DEVELOPMENT AND CLINICAL APPLICATIONS OF INTRAVENOUS LASER BLOOD IRRADIATION (ILBI)

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Extracorporeal irradiation of blood using ultraviolet light has been well-documented particularly in the Russian literature as having efficacy in the treatment of a number of diseases and conditions, but the technique required a high level of technical skill and was relatively invasive. The extracorporeal approach was necessary due to the poor penetration of UV light into living tissue. The development over the past 3 decades of efficient and comparatively inexpensive laser devices delivering low levels of laser energy in the visible red and near infrared wavebands offered deep penetration of light into living tissue and allowed the application of the transcutaneous approach for irradiating blood *in vivo*. This approach, although noninvasive, could not deliver laser energy efficiently and precisely to the main target, *i.e.*, the blood, due to the non-specificity of these wavebands for hemoglobin, so the next stage was the minimally invasive delivery of laser energy concentrated directly into the blood itself using the intravenous approach, and intravenous laser blood irradiation (ILBI) successfully developed. Applications rapidly expanded in the 1980's and 1990's, including heart diseases and arrhythmias, pulmonary disease, problems of the exocrine and endocrine systems, treatment of postoperative sepsis, oncology and autoimmune disease, amongst others. Currently in Russia, many pathologies are successfully treated with ILBI, and the successfully treated patient numbers have reached the hundreds of thousands. The current review article traces the development of ILBA, examines devices and wavelengths used, and categorizes clinical applications. Based on the available data, we can conclude that ILBI improves the rheological properties of the irradiated blood thereby stimulating blood and tissue cells and enhancing the autoimmune system. ILBI offers high efficacy, shorter treatment periods and increased treatment latency. When used in combination therapy, ILBI improves the efficacy and results of the other therapy or therapies. Finally, it would appear that a frequency modulated beam is more efficient than the same system or wavelength applied in continuous wave.

Key Words: Intravenous laser therapy, cardiovascular disease, cardio-pulmonary disease, dermatological disease, endocrine disease, musculoskeletal disease, frequency modulation

Introduction

Extracorporeal irradiation of blood using ultraviolet (UV) light was extremely popular in the 1970's and 80's and has been well-documented in the Russian literature as having efficacy in the treatment of a number of diseases and conditions. This technique, however, requires a relatively invasive technique to introduce blood extracorporeally to the irradiation chamber, a

high level of technical skill and the maintenance of an extremely strict sterile field. The poor penetration of UV light into living tissue necessitated the extracorporeal approach to irradiation of blood. The development in the late 1970's of reliable and comparatively inexpensive laser systems capable of delivering low incident levels of laser energy in the visible red and near infrared wavebands, so called low level laser therapy or LLLT, provided light sources which were capable of deep penetration into living tissue so that transcutaneous irradiation of the superficial blood vessels was possible. However, neither of the above-mentioned

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wavebands is selectively absorbed in haemoglobin, so precise irradiation of blood alone was impossible. This led to the development of the intravenous approach, facilitated by the ability of visible red light to be delivered via flexible quartz fibres capable of being introduced down needle-based delivery devices. Red light was selected because of its better absorption in haemoglobin compared with plasma, and the fact that the laser energy can be seen in the target vessel transcutaneously. The first reports on intravenous laser blood irradiation (ILBI) in animal experiments appeared in 1978 from Meshalkin E.N. and Sergievsky V.S.¹⁾, and reports on clinical applications of ILBI started to appear in the 1980's. Meshalkin E.N. (1984)¹⁾ and Kipshidze N.N. (1986)²⁾ succeeded in using ILBI for the treatment of ischemic heart disease and different types of cardiac arrhythmias. Kraskov A.M. (1986) demonstrated the efficacy of ILBI in the treatment of septic endocarditis.³⁾ Zemskov V.S. and colleagues (1984)⁴⁾, Babadjanov R.A. (1986)⁵⁾, and Gushcha A.L. (1988)⁶⁾ used ILBI for the treatment of acute destructive pancreatitis.

Voronina V.A. (1985) started using ILBI for integral medical measures in the treatment of peritonitis.⁷⁾ Sitchev P.S. (1986) used ILBI as a preventive measure against purulent septic complications in surgery.⁸⁾ Mokeyev A.F. (1986) started using ILBI for integral treatment of hepatic icterus⁹⁾ and Mikhailov V.A. (1989)¹⁰⁾ and Gamaleyeva N.F. (1989)¹¹⁾ applied ILBI in the field of oncology.

In October 1989, the Council of Ministers of the USSR awarded the State Prize of the USSR (No 21488) to a group of medical scientists (Korochkin I.M., Kapustina G.M., Kipshidze I.N., Chapidze G.E., Bokhoa M.P., Marsatiaschvilli L.A., Stepanishcheva N.I., Sergievsky V.S., Agov B.C.) for the development of helium neon (HeNe) laser intravenous irradiation of blood in the treatment of ischemic heart disease. Currently, ILBI is routinely used in Russia in the monotherapy and combination therapy for an extremely wide range of pathological conditions, with the numbers of successfully-treated patients reaching several hundreds of thousands.

ILBI Apparatus and Contraindications

Systems used

The main laser therapy systems used in ILBI are currently the continuous wave (CW) HeNe laser (632.8 nm, output at fibre tip of 1-2 mW) and a variety of semiconductor (diode)-based laser systems (wavelengths ranging from 640 nm – 670 nm, 1-2 mW output

power). However, from 2002 frequency-modulated diode laser energy (640 nm – 670 nm, 1-2 mW output power and the same total dose) has been used more and more as it has been shown by the author¹²⁾ and others (Serov V.A.¹³⁾ and Nasedkin A.N.¹⁴⁾ to increase the efficacy of the intravenous laser treatment of blood, and to extend the range of diseases which responded most effectively to ILBI.

Contraindications of ILBI

With regard to the contraindications associated with ILBI, there are two classes of contraindications based on the total clinical experience as reported by the various researchers, namely absolute and relative contraindications. In the case of absolute contraindications, the name speaks for itself. The category of relative contraindication is evolved from the data, taking into account that the reports from researchers are sometimes contradictory.

