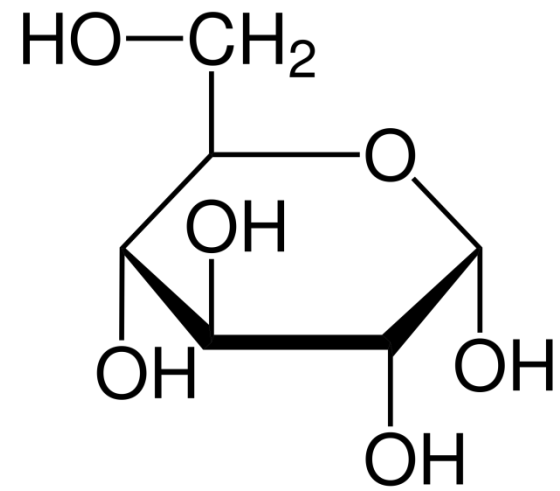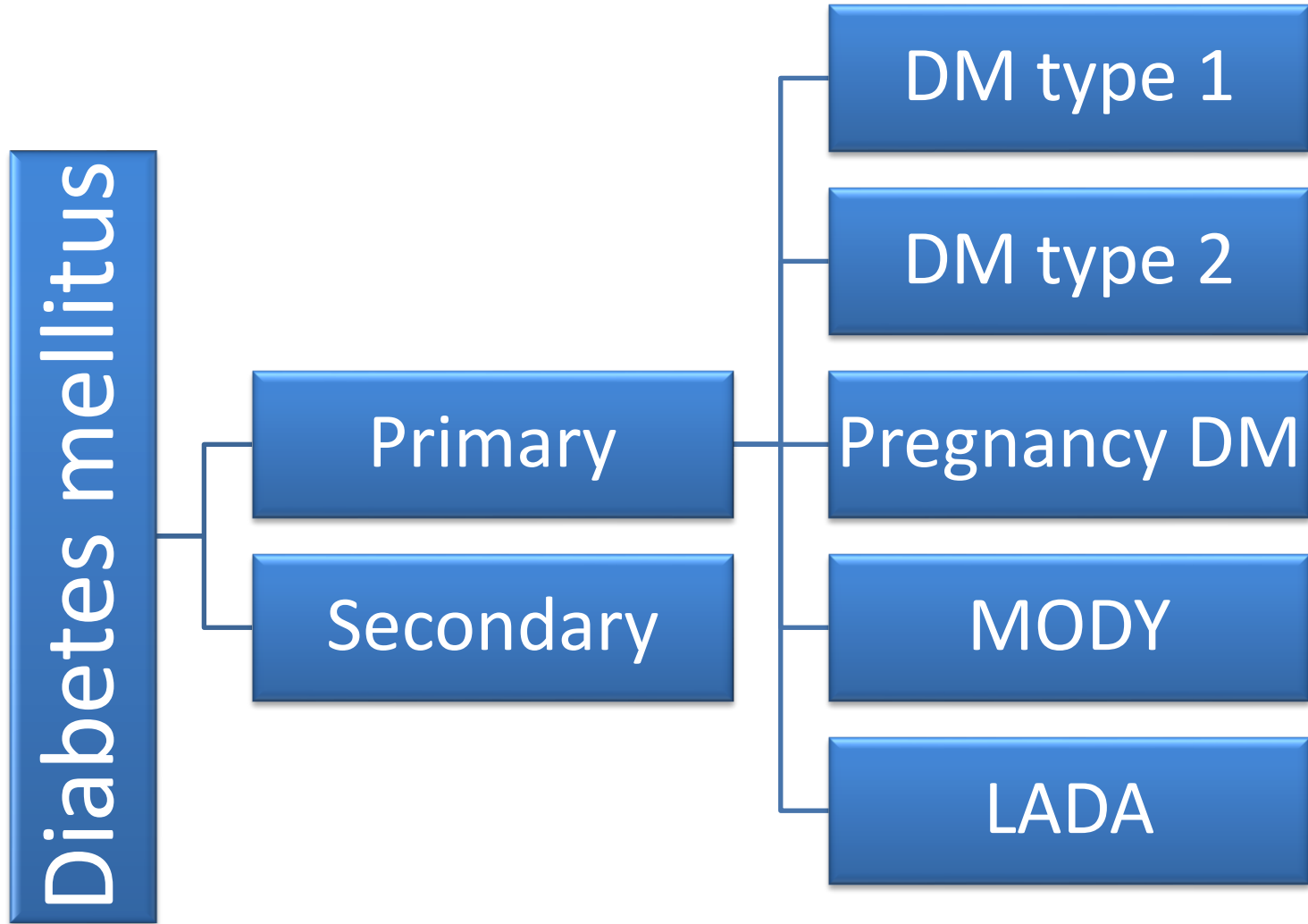# Diabetes mellitus

