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Dr. Genady Kostenich

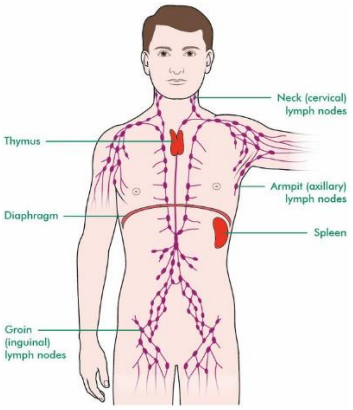
Immune System. Our immune system is essential for our survival. The immune system is the body's defense against infections. Without an immune system, our bodies would be open to attack from bacteria, viruses, parasites, and more. It is our immune system that keeps us healthy as we drift through a sea of pathogens. Immune function within our body is controlled by a system of biological structures and processes that protects against diseases by identifying and destroying pathogens and tumor cells. Multiple complex mechanisms and pathways have developed in order for our immune system to react and adapt to the surrounding environment while maintaining life and health. Many cells and organs work together to protect the body. White blood cells, also called leukocytes, play an important role in the immune system. White blood cells are on constant patrol and looking for pathogens. When they find a target, they begin to multiply and send signals out to other cell types to do the same. Our white blood cells are stored in different places in the body, which are referred to as lymphoid organs. These include the following: Thymus — a gland between the lungs and just below the neck. Spleen — an organ that filters the blood. It sits in the upper left of the abdomen. Bone marrow — found in the center of the bones, it also produces red blood cells. Lymph nodes —small glands positioned throughout the body, linked by lymphatic vessels.

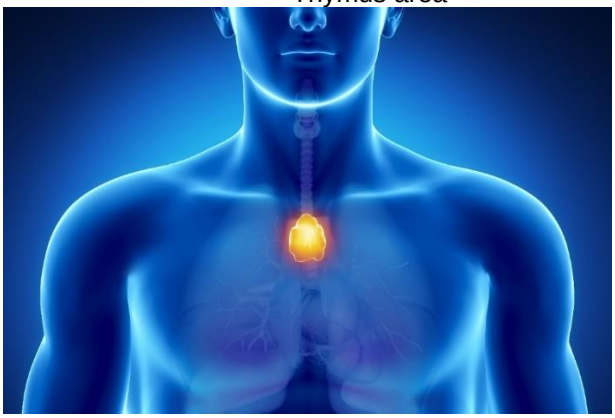
Low-power Laser Therapy (LPLT) – a helpful way to strengthen our immune system and fight off disease.

Immune activation is one of many biochemical responses observed with therapeutic lasers. Numerous scientific publications demonstrate that LPLT with red-infrared irradiation causes various systemic immunomodulatory effects. Laser therapy has been shown to act directly and selectively on the autoimmune system, restoring immuno-competence to cells. Proliferation of lymphocytes after exposure to laser is suggestive of a complex interaction at the cellular immune response level. LPLT has been shown to increase cytokine production in human peripheral blood mononuclear cells as well as stimulates both the phagocytic and chemotactic activity of human

leukocytes. The results indicate that even a single dose of low power laser irradiation can modulate immune responses depending on the immunological status of the organism. 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. The results of studies demonstrate that *low-power laser irradiation showed more effective immunomodulatory effects when applied on the area of lymphoid organs, particularly on thymus projection zone.*

Thymus area





HANDY CURE S'

HANDY CURE S' is a home-use LPLT device that comprises a combination of several light irradiation sources with static magnetic field. The device utilizes low-level super-pulse infrared laser, infrared and red light emitting diodes and static magnetic field in the unique arrangement causing synergistic therapeutic effect. HANDY CURE S' is recommended for various medical applications *including immunomodulatory effect* that can be achieved by irradiating projection zones of lymphoid organs such as thymus gland, spleen and various sites of lymph nodes located throughout of the body.

Below is a review of selected scientific studies that have been published relating to immune modulation effects of LPLT.

