the rate of metabolic processes. We attempted to produce a direct effect of LLI on the region of the higher autonomic centers and pituitary body in order to modulate the level of endogenous hormones. However, it would be a misinterpretation of the experimental data to conclude that our findings are a result exclusively of changes in the functional activity of the endocrine gland subjected to laser radiation. The entire array of changes induced in the organism by laser radiation should be taken into account. We consider that the immunobiological effects resulting from transcerebral laser irradiation are more diverse than in the case of treatment with hormonal preparations.

The obtained phase changes of serum opioid level is probably dictated by the progressive depletion of the opioid system under laser irradiation. Both immunodepression and the effect on the endogenous opioid system are most pronounced under a pulse mode of irradiation, probably due to the induction of bioresonance effects in the irradiated tissues [4].

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Immunological Screening and Immune Correction in Cardiosurgery of Infants

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The early-onset complications of cardiovascular surgery in congenital heart disease (CHD) can be caused by infection of both endogenous and exogenous origin. The diagnosis of infectious endocarditis as well as of focal infection of other localization is extremely sophisticated in infants with CHD. This is due to the general gravity of the state of a child with CHD, and also to the frequency of latent, nonobvious, and atypical forms occurring against the background of altered immunoreactivity. In a series of reports it was shown that circulatory insufficiency and arterial hypoxemia induce significant derangement in the functional state of the immunocompetent organs and cause the development of secondary immunodeficiency (SID) [1,2,4]. A lowered immunoreactivity associated

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TABLE 1. Spontaneous and Induced NTB Test Index as a Function of Severity of Circulatory Decompensation and General Stigmatization in "Pale" CHD Patients and of Degree of Arterial Hypoxemia in "Blue" CHD Patients

Symptom	NTB spontaneous test	NTB induced test
Circulatory insufficiency		
Stage I	24.20±3.19	28.00±3.94
Stage II	31.64±5.70	26.44±4.43
Stage III	58.32±2.60	54.31±6.20
No stigmatization	26.86±4.84	29.64±5.23
Moderate stigmatization		
(less than 5 stigmata)	27.88±6.81	30.13±13.80
Severe stigmatization		
(more than 5 stigmata)	51.00±11.43	45.83±10.96
Blood saturation with oxygen		
less than 50%	43.00±3.25	37.50±4.72
50–80%	35.38±2.83	34.15±5.54

with multiple stigmatization accompanying malformations of the internal organs and reflecting connective tissue dysplasia has been described [1]; precisely at an early age, constitutional anomalies, an aggravated allergological anamnesis, acute and chronic diseases of the mother, and occupational and environmental hazards of pregnancy play an important role in the derangement of the immune status.

The goal of this study was to elaborate immunological criteria for the diagnosis of manifest and/or latent infection in order to substantiate the surgical tactics and individual immune correction in the pre- and postoperative period.

MATERIALS AND METHODS

During 1988-1991 110 patients were examined, including 69 children with "pale" CHD and 41 with "blue" CHD. The patients were aged 1 to 4.5 years (mean age 2.43±0.18 years). We used the immunological tests of the first level [3], which are most simple yet informative enough for a general assessment of gross defects in the cellular and humoral immunity [3]. The following criteria served as clinical indications for the examination of a total of 57 children: 1. Complicated situations requiring a differential diagnosis a) progressive circulatory decompensation and cardiomegaly during the 1-6 months preceding the present admission; b) febrile rises of body temperature without any association with any visible respiratory viral and/or focal chronic infection (tonsillitis, pyelonephritis, etc.); c) hepato- and splenomegaly unexplained merely by the circulatory decompensation; d) arrhythmia, ECG-detected severe myocardial and pericardial alterations unconnected with surgical trauma; e) hypofunction and/or thrombosis of an earlier-performed aortopulmonary shunt. 2. Cases requiring verification of the phase activity of infectious endocarditis; a) vegetations on the heart valves revealed by echography; b) induration of the casps of heart valves revealed by echography; c) thromboembolisms in the anamnesis; d) endocarditis with positive hemoculture in the anamnesis; e) septicemia with positive hemoculture. 3. Cases with a well-defined symptomatology of focal complications or intercurrent diseases: a) otolaryngeal pathology; b) acute respiratory infections and pneumonia; c) urinary tract infections; d) mediastinitis; e) superficial suppuration of the operative wound. A systematic examination of 53 CHD patients with no intercurrent diseases and stably normal temperature in the 4-6 months preceding hospitalization and at the time of examination, and with normal laboratory findings, as well as of age-matched healthy children was also carried out.

