Response to Blue Light in Humans

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Rapid and slow responses to photohemotherapy with blue light were studied in 61 patients with various diseases. Changes in blood rheology, coagulation, immunological, and biochemical parameters, and respiratory function of the lungs were studied. The observed reactions indicate enhanced metabolism and energy production in the body.

Key Words: *blue light; photohemotherapy*

The term "response to blue light" now accepted in photobiology unites a group of photoregulatory processes differing by physiological manifestations, which are induced by the blue-violet band of the spectrum. Responses to blue light (BL) are best studied in plants and fungi. Their photoregulatory systems with maximum activity spectra of 420, 450, and 480 nm ensure regulation of the rate and vector of cell growth, differentiation, biological mobility, circadian rhythms, and carotenoid production.

Photoreceptor pigment (cryptochrome) absorbing in the blue spectrum belongs to flavines. Photochemical activity of flavine is due to transition from the basal into excited singlet state upon BL energy absorption, and then into a triplet state characterized by high catalytic activity [14].

Responses to BL can be fast and slow. Fast responses manifest by immediate activation of photosynthesis and changes in stomatal resistance to carbon dioxide diffusion into chloroplast. This effect is attributed to the effect of BL on guard cell membrane containing integral flavine, to stimulation of electron transport, changes in proton gradient, and increased energy potential of guard cells [1,3-5]. This regulatory mechanism ensures opening of the stomata in the dawn, when photosynthetic mechanism is inactive, while weak early morning light consists mainly of blue rays.

Slow responses are associated with the effect of BL on the genetic apperatus. The activity of photosynthesis and potential activity of electron transfer are higher in plants grown under BL, which allows effective photosynthesis at high-intensity light [4,5,7].

Bearing in mind the unity of plant and animal world, we can expect that BL is also involved in the regulation of various processes in animals.

The effects of color light on the development, growth, and intensity of metabolic processes were studied starting from the middle of the nineteenth century. Experiments were carried out on piglets, calves, trout ovicells, frogs, fly larvae, tadpoles, *etc.* Blue light stimulated the development and growth in comparison with other types of illumination almost in all experiments. Moreover, BL increased motor activity of salamander embryos: 1 movement/min in the shadow, 6 in red light, 8 in green light, and 46 movements/min in blue light [9].

The intensity of metabolism is highest in BL. Tadpoles exposed to BL die from starvation sooner than in other types of illumination. Almost 100 years ago B. S. Kogan [6] discovered «the maximum intensity of vital processes with predominance of more perfect metamorphosis» in dogs exposed to BL.

The effect of BL on cells and subcellular structures in animal tissues is dose-dependent. High doses cause a photodynamic injury to mitochondria, chromosomes, and erythrocyte membranes [13] involving endogenous photosensitizers. N. L. Vekshin [1] investigated photoinduced synthesis of ATP in rat liver mitochondria and showed that BL in low doses stimulated energy production.

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Humans are known to respond to BL. Blue light phototherapy was widely used in Russia and Europe for four decades until the era of antibiotics. Analgesic, absorbing, and bactericidal effects of BL were noted. At present BL is used only in the treatment of neonatal hyperbilirubinemia and some skin diseases. H. Kost *et al.* [11] offered blood irradiation for the treatment of coronary disease and essential hypertension; exposure to BL decreased the concentrations of LDL in the blood. We studied human responses to BL irradiation of the blood on a wider scale. In fact, irradiation of the body surface is equivalent to exposure of the blood in skin capillaries, because tissue permeability for BL is very low.

MATERIALS AND METHODS

Blood was extracorporeally exposed to BL (a variant of UV irradiation of the blood). Blood (150 ml) was exfused from the ulnar vein into a sterile flask with glucigar and immediately infused back at a rate of 60 drops/min. Blood was irradiated with BL through a transparent plastic tube of a blood transfusion system. A 10-cm fragment of the tube was placed parallel to BL source at a distance of 2 cm. The source of BL was a DRB-8 lamp coated from the inside with blue luminophore, which cuts UV radiation. Maximum emission wavelength was 439 nm, power density 0.16 W/cm^2.

Blood for the analysis was collected from the vein into dry heparin or citrate before and immediately after reinfusion over the entire course of treatment (5-6 sessions every other day).