Immune-modulating Effects of Therapeutic Lasers

By William J. Kneebone, CRNA, DC, CNC, DIHom

Therapeutic laser has been shown to have many interesting effects on immune function. Immune function within our body is controlled by a system of biological structures and processes that protects against diseases by identifying and destroying pathogens and tumor cells. It can detect many different types of invaders—from viruses to parasitic worms—while distinguishing them from its own healthy cells and tissues. This identification and detection is ever changing as pathogens rapidly change and adapt to the host in a way that circumvents many immune responses. Multiple complex mechanisms and pathways have developed in order for our immune system to react and adapt to the surrounding environment while maintaining life and health.[1]

Studies of Laser Effects on the Immune System

Kut'ko et al[2] performed a study that looked at the influence of endovascular laser therapy and of antioxidants on clinical immunological indices and energy metabolism This was analyzed 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.

Ganju et al[3] performed a study that analyzed the effect of laser on immune response in rats. A group of rats were exposed to 0.225 mu j/cm2 for 90 min for three days in specially designed fiberglass chambers. The whole body exposure of rats to 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.

Fujiaki et al[4] coducted a study to examine the effects of low-level laser therapy (LLLT) on production of reactive oxygen (ROS) species by human neutrophils. LLLT is an effective therapeutic modality for inflammatory conditions. An infrared diode laser (GaAlAs), 830-nm continuous wave (150 mW/cm2) was used for treatment). After irradiation, ROS production by neutrophils was measured using luminol-dependent chemiluminescence (LmCL) and expression of CD11b and CD16 on neutrophil surface was measured by flow cytometry. The LmCL response of neutrophils was reduced by laser irradiation at 60 minutes prior to the stimulation with opsonized zymosan and calcium ionophore. The attenuating effect of LLLT was larger in neutrophils of smokers than non-smokers, while the amount of produced ROS was larger in neutrophils of smokers. Expression of CD11b and CD16 on neutrophil surface was not affected by LLLT. The results indicate that attenuation of ROS production by neutrophils may play a role in the effects of LLLT in the treatment of inflammatory tissues. There is a possible utility of LLLT to improve wound healing in smokers.

Takaduma[5] reports that both visible and infrared light have been shown to act on immune system cells in a number of ways, activating the irradiated cells to a higher level of activity. Infrared laser therapy has been shown to increase both the phagocytic and chemotactic activity of human leukocytes in vitro. This is an example of photobiological activation. Photobiological cell-specific destruction is possible by using doses of low incident laser energy on cells which have been photosensitized for the wavelength of the laser—such as in photodynamic therapy (PDT) for superficial cancers. Laser therapy has

also been shown to act directly and selectively on the autoimmune system, restoring immuno-competence to cells.

Kolarova[6] reported that doses of 5–10 J/cm^2 induced a significant increase in phagocytic activity of leukocytes in vitro.

Duan[7] has demonstrated a respiratory burst in bovine neutrophils after HeNe irradiation.

Schindal et al[8] described an experiment on the immune modulating effect of a HeNe laser on e. coli endotoxin pre-immunized rabbits. The influence of transcutaneously-applied low-power laser light on differential blood count and rectal temperature. After three initial immunizations, animals were either given a booster with 5mg/kg of endotoxin or with pyrogen-free saline solution. Both groups underwent laser irradiation with two different wavelengths of red laser and a sham application. The lymphocyte values were considerably higher and the neutrophils were significantly lower in the laser treated group 23 to 24 hours post treatment. The differential blood counts returned to normal levels in the boostered rabbits and continued to rise in the non-boostered rabbits post laser irradiation. Rectal temperature increased after laser treatment, especially in the non-boostered animals. The results indicate that a single dose of low power laser irradiation can modulate immune responses depending on the immunological status of the organism.

Inoue et al[9] studied the effect of 830 nm laser on tuberculin reactions in vivo. Laser was shown to suppress this well-known immunological test for the evaluation of cellular immunity.

Funk et al[10] performed a study demonstrating that He Ne laser increases cytokine production in human peripheral blood mononuclear cells in vitro.

