MODY 2 diabetes in Siberia: 3 years of follow

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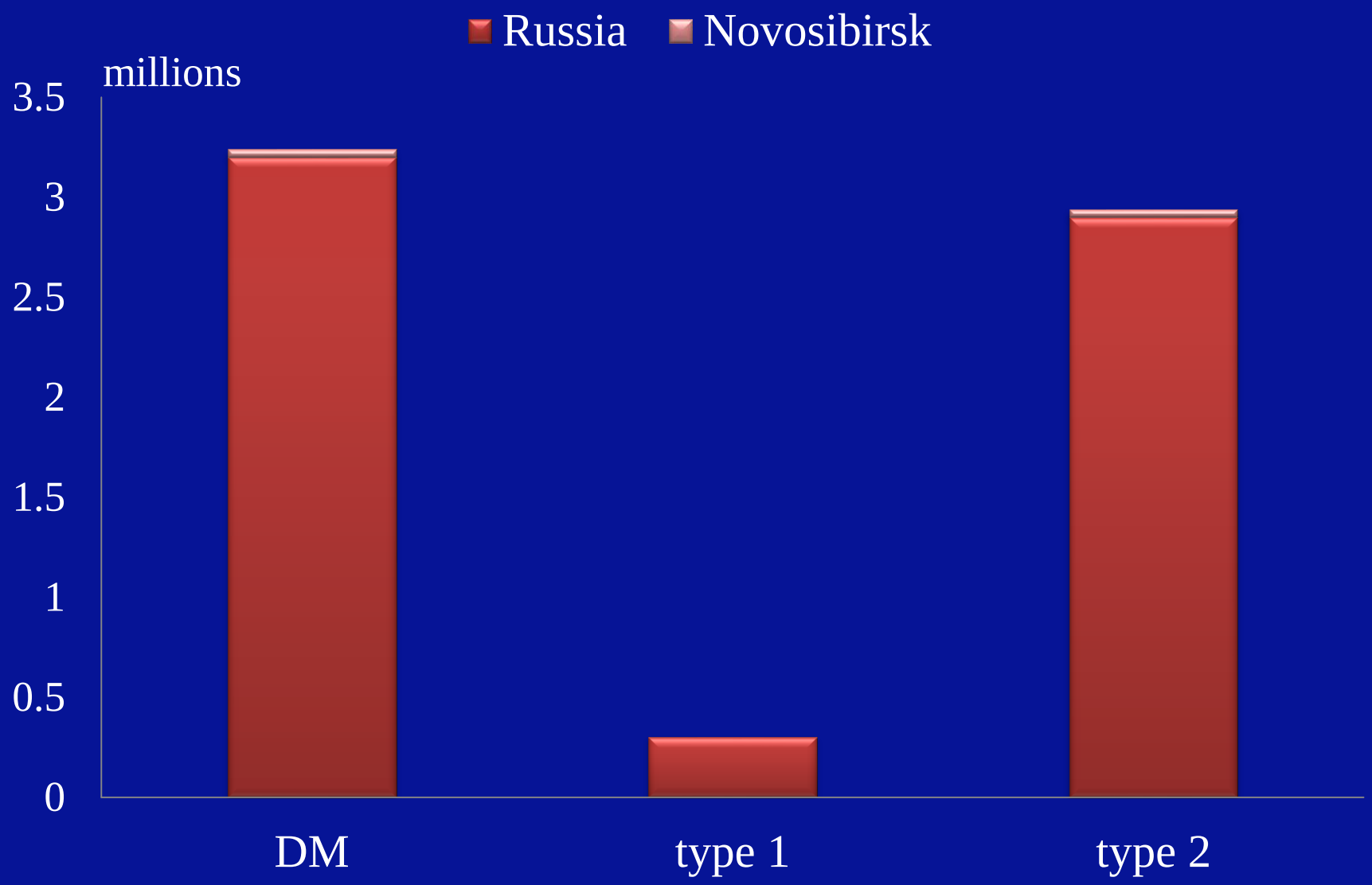
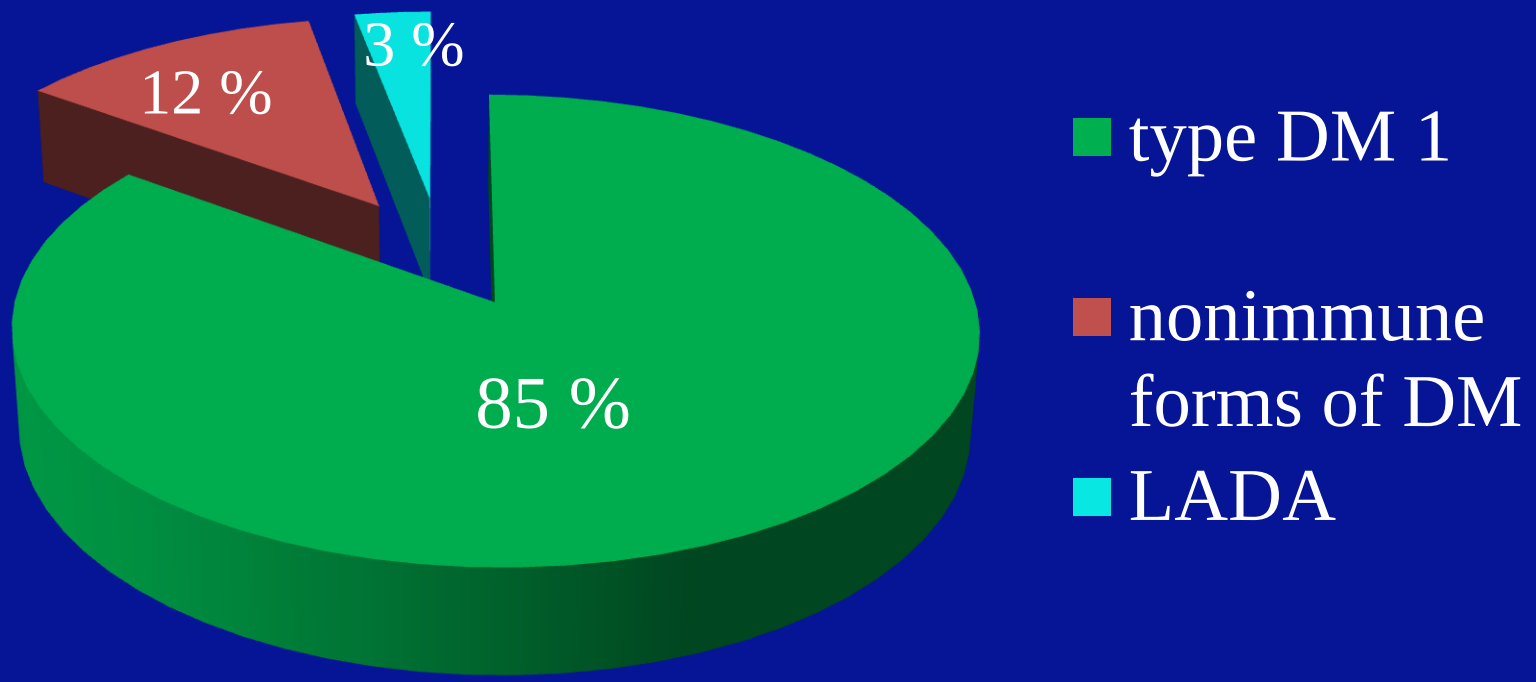
Russia