Definition of DM

Fasting glycaemia in venous blood $\geq$ 7 mmol/l

- Frequency in general population 5 %
- Czech population: 10 %!
- 90 % = DM type 2

DM type 1

- IDDM (insulin dependent DM)
- without any production of insulin
- Fast progression, ketoacidosis
- Children, adolescents (7-10 % from all diabetics)
- genetic predisposition (defective expression of HLA antigens + T lymphocyte reaction)
- Inflammation, viral infections
- Antibodies
  - Beta cells (ICA – Islet Cells Ab)
  - Insulin (IAA - Inzulin AutoAb)
- Ther.: insulin.

DM type 2

- Adults, old people
- Partial production of insulin
- inzulin resistance (defective transport of signal inside the target cell)
- Ther.: PAD + insulin
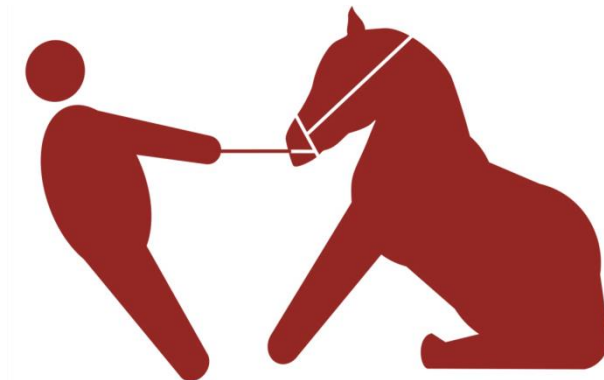
Pregnancy DM, MODY, LADA

Pregnancy DM (effect of placental hormones)

MODY (Maturity Onset Diabetes of the Young)

- Young people

- Inherited (causal genes are known)

- Defective secretion of insulin from beta cells

LADA (Late Autoimmune Diabetes of Adult)

- DM of adults with auto-antibodies (ICA, IAA)

Secondary DM

- Afer pancreatectomy (i.e. due to cancer)
- Chronical pancreatitis = destruction of functional tissue
- Very unstable type of DM (destroyed also cells producing glucagon)
- Therapy with insulin
- Exocrine pancreatic insufficiency as well

Prediabetes

Glycaemia

- fasting: 5,6 - 6,9 mmol/l   (IFG)
- After 2 hrs: 7,8 - 11,0 mmol/l   (IGT)

