Federal State Budgetary Educational Institution of Higher Education
FAR EASTERN STATE MEDICAL UNIVERSITY
MINISTRY OF HEALTH OF THE RUSSIAN FEDERAL STATE BUDGETARY INSTITUTION

Interregional Scientific and practical conference with international participation
dedicated to the International Children's Day
Interdisciplinary aspects of child and adolescent health

Hypoglycemia in children. We form knowledge, expand clinical thinking

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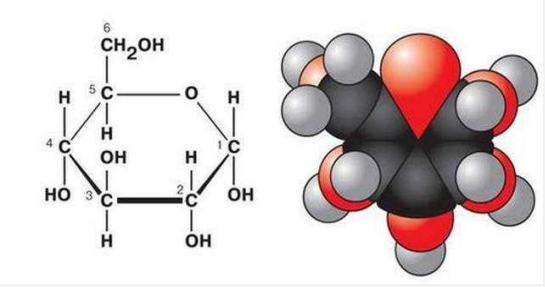
Interregional scientific and practical conference

Khabarovsk FESMU

June 5, 2025



The relevance of the problem of hypoglycemic conditions in children in pediatrics

There are more than 50 etiological factors of hypoglycemic conditions
20 are the causes of the transient course of hypoglycemia in newborns
> 25 of the recurrent course of HS in children and adolescents.

Hypoglycemia leads to various neurological disorders in postnatal life associated with the damaging effect of low glucose levels on brain neurons

Mechanisms of the damaging effect of hypoglycemia

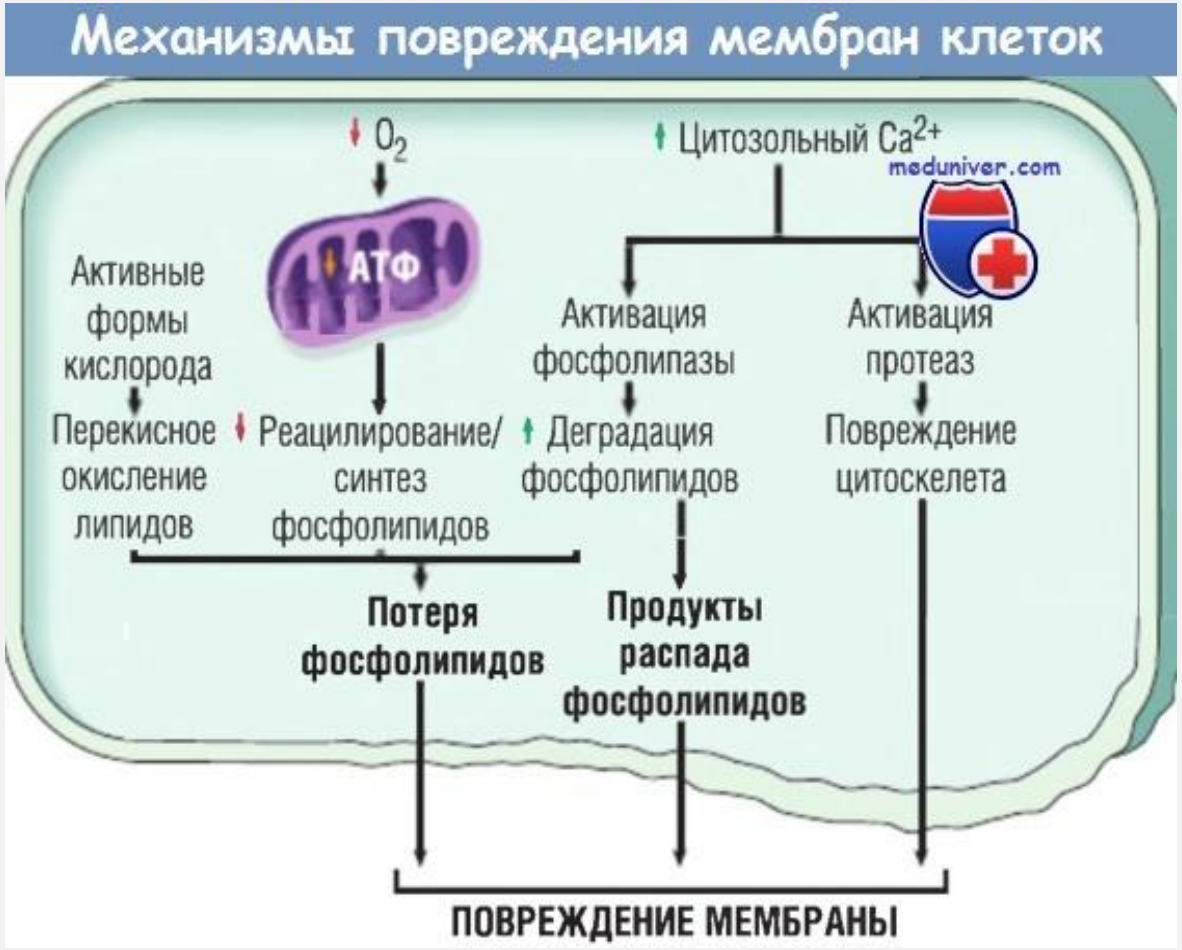
Increased lactate production
Development of tissue acidosis
Decreased levels of creatine phosphate and ATP in brain cells
Depolarization of the neuron membrane
Tissue electrolyte disorders: potassium influx into the extracellular space
Intracellular elevation of Na, Cl, Ca levels, accumulation of fluid in neurons
Release of free radicals
Activation of prostaglandins, thromboxanes and leukotrienes

Edema of neurons, atrophy of glial cells, demyelination of white matter. Vasospasm due to intracellular Hyperca++, hypoxia of brain tissue, damage to cell membranes

Consequences of hypoglycemia

Irreversible damage to cell membranes ,
selective death of neurons

- convulsive syndrome
- delayed psychomotor development
- decreased IQ
- scores impaired cognitive functions
- Secondary dysfunction of organs and systems (liver, myocardium, skeletal muscles)



The more severe and prolonged the hypoglycemia, the younger the age of the child at the onset of hypoglycemia, the higher the risk of persistent irreversible neurological disorders *(M. Shperling, 1999).*

Definition and definitions of hypoglycemic conditions (HS)

- Hypoglycemia is not an independent disease.
- The symptoms of hypoglycemia are nonspecific
- clinical manifestations can occur in various diseases

HS is a laboratory-clinical symptom complex caused by a decrease in blood glucose concentration below the physiological minimum, or a rapid drop in glycemia from high numbers to significantly lower ones, which is accompanied by polymorphic and vivid clinical symptoms

The duration of the etiological diagnosis of the causes of HS is unreasonably delayed reaches 1.8- 4.8 years old

Reasons for untimely care and lack of pathogenetically adequate treatment

1. The presence of neuropsychiatric disorders, convulsive syndrome, similar to other diseases

75% patients are misdiagnosed neurological diseases

Epilepsy - in 34% of cases
Brain tumors – in 15%
Autonomic dysfunction – in 11%
Diencephalic syndrome – in 9%, Psychosis, neurasthenia – in 3%

2. Lack of awareness of specialists about modern methods and algorithms of etiological diagnostics: at least 7 stages of laboratory diagnostics, including performing molecular genetic studies (genes KCNJ11, ABCC8, etc.)

3. Erroneous interpretation of the results of the glycemic level in age groups

Миняйлова Н.Н., Железняк О.С., Ровда Ю.И., Ведерникова А.В. Шмакова О.В. Гипогликемии у детей после неонатального периода: ряд важных аспектов в клинической практике (часть 1) //Мать и Дитя. 2021. №3(86). С. 27-35.