The population in Russia is 146 519 759 people, in Novosibirsk – 1,584,000

The number of patients with DM in Russia

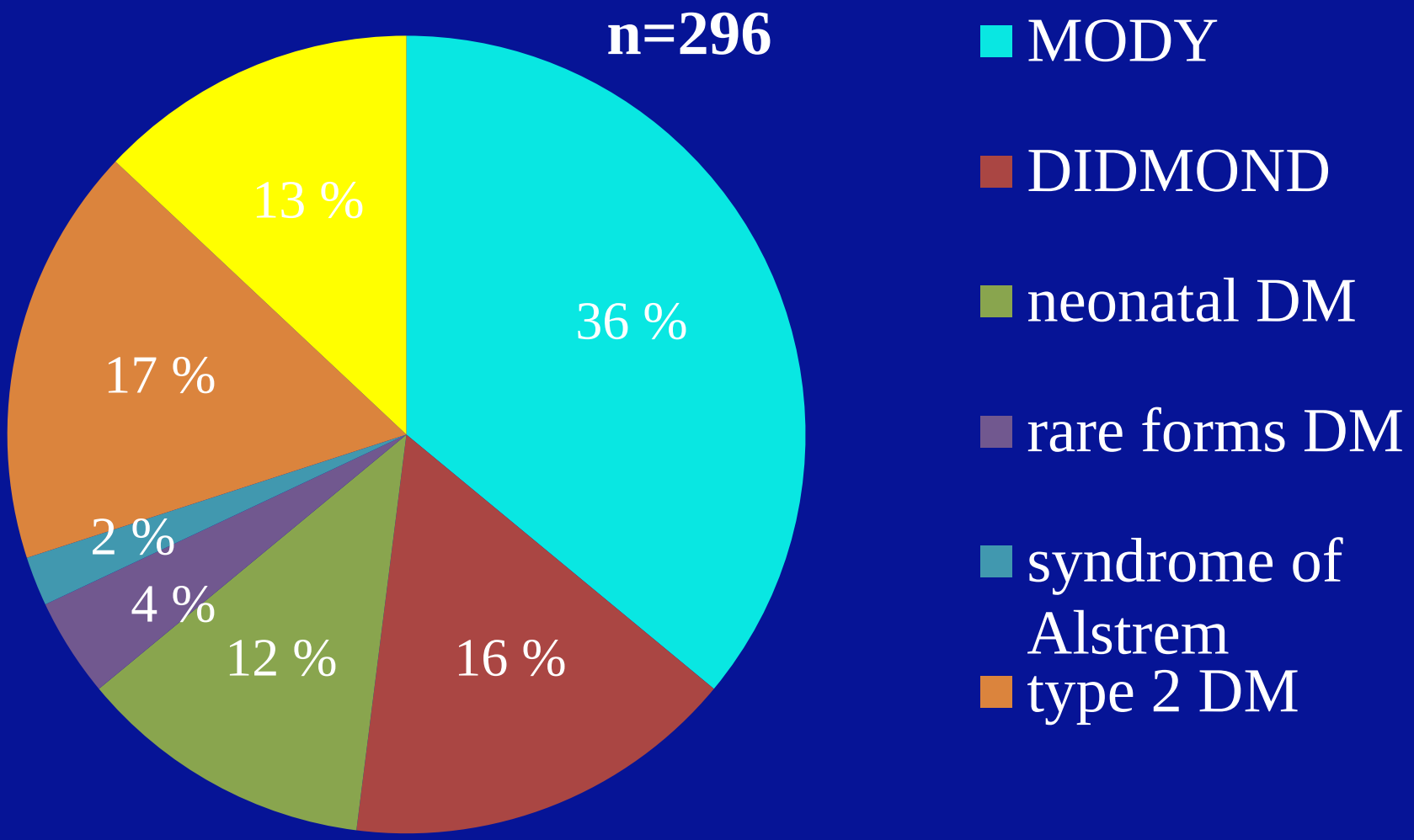


Prevalence of DM in youth in Russia*



* Kuraeva, T., Zilberman L., Titovich E., Peterková V. Genetics of monogenic forms of diabetes .Diabetes. - 2011. - № 1. - P. 20-27.

The prevalence of nonimmune forms of DM in Russia*



*Peterková V. et al. Molecular genetics and clinical features monogenic forms of diabetes. Herald RAMN.- 2012. - № 1.- pp 81 - 86.

Clinical characteristics of MODY and type 2 diabetes

CHARACTERISTIC	MODY	TYPE 2 DIABETES
Mode of inheritance	Monogenic, autosomal dominant	Polygenic + environment
Age of onset	Childhood, adolescence or young adulthood (<25yr)	Adulthood (40-60yr) occasionally adolescence (obese)
Pedigree	Usually multigenerational	Rarely multigenerational
Penetrance	80-95%	Variable (~10-40%)
Body habitus	Nonobese	Usually obese
Metabolic syndrome	Absent	Usually present

