

THIEME FLEXIBOOK

Photo- chemotherapy

Information for Doctors and Patients

Gerhard Weber

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Gerhard Weber

Photochemotherapy

Information for Doctors and Patients

Translated by Gerhard Behr

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Foreword

This monograph heralds a new way of treating skin disease. Written in a lucid, personal style by an internationally recognized pioneer in this field, it is a welcome and much needed translation of a volume which originally appeared in German. It presents the vast experience Professor Weber has had in treating several thousand patients with the combination of a special band of ultraviolet light and complementary chemicals. Holding firm to the tenet that a well informed patient is essential to real therapeutic success, Professor Weber has written for the patient as well as the physician. It is thus a book unique not only in subject matter, but in its dual presentations for both patient and doctor.

Photochemotherapy is a burgeoning field. A whole industry has sprung up to respond to the demand for radiant canopies, cabinets, boxes and screens. Originally concerned with psoriasis, this new form of light therapy has extended its usefulness to other diseases of the outer sheath of the body, viz. vitiligo, mycosis fungoides, atopic dermatitis and, most recently, urticaria pigmentosa. Known under the acronym PUVA, its effects largely stem from the selective psoralen-ultraviolet light band A, induced damage to DNA. As with all therapies, both the physician and the patient should know its hazards; premature aging of the skin, as well as carcinogenesis. It is too early to assess these or other untoward effects, but Professor Weber gives a solid and fair appraisal of the knowledge at the time of his writing.

All of the subject material is presented in the forceful fashion of one who not only has treated psoriasis in all its forms, but who has personally experienced the clutch of this disease. The result is a practical book for not only physician, but patient, written with verve by one who is both.

Until recently, the physician has recognized and dealt only with the harmful effects of the interaction of light and chemicals within the skin. Professor Weber's work introduces us to the converse of this. In his book he skillfully teaches how to heal by the felicitous conjunction of near-ultraviolet light and photoactivated psoralens. All this is graced by scholarship, experience and historical sense. Here is a manual that deserves the wide readership accorded to the new, the practical, and the significant.

Philadelphia, March 1980

WALTER B. SHELLEY, MD

Preface

When the Egyptian dermatologist Abdel Monem El Mofty discovered in 1947 that the extract of a plant which grew wild on the shores of the Nile would cure the pigment defect of vitiligo after exposure to the sun, he did not foresee the far-reaching effects of his discovery. Twenty-five years of research throughout the world were needed to uncover the secrets of this method of treatment and to establish photochemotherapy. Dermatologists of many countries examined the potential of photochemotherapy. The collected results justify the conclusion, that the value of this new form of therapy is still inestimable. Several dermatoses which formerly were incurable or extremely difficult to treat can now be cured or cleared for prolonged periods by photochemotherapy. There can be no doubt that it is the greatest advance in dermatological therapy since the discovery of cortisone. Nevertheless, an exact understanding of photochemotherapy by dermatologists is necessary to ensure optimal results and to avoid side effects. The patient also must be well informed to be able to contribute to his cure. The large number of publications indicates that photochemotherapy is not a simple subject and that specialized knowledge is necessary. This book aims at giving the scientific facts, describing the available technical equipment and discussing the effects and side effects of the medication used. Patients and doctors should learn all the known facts, since photochemotherapy is not a secret science but the fascinating result of centuries of progress with a single aim: to cure skin diseases.

We wish to express our sincere gratitude to the publishers, Georg Thieme, for their valuable assistance in making it possible to provide doctors and patients with comprehensive information on this important subject, and to Dr. G. Behr who did his best to meet my wishes in the translation.

Nürnberg, 1978

GERHARD WEBER

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Introduction

In the last 20 years medicine has made more progress than in the previous century. This can be recognized by the discovery of antibiotics, cortisone, chemotherapy for cancer and the groups of drugs used in the treatment of diabetes and hypertension. The present generation of doctors uses as a matter of course modern diuretics, the artificial kidney and infusion therapy. Each of these examples owes its development to a process that started with the discovery of a new substance in nature or in the test tube. Intention and chance were of equal importance in the collection and testing of many hundreds of soil samples from all over the world to find a new and highly effective antibiotic, or when chemical synthesis produced a substance that unexpectedly proved to be a diuretic of unrivaled effectiveness and tolerance. However, it always takes a long time to develop a new synthetic or natural material into a drug for routine application.

An exception to this rule for the production of new medications is a form of treatment that we call "black light" or "photochemotherapy." It is unique in every way. This therapeutic principle was not discovered by systematic research, in the chemist's test tube or in the numerous laboratories of the pharmaceutical industry, or in the university departments of pharmacology. Many independent discoveries stretching over centuries were needed to produce in photochemotherapy a new method of treatment for several skin diseases.