Absolute group:

- Cardiogenic shock.
- Expressed arterial hypotension
- Stagnant cardiopathy
- Circulatory inefficiency, stages II b and III
- Anemia (Hb less than 60 g/l)
- Sick sinus syndrome
- Existence of blood coagulopathies (angiostasis, *et cetera*)

Relative group:

1. Oncological diseases. The author (1989) has used ILBI to treat different oncological diseases.¹⁰⁾ Both preoperative HeNe intravenous laser blood irradiation and external transcutaneous semiconductor laser irradiation have been used in 56 oncology patients, both as mono- and combination therapy. The external semiconductor laser irradiation was the most effective and showed strong immunostimulating and tumor static effect and decreased postoperative complications, demonstrating good photoactivation of the immunomodulatory system; however, now we use only infrared lasers, due to the fact that it is impossible to calculate the exact dose of a laser radiation which could be received by tumor cells circulating in the blood.
2. Acute forms of specific infectious diseases (lues, brucellosis).
3. Dysmenorrhea
4. The first half term of pregnancy where there is the potential for an abortion.
5. Acute zymosis, either respiratory or viral.

CLINICAL APPLICATIONS

Diseases of the Cardiovascular System

Stenocardia: Koryakov A.I. and Rojdestvenskaya E.D. (1999) confirmed the connection between angina and rheological ILBI effect in patients with cardiovascular insufficiency.¹⁵⁾ Belousov S.S. (1990) studied the therapeutic effect of ILBI on two pathophysiologically distinct forms of myocardial ischemia with stable and unstable processes. The investigation showed that patients with unstable stenocardia got the best results. Patients from both groups demonstrated up to 67% decrease in spontaneous aggregation of thrombocytes and 17% in the aggregation of erythrocytes. Compared with the control group, ILBI patients demonstrated positive clinical effects on average 3 - 5 days earlier. Seventy-six percent and 17% patients in the basic groups respectively demonstrated sedative and diuretic effects of ILBI. Patients with an atrioventricular extra systole showed an antiarrhythmic effect.¹⁶⁾

Mikhailov V.A. et al. reported in 1999 on a clinical trial with 80 patients having stenocardia tension of class II-III class. There were 3 groups, the control untreated group (n=20), a group treated with HeNe ILBI (n=40, 632.8 nm, 1 mW, 0.9 J/cm²/session) and frequency modulated IR transcutaneous diode laser therapy (n=20, 630 nm, 5 mW/cm², 0.787 J/cm²/session). The HeNe group and the diode laser group showed improvements of 27% and 10%, respectively, compared with the control group. Treatment latency was from 1.5 - 2 months after the first course and 2-3 months after the second course. In 7.5% of the patients, the treatment effect lasted for 6 months.¹⁷⁾

A clinical trial on the use of Intravenous Frequency Laser Therapy (IFLT) (wavelength 640 nm., dose 0.8 - 0.9 J/cm²) in 26 patients with stenocardia of functional class 3-4 demonstrated that the positive results of the IFLT lasted for 2.5-3 months on average, with 6.4 months in 15.3% of patients.¹²⁾

Kapustma G.M., Moskvina S.V. and Titov M.N. reported in 1999 on the efficacy of intravascular laser therapy for unstable stenocardia of classes I to III. There were 177 patients in total: 74 patients were treated with the HeNe laser, 83 patients were treated with a semiconductor laser (630 nm), and the remaining 20 patients made up the control group, who were treated with conventional chemotherapy. The result was classed as "good" if the stenocardia attacks disappeared completely; "satisfactory" if the number of attacks and the number of nitroglycerin pills required by the patient decreased by up to 50 %, and it was

considered "negative" if no effect was observed. For patients suffering from unstable stenocardia with prethrombotic syndrome, the hemostasis was corrected using intravascular HeNe laser therapy every other day. For patients suffering from progressing and primary stenocardia with prethrombotic syndrome, the most effective treatment was prolonged HeNe laser therapy every other day (5 to 8 sessions). If the initial level of antithrombin-III was high, then combined HeNe laser therapy was recommended with the traditional method of the treatment.¹⁸⁾

In another controlled trial in 1990, Belousov S.S. and colleagues studied the therapeutic effect of ILBI in two pathophysiologically distinct forms of stable and unstable flow stenocardia. The patients treated with ILBI had a positive clinical effect appearing on average about 3 to 5 days earlier than those in the control group. A sedative and a diuretic effect after ILBI were experienced by 76% and 17% of the treatment group patients, respectively. Patients with an atrioventricular extra systole experienced an antiarrhythmic effect.¹⁶⁾

In 1990, Ananchenko V.G. et al.¹⁹⁾ reported a study on the influence of ILBI on clinical flow and the level of activity of lymphocytic-related enzymes in the peripheral blood of patients with ischemic heart disease. The results showed that the patients with functional class 3 to 4 stenocardia experienced decreased frequency, intensity and duration of their stenocardia attacks or even their complete disappearance, coupled with some improvement in their endurance to common physical stress. Apart from that, asthenia (general weakness) improved, their sleep normalized, and their mood improved. Some additional indications on the effect of ILBI against angina can be found in the works of Belousov G.G et al. (1990).¹⁶⁾

Arterial Hypertension: In a 1990 study on ILBI from Belousov S.S. et al., systolic and diastolic arterial pressure decreased; pulse rates dropped; and blood-clotting time was prolonged on average by 27 %. Biochemical blood analysis showed an average of 17% decrease in the urea and creatinine levels.¹⁶⁾

While investigating ILBI for patients with primary vascular forms of hypertension of the small circle, Konopleva L.F. and colleagues (1990) reported a marked decrease of systolic pressure in the pulmonary artery by 18%, improvement of hemorheology parameters including a 28% decrease in blood viscosity, 23% in thrombocytes aggregation and a 20% increase in deformation of erythrocytes. The positive shifts in the main parameters of endocardiac hemodynamics and hemorheology were stable for 6 months after com-

bined ILBI treatment in an average of 73% of patients.

