

Immune Response

[Biofizika](#). 2006 May-Jun;51(3):509-18.

[Effect of low-intensity laser radiation (632.8 nm) on immune cells isolated from mice]

[Article in Russian]

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The effect of in vitro exposure to low-power laser light with a power density of 0.2 mW/cm² and a wavelength of 632.8 nm induced by helium-neon laser on the functional activity of macrophages and splenic lymphocytes was studied. If the exposure period did not exceed 60 sec, the stimulation in interleukin-2 (IL-2) and nitric oxide (NO) production, as well as an increase in the activity of natural killer cells were observed. The increase of irradiation dose by prolongation of the exposure duration up to 180 s induced a significant decrease in NO production and natural killer cell activity, but IL-2 production was not different from the control level. A remarkable decrease in interferon-gamma (IFN-gamma) production was observed following laser light exposure of cells for 60 or 180 s, whereas under lower doses (exposure for 5 or 30 sec) IFN-gamma production increased. Irradiation of isolated macrophages induced a significant stimulation of cellular tumor necrosis factor-alpha (TNF- alpha) production at all doses used, and, what is more important, an enhancement in both TNF-alpha and interleukin-6 (IL-6) production was revealed as early as after a 5-s exposure. In this case, more prolonged exposure periods, 60 and 180 s, either did not induce changes in IL-6 production (in macrophages) or decreased IL-6 production (in lymphocytes). Thus, upon in vitro exposure of cells to extremely low-power laser light, a basic tendency was observed: short-term irradiation predominantly induced stimulation in secretory activity of cells, whereas prolongation of exposure mainly induced immunosuppression. The only exception to the rule was a change in interleukin-3 (IL-3) production, which decreased after short-time exposure, but, on the opposite, increased when the cells were exposed for 180 s. In addition, a high sensitivity to extremely low-power laser light was supported by expression of the inducible heat shock protein, Hsp70, the effect being observed at all doses used, including the exposure for 5 s. At the same time, expression of another heat shock protein, Hsp90, was somewhat reduced after irradiation of cells with laser light.

[Photodermatol Photoimmunol Photomed](#). 2006 Feb;22(1):33-8.

Effects of low-power laser radiation on mice immunity.

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Background/purpose: Because of large interest in biological effects of laser radiation used in laser therapy, the effect of extremely low-level red laser light intensity on the immune cell activity has been studied in the animal model with well-characterized macrophage and T cell populations as responder cells producing cytokines, protective proteins, active oxygen, and nitric compounds. To study of the possible side effects of laser immunotherapy we monitored the productions of cytokines, nitric oxide (NO), and heat shock protein 70 (Hsp70) in mice subjected to a periodic laser exposure for 1 month. Methods: Helium-neon laser radiation with the power of 0.2 mW/cm² and wavelength of 632.8 nm was applied on two different mouse skin surfaces, i.e. a thymus projection area or a hind limb. Healthy NMRI male mice were irradiated repeatedly with laser light for 1 min with 48-h intervals for 30 days. The animals were divided into three groups of 25 mice. The first and the second groups were exposed to laser light, on the thymus and hind limb area, respectively. The third, sham-irradiated group served as a control. Early and prolonged effects of laser radiation on the levels of NO (by Griess assay), Hsp70 (by Western blot assay), tumor necrosis factors (TNF-alpha and TNF-beta) (by cytotoxic assay using L929 cells as targets), and interleukin-2 (IL-2) (by ELISA assay) were determined. Results: The dynamics of immune responses to low-power laser light intensity was shown to be dependent on two factors, i.e. the cumulative dose and the localization of the irradiated surface. Besides, various populations of cells demonstrated different sensitivity to laser radiation, with T cells being more responsive among examined populations of the cells. Low intensity laser light induced an immune cell activity when the exposure duration did not exceed 10 days, while a more prolonged period of treatment generated more severe changes in the immune system, up to immunosuppression. The treatment of the thymus zone resulted in more pronounced changes in the cytokine production as well as in NO and Hsp70 synthesis. Conclusion: Low-power laser irradiation showed more effective immunomodulatory effects when applied on the thymus projection area. The rise in IL-2 and Hsp70 production related to a short-term effect of laser application may be reversed after repeating laser treatment. We suggest that for the support of immune system stability, the prolonged laser therapy should be accompanied by supplementary methods.

[Photodermatol Photoimmunol Photomed](#). 2003 Aug;19(4):203-12.

Immunomodulatory effects of low-intensity near-infrared laser irradiation on contact hypersensitivity reaction.