Criteria for hypoglycemic condition

Hypoglycemia in children is a decrease in blood glucose levels below

2.8 mmol/l

in full-term newborns

< 2.2 mmol/l

in premature infants

< 2.0 mmol/l in the first 3 hours of life

Симптомы и признаки гипогликемии

Адренергические

- Тахикардия
- Мидриаз
- Беспокойство
- Агрессивность
- Дрожь
- Тошнота
- Гиперсаливация
- Диарея
- Обильное мочеиспускание

Нейрогликопенические

- Астения
- Снижение концентрации внимания
- Головная боль
- Чувство страха
- Спутанность сознания
- Дезориентация
- Галлюцинации
- Амнезия
- Нарушение сознания
- Судороги
- Речевые, зрительные, поведенческие нарушения
- Кома

Холинергические

- Холодный пот
- Сильный голод
- Парестезии

Эндокринология И.И. Дедов, Г.А. Мельниченко, В.В. Фадеев 2015

Indications for urgent determination of glycemic level in clinical practice

clinical symptoms

- Impaired consciousness (of any degree)
- Vomiting and regurgitation
- Diarrhea
- Abdominal pain (or severe anxiety)
- Hypothermia
- Arterial hypotension
- Cardiac arrhythmia
- Seizures
- Exicosis (of any degree)

Clinical manifestations of hypoglycemia in newborns

They can be "asymptomatic", the clinical manifestations of the symptoms are nonspecific and diverse

The most common clinical symptoms

Eye symptoms: "floating" circular eye movements, nystagmus, decreased eye muscle tone and disappearance of the oculocephalic reflex

Weak high-frequency high-pitched unemotional scream, loss of communication skills, weakness, regurgitation, anorexia, lethargy, poor movement or tremor, twitching, increased excitability, irritability, increased Moro reflex

Less frequent clinical symptoms

Rhythmic tremor

Increased muscle tone and periosteal reflexes, reflexes of newborns

Seizures

Apnosis

Cyanosis: perioral, general or acrocyanosis

Body temperature instability, hypothermia

Tachycardia and tachypnea

Arterial hypotension

- **THE IMPORTANCE OF MEDICAL HISTORY**

The list of drugs used by pregnant and breast-feeding mothers that most often cause "medicinal" hypoglycemia in newborns: fluoroquinolones, pentamidine, beta-blockers, ACE inhibitors, antiepileptic drugs (valproic acid, phenytoin), antidepressants

Laboratory and clinical manifestations of hypoglycemia in children and adolescents

A decrease in the level of glycemia < 3.3 mmol/l is accompanied not only by a reaction of the central nervous system, but also by the autonomic nervous and endocrine systems, forming a diverse clinical picture

Гипогликемия стадии	Показатель глюкометра, ммоль/л	Симптомы
Легкая	ниже 2,8	Тревожность, тошнота, голод, озноб, онемение губ и пальцев на руках, тахикардия
Средняя	ниже 2,5	Проблемы с речью, концентрацией, мышлением, движением. Голова сильно болит и кружится, возникают проблемы со зрением
Тяжелая	ниже 2, 2	Судороги, потеря сознания. Снижение температуры тела. Возможен эпилептический припадок, кома

Classification of hypoglycemia by time of manifestation

Occurring on an empty stomach (fasting or spontaneous)

Fasting hypoglycemic syndrome is initiated by an organic pathology in which insulin and/or insulin-like substances are secreted offline, regardless of the level of glycemia

Postprandial, occurring 2-4 hours after eating (reactive or alimentary hypoglycemia)

observed in various conditions, the main pathogenetic feature of which is an imbalance and inconsistency of the processes of glucose intake from the intestine with the action of factors regulating its plasma level

Defects at any stage of glucose homeostasis and its regulation can lead to the development of hypoglycemic syndrome

Depending on the causes of hypoglycemia, they are classified into

- **Oxidation associated with substrate deficiency**

  These conditions are the result of a discrepancy between high metabolic needs and low reserves of substances necessary for gluconeogenesis

- **Related to excessive insulin production**

  occur with congenital hyperinsulinism (persistent hyperinsulinemic hypoglycemia of newborns), which is caused by mutations in the genes responsible for the functioning of beta cells of the pancreas and insulinomas, which is an extremely rare condition in childhood.

Iatrogenic – insulin therapy, treatment of diabetes

- **Transient hyperinsulinemic hypoglycemia –** observed in children born with asphyxia, diabetic fetopathy, and fetal erythroblastosis.

Hyperinsulinism

- **Hyperinsulinemic hypoglycemia (HH)**

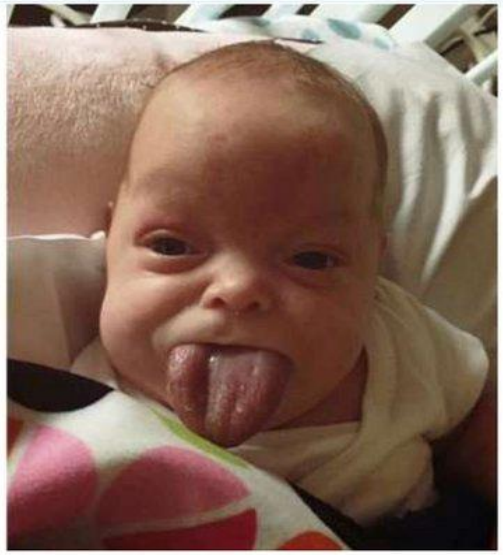
  they are a consequence of hyperproduction of insulin
- **Persistent**

  with congenital hyperinsulinism insulinomas
- **Transient**

  syndromes

  Beckwith—Wiedemann, diabetic fetopathy, prolonged neonatal hyperinsulinism

Beckwith—Wiedemann syndrome



Diffuse beta-cell hyperplasia
Autosomal dominant type of inheritance
Frequency - 1:13,700 newborns

Etiology
Mutation or deletion at the 15p15.5 locus

Hyperinsulinemia
Hyperlipidemia
Hypocalcemia

Гипогликемия умеренная, самопроизвольно исчезающая во втором полугодии.
Макросомия, висцеромегалия, гепатоспленомегалия, пупочная грыжа, характерная борозда на мочке уха, асимметричный рост одной или нескольких частей тела/органов (гемигиперплазия), аномалии развития почек.
Ускорение костного возраста, врожденные пороки сердца, эмбриональные опухоли, задержка умственного развития, гипогонадизм, крипторхизм, аномалии развития матки.
Наиболее частая коморбидная жизнеугрожающая патология- гепатобластома, опухоль Уильмса, рабдомиосаркома, адренокортикальная карцинома, нейробластома.

