Phototherapy: Treatment With Light

"In the next 10 years, light will become as important as drugs"

This is the second of two articles on photobiology. Last week's dealt with basic research into the effects of light on organisms. This week's focuses on clinical applications of light.

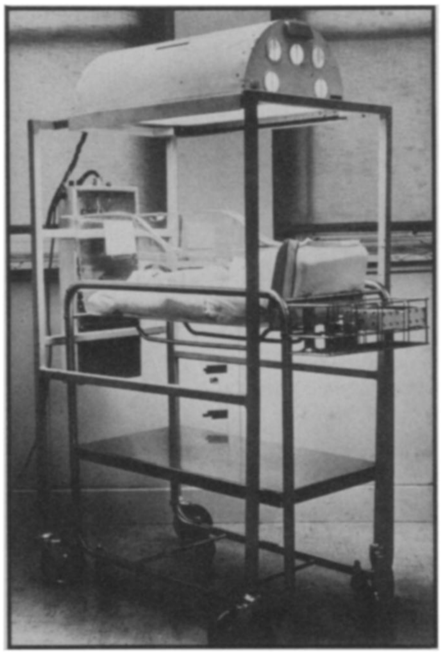
by Dietrick E. Thomsen

Light is associated in human psychology, religion and folklore with everything that is good, beautiful and health giving. Light can do us good physically as well as spiritually, not only in terms of our general health but as a therapeutic agent for specific conditions. A number of particular therapeutic applications of light are under development, and the future is likely to see more. Says Thomas P. Vogl of the Westinghouse Research Laboratories in Pittsburgh and Columbia Presbyterian Medical Center in New York, "In the next ten years light will become as important as drugs."

Yet light is so commonplace that it has largely escaped the attention of physiologists. Only now are biologists studying the effects of light on living organisms, and very little is yet known about long-term effects of exposure to light and other possible hazards of phototherapy. Sanguine as he is about the prospects, Vogl cautions: "I believe that if light came in gelatin capsules, the FDA would not, for better or for worse, permit the routine clinical use of phototherapy in view of our limited knowledge about the mechanisms and effects involved."

It might also be remarked that we know very little about how aspirin works and we do know certainly that misused aspirin can kill, yet we don't even need a prescription to get it and swallow it at will. Light is even more ubiquitous than aspirin and easier to get, and in spite of any lack of knowledge, it is being used therapeutically day in and day out because it does things that are needed and beneficial.

Lasers might be called the Robert Redford of phototherapy. They have glamour, zap and pizzaz; they do dramatic things, and their medical uses have been publicized from time to time. Less well publicized and less dramatic, but perhaps more surprising are the therapeutic effects of ordinary sunlight and fluorescent light. One expects much of lasers. It is in their nature to do prodigious things; on the other hand there is evidence that run-of-the-mill fluorescent bulbs can be used to do such things as help shrink tumors.



Over-the-bassinet phototherapy unit.

To start from the natural and proceed to the artificial, let us begin with sunlight and bilirubin. Bilirubin is a yellow dye. It is the product of the breakdown of red blood cells that goes on in the body all the time. In adults this is usually no problem; the liver excretes the bilirubin.

In newborn babies it can become a difficulty. Because the liver is immature, bilirubin builds up in the blood. A large number, maybe a majority, of newborns develop jaundice in the first few days of life, says Vogl. In some babies this can cause serious problems. Bilirubin is fat-soluble and causes blood and brain damage. It can lead to cerebral palsy and even death.

In 1958 a doctor in England named Cremer found that babies laid in bassinets near windows became less jaundiced than those in darker parts of the nursery. Test-tube experiments showed that the blue portion of the spectrum could deal with bilirubin. Out of this came a procedure that is the first large-scale application of light as a clinical tool, as a pharmaceutical agent, says Vogl. Characteristically the infant is exposed to eight or ten fluorescent tubes about 20 or 30 inches away. Phototherapy is becoming increasingly popular: Roughly 10 percent of the infants born in the United States are exposed to this treatment.