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BACKGROUND/PURPOSE: Contact hypersensitivity (CHS) reaction is a useful model for studying the skin immune system and inflammatory reactions in the skin. In this study, an experimental model of CHS reaction was employed to assess immunomodulatory effects of near-infrared (near-IR) low-intensity laser (LIL) irradiation, which is used as adjuvant therapy in dermatology, physical medicine, rheumatology, etc., because of its declared anti-inflammatory, biostimulative and analgesic effects. **METHODS:** The effects of near-IR LIL irradiation ($\lambda=904$ nm, irradiance 60 mW/cm², fluence 3.6 J/cm²) on CHS reaction to 1-chloro-2,4-dinitrochlorobenzene (DNCB) in Albino Oxford rats were examined by irradiating experimental groups of animals before the induction phase of CHS reaction, while nonirradiated animals and animals that received vehicle instead of hapten served as controls. Ear-swelling assay, histopathological examination of H&E preparations of ear skin, computer-assisted image analysis of dermal infiltrate, ear skin organ culture with the determination of cutaneous production of tumour necrosis factor-alpha (by ELISA assay) and nitric oxide (by Griess' assay) were used for measuring the effects of LIL in the elicitation phase of CHS reaction. Cellularity, dendritic cell content, flow cytometry and proliferation assays (spontaneous and in the presence of IL-2 and concanavalin A) of the draining lymph node cells (DLNC) were performed for the assessment of LIL irradiation effects in the induction phase. **RESULTS:** In the irradiated group of animals, ear swelling was significantly diminished compared to control animals (101 \pm 11.5% vs. 58 \pm 11.6%, $P<0.01$). This was accompanied by a highly significant decrease in the density of dermal infiltrate (22 \pm 0.81 vs. 14.2 \pm 1.75 cells per unit area, $P<0.01$) and a significant decrease in nitrite levels in the medium conditioned by organ-cultured ear skin (17.63 \pm 1.91 vs. 3.16 \pm 1.69 μ M NaNO₂; $P<0.01$), while TNF-alpha concentration was not changed. Cellularity and dendritic cell content in DLNC population, as well as the expression of TCR-alpha, CD4, CD8 and CD25, were not changed between irradiated and nonirradiated animals. Proliferation rates of DLNC cultured for 72 h were significantly lower in irradiated animals (17.3 \pm 4.1 vs. 13.9 \pm 0.9 x 10³ c.p.m.; $P<0.01$). In cultures of DLNC with added rIL-2 or 0.5 μ g/ml of concanavalin A, proliferation rates were also significantly decreased in irradiated animals (34.7 \pm 3.5 vs. 31.2 \pm 2. c.p.m. in IL-2-supplemented culture, $P<0.01$; 70.9 \pm 6.4 vs. 58.3 \pm 9.1 x 10³ c.p.m. in concanavalin A-supplemented culture, $P<0.01$). However, this effect was overcome in the presence of the higher concentration of concanavalin A (2.5 μ g/ml) (nonirradiated 38.7 \pm 3.1, irradiated 123.1 \pm 7.3 x 10³ c.p.m., $P<0.01$). **CONCLUSION:** LIL irradiation showed a systemic immunomodulatory effect on CHS reaction to DNCB in rats. Decreased ear swelling observed in the elicitation phase was associated with diminished proliferative responses of the DLNC in the induction phase of CHS reaction. Further experimental work is needed to examine the possible mechanisms of these effects.

[Lik Sprava](#). 2004 Mar;(2):30-5.

[Effect of low intensity helium-neon laser and decimeter electromagnetic

irradiation on functional indices of immune cells in patients with rheumatoid arthritis]

[Article in Russian]

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Clinical, laboratory, and immunoassay of 58 patients with rheumatoid arthritis, first and second degree of activity was carried out. Low-energy helium-neon laser exposure and decimeter electromagnetic radiation (DMEM) of peripheral blood was given along with the use of non-steroidal antiinflammatory drugs and methotrexate. Peculiarities of this magnetic-laser effect on proliferation response and apoptosis of mononuclear leucocytes in vitro and in vivo have been revealed. It was also established that the application of DMEM-therapy brought patients with RA in shorter period of time to clinical improvement evaluated by ACR criteria.

[Eksp Klin Gastroenterol.](#) 2004;(4):29-32, 108.

[State of humoral immunity and phagocytic activity of neutrophils in patients with ulcer and effect of low-intensity laser therapy]

[Article in Russian]

[Burduli NM,](#) [Gutnova SK.](#)

The aim of our investigation was to study the influence of low-intensity laser therapy at the immunologic parameters and Helicobacter pylori (HP) microbial contamination in patients with exacerbation of peptic and duodenal ulcer. 100 patients aged 18-65 were examined and divided into 2 groups. The experimental group (75 patients) underwent a complex drug and laser therapy of various therapeutic techniques. The control group (25 patients) underwent only drug therapy. The results of this study show the immunocorrective effect of different methods of low-intensity laser therapy in the exacerbation period and more essential decrease of HP microbial contamination in the experimental group.