The difference may be due to the fact that the effective principle of black light treatment is not a single substance or a combination of medications. On the contrary, there is a combination of two unconnected components. Both of these existed in nature, but were unrelated to each other and showed no indication of therapeutic usefulness to man. One component is the vegetable substance 8-methoxypsoralen; the other is a kind of radiation belonging to ultraviolet light A, which previously had no practical medical importance.

Combined effects of light and biological substances have been known for a long time. Light is the basis of vegetable and animal growth. A typical example is the photosynthesis of chlorophyll. Light and chlorophyll together produce the growth of plants in nature. More than 100 years ago, man began to use such natural processes, where light and photochemical substances are combined to form the basis of photography. A few decades later, Roentgen discovered x-rays and the process where invisible light, i.e., short wave radiation and photosensitive substances, are used to demonstrate the contrast between bones and soft tissues of the body. Then, half a century later, television, which is based on a photochemical principle, was developed. But, until recently, medicine has not been able to make therapeutic use of photochemistry.

● The Oriental Discovery

How did we come to discover black light or photochemotherapy? More than 2000 years ago, the ancient Egyptians found the drug in the seeds of a plant, and some 10 years ago the light source for ultraviolet A was discovered in the United States. It is fascinating, however, that light and plant extract can only produce an effect in the presence of human or animal cells. Such an effect does not otherwise exist in nature. We therefore need three components—light, the plant extract 8-methoxypsoralen and the human cell—to demonstrate the existence of a previously unknown principle, photochemotherapy, which is of great importance for the restoration of human health. It can be said without exaggeration that the value of this therapy and its consequences, is still inestimable.

All it took for this unknown principle to be discovered was the awareness and interest of an Egyptian dermatologist, with no aid from the potential resources of industry. Thus, while years usually pass before all the possibilities and effects of a medication can be recognized, this delay was avoided. Two doctors, a German and an Iranian, were able within a few months to discover the essential therapeutic possibilities of black light. It is important to mention that the academic establishment for years ignored the obvious possibilities of black light therapy, in spite of the fact that 10 years previously American research workers had discovered that the substance 8-methoxypsoralen, from the Egyptian plant *Ammi majus* Linn., could be stimulated to a photobiological process by ultraviolet light A.

Why a Book for Doctor and Patients?

This exciting story of the origin of a new form of treatment might have remained unwritten, like so many other tales of medical science. However, the valuable opportunity was seized to explain to patients with skin diseases the nature of the disease and the new method of treatment. It may be questioned why the patient must understand this particular treatment. In contrast to other therapies, which produce an improvement or a cure of a skin disease without any essential contribution by the patient, photochemotherapy is dependent on the patient's cooperation and will not be successful without it.

After many conversations with my patients, I am convinced that black light therapy changes the doctor/patient roles without devaluing them. The patient, who in the true sense of the word is usually "patient," must become an active collaborator if success is to be achieved. But the doctor must exercise forbearance and treat each one of his patients as an individual and not according to a "three times a day" routine, a routine that has proved effective with other medications. This peculiarity of black

light or photochemotherapy is due to its individual application and the related reaction of disease and patient. This is the difference from other methods of treatment, which progress more or less without the patient's collaboration. For example, a penicillin injection will be effective if the organisms it is supposed to destroy are penicillin sensitive. In this case, the patient cannot contribute to his cure. Photochemotherapy, however, loses a large part of its effect if the patient is uncooperative. To avoid this, I have utilized knowledge and discernment, questions and answers of doctor and patient, so that both can attain the basis for optimal photochemotherapy. As in many other disciplines, it often happens that a doctor uses professional jargon. This is not an attempt at mystification of an obscure situation; rather, it is useful for international communications among doctors. On the other hand, it is often necessary to explain to the patient those events, incidents or symptoms of his disease or treatment that are familiar to the doctor. To facilitate the reading and thereby the comprehension of this book, each section that is meant mainly for patients has been marked with a circle (●), and those sections containing technical or professional information primarily of interest to doctors have been marked with a square (■). Chapters of general interest are not marked. I do not find it difficult to speak the language of both the doctor and the patient, because I have long been a patient and I am a doctor. My main task is, by a comprehensive explanation, to unite doctor and patient in collaboration with the aim of curing skin diseases.