RESULTS

Assessment of the validity of using the nitrotetrazolium blue (NTB) test as a diagnostic criterion of manifest or latent infection in CHD patients revealed that: 1) even in the absence of infectious complications the enzymatic activity of neutrophils according to the NTB test (both spontaneous and induced) is elevated in the children with "pale" and, especially, "blue" CHD, as compared to the age-matched healthy children (on average, 20-40% and 11-13%, respectively); 2) the values of the induced NTB test in the CHD patients having no infectious complications are lower than those of the spontaneous test, in contrast to the situation in healthy children, in which case the figures of the induced test exceeded those of the spontaneous test by 3-6%. The difference between the indexes of the induced and spontaneous test is conventionally named the phagocytic reserve.

Thus, the phagocytic reserve in this category of patients was substantially limited, even in the absence of inflammation. It was also established that the figures of the spontaneous NTB test in the patients

without infectious complications are reliably increased (with a corresponding fall of the phagocytic reserve as detected in the induced test) in the following situations: a) in the course of an increase of circulatory decompensation in the children with "pale" CHD; b) in the course of a rise of hypoxemia in the patients with "blue" CHD; c) depending on the general stigmatization reflecting the degree of connective tissue dysplasia (Table 1).

Thus, the obtained results serve as evidence for the invalidity of using the "standards" obtained during the examination of healthy children in the diagnosis of infectious complications in CHD patients, as intoxication of purely metabolic genesis (hypoxia, hypoxemia) significantly changes the values of the NTB test.

The following peculiarities of SID in CHD patients were demonstrated:

1. In the absence of infectious complications and intercurrent diseases: a) the total number of leukocytes, neutrophils, and lymphocytes does not differ in the patients with "blue" vs. "pale" CHD and corresponds to the standard for healthy children of similar age; b) the children with "blue" CHD manifest a significant reduction in the relative and, especially, the total number of T lymphocytes, when compared to the patients with "pale" CHD and, particularly, to the healthy children; c) the values of the leukocyte index of intoxication (LII) are less than 1.0, yet, particularly in the "blue" CHD they exceed those in the healthy children; d) even a pronounced increase in the neutrophil enzyme activity (raised value of NTB test) does not ensure a respective increase in the absorbing and bactericidal capacity, as proved by the drop of the absolute phagocytic index (API) two and more times as compared to the healthy children, and the decrease of bactericidal activity as well; the reduction of API was of similar severity in the groups of "blue" and "pale" CHD; e) the levels of IgG and IgA did not differ in the patients with "blue" vs. "pale" CHD and were within normal ranges, while the level of IgM was slightly elevated in the patients of both groups.

2. Under conditions of infectious complications: a) the T-lymphocyte content in "pale" CHD patients showed no significant change. In "blue" CHD patients the absolute number of T lymphocytes was 2-fold lower than in the "pale" CHD group, and 3-

TABLE 2. Neutrophil Functional Activity, T–Cell Content, and Immunoglobulin and CIC levels in CHD Patients without (I) and with Inflammatory Complications (II)

Disease type	Value	I	II
"Pale" CDH	NTB spontaneous test, %	33.7±6.3*	57.1±9.1*
	NTB induced test, %	30.5±3.4	47.5±9.2
	API	4387.7±1704.9	6385.9±3441.3
	Bactericidal index		0.75±0.2
0.92±0.3			
	T–lymphocyte content		
	percentage	40.7±3.1	39.4±5.6
	absolute	1349.0±334.4*	1422.9±1253.3
	CIC, arbitrary units		83.9±7.7
95.3±12.1			
	Ig, mg%		
	G	760.7±162.3	884.5±288.6
	A	98.9±11.5	105.4±99.6
	M	162.2±70.9	183.3±75.1
	LII	0.58±0.1*	1.37±0.2*
"Blue" CDH	NTB spontaneous test, %	37.3±4.2*	61.9±9.9*
	NTB induced test, %	35.5±4.3	42.4±9.2
	API	5129.98±3813.5	3545.7±2581.5
	Bactericidal index	0.84±0.58	0.58±0.2
	T–lymphocyte content		
	percentage	35.1±2.3	23.8±6.5
	absolute	687.7±153.8*	369.5±187.9*
	CIC, absolute unite	74.0±7.6	83.6±7.2
	Ig, mg%		
	G	734.3±134.2	747.9±213.4
	A	101.8±52.6	66.5±24.9
	M	351.1±268.7	306.4±226.6
	LII	0.70±0.15*	1.60±0.3*

Note: an asterisk indicates significant differences in values when group I and group II are compared ($p<0.001$).