Maple syrup disease (valinoleucinuria)

Mutation in the gene 1p21.2, g14.4,19g13.2 1:225,000 autosomal dominant type of inheritance

- **defective metabolism of leucine, isoleucine and valine**
- It is caused by the insufficiency of alpha-keto acid dehydrogenase
- **Manifestations**: hypoglycemia, ketonuria, ketonemia, vomiting, characteristic odor of urine, severe damage to the central nervous system.
- Leucine hypoglycemia can be suspected when**, after eating a high-protein meal, muscle stiffness, cramps, pallor, sweating, progressive hypotrophy, vomiting, lethargy, and coma occur.**
- **Hypoglycemia, ketonemia/uria,**
- **Diagnostic test**

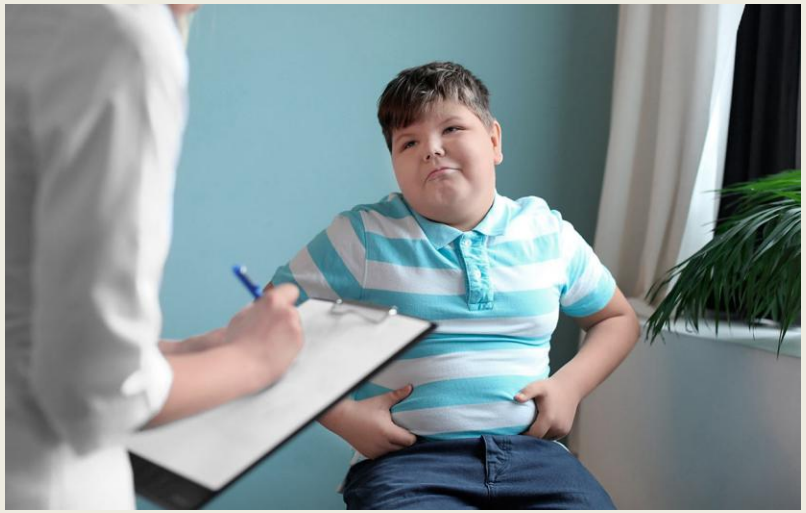
leucine sensitivity test (leucine at a dose of 150 mg/kg reg os, with increased sensitivity to leucine, blood glucose decreases, and insulin levels increase)

Ketotic hypoglycemia syndrome requires the exclusion of endocrine diseases

- **Diabetes mellitus** (overdose of insulin, sugar-lowering drugs, insulin resistance).
- **Insufficient production of counterinsular hormones**
- Typical: from the age of 1.5—2, episodes of ketotic hypoglycemia are noted, usually in the morning and/ or against the background of infectious diseases.
- At risk are children receiving long-term courses of anticonvulsant therapy without effect, who have indications of prolonged jaundice in the neonatal period, increased fractions of bilirubin and hepatic transaminase.
- **Adisson's disease, autoimmune adrenalitis –** adrenal insufficiency accompanied by hypotension and hypoglycemia.
- **The presence of EGFR and ketotic hypoglycemia** is an indication to exclude deficiency of growth hormone and other tropic hormones of the pituitary gland
- **Laron's dwarfism** is a high level of inactive GH, spontaneous hypoglycemia, phenotype : stunting, mandibular hypoplasia, saddle-shaped nose, high voice, sexual infantilism (see photo)

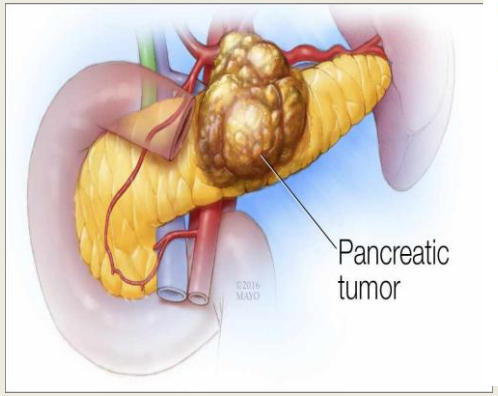
Functional hyperinsulinism in obesity

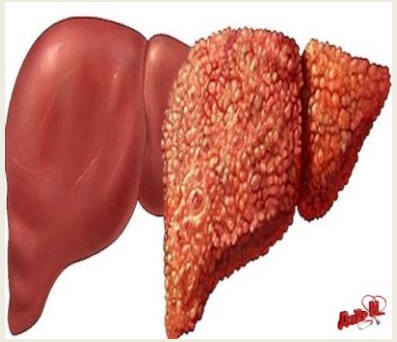
- **Excess body weight and obesity** are a significant cause of various forms of hyperinsulinism, which are widespread in childhood and adolescence.
- The central position in these processes is occupied by the nuclei of the posterior hypothalamus, the "food center" that change a person's eating behavior, the feeling of hunger or satiety.
- **Impaired secretion of neuropeptide Y, hyperliptinemia, leptin resistance**
- **Decreased sensitivity of beta-adrenergic receptors in adipose tissue to sympathomimetics (adrenaline, norepinephrine)**
- **Decreased glucagon secretion**
- **Eliminate type 2 diabetes!**

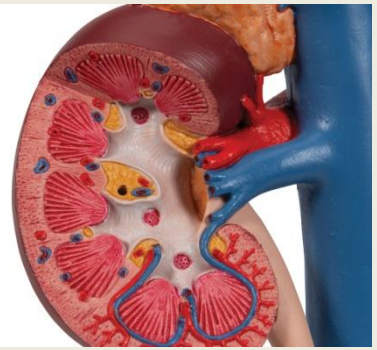


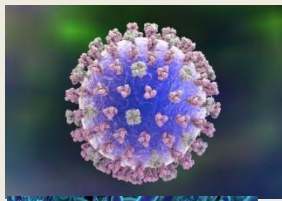
Hypoglycemia in somatic pathology

- **Diseases of the intestine and pancreas, with impaired digestion and absorption of carbohydrates:** infectious enteritis, severe food allergies, chronic pancreatitis
- **Intestinal malabsorption syndrome, disaccharidase deficiency, celiac disease, cystic fibrosis, exudative enteropathy.**
- **Tumors outside the pancreas –** fibroids, sarcomas, neuromas- liver cell carcinoma, tumors of the adrenal glands, due to increased production of IGF
- **Kidney diseases with impaired glucose reabsorption -** renal glucosuria, tubulopathy
- **Liver diseases:** cirrhosis, chronic hepatitis, fatty non-alcoholic liver disease
- **Severe course of infectious diseases**
- **Mismatch of resources with increased energy demand**
- **Hereditary diseases based on impaired carbohydrate metabolism:** glycogenoses, aglycogenoses, enzyme deficiency of fructose-1,6-diphosphatase, glucose-6-phosphatase and others



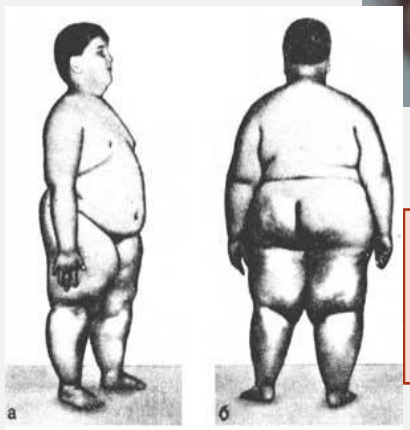






Dysregulatory hypoglycemia in adolescents

- **Vegetative vascular dystonia syndrome (VSD)** is n.Vagus hypertension with hyperinsulinemia during vegetative crises or panic attacks
- **Chromosomal and hereditary/genetic syndromes**
- **Babinsky-Frolich -** along with the vagal-insular component of pathogenesis, there is often dysfunction or damage to the adenohypophysis, deficiency of CTT, ACTH, TSH, cortisol and thyroid hormones
- **Kleine-Levine syndrome –** "sleeping beauty" - hypersomnia, apathy, "narrowing" of consciousness, bulimia and aggressiveness, chronic hypoglycemia with damage to the hypothalamus and increased tone of the parasympathetic nervous system.
- **Cyclical acetonemic vomiting syndrome occurs in preschool and school–age children,** characterized by periodic vomiting attacks with the smell of acetone in the exhaled air and pronounced ketonemia and ketonuria. Possible causes include enzymopathies caused by mutations in mitochondrial DNA at loci 16519T and 3010A.