Blood and plasma viscosity were measured in a Lowshear rotation viscosimeter, hematocrit on a high-speed centrifuge (Autocrit), activated partial thromboplastin time (APTT), prothrombin time (PTT), thrombin time (TT), and factors VIII and IX by Reanal kits. Platelet aggregation was studied on an Elvi-840 platelet aggregometer using ADP, epinephrine, and ristomicin as inducers (all reagents were from Reanal), biochemical parameters of the blood were evaluated on an Impact-400 autoanalyzer, immunological parameters were evaluated routinely, and respiratory function of the lungs was studied by computer-aided spirometry.

Studies were carried out in 18 patients with chronic obstructive bronchitis, 32 with intermittent claudication, 12 with cerebral circulation disorders, and 9 with infectious allergic myocarditis.

RESULTS

Blood viscosity in all patients dropped by 16.7±3.9% immediately after reinfusion. The most pronounced decrease was 30%, which is significant for such stable parameter as viscosity. The decrease in blood viscosity was deteremined by decreased hematocrit: it correlated with viscosity shifts and sometimes reached 8 vol.%. Plasma viscosity also decreased, but to a lesser extent: by 8.3±1.5%, which correlated with a decrease in total protein concentration. Hemoglobin concentration decreased in proportion to decrease in hematocrit.

Hence, rapid response to reinfusion of BL-exposed blood manifested by increased blood fluidity.

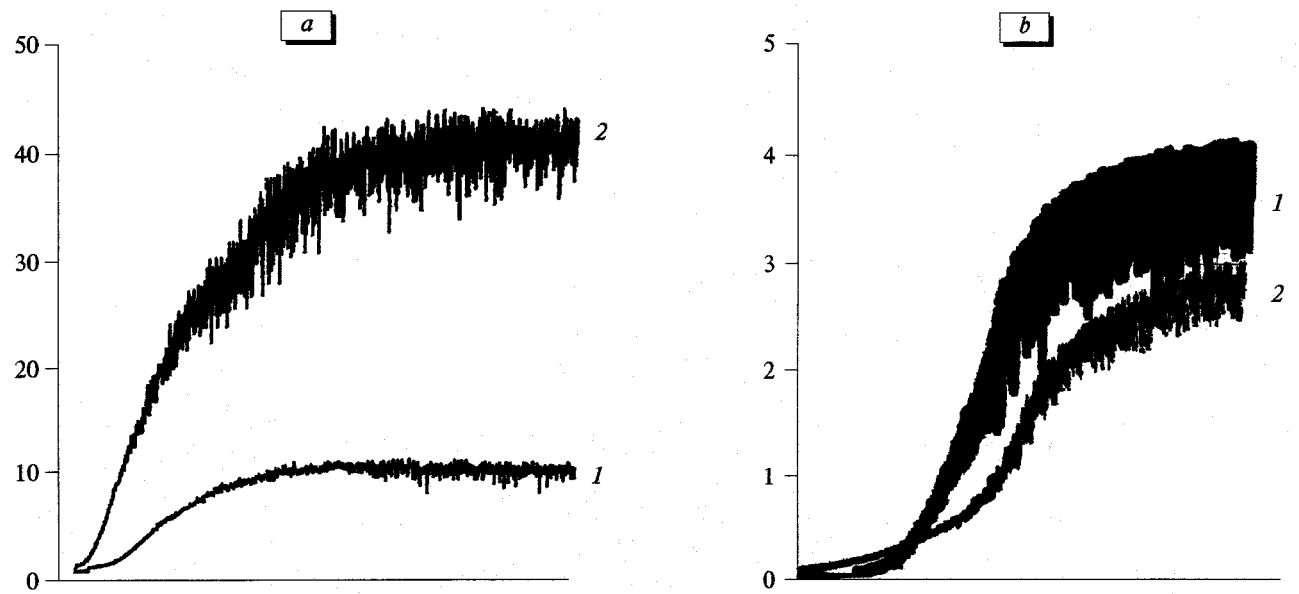

Fig. 1. Effect of blue light photohemotherapy on platelet aggregation (*a*) and hyperaggregation (*b*). *1*) before exposure; 2) after exposure. a) recovery of ristomicin-reduced activity; b) normalization of agristine-induced aggregation.