The History of Photochemotherapy

● Abdel Monem El Mofty

It started on an early summer day in 1947 when two women came to consult the Egyptian dermatologist Dr. Abdel Monem El Mofty. They lived in the country near the shores of the Nile and had come to Cairo for treatment of their skin disease. This was a common occurrence, as neither of these patients was suffering from a serious or rare disease. But one thing attracted the doctor's attention. Apart from their rather trivial complaints, both women showed numerous irregular whitish patches which contrasted with the naturally dark skin of the fellahin women. For the experienced dermatologist, it was easy to diagnose vitiligo in both patients. This is often erroneously called "white-spot disease" by the general public, but to the dermatologist it means a different, more serious disease (lichen sclerosus). Vitiligo is caused by inability of the human skin to form the pigment melanin. Therefore the affected skin remains white and even the strongest sunlight will not produce any tanning. El Mofty had seen hundreds of such patients in his medical practice and had to tell

them that an effective treatment did not exist. He was surprised that neither of the two peasant women complained that the vitiligo impaired her appearance.

As he thought about this, he noticed that the white skin patches of one of the women contained brown, round or oval, partly confluent pigment spots. Also the surrounding healthy skin was darker brown than any he had ever noticed in such patients. El Mofty did the obvious. He compared these changes with the skin of the other patient, and with increasing excitement he noticed again the unusual over-pigmentation of the normal skin which surrounded the diseased patches. El Mofty was not surprised that the diseased skin of these patients had partly started to become brown again. Such spotty tanning of the white areas can occur spontaneously, but never at the same time as increased tanning of the surrounding healthy skin. At this moment, El Mofty was aware that the whole situation was unusual. It was unusual that both women had consulted him not because of the vitiligo but because of relatively trivial skin diseases. Vitiligo has no “disease value”; it does not diminish an individual’s physical powers in any measurable or recordable way. But it has a lasting psychological effect that can lead to severe depression. The piebald discoloration of the skin, which becomes more obvious if the normal skin is darkly pigmented, is a permanent stigma in colored subjects. In our latitude, vitiligo is a problem only during the summer months when after sunbathing the contrast with the tanned normal skin becomes noticeable. Anyone who has heard the complaints of these patients knows that the common textbook description of the disease as a “cosmetic lesion” is a serious understatement.

Since these two women did not consult El Mofty because of their vitiligo, obviously they did not consider the disease a problem – perhaps because both of them showed signs of repigmentation. But could such a rare event occur twice on the same day?

These considerations stimulated El Mofty to a comprehensive interrogation of the patients, which led to a series of actions that resulted in surprising discoveries and the beginning of photochemotherapy.

● The Plant *Ammi majus* Linn.

The women told El Mofty that they suffered little anxiety from the depigmentation of their skin, as everybody in their village knew a treatment that would help them when new patches appeared. It was only necessary to eat the seed of a plant that grew on the shores of the Nile. To be sure, it was necessary to expose the skin for a day afterward to the sun. Blisters, which hurt, would then form on the white skin. When they healed, the skin would be lightly tanned. We know today how thin was the thread on

which at this moment the discovery of photochemotherapy depended, because only one in five patients with vitiligo shows improvement through eating the seeds of the plant and exposing the skin to sunlight. Chance had introduced to El Mofty simultaneously two patients with resolving vitiligo. This occurrence and his acute observation enabled him to seize that chance. Undoubtedly, doctors and healers had for centuries ignored such cases of diseased skin because they lacked the Egyptian doctor's awareness and opportunity.

Doctor El Mofty's work stimulated a frenzy of research all over the world, but in 20 years it failed to produce any further understanding than he had gained during the first two years of his work. Chance had chosen this doctor, alone and at that moment, to make his discovery. However, another 25 years were to pass before the real value of his discovery was recognized, when two other doctors, an Iranian and a German, discovered the great possibilities of photochemotherapy and presented it for use in dermatology.

Doctor El Mofty told me that, after his conversation with the fellahin women, he sent for the plants and seeds to have them classified by a botanist. Further developments proved that the doctor was now fully equipped to explore this therapeutic principle and to promote its use under modern medical conditions.

● The Treatment of Vitiligo in the Middle Ages

The examination of the plants and seeds at the Botanical Institute of the University of Cairo showed that they were umbelliferous plants, common in the delta of the Nile and known under the name *Ammi majus* Linn. When studying the sources of older Egyptian medicine, it was surprising to find that in the 13th century Ibn El Bitar had described this plant in his book *Mofradat al Adwiya* under the name *Aatrillal*. This is a Berber word that means "bird foot." It is identical with the Egyptian name *Regl El Ghorab*. Galen had already called it *Ammi*, while during the time of Charlemagne it was known as *Ameum*. It was of extreme medical interest to read in Ibn El Bitar's text that the seed of this plant was used in northwest Africa for the treatment of vitiligo and similar loss of pigment of the skin. His prescription reads: "Mix 1 derum (about 3g) of