ORIGINAL RESEARCH PAPER
Volume-9 | Issue-5 | May-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

INTRAVENOUS C BAND ULTRAVIOLET LIGHT THERAPY (IVUVLT) AS A TREATMENT FOR BACTERIAL AND VIRAL INFECTIONS INCLUDING COVID 19

Medicine

Sagar Jawale*
Jawale Institute of Pediatric Surgery,VigyanYog Foundation,Jalgaon, Maharashtra, India
*Corresponding Author

ABSTRACT

Introduction: Antibiotic resistance developed by micro-organisms is getting scary day by day and WHO estimates that drug-resistant diseases could cause 10 million deaths each year by 2050 and loss of up to 100 trillion USD to the whole world. To solve this problem, I started my own research to find a solution to this upcoming disaster. I have invented a new therapy called Intravenous Ultraviolet Light Therapy (IVUVLT) which is likely to be effective in variety of bacterial and viral infections including covid19.

Materials and Methods: Intravenous Ultraviolet Light Therapy (IVUVLT) illuminates ultraviolet light of 254 nm wavelength into a peripheral vein with a fiber optical device. The device is made up of a 3-watt ultraviolet light bulb of quartz material. A PMMA (Poly methyl methacrylate) fiber carries UV light of 254 nm wavelength and delivers it through an angiocath to the patient's blood in a peripheral vein.

Discussion: The UV light of 254 nm wavelengthkills all bacteria, viruses, fungi and molds in 60 seconds. PMMA material is non-reactive to blood and already FDA approved for use inside human body. The device for IVUVLT is commercialized for a reasonable cost of Rs. 15,000. The probe of the device is reusable, detachable and sterilized by ETO gas or by putting in Formalin chamber for 30 minutes. IVUVLT and its device are reported for the first time in medical literature.

UV light of 254 nm wavelength is a non- ionizing radiation and proved to be safe in many studies done on human body. The blood cells are exposed to UV light only for few seconds and the progenitors in bone marrow are not exposed keeping them safe.Ultraviolet Blood Irradiation (UBI) is a procedure that exposes the blood to UV light to heighten the body's immune response and to kill infections. It is similar to IVUVLT in many ways and has shown positive effects on RBCS, neutrophils, lymphocytes, on phagocytosis and on redox status.The light of 254 NM splits the 2% dissolved Oxygen in the blood and converts it into molecular Ozone O3. Ozone is a non-toxic gas and kills all micro-organisms like bacteria, fungi, viruses and molds in just 60 seconds. It is effective in little concentration as 0.04 ppm and human toxicity starts at 3 ppm indicating a huge safety limit. Ozone is a strong modulator of immune system. Inside the blood, it creates a mild oxidative stress which makes the immune system produce a large quantity of Interferons, agents that attack micro-organisms and kills them. No resistance is reported toOzone and UV light making them a never-failing solution to micro- organisms. There are numerous studies in the medical literature which show that the UV light kills bacteria and viruses in the animal studies as well as studies done on human body.

IVUVLT is going to be effective against vast number of viral infections such as HIV- AIDS, COVID 19, Swine flu, Dengue fever, Japanese encephalitis, Rabies, viral diarrheas, rabies etc. which kill millions of people yearly worldwide. It will also be effective against bacterial septicemia, tetanus, meningitis, Diphtheria and against Methicillin-resistant Staphylococcus aureus (MRSA) etc. It will also be effective against systemic fungal infections and molds. The therapy will work against unknown organisms leading to pyrexia of unknown origin (PUO). I do not claim to know everything about IVUVLT. A lot of research and numerous clinical trials will be necessary to know about its exact mechanism of action, dosages and indications. This is only the beginning of this kind of research.

Conclusions: IVUVLT is a potentially safe, cheap and effective therapy for septicemia secondary to vast majority of viral and bacterial infections including Covid19. We need more research and a greater number of patients to know more about it. The therapy has a potential to save many patients worldwide from variety of infections. The therapy can be used as an immediate measure in epidemics and pandemics for new infections with unknown micro-organisms even before a specific vaccine and treatment is developed.

KEYWORDS

Ultraviolet C band Ultraviolet Light Therapy (IVUVLT), Ultraviolet blood irradiation, Antibiotic resistance, Therapy for antibiotic resistance, Therapy for Covid 19 infection.

INTRODUCTION:

Antibiotic resistance developed by micro-organisms is getting scary day by day. WHO estimates that if no action is taken, then drug-resistant diseases could cause 10 million deaths each year by 2050 and damage to the economy as catastrophic as the 2008-2009 global financial crisis.[1]By 2030, antimicrobial resistance could force up to 24 million people into extreme poverty.

Initial research, looking only at part of the impact of antibiotic resistance, shows that a continued rise in resistance by 2050 would lead to 10 million people dying every year and a reduction of 2% to 3.5% in Gross Domestic Product (GDP). It would cost the world up to 100 trillion USD. [2,3] To solve this problem, I started my own research to find a solution to this upcoming disaster. I started experiments to find an alternative to antibiotics and antiviral agents so that such a therapy can be applied as adjuvant or an alternative to the antibiotics and antivirals, totally replacing them. The micro-organisms develop resistance to drugs very fast. Before the first birthday of an antibiotic or antiviral drug, the micro- organisms have already developed resistance making them partially or totally worthless.

Bacteria may Demonstrate any of the five general mechanisms of antibiotic Resistance. Lack of entry; Decreased cell permeability, Greater exit; Active efflux, enzymatic inactivation of the antibiotic, altered target; modification of drug receptor site, synthesis of resistant metabolic pathway,etc.[4] Antiviral drug resistance is mediated most often by mutations in the molecular targets of drug therapy, and the development of drug resistance is the most compelling evidence that an antiviral drug acts specifically by inhibiting the virus rather than its cellular host.[5]

That is the reason we have to have entirely fresh and unbiased view towards the problem so that the new therapy does not have the above drawbacks.Numerous agents successfully kill micro- organisms in vitro in a petri dish such as alcohol, iodine, formalin, heat etc. But they are too toxic to be used inside the human body for killing micro-organisms.

I have invented a new therapy called Intravenous Ultraviolet Light Therapy (IVUVLT) which is reported for the first time in medical literature. Since the vast number of studies and clinical trials will take a lot of time, I am writing the theoretical aspect of IVUVLT in this article.

MATERIALS AND METHODS:

Intravenous Ultraviolet Light Therapy (IVUVLT)illuminates ultraviolet light of 254 nm wavelength into a vein with fiber optical device. The complete specifications of the Device for Intravenous Ultra Violet Light Therapy (IVUVLT) are as follows: The device is made up of a 3-watt ultraviolet light bulb(Figure 1) (1)made up of quartz material. It is filled up with a low- pressure mercury vapor and inert noble gas called Argon. The tube produces UV light when an electric current pass between two electrodes called cathodes.(Figure 2) (2) The electric current excites mercury vapor in the tube, generating radiant energy, primarily in ultraviolet range of 254 NM. Since light produced is cold in nature, it is also known as cold cathode. The power of bulb is 3 Watt. The length of the bulb is 40mm and diameter of 15 mm. This bulb is powered by a 3 -watt driver. The bulb and a cooling fan are fitted in a metal box. The metal box has a female metal connector. (Figure 1) (3) On the side of the bulb, this metal connector has a biconvex lens of 10 mm focal length. (Figure 2) (5) To this female

metal connector, a male FC connector is attached. (Figure 1) (5) It is detachable in nature. The male metal ferrule has PMMA (Polymethyl methacrylate) fiber of 1 meter in length fixed into it.(Figure 1) (4) The PMMA fiber is covered by a polylecithin black colored sleeve to avoid loss of light. The distal 2 inches of the PMMA fiber are bare without this sleeve which enters through an angiocath (Figure 1) (7) into patient's body. The lens of 10 mm focal length concentrates UV light of 254 nm wavelength on the tip of the PMMA fiber fixed into the ferrule. The PMMA fiber travels light from the bulb till the opposite end of the fiber. This opposite end of the fiber is 1 cm longer than the angiocath and goes through the angiocath (Figure 1) (8) into a peripheral vein of the patient, thus illuminating blood in that vein. The PMMA fiber used is of front and side illuminating type so that maximum illumination occurs in the vein. The probes for INUVLT comes in 3 different sizes. Neonatal, pediatric and adult. The neonatal size has PMMA fiber of 0.25 mm diameter which goes through no. 24 angiocath. The pediatric size has PMMA fiber of 0.5 mm diameter that goes through no. 22 angiocath. The adult size has PMMA fiber of 1 mm diameter that goes through no. 16 angiocath.