Katsuyama et al[11] performed a study that demonstrated a suppressive effect of diode laser irradiation on picryl contact sensitivity in a rat model. The thickness of the right ear was used as an indicator to various doses of 830 nm laser irradiation. Laser therapy suppressed the cutaneous inflammation due to picryl contact sensitivity in an exposure–time dependent manner. This suppressive effect was restricted to within the radiation site. Remote irradiation to the proximal portion of the tail had no effect.

Yu et al[12] performed a study in which they used an argon pumped dye laser at a wavelength of 630 nm to determine the effects of laser therapy on the immune system. Rats with experimentally-induced sepsis via cecal ligation received laser therapy at 5 J/cm^2. At sixty days, the survival rate was 79% for the laser group and 42% for the control group. Ex vivo lymphocyte proliferation was 180 in the laser group and 130 in the control group. Enhanced ATP synthesis was observed in the laser group.

Mikhailov et al[13] performed a study on patients with Hashimoto's thyroiditis. Forty two patients were treated with 10 applications of 2.4 J/cm2 via an 890nm laser and targeted the thymus projection zone, vascular junction, and the thyroid gland. A control group of similar size was given L-thyroxin, 100 mg/day. All laser-treated patients experienced a decrease in the feeling of squeezing in the area around the thyroid and a decrease in facial edema. The thyroid gland became softer on palpation and smaller on ultrasound examination. There was also a decreased number of patients that caught winter colds in the laser group. The immunoregulatory index (Th/Ts) normalized from 7.5 to 4.2%. The laser effects were still noticeable in 78% of the laser patients four months after treatment. This index was only slightly changed in the control group.

Summary

We can see from the above studies that many significant immune modulating effects have been observed in response to therapeutic laser. Immune activation is one of many biochemical responses observed with therapeutic laser.

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

Effects of low-power laser radiation on mice immunity.

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Author information

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Abstract

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.

Lasers Surg Med. 2000;26(4):357-63.

Laser modulation of angiogenic factor production by T-lymphocytes.

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In previous investigations, small variations in the energy densities of low level light therapy (LLLT) were found to produce significant differences in the proliferation of resting T-lymphocytes in vitro. Pulsing these cells with mitogen in addition to laser therapy produced inhibitory effects regardless of the amplitude of the energy density used. In the current study, the effect of LLLT on the production of angiogenic factor(s) by T-lymphocytes was investigated in vitro.

STUDY DESIGN/MATERIALS AND METHODS:

Human T-cells isolated from peripheral blood were prepared in suspension either with or without addition of mitogen. Cell suspensions were irradiated with laser by using the following energy densities: 1.2, 3.6, 6.0, and 8.4 J/cm(2). Wavelength, pulsing frequency, and power output were kept constant at 820 nm, 5,000 Hz, and 50 mW, respectively. After either 3 or 5 days of incubation, lymphocyte supernatants were collected and added as conditioned media to cultured endothelial cells (ECs). The effect on the proliferation of these ECs was assessed over a 72-hour period by using a methylene blue assay.

RESULTS:

Endothelial cell proliferation increased significantly when incubated with conditioned media collected from resting T-cells exposed to 1.2 and 3.6 J/cm(2). Day 5 conditioned media produced similar patterns of EC proliferation to that of day 3 but at lower magnitude. Pulsing of T-lymphocytes with mitogen in addition to laser irradiation significantly lessened their angiogenic capability. Conditioned media from 3.6 J/cm(2) laser-treated T-cells induced the maximal EC proliferation in all groups studied.

CONCLUSION:

It would seem that laser therapy stimulates lymphocytes to produce factor(s) that can modulate EC proliferation in vitro; this effect on the lymphocytes is influenced by (1) the amplitude of energy density used for T-cell irradiation, (2) exposing T-cells to both mitogen and laser, and (3) the duration of T-cell incubation in culture.

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

Possible application of the laser in immunobiology.

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Abstract

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.

Photomed Laser Surg. 2008 Oct;26(5):451-3. doi: 10.1089/pho.2007.2218.