M. Vaxillaire et al., 2006

Definition of MODY

S. Fajans и R.Tattersall entered abbreviation of MODY in 1965 year

↓

first mutation (gene glucokinase) was diagnosed in 1992

↓

five subtypes of MODY were identified in 2002

↓

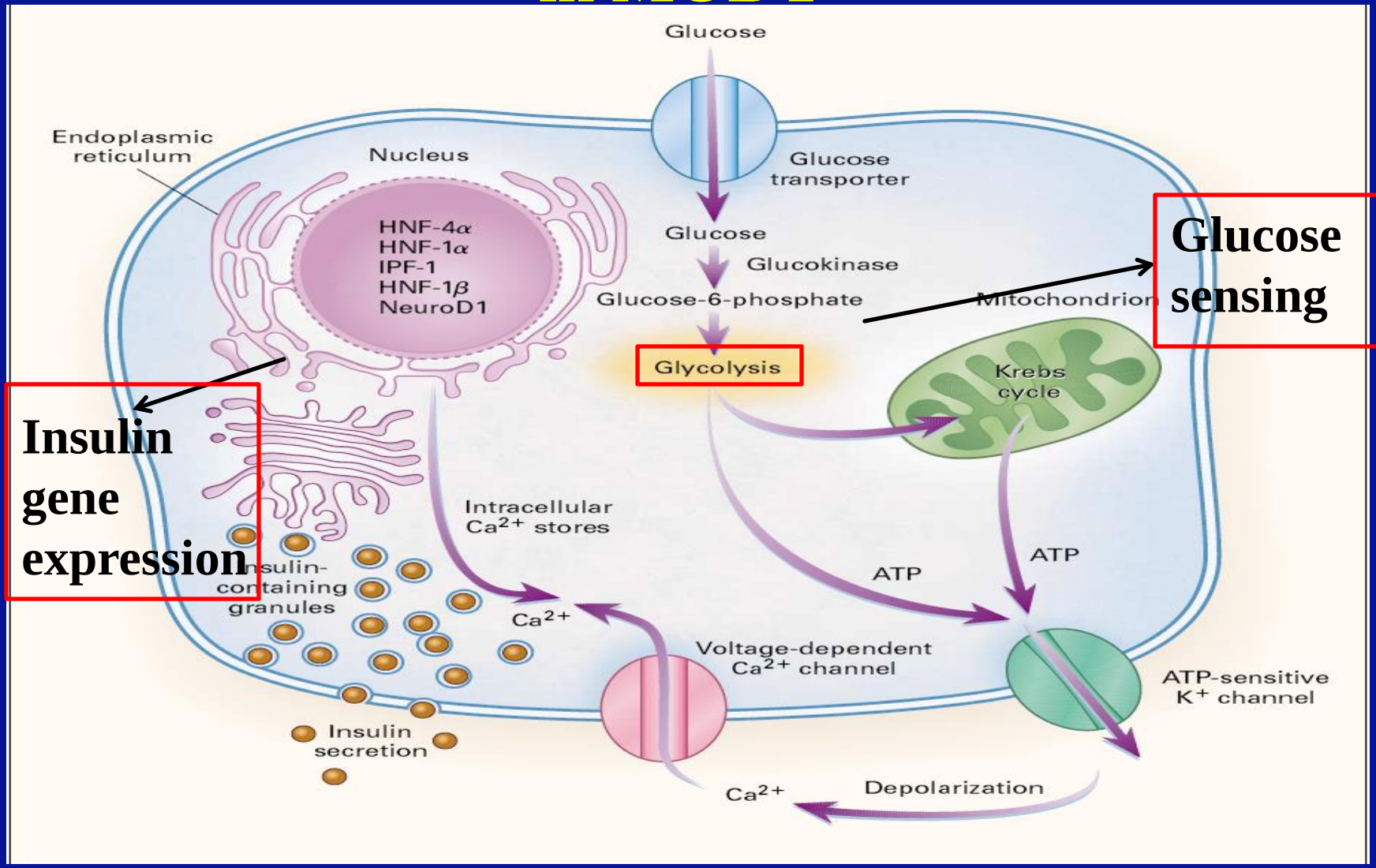
NOW: 13 subtypes of MODY

Characteristics of MODY diabetes*

- relatives with disorders of carbohydrate metabolism;
- manifestation of DM before the age of 25 years;
- the absence of ketoacidosis;
- good compensation (HbA1c ≤ 7%) diabetes;
- long-term (at least 1 year) remission ("honeymoon diabetes") without periods of decompensation;
- preservation of the secretory activity of beta cells (the level of C-peptide is in the normal range or slightly reduced);
- Absence of markers of autoimmune response against beta cells (antibodies to beta-cells, GAD, insulin);
- Absense of obesity;
- absence of association with HLA.

*M. Vaxillaire et al., 2006, Ch. Henzen, et al., 2012 ;

Pancreatic β-Cell and the Proteins Implicated in MODY



N Engl J Med, Vol. 345, No. 13, September 27, 2001

MODY types*

HNF 4a (hepatocyte nuclear factor)

