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NEW APPROACH TO THE PROPHYLAXIS AND TREATMENT OF AGE - RELATED PATHOLOGY

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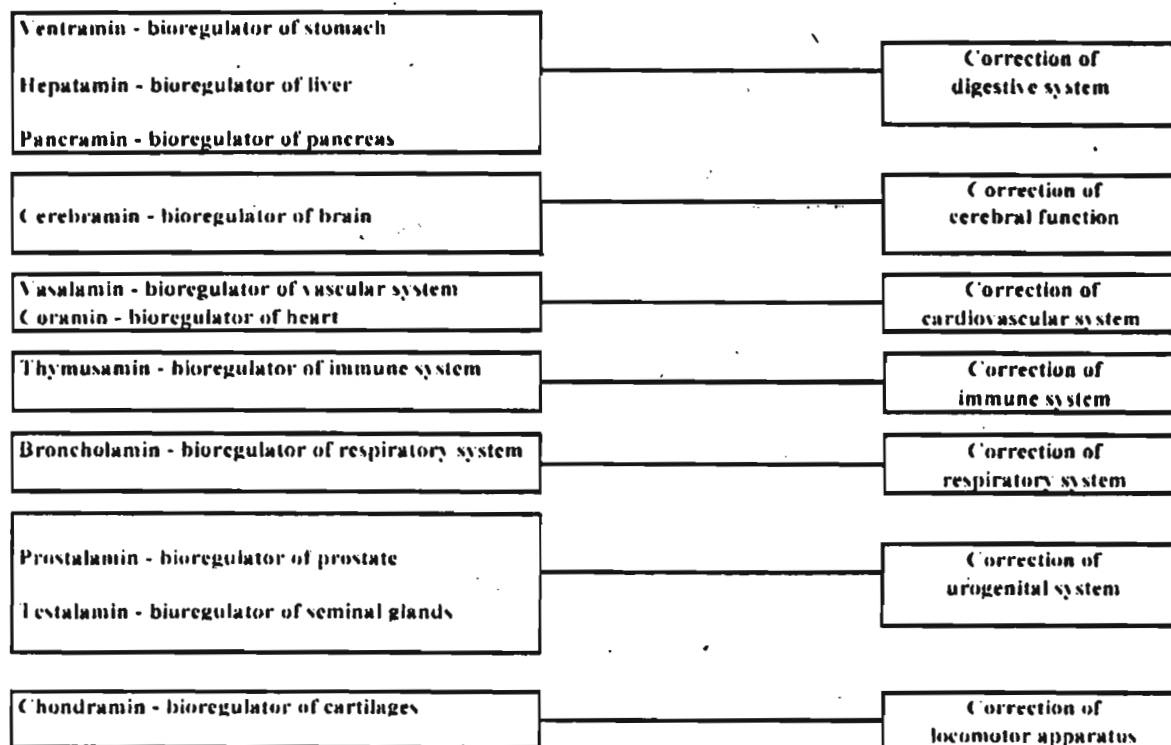
As known, aging leads to homeostatic disbalance in an organism (1). Our new approach to the problem of preventing age-related pathology development is connected with peptide bioregulators application. Peptide bioregulators (Cytomedins) contain physiologically active substances extracted from animals' organs and tissues which play the most important role in regulation of the body functions (2).

During the last twenty years of experimental studies of Cytomedins efficiency, we noticed an inhibition of age-related metabolic, endocrine and immune abnormalities leading to life span extension by 15 - 40 % (3-5). The rate of development of age-related pathology is linked with the state of both endocrine and immune systems (6). The most important organs responsible for their functioning (epiphysis and thymus) are subjected to the process of early involution (7,8). Based on results of clinical researches, the complex application of Epithalamin and Thymalin (peptide bioregulators extracted from cattle epiphysis and thymus) slowed down the appearance of age-related

changes in neuroendocrine and immune systems of an organism, that resulted in stabilization of laboratory indices, reduction of frequency of infectious diseases development and reduction of relapses of chronic pathologic processes.

Our recent achievement is food additives - Cytamins (Figure 1). They are developed on a base of peptide bioregulators. Cytamins are produced from cattle organs and tissues (brain, liver, prostate, heart, thymus, bronchial tubes, cartilages, pancreas, vessels, stomach, seminal glands) and represent ecologically pure complexes of peptides and nucleic acids, including physiological concentrations of mineral substances, trace elements and vitamins in easily assimilating form. These substances promote optimum performance and high-grade feeding of organs and tissues and can be used for effective prophylaxis of age - related abnormalities (degeneration of cerebral cells, atherosclerotic lesions, reduction of sexual dysfunction etc.). The application of Cytamins is recommended also in geriatric patients:

Figure 1

Classification of Cytamins

• For increase of body resistance to influences of the adverse ecological, and climatic environment and of psycho-emotional stress;

• For the prevention of various pathological states and complications;

• For accelerated rehabilitation after diseases, traumas and surgical operations;

• As geroprotectors.