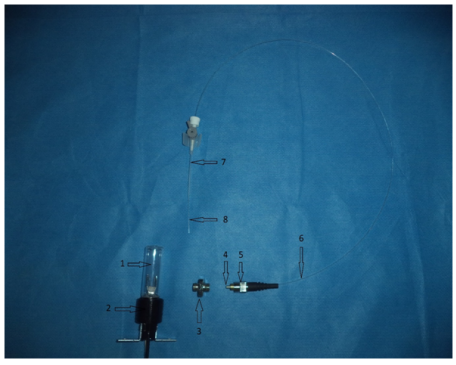

Figure 1: Showing complete assembly of the device for IVUVLT

1)3- watt quartz UV bulb 2) Bulb holder 3) Female FC connector 4) PMMA - fiber at tip of the ferrule 5) Male FC connector 6) PMMA fiber 7) No. 18 angiocath 8) PMMA fiber coming out of the angiocath

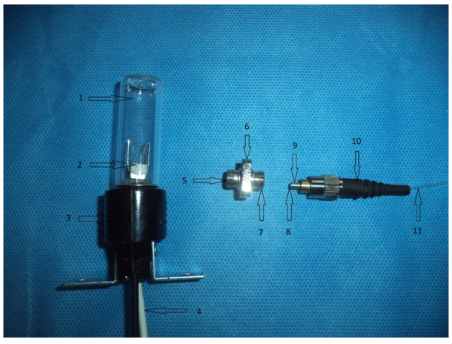

Figure 2: Showing details of the assembly of IVUVLT device

1)3- watt quartz UV bulb 2) Filament 3) Bulb holder 4) Electric wires 5) Lens 6)Female FC connector 7) Threads for male FC connector 8) PMMA - fiber at tip of the ferrule 9) Ferrule of FC connector 10) Male FC connector 11) PMMA fiber

Theprocedure for using the device on the patient is as follows. The probe made up of PMMA fiber is sent for sterilization by Ethylene Oxide gas or kept in Formalin chamber for 30 minutes before use. A peripheral vein of large size and relatively straight course is selected for the therapy. The site is prepared by applying spirit. An angiocath of appropriate size is selected and introduced into the vein. The stylet is removed and the PMMA fiber now put into the vein. The proximal part of the fiber with ferrule is fixed into the female connector on the box and the device switched on. Now, the UV light starts illuminating the blood into the vein. Alternatively, the PMMA fiber can be put into a vein for 6 inches by performing Saphenous vein or Cephalic vein cut down procedure. The probe here is slightly different than described above. It has 6 inches area bare distally to illuminate the vein. Therapy time is 3 hours.

DISCUSSION:

I wanted an energy which kills mico-organisms efficiently and still does not produce any significant damage to the human body. I also wanted my new energy to be free of antibiotic resistance.In my research, I found 2 such energies which are part of the nature and having above qualities. One is sunlight and another is Ozone gas.

Since time immemorial, sunlight is killing micro-organisms and saving us from them.[6]The sunlight is 10 % ultraviolet by volume which has antimicrobial activity. Out of total sunlight, only 1% sunlight is C band ultraviolet which as maximum antimicrobial activity with wavelength of 100–280nm. Maximum antibacterial and antiviral activity of C band ultraviolet light was found in the wavelength of 254 nm.[7] Hence it is used in my device to kill micro-organisms.Ultraviolet (UV-C) light kills or inactivates microorganisms by destroying nucleic acids and disrupting their DNA, leaving them unable to perform vital cellular functions.Wavelengths between about 200 nm and 300 nm are strongly absorbed by nucleic acids. The absorbed energy can result in defects in pyrimidine dimers. These dimers can prevent replication or can prevent the expression of necessary proteins, resulting in the death or inactivation of the organism. My device uses a low-pressure mercury lamp that effectively generate UV radiation at 254nm wavelength. Even today ultraviolet in sunlight kills micro-organisms as efficiently as before. Viruses like HIV die within 8 seconds of exposure to ordinary sunlight. Micro-organisms and sunlight both are present since millions of years. Still micro-organisms could not develop resistance to the ultraviolet light.The 1903 Nobel Prize for Medicine was awarded to Niels Finsen for his use of UV against lupus vulgaris, tuberculosis of the skin.

For more than 100 years now, billions of people are drinking water treated by C band ultraviolet light. In UV water purifiers, the water moves through a transparent glass tube with a speed of 100ml per minute. Around this glass tube an ultraviolet tube light with 254 NM ,20 Watt is placed. As water is exposed to UV light 99.99% micro-organisms are killed. [8] Dosages of UV light for a 99.99 % killing of most bacteria and viruses range from 2,000 to 8,000 µW·s/cm

The ultraviolet light of 254 nm wavelength is invisible light and does not pass through ordinary glass. Hence, the bulb used in the device is made up of special quartz material. The ultraviolet light also can- not pass through glass fiber. Hence a special fiber made up of PMMA[9] (Poly methyl methacrylate) is used for the purpose. PMMA is already FDA approved[10] to be used on human body for a variety of purposes.Polymethyl methacrylate (PMMA), commonly known as bone cement[10], and is widely used for implant fixation in various Orthopedic and trauma surgery.In the 1970's, the U.S. Food and Drug Administration (FDA) approved bone cement [10] for use in hip and knee prosthetic fixation. PMMA has also been used[11] for (a) bone cements; (b) contact and intraocular lens; (c) screw fixation in bone; (d) filler for bone cavities and skull defects; and (e) vertebrae stabilization in osteoporotic patients.

Application of UV light to kill micro-organisms in the human body is challenging. There are types of sepsis, one is localized tissue infection and the another is generalized septicemia where the micro-organisms are present in the blood. The micro-organisms in the blood need to be killed immediately as it is far more dangerous than tissue infection.

The blood flows through peripheral circulation with a speed of 25-40 ml per minute [12] which is 4 times slower than the ultraviolet water purifier. It means the blood will be exposed to UV light 4 times more than water making it 4 times more effective. The physics of light tells us that the light is absorbed best by the opposite color. The red color of blood is almost opposite of ultraviolet. That makes the blood absorb maximum UV light making the therapy super effective.With exposure to UV light, bacteria and viruses in the bloodstream absorb five times as much photonic energy as the red and white blood cells.Thus, IVUVLT directly kills micro-organisms in the blood as it moves across the light drop by drop. The total blood volume in adult is about 5 liters. With a blood flow of 25-40 ml per minute, it will take about 3 hours for the complete blood to pass across the UV light in a peripheral vein. Hence the therapy time is kept as 3 hours.

The device is reusable and is commercialized for a reasonable cost of Rs. 15,000. The probe of the device is detachable and sterilized by ETO gas or by putting in Formalin chamber for 30 minutes.The application of the device requires minimal skills and even a staff nurse can apply it on the patient. Hence it can be used in epidemics to be applied on large number of children and adults. The therapy is extremely affordable and

the running cost per therapy sessions is only pennies. Hence it has a potential to have a huge positive impact on public health worldwide.

The argument of safety of my device is as follows. PMMA material is biocompatible and already approved by FDA to be used inside the human body. It is inert material and does not react with blood. The device illuminates the blood flowing through a vein. The blood is exposed to UV light only for few seconds. Although very few cells can develop mutations, they are easily killed by the immune system. Every day, our body produces cancer cells but the immune system kills them and does not allow developing cancer. The blood cells have a life of only 120 days and they die after that time span. The progenitors of blood cells in the bone marrow have a long life as much as the human body and they are not exposed by the therapy. The progenitors in the bone marrow retain full capacity of blood regeneration.