GCK,

HNF-1a,

IPF (insulin promoter factor),

HNF-1b,

NEUROD1

KLF-11,

CEL,

PAX-4,

INS,

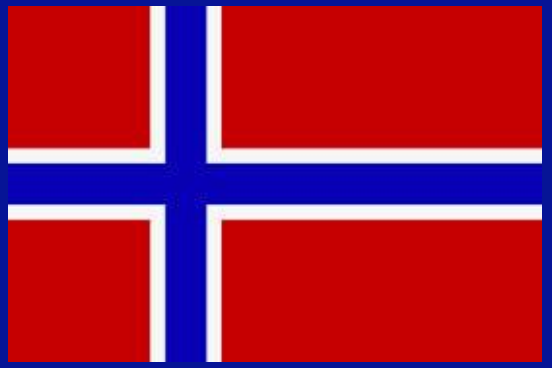
BLK

New types (2012) { ABCC8, KCNJ11

•Ch.. Henzen, 2012, B. Johansson,.2011, Bowman et al ., 2012

Prevalence of subtypes MODY diabetes

- MODY 2-5% of all cases of diabetes, in the UK up to 10%.
- MODY 3: ↑



- MODY 2: ↑

Prevalence of subtypes MODY diabetes in Russia

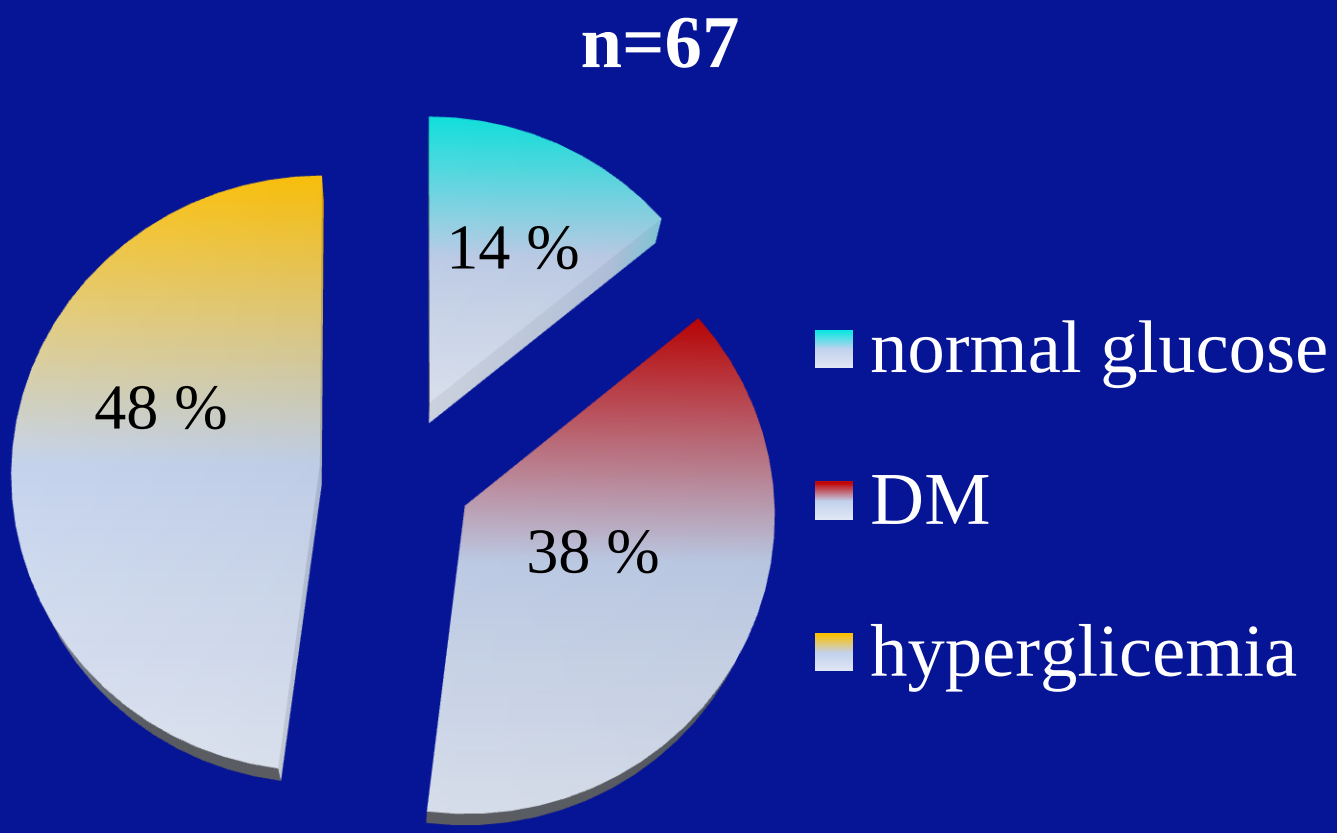
MODY 2 = MODY 3

Phenotype of MODY 2*

- ~~Symptoms;~~
- Can begin to
- Good compensation;
- Moderate fasting hyperglycemia (not more than 6.5 mmol / l);
- OGTT: increase in blood glucose of less than 3.5 mmol / l;
- Neuropsychiatric disorders 7.5%;
- Absence obesity.

*A. Senatorova et al., 2009

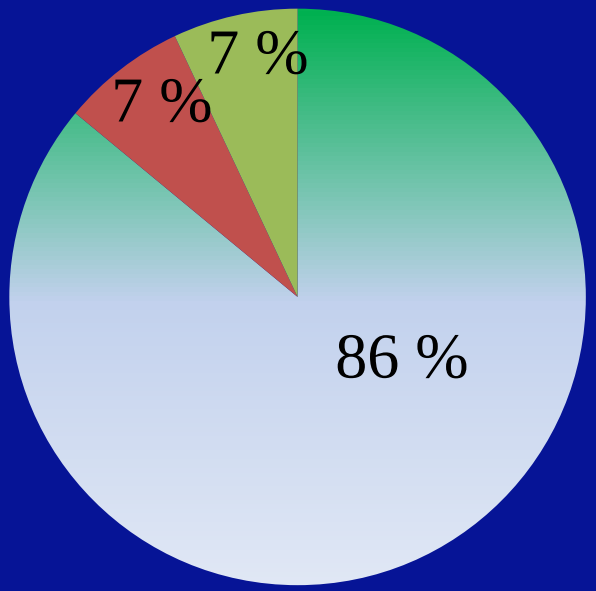
Characteristics of carbohydrate metabolism in MODY 2



2 Russian Congress «Innovative technologies in endocrinology» (may 2014)

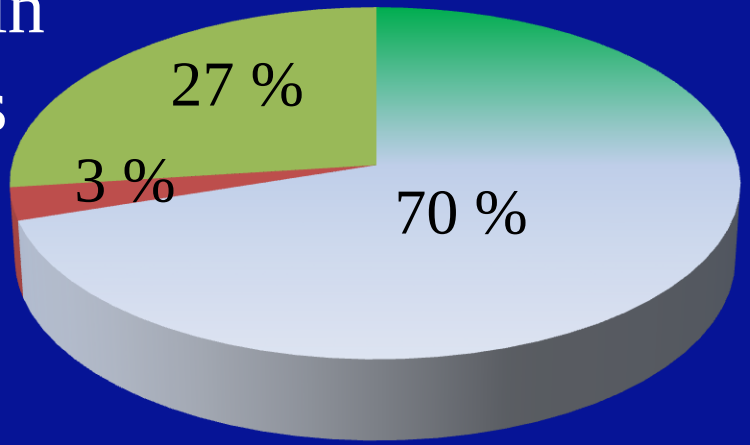
Treatment of MODY 2

Children



diet
insulin
drugs

Adult



diet
insulin
drugs

2 Russian Congress «Innovative technologies in endocrinology» (may 2014)

MODY GCK in Siberia*

- **The purpose:** to identify the clinical features of MODY GCK diabetes which we need to follow of this group of patients.

**The reported study was supported by RSCF, research project No. 14-15-00496.*

- **Materials and methods:**

- diagnose of MODY GCK during the molecular genetic testing of glucokinase gene;
- once a year: full clinical examination, blood samples for biochemical research, determination of C-peptide and TSH, antibodies to b- cells, microalbuminuria, abdominal ultrasound, heart and thyroid ultrasound, examination of ophthalmologist.