синдром Бабинского-Фрелиха

Ятрогенные гипогликемии

- **alcohol-related poisoning substances**

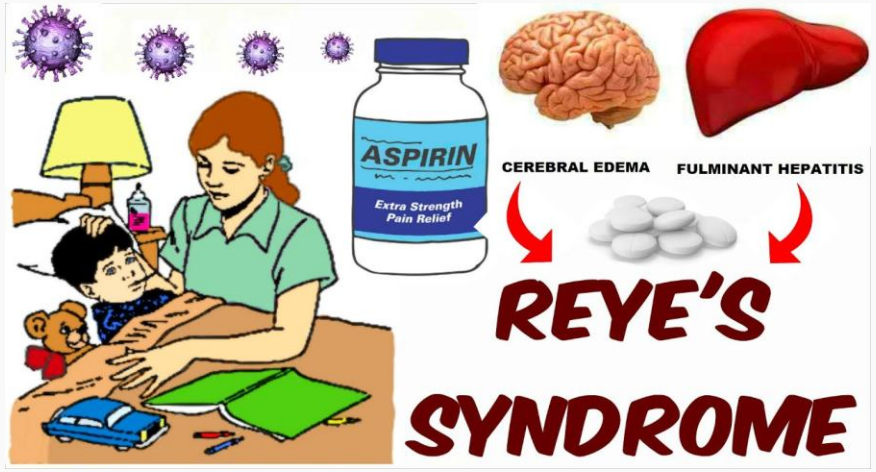
  aspirin

  beta-blockers

- **Reye's syndrome**

  is a disease of children and adolescents that occurs with epileptoid encephalopathy, hepatomegaly, and fatty degeneration of organs. Hypoglycemia occurs with vomiting, impaired consciousness and breathing

- **There is a deficiency of gluconeogenesis and malabsorption due to liver and intestinal dystrophy**



Ray's syndrome

It occurs mainly in children aged 1-10 years, under the influence of viral infections (chickenpox, influenza, etc.) and intoxication (primarily with aflotoxin, acetylsalicylic acid), it is a variant of the acute course of fatty hepatosis with the development of severe portal liver failure.

Severe selective damage to the mitochondria of hepatocytes was detected with a violation of the mitochondrial segment of the urea cycle (carbamoyl phosphate synthetase and ornithine carbamoyltransferase enzymes), which leads to a sharp increase in the level of ammonia in the blood, the disappearance of citrulline in the liver, encephalopathy, hypoglycemia, vomiting

Hypoglycemia in diseases of glycogen accumulation E 74.0 glycogenoses

- Hereditary diseases, based on a genetic defect in the production of enzymes involved in carbohydrate metabolism.
- Frequency 1: 40,000 12 types of autosomal recessive inheritance
- A characteristic common feature is the impossibility of the process of glycogen synthesis and breakdown, excessive deposition of glycogen in myocytes, hepatocytes and other cells of the body.
- Clinical symptom complex from birth:

  fasting hypoglycemia or postabsorption 0.6-3 mmol/l

  Hepatomegaly

  muscle weakness

  liver, heart, respiratory, and kidney failure.

Laboratory diagnosis:

lactic acidosis – lactic acid 3-10 mmol / l, increased levels of triglycerides, total cholesterol, LDL, VLDL, uric acid, liver enzymes.

biochemical blood analysis, morphological examination of biopsy material of muscles and liver, determination of enzyme activity, molecular genetic tests. Treatment is based on therapeutic nutrition, medical correction

Types of glycogenoses accompanied by hypoglycemia

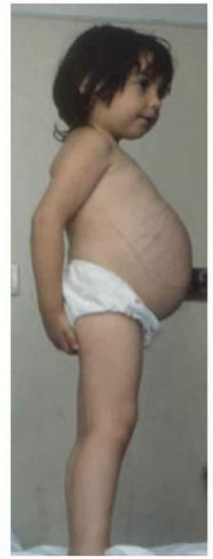
Печеночные формы
Гипогликемия +

Смешанные формы
Гипогликемия -

Мышечные формы
Гипогликемия -

Тип гликогеноза, название болезни	Молекулярная причина болезни	Структура гликогена	Основные органы, ткани и клетки, депонирующие гликоген
I тип, болезнь Гирке	Дефицит глюкозо-6-фосфатазы	Нормальная	Печень, почки
II тип, болезнь Помпе	Дефицит кислой α-1,4-глюкозидазы	»	Печень, селезенка, почки, мышцы, нервная ткань, эритроциты
III тип, болезнь Форбса, или болезнь Кори	Полное или частичное отсутствие активности амило-(1→6)-глюкозидазы и(или) гликогенветвящего фермента	Короткие многочисленные внешние ветви (лимит-декстрин)	Печень, мышцы, лейкоциты, эритроциты
IV тип, болезнь Андерсена	Отсутствие 1,4-глюкан-6-α-глюкозилтрансферазы	Длинные внешние и внутренние ветви с малым числом точек ветвления (амилопектин)	Печень, мышцы, лейкоциты
V тип, болезнь Мак-Ардла	Недостаточность фосфорилазы мышц	Нормальная	Скелетная мускулатура
VI тип, болезнь Герса	Недостаточность фосфорилазы печени	»	Печень, лейкоциты
VII тип, болезнь Томсона	Недостаточность фосфоглюкомутазы	»	Печень и(или) мышцы
VIII тип, болезнь Таруи	Недостаточность или полное отсутствие фосфофруктокиназы мышц	»	Мышцы, эритроциты
IX тип, болезнь Хага	Недостаточность киназы фосфорилазы *b*	»	Печень

Glycogen storage disease type 1
Clinical features



GSD1a/GSD1b

Short stature - delayed puberty
Liver and kidney enlargement
Fasting hypoglycemia
Hyperlipidemia and hyperuricemia

Chronic renal disease
Liver adenoma
Osteoporosis

GSD1b

Neutropenia/Neutrophil dysfunction
Recurrent infections

Inflammatory bowel disease

- **Болезнь Гирке.**
- **Болезнь Кори.**
- **Болезнь Андерсена.**

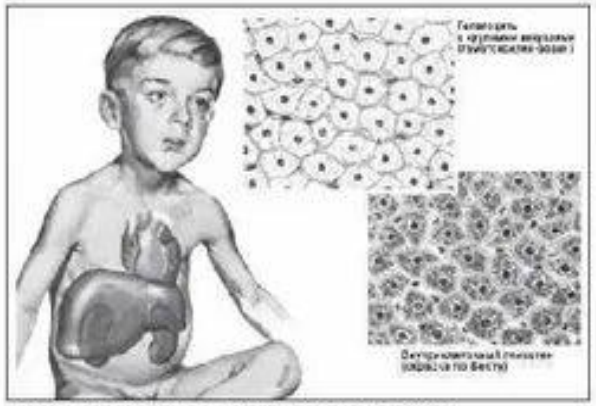


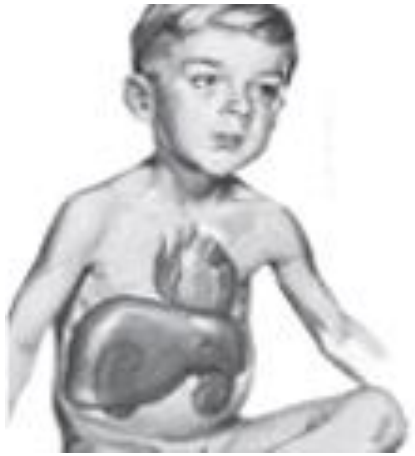
Рисунок 2. Симптомы болезни Гирке (по F. Netter, 2001)

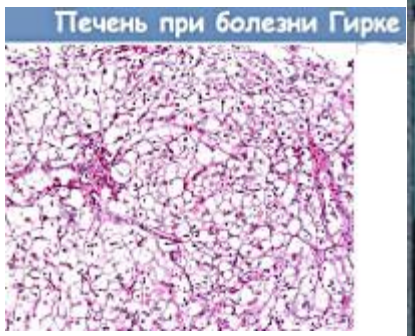
Гликогенозы проявляются избыточным накоплением гликогена, в результате у больных отмечается гипогликемия.