Ultraviolet light of 254 NM is safe and is a non-ionizing radiation. Ionizing radiations start at 100 NM and below and are harmful to the body which are not used in this therapy. It takes thousands of hours of exposure to UV light to develop cancer. Here, therapy time is only 3 hours which is far less than that. Since blood is flowing in peripheral vessels with a speed of 25-40 ml per minute, the blood cells are exposed to UV light only for few seconds. There are studies now which show that when human wounds were exposed by UV light to kill the micro-organisms in the wound, the cells of the wound showed no damage by UV light of 254 NM wavelength. [13]

Ultraviolet Blood Irradiation (UBI) (Figure 3)is a procedure that exposes the blood to UV light to heighten the body's immune response and to kill infections.It was extensively used in the past when there were no antibiotics and antiviral drugs.No side effects were noted in the patients who underwent UBI in the past with long follow ups. IVUVLT has a lot of things in common to UBI. IVUVLT will have same benefits as UBI which is extensively studied in the past.THE UBI technique involves removing approximately 3.5 mL/kg venous blood, citrating it for anticoagulation, and passing it through a radiation chamber and reinfusing it[14].Exposure time per given unit amount was approximately 10 seconds, at a peak wavelength of 253.7 nm (ultraviolet C) provided by a mercury quartz burner and immediately re-perfused[14]. In this technique, only a small amount of blood is treated instead of entire blood volume. IVUVLT is superior to UBI as it covers whole blood volume compared to UBI whichcovers only 10-15 % of the total blood volume.

The use of UBI has been described to affect many different components of the blood. UBI can alter the function of leukocytes as proven in many in vitro studies. UV can increase stimulator cells (Figure 3) in mixed leukocyte cultures, modulate helper cells in mitogen-stimulated cultures, (Figure 2) UV can also reverse cytokine production (Figure 3) and block cytokine release. UV can disturb cell membrane mobilization.

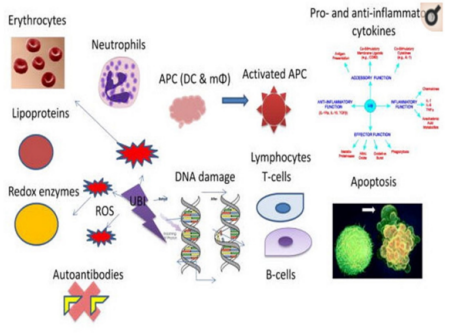

Figure 3: Showing mechanism of action of ultraviolet blood illumination

Following are numerous studies which show that the UV light kills bacteria and viruses in the animal studies as well as studies on human body. In 1801 Johann Wilhelm Ritter, a Polish physicist working at the University of Jena in Germany discovered a form of light beyond the violet end of the spectrum that he called “Chemical Rays” and which later became known as “Ultraviolet” light [15]. In 1845, Bonnet [16] first reported that sunlight could be used to treat tuberculosis arthritis (a bacterial infection of the joints).

In the second half of the 19th century, the therapeutic application of sunlight (known as heliotherapy) gradually became popular. In 1855, Rikli from Switzerland opened a thermal station in Veldes in Slovenia for the provision of heliotherapy [17]. In 1877, Downes and Blunt discovered [18] by chance that sunlight could kill bacteria. They noted that sugar water placed on a window-sill turned cloudy in the shade but remained clear while kept in the sun. Upon microscopic examination of the two solutions, they realized that bacteria were growing in the shaded solution but not in the one exposed to sunlight.

In 1904, the Danish physician Niels Finsen was awarded the Nobel Prize in Physiology or Medicine for his work on UV treatment of various skin conditions. He had a success rate of 98% in thousands of cases, mostly the form of cutaneous tuberculosis known as lupus vulgaris [19]. Walter H Ude reported a series of 100 cases of erysipelas (a cutaneous infection caused by Streptococcus pyogenes) in the 1920s, that were treated with high cure rates using UV skin irradiation [20].

Emmett K Knott in Seattle, WA reasoned that the beneficial effect of UV irradiation to the skin might (at least partly) be explained by the irradiation of blood circulating in the superficial capillaries of the skin. With his collaborator Edblom, an irradiation chamber was constructed to allow direct exposure of the blood to UV light. The irradiation chamber was circular and contained a labyrinthine passage connecting the inlet and outlet ports underneath the quartz window that formed the top of the chamber. The irradiation chamber was so designed as to provide maximum turbulence in order: (a) to prevent the formation of a film of blood on the chamber window that would absorb and filter out much of the UV; (b) to insure that all the blood passing through the chamber was equally exposed to UV [21].

Knott and co-workers then carried out a series of experiments using UV irradiation of blood extracted from dogs that had been intravenously infected with Staphylococcus aureus and hemolytic Streptococcus, and then the treated blood was reinfused. They found that it was unnecessary to deliver a sufficient exposure to the blood to kill all the bacteria directly. It was also found unnecessary to expose the total blood volume in the dogs. The optimum amount of blood to be irradiated was determined to be only 5–7% of the estimated blood volume or approximately 3.5 mL per kg of body weight. All the treated dogs recovered from an overwhelming infection (while many dogs in the control group died), and none showed any ill effects after four months of observation [21].

The first treatment on a human took place in 1928 when a patient was determined to be in a moribund state after a septic abortion complicated by hemolytic streptococcus septicemia. UBI therapy was commenced as a last resort, and the patient responded to treatment and made a full recovery [21]. She proceeded to give birth to two children.

Hancock and Knott [22] had similar success in another patient with advanced hemolytic streptococcal septicemia. These workers noted that in the majority of cases, a marked cyanosis was present at the time of initiation of UBI. It was noted that during (or immediately following) the treatment a rapid relief of the cyanosis occurred with improvement in respiration accompanied by a noticeable flushing of the skin with a distinct loss of pallor.

These observations led to application of UBI in patients suffering from pneumonia. In a series of 75 cases in which the diagnoses of pneumonia were confirmed by X-rays, all patients responded well to UBI with a rapid fall in temperature, disappearance of cyanosis (often within 3–5 minutes), cessation of delirium if present, a marked reduction in pulse rate and a rapid resolution of pulmonary consolidation. A shortening of the time of hospitalization and convalescence occurred regularly.

The knowledge gained in these successful studies led to the redesign of the irradiation chamber to give a more thoroughly uniform exposure and led to the “Knott Technic of Ultraviolet Blood Irradiation.” A number of redesigned irradiation units were manufactured and placed in the hands of physicians interested in the procedure, so that more clinical data could be accumulated [23]. The technique involved removing approximately 3.5 mL/kg venous blood, citrating it for anticoagulation, and passing it through a radiation chamber and reinfusing it. Exposure time per given unit amount was approximately 10 seconds, at a peak wavelength of 253.7 nm (ultraviolet C) provided

by a mercury quartz burner and immediately re-perfused [21].

George P Miley at the Hahnemann Hospital, Philadelphia, PA published a series of articles on the use of the procedure in the treatment of thrombophlebitis, staphylococcal septicemia, peritonitis, botulism, poliomyelitis, non-healing wounds, and asthma [23–36].

Henry A Barrett at the Willard Parker Hospital in New York City, in 1940 reported on 110 cases including a number of infections. Twenty-nine different conditions were described as responding including the following: infectious arthritis, septic abortion, osteoarthritis, tuberculosis glands, chronic blepharitis, mastoiditis, uveitis, furunculosis, chronic paranasal sinusitis, acne vulgaris, and secondary anemia [37, 38].

EV Rebbeck at the Shadyside Hospital in Pittsburgh, PA, reported the use of UBI in Escherichia coli septicemia, post-abortion sepsis, puerperal sepsis, peritonitis, and typhoid fever [39–43].Robert C Olney at the Providence Hospital, Lincoln, NE, treated biliary disease, pelvic cellulitis and viral hepatitis with UBI [42–46].

UV irradiation of blood was hailed as a miracle therapy for treating serious infections in the 1940s and 1950s. However, in an ironic quirk of fate, this time period coincided with the widespread introduction of penicillin antibiotics, which were rapidly found to be an even bigger miracle therapy. Moreover, another major success of UBI, which was becoming used to treat polio, was also eclipsed by the introduction of the Salk vaccine. Starting in the 1960s UBI fell into disuse in the West and has now been called "the cure that time forgot" [47].

Effect of UV light on red blood cells is as follows. Anaerobic conditions were reported to strongly restrict the process by which long wave ultraviolet light could induce loss of K+ ions by red blood cells. Kabat showed that UV-irradiation could have an effect on the osmotic properties of red blood cells, altering their submicroscopic structure and affecting the metabolism of adenine nucleotides. Irradiation times (60, 120, 180, 240 and 300 minutes) were used. ATP decreased while content while ADP, AMP and adenine compounds increased. It was also found that hypotonic Na+ and K+ ion exchange and hematocrit values increased. [48]

UV light illumination on Rh-positive blood significantly increased the Immunoadsorption activity. Immunoadsorption is a blood purification technique used to eliminate pathogenic antibodies. Vasil'eva et al [49] studied varying irradiation levels of UV on both red blood cells and leucocyte-thrombocyte suspensions. The immunosorption activity increased immediately after irradiation in the whole blood and red blood cells, however, the Immunoadsorption capacity in leucocytic – thrombocytic suspensions was lost after two days later.