The author summarizes his results here in a recent study on Intravenous Frequency Laser Therapy (IFLT) (wavelength, 640 nm; course dose 0.8-0.9 J) in 76 patients with stage II-III hypertension. Positive results lasted on average 2.7 months, systolic blood pressure decreased by 22.2% and diastolic by 8.3%. In 1 patient the positive results lasted for 8 months.¹²⁾

Acute Myocardial Infarction (AMI)

Savitsky S.Y. and Popova L.I. (1989) studied the influence of intravenous blood laser exposure in the case of acute myocardial infarction on neurohumoral regulation of the metabolism. They established that the exposure to ILBI allowed normalization of a number of regulatory processes in the case of acute myocardial infarction. The elevated levels of adrenocortical hormone, hydrocortisone and vasopressin significantly decreased on the 7th post-treatment day in the group receiving LT. After ILBI treatment, patients with myocardial infarction showed a 38% increase in their pO₂ in capillary blood in comparison with the initial level.²⁰⁾

This correlates with the 1989 findings of Gamaleya N.F. and Stadnik V.Y. who demonstrated a decrease in arterial pCO₂. Kapustina G.M. et al. (1999) observed 213 patients with an acute myocardial infarction (AMI) who had been treated with invasive laser therapy. Invasive laser therapy was applied in the early phase of infarction, and was noted to improve rheological blood properties, help the microcirculation to recover and reduce hypoxia in the peri-infarction zone thus limiting the extent of the region of necrosis. Investigation of serum creatinine phosphokinase (CPK) activity demonstrated that for patients who received laser treatment in the first six hours following a myocardial infarction the total peak of enzyme activity was observed 3 to 6 hours earlier than in untreated patients and complete normalization occurred 2 to 3 days earlier. These positive CPK dynamics can be considered as an indication that the necrotic zone has been localized, and these results are in agreement with the scintigraphy findings of the myocardium with 99 Tc pyrophosphate.¹⁸⁾

Antiarrhythmic Effect: Malinovskaya P.E. et al. (1989) highlighted the ILBI-associated antiarrhythmic effect in patients with cardiovascular diseases²¹⁾ and a combination of antiarrhythmic and anesthetizing effects were described in a study from Domnikov A.D. and colleagues (1989). In diabetes mellitus patients, Donish R.M. and colleagues (1989) demonstrated favorable

tendencies in the autonomous regulation of the heart using cardiomyography (according to Baevsky R.M.) following laser treatment. This was particularly noted during intense physical exercise post ILBI. Changes included activation of the autonomous cardiac regulation as already mentioned, and a decreased influence of the central nervous system on the regulation of cardiac activity. The cardiac rhythm was favorably influenced by increased parasympathetic and decreased sympathetic activity, confirmed by the index of vegetative equilibrium. The value of the humoral regulation of heart activity also increased.²²⁾

The author, demonstrated the use of IFLT (wavelength, 640 nm; course dose, – 0.9 J) in 27 patients with cardiac arrhythmia, with a follow-up of from 1 to 3 years. IFLT was combined with medical therapy. Clinical improvement was seen in 54 % of patients, with an average therapeutic latency of 1.4 months.¹²⁾

Autonomic Vascular Dystonia: Grigorash G.A. et al. (1990) used ILBI for patients with various postoperative complications and widespread sympathetic hypertension and tonus. They were able to demonstrate a return to self regulation with ILBI (power at the fiber, 1.4 mW, power density 0.8 mW/cm², 30 - 40 min/session giving a dose of approximately 14 – 19 J/cm²).²³⁾

ILBI for patients with increasing sympathetic-mediated tonus, as reported by Olesin A.I. and colleagues in 1995, resulted in a positive influence on the heart function and achieved centralization of cardiac rhythm control.²⁴⁾

The author applied Intravenous Frequency Laser Therapy (IFLT) (wavelength, 640 nm; course dose 0.8 - 0.9 J) in combination with medical therapy in 43 patients with autonomic vascular dystonia over a 1-3 yr period. Significant clinical effects were seen in 72% of the patients including reduction in headaches and dizziness, and normalization of blood pressure. The positive clinical effects lasted on average for 2.8 months.¹²⁾

Atherosclerosis: Patients with stenosing atherosclerosis of branches of the abdominal aorta and arteries of lower limbs were very successfully treated with ILBI by Savitskiy S.Y. and Popova L.I. in 1989. Treatment with ILBI resulted in stabilization of ischemia, improvement in the rheographic index (rheography is a cardiovascular functional test which gives a graphical record of the flow of blood) and appearance of the blood flow pulse. At the same time positive changes were registered on thermograms and capillaroscopy.²⁰⁾

The author in 1999 reported treatment of 156

patients (average age 61.2 yr, predominantly male) with Fontaine 2nd – 3rd degree peripheral atherosclerotic obliterans. The patients had 2nd degree regional ischemia. Limb ischemia had been present on average for 5.2 yr. (range, 5 - 30 yr). ILBI (633 nm; 15-30 min over 7-10 procedures; power 1.5 - 2 mW) was applied in combination with transcutaneous laser therapy (1264 nm; power, 2 mW). The application of this combination LLLT realized a good clinical effect in 84.3% of the patients. The use of LLLT saved the load-bearing function of the feet in most patients, improved patients' quality of life, reduced the incidence of physical inability and was associated with reduced social expenses.²⁵⁾

Obliterating Endarteritis, Thrombophlebitis and Trophic Ulcers:

Accerman G.L. *et al.* (1989) successfully applied ILBI with the HeNe laser in the treatment of obliterating endarteritis of the lower limbs. Simultaneous normalization of rheological blood and immunological indices was clearly seen.²⁶⁾ Bulavkin V.P. *et al.* (1992) treated 41 patients with obliterating endarteritis and its complications. There were 3 groups of patients. One group (n=21) underwent treatment with a combination of ILBI (630 nm, power at the fiber tip, 2.6 mW; 5-7 sessions) and hemosorbition (a form of dialysis popular in Russia employing specific absorbents to detoxify the blood); and one group each of 10 patients who underwent ILBI only and hemosorbition only. The best effects were observed in the combination group with positive effects (less pain, decreased inflammation, healing of ulcers seen in 19 of the 21 patients. Ten patients underwent minor surgery (finger amputation in 6 patients; amputation of planta in 1 patient and removal of necrotic tissue in 3 patients). Using ILBI on patients with trophic ulcers and thrombophlebitis demonstrated positive effects in reports from Kovkalo D.N. *et al.* (1990).²⁷⁾

Myocarditis: Sundukov *et al.* (1996) Used ILBI in combination treatment for early myocarditis associated with diphtheria. They reported positive results from this complementary therapeutic approach in the treatment of these patients.