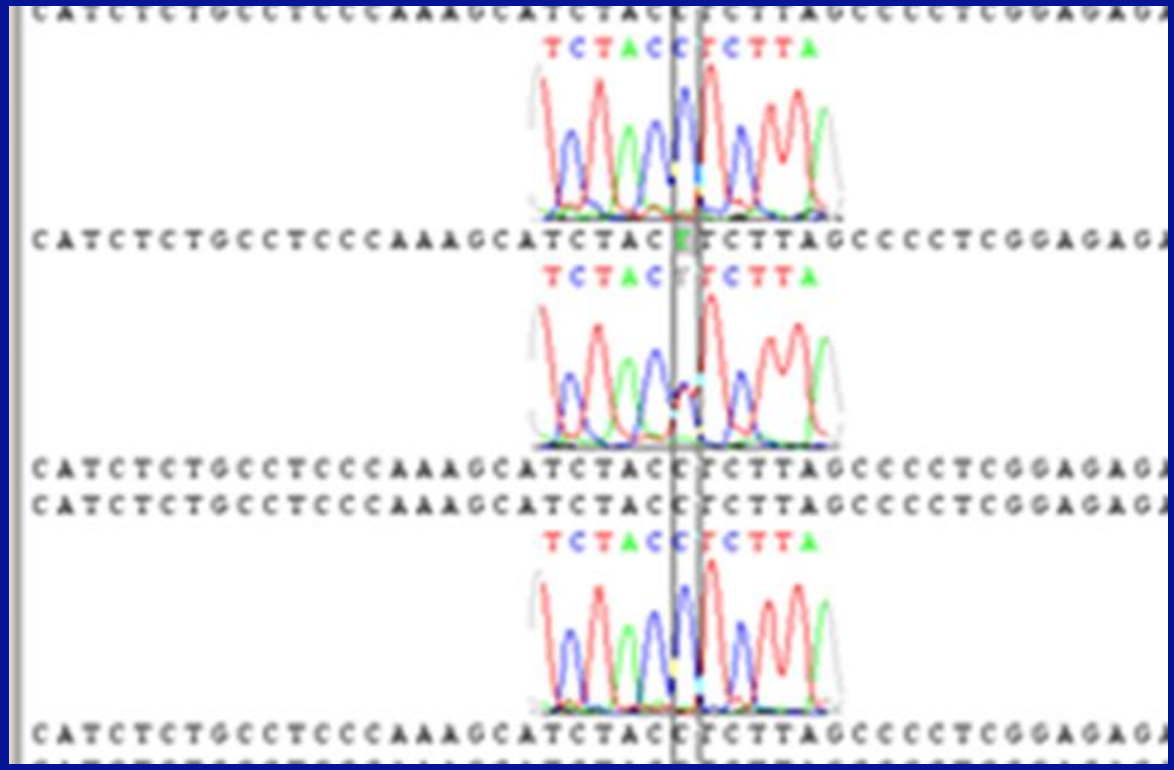
Results

Patients with MODY GCK:

- 14 peoples (8 probands +6 relatives)= 6 males (43%) and 8 (57%) female.
- The average age of the probands was 12 ± 2,6 years.
- Age of onset ranged from 3 months to 32 years.
- Median of duration of diabetes was 3 years.
- Hereditary: 93% of patients had relatives with disorders of carbohydrate metabolism, 1 patient had mutation “de novo”.

Results

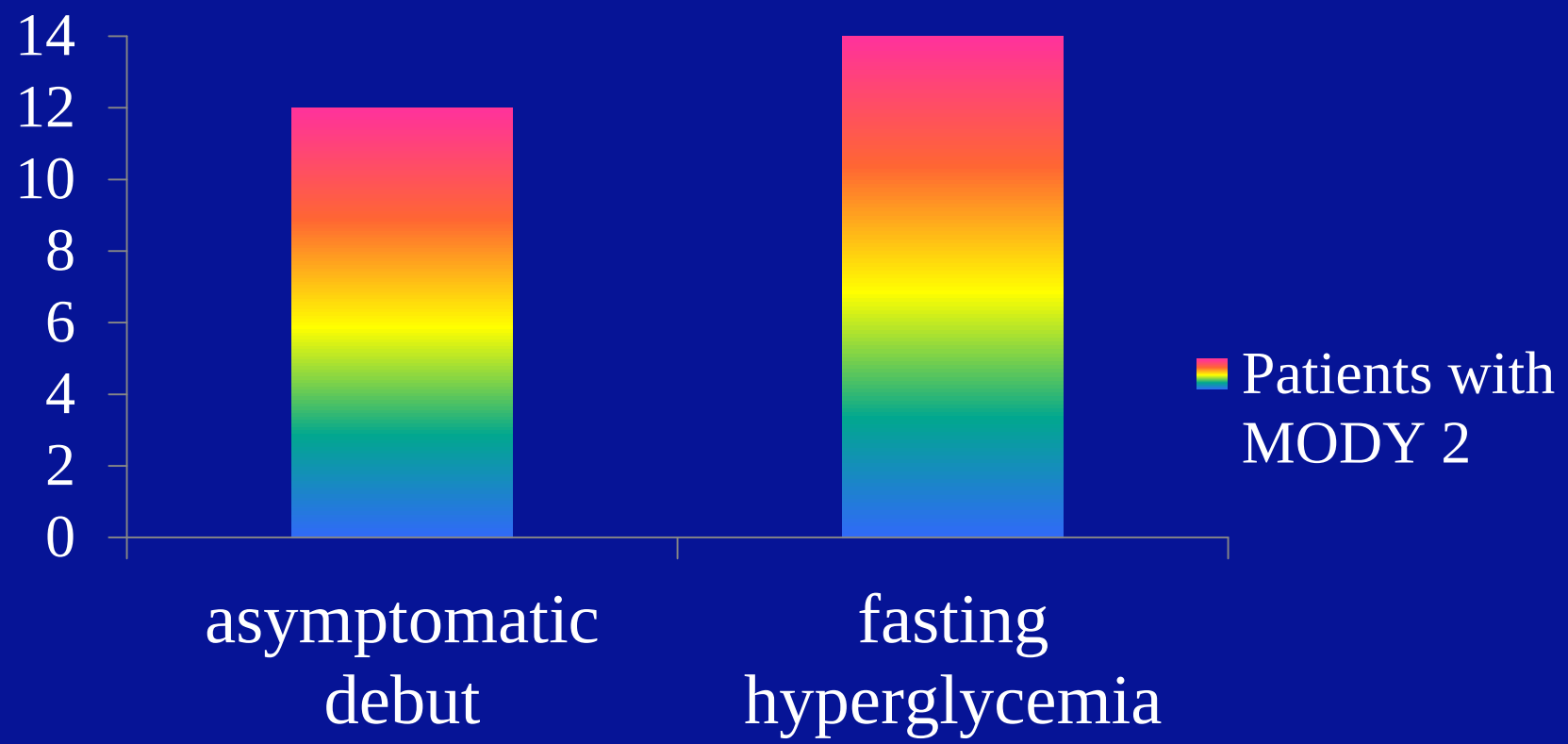
- Mutations were in 1 ekzon, 3, 4, 5, 7 of GCK gene.