Making the diagnose of DM
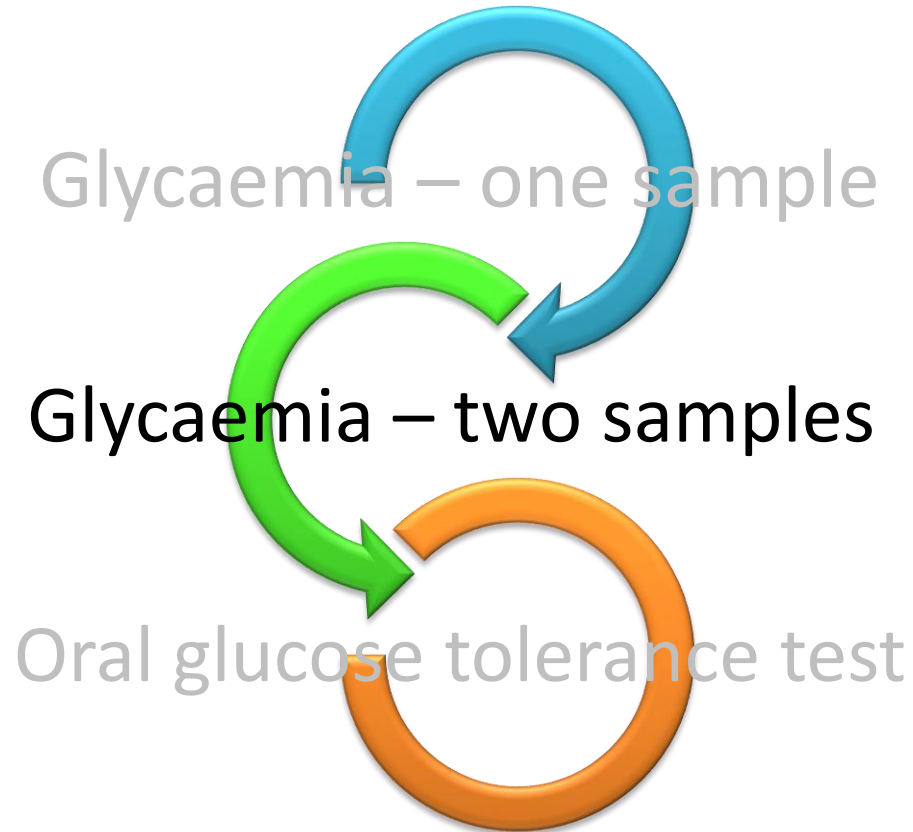
Glycaemia – one sample

Glycaemia – two samples

Oral glucose tolerance test
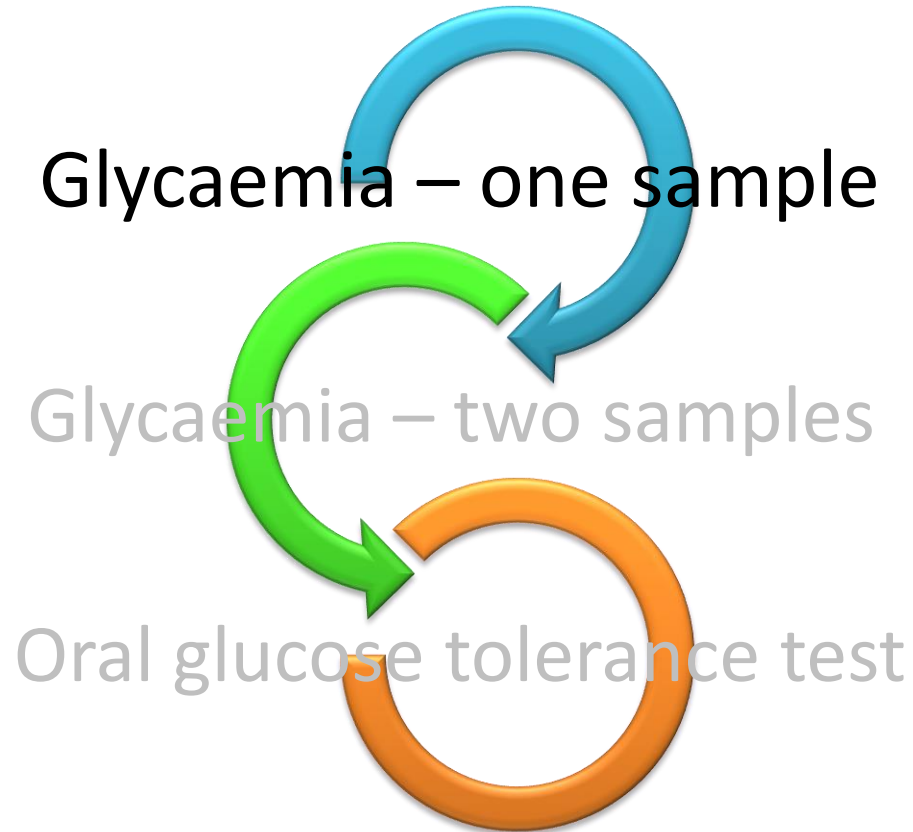
Glycaemia – taken once

- Fasting glycaemia $\geq$ 7,0 mmol/l

- Post-prandial glycaemia $\geq$ 11,0 mmol/l

- + typical clinical symptoms (polyuria, polydypsia, losing weight)