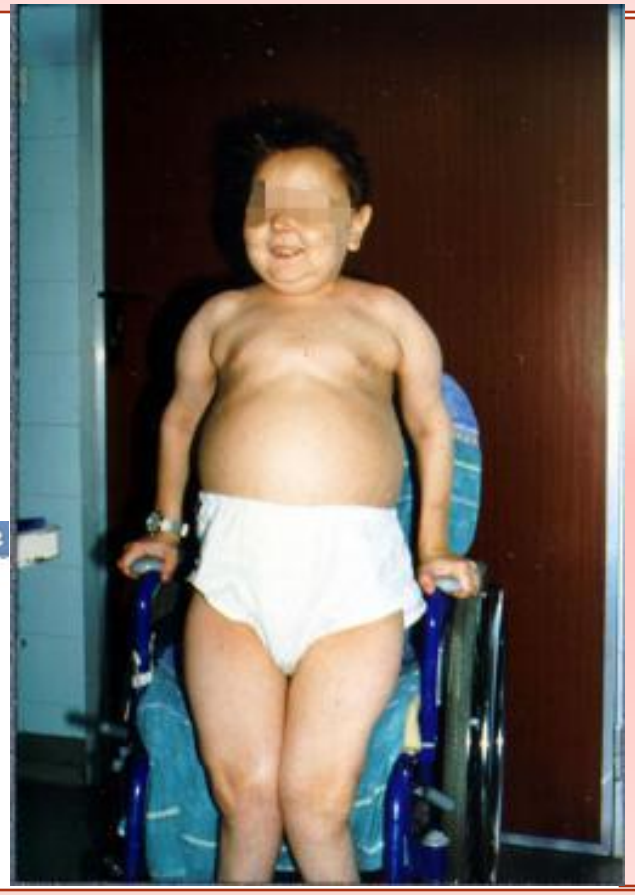
Электронный ресурс www/http://vse-pro-geny.com/ru_disease_type_autosomno-recesuvni-hvoroby_1_Hvoroba-Girke **Фото транспортировано** https://ru.wikipedia.org/wiki

Gierke's disease type Ia (1:100,000) Gene mapped on 17q21.31.

The autosomal recessive type of inheritance, caused by **mutations in the G6 PC gene** encoding glucose-6-phosphatase, leads to enzyme deficiency in the liver, kidneys, intestinal mucosa, and islets of beta cells of the pancreas and gallbladder.
Blockade of gluconeogenesis, accumulation of glycogen, lactate, impaired oxidation of fatty acids, hypertriglyceridemia, hyperuricemia





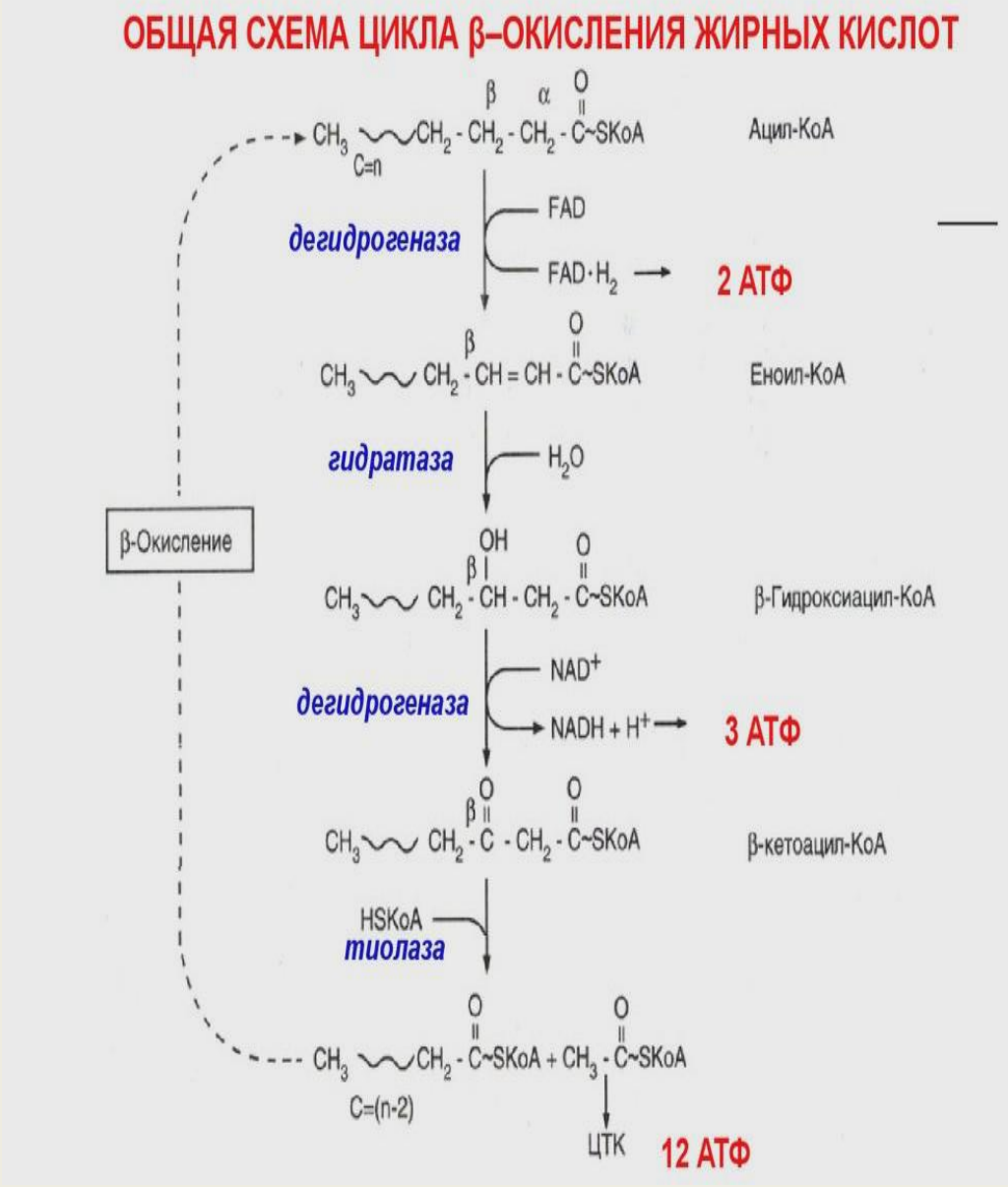


Clinical symptoms:
from birth, lack of appetite, vomiting,
hypoglycemic seizures,
a coma. Progressive
Liver enlargement ,
Nephromegaly due to
glycogenic intoxication.
Lagging FR –growth, mass,
Pronounced disproportionality:
doll-like face, large head,
short neck and legs, muscular hypotension,
delayed sexual and NPD development with
satisfactory NPD, pulmonary
hypertension, gout, nosebleeds

Gierke's disease type Ib - Mutations in the SLC37A4 gene lead to a deficiency of the enzyme glucose-6-phosphatase translocase (transporter deficiency) and account for approximately 20% of diseases.