Questions arise. We know that light reduces serum bilirubin at least in the first millimeter of skin. We do not know the chemical details of the process nor what the breakdown products are and how they affect the baby. "We don't know what light does to infants," says Vogl. We do know that in simple systems—which are bad models for living babies—light at these intensities has a profound effect on the development of cells.

Still "no serious short-term effects have been found," says Vogl, and the only alternative treatment is an exchange transfusion, in which all of the baby's blood is replaced. This is a procedure that Vogl characterizes as "not without risks." The chance of disaster is about one-tenth of a percent in big medical centers where such transfusions are done frequently. In small hospitals, where many babies are born, the personnel are less practiced at exchange transfusions and the risk is "much higher." Phototherapy is a tempting alternate treatment.

Long-term undesirable effects, if there are any, have yet to show up. One way of possibly minimizing any adverse long-term effects is to decrease the total light exposure by using intermittent instead of continuous phototherapy. There is evidence that it takes a few hours for the bilirubin to move in and out of the bloodstream from the skin, and this is an argument that intermittent exposure may be as effective as continuous exposure.

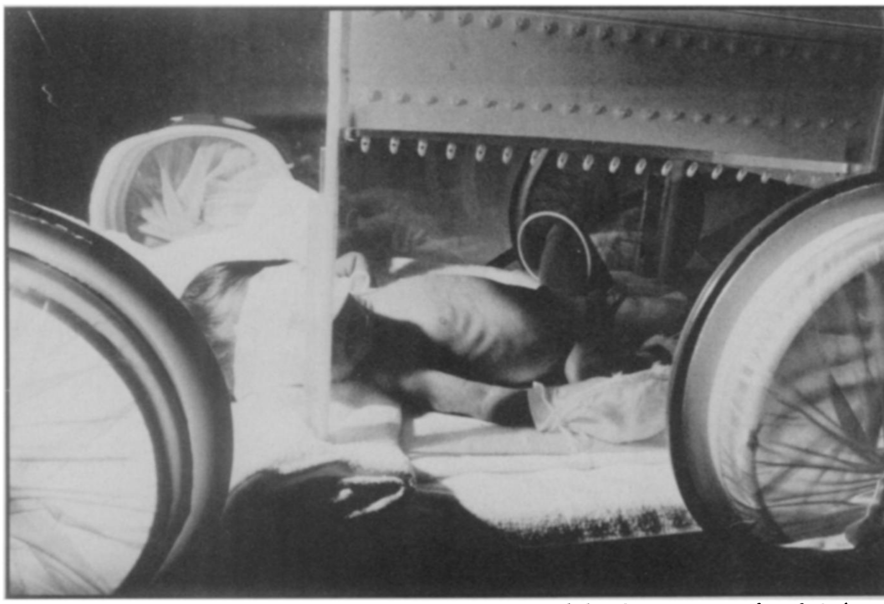
Vogl's summary opinion is that "unfortunately, the experiments which we and others have done just scratch the surface of the problem, and many more, carefully executed, experiments are required before the safety and best way of administering phototherapy is conclusively determined."

Bilirubin is one example of the important role that dyes play in photobiological processes. Porphyrins are another. Porphyrins are a class of dyes that render living tissue extremely sensitive to light. Porphyrins catalyze the singlet state of oxygen, and the singlet oxygen reacts with proteins in a way that is damaging to tissue. Patients who have ingested excess amounts of porphyrins can suffer severe skin lesions and even death on exposure to light. Sometimes they have to stay indoors for weeks or even months until the porphyrins are metabolized away.

Can such a property be used to do away with tissue that one doesn't want? The answer is, yes, it can be used to reduce tumors. The work is described by Antony F. McDonagh, who speaks for himself and five others, all of the University of California Medical School at San Francisco.

There is a porphyrin, hematoporphyrin, that accumulates preferentially in malignant tissue. Exposure to light then tends to destroy the tissue. McDonagh suggests that such a procedure might be used on tumors untreatable by other means, inoperable tumors of the brain for example. Often tumors of the brain can't be removed without damaging the brain.

