Energy Tropic Therapy in Modern Pediatrics

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Abstract. The article is devoted to the problems of using metabolic drugs that affect intracellular energy exchange processes. These drugs, which are proposed to be called energotropic, are becoming increasingly popular in modern medicine. The more urgent the task of determining the area of pathogenetic justification for their purpose becomes. The authors propose for discussion a range of indications for energotropic therapy. Various examples of the successful use of energotropic drugs in pediatrics are discussed. Keywords: mitochondrial diseases, secondary mitochondrial deficiency, energy-deficient diathesis, metabolic therapy, energy-tropic drugs, indications for use.

INTRODUCTION
In modern medicine, the doctrine of multisystem disorders of cellular energy exchange (mitochondrial pathology) occupies an increasingly important position. The key area of this branch of medicine is hereditary syndromes, which are based on mutations of genes responsible for mitochondrial proteins (Kearns-Sayre, MELAS, MERRF, Pearson, Barth syndromes, etc.). However, the class of conditions characterized by mitochondrial deficiency is by no means limited to these “primary” mitochondrial diseases. A huge number of diseases include disorders of cellular energy exchange as “secondary” links in pathogenesis. Among them: chronic fatigue syndrome, migraine, cardiomyopathies, glycogenosis, connective tissue diseases, diabetes, rickets, tubulopathies, pancytopenia, hypoparathyroidism, liver failure and many others.

MATERIALS AND METHODS
The study of these disorders is of particular importance for practical medicine due to the availability of fairly effective therapeutic correction options. However, it should be taken into account that the range of pathological disorders of cellular energy metabolism is extremely large (damage to various parts of the Krebs cycle, respiratory chain, beta-oxidation, etc.). And although the range of corresponding metabolic drugs, which we propose to call “energotropic”, is also quite wide, it is not always possible to identify specific point damage to mitochondria and accurately select the appropriate drug. In this regard, the most effective in wide clinical practice may be complexes of energy-tropic drugs that have the ability to simultaneously influence several key stages of cellular energy metabolism. Coenzyme Q10, carnitine, B vitamins and many other energy-tropic drugs are widely used in modern medicine. However, as with other metabolic drugs, the rational basis for their use is poorly developed, effective approaches are often underused or ineffective ones are overestimated, drugs are used chaotically, without sufficient knowledge about their capabilities and features, without planning a treatment strategy from the standpoint of feasibility.

RESULTS AND DISCUSSION
One of the essential aspects of the formation of rational treatment approaches is the creation of a clear idea of what categories of patients and in what cases need medicinal assistance. A clear delineation of indications is needed for energotropic drugs no less than for any others. In our article we will consider the issue of the spectrum of diseases that require energy-tropic correction. Identifying the area of pathogenetically appropriate use is one of the prerequisites for developing a rational concept for the use of drugs. Based on our data, as well as data from other authors, we offer a list of indications for the use of energotropic drugs. So, what therapeutic measures require energy-tropic reinforcement? We believe that these should include: Treatment: mitochondrial diseases; “secondary” (endogenous and exogenous) mitochondrial disorders in other diseases and conditions. - Prevention: possible complications of various diseases in patients with energy-deficient diathesis; premature pathological disorders associated with old age.
Rehabilitation measures for various chronic diseases.
The detailed list of indications we offer is presented in the Appendix. We will try to dwell on the justification of a number of positions on this list.

Mitochondrial diseases
The concept of “mitochondrial diseases” was formed in medicine at the end of the twentieth century thanks to hereditary diseases discovered shortly before, the main etiopathogenetic factors of which are mutations of the genes responsible for the synthesis of mitochondrial proteins. First of all, diseases associated with mutations in mitochondrial DNA, discovered in the early 60s, were studied. This DNA, which has a relatively simple structure and resembles the circular chromosome of bacteria in its structure, was quickly studied in detail (the complete primary structure of human mitochondrial DNA was published in 1981), and already in the late 80s its leading role was proven mutations in the development of a number of hereditary diseases. The latter include: Leber hereditary optic atrophy, NARP syndrome (neuropathy, ataxia, retinitis pigmentosa), MERRF syndrome (myoclonus epilepsy with “ragged” red fibers in skeletal muscles), MELAS syndrome (mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes), Kearns-Sayre syndrome (retinitis pigmentosa, external ophthalmoplegia, heart block, ptosis, cerebellar syndrome), Pearson syndrome (bone marrow damage, pancreatic and hepatic dysfunction) and many others. The number of descriptions of such diseases is growing every year and now. Epidemiological data on these diseases are being clarified (according to the latest data, the cumulative frequency of hereditary diseases associated with mitochondrial DNA mutations reaches a fairly high value - 1:5000) [2].

Hereditary mitochondrial defects associated with damage to the nuclear genome have been studied to a lesser extent. To date, relatively few of them are known (among them are various forms of infantile myopathies, Alpers disease, Ley disease, Barth disease, Menkes disease, carnitine deficiency syndromes, certain enzymes of the Krebs cycle and the mitochondrial respiratory chain). Meanwhile, it can be assumed that their number should be much larger, because the genes encoding information for 98% of mitochondrial proteins are located precisely in the nucleus.

In general, we can say that the study of diseases caused by hereditary disorders of mitochondrial functions has made a kind of revolution in modern ideas about the medical aspects of human energy metabolism. In addition to the contribution to theoretical pathology and medical systematics, one of the main achievements of medical “mitochondriology” was the creation of effective diagnostic tools (clinical, biochemical, morphological and molecular genetic criteria for multisystem mitochondrial failure), which made it possible to evaluate multisystem disorders of cellular energy metabolism.

The diagnostic tools mentioned above have made it possible today to identify a large number of chronic diseases, one of the pathogenetic links of which is secondary mitochondrial failure. Their list, reflected in the Appendix, is far from complete, and is expanding to this day [3].

All these disorders are polymorphic, can have varying degrees of severity and are of interest to medical specialists in various fields - neurologists, cardiologists, neonatologists, nephrologists, surgeons, urologists, otolaryngologists, pulmonologists, etc.

According to our data, at least a third of all disabled children in the symptom complex of their diseases have signs of a multisystem disorder of cellular energy. It should be noted that in recent years the number of children with diseases accompanied by a high probability of tissue hypoxia has increased significantly.

CONCLUSION
All of the above indicates the need for targeted research to refine the composition of energy-tropic complexes, carefully select doses of active substances, and determine optimal prescription regimens, including taking into account chronobiological rhythms.

The question of the possibility of complex use of energy-tropic agents is practically important. The above examples indicate the need for the complex use of such agents as L-carnitine and coenzyme Q10, coenzyme Q10 and magnesium. However, for each nosological form, its own specialized complexes must be developed, including the most pathogenetically significant components of cellular energy exchange (for example, cytochrome C, succinic acid, etc.)

REFERENCES