- Mutation 60 C > T

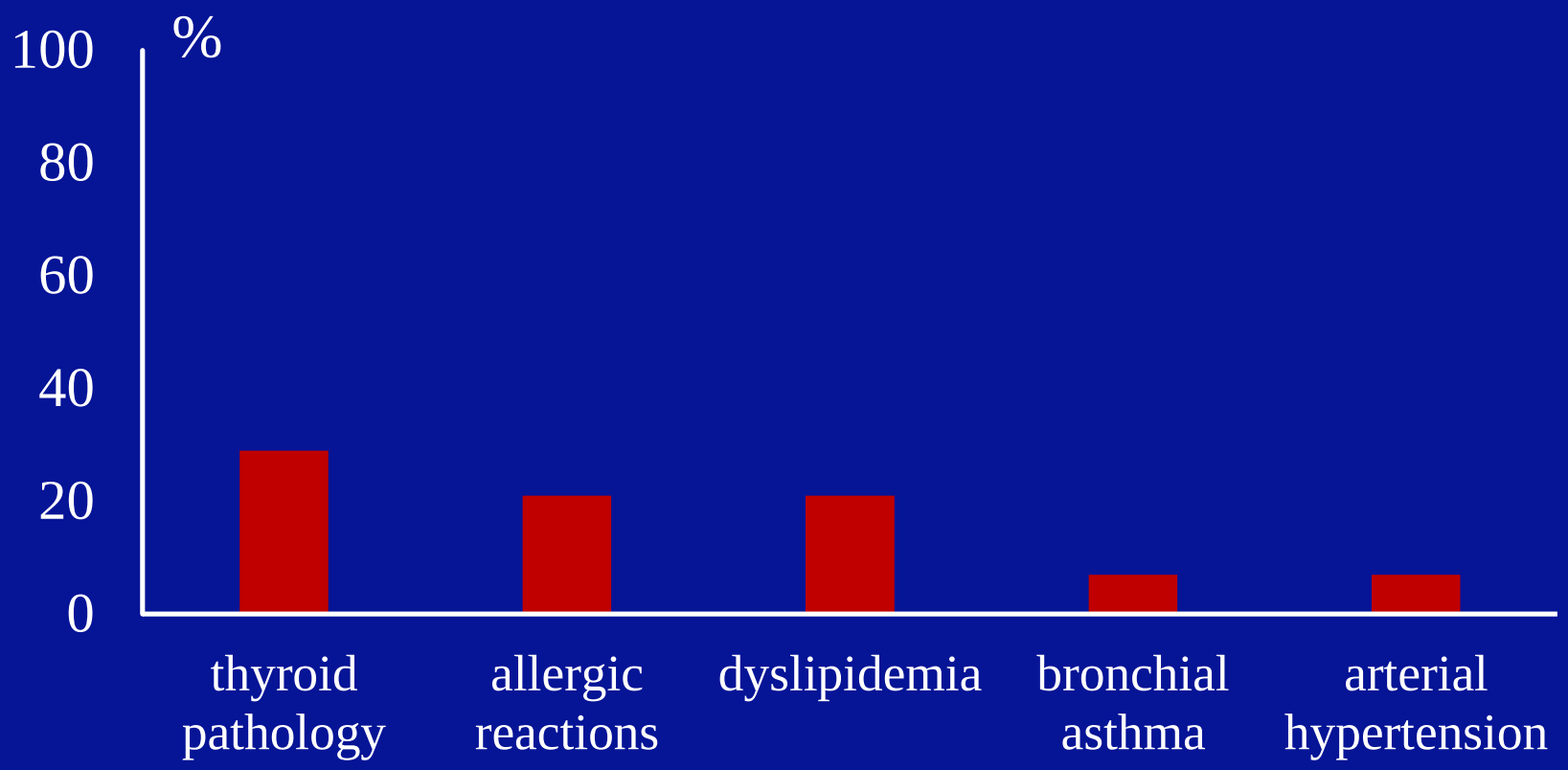
Results

DEBUT:



Results

DEBUT:



Results

- Diabetes complications:

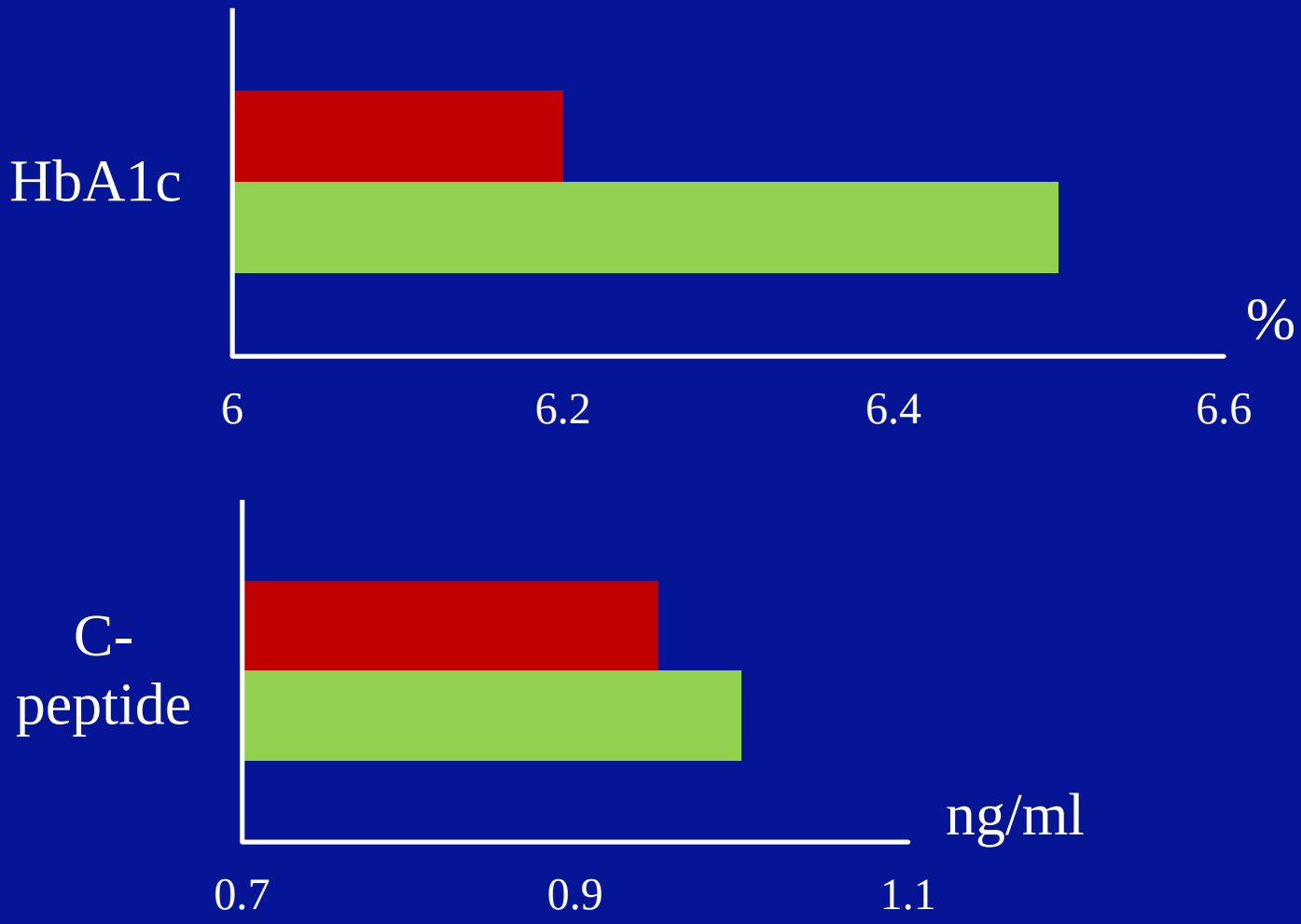
1 patient (7%) had diabetic nephropathy, chronic kidney disease, Stage 1, category 2 (A2).

