-pharmacological treatment:** restriction of carbohydrate intake, preference of foodstuffs with lower glycemic index, physical activity, applies to both types of DM
- **type 1 DM** – insulin therapy is necessary
- **type 2 DM** – at the beginning, the treatment with peroral antidiabetics or non-insulin injectable antidiabetics (GLP-1 RA) is sufficient, with the disease progression insulin therapy may be necessary
- patients with type 1 DM need to be treated with intensive insulin therapy: basal-bolus regimen (basal insulin once daily in the evening and short or rapid acting insulin 3 times daily before main meals) or continuous subcutaneous insulin infusion by insulin pump
- simpler insulin regimens may be used in patients with type 2 DM, usually in combination with oral antidiabetics at the beginning of insulin treatment (e.g. only basal insulin once daily, premixed insulins twice daily)

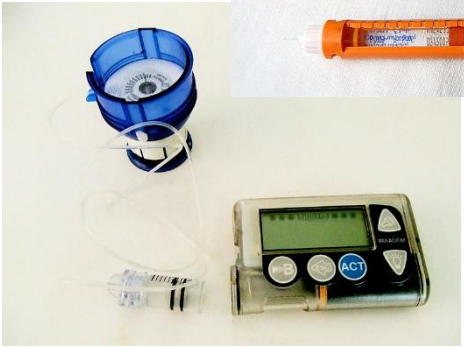


Insulin Therapy

Insulin Administration

- **subcutaneously** using an insulin syringe, insulin pen (disposable pre-filled insulin pens or older reusable cartridge-type pens) or insulin pump
- in acute conditions **during hospitalization, intravenous administration** of short acting insulin with an infusion pump is also possible





Types of Insulin

- **short acting insulin** – used as boluses before meals
- **long acting insulin** – used to cover basal need of insulin, administered once daily or twice daily (in the morning, in the evening)
- *pre-mixed insulin* – a combination of short and long acting insulins (e.g. 50/50 or 30/70 ratio)

Literature for Self-study:

- Jindřich Špinar, Ondřej Ludka a kolektiv – Propedeutika a vyšetřovací metody vnitřních nemocí (in Czech)
- Czech guidelines of Czech Diabetes Society (in Czech): https://www.diab.cz/standardy
- Czech guidelines for general practitioners – Diabetes mellitus (in Czech): https://www.svl.cz/doporucene-postupy/doporucene-postupy-pro-pl-zpracovane-od-2020/
- Pavlína Piťhová - Inzulinové režimy z klinického pohledu (in Czech): https://www.internimedicina.cz/pdfs/int/2010/11/02.pdf
- Tulane University - Insulin Regimens (in English): http://tmedweb.tulane.edu/pharmwiki/doku.php/insulin_regimens