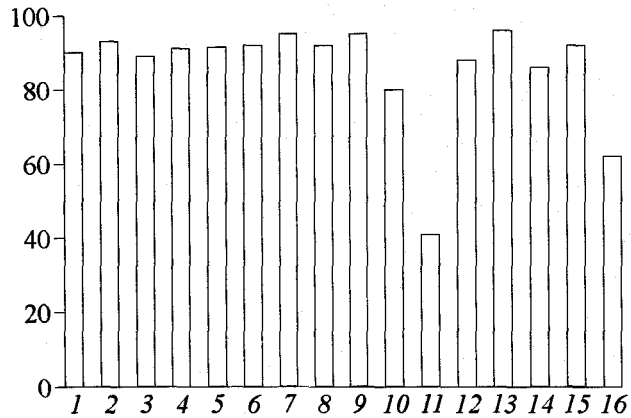

Fig. 2. Changes in biochemical parameters of the blood immediately after reinfusion of blood exposed to blue light. Pre-exposure values are taken for 100%. *1*) total protein; *2*) albumin; *3*) acid phosphatase; *4*) alanine aminotransferase; *5*) asportate aminotransferase; *6*) glutamyltransferase; *7*) lactate dehydrogenase; *8*) amylase; *9*) creatine phosphokinase; *10*) cholesterol; *11*) triglycerides; *12*) LDL; *14*) glucose; *15*) creatinine; *16*) bilirubin.

Changes in blood viscosity and hematocrit were not caused by erythrocyte deposition, but were due to intravascular dilution with interstitial fluid with a low content of high-molecular proteins. The effect decreased but did not completely disappear after 24 h. After the end of the course blood viscosity remained below the initial level (slow response).

Blue light did not modify *in vitro* blood rheology, except very long exposure inducing photohemolysis.

Rapid response of the blood coagulation system consisted in a negligible (2-3 sec) shortening of APTT, PTT, and TT and increased factor VIII and IX activities.

Changes in platelet aggregation depended on its initial intensity (Fig. 1). It sharply increased if it was initially suppressed, while activity of platelets in the "reutz" form decreased. Platelet activity increased only in cases with drug-induced inhibition, but not in genetic defects.

Changes in the biochemical composition of the blood are presented in Fig. 2. Total protein content decreased by 10%, which allowed to differentiate dilution from metabolic shifts. Minor changes in glutamyl transferase, lactate dehydrogenase, acid phosphatase, serum glutamic and pyruvic transferases, and amylase activities were caused by dilution. However, dilution could not be responsible for decreased concentrations of cholesterol, triglycerides, LDL, and glucose. These shifts were apparently due to metabolic changes, and unlike H. Kost *et al.* [11] we observed a rapid response. As for glucose, hypoglycemic effect of BL after body surface irradiation was well known at the beginning of the twentieth century, when BL was recommended for treating diabetes mellitus.

A relative decrease in bilirubin concentration in patients with normal bilirubin values seems to be significant, but the absolute decrease did not exceed 0.5-1 mg/100 ml. A decrease in bilirubin level can be attributed to its oxidation as a result of activation of photodynamic processes.

Hence, phototherapy with BL induces no damage to organs (activities of damage marker enzymes in the blood do not increase), but decreases the concentrations of atherogenic lipids, sugar, and bilirubin. These shifts progress and stabilize after completion of the course of phototherapy.

In patients with chronic obstructive bronchitis phototherapy significantly increased the index of phagocytosis, bactericidal activity of neutrophils, T and B lymphocyte counts, and the T helper/T suppressor ratio from 1.1±0.12 to 3.17±0.15. Hence, infusion of

TABLE 1. Effect of Blue Light Photohaemotherapy on Parameters of Computer-Aided Spirometry in a Female Patient with Chronic Obstructive Bronchitis

Parameter	Normal value	Initial		After 1st session		After 4th session	
		abs.	% of norm	abs.	% of norm	abs.	% of norm
Vital lung capacity, liters	4.13	2.86	69.23	3.25	78.67	3.72	90.05
Functional vital lung capacity, liters	4.03	2.87	71.30	3.51	87.20	3.96	98.39
Forced expiration volume, liter/sec	3.47	1.82	52.48	2.17	62.57	2.59	74.68
Expiration to inspiration ratio, %	84.21	63.41	75.30	61.82	73.41	65.40	77.66
Expiration volumic rate, liter/sec							
peak	7.36	3.55	48.23	4.14	56.25	5.62	76.36
immediate at 25th sec	6.72	3.08	45.80	4.07	60.52	4.98	74.05
maximal at 50th sec	5.07	1.52	30.00	2.67	52.70	2.89	57.05
immediate at 75th sec	2.57	0.70	27.24	1.15	44.75	1.14	44.36
Mean volumic rate of minute ventilation at 25-75th sec, liter/sec	4.24	1.42	33.47	2.39	56.33	2.48	58.45