DISEASES OF THE PULMONARY SYSTEM

Acute and Chronic Bronchitis: In a controlled study, Scheligina N.M. *et al.* (1989) used combination ILBI in the treatment of acute and chronic bronchitis. They achieved clinical remission in a shorter period and which lasted much longer in comparison with the control group.²⁸⁾

Bart B.Y. and colleagues reported in 1995 on the results of 5 years experience with ILBI (HeNe laser, 632.8 nm; power, 1 mW). The efficacy of ILBI treatment in 360 patients with chronic bronchitis and bronchial asthma was assessed. By the end of the course of treatments (5-7 sessions), 352 patients (97.8%) felt some improvement in expectoration with a decreased incidence of associated tussis.²⁹⁾

In a study on ILBI combined with transcutaneous laser blood irradiation, Ananchenko V.G. and colleagues (1999) compared the combined laser therapy with conventional treatment in a total of 59 chronic obstructive bronchitis (COB) patients (32 in the experimental group and 27 in the control group). In addition to the conventional examination methods and assessment of the treatment effect, cytological and bacteriological tests of bronchoalveolar lavage (BAL) precipitate smears were carried out. The treatment of COB with the combination laser therapy approach compared with the non-laser treated controls demonstrated a better anti-inflammatory action, promoted the normalization of mucociliary transport, activated phagocytosis and immune defense, cleared up the bronchial tree, reduced obstructions and effectively managed any exacerbated symptoms. Hospitalization was 4 days less in the laser treated group. The authors concluded that the combination of intravenous and transcutaneous blood irradiation had clear advantages in comparison with the conventional approach.¹⁹⁾

In 1999, the author reported on the treatment of 42 chronic bronchitis patients (a history of up to 10 years) with a combination of ILBI (632.8 nm transcutaneous laser therapy (890 nm) and drug therapy. A further 10 patients received only drug therapy (control group). In the combination therapy group, the efficacy of treatment was very good and remission of bouts of exacerbation of the symptoms of chronic bronchitis was extremely sturdy, lasting for a minimum of 3 months over a long follow-up period.^{30),31)}

Acute and Chronic Pneumonia: The first publications of the successful ILBI application in treating acute pneumonia came from Kavkalo D.N. *et al.* (1989)³⁾ and Scheligina N.M. and colleagues (1989).²⁸⁾ These groups applied ILBI in combination therapy for chronic pneumonia, and found that clinical remission of the disease was longer and more robust in comparison with the control groups. Clinical improvement was confirmed by normalization of the hemographic findings, the acute phase reaction indices and in respiratory functions. Following ILBI combination therapy, a statistically significant increase of both volumetric and

fast track indexes were registered compared with the controls.

Forty-nine patients with acute pneumonia received ILBI (630 nm) in combination with transcutaneous laser therapy (890 nm) and drug therapy in a 1999 study by the author and colleagues. A further 10 patients received only drug therapy (control group). The results showed that the period of convalescence for patients with acute pneumonia treated with the combination therapy was 4 to 6 days shorter than in the control group, and the treatment efficacy was maintained over a long follow up period.^{30),31)}

Bronchial Asthma: As stated above, Bart B.Y. et al. in 1995 published the results of their experience with 5 years of ILBI application (HeNe laser, 630 nm; power, 1 mW) for chronic bronchitis and bronchial asthma. By the end of the treatment course (5-7 sessions) more than 90% of the patients had much better respiratory function combined with decreased doses of corticosteroids prescribed for their bronchial asthma.²⁹⁾

In a 1995 study from Fedorova T.A. et al, 250 patients were treated with ILBI, (42% of whom had bronchial asthma and 58% had allergic reactions). The influence on the cytological factors of hemostasis, the increase of neutrophil phagocytic activity and higher numbers of T-lymphocytes were observed. This could be the result of the anti-inflammatory and detoxification effects of the treatment.³²⁾

Ostronosova S. and colleagues (2000) examined 532 bronchial asthmatic (BA) patients. Laser therapy (LT) was applied to 286 patients for the purpose of rehabilitation and the effectiveness of this treatment was evaluated. Efficacy was based on the dynamics of clinical and cytochemical parameters such as the levels in the peripheral blood of catecholamines (CC), serotonin (S) and histamine (H), lung function (LF) and bronchial reactivity. LT led to an improvement not only in the clinical parameters but also in LF. Bronchial hyper-reactivity decreased, initially reduced CC concentrations increased and initially increased levels of S and H levels were reduced. The best LT results were noticed both in mild and moderate atopic BA and in mild infectious-dependent BA.³³⁾

The author and colleagues in 1999 reported on 39 patients with chronic bronchial asthma who were treated with a combined regimen of ILBI (630 nm) transcutaneous laser therapy (890 nm) and drug therapy, while a further 10 patients received only drug therapy as the control group. Patients in the combination treatment group reported a decrease in the number of bronchospasms and the doses of bronchodilators and

glucocorticoids following the intravenous and transcutaneous LLLT. Their asthma remained in remission for 3 – 6 months, after which the patients required a 'top-up' session of LLLT. (10-year follow-up)^{30),31)}

Tuberculosis: Akhunov Sh.B. *et al.* (1995) treated 17 patients (22 patients in the control group) with destructive pulmonary tuberculosis along with conventional therapy being applied together with ILBI (wavelength, 630 nm; power density, 4-6 mW/cm²; treatment time, 10 min; 15 sessions in a day). The absence of bacteria in expectorate for up to 3 months was detected for 82.4 % patients in the ILBI group, compared with 73.6% in the control group. In conclusion, TB foci clearance lasted from 4 to 6 months in 62.3 % and 76.2 %, respectively, and 19.1 % and 65.3 %. Respectively, in the control group.³⁴⁾

DERMATOLOGICAL DISEASES

Atopic Dermatitis (AD): Prochorenkov V.I. et al. (1990) reported on the treatment of 25 patients with atopic dermatitis with ILBI (wavelength, 0.63 microns; power at the fiber tip, 12.3 mW; exposure time 30-40 min over 8-10 sessions). All the patients had positive therapeutic effects. In a 2002 study by Arakelyan H.S. 89 patients took part. The study period was from 6 months to 17 years. Ninety-seven percent of the patients had previously and sporadically taken different medications (H1 histamine inhibitors, oral and topical glucocorticoids, immunomodulators, etc.) to control their AD. In 11.5 % of patients such treatment had caused paradoxical effects, exacerbating the disease; for the rest of patients treatment had predominantly short term remission and a moderate positive clinical effect. Laser therapy combined with phytoceutical application had proved to be an effective method of AD treatment, and according to the preliminary results of Arakelyan's randomized open trial, the combination of external and ILBI with phytoceutical application was the most effective mode of trialed integrative therapy.