Making the diagnose of DM

Glycaemia – one sample

Glycaemia – two samples

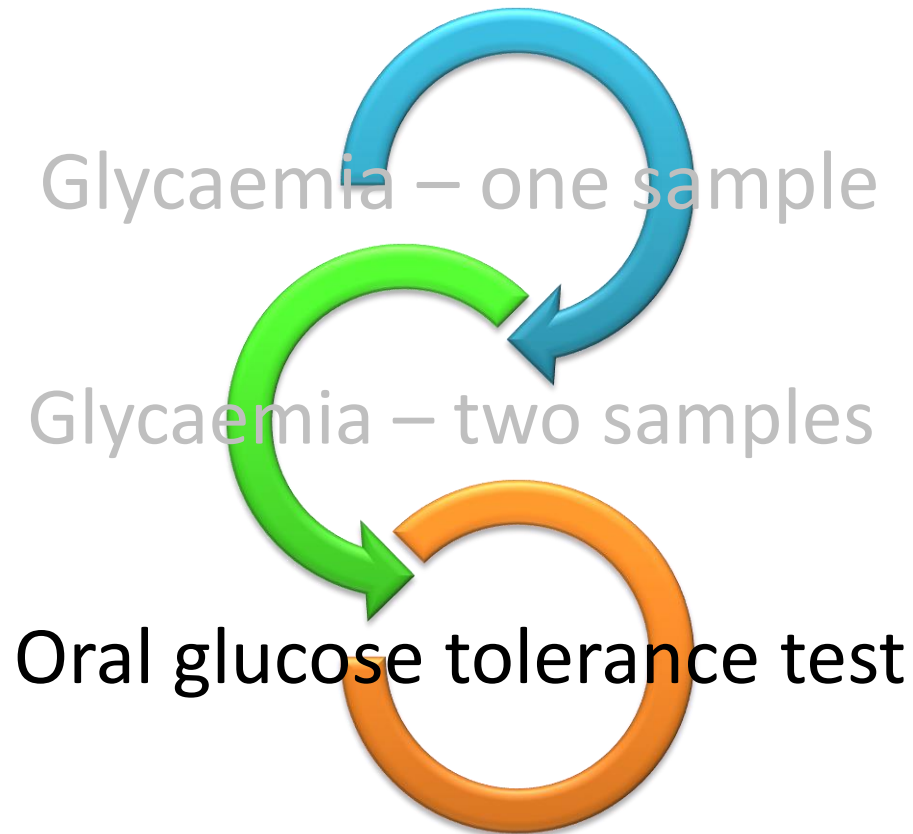Oral glucose tolerance test

Glycaemia – two blood samples

Taken repeatedly during time

- Fasting glycaemia $\geq$ 7,0 mmol/l

- Post-prandial glycaemia $\geq$ 11,0 mmol/l

- Clinical symptoms don´t have to be present to make diagnosis

Making the diagnose of DM

Glycaemia – one sample

Glycaemia – two samples

Oral glucose tolerance test

OGTT

Indication

- Fasting glycaemia up to 6.9 mmol/l

Contraindication

- Fasting glycaemia $\geq$ 7 mmol/l

- Acute disease

- till 6 weeks after surgery

- Fever

- Menstruation

How to prepare the patient

- 3 days prior the test ordinary intake of sacharides
- Avoid of any physical exercise
- 24 hrs prior the test don´t drink any alcohol beverages (including beer)
- 10-14 hrs. prior the test avoid smoking
- 10-14 hrs. be fasting before starting OGTT
- Drink only pure water

OGTT

- Venous blood sample („fasting" sample)
- Drink standard amount of sweetened liquid (75 g of glucose in 250 ml of water)
- Relax for 2 hrs.
- During the test don´t eat, drink, smoke
- 2nd blood sample after 2 hrs.