Results

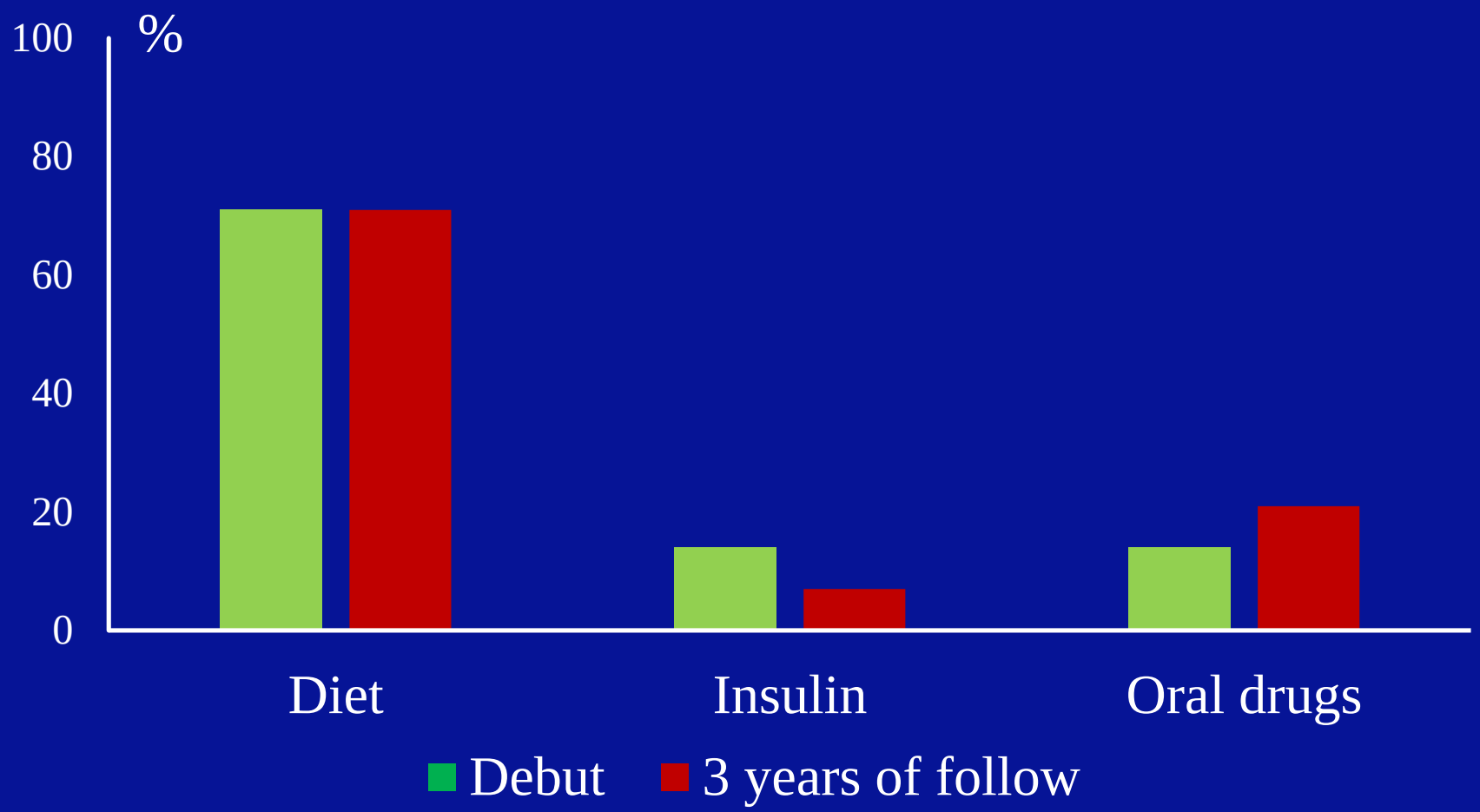
3 YEARS OF FOLLOW UP:

- Overweight and obesity were not detected in any patient.
- The same patient had no progressive diabetic nephropathy.
- Biochemical analysis: no changes.

Results



Results


%
100
80
60
40
20
0
Diet
Insulin
Oral drugs
Debut
3 years of follow

Conclusions

1. The earliest age of clinical manifestations of disorders of carbohydrate metabolism in MODY 2 diabetes was six months which should be considered in the differential diagnosis with type 1 diabetes because it is also manifest in a younger age group.

2. MODY 2 diabetes had oligosymptomatic onset, soft flow, good compensation of carbohydrate metabolism, no complications, no need for exogenous insulin in most cases.