A two-phase polymer system including poly-dextran was used to study a one-hour UV exposure of blood for autotransfusion. They found that the cell surface properties of circulating erythrocytes were altered, which contributed to the prolongation and more effective therapeutic benefit of autotransfusion.Snopov et al [50] suggested that some structural disturbances in the state of the erythrocyte glycocalyx were related to UV-irradiation when it was used as a clinical treatment. Cytochemical and iso-serological methods were used to show that blood autotransfusions were improved after UV irradiation.

Ichiki et al [51] showed that the erythrocyte cellular volume and the membrane potential were changed by UV irradiation. Lower doses (< 0.1 J/cm2) increased polymorphonuclear leukocyte production of peroxides (H2O2) which was the most pronounced among different blood cells, However an increased dose decreased the production, while the peroxide production in platelets was lowest at the lower dose, but it increased abruptly at doses above 0.4 J/cm2.

The UV light exposure had following effect on neutrophils. The pro-oxidative effects of UBI on neutrophils could be inhibited by arachidonate or lysophosphatidylcholine (LPC), as well as the complex-forming agent alpha-tocopherol. These compounds inhibited the interaction of UVR with phagocytes [52]. In chronic inflammatory disease, the concentration of large IC-IgG, IgM, and small IC-IgM immunocomplexes showed a linear and inverted correlation when UBI was carried out on autotransfused blood [20]. The function of UV-B irradiated mononuclear cells derived from human peripheral blood could be enhanced by deoxyribonucleoside supplementation, and also T-lymphocyte survival was enhanced after UV-B or UV-C exposure [53]

Artiukhov suggested that nitric oxide (NO) generation by photomodified neutrophils was due to the activation of iNOS synthesis that was de novo upregulated by UV-irradiation, which also had an effect on TNF-alpha production. Irradiation with a lower dose (75.5J/m2) improved the maintenance of physiological homeostasis through an effect relative to the native level of NO. While higher doses (755 and 2265 J/m2) were delivered to neutrophils this led to different effects by increasing the concentration of NO metabolites. Cells treated with UV-irradiation in the presence of cycloheximide (a transcriptional inhibitor of protein synthesis) could prevent the activation of iNOS synthesis. High dose UV-irradiation (755 J/m2) of blood cells showed a positive correlation between NO and TNF-alpha concentrations [54].

Zor'kina carried out a series of thirty-day rabbit experiments, suggesting that alleviation of chronic stress with hypodynamia after UBI, was caused by neutrophilic mobilization and lowered coagulation. These effects contributed to improvement of body function under long-term hypodynamia and lessening of chronic stress. UBI enhanced an adaptive process to reduce stress through activated neutrophils, lowering of disseminated intravascular coagulation, and changed atherogenic metabolism[56].

UV light illumination has following effect on lymphocytes. UBI can be useful in organ transplantation and in blood transfusion particularly in the UVB range, since immunological function and immunogenicity could be suppressed in a dose-dependent manner. Although UBI can decrease lymphocyte viability, UVC irradiation appears to be the most effective among the three spectral regions. UVB and UVC irradiation can abolish proliferative and stimulatory ability as well as the accessory/antigen-presenting ability of leukocytes in vitro. Cell-surface properties, calcium mobilization, cytokine production and release, and other sub cellular processes could be changed by UV irradiation [57]. Areltt et al [58] used the "Comet" assay for strand breakage (single cell gel electrophoresis) as an indicator of nucleotide-excision repair to prove that circulating human T–lymphocytes were exquisitely hypersensitive to the DNA-damaging and lethal effects of UV-B radiation, raising the possibility that UV-B may make a contribution to immunosuppression via a direct effect on extracapillary T-lymphocytes.

Schieven et al observed that after surface immunoglobulin cross-linking, UV-induced tyrosine phosphorylation in B cells was very similar to that seen after Ca2+ signaling in T cells. This means that the UV irradiation effect on lymphocyte function could induce both tyrosine phosphorylation and Ca2+ signals. Ca2+ channels in lymphocyte membranes are sensitive to UV irradiation, and moreover UV radiation can cause damage DNA through activation of cellular signal-transduction processes. UV radiation depending on dose and wavelength can not only induce tyrosine phosphorylation in lymphocytes, but also induce Ca2+ signals in Jurkat T cells and associated proteins synthesis. Furthermore, the pattern of surface immunoglobulin cross-linking was very similar to the UV-irradiated B cells and Ca2+-treated T-cells. In this research it was found that CD4+ and CD8+ normal human T-lymphocyte cells gave strong reactions during UV-irradiation induced producing Ca2+ responses [59].

In another similar study, Spielberg et al [60] found that UV-induced inhibition of lymphocytes accompanied by a disruption of Ca2+ homeostasis, and compared the UV effect with gamma irradiation, which have different effects on lymphocyte membranes. They found the presence of Ca2+ channels in lymphocyte membranes that were sensitive to UV irradiation. Indo-1 and cytofluorometry, was used to measure [Ca2+]I kinetics was in UVC- or UVB-exposed human peripheral blood leukocytes (PBL) and Jurkat cells in parallel with functional assays. The UV-induced [Ca2+]i rise was predominantly due to influx of extracellular calcium, and it was more pronounced in T than in non-T cells. It was observed that [Ca2+]i increased within 2–3 h of irradiation; these increases were UV-dose dependent and reached maxima of 240% and 180% above baseline level (130 nM) for UVB and UVC. The UV-induced more [Ca2+]i rise in T cells than in non-T cells, due to the influx of extracellular calcium. UV-induced calcium shifts and UV irradiation on the plasma membrane decreased the sensitivity of response to phytohemagglutinin (PHA) and its ability to stimulate a mixed leukocyte culture, because UV produces [Ca2+]i shifts.

A series of studies confirmed that UVR irradiated lymphocytes were not able to induce allogeneic cells in a mixed lymphocyte culture (MLC) as first reported by Lindahl-Kiessling [61,62,63]. Clusters formed by specialized accessory cells such as dendritic cells (DC), after mitogenic or allogenic stimulation, were necessary for lymphocyte activation to occur. Aprile found that UV irradiation of DC before culture completely abrogated the accessory activity and was able to block both cluster formation and proliferation [64].

UV-induced differentiation of human lymphocytes could accelerate the repair of UV-irradiation damage in these cells [65]. Exposure to UV irradiation was more effective than combination of UV-irradiation with methyl methane sulfonate (MMS) in the unscheduled DNA synthesis value, especially when MMS was given prior to the UV-irradiation (either at 2 hour or 26 hours incubation) because the MMS has an effect on the DNA repair polymerase by alkylating DNA [66]. Photo modification of HLA-D/DR antigens could be a trigger mechanism for activation of immunocompetent cells by UV-irradiation. Lymphocytes were isolated from a mixture of non-irradiated and UBI irradiated blood at different ratios (1:10, 1:40, 1:160) [68].

Pamphilon reported that platelet concentrates (PC) could become non-immunogenic after being irradiated with ultraviolet light (UVL) and stored for 5 d in DuPont Stericell containers. Lactate levels, beta-thromboglobulin and platelet factor were increased, while glucose levels were decreased with an irradiation dose of 3000 J/m2 at a mean wavelength of 310 nm in DuPont Stericell bags[69].Ultraviolet B (UVB) irradiation of platelet concentrate (PCs) accelerated downregulation of CD14 and nonspecifically increased the loss of monocytes by inhibiting the upregulation of ICAM-1 and HLA-DR. However, UV radiation of platelet concentrates reduced the induced immunological response in a cell suspension [70,71,72].

Deeg et al studied a model where administering blood transfusions to littermate dogs led to rejection of bone marrow grafts even though the grafts were DLA-identical, while untransfused dogs uniformly achieved sustained engraftment. UBI of the blood before transfusion prevented bone marrow graft rejection in vivo. 9.2 Gy of total body irradiation (TBI) was also used and 2.8±2.1×108/Kg donor marrow cells were infused, and whole blood was exposed for 30 minutes to UV light for 1.35 J/cm2, then injected into the recipient dogs. The control group transfused with sham-exposed blood rejected grafts, while no rejection appeared in the treatment group, which received UV-exposed blood before transplanted marrow. UV irradiation of blood lessened activation of DC by eliminating a critical DC-dependent signal; therefore, subsequent DLA-identical marrow graft was successfully engrafted [73].