OGTT

1. Fasting for 8 - 12 hours

3. Glucose drink

2. Blood is withdrawn to test fasting blood glucose level

4. Blood samples are drawn for three times with the time interval of one hour

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Evaluation
(non-pregnant, men)

Glucose	Interpretation		
(mmol/l)	Without DM	Pre -DM	Diabetes mellitus
Fasting	< 5,6	5,6 - 6,9 IFG	≥ 7,0
in 2 hrs	< 7,8	7,8 - 11,0 IGT	≥ 11,1

OGTT – pregnant

- DM in pregnancy → fetal and maternal complications
- Perform between 24th – 28th week of pregnancy
- Same preanalytical conditions
- Same dosis of glucose
- Blood samples: 0 – 1 – 2 hrs.
- Worse tolerance

Evaluation (pregnant)

Without DM in pregnancy	Fasting glucose < 5,1 mmol/l
Pregnancy DM	Fasting glucose ≥ 5,1 mmol/l
Pregnancy DM	Glucose after 1 hour ≥ 10,0 mmol/l
Pregnancy DM	Glucose after 2 hrs. ≥ 8,5 mmol/l

Presence of glucose in urine is not important in diagnostic process.

DM under control

Fasting glycaemia

- Measured by M.D.

- Patients by themselves („self monitoring")

Post-prandial glycaemia (in 2 hrs after food)

Glycemic profile

Continuous measuring of blood sugar

Glycosuria

- Glycosuria is present if the blood sugar exceeds approx. 10 mmol/l for 15 mins. Highly individual
- Only self monitoring, not for making diagnose

Ketonuria

- Is not recommended for making the diagnose

Non – enzymatic glycation of proteins

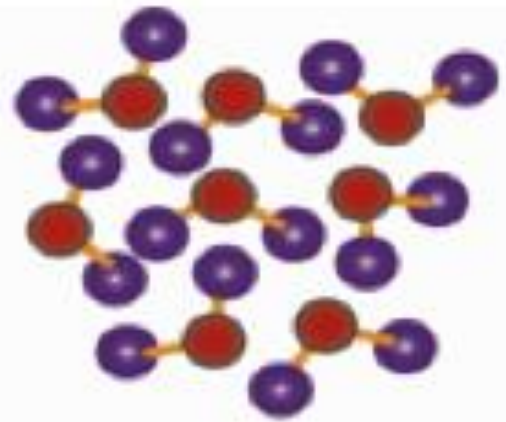Glucose is binding to proteins without presence of enzymes.

2 phases of reaction:

- reversible (Schiff base)

- irreversible (Amadori product)

AGEs = advanced glycation endproducts - lead to vessel damage

PROTEIN MOLECULES + SUGAR MOLECULES → GLYCATED PROTEIN

Glycated hemoglobin (HbA$_1$c)

Globin = protein contained in erythrocytes, 3 derivates

- HbA$_1$a

- HbA$_1$b

- HbA$_1$c = stable fraction

- Average glycaemia during last 8-12 weeks

- Lifetime of ery: 100-140 days (average: 120 ± 10 days)

Results

Results in mmol/mol
- < 42   physiological ranges
- 43 - 53   +- compensated DM
- > 53   poorly compensated DM

Tests for secretion of insulin

- Insulin

- C-peptide

Insulin like a marker

- Non - stable
- It is impossible to distinguish endogenous insulin and insulin applied artificially
- Passing through liver – quick destruction

C-peptide (connecting peptide)

- β-cells of pancreas produce proinsulin
- C peptide is not contained in exogenous insuline (medication)
- Only own production of insulin
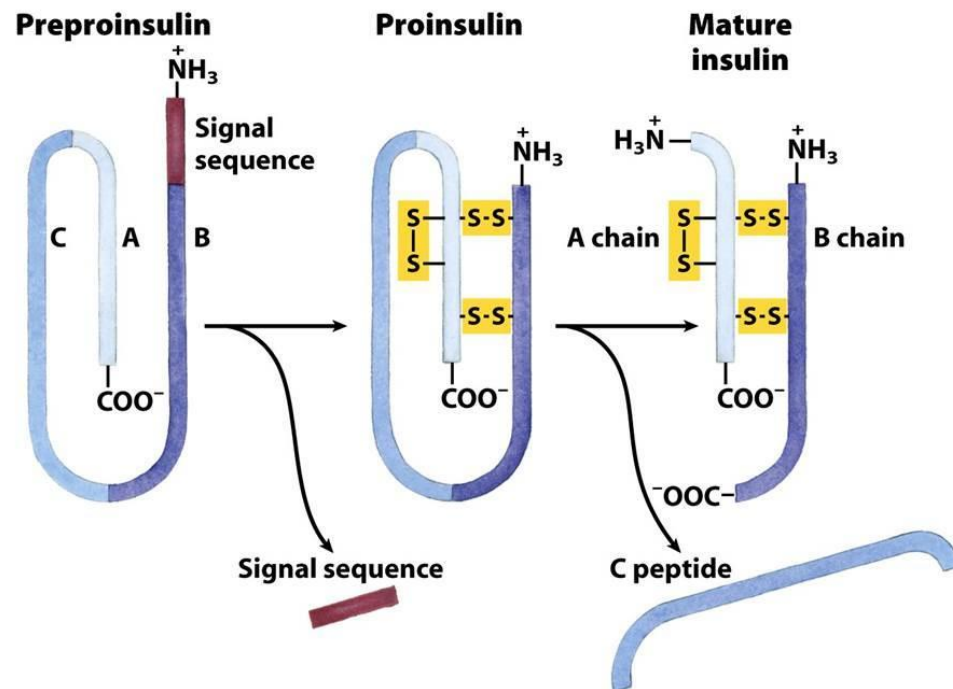
C-peptid