Psoriasis: (1992) Forty-two patients with psoriasis (age 19-64 years, prolongation of disease from 6 month to 52 years) were treated in a 1992 study reported by Shakmatov D.A. and Rakcheev A.P. ILBI was used with a HeNe laser (output power, 2 - 8 mW; exposure time, 15-60 min.). After 3-5 sessions, alleviation of joint pain was obtained. Dermatitis was seen to decrease by 23-26 days, and remained stable for 7-10 days.³⁵⁾

Herpes: The author applied diode laser ILBI (wavelength, 640 nm., course dose 0.9 J) in 38 patients with

herpes over a 1 – 5 year period. A positive clinical effect was observed in 32 of the 38 patients.¹²⁾

Neurodermatitis: Forty-nine patients with neurodermatitis were treated by the author with follow-up over a 1 – 5 year period. Laser therapy using ILBI (wavelength, 640 nm; course dose – 0.9 J) was combined with transcutaneous laser therapy (630 nm). In 36 out of the 49 patients, a positive clinical effect was observed.¹²⁾

Eczema: The author treated 23 patients with eczema with a follow-up period of 1-3 years using a combination of ILBI (640nm) and laser therapy (630 nm) immunomodulation therapy with an IR diode laser (890 nm) and medical treatments. Positive clinical effects were observed in 67 % of the patients treated.¹²⁾

Allergodermatosis: Fifty-two allergodermatosis patients were treated by the author with a 1-5 year follow-up. Combination laser therapy with ILBI (630 nm) and transcutaneous laser therapy (890 nm) was applied, with a being achieved in 34 patients.¹²⁾

DISEASES OF THE ENDOCRINE SYSTEM

Diabetes: Donich R.M. *et al.* (1989) applied ILBI to patients with diabetes mellitus: the general state of the patients health improved, pain in the low limbs disappeared and pain in the heart area weakened.²²⁾

Mikhailov V.A., Proshanova A.I. In 1999, in a prospective double-blind study, the author and colleague evaluated the effect of LLLT on clinical characteristics and biochemical findings over a treatment period of about 2 years. One hundred and eighty-seven patients from 50 to 75 years old with non insulin-dependent diabetes mellitus (NIDDM) were included in this study. All patients had been suffering from micro- and macro vascular disorders of the lower limbs for more than 2 years. One hundred and seventy-six patients with microvascular disorders (formed group 1, treated with ILBI at 630 nm.) Eleven overweight patients of more than 130% in comparison with normal weight and macrovascular complications formed group 2 and were treated with transcutaneous laser therapy (890 nm; frequency, 1000 Hz) and with visible red diode irradiation (640 nm; output power, 60 mW). 4 patients of the 1st group avoided major amputation. Only limited minor surgery for planta was used in these cases. Furthermore, after repeated courses of therapy the period of remission and the period or repeat treatment was established.³⁶⁾

The author used Intravenous Frequency Laser Therapy (IFLT) (wavelength, 640 nm; dose, 0.9 -1.2 J) for 21 patients with NIDDM and 9 patients with insulin dependent diabetes mellitus (IDDM). In 17 of the 21 NIDDM patients, positive dynamics were observed post-treatment: decrease in macro- and microvascular disorders, stabilization of blood sugar level and a decreased drugs dosage. In 5 of the 9 IDDM patients, positive dynamics were also observed: including stabilization of the daily blood sugar level. In 2 patients, diabetic drugs were able to be substituted for insulin.¹²⁾

Kovalyova T.V. *et al.* (2001) observed 205 patients with NIDDM and 54 with IDDM over 2 years in the outpatient department. The lipid normalizing effect of combination laser therapy was used together with antioxidant therapy (about 600 mg a day). They repeated the treatment course within 9 months. The repeated courses were given in 3 and 6 months. Each course consisted of 8-10 ILBI sessions with a visible red laser (630 nm; output power at the fiber tip, 2 mW; exposure time, 15-30 min). Simultaneously, a percutaneous procedure with near-IR LLLT (890 nm; output power at the fiber tip, 5 - 20 mW) was performed in combination with magnetic nozzles on the gastrocnemius muscle, liver, pancreas, and spleen projections (frequency, 150 Hz; exposure time, 4 min per zone). Combined laser therapy is believed to help decrease the intake of hypolipidemic and lipotropic agents, and following this approach a prolonged effect in respect to the most important, pathogenetically significant deviations of the lipid metabolism were observed: namely a significant increase in the level of HDL-c in the post-treatment follow-up, which lasted for up to 6-10 months, and a concomitant decrease in LDL-c levels. Simultaneously a significant decrease in total cholesterol was noted and triglycerides were either normal or within the upper normal limits. The LDL/HDL-c ratio was reduced by two-fold.³⁷⁾

DISEASES OF THE LOCOMOTIVE SYSTEM

Rheumatoid Arthritis: Alikhanov B.A. *et al.* in 1992 studied 90 patients with rheumatoid arthritis who were divided into 3 groups. The 1st group consisted of 20 patients who received chlorbutol (dose 10-15 mg. a day). The 2nd group (n=40) received a combinations of chlorbutol and ILBI (wavelength, 632.8 nm; power, 1 mW/cm²; exposure time, 20 min.). The 3rd group (n=30) received only ILBI at the above parameters. In 3-6 months, 12 of the 20 patients in group 1 developed hematological complications compared with group 2, where hematological complications were seen in only

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3 of the 40 patients. In group 3, a positive effect was found only in sero-negative patients.³⁴⁾

Chronic Arthritis: In an 80 patient study, the author assigned patients to 4 groups: In group 1, ILBI was applied in 20 patients (wavelength, 630 nm; dose, 0.9 J.); in group 2, IFLT was applied in 20 patients (wavelength, 640 nm; dose, 0.9 J.) a combination of IFLT with percutaneous near IR LLLT (890 nm) was used in group 3 (n=20); and for group 4, only percutaneous near IR LLLT (890 nm) was applied in 20 patients. The greatest efficacy was seen in group 3 who received combined laser therapy (IFLT + LLLT), with significantly decreased pain syndrome and improved joint activity and mobility. The effect after treatment lasted for an average of 2.7 months.¹²⁾