Oluwole et al [74] suggested that transfusion of UV-irradiated blood into recipients could be used prior to heart transplantation to inhibit immune response and reduce lymphocyte reaction. Three strains of rats (ACI, Lewis, W/F) were used for heart transplantation in his research. When ACI rats received a Lewis rat heart, giving 1 mL transfusion of donor-type blood with or without UV-irradiation transfusion at 1,2, and 3 weeks prior to the transplantation, the mixed lymphocyte reaction with ACI lymphocytes showed a weaker response to Lewis lymphocytes than without UBI and the similar results were obtained with the other two strains of heart transplantation. UV irradiation of donor rhesus-positive blood can be used for increase in therapeutic effect of blood exchange transfusion in children with rhesus-conflict hemolytic disease [75].

Kovacs et al [76] found that DNA repair synthesis was dependent on the dose of UV-C light between 2 and 16 J/cm2. This was evaluated in irradiated and unirradiated lymphocytes in 51 healthy blood donors. Irradiation (253.7 nm) of 2,4,8 and 16 J/m2 was used, then DNA synthesis was measured by [3H] thymidine incorporation in the presence of hydroxyurea (2mM/2 ×106 cells) added 30 min before irradiation to inhibit the DNA-replicative synthesis. No significant age-related difference was seen between 17 and 74 years.

Teunissen et al [77] suggested that UVB radiation neither selectively affects Th1 or Th2 nor CD4 or CD8 T cell subsets. Compared with different dose of UVB irradiation, although the phototoxic effect was not immediately apparent, low doses of UVB (LD50: 0.5–1 mJ/cm2) irradiation were sufficient to kill most of T cells after 48–72 hours. There was a dose dependent reduction of all cytokines (IL-2, IL-4, IL-5, IFN-γ, TNF-a) 72h after irradiation. This fall in cytokine production was correlated with loss of viability so the reduction of cytokine production may be caused directly by cell death. However, the ratio of CD4+ or CD8+ T cell subsets, and the expression of CD4 and CD8 compared with the un-irradiated control, was not altered by UVB, suggesting that neither of the two T cell subsets was selectively affected.

UV light has following effect on phagocytic activity. Phagocytic activity (PhA) was one of the first mechanisms to be proposed to explain the immune correction by UBI therapy, In Samoı lova's research, non-irradiated blood mixed with 1:10 volumes of irradiated blood were used to test PhA of monocytes and granulocytes. An increase of 1.4–1.7 times in PhA compared with non-irradiated blood, was seen when UV-irradiated blood was transfused into healthy adults. The enhancement of PhA depended on its initial level and may occur simultaneously with structural changes of the cell surface components [79].

Simon et al [82] showed that UVB could convert Langerhans cells (LC) or splenic adherent cells (SAC) from an immunogenic to a tolerogenic type of APC (LC or SAC). In his research, single dose of irradiation (200J/m2) was used on LC and SAC. The Th1 loss of response after preincubation with keyhole limpet hemocyanin (KLH) was studied with UVB-LC or UVB-SAC. Furthermore, the loss of responsiveness was not related to the release of soluble suppressor factors but was Ag-specific, MHC-restricted, and did not last for a long time. Functional of allogeneic LC or SAC delivery a costimulatory signal(s) was interferes by UVB, because unresponsiveness by UVB-LC or UVB-SAC could not induce by unirradiated allogeneic SAC.

UV-irradiation increased phagocytic activity of human monocytes and granulocytes; the improvement in phagocytic index was related to the irradiation dose, and the initial level. A lower initial level would increase proportionately more than a higher initial level after UV-irradiation. It was found that UV irradiation enhanced the phagocytic activity directly [83].

UV light has following effect on low-density lipoprotein (LDL). Roshchupkin et al [81] found that UV irradiation played a core role in lipid peroxidation in the membrane of blood cells. UV irradiation on blood stimulated arachidonic acid to be produced by a cyclooxygenase catalyzed reaction. UV induced a process of dark lipid autoperoxidation that continued for some time afterwards producing free radicals. It contributed to lipid photoperoxidation producing lipid hydroperoxides.

An UV irradiated lipid emulsion greatly enhanced reactive oxygen species (ROS) production by monocytes. Highly atherogenic oxidized LDL could be generated in the circulation. UV irradiation of the lipid emulsion called “Lipofundin” (largely consisting of linoleic acid oxidized either by lipoxygenase, Fe3+ or ultraviolet irradiation) was injected into rabbits. Blood samples were taken from the ear vein with EDTA before and 6 hours after lipofundin treatment. Though UV-oxidized lipofundin induce less chemiluminescence from monocytes compared with Fe3+ oxidation, it lasted 2.3 times longer. UV–oxidized lipofundin could more effectively stimulate H2O2 production by cells, than LDL altered by monocytes, even with the same concentration of thiobarbituric acid reactive substance (TBARS). Six hours after injection of oxidized lipofundin, the lipid peroxide content was significantly increased; however neutral lipids of LDL separated from rabbit plasma showed no significantly difference to the monocyte-oxidized human LDL [82].

Salmon [83] found that UVB (280–315 nm) irradiation could easily damage LDL and high-density lipoprotein (HDL) tryptophan (Trp) residues. The TBARS assay was used to measure the photooxidation of tryptophan residues which was accompanied by the peroxidation of low- and high-density lipoprotein unsaturated fatty acids. Vitamin E and carotenoids naturally carried by low- and high-density lipoproteins, were also rapidly destroyed by UVB. However, UVA radiation did not destroy tryptophan residue and lipid photoperoxidation.

UV radiation (wavelength range 290–385 nm) easily oxidized lipoproteins contained in the suction blister fluid of healthy volunteers, which is a good representative of the interstitial fluid feeding the epidermal cells. Apolipoprotein B of LDL and apolipoprotein A-I and II were all changed in the same way under UV irradiation. The single tryptophan residue of albumin was highly susceptible to photo-

oxidation during irradiation. UVA irradiation of undiluted suction blister fluid induced apo-A-I aggregation; however, purified lipoproteins were not degraded. During UV irradiation of suction blister fluid, antigenic apolipoprotein B is fragmented and polymerized. Activated oxygen radicals in the suction blister fluid during UV irradiation were derived from lipid peroxidation in HDL. Furthermore, they suggested that lipid peroxidation of was caused by a radical chain reaction and could transfer the initial photodamage. UV-light irradiation could play an important role in triggering inflammation and the degeneration caused by induced lipoprotein photo-oxidation with systemic effects. [84]

Artyukhov et al [85] found that dose-dependent UV-irradiation could activate the myeloperoxidase (MPO) and the NADPH-oxidase systems and lipid peroxide (LPO) concentration in donor blood. Two doses of UV-light were used (75.5 and 151.0 J/m2) in UV-induced priming of neutrophils (NP). A higher dose activated more free radicals and H2O2 from NP than a lower dose. Two groups were divided by the type of relationship between MPO activity and UV light dose (from 75.5 to 1510J/m2). A low enzyme activity (group 1) increased under the effect of UV exposure in doses of 75.5 and 151.0 J/m2, while in group 2 this parameter decreased. MPO activity showed the same result in dose-dependent UV-irradiation; however, increasing the dose to 1510J/m2 did not increase the activity of MPO. In the next series of experiments, LPO concentration was evaluated after UV exposure of the blood. Two groups of donors were distinguished by the relationship between blood content of LPO and UV exposure dose. UV irradiation at low doses (75.5–151.0 J/m2) decreased initially high LPO and increased initially low LPO levels. In phagocytes, NADPH-oxidase plays one of the most important role of photoacceptors for UV light. Which cause the superoxide concentration to increase after UV-irradiation by activating the enzyme complex. UV irradiation decreases intracellular pH that is raised by activation of NADPH-oxidase complex.

UBI can reduce the free radical damage and elevate the activity of antioxidant enzymes after spinal cord injury in rabbits. 186 rabbits were divided into 4 groups randomly, (control, blood transfusion, injured and UBI). UV irradiation (wavelength 253.7nm, 5.68×10−3 J/cm2) were used in the treatment group at 47, 60 and 72 hours after surgery. Free radical signals (FR), malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione peroxidase (GSH-PX) were measured. In the treatment group, SOD and GSH-PX were highly increased and showed significant differences compared with other groups; while FR and MDA decreased significantly in the UBI groups compared to the other groups. UV-irradiated blood decreased MDA and FR content in the spinal cord tissue. They also suggested that two factors contributed to increased SOD and GSH-PX activity: one was that UV irradiation induced the (lowered) SOD, GSH-PX return to normal levels, the other was that a decrease in the formation of FR, led to SOD and GSH-PX increases, especially at 48 and 72 hours after injury [86].