Электронный ресурс www/http://vse-pro-geny.com/ru_disease_type_autosomno-recesuvni-hvoroby_1_Hvoroba-Girke
Фото транспортировано https://ru.wikipedia.org/wiki/

- **Defects of hereditary metabolic defects of β-oxidation of fatty acids**
- **The group of hereditary metabolic diseases includes more than 20 nosological forms**
- They are characterized by a similar pathogenesis with a violation of the conversion of free fatty acids into acetyl-CoA, necessary for the production of ketone bodies
- With insufficient secretion of KT**, excessive glucose consumption by body tissues** occurs, which leads to hypoglycemia.
- The block of stages of mitochondrial oxidation of fatty acids ends with the **accumulation of intermediate reaction products in tissues**, forming an extremely variable clinical picture.
- **The disease can manifest itself at any age,**
- **In 70% of patients, the first symptoms occur in the neonatal period.**



Электронный ресурс www/http://vse-pro-geny.com/ru_disease_type_autosomno-recesuvni-hvoroby_1_Hvoroba-Girke

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Deficiency of the enzyme acyl-CoA dehydrogenase of short, medium and very long carbon chain fatty acids is a hereditary disease from the group of defects in mitochondrial β–oxidation of fatty acids

- **E71.3 - Disorders of fatty acid metabolism**

  Frequency 1:5,000 \9,000

Clinical forms of the disease

- **systemic disease** with damage to the heart and liver
- **hepatic form**
- **myopathic form**

According to the timing of the first signs :

- **neonatal** (½ of patients);
- **children with manifestation during the first two years of life (about 40% of patients);**
- **late (less than 10%)**

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Etiology	**Mutation of the ACADVL gene encoding acyl-CoA dehydrogenase of very long-chain fatty acids**
Mechanism	Deficiency of acyl-CoA dehydrogenase of fatty acids with a very long carbon chain === blocking (or a sharp decrease in the activity of mitochondrial β–oxidation at the level of fatty acids
Pathogenesis of the formation of symptoms and syndromes	A sharp decrease in ketogenesis, accumulation of fatty acids, increased formation of dicarboxylic acids, metabolic acidosis hyperammonemia, secondary carnitine deficiency, toxic damage to brain tissue, heart, liver, inhibition of a number of enzymes, the cycle of urea synthesis and gluconeogenesis
Factors that provoke hypoglycemia	Metabolic stress in case of intercurrent infectious diseases, starvation, eating fatty foods, physical or emotional overload, etc.
The debut	In 50% of infants and young children

The clinical picture

of up to 5% of all cases of "sudden" infant death is associated with defects in OGK and ketogenesis

CNS depression, delayed psychomotor development, seizures, coma,

respiratory disorders

Liver damage: **fatty infiltration,** accumulation of products of imperfect ketogenesis, may be mild, manifested by a slight **increase in the level of hepatic transaminases and moderate hepatomegaly, acute liver failure**

Abdominal pain

Neuropathy

Tubular insufficiency

Life-threatening cardiac disorders are leading in childhood and can lead to severe complications, up to death due to:

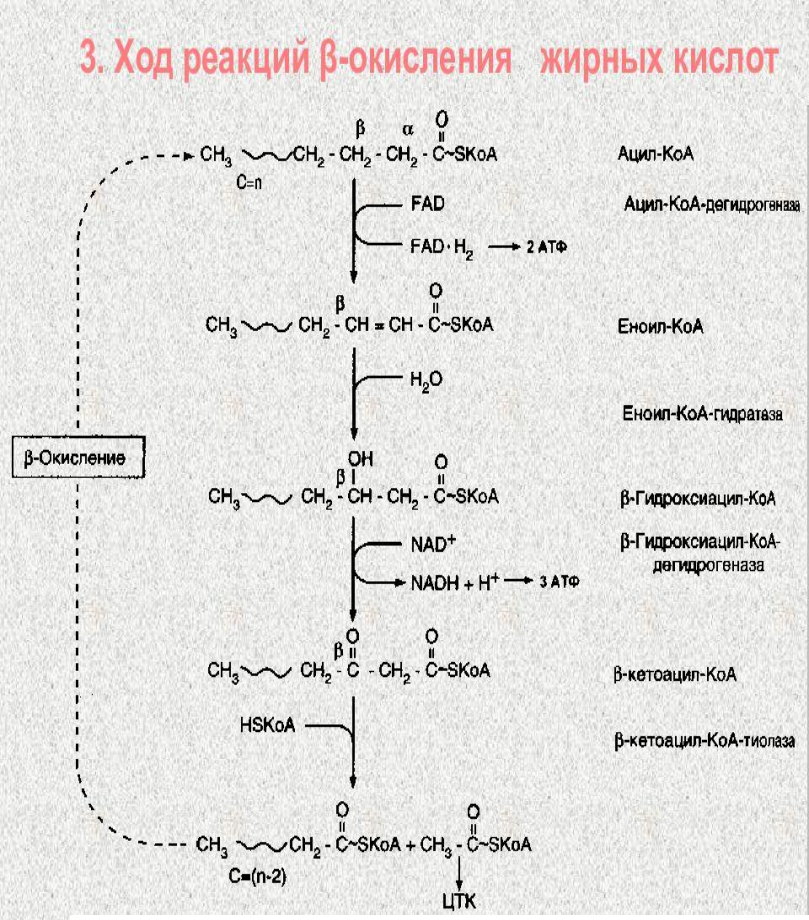
cardiomyopathy (hypertrophic, dilated),

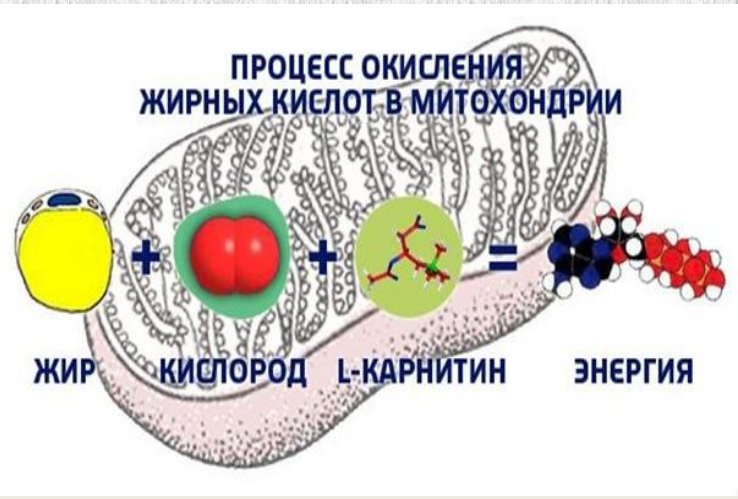
cardiac arrhythmias

, congestive heart failure

In adults, symptoms of myopathy, rhabdomyolysis, muscle weakness,

myalgia, and myoglobinuria





_Нарушения_митохондриального_β-окисления_жирных_кислот_2021.pdf

https://diseases.medelement.com/disease/

Given the high risk of acute complications, screening for OCD defects should be performed in all patients with persistent hypoketotic hypoglycemia.