Marker of endogenous insulin secretion

- Normal ranges: 1,1 - 4,4 μg/l

Acute complications of DM

Hyperglycaemia

Ketoacidosis

Diabetic coma

Hyperglycaemia

- Rises up the blood osmolarity
- Water is going from ICF to ECF
- Exceeded renal „treshold" for glucose = osmotic diuresis → dehydration, feeling thirsty
- When treating serious hyperglycaemia with MAc, the kalemia has to be controlled regularly! (relation between potassium and pH!)
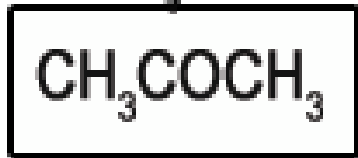- Substitution of hypokalemia, lot of infusions
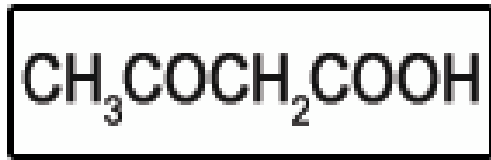
Ketoacidosis

- DM type 1
- Normal situation: insulin inhibits lipolysis
- Pathological situation: insulin is missing

↓

→ hyperglycaemia + lipolysis → production of ketoacids → decreasing of pH → MAc, Kusmaull´s breathing

Ketoacids

Kyselina acetooctová   Kyselina β-hydroxymáselná

$$\boxed{CH_3COCH_2COOH} + NADH + H^+ \longleftrightarrow \boxed{CH_3-CHOHCH_2-COOH} + NAD^+$$

$\downarrow -CO_2$

$\boxed{CH_3COCH_3}$

aceton

Drunk or diabetic?

Keto-substances smells similarly to alcohol (mainly aceton)

Diabetic coma

During hyperglycaemia (deficit of insulin→ MAc)

- Due to hyperosmolarity of ECF, the water moves from nerve tissue to ECF

- Treating of serious hyperglycaemia has to be very slow. If the glycaemia is decreased too quickly, then the brain edema can occur.

During hypoglycaemia (too much of insulin applied or food intake was missed/forgotten)

Late complications of DM

- ## Macroangiopathy (atherosclerosis)
  - Lipids (apolipoproteins)

- ## Mikroangiopathy
  - Nephropathy
  - Neuropathy
  - Retinopathy

Mechanism of vessel injury: glycation of proteins

Albuminuria

= low concentration of albumin in urine

- Physiological: < 30 mg/day
- Diagnosic strips: > 150 mg/l
- MAU: 30-300 mg/day

- early indicator of diabetic nephropathy
- should be taken every 6 months

Results of albuminuria (MAU)

	Normal excretion	microalbuminuria	Proteinuria
Collection of urine during 24 hrs	< 30 mg/day	30 - 299 mg/day	≥ 300 mg/day
Timed sample	< 20 μg/min	20 - 200 μg/min	> 200 μg/min
Random sample** (ACR)	< 2,5 (M) < 3,5 (F) g/mol creat.	2,5 - 30 3,5 - 30 g/mol creat.	30 g/mol kreat.

** second morning urine.

ACR = Albumin/Creatinin Ratio