Cytamins do not contain conservatives and have no contraindication and side effects. Food additives are made as tablets and capsules covered by an enteric coating, interfering destruction of active components by enzymes of stomach juice that prevent their absorption in small intestine.

We can also suggest our patients one of the most promising methods of

investigation: molecular-genetic diagnosis of predisposition to different kinds of cardiovascular pathology, metabolic disturbances and insulin resistance (Figure 2).

At the moment we are capable of determining the following gene allelic variants:

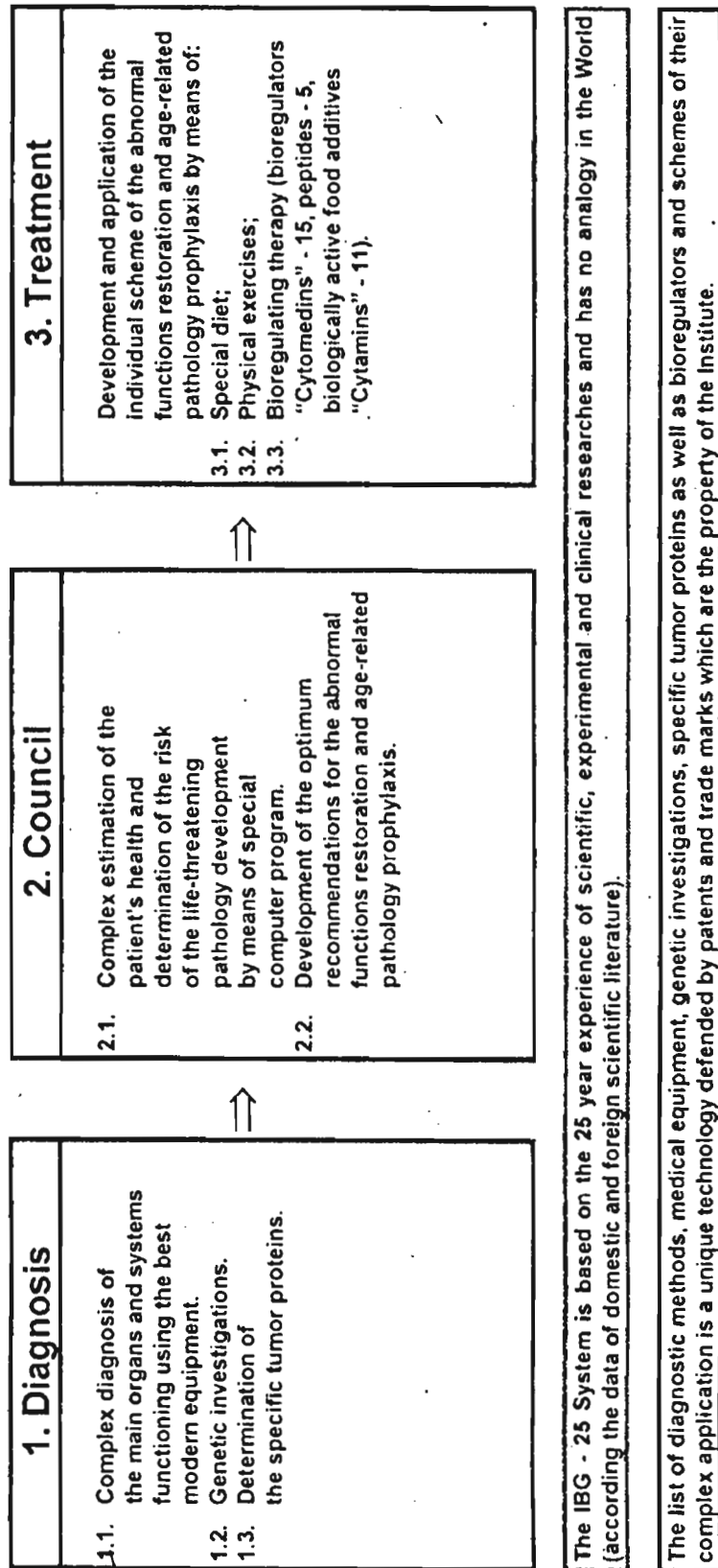
- Apolipoprotein E
- Apolipoprotein CIII
- Lipoprotein (a)
- Angiotensinogen
- Angiotensin-converting enzyme
- Factor V of blood coagulation system
- Factor VII of blood coagulation system
- Plasminogen activator inhibitor - I
- Paraoxonase