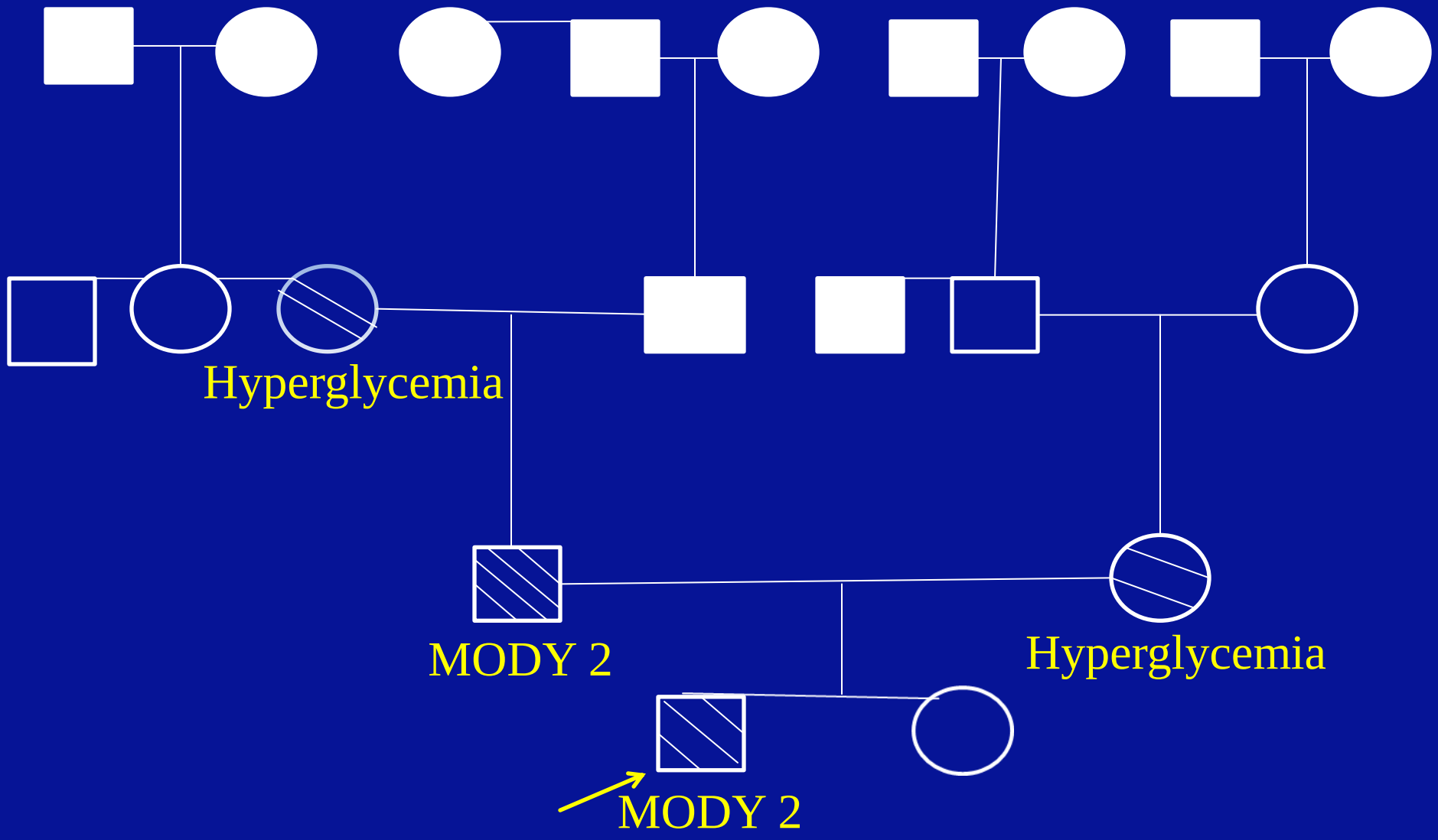
Clinical case

- Patient D. (boy) 2002 year of birth.
- 2010 year: thirst, itchy skin. Fasting hyperglycemia 6,5 mmol/l (capillary blood), postprandial hyperglycemia 8,9 mmol/l, HbA1c 5,9 %. Antibodies to b cells, GAD negative.
- The patient had diabetic nephropathy, chronic kidney disease, Stage 1, category 2 (A2).

Clinical case

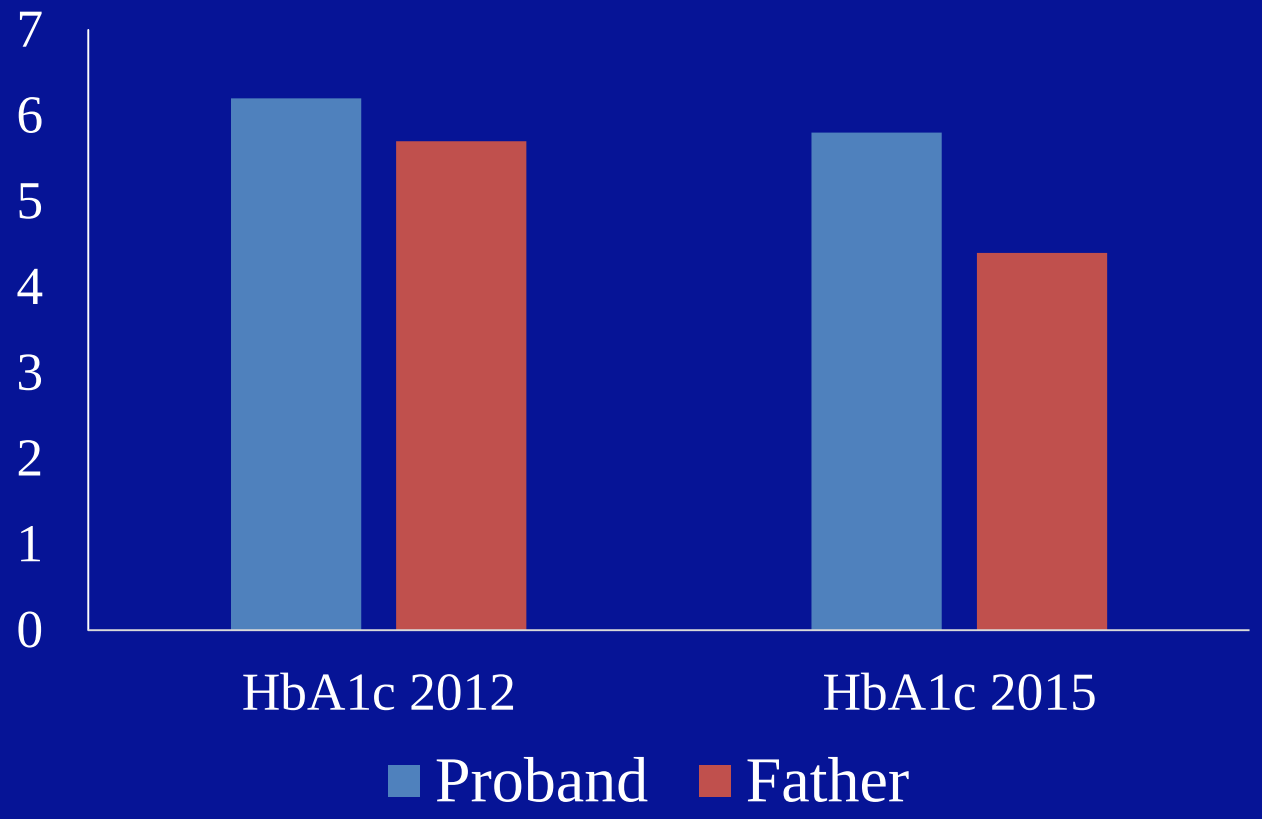
- Relatives of the patient did not have diagnosis of diabetes.
- 2012 genetic research of GCK gene. Mutation 146 (146C > G) was detected.
- Probands parents were examined. Father had asymptomatic fasting hyperglycemia. He was examined and same mutation was detected.

Pedigree



Clinical case

- Probands father had mild hypertension.



Clinical case

- Treatment in 2012:
- Patient: Insulin (4-6 U Detemir)
- Father: diet.
- Treatment in 2015:
- Patient: glibenclamid ¼ tab 1,75mg
- Father: diet.

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Thank you for your attention!