Diagnosis of disorders of OGK and ketogenesis:

- Spectral assessment of carnitine levels

- Investigation of lactate, amino acid levels in blood and/or urine, creatine phosphokinase, tetradecenoyl carnitine C

- Tandem mass spectrometry and gas chromatography are the most accurate diagnostic method.

- Molecular genetic research

The collection of biological material for examination (blood or urine) should be carried out as soon as possible after the onset of symptoms.

- Treatment of OCD disorders depends on the insufficiency of a particular enzyme

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A clinical example

КГБУЗ ДККБ им. А.К.Пиотровича минздрава Хабаровского края,
леч.врач - Шарова Ю.В., зав. отд. К.м.н. Козлова Е.А.

THE GIRL IS 10 MONTHS OLD. HOSPITALIZED IN THE HOSPITAL FOR EMERGENCY INDICATIONS, AGE 10 MONTHS, PHYSICAL DEVELOPMENT: 11 KG, HEIGHT 92 CM.

Complaints on admission	**Hyperthermia 37.4, marked lethargy, adynamia, phase slurred speech, somnolence, single vomiting, impaired consciousness, seizures, hepatomegaly. Inpatient treatment is 13 days. ICU for 7 days. The severity of the condition is caused by symptoms of hypoglycemia, exsicosis, and CNS depression.**
Diagnosis upon admission	**A04.9 Bacterial intestinal infection of unknown etiology, severe gastroenterocolitis, toxicosis. Hypoglycemic state. Parenchymal hepatitis. Anemia deficiency of moderate severity, mixed etiology.**
Clinical blood analysis	**Hb- 94g\l, erythrocytes 3.0 x1012g\l, L-7.4 x 109g\l, N-2%,c-13%, e- 3%, lymph- 81%, mon- 3% ESR 3 mmh – anemia of moderate severity. In dynamics - leukocytosis 24x10 9 g/l, neutrophilosis 70%**
Glycemic profile	**upon admission 0.9 mmol / l, monitoring - 3.2 -3.8 mmol / l , history of acute respiratory viral infections, at night - hypoglycemia 1.8-2.2 mmol / l, glucose correction. COS – pH 7,390 pCO2 29.8, pO2 72.6, BE (ecf) -7.3, HCO3(std) 19.5, lactate 4.18 mmol/L**
Biochemical blood analysis	**Total protein 51 g/l; Albumin 41 g/l; AST 84 ; ALT 89 Alkaline phosphatase 115 e/l; LDH 480 units/l; OHSS 42.6 mmol/l; CRP 7.8; CK 414 units/l; LDH 1280 units/l; Amylase 67 mg/day x l.; Calcium 2.5 mmol/L; Serum iron 30.9 mmol/L; CRP 0 ; GGTP 36 units/L; CK 2461 units/L; potassium 4.61 mmol/L, sodium 136 mmol/L, calcium 1.15 mmol/*l**
The coprogram Study of intestinal pathogens	Fatty acids +, mucus ++, leukocytes 1-2 in vision – without pathology of feces on eggs of worms, tank. Fecal culture, feces for rotaviruses- (ELISA antigen)- without pathological changes
Conducted research	**Spinal tap, R-graph of the OGC, CT of the brain, CT of the chest -- without pathology, ECG- hypokalemia consultation with a neurologist, M-ECHO, Dopplerography GM - edema GM, vasospasm** Lipid profile study - Total_cholesterol 3.38 mmol/L; B-lipoproteins 22 units; Triglycerides 1.05 mmol/l; HDL 0.56 mmol/L; LDL 2.81 mmol/L; VLDL 0.21 mmol/l; Atherogenicity index 2.93 units; CMT negative – dyslipidemia Ultrasound of the OBP - hepatomegaly, diffuse changes in liver parenchyma, oculist's examination - retinitis pigmentosa The study of hormones T4 sv. - 18. 4 pmol/l, TSH 4.7 (norm 0.23-3.4), at TPO 1.1 honey/ml, cortisol 655 mmol /l Pharyngeal and nasal smear on flora - pharynx- abundant growth of Staph.aureus sensitive to oxacillin, ampicillin, azithromycin, lincomycin, cefotaxime, nose- scant growth of Staph.aureus

Hereditary history	Burdened by the female line of kinship – the child's mother, aunt and grandmother - hypertension, **obesity**, autoimmune thyroiditis, hypothyroidism, nodular goiter, **type 2 diabetes mellitus**, unidentified diseases of the visual organs, steatohepatosis - a consultation of a geneticist and an endocrinologist is indicated !
Anamnesis vitae The course of pregnancy	**The first pregnancy, the threat of termination of pregnancy at 16 weeks, acute respiratory viral infections in the 2nd trimester, fatty hepatosis of the pregnant woman (inpatient treatment, prevention of fetal respiratory disorders syndrome).**
Childbirth	**Operative delivery (ACS) according to emergency indications: acute hepatosis of a pregnant woman at 31 weeks**
The neonatal period	**Histology of the placenta: leukocyte-necrotic deciduitis, impaired implantation and placentation, chronic placental insufficiency.** **The Apgar score is 7- 8 points. The condition is of moderate severity.** **Fetal development delay - Weight 1630 g, height 40 cm, head circumference 29 cm, chest- 27 cm.** **The maximum loss of body weight is 11%.** **Neonatal screening: 17 OPG - 5.76 mmol/L, IRT - 36.34 ng/ml, phenylalanine - 1.09 mg/dl, galactose -0.10 mg/dl.**
The 2nd stage of nursing KGBUZ Perinatal Center of the Ministry of Health named after G.S.Postol	**Normoglycemia, secondary transient hypocorticism, transient hypothyroidism.** **Hormone replacement therapy - Cortef 2.5 mg, Eutirox 6.25 mcg/day, Aquadetrim 1000 units per day**
Developmental dynamics in the 1st year of life (1-10 months)	**Frequent regurgitation, lethargy, salivation, delayed psychomotor development: keeps his head from 5 months, at 10 months. –does not sit confidently, does not turn over, stands with support, pronounced general muscular hypotension, limb hypotension. Diagnosis: encephalopathy of complex origin (posthypoxic, posthemorrhagic, syndromic?). Anemia deficiency of mixed genesis, moderate severity - Hb 78-82-96 g/l, er.-2.6-3.0 x1012g /l. At the outpatient stage, symptomatic therapy was performed: iron preparations, rickets prevention, nootropic drugs, without effect.**

Stages and criteria of diagnosis

Clinic of recurrent metabolic decompensation against the background of intercurrent ARVI (acute respiratory viral infection) diseases

Delayed NPR, hepatomegaly, diffuse changes in liver parenchyma, dyslipidemia

Daily monitoring of glycemic levels : nocturnal hypoglycemia of 1.8 - 2.2 mmol / l was observed at 2 a.m., normalization by infusion of 10% glucose

The burden of a hereditary history

- **Differential diagnosis:** glycogen disease, kidney disease, organic diseases of the central nervous system, liver, endocrine diseases (thyroid, parathyroid, adrenal glands)
- **Main: ICD 10 (E71.3) Fatty acid metabolism disorder: deficiency of long-chain 3-hydroxy-acyl-CoA fatty acid dehydrogenase, childhood form, with liver damage, myopathy, retinitis pigmentosa. The period of metabolic decompensation .**
- **Concomitant: Dysplastic cardiopathy: grade 1 mitral valve prolapse. Anemia is iron deficiency, mild, mixed, normoregenerative. Subclinical hypothyroidism.**

- **She was sent to the Russian Children's Clinical Hospital (RDKB) to confirm the diagnosis — branch of the Federal State Budgetary Educational Institution of Higher Medical Research named after N.I. Pirogov of the Ministry of Health of the Russian Federation (Moscow)**
- **Methods of diagnosis confirmation - biochemical method - tandem mass spectrometry (MS/MS); increased concentration of tetradecenoyl carnitine (C14:1 is the main diagnostic marker), exceeds 0.7 mmol/L (norm up to 0.43);**
- **Molecular genetic study: revealed a mutation** with 1528G>C, (p.Glu510Gln), (CM940884, previously described as p.Glu474Gln) in a homozygous state.