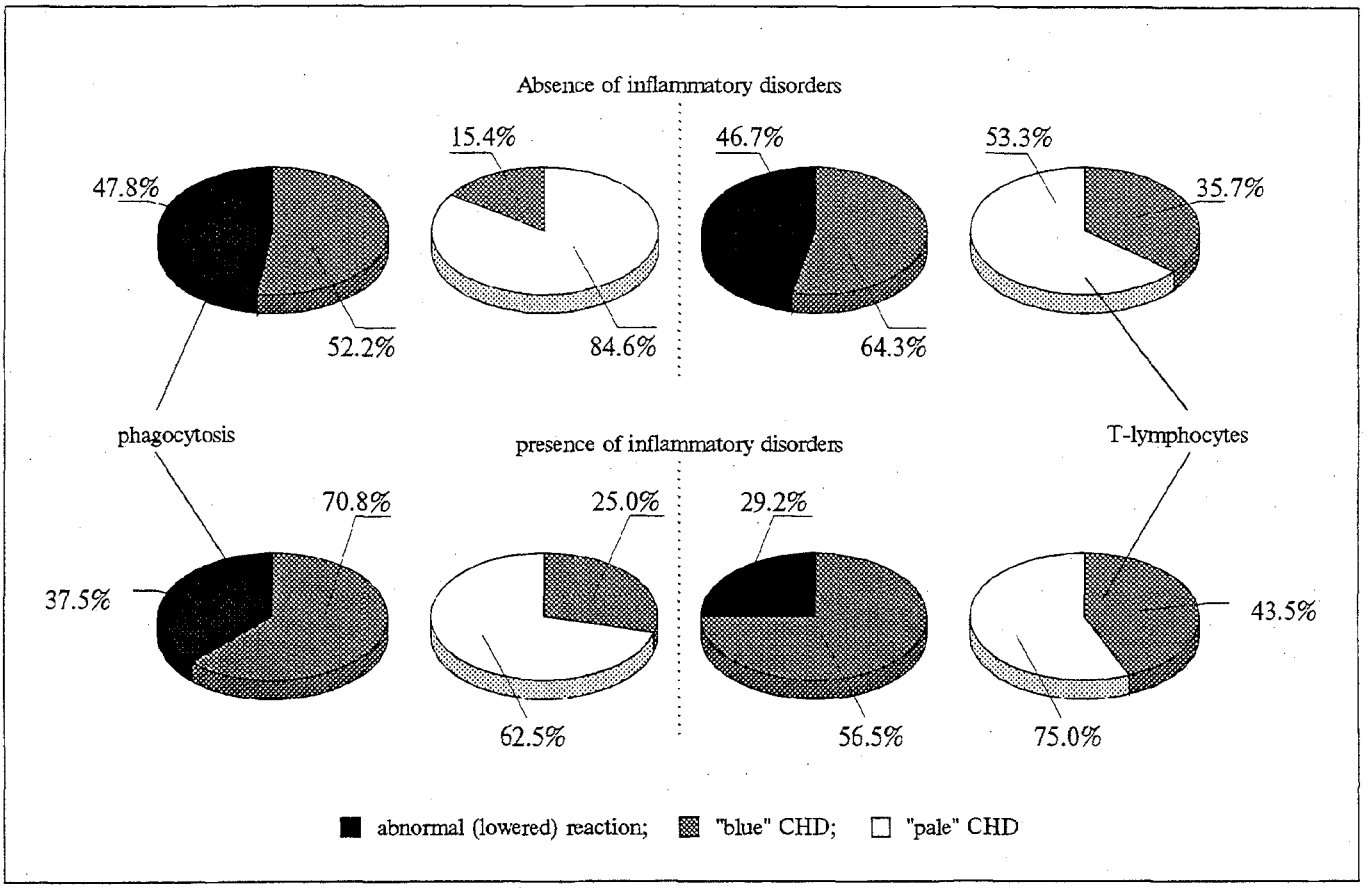

Fig. 1. Types of immune reactions in patients with congenital heart disease (CHD).