Intracellular ATP level increases in lymphocytes irradiated with infrared laser light of wavelength 904 nm.

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OBJECTIVE:

Red and near-infrared laser irradiation is reported to have a range of biological effects on cultured cells and different tissues, leading to the hypothesis that laser light can affect energy metabolism. Increased adenosine triphosphate (ATP) synthesis has been reported in cultured cells and rat brain tissue after irradiation at 632.8 nm and 830 nm, respectively. This study investigated whether diode pulsed laser irradiation enhances ATP production in lymphocytes.

MATERIALS AND METHODS:

Aliquots (500 microL) of an extract of cultured lymphocytes of the Molt-4 cell line were irradiated with diode laser light (lambda = 904 nm, pulsed mode, 6 kHz frequency) with an average emission power of 10 mW for 60 min. A Spectra Physics M404 power meter was used to measure light intensity. Controls were treated similarly but not irradiated. The amount of ATP was measured by the luciferin-luciferase bioluminescent assay.

RESULTS:

The amount of ATP in irradiated cell cultures was 10.79 +/- 0.15 microg/L (SD; n = 10), and in non-irradiated cell cultures it was 8.81 +/- 0.13 microg/L (SD; n = 10). The average percentage increase of irradiated versus control cell cultures was about 22.4% +/- 0.56% SD ($p < 0.001$).

CONCLUSION:

This significant increase is probably due to laser irradiation; it cannot be attributed to any thermal effect, as the temperature during irradiation was maintained at 37.0 degrees +/- 0.5 degrees C. Thus the therapeutic effects of the biostimulating power of this type of laser are identified and its indications may be expanded.

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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Department of Dermatology and Institute for Medical Research, Military Medical Academy, Belgrade, Serbia and Montenegro.

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+/-11.5% vs. 58+/-11.6%, P<0.01). This was accompanied by a highly significant decrease in the density of dermal infiltrate (22+/-0.81 vs. 14.2+/-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+/-1.91 vs. 3.16+/-1.69 microM 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+/-4.1 vs. 13.9+/-0.9 x 103 c.p.m.; P<0.01). In cultures of DLNC with added rIL-2 or 0.5 microg/ml of concanavalin A, proliferation rates were also significantly decreased in irradiated animals (34.7+/-3.5 vs. 31.2+/-2. c.p.m. in IL-2-supplemented culture, P<0.01; 70.9+/-6.4 vs. 58.3+/-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 microg/ml) (nonirradiated 38.7+/-3.1, irradiated 123.1+/-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.

Mol Cell Biochem. 1997 Apr;169(1-2):51-9.

Infra-red laser irradiation enhances interleukin-1 receptor antagonist, increases 3H-thymidine incorporation and the release of [3H]arachidonic acid in human monocytes.

Reale M1, Orso C, Castellani ML, Barbacane RC, Placido FC, Porreca E, Di Febbo C, Cataldo I, Vacalis D, Anogianakis G, Trakatellis A, Conti P.

Abstract

The effect of infra-red laser irradiation has been experimented on various biological systems and particularly in human tissues, in vitro as well as in vivo. In order to examine the influence of laser irradiation on cells of the monocytic lineage we have irradiated human peripheral blood mononuclear cells with an infra-red laser at a wavelength of 904 nm, at 2000 Hz frequency and 15 mW for 2 min. Here, we report that laser irradiation for 2 min. at different preincubation times (T = 0 and T = 30 min) enhances LPS (10 micrograms/ml or PHA (10 micrograms/ml, suboptimal concentration)-stimulated monocytes by modifying cell proliferation, as judged by [3H] thymidine incorporation. IL-1 receptor antagonist (IL-1ra) along with an increased release of [3H] Arachidonic acid production, is also influenced by laser irradiated monocytes when treated for 2 min after 1 h incubation. IL-1RA production increased 4-5 fold after laser irradiation, while 3H-arachidonic acid incorporated from PMA-stimulated cells increased and the effect was significant at T = 0 and T = 30 min; while at T = 1 h the effect was negligible. These results may provide new information regarding the effect of laser irradiation on the immune system.