Treatment

- **Maintaining the energy value of a diet of** at least 100 kcal/kg for infants and young children;
- **Frequent feeding up to 6-8 times a day** (including early breakfast at 6-7.00 and late dinner at 22.00), intervals between feedings no more than 3 hours..
- **Additional administration of 1-2 night feedings at glucose concentrations below 2.5 mmol/l**
- **Additionally, the introduction of raw corn starch.** Starch is mixed with water. For young children, the target dose of corn starch is about 1.6 g / kg (every 3-4 hours, including overnight intake).
- **Low fat content** (for infants, no more than 25% of the energy value of the entire diet, for children 1 year of age – **no more than 20%);**
- **To compensate for the fat component, the use of fat emulsions enriched with SCT is eliminated by 50%,** Monogen fat emulsion at the rate of 1.3 g/kg/ day – 20 ml/day,
- **MCT-Oil** , natural oils- sources of medium-chain (SCT) fatty acids (coconut and palm oils)
- **EXCLUDE FROM THE DIET the main food sources of long-chain fatty acids:**
- human milk, standard infant formula, fish; seafood; brown seaweed; fish oil
- special food additives containing fish oil or long-chain polyunsaturated fatty acids, vegetable fats rich in very long-chain fatty acids (low-oleic sunflower, rapeseed, corn oils), some animal products: milk, cottage cheese, fermented dairy products, pork meat, lard, sausages

Parent education

Recommendations for outpatient follow-up

Participation, strict fulfillment of doctor's prescriptions

Vaccination, !! medical withdrawal from vaccination with live vaccines

prevention of viral and bacterial infections, stressful situations, injuries, emotional and physical stress.

Early detection of crisis precursors: decreased emotional tone, lethargy, drowsiness, refusal to eat, vomiting, fever, especially at the onset of an infectious disease. .

At the first symptoms of a metabolic crisis, it is urgent: a call to the NSR, urgent hospitalization

before the arrival of the NSR doctor, immediate therapy at home: in the presence of a temperature < 38.5 C, absence of vomiting, refusal to eat and neurological disorders, continuation of basic metabolic therapy, maximum restriction of intake of natural protein from food for up to 12 hours.

If the temperature is > 38.5 C, antipyretics, including Ibuprofen at a dose of 10-15 mg / kg / day, sufficient fluid intake (glucose solution and maltodextrin, sweet compote, jelly) **of at least 120 ml / kg.**

If the patient is in stable condition, continue the planned symptomatic therapy.

Dietary restrictions in case of crisis: completely eliminate fat intake during the acute crisis (for 24-48 hours), then introduce a minimum amount of medium-chain fats while maintaining a high caloric content (at least 100-115 kcal / kg) of the diet mainly due to carbohydrates; avoid starvation.

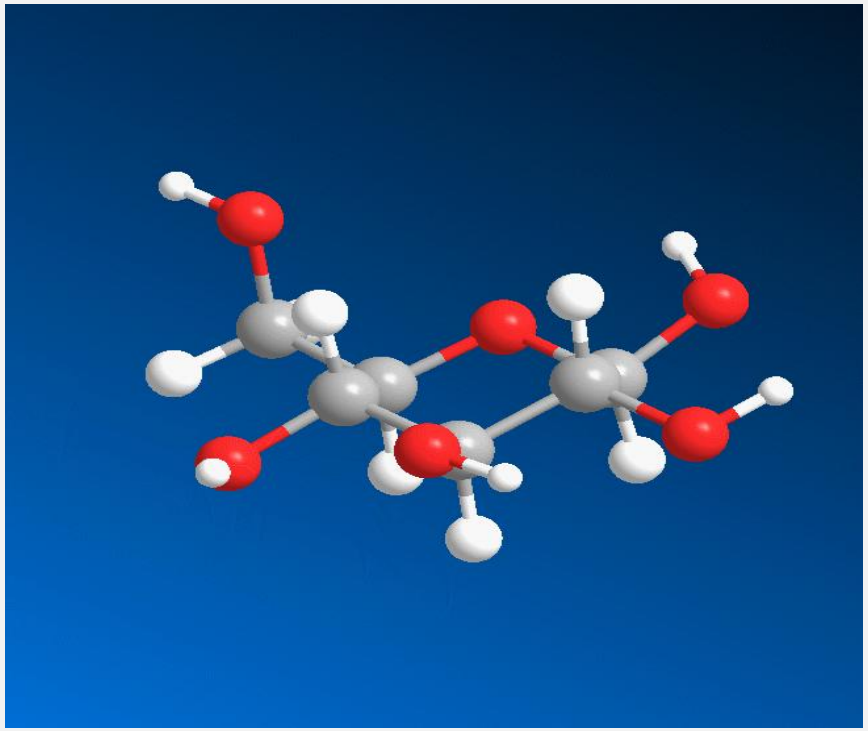
- ***It is recommended to monitor the content of pathological metabolites in blood serum or urine by tandem mass spectrometry once every 6-12 months.***
- **Follow-up: pediatrician, endocrinologist, neurologist, gastroenterologist, geneticist, cardiologist,**
- **nutritionist, ophthalmologist**
- **!! medical.withdrawal from vaccination with live vaccines**
- **Glycine up to 0.6 g / day (promotes the elimination of toxic acyl radicals)**
- **Levothyroxine sodium (Eutirox) 12.5 mcg x 1 time per day – 1 month, followed by ultrasound examination of the thyroid gland and hormonal profile (TSH, SvT4), consultation with an endocrinologist, patient administration**
- **Aquadetrim 4 drops (2000ED)** 1 time a day constantly
- **Levocarnitine (Elcar 30%) (300 mg / ml)** at the rate of 20 mg / kg / day 0.5 ml x 2 times a day for a long time. In a crisis situation, it is possible to increase the dose of 50-100 mg / kg / day.
- **Folic acid ½ t * 1 time per day –** for a long time.
- **iron (III) hydroxide polymaltosate 3 mg/kg/day ,** further blood biochemistry serum iron, OHSS CST
- **Neuroprotectors: choline alfoscerate (drinking solution)** 3.5 ml x 1 time (morning) – 5 days, then 3.5 ml x 2 times (morning, afternoon)
- **B vitamins 25 mg/kg**
- **monitoring of urea levels, AST, ALT, ALP, CK, LDH 1 time per month**
- **Scheduled hospitalization to the pediatric department 2 times a year**

Family support examination of mother, family members, siblings

Indications:

- Complicated course of pregnancy in the mother (uncontrollable vomiting, enlarged liver
- Increased transaminase activity, hyperbilirubinemia, fatty liver

liver dystrophy)



THANK YOU FOR YOUR ATTENTION

SUCCESS IN DIAGNOSIS AND TREATMENT

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