Figure 2 Molecular - Genetic Diagnosis of Predisposition to Different Kinds of Pathology

GENES	POLYMORPHISM	PATHOGENESIS	PATHOLOGICAL STATES
Apolipoprotein E	Apo E3 Apo E4 Apo E2	Apo E2 isoform is defective in mediating the clearance of remnant lipoproteins by hepatic receptors \Rightarrow hypercholesterolemia, hypertriglyceridemia Apo E4 isoform is associated with hypercholesterolemia	type III hyperlipoproteinemia
Apolipoprotein CIII	S1 S2	S2 allele is associated with inhibition of LPL activity \Rightarrow high level of triglycerides	risk of thrombosis
Lipoprotein (a)	C T	C allele is associated with increase of Lp (a) level \Rightarrow attenuates activation of plasminogen to plasmin \Rightarrow inhibition of fibrinolysis	risk of thrombosis
Angiotensinogen	C T	C is associated with high level of Ang \Rightarrow increased formation of Angiotensin II \Rightarrow high vasoconstrictor activity	essential hypertension
Angiotensin-converting enzyme	Insertion Deletion	D allele homozygotes are associated with plasma ACE level twice as high as one in I allele homozygotes \Rightarrow increased formation of Ang II \Rightarrow high vasoconstrictor activity	hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy, risk factor for myocardial infarction in young persons, left ventricular hypertrophy
Plasminogen-activator inhibitor 1	4G 5G	I allele is associated with low insulin sensitivity	insulin resistance
Factor V of coagulation	Mutation - replacement of Arg 506 with Gln	High level of Ang II increases plasma PAI - 1 (plasminogen activator inhibitor) activity \Rightarrow inhibition of fibrinolysis 4G is associated with increase in plasma PAI - 1 activity \Rightarrow inhibition of fibrinolysis	risk of thrombosis risk of thrombosis
Factor VII of coagulation	M1 M2	Mutated factor V is less sensitive than normal one to activated protein C - mediated inactivation \Rightarrow disturbance in inhibition of coagulation	venous thromboembolism which tends to occur in conjunction with surgery, fractures, inflammatory states
Paraoxonase	A B	M1 allele is associated with high secretion of factor VII B allele is associated with high plasma concentration of Tg and LPL cholesterol	risk of thrombosis atherosclerosis

Figure 3

**System
of complex diagnosis and rehabilitation of the organism's main functions and age - related
pathology prophylaxis in the patients treated in the Institute of Bioregulation and Gerontology
(IBG - 25 System)**



Due to the investigation we can diagnose predisposition to the pathological states:

- Venous thromboembolism which tends to occur in conjunction with surgery, fractures, inflammatory states (9);
- essential hypertension (10);
- coronary heart disease, acute myocardial infarction (11-16);
- hypertrophic cardiomyopathy (11);
- idiopathic dilated cardiomyopathy (11);
- left ventricular hypertrophy (11);
- insulin resistance (16, 17);
- type III hyperlipoproteinemia (18).

In the case of venous thromboembolism any serious trauma as hip fracture can result in sudden death.

The coronary heart disease is initiated by thrombosis, high vasoconstrictor activity or atherosclerotic vascular lesion (9). In the cases of hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy and left ventricular hypertrophy, the disease can progress very quickly causing the patient's disability. Insulin resistance is mostly associated with non-insulin dependent diabetes mellitus.

As the mechanism of pathogenesis is known we can recommend the examined patients the prophylaxis or treatment of the determined diseases.

Treatment

Basic directions

Hypercoagulability - prophylactic anticoagulant therapy in situations known to provoke thrombosis (eg. major surgery) (9).

Hypercholesterolemia - recommendation of a special diet plan with low saturated fat, low cholesterol, limited sodium.

- High plasma ACE activity - inhibitors of ACE.
- Fibrinolytic abnormalities - fibrinolytic therapy.
- The main direction - complex application of food additives (Cytamins) or peptide bioregulators (Cytomedins) for restoration of functional activity of injured organs and systems. For example, in the case of predisposition to non-insulin dependent diabetes mellitus we suggest complex therapy with Epithalamin (increases the blood glucose level), Pancramin (food additive capable to normalize the pancreas function), special diet etc.

The new method of investigation allows to prognosticate the patients' health condition in the nearest future and prolong their active life by timely prophylaxis of the determined pathology.

It is necessary to emphasize that the diagnosis of the expected diseases and their complex treatment with peptide bioregulators are unique and carried out only in St. Petersburg's Institute of Bio-regulation and Gerontology (Figure 3).

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