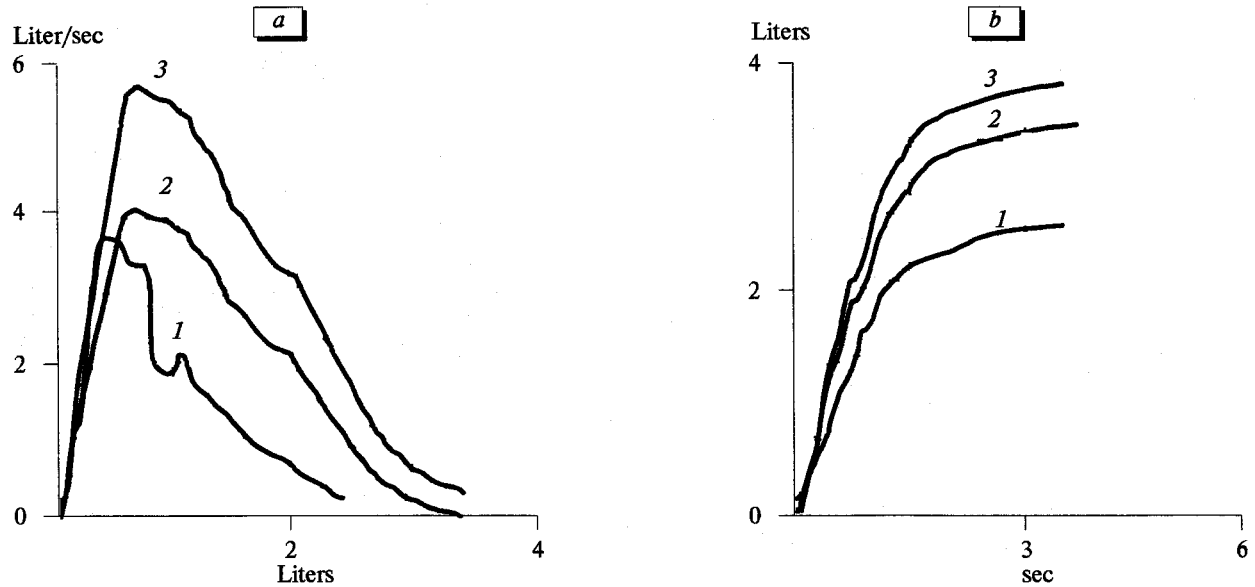

Fig. 3. Pulmonary function of a female patient with chronic obstructive bronchitis treated by blue light photochemotherapy. Flow-volume(*a*) and volume-time (*b*) curves. *1*) before therapy; *2*) after the 1st exposure; *3*) after the 4th exposure.

BL-exposed blood stimulated immunity. Similar results were obtained in nude mice and humans exposed to UVA-1 and BL (body surface exposure) [10]. The method is used for immunity stimulation in cancer patients treated by radiotherapy.

To demonstrate rapid functional responses to BL, we examined the respiratory function of the lungs in patients with chronic obstructive bronchitis. Infusion of irradiated blood rapidly improved the major parameters of respiratory function of the lungs (Fig. 3, Table 1), the effect increasing during the course of therapy (slow response).

Thus, direct irradiation of a small volume of blood followed by its reinfusion into the circulation caused rapid and intense changes in homeostasis. Blood viscosity decreased due to endogenous dilution; the mechanism of this phenomenon is not clear. According to hemorheological laws, these shifts increase volume rate of bloodflow, stroke volume, and cardiac output, and decrease total peripheral resistance. Presumably, all these changes are to compensate for increased requirements of energy systems of the cell caused by its transition to more intense functioning. Changes in the functional capacity of the lungs can serve the same purpose. Biochemical shifts in the blood reflect activation of metabolism. A shift in the blood clotting system towards hypercoagulation is usually accompanies metabolic stress [8].

Pathological signs more rapidly disappear in patients exposed to BL and cure can be attained even in cases when drug therapy is ineffective.

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