Osteochondrosis: IFLT (wavelength, 640 nm, dose, 0.9 J.) was applied in 21 patients with osteochondrosis during the aggravation period. The treatment was effective, with an average latency period of 4.7 months.¹²⁾

Osteomyelitis: Shkrob L.O. et al. (1995) studied the efficacy of ILBI in 152 patients with chronic hematogenous and 53 with posttraumatic osteomyelitis. The improvement in immunological parameters was marked, which allowed surgical intervention with reduced postoperative complications.³⁸⁾

DISEASES OF URINOGENITAL SYSTEM ORGANS

Benign Prostatic Hyperplasia (BPH): In a study published in 2000, Neimark A.I. and Muzalevskaya N.I. administered LLLT in the form of ILBI, or transrectal and transurethral prostatic irradiation, or a combination of the two approaches as preoperative preparation and correction of immunity disturbances for patients with benign prostatic hyperplasia (BPH). The response to the treatment was evaluated by positive changes in immune status and bacterial contamination of the urine and prostatic tissue. Conventional preoperative preparation (such as antiseptics, antibiotics and phytotherapy) usually fails to correct the signs of T-cell immunodeficiency, depression of phagocyte activity of neutrophils and to achieve a significant reduction in bacteriuria. Laser therapy in the form of intravenous laser blood irradiation, has a positive immunomodulatory effect on cellular immunity. It firstly normalizes the proportion of T-helpers at first and secondly acts on T-suppressors and neutrophil phagocytosis. The antibacterial effect of this technique on the urinary microflora

and prostatic tissue is not very high. Local laser therapy is a potent immunoactivator for T- and B-lymphocytes, it increases the proportional index of immunoregulatory cells, and activates neutrophil phagocytosis. It also has an antibacterial effect against gram-negative urinary microflora and the prostate tissue. The combined laser therapy approach produced the highest immunomodulating action for T-lymphocytes and immunoactivation of B-lymphocytes, potentiated the phagocytic ability of neutrophils, elevated the index of immunoregulatory cells, but was unable to correct their imbalance completely. The highest antibacterial effects were also noted with combined laser therapy, including the bacterial group *Proteus-Providencia*. Preoperative low-intensity laser therapy for BPH reduced the number of postoperative pyoinflammatory complications, hospital stay and severity of the postoperative period.³⁹⁾

Acute and Chronic Adenitis: The author studied 59 patients with acute and chronic adenitis. (follow-up period 1-7 years). Thirty-nine patients were treated with combined laser therapy (ILBI combined with transcutaneous 890 nm laser therapy) and medicinal therapy. A group of 20 patients were treated with only medicinal therapy as controls. The period of recovery of patients with acute adenitis was 3 to 4 days less than in the control group. Patients with chronic adenitis had a much shorter period of treatment (4-5 days less) in comparison with the control group.¹²⁾

Acute Pyelonephritis: The author has treated 18 patients with acute pyelonephritis (follow-up period 1-7 years). Laser therapy (ILBI) was used (630 nm) along with transcutaneous laser therapy (890 nm) and medicinal therapy. Some reduction of inflammation-related heat was achieved in 4-5 days, reduction of the painful symptoms (lumbar area) in 3-4 days. Normalization of the blood chemistry was marked in 5-6 days. In the control group, which was treated with medicines only, these parameters improved in 6-8 days.¹²⁾

Chronic Prostatitis: Thirty-one patients (follow-up period 1-7 years) were treated by the author. Laser therapy (ILBI, 630 nm) was used in combination with transcutaneous laser therapy (890 nm) and medicinal therapy. The reduction of the pain was observed after 3 to 4 sessions.¹²⁾

Impotence: The author has treated 34 male patients with impotence (follow-up period 1-7 years). Laser therapy (ILBI, 630 nm) was used along with transcuta-

neous laser therapy (890 nm 0.89 microns.), kryolaser massage and medicinal therapy. The improvement of erectile functions was observed in 24 of the 34 patients.¹²⁾

Adenoma of the Prostate: Seventy-three patients (follow-up period 1-7 years) were treated in a study by the author. Laser therapy (ILBI, 630 nm) was combined with transcutaneous laser therapy (890 nm) and medicinal therapy. The frequency of nocturia decreased from 5 to 8 times to 3 to 4 times a night in 50 of the 73 patients (68%). The period of remission lasted from 3 to 6 months, then the patients repeated the course of treatment.¹²⁾

Renal Problems: In 1995, Sernjak R.S. *et al.* treated 32 patients with purulent - septic complications and hemodialysis problems after kidney allotransplantation. They were divided into two groups: group 1, treated with haemodialysis, hemosorption, plasmapheresis and endolymphatic introduction of antibiotics; and group 2 who were treated similarly to group 1, but with the addition of intravenous arterial blood irradiation with HeNe laser energy (632.8 nm, power density at the end of the fiber, 1.5-2 mW/cm²; irradiation time - 50-90 min). In group 2 the levels of urea, creatinine, bilirubin, fibrinogen, thrombokinase B2 and so on. B2, sex hormones and other factors all decreased and a significantly greater bacteriocidal effect was recorded together with an increased regenerative process.⁴⁰⁾

Lebedkov E.V. *et al.* (1995) treated 24 patients with terminal renal failure. Twelve patients underwent hemodialysis in the control group, compared with another 12 patients who additionally received ILBI (wavelength, 630 nm; output power, 1 mW; treatment course, 10 sessions over 4 weeks, repeated twice in 1 year) to treat cardio-vascular and other system complications. The patients in group 2 who received ILBI experienced complications more seldom than the control group patients; their high blood pressure decreased due to a parasympathetic-mediated decrease of their general peripheral resistance and increased cardiac output; and the level of triglycerides, pre-beta lipoproteins, and cholesterol significantly decreased. Finally, the frequency of hospitalization decreased by 1.8-fold in the ILBI group in comparison with the control group.⁴¹⁾

