Brief History of Phototherapy

It has been known for some time that light has as a myriad of therapeutic effects. Since 1400 AD, many major civilizations were using sunlight in the treatment of skin diseases, including vitiligo, cancer, and psoriasis. The Egyptians built special light healing temples that used sun and colored light for various healing purposes. Along with the Egyptians, the Assyrians and the Babylonians all practiced therapeutic sun healing, called heliotherapy. Herodotus, a famous Greek physician, was thought to be the father of heliotherapy and emphasized the importance of sun exposure for the renewal of health. The Greek city, Heliopolis, was known for its healing temples and light rooms, which had windows covered with various colored cloths which were thought to have different healing properties. Many believed that the red light of the sun contributed to these therapeutic effects.

As time went on, many others became interested in heliotherapy. In 1855, Arnold Rikli, a natural healer from Switzerland, developed helio-hydroscopic treatment centers in Bled, Slovenia (Liberman, 1991). Individuals who lived at these centers resided in special houses, bathed and sun tanned in the nude. Rikli believed that the sun, air, and water were the sources of health and healing. However, it was not until the 1870s that scientists in the field of light therapy became fully aware of the healing properties of light.

In 1876, Augustus Pleasontan developed a theory that blue light from the sun was beneficial in the growth of plants as well as in the health of humans and animals (Liberman, 1991). His theory was based on his observations that plants grew best in the spring when the sky was bluer. He performed experiments on the growth of grapes that were exposed to natural sunlight and blue light (Liberman, 1991). The results showed that grapes exposed to blue light grew faster than those exposed to direct sunlight. In animals, he found that blue light elevated fertility and increased the rate of physical maturation. Pleasanton also found that blue light, from either the sun or an artificial source, was an effective means of stimulating the secretory glands and nervous system in humans. He found this to be beneficial in the treatment of various diseases, especially those accompanied with pain. Even though his theory was never fully adopted in the scientific community, his blue light theory is considered to be the birth of modern chromotherapy (Liberman, 1991).

A year later, Dr. Seth Pancoast, a renowned physician, filtered sunlight through blue and red glass. This caused the acceleration or relaxation of the nervous system which created balance in the body (Liberman, 1991). These results were published in his book, *Blue and Red Lights.* While Pancoast's findings were significant, Dr. Edwin Babbitt's book, *The Principles of Light and Color*, took the medical profession by surprise.

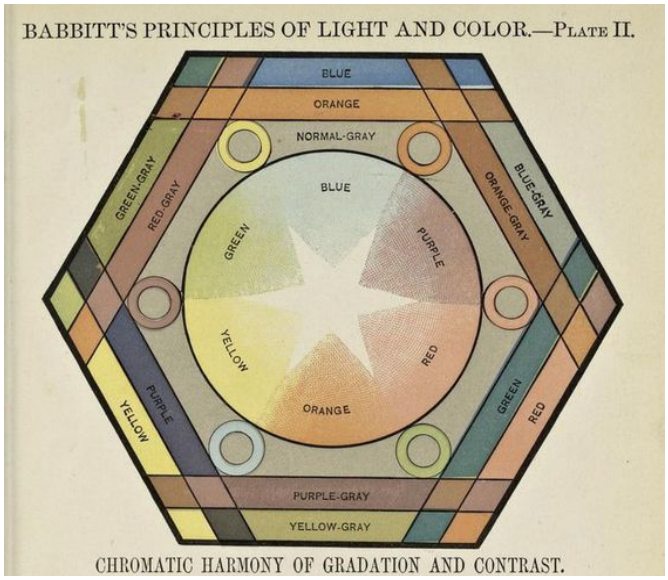

Figure 1: Dr. Edwin Babbitt's Chromo Disk. Obtained from: Babbitt, 1878

Unlike Dr. Pancoast, who treated his patients with blue and red light, Dr. Babbitt treated his patients with both artificial and natural light (Liberman, 1991). One of the devices he created was the Chromo Disk, (figure 1). The Chromo Disk can be fitted with different filters and then focused on different areas of the body for various treatments. He also developed Solar Elixirs by exposing bottled water to sunlight that was filtered through a Chromo Lens, which was similar to his Chromo Disk. Babbitt claimed that this "sensitized" water retained the energy and vital elements of the different colors and was able to have unbelievable healing powers. By incorporating different hues of color, Babbitt was not only able to expand is treatment capabilities, but he was able to open a new interest in light and color in the treatment of various ailments.

Also in 1877, Arthur Downes and Thomas Blunt accidently discovered that ultraviolet light was able to kill bacteria. Downes and Blunt found that sugar water remained clear when exposed to sunlight and sugar water in the shade remained cloudy. Microscopic examination showed bacterial growth in the shaded solution but not in the sunlight solution. It was during the 1880s and 1890s that great advances were made with ultraviolet light. These included using

UV light as an anti-bacterial in hospitals, operating rooms as well as the treatment of wounds and scars. The 1890s introduced two important contributions to the field of light therapy, the use of sunlight to treat rickets and Niels Finsen's use of red light to cure lupus vulgaris.

The most common cause of rickets is a lack of vitamin D, which results in inadequate calcium and phosphorous absorption. This causes the deformation of bones in children and osteomalacia in adults (Holick, 2006). However, in 1890, Dr. Theobald Palm observed an inverse relationship between the incidence of rickets and the amount of sunlight the country was exposed too. He observed countries that were exposed to more sunlight had a lower incidence of rickets (Palm, 1890). It was later understood that when exposed to sunlight, the skin underwent a series of reactions to produce vitamin D, which caused an increase in bone mineralization (figure 2). It is now known that sunlight acts as the catalyst for the reactions that produce the body's main source of vitamin D.

During the same year, Niels Finsen began his famous work on the treatment of smallpox scars and lupus vulgaris with light. Suffering from Niemann Pick Disease, Finsen was inspired to explore the effects of sunlight on living organisms. In 1893, Finsen observed that red light had a beneficial effect on smallpox scars. When exposed to red light, there was significant improvement in the pitting of these scars. One patient who was exposed to red light for nine days had complete clearing of pitting (figure 3). There were specific requirements for this treatment however (Finsen 1895). The patient had to stay in a room away from chemical rays and only exposed to red light, the treatment should be started as soon as possible, and the patient should be exposed to red light until the vesicles have dried up (Finsen 1895).

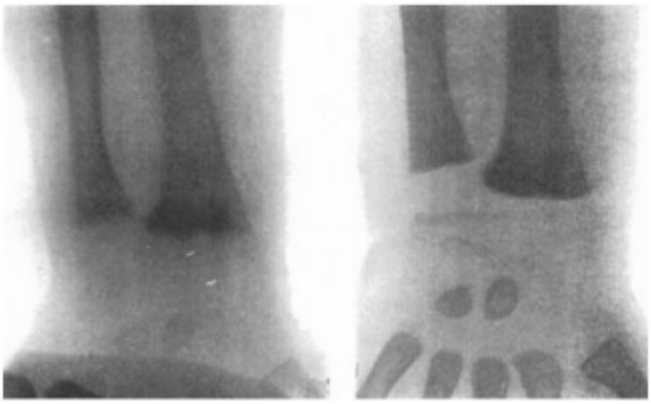

Figure 2. X-rays of rickets untreated (left) and treated with UV light (right). Obtained from: Holick, 2006.

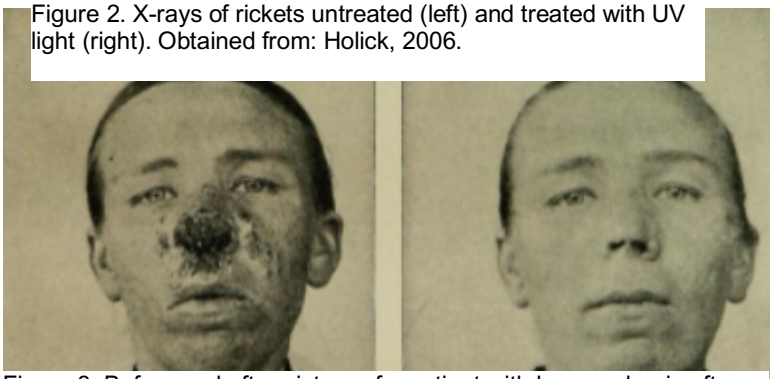

Figure 3: Before and after picture of a patient with lupus vulgaris after undergoing treatment via Finsen light.

Inspired by the 1887 paper written by Downes and Blunt, Finsen set out to apply this phenomenon in living tissue. He reasoned that the causative agent of lupus vulgaris could be killed by sunlight. At first, he used natural light in his initial clinical trials, but eventually developed a lamp that generated bright artificial light via electric carbon

arcs (Grzybowski 2012). The lens of the lamp was made out of regular glass; however, Finsen found that quartz was able to separate the light and form UV rays (Grzybowski, 2012). This lamp later became known as the Finsen lamp (figure 4).

In 1895, Niels Mogensen, a Danish engineer, who suffered from lupus vulgaris, became Finsen's first patient (Gotzsche, 2012). Mogensen had tried a number of treatment methods ranging from various medications to surgery, but none of them worked. However, when exposed to the Finsen light for four days, Mogensen showed dramatic improvements. These results mark the start of the use of phototherapy in dermatology (Grzybowski, 2012).

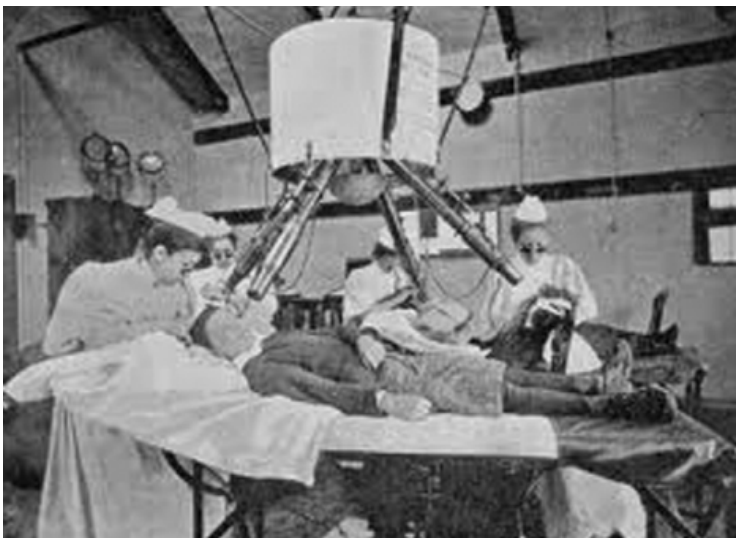

Figure 4: Finsen light used in the treatment of lupus vulgaris.
Obtained from Grzybowski 2012

In 1896, the Medical Light Institute was founded and on August 12, 1896, the first two patients underwent treatment. Over the years, 804 patients were treated for lupus
and the use of Finsen lamps were used for many decades (Grzybowski, 2012). Finsen
gained world recognition for his work which influenced many more pioneers in the field of light therapy. In 1903, Niels Finsen received the Nobel Prize for Physiology and Medicine and is known as the father of photobiology (Liberman, 1991). Around the same time as Niels Finsen, Dr. John Kellogg, who is most known for the invention of Corn Flakes cereal, was also experimenting with light therapy. In 1891, Kellogg created his first incandescent light bath to treat certain disorders such as diabetes, obesity, depression, and fatigue (Kellogg, 1927).

At the start of the nineteenth century, one of the first organized uses of sun exposure was used in the treatment of tuberculosis. In 1903, Dr. Auguste Rollier
opened the first hospital in Switzerland that successfully used sunlight to treat tuberculosis and rachitis by exposing his patients for various periods of time in the sunlight (Roelandts 2002). Following Rollier, two scientists would develop the foundations for modern day phototherapy. Dinshah P. Ghadiali and Dr. Harry Riley Spitler.

Both Dr. Spitler and Dinshah Ghadiali studied and validated the work of their predecessors', Babbitt, Pleasontan, and Pancoast (Liberman, 1991). Dinshah started his work in 1897 and began to examine the chemical elements that makeup living

things. Dinshah, along with Babbitt, also noticed that when a chemical element is in its excited states, it gives of a distinctive spectral emission line, called a Fraunhofer line (Liberman, 1991). Dinshah also observed that when an excited element is exposed to white light, the element would absorb the energy of that light. With this discovery, he reasoned that if excited elements are able to give off light as well as absorb light, then the human body would be able to absorb light as well. He began to study the Fraunhofer spectrums of the elements that comprise the human body to determine their specific color. He reasoned that the color emitted by an element of the body was related to the function of a specific part of the body. After twenty-three years of scientific work and clinical trials, Dinshah developed the Spectro-Chrome system of healing (figure 5). This system had five different colored filters with a normal light bulb that would shine on a specific part of the body (figure 6).

Figure 5: Spectro-Chrome

He theorized that the different colors would aid in the specific elements function in the body (Liberman, 1991). For example, purple was used in conditions related to the heart or reproductive system and indigo was used in the aid of pain, bleeding, and abscesses. (Liberman, 1991). While Dinshah's work was not scientifically proven, those who have used his method have shown it to be very successful. One person was chief surgeon at Philadelphia Women's Hospital, Dr. Katie Baldwin. Dr. Baldwin used the Spectro-Chrome light on her patients for many years and found that by using the light, she was able to produce quicker and more accurate results with colors than with medicine alone.

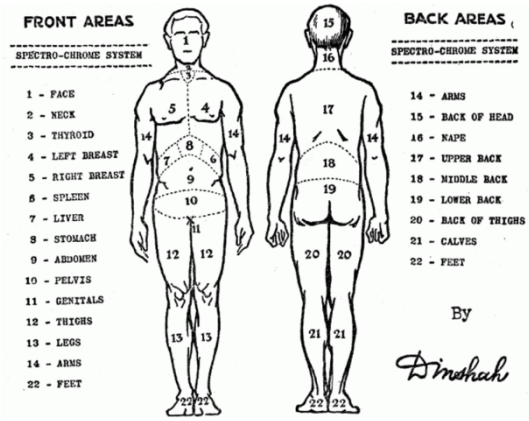

Figure 6: Dinshah's Spectro-Chrome chart.
Obtained from Liberman 1991

During the same time Dinshah was developing the Spectro-Chrome system, Dr. Riley Spitler was developing his theory of Syntonics, in which he used light to treat the body through the eyes. In 1923, he began experimenting on rabbits that were living in various colored environments. After 18 months, Spitler began to notice that some of the rabbits

began to have abnormal side effects, such as loss of hair, digestive problems, as well as sterility. Spitler knew that there were imbalances in the autonomic nervous system as well as the endocrine system. He concluded that the part of the brain that controls the autonomic and endocrine system is also connected to the eyes (Liberman, 1991). While environment, nutrition, and exercise play a major role in our lives, based on the research from Spitler, light might play the most significant role in altering our bodies function.

In 1927, Spitler began to develop the first light-dispensing device for ocular therapy. His medical and optometric degree helped him realize that ocular light therapy could enhance the various control centers in the brain. Spitler was not focused on the color of light used, but rather the frequency of the different colors of light. He created a treatment system based on the fact that not all individuals process light the same way. The principles that Spitler created are known as Syntonics, which refers to creating a physiological balance in the nervous system (Liberman, 1991). When Spiller's methods are applied via the eyes, Syntonics automatically brings the bodies functions into balance with the environment, which results in better vision. In 1933, Spitler, who is known as the father of colored light therapy, developed the College of Syntonic Optometry, which is at the forefront of research in ocular phototherapy.

During the 1940s, Dr. Emmitt Knott began to further the research of Dinshah and Spitler. Instead of focusing on one part of the body, Knott administered light to the whole body by radiating blood with UV light. A small of sample of blood was radiated through his haemoirradiation machine (figure 7) and then transfused back into the body, this treatment is known as Ultraviolet Blood Irradiation (UBI).

Knott used UBI on his first patient who had sepsis and within 24 hours, the patient was cured. By 1942, over 80,000 patients were treated with UBI with a success rate of 95%.

Figure 7: Knott's hemoirradiator machine

After World War II, when antibiotics started to become available, the use of light therapy started to become more and more unpopular. Treatment of diseases that could not be supported by scientific fact were considered doubtful. However, things began to change around the 1960s. With the invention of the laser in 1960, Endre Mester, a Hungarian physician began to use lasers in the treatment of malignant tumors. In 1965, Mester implanted tumor cells in the skin of mice, exposed them to a high-powered ruby laser, and expected the laser to destroy the tumor cells (Gaspar, 2009). However, to his surprise, Mester noticed that the incisions made on the skin began heal faster when exposed to light. Instead of destroying the tumor, the laser promoted tissue growth. This discovery opened up the field of monochromatic light therapy. To further his research, Mester began to expose burns, skin defects, and

diabetic ulcers to red light and observed that these wounds healed faster when exposed to light. Since Mester discovered the healing power of red light, he found that light between 600 to 1,000 nanometers was found to be the most beneficial (Gaspar, 2009).

This range of wavelength has been shown to promote the healing of muscle, bone, nerves, and skin. Endre Mester is accredited with the discovery of low-level laser therapy, now known as photobiomodulation (Gaspar, 2009).

In 1970, Dr. John Ott began to experiment with the growth of plants under various types of light. He found that plants grew best when exposed to a full spectrum of light. With this discovery, he focused his research on using full spectrum lights and the effect they had on human physiological functions. Ott discovered that the color temperature of lights has beneficial effects on mental health, behavior, and academic performance.

In the 1990s, there was an increase in the use of low-level light therapy. In 1996, Michael Conlan began to research the effects of near-infrared laser light therapy on wound healing (Conlan et al., 1996). Also in the 1990s, NASA began researching the

effects of light emitting diodes (LEDs) on wound healing. Their results show that when exposed to LED, there was a 140-200% increase in cellular growth in mouse muscle and skeletal cells (Whelan et al., 2001). They concluded their results would greatly increase the healing time of wounds when this application is applied to humans.

While Finsen was able to treat lupus vulgaris with his Finsen light, it was not until the early twentieth century that reports of light therapy was used in the treatment of cancers. This therapy is known as photodynamic therapy (PDT). Photodynamic therapy is a type of treatment that uses light and a photosensitizing agent to cause cellular death (figure 8). (Ackroyd et al.,2001). It is mainly used in the treatment of cancers

particularly lung, skin, and bladder, as well as in non-cancerous conditions, such as aged-related macular degeneration (AMD), psoriasis, and even herpes. Along with photobiomodulation reports of PDT can be traced back to the ancient Egyptians. They were able to cure vitiligo by ingesting plants containing light-activated psoralens, which absorb ultraviolet light. However, it was not until 1900 when a German medical student by the name of Oskar Raab discovered that paramecia were able to be killed when exposed to various types of dyes. He and his mentor, Dr. Herman von Trappeiner, were studying the effects of acridine on the protozoa that cause Malaria when they found that the combination of acridine red and light had a lethal effect on a paramecium (Ackroyd et al., 2001). Raab went on to discover that the combination of acridine red and light were stronger than either substance alone. It was through this experiment that Raab discovered the optical property of fluorescence and concluded that a transfer of energy caused the lethal effect from the light to the chemical substance.

In 1903, Trappeiner, along with a French dermatologist named Jesionek used a combination of topical eosin and white light in the treatment of skin tumors (Ackroyd et al., 2001). Trappeiner went to further describe the requirement of oxygen in photosensitization reactions. The first reported use of human photosensitization with porphyrins was in 1913. Fredrich Meyer-Betz injected himself with 200 mg of hematoporphyrin and experienced pain and swelling when his skin was exposed to sun light (Ackroyd et al., 2001). In 1924, Policard was the first to demonstrate the localization of a fluorescent porphyrin in a tumor. He observed the red fluorescence of a porphyrin in a rat sarcoma when exposed to the ultraviolet light from a Woods lamp (Ackroyd et al., 2001). The history of PDT remained dormant for several years until 1960, when Lipson and Schwartz demonstrated that a hematoporphyrin derivative (HpD) was able to cause

fluorescence in neoplastic lesions during surgery (Sibata et al, 2000). Using light irritation for tumors marked the beginning of photodynamic therapy as a treatment option for cancer (Sternberg et al., 1998).

In 1972, following Lipson and Schwartz, Ivan Diamond proposed that hematoporphyrin might be able to serve as a selective photosensitizing agent in the treatment of cancers when exposed to light (Diamond et al., 1975). Diamond et al studied the effects of white light activation of hematoporphyrin on glioma cells both *in vitro* and *in vivo*. They observed when cells were exposed to white light for 50 minutes hematoporphyrin caused 100% cellular death. Diamond et al observed similar results in their *in vivo* experiments; tumor volume was suppressed for 10 to 20 days after exposure to white light (Diamond et al., 1972). From these experiments, they concluded that PDT offered a new approach for the treatment of brain tumors and other forms of cancer that are resistant to other forms of treatment (Ackroyd et al., 2001).

A major milestone in the history of PDT occurred in 1975 when Thomas Dougherty and colleagues reported the complete cure of a tumor following administration of HpD and activation with red light. Dougherty et al administered mice 2.5 – 5.0 mg/kg of HpD and exposed them to red light for three hours a day, over a five-day period. Their results showed that 48% of the mice were cured of their tumor (Ackroyd et al., 2001). Following Dougherty's work, in 1976, Kelly and Snell were the first to use porphyrin based-PDT in the treatment of bladder cancer in humans. Their results showed that fluorescence was only seen in malignant and premalignant areas of the tumor, indicating that HpD could be used in the diagnosis and treatment of bladder cancer.

In 1978, Dougherty set out to use HpD to treat twenty-five patients with 113 various types of cancers. His results showed that of the 113 cancers treated with HpD and exposed to red light, 98 lesions completely degenerated and 13 partially degenerated (Dougherty et al., 1978). This study demonstrated that photodynamic therapy was able to be successfully used in the treatment of various malignant tumors. Since Dougherty and Kelly, there have been a myriad of studies showing the effectiveness of PDT in the treatment of tumors.

In 1993, the first photosensitizer, Photofrin, was approved for clinical use in the treatment of bladder cancer in Canada and eventually in the United States. While there are only a few photosensitizers that are being used in the treatment of cancers, such as Levulan and Visudyne, Photofrin remains the sensitizer with the most indications for use. The largest study that was performed with Photofrin was on the condition known as, Barrett's esophagus, an abnormal change in the cells of the esophagus. Barrett's esophagus also has a strong association with esophageal cancer.

In 1999, Overholt et al treated 100 patients with dysplastic Barrett's esophagus using photodynamic therapy. His results showed that PDT, along with exposure to light, was able to eliminate Barrett's mucosa in 43 patients, and 80% of patient's mucosa returned to normal epithelium. Various clinical trials have shown the success of PDT in the treatment of cancers in the skin, head and neck, oral, and other nonmalignant diseases (Overholt et al., 1999).

From sunlight to high powered lasers to specific molecules that target tumors, the evolution of light therapy has progressed exponentially. While light therapy can treat a variety of conditions ranging from wounds to rickets to cancer, this field of science is still being explored. New photosensitizers are being researched for photodynamic therapy. These are intended to have an increase in tumor selectivity, a decrease in side effects such as the duration of photosensitivity. Research is also being explored into the efficacy of light delivery into various tissues and a better understand of the optical properties of various tissues. Advances in low laser light therapy (LLLT), or photobiomodulation (PBM) are also being researched, which will help widen the application of this type of therapy in medicine. Such advances are the use of PBM in hair regrowth, the treatment of strokes, spinal cord injuries, as well as degenerative nerve diseases. With so

many advances being made in both fields of light therapy, the day might not be far off when light sources will be common in homes and used for the treatment of joint pain, cuts, aches, and bruises.

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