So McDonagh and his associates, Ivan Diamond, Steven G. Granelli, Surl Nielsen, Charles B. Wilson and Richard Jaenicke, started with a test-tube study of the effect of light and hematoporphyrin on cells of rat glioma, a tumor of the rat's brain. They used a bank of four to eight 20-watt fluorescent lights located one foot above the cells. In eight minutes all the cells in the sample were dead. The effect turned out to be less as the dosage of the drug was less, but the rate of uptake of the porphyrin did not bother the process. Neither porphyrin alone nor light alone had any effect. Only the combination.


Photos: Thomas R. C. Sisson/Temple Univ.

Inside-the-incubator phototherapy unit to reduce bilirubin in jaundiced infants.

In studies with living animals, glioma cells were injected into their flanks. This is a way of getting a brain tumor on the leg. For experimental purposes that is a good place to have one because it is exposed; its diameter can be measured and its volume calculated. The experimenter can get some quantitative idea of what he is doing.

After three to five hours illumination there was a striking difference in the volume of the tumor, says McDonagh, but "we haven't been successful enough." It doesn't kill all. The kill rate is 75 to 90 percent. Cells on the rim of the tumor farthest from the light can survive, and the tumors will regrow. But they were using "a puny light source." They increased the power of the source to 5,000 watts. Then 40 minutes exposure killed 90 percent of the tumor. "One rat had no viable tumor cells left," McDonagh reports. Experimentation continues, but the conclusion so far is: "Photodynamic therapy offers a new approach to the treatment of brain tumors and other neoplasms resistant to existing forms of therapy."

Finally, but by no means least, there are the lasers, the glamour boys of phototherapy. Unlike puny, 20-watt bulbs, they provide coherent, highly intense burst of light. Much of their work is of the "Zap! You're disintegrated" character. They are becoming an important surgical tool; they do some things knives can and some things knives can't. Some of their current applications are described by Donald E. Rounds of the Pasadena Foundation for Medical Research in Pasadena.

Ophthalmology was one of the branches of medicine first to apply lasers. Much publicity has been made about the lasers ability to spot-weld detached retinas, reattaching them to the back of the eyeball. Lasers are also useful in other retinal problems such as retinal edema and a disease of diabetics in which new capillaries form on the retina and become engorged with blood and interfere with sight. The capillaries often rupture and release blood into the eye. Laser light can destroy them. A great advantage, of course is that these retinal therapies can be accomplished without cutting into the eye.

The ability of laser light to destroy blood-engorged capillaries leads to a use in dermatology, the eradication of port-wine marks. These are a frequent kind of birthmark, in which capillaries just under the skin become engorged with blood, forming a mark with a purplish color. Laser light can erase them. Lasers are also better than sanding for getting rid of tattoos.

There has been some experimental work, says Rounds, on treating pigmented tumors, melanomas, with laser light. But the destructive action of lasers on tissue is explosive. The light causes a sudden rise in temperature that vaporizes water. The steam blows the tissue apart. Applied to melanomas, high-energy laser light tends to create airborne tissue and spread tumorus matter around. This is undesirable so, says Rounds, high-energy lasers may not be the way to go in treating melanomas.

There is a growing use of far-infrared carbon-dioxide lasers as substitute for surgical knives. The laser beam can cut tissue like a knife, and the incision is bloodless because the laser light seals blood vessels as it goes. It can also be used to vaporize tumors in places where it would be difficult to use a knife on them. Furthermore use of flexible light guides can deliver laser energy to natural body orifices where it's difficult to reach. Using a tube in the throat surgeons can burn polyps off vocal cords—literally burn them. "A great deal of smoke comes off," say Rounds. The treatment destroys the tumor but leaves the surrounding tissue, which heals readily.

From light bulb to laser the medical applications of light seem likely to increase as time goes on. As they do, they will create a necessity for a great deal of pure scientific work in photobiology. As Vogl points out, for maximum efficacy and safety in phototherapeutic procedures scientists must understand the details of how light interacts with physiologically important substances. □