NEUROLOGIC DISEASES

Encephalopathy: Fedin A.I. *et al.* (1991) showed that ILBI has positive influence on the brain functional condition and the general emotion of patients with athero-

sclerotic dysfunctional circulatory encephalopathy. In a 2000 study, Gonchar-Zaykin A.P. and colleagues reported on the efficacy of ILBI (630 nm; exposure time, 60 min over 3-6 sessions) for 29 patients with stage I – III encephalopathy (group 1) compared with 34 patients who were not treated with ILBI as controls (group 2). The longest interval between ILBI sessions was 3 months, and ILBI was recommended for those patients in whom the efficiency of pharmaceuticals was low. As the result of ILBI treatment all the patients began to feel much better, their physical and psycho-emotional activity increased, and their complaint regarding headaches, vertigo, nausea and tinnitus became considerably less. In group 1 the arterial pressure at stage I significantly ($P < 0.05$) decreased by 60%, at stage II, 49 %, and at stage III, 20%. The rheoencephalographic index improved: at stage I it was 90%, at stage II, 56% and at stage III, 10%; the rheography index increased from 0.5 to 1.3 Ω ; asymmetrical pulse filling decreased, especially for the patients with dysfunctional circulatory encephalopathy (DE) stages I and II; vessels tonus normalized; and the venous outflow improved considerably. In addition, the extent of neurological symptoms such as oral automatism, muscle hypertonus, and autonomic-regulated vascular dysfunction decreased. The health of the group 2 patients also improved with a rheoencephalographic index in stage I patients of 60% and in stages II and III of 33%. From the results of this study, ILBI was shown to increase the functional condition of the central nervous system of DE patients, and to reduce the resistance of an organism to pharmacotherapy. The greatest effect for ILBI was observed in patients with stage I and II DE.⁴²⁾

Schizophrenia: Kutko I.I. *et al.* (1996) used the ILBI method for 62 patients with both simple and paranoic schizophrenia. Almost all the patients were prescribed neuroleptics at different doses according to their own regimen, and this was not subjected to any considerable changes during the period preceding, during and following ILBI treatment. The only condition for inclusion of schizophrenic patients in the ILBI treatment subjects was the absence of psychomotor excitation.⁴³⁾

Nineteen schizophrenic patients treated with typical 5h neuroleptics were studied in a report from Saikin M.A. *et al.* (2001). All of them demonstrated extrapyramidal symptoms (EPS), resistant to trihexifenidil treatment. ILBI was performed every day (630 nm; output power at the fiber tip, 8 mW; treatment time, 15 min per session; 8-12 sessions per treatment course,) Neuroleptic therapy and trihexifenidil treatment were

unchanged throughout the treatment period. The overall efficacy of ILBI was 79% (with a 50% reduction in the Simpson-Angus score). The ILBI treated subjects were characterized by the prevalence of akinesia against a background of rigidity symptoms before treatment. The symptoms of akinesia and tremor showed a slight reduction after ILBI, and bouts of clinical depression and cognitive disturbances were significantly reduced concomitantly with a reduction in EPS.⁴⁴⁾

Muzychenko A.P. *et al.* (2001) applied ILBI in 21 psycho – pharmacotherapy-resistant patients with paroxysmal schizophrenia. A reduction in depressive disorders was recorded during 2-3 weeks.⁴⁵⁾ In a 2001 study from Mosolov N.S. and colleagues 43 schizophrenic patients were included, split into two groups: group 1 (n=22) with prevalence positive schizophrenia; and group 2 with prevalence negative symptoms. ILBI was performed daily (wavelength, 630 nm; output power at the fiber tip, 8 mW; 15 min/session over 8-12 sessions) ILBI achieved an overall efficacy of 55.8% (with a 25% reduction in the PANSS score). Treatment was scored at 59.8% in group 1 and 52.4% in group 2 patients. In group 1 patients a distinct reduction in psychotic symptoms was observed and recorded. Patients from the 2nd group expressed marked psychostimulatory action.

Multiple Sclerosis: Mikhailov V.A., the author has been using IFLT (wavelength, 640 nm; dose, 0.9- 1.6 J) for 6 patients with the cerebrospinal form of multiple sclerosis. (follow-up period 1-7 years). Disease remission lasted 2.9 months on average, in comparison with 10 patients who had ILBI where the effect lasted for 2.1 months.¹²⁾

Parkinsonism: Nine patients with parkinsonism (follow-up period 1-6 years) have been treated by the author, 6 with a combination of laser therapy (IFLT), kryolaser massage, transcutaneous laser therapy (890 nm), massage of the head and medicinal therapy, the remaining 3 patients receiving ILBI instead of IFLT. Reduction of tremor, reduction of unsteadiness of gait and improvement of the general state of health were achieved in all patients. The period of remission of the patients who received ILBI was on average-2.1 months, compared with 3.4 months for the IFLT patients.¹²⁾

Severe Alcohol Intoxication-Related Coma: Idrisova L.T. and colleagues presented clinical data in an article published in 2000 on the therapeutic effects of intravenous laser blood irradiation (ILBI) in severe alcohol intoxication complicated by alcohol-induced

coma. ILBI effectiveness was assessed by EEG changes within the 3 post-comatose days. Changes in brain biopotentials in various post comatose periods were unidirectional. Positive results were achieved after low-intensity laser radiation.⁴⁶⁾

DISEASES OF GASTROINTESTINAL TRACT:

Stomach and Duodenal Ulcers: In articles published in 1989 and 1990, Yepishin N.M. and colleagues reported on 40 patients with stomach and duodenal ulcers who were treated with a semiconductor laser in transcutaneous therapy, and the HeNe laser in ILBI. Thirty-one of the 40 patients showed complete healing of their ulcers, with a marked decrease in ulcer size in the others. Semiconductor irradiation was more effective for stomach ulcers but in the case of duodenal ulcers ILBI appeared more effective (2 years was the follow up period).^{47),48)}