[Photomed Laser Surg.](#) 2004 Dec;22(6):504-8.

Cell survival, DNA, and protein damage in B14 cells under low-intensity near-infrared (810 nm) laser irradiation.

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OBJECTIVE: The aim of this study was to reveal the possible cytotoxic and genotoxic effects of low-intensity (200 mW) near-infrared (810 nm) laser irradiation, using B14 cell line. **BACKGROUND DATA:** Laser therapy is widely used in biomedical treatment of many diseases, but the possible molecular mechanisms of laser actions remain unclear and the damaging effects of laser irradiation are still controversial. The side effects of laser therapy involve the generation of reactive oxygen and nitrogen species which in turn initiate lipid peroxidation, protein damage or DNA modification. **METHODS:** B14 cells and suspension of human erythrocyte membranes were irradiated with near-infrared (810 nm) therapy laser at different radiant exposures (3.75-15.0 J/cm²) and light power (fluency rate) 200 mW at 22 degrees C. Laser induced cellular oxidative damage was measured in terms of cell survival, DNA damage, measured using the method of single cell gel electrophoresis (Comet assay), protein damage measured as protein carbonyls formation. **RESULTS:** No substantial changes of cell survival under B14 cells irradiation at radiant exposures 3.75-11.25 J/cm²) were observed. Similarly, neither considerable light-induced DNA damage or protein carbonyls accumulation was revealed. On the contrary, laser irradiation has led to decrease of cell protein carbonyl groups level in a dose-dependent manner. Additionally, using human red blood cell membranes as model membranes and biological oxidant HOCl we observed that laser irradiation resulted in a decrease of the level of membrane protein carbonyl groups accumulated under oxidative HOCl treatment. **CONCLUSIONS:** We can conclude that laser irradiation used (810 nm, 200 mW, 3.75-11.25 J/cm²) did not produce any considerable cytotoxic or genotoxic effects in B14 cells. Moreover, laser irradiation reduced cellular protein damage (protein carbonyl groups) produced by biological oxidant HOCl.

[Lasers Surg Med.](#) 1997;20(4):451-60.

Helium-neon laser irradiation is not a stressful treatment: a study on heat-shock protein (HSP70) level.

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BACKGROUND AND OBJECTIVE: Helium-neon (He-Ne) laser irradiation has been clinically used to reduce chemotherapy-induced mucositis. This work was designed to find out if this treatment is stressful at the cellular level by studying its effects on the level of the stress-inducible heat shock proteins. **STUDY DESIGN/MATERIALS AND METHODS:** Human desmodontal and mouse L929 fibroblasts were irradiated using a 60 mW laser by a single application of 1.5 and 3J/cm² in continuous mode. Heat shock protein level was studied by gel electrophoresis and Western blotting using monoclonal antibodies. **RESULTS:** He-Ne treatment does not induce heat shock protein synthesis in human desmodontal nor in mouse fibroblasts at the energy densities used in this study. **CONCLUSIONS:** These results indicate that the treatment is not stressful at the cellular level.

Indian J Exp Biol. 1999 May;37(5):444-9.

Immunomodulatory effect of laser on whole body exposure.

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All biomedical laser applications are based on the interaction of laser light with biological system. During the past decade considerable evidence has accumulated demonstrating that non-thermal exposure to laser can elicit cellular changes in the immune system. In the present study, we have analyzed the effect of laser on immune response in rats. A group of rats were exposed to 0.225 mJ/cm² for 90 min for 3 days in specially designed fiberglass chambers. The whole body exposure of rats of He-Ne laser modulated both the humoral and cellular responses to tetanus toxoid stimulation. Plain red light used as a control for red laser light showed an appreciable degree of response as compared to the control groups, but not to the extent of the response to laser. Non-responders turned responders after exposure to laser. There was no response in unimmunized groups when exposed to laser and red light alone. The early and heightened immune response and proliferation of lymphocytes after exposure to laser is suggestive of a complex interaction at the cellular immune response level.

[J Photochem Photobiol B](#). 1992 Dec;16(3-4):347-55.

Cytokine production after helium-neon laser irradiation in cultures of human peripheral blood mononuclear cells.

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The effects of laser light on the immune system have not been extensively characterized. Low-power laser sources, such as the helium-neon (He-Ne) laser with a wavelength of 632.8 nm, have been found to produce photobiological effects with evidence of interference with immunological functions. We have investigated the effects of He-Ne laser irradiation on Ficoll-Hypaque-isolated human peripheral blood mononuclear cells (PBMC). Cultured cells were irradiated for various times at two selected intensities and then stimulated with different mitogens. The rate of incorporation of ³H-thymidine into the DNA of stimulated cells decreased with increasing energy density. The levels of interleukin-1 alpha (IL-1 alpha), interleukin-2 (IL-2), tumour necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) in supernatants of the cultures were determined (irradiated either before or after stimulation). When stimulating cells after irradiation, significantly increased levels of all cytokines were detected after 30 min of

irradiation (18.9 J cm⁻²), whereas after 60 min of irradiation (37.8 J cm⁻²) cytokine levels were found to be significantly decreased.

Bull Exp Biol Med. 2001 Apr;131(4):399-402.

Healing of bone fractures of rat shin and some immunological indices during magnetic laser therapy and osteosynthesis by the ilizarov method.

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The effect of magnetic and laser therapy on healing of bone fractures and blood levels of T and B lymphocytes was studied in rats during osteosynthesis by the Ilizarov method. Laser therapy induced changes in cells attesting to stimulation of reparative processes and normalization of immunological parameters.

Zh Vopr Neurokhir Im N N Burdenko. 1999 Jan-Mar;(1):20-5.

[The possibility of immunocorrection in spinal-spinal cord trauma by using intravenous laser irradiation]

[Article in Russian]

Stupak VV, Rodiukova EN.

The natural defense factors of the body and the cell factors of immunity were studied in 60 patients with acute and early spinal trauma. Immunodeficiency develops in 100% of cases with acute and early spinal trauma. Blood intravenous laser radiation at wave lengths of 632 and 830 nm was shown to produce an immunostimulating effect.

Zh Nevropatol Psikhiatr Im S S Korsakova. 1996;96(2):34-8.

[The effect of endovascular laser therapy and antioxidants on the immune status and energy metabolism of patients with treatment-resistant forms of schizophrenia]

[Article in Russian]

Kut'ko II, Frolov VM, Pustovoi IuG, Pavlenko VV, Rachkauskas GS.

The influence of endovascular laser therapy and of antioxidants on clinical immunological indices and energy metabolism was analysed in 148 schizophrenic patients including 86 patients with shift-like progredient (first group) and 62 patients with continuous-progredient (second group) forms of the disease. Positive trends in psychosis course were observed in 57% of cases in the first group and in 41.9% of patients of the second group. Pronounced improvement of the immunological indices was observed in

patients with positive clinical dynamics: decreased peripheral blood immunocytes sensitization to the brain, hepatic, thymus tissue antigens as well as ATP elevation which was evidence of the improvement of energy metabolism.

[Keio J Med.](#) 1993 Dec;42(4):180-2.

Possible application of the laser in immunobiology.

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The human immune system acts a defence mechanism against exogenous or indigenous potentially harmful bodies, such as bacteria and viruses. The major histocompatibility complex (MHC class I and class II antigens) form key elements of legitimate body components, and the organization of MHC molecules allows T-lymphocytes to distinguish between legitimate and foreign bodies. On detection of a foreign component, T-cells activate the necessary pathways for destruction of the foreign body. Occasionally however the system breaks down and the result is a disease of an autoimmune nature. Both visible light and infrared low reactive-level laser therapy (LLLT) has been shown to act on immune system cells in a number of ways, activating the irradiated cells to a higher level of activity. Infrared LLLT has been shown to increase both the phagocytic and chemotactic activity of human leukocytes in vitro, for example. This is an example of photobiological activation. Photobiological cell-specific destruction is also possible using doses of low incident laser energy on cells which have been photosensitized for the specific wavelength of the laser, such as in photodynamic therapy (PDT) for superficial cancers. LLLT has also been shown to act directly and selectively on the autoimmune system, restoring immunocompetence to immunocompetence cells. Although much more research needs to be done, there are enough experimental and clinical data to show that the laser, and LLLT in particular, has a possibly exciting role both in immunobiological therapy for diseases of the immune system, and to activate and boost the normal reaction of the immune system components against harmful foreign bodies.

[Probl Tuberk.](#) 1991;(6):26-9.

[Effect of low-energy laser irradiation of bronchial mucosa on systemic and local immunity in patients with chronic bronchitis]

[Article in Russian]

Ivaniuta OM, Chernushenko EF, Dzublik AIa, Tyshko NA, Naida IV, Kulik IV.

The effectiveness of endobronchial low-energy laser therapy was studied in 28 patients with chronic nonobstructive bronchitis concurrent with thinning of bronchial mucosa. The course of treatment made it possible to obtain positive dynamics of most parameters of immunologic reactivity in CNB patients. Systemic immunity parameters, except for

the NST and concentration of circulating immune complexes, underwent essential normalization. Marked positive changes were found in the parameters characterizing functional activity of alveolar macrophages: there was a 2.5-fold increase in adhesive properties and over 1.3-fold increase in the percentage of phagocytes. The level of secretory IgA rose significantly (by 3.5 times). Hence, a manifested therapeutic effect of this therapeutic method is mainly associated with its immune-stimulating action.