fold lower than in the healthy children of the same age; b) LII provides valid information concerning the addition of inflammation, and its value can significantly exceed 1; c) the spontaneous NTB test is increased in 92% of CHD patients, its value exceeding 60% in "blue" CHD and 48% in "pale" CHD; d) in 8% of cases characterized by extremely low (0-8%) figures of the NTB test one should discriminate between an initial (inborn) functional deficiency of the granulocytes and blockade of the granulocyte receptors due to the excess of antigen. Differential diagnosis is made by comparison with the clinical symptomatology and the indexes of immunological follow-up screening in the course of therapy; e) in "pale" CHD patients the direction of changes in the phagocytic function of the neutrophils is normal, although quantitatively insufficient. This is proved by the weaker than normal rise of API and bactericidal index; f) "blue" CHD patients with infectious complications exhibit an aggravation of the phagocytosis dysfunction syndrome with a considerable drop of API and marked inhibition of the bactericidal properties of cells, i.e., the phenomenon of toxogenic immunosuppression becomes more pronounced; g) dysfunction of the B-lymphocyte system in CHD patients with inflammation is characterized by an abnormal dynamics of the main Ig classes. While the IgG level remains unchanged, the IgA concentration falls (in "blue" CHD patients as reliably as by 45%). Simultaneously there is a 3-4-fold rise of IgM, providing evidence of the preeminent participation in the primary immune response of IgM, rather than IgG (as occurs in the normal situation); h) the concentration of circulating immune complexes (CIC) exceeds 80 arbitrary units, indicating alterations of CIC clearing and elimination processes an the risk of infectious and immune complex complications (Table 2).

Thus, SID in CHD patients is complex and is characterized by the combined destruction of the general humoral immune response and of the T-lymphocyte and neutrophilic granulocyte systems resulting from the action of hypoxia and hypoxemia upon the immunocompetent cells. The analysis showed that the initial SID (as assessed by phagocytosis and T-lymphocyte changes) is aggravated in 50% of "pale" CHD patients and 75% of "blue" patients with infectious complications (Fig. 1).

On the basis of the results of our study, we believe it worthwhile to recommend the following therapeutic measures:

1. In the critical infectious process of high activity, against the background of massive antibacterial

and heparin therapy transfusiological methods of immune correction and detoxication should be used for the purpose of controlling the toxogenic immunosuppression, including infusion of Hemodes, native and immune plasma, ultraviolet-irradiated autologous blood, immunoglobulins of different classes and polyimmune preparations.

2. In a deficit of the T-lymphocyte component of immunity, thymic hormone preparations should be used in order to promote differentiation and maturation of T lymphocytes, as well as for an indirect correction of phagocytosis dysfunction.

3. If the syndrome of phagocytosis dysfunction (including all or certain stages of the process) predominates in the immunohematological status, in order to stimulate the metabolism of phagocyting cells preparations of yeast RNA (Na nucleinate) may be used; granulocyte repopulation can be promoted by pyrimidine derivatives (e.g., methyl uracil). Complex therapy includes vitamins E, A, and C and nonvitamin cofactors (lipoic acid, carnitine chloride, potassium orotate) possessing immunomodulatory activity.

4. Immediately after the withdrawal of antibacterial therapy and during the reconvalescence period (3-6 months after surgery) homeopathic immunocorrecting preparations are prescribed, taking into consideration the constitutional parameters of the children, the pattern and localization of the infectious process, and specific features of reactivity.

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The Effect of Serotonin Interaction with Cells

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The study of the mechanisms of serotoninergic immunomodulation is of both particular and general interest, as the effects of serotonin are realized via the neuroendocrine system [2,3,7,17]. It has been shown that the inhibitory action of high doses of serotonin is mediated via the hypothalamo-hypophyseal-adrenal system [8,9], while its stimulatory effect (low doses) is mediated via the vagus nerve [11]. The following facts, besides the ones mentioned above, served as the premises for this study: 1) immunocompetent organs and tissues contain cells bearing heterogenous receptorlike serotonin-binding structures [10-12,22]; 2) the level of specific binding of serotonin by these cells and also by the synaptosomes depends on the dose of antigen introduced [14]; 3) the biological effect of serotonin upon the cells of immunocompetent organs *in vitro* can be further observed *in vivo* following administration of these cells into syngenic recipients and is expressed as opposite changes of the function of amine-treated cells [11]. Thus, there are data concerning opposite regulatory effects of serotonin on the same immunological phenomenon, depending on the targeted action of serotonin on spe-

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