The light of 254 NM splits the 2% dissolved Oxygen in the blood and converts it into molecular Ozone (O3). Ozone is a non-toxic gas and kills all micro-organisms like bacteria, fungi, viruses and molds in just 60 seconds. (54,55)It is effective in little concentration as 0.04 ppm and human toxicity starts at 3 ppm indicating a huge safety limit. No resistance is reported to Ozone making it a never-failing solution to micro- organisms. French people are drinking Ozonated water for more than 100 years now without problem. Ozone is a strong modulator of immune system(90). Inside the blood, it creates a mild oxidative stress which makes the immune system produce a large quantity of Interferons, agents that attack micro-organisms and kills them. Ozone is a twin brother of Oxygen, hence can even enter a cell and cross blood brain barrier. Thus, the Ozone generated in minute quantities in the blood can kill the tissue infection.Ozone destroys micro-organisms by attacking the glycoproteins and glycolipids in the cell membrane that results in rupture of the cell.

IVUVLT is going to be effective against vast number of viral infections such as HIV- AIDS, COVID 19, Swine flu, Dengue fever, Japanese encephalitis, Rabies, viral diarrheas, Hepatitis B and C, rabies etc. which kill millions of people yearly worldwide. It will also be effective against bacterial septicemia, tetanus, meningitis,Diphtheria and against Methicillin-resistant Staphylococcus aureus (MRSA) etc. It will also be effective against systemic fungal infections and molds.The therapy will work against unknown organisms leading to pyrexia of unknown origin (PUO). There are thousands of mico-organisms which can infect human body, but we have diagnostic tests and specific treatment only for few of them.IVUVLT can act against all micro-organisms as UV light and Ozone kill them all in Vitro.Penicillin was the greatest discovery of 19 th century but lost its charm due to antibiotic resistance. Since micro-organisms can- not develop resistance to UV light and Ozone, this therapy will ultimately prove to be a bigger discovery than penicillin.

I do not claim to know everything about IVUVLT. A lot of research and numerous clinical trials will be necessary to know about its exact mechanism of action, dosages and indications. This is only the beginning of this kind of research.

CONCLUSIONS:

IVUVLT is a potentially safe, cheap and effective therapy for septicemia secondary to vast majority of viral and bacterial infections including Covid19. Since, the micro-organisms can-not develop resistance to UV light and Ozone gas, IVUVLT will always be effective against them. IVUVLT and its device are reported for the first time in the medical literature. It may be useful in organ transplanted patient due to its immune-modulatory effect. We need more research and a greater number of patients to know more about IVUVLT's exact indications, dosages and mechanism of action. The therapy has a potential to save many patients worldwide from variety of infections. The therapy can be used as an immediate measure in epidemics and pandemics for new infections with unknown micro-organisms even before a specific vaccine and treatment is developed.

REFERENCES:

1) https://www.who.int/news-room/detail/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis.
2) Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? Marlieke E. A. de Kraker ,Andrew J. Stewardson, Stephan Harbarth PLOS MEDICINE. Published: November 29, 2016 https://doi.org/10.1371/journal.pmed.1002184
3) Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. The Review on Antimicrobial Resistance. Chaired by Jim O'Neill. December 2014
4) Physiological and Biochemical Mechanisms of Drug Resistance BSCI 424 PATHOGENIC MICROBIOLOGY.Fall 2000
5) Mechanisms of Resistance to Antiviral Agents Authors: Robert W. Shafer, Sunwen Chou Chapter 111: Publication Year: 2015.Category: Clinical Microbiology. Book DOI: 10.1128/9781555817381.Chapter DOI: 10.1128/9781555817381.ch111
6) The Bactericidal Effect of Sunlight-The discovery of the damaging effect of sunlight on bacteria Philip E. Hockberger* Journal of Photochemistry and Photobiology B: Biology 58 (2000) 185–191. www.elsevier.nl / locate / jphotobiol Department of Physiology, Northwestern University Medical School, 303 E. Chicago Ave., Chicago, IL USA Received 26 September 2000; accepted 2 October 2000
7) Fungi/Bactericidal and Static Effects of Ultraviolet Light in 254 and 354 nm Wavelengths 1)BerrinOzcelik Research Journal of Microbiology 2(1), 42-49, 2007. ISSN:1816-4935 Faculty of Pharmacy, Gazi university, 06330 Ankara, Turkey
8) Ultraviolet germicidal irradiation in tap water contaminated by Aspergillusspp J Prev Med Hyg. 2017 Dec; 58(4): E315–E319. Published online 2017 Dec 30. doi: 10.15167/2421-4248/jpmh2017.58.4.777. PMCID: PMC5912791. PMID: 29707663 M. SISTI,* G.F. SCHIAVANO, M. DE SANTI, and G. BRANDI
9) Exposure and Development of Poly (Methyl Methacrylate) Using 254nm Light Source and IPA/Water Robert W. Johnstone; Ian G. Foulds; M. ParameswaranPublisher: IEEE. 2007 Canadian Conference on Electrical and Computer Engineering
10) Bone cement RajuVaishya, (MS, MCh, FRCS),a, Mayank Chauhan, (MS Orth),b and AbhishekVaish, (MBBS)c J ClinOrthop Trauma. 2013 Dec; 4(4): 157–163.Published online 2013 Dec 15. doi: 10.1016/j.jcot.2013.11.005. PMCID: PMC3880950 PMID: 26403875
11) PMMA: an essential material in medicine and dentistry.Frazer RQ1, Byron RT, Osborne PB, West KP. J Long Term Eff Med Implants. 2005;15(6):629-39.PMID:16393131. DOI:10.1615/jlongtermeffmedimplants.v15.i6.60
12) Continuous infusion indicator dilutionmeasurement of limb blood flow and vascularresponse to magnesium sulfate innormotensive and hypertensive men Henry W. Overbeck, Robert M. Daugherty Jr., Francis J.HaddyJ Clin Invest. 1969;48(10):1944-1956. https://doi.org/10.1172/JCI106161.
13) 207-nm UV Light—A Promising Tool for Safe Low-Cost Reduction of Surgical Site Infections. II: In-Vivo Safety StudiesManuela Buonanno, MildaStanislauskas, Brian Ponnaiya, Alan W. Bigelow,Gerhard Randers-Pehrson, YanpingXu, Igor Shuryak, LubomirSmilenov, David M. Owens, David J. Brenner Published: June 8, 2016. https://doi.org/10.1371/journal.pone.013841814)
14) Ultraviolet blood irradiation: Is it time to remember "the cure that time forgot"? XimingWu,a,b,cXiaoqingHu,b,c,d and Michael R. Hamblinb,c, J PhotochemPhotobiol B. Author manuscript; available in PMC 2017 Apr 1.Published in final edited form as:JPhotochemPhotobiol B. 2016 Apr; 157: 89–96.Published online 2016 Feb 5. doi: 10.1016/j.jphotobiol.2016.02.007.PMCID: PMC4783265. NIHMSID: NIHMS761387. PMID: 26894849
15) Reception and discovery: the nature of Johann Wilhelm Ritter's invisible rays. Studies in History and Philosophy of Science Frercksa J, Weberb H, Wiesenfeldt G Part A. 2009;40:143–156. [Google Scholar]
16) Traite des Maladies des Articulations. Bonnet A. Bailliere; Paris: 1845. [Google Scholar]
17) Photodermatologie in Dresden-einhistorischerAbriss. Festschrift anlasslich des 75. Barth J, Kohler U. Geburtstages von Prof. Dr. Dr. Dr. h.c. H.-E. Kleine-Natrop (1917–1985) Dresden. 1992 [Google Scholar]
18) Researches on the effect of light upon bacteria and other organisms.Downes A, Blunt TP. Proc Royal Soc London. 1877;26:488–500. [Google Scholar]
19) Phototherapy.Finsen NR. Edward Arnold; London: 1901. [Google Scholar]
20) Ultraviolet Radiation Therapy in Erysipelas.Ude WH. Radiology. 1929;13:504. [Google Scholar]
21) Development of ultraviolet blood irradiation.Knott EK. Am J Surg. 1948;76:165–171. [PubMed] [Google Scholar]

22) EK Irradiated blood transfusion in the treatment of infections. Hancock VKK, Northwest Med. 1934:200. [Google Scholar]
23) Ultraviolet blood irradiation further studies in acute infections. Miley G, Christensen JA. Am J Surg. 1947;LxxIII:486–493. [PubMed] [Google Scholar]
24) Uv irradiation non healing wounds. Miley G. Am J Surg. 1944;LXV:368–372. [Google Scholar]
25) Recovery from botulism coma following ultraviolet blood irradiation. Miley GP. The Review of gastroenterology. 1946;13:17–19. [PubMed] [Google Scholar]
26) Ultraviolet blood irradiation therapy of apparently intractable bronchial asthma.Miley GP, Seidel RE, Christensen JA. Archives of physical medicine and rehabilitation. 1946;27:24–29. [PubMed] [Google Scholar]
27) The control of acute thrombophlebitis with ultraviolet blood irradiation therapy. Miley G. Am J Surg. 1943:354–360. [Google Scholar]
28) Efficacy of ultraviolet blood irraidation therapy in the control of staphylococcemias.Miley G. Am J Surg. 1944:313–322. [Google Scholar]
29) Ultraviolet blood irraidation therapy in acute poliomyelitis.Miley G. Arch Phys Therapy. 1944:651–656. [Google Scholar]
30) Disappearance of hemolytic staphylococcus aureus septicemia following ultraviolet blood irradiation therapy. Miley G. Am J Surg. 1943:241–245. [Google Scholar]
31) The knott technic of ultraviolet blood irradiation in acute pyogenic infections.Miley G. New York state Med. 1942:38–46. [Google Scholar]
32) Present status of ultraviolet blood irradiation (Knott technic) Miley G. Arch Phys Therapy. 1944:368–372. [Google Scholar]
33) Ultravilet blood irradiation.Miley G. Arch Phys Therapy. 1942:536. [Google Scholar]
34) Ultraviolet blood irradiation therapy (knott technic) in acute pyogenic infections. Miley G. Am J Surg. 1942:493. [Google Scholar]
35) The knott technic of ultraviolet blood irradiation as a control of infection in peritonitis. Miley G. The Review of gastroenterology. 1943:1. [Google Scholar]
36) Preliminary report of results observed in eighty cases of intractable bronchial asthma.Miley GP, Seidel RE, Christensen JA. Arch Phys Therapy. 1943:533. [Google Scholar]
37) The irradiation of autotransfused blood by ultraviolet spectral energy. Barrett HA. Result of therapy in 110 cases. Med clin North America. 1940 721.1040. [Google Scholar]
38) Five years' experience with hemo-irradiation according to the Knott technic.Barrett HA. Am J Surg. 1943;61:42–53. [Google Scholar]
39) Double septicemia following prostatectomy treated by the knott technic of ultraviolet blood irradiation.Rebbeck EW. Am J Surg. 1942;57:536–538. [Google Scholar]
40) Preoperative hemo-irradiations.Rebbeck EW. Am J Surg. 1943;61:259–265. [Google Scholar]
41) Ultraviolet irradiation of autotransfused blood in the treatment of puerperal sepsis.Rebbeck EW. Am J Surg. 1941;54:691–700. [Google Scholar]
42) Ultraviolet irradiation of autotransfused blood in the treatment of postabortional sepsis.Rebbeck EW. Am J Surg. 1942;55:476–486. [Google Scholar]
43) Ultraviolet Irradiation of Blood in the Treatment Of Escherichia coli Septicemia.Rebbeck EW. Arch Phys Therap. 1943:158–167. [Google Scholar]
44) Ultraviolet blood irradiation in biliary disease; Knott method. Olney RC. Am J Surg. 1946;72:235–237. [PubMed] [Google Scholar]
45) Ultraviolet blood irradiation treatment of pelvic cellulitis; Knott method. Olney RC. Am J Surg. 1947;74:440–443. [PubMed] [Google Scholar]
46) Treatment of viral hepatitis with the Knott technic of blood irradiation. Olney RC. Am J Surg. 1955;90:402–409. [PubMed] [Google Scholar]
47) Ultraviolet Blood Irradiation Therapy (Photo-Oxidation): The Cure That Time Forgot. Rowen RJ. Int J Biosocial Med Research. 14:115–132. [Google Scholar]
48) Effect of UV-irradiation of shifts of energy-rich phosphate compounds: ADP, ATP and AXP in human red blood cells represented by a trigonometrical polynomial. 34. Kabat IA, Sysa J, Zakrzewska I, Leyko W.Zentralblatt fur Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene ErsteAbteilungOriginaleReihe B: Hygiene, praventiveMedizin. 1976;162:393–401. [PubMed] [Google Scholar]
49) Changes of immunosorption properties in the blood and its components at various times after UV-irradiation.Vasil'eva ZF, Samoilova KA, Shtil'bans VI, Obolenskaia KD, Vitiuk NG. Gematologiiaitransfuziologiia. 1991;36:26–27. [PubMed] [Google Scholar]
50) Functional and structural changes in the surface of human erythrocytes following irradiation with ultraviolet rays of various wave lengths. V. Modification of the glycocalyx in autotransfusions of UV-irradiated blood. Snopov SA, Aritsishevskaia RA, Samoilova KA, Marchenko AV, Dutkevich IG. Tsitologiia. 1989;31:696–705. [PubMed] [Google Scholar]
51) Generation of active oxygens, cell deformation and membrane potential changes upon UV-B irradiation in human blood cells. Ichiki H, Sakurada H, Kamo N, Takahashi TA, Sekiguchi S. Biological & pharmaceutical bulletin. 1994;17:1065–1069. [PubMed] [Google Scholar]
52) Activation of neutrophil membrane-associated oxidative metabolism by ultraviolet radiation. Savage JE, Theron AJ, Anderson R. The Journal of investigative dermatology. 1993;101:532–536. [PubMed] [Google Scholar]
53) Effect of the UV irradiation of autologous blood on the humoral link in the immune response of patients with chronic inflammatory processes. Ivanov EM, Kapshienko IN, Tril NM. Voprosykurortologii, fizioterapii, ilechebnoifizicheskoikultury. 1989:45–47. [PubMed] [Google Scholar]
54) Effect of deoxyribonucleosides on the hypersensitivity of human peripheral blood lymphocytes to UV-B and UV-C irradiation.Green MH, Waugh AP, Lowe JE, Harcourt SA, Cole J, Arlett CF. Mutation research. 1994;315:25–32. [PubMed] [Google Scholar]
55) Level of nitric oxide and tumor necrosis factor-alpha production by human blood neutrophils under UV-irradiation. Artiukhov VF, Gusinskaia VV, Mikhileva EA. Radiatsionnaiabiologiia, radioecologiia/Rossiiskaiaakademiianauk. 2005;45:576–580. [PubMed] [Google Scholar]
56) Effect of UV-irradiation of blood on the course of adaptation to conditions of hypodynamia. Zor'kina AV, Inchina VI, KostinIa V. Patologicheskaiafiziologiiaieksperimental'naiaterapiia. 1996:22–24. [PubMed] [Google Scholar]
57) Manipulation of immunity and immunogenicity Deeg HJ. Ultraviolet irradiation in transplantation biology. Transplantation. 1988;45:845–851. [PubMed] [Google Scholar]
58) Hypersensitivity of human lymphocytes to UV-B and solar irradiation.Arlett CF, Lowe JE, Harcourt SA, Waugh AP, Cole J, Roza L, Diffey BL, Mori T, Nikaido O, Green MH. Cancer research. 1993;53:609–614. [PubMed] [Google Scholar]
59) Ultraviolet radiation induces differential calcium signals in human peripheral blood lymphocyte subsets. Journal of immunotherapy with emphasis on tumor immunology. Schieven GL, Ledbetter JA. official journal of the Society for Biological Therapy. 1993;14:221–225. [PubMed] [Google Scholar]
60) UV irradiation of lymphocytes triggers an increase in intracellular Ca2+ and prevents lectin-stimulated Ca2+ mobilization: evidence for UV- and nifedipine-sensitive Ca2+ channels. Spielberg H, June CH, Blair OC, Nystrom-Rosander C, Cereb N, Deeg HJ. Experimental hematology. 1991;19:742–748. [PubMed] [Google Scholar]
61) Applications of ultraviolet light in the preparation of platelet concentrates Pamphilon DH, Corbin SA, Saunders J, Tandy NP. Transfusion. 1989;29:379–383. [PubMed] [Google Scholar]
62) Inability of UV-irradiated lymphocytes to stimulate allogeneic cells in mixed lymphocyte culture. International archives of allergy and applied immunology.Lindahl-Kiessling K, Safwenberg J. 1971;41:670–678. [PubMed] [Google Scholar]
63) Dissimilar effects of ultraviolet light on HLA-D and HLA-DR antigens. Slater LM, Murray S, Liu J, Hudelson B. Tissue antigens. 1980;15:431–435. [PubMed] [Google Scholar]
64) Ultraviolet irradiation of canine dendritic cells prevents mitogen-induced cluster formation and lymphocyte proliferation. Aprile J, Deeg HJ. Transplantation. 1986;42:653–660. [PubMed] [Google Scholar]
65) DNA repair in the UV irradiation of human peripheral blood lymphocytes (healthy donors and xeroderma pigmentosum patients) in relation to the dedifferentiation process in phytohemagglutinin exposure. Genter EI, Zhestianikov VD, Mikhel'son VM, Prokof'eva VV. Tsitologiia. 1984;26:599–604. [PubMed] [Google Scholar]
66) The modifying action of methylmethanesulfonate on unscheduled DNA synthesis in the UV irradiation of human peripheral blood lymphocytes.Genter EI, Mikhel'son VM, Zhestianikov VD. Radiobiologiia. 1989;29:562–564. [PubMed] [Google Scholar]
67) The effect of UV irradiation and of UV-irradiated autologous blood on the functional state of human peripheral blood lymphocytes.Volgareva EV, Volgarev AP, Samoilova KA. Tsitologiia. 1990;32:1217–1224. [PubMed] [Google Scholar]
68) Platelet concentrates irradiated with ultraviolet light retain satisfactory in vitro storage characteristics and in vivo survival. Pamphilon DH, Potter M, Cutts M, Meenaghan M, Rogers W, Slade RR, Saunders J, Tandy NP, Fraser ID. British journal of haematology. 1990;75:240–244. [PubMed] [Google Scholar]
69) Effect of storage and ultraviolet B irradiation on CD14-bearing antigen-presenting cells (monocytes) in platelet concentrates. Fiebig E, Lane TA. Transfusion. 1994;34:846–851. [PubMed] [Google Scholar]
70) Ultraviolet irradiation of platelet concentrate abrogates lymphocyte activation without affecting platelet function in vitro. Kahn RA, Duffy BF, Rodey GG. Transfusion. 1985;25:547–550. [PubMed] [Google Scholar]
71) The role of UV radiation in the prevention of human leukocyte antigen alloimmunization Andreu G, Boccaccio C, Klaren J, Lecrubier C, Pirenne F, Garcia I, Baudard M, Devers L, Fournel JJ. Transfusion medicine reviews. 1992;6:212–224. [PubMed] [Google Scholar]
72) Platelet transfusions irradiated with ultraviolet-B light may have a role in reducing recipient alloimmunization. Blood coagulation & fibrinolysis. Tandy NP, Pamphilon DH. an international journal in haemostasis and thrombosis. 1991;2:383–388. [PubMed] [Google Scholar]
73) Ultraviolet irradiation of blood prevents transfusion-induced sensitization and marrow graft rejection in dogs.Deeg HJ, Aprile J, Graham TC, Appelbaum FR, Storb R. Blood. 1986;67:537–539. [PubMed] [Google Scholar]
74) Prolongation of rat heart allografts by donor-specific blood transfusion treated with ultraviolet irradiation.Oluwole SF, Iga C, Lau H, Hardy MA. The Journal of heart transplantation. 1985;4:385–389. [PubMed] [Google Scholar]
75) The activation of the immunosorptive properties of blood during its UV irradiation at therapeutic doses.Vasil'eva ZF, Shtil'bans VI, Samoilova KS, Obolenskaia KD. Biulleten' eksperimental'noibiologiiimeditsiny. 1989;108:689–691. [PubMed] [Google Scholar]
76) Age-related variation in the DNA-repair synthesis after UV-C irradiation in unstimulated lymphocytes of healthy blood donors. Kovacs E, Weber W, Muller H. Mutation research. 1984;131:231–237. [PubMed] [Google Scholar]
77) Effect of low-dose ultraviolet-B radiation on the function of human T lymphocytes in vitro. Teunissen MB, Sylva-Steenland RM, Bos JD. Clinical and experimental immunology. 1993;94:208–213. [PMC free article] [PubMed] [Google Scholar]
78) Changes in the leukocyte phagocytic activity of donor blood after its UV irradiation. II. Simulation of the effect of the autotransfusion of UV-irradiated blood. Samoilova KA, Obolenskaia KD, Freidlin IS. Tsitologiia. 1987;29:1048–1055. [PubMed] [Google Scholar]
79) Ultraviolet B radiation converts Langerhans cells from immunogenic to tolerogenic antigen-presenting cells. Induction of specific clonal anergy in CD4+ T helper 1 cells.Simon JC, Tigelaar RE, Bergstresser PR, Edelbaum D, Cruz PD., Jr Journal of immunology. 1991;146:485–491. [PubMed] [Google Scholar]
80) Changes in the leukocyte phagocytic activity of donor blood after its UV irradiation. I. Its relation to the irradiation dose and initial level of phagocytic activity. Obolenskaia KD, Freidlin IS, Samoilova KA. Tsitologiia. 1987;29:948–954. [PubMed] [Google Scholar]
81) Free-radical and cyclooxygenase-catalyzed lipid peroxidation in membranes of blood cells under UV irradiation.Roshchupkin DI, Murina MA. Membrane & cell biology. 1998;12:279–286. [PubMed] [Google Scholar]
82) Activation of human blood monocytes by oxidized polyunsaturated fatty acids: a possible mechanism for the generation of lipid peroxides in the circulation.Gorog P. International journal of experimental pathology. 1991;72:227–237. [PMC free article] [PubMed] [Google Scholar]
83) UVB-induced photoperoxidation of lipids of human low- and high-density lipoproteins. A possible role of tryptophan residues. Salmon S, Maziere JC, Santus R, Morliere P, Bouchemal N. Photochemistry and photobiology. 1990;52:541–545. [PubMed] [Google Scholar]
84) Alteration of lipoproteins of suction blister fluid by UV radiation. Salmon S, Haigle J, Bazin M, Santus R, Maziere JC, Dubertret L. Journal of photochemistry and photobiology B, Biology. 1996;33:233–238. [PubMed] [Google Scholar]
85) Effect of UV irradiation on functional activity of donor blood neutrophils. Artyukhov VG, Iskusnykh AY, Basharina OV, Konstantinova TS. Bulletin of experimental biology and medicine. 2005;139:313–315. [PubMed] [Google Scholar]
86) Ultraviolet blood irradiation and oxygenation affects free radicals and antioxidase after rabbit spinal cord injury.Dong Y, Shou T, Zhou Y, Jiang S, Hua X. Chinese medical journal. 2000;113:991–995. [PubMed] [Google Scholar]
87) Antimicrobial activity of ozonated water.Białoszewski D1, Bocian E, Bukowska B, Czajkowska M, Sokół-Leszczyńska B, Tyski S.Med SciMonit. 2010 Sep;16(9):MT71-5. international medical journal of experimental and clinical research 16(9):MT71-5 • September 2010
88) Antimicrobial Effect of Ozone Made by KP Syringe of High-Frequency Ozone GeneratorDomagoj Prebeg,1 Marina Katunarić,1,2 Ana Budimir,2 BožidarPavelić,corresponding author1,2 Sanja Šegović,1,2 and Ivica Anić1,2 ActaStomatol Croat. 2016 Jun; 50(2): 134–142.doi: 10.1564/asc50/2/6 PMCID: PMC5080568. PMID: 27789911
89) Systemic Ozone Therapy by Rectal Insufflation for Immunoglobulin A Deficiency Jacqueline Díaz-Luis Silvia Menéndez-Cepero Consuelo Macías-Abraham LucíaFariñas-Rodríguez About the authors
90) Ozone therapy as a primary and sole treatment for acute bacterial infection: case report Med Gas Res. 2018 Jul-Sep; 8(3): 121–124.Published online 2018 Sep 25. doi: 10.4103/2045-9912.241078. PMCID: PMC6178636. PMID: 30319768. Robert Jay Rowen, MD*