Acute Surgical Pathology of the Stomach: Recently ILBI has begun to be applied widely for complex treatment and to preventive measures in cases of purulent - septic complications in surgical practice (Sychev P.S., 1986⁸⁾; Maslova M.G. *et al.*, 1989⁴⁹⁾; Lisienko V.M. *et al.*, 1990)⁵⁰⁾, in a combination of medical measures in cases of peritonitis (Voronina V.A., 1985).⁷⁾ ILBI was successfully applied to decrease the degree of hypoxia in tissues, to correct nonspecific organism resistance and to increase the efficiency of detoxification and bacteriocidal therapy in treating purulent - septic post-surgical complications Zemskov B.S. *et al.*, 1984⁴⁾; Guscha A.L. *et al.*, 1988).⁶⁾ Patients with pancreatonecrosis registered decreased levels of lactate dehydrogenase, gamma-glutamine transferase and alpha-amylases just after the third session of HeNe ILBI (output power, 1.4 - 2 mW; power density, 0.8 mW/cm², treatment time, 30 min). Patients with hemorrhagic pancreatonecrosis showed the following decreased levels: 1.7-fold in blood trypsin; 2.4-fold in lipase; 1.8-fold in alkaline phosphatase and alanine aminotransferase; 1.7-fold in asparagine transferase; and 1.4 in sorbitol dehydrogenase. Concomitantly with an increase in antioxidant enzymes (glutathione peroxidase and reductase in erythrocytes and plasma, superoxide dismutase, transferrin and ceruloplasmin) the level of diene conjugates, hydroperoxide and malonic dialdehyde decreased. Simultaneously an increase in the potential energy of erythrocytes was detected as measured by their increased DNA contents and electrophoretic mobility of glucose-6-phosphatase (Dedenko I.K., 1989).⁵¹⁾

Galtchenko L.I. and co-workers (1995) studied 70

patients with acute cholecystitis who were treated with ILBI (wavelength, 630 nm; power output at the fiber tip, 2-3 mW; treatment time - 60 min over 5-7 sessions) and [D-Ala2, Leu5]-enkephalyl-Arg (Dalargin, 2 mg i.m.). The control group (n=70) were treated with only Dalargin. Improvement in liver function, reduction of sex hormones and the activation of antioxidant and enzymatic systems were marked in the ILBI group compared with the control. ⁵²⁾

Nineteen patients with acute peritonitis (11 patients with local peritonitis and 8 with total peritonitis) were treated with ILBI in a study by Korabojev U.M. et al. in 1995. The ILBI parameters were as follows: wavelength, 630 nm; output power at fiberoptic tip, 8-10 mW; treatment time 60 min per session per day over 5 to 7 sessions; target vessel, the cubital vein). The application of ILBI was seen to increase the metabolic and immune processes. ⁵³⁾

Martino A.A. and Pavlenko V.V. (1995) treated 34 patients with acute pancreatitis with ILBI. After 2 to 3 sessions, the pain symptoms decreased; a decrease was seen in diastase and amylase levels; and a reduction in blood toxicity and pancreatic edema. ⁵⁴⁾

In a study published in 1995, Rakimov R.S. and colleagues assessed the results of the use of ILBI in combined treatment of 46 children (ages-1-15 years) with widespread peritonitis. The results demonstrated that ILBI produced positive clinical laboratory dynamics as well as a faster healing process than normal with a reduction in postoperative scarring. In addition, the number of hospital days was reduced by 5-7 days. ⁵⁵⁾

Acute and Chronic Hepatitis: Makashova V.V. (2002) applied ILBI in combined treatment for patients with acute viral hepatitis. The study results showed that ILBI promoted earlier disappearance of blood toxicities and cholestasia, faster decrease in aminotransferase activity, transmembrane enzyme of gamma-glutamine aminotransferase, and the bilirubin levels; ILBI decreased disturbances in the peroxide-radical oxidant and antioxidant systems; it decreased free-radical oxidation, and increased the quantity of SD4 and SD8; ILBI normalized the contents of circulatory immune complexes and redressed low neutrophil functional activity; in addition. ILBI stimulated stabilization of cellular membranes, and improved the functional state of various cells (hepatocytes, thrombocytes, T- and B - lymphocytes, neutrophils), thereby starting a cascade of secondary biochemical and physiological reactions that led to hepatoprotective and immunomodulating effects, thus reducing the duration of infusion therapy and hospital stay. ⁹⁾

OPHTHALMOLOGY

Bakshinsky P.P. and colleagues (1995) used LLLT in 82 patients with severe posttraumatic uveitis (eye inflammation) who could not be treated with traditional anti-inflammatory therapy. Patients were divided into 3 groups: group 1 received treatment with an infrared semiconductor pulsed laser, group 2 received intravenous exposure of blood to HeNe laser and group 3 received both treatments. The treatment efficiency was monitored by measuring levels of lipid peroxides and superoxide dismutase in the lachrymal fluid. Treatment proved to be effective. Best results were attained in group 3, *i.e.*, by applying both treatment methods, as shown by the earlier normalization of levels of lipid peroxidation products and superoxide dismutase activity compared with groups 1 and 2. ⁵⁶⁾

An analysis of the clinical efficacy of ILBI in 45 patients (total of 79 eyes) was carried out in a study by Evgrafov V.Y. (2000). The ILBI course was started 3 to 5 days after pan retinal laser or cryocoagulation. ILBI caused a significant increase in the photosensitivity of the fovea (from 26.7 ± 0.8 up to 29.5 ± 0.4 Db) and decreased the total photosensitivity deficit (from 245 ± 34 to 204 ± 89 Db). Value indexes significantly exceeded the initial level. After the ILBI treatment the contents of antithrombin III in the blood plasma increased from an average of 58% (range, 44-67%) up to 87% (range, 63-95%) for the median and quarter intervals; the contents of fibrinogen rose from an average of 5.9 mg/ml (range, 4.9-7.0 mg/ml) up to 4.2 mg/mls (range, 2.2-5.5 mg/ml at the median and quarter intervals). The use of ILBI demonstrated a considerable improvement in all studied parameters, and the beneficial effect was retained for 1 to 4 months after the treatment course.

OTOLARYNGOLOGY

Paltchun V.T. *et al.* (1996) ⁵⁷⁾ used ILBI for treating neurosensory ear problems and Meniere's disease. The results obtained showed that after a course of ILBI patients with neurosensory ear disturbance noticed a decrease in their tinnitus symptoms, with hearing improvement of from 5-20 Db. The same effect was not observed after ILBI. Patients with Meniere's disease reported decreased severity of their tinnitus symptoms after ILBI and they completely disappeared when head turning was carried out. The same results were obtained in a report by Patiakina O.K. and Scheremet A.C. (1997), who observed positive effects after ILBI lasting for 5 to 6 months. ⁵⁸⁾

CONCLUSIONS

1. The application of ILBI in the treatment of various diseases improved rheological properties of blood, stimulated blood cells, and enhanced the metabolic processes in tissues including the improvement of cellular and humoral immunity.
2. The overall efficacy of ILBI was very high, resulting in a reduced period of treatment as well as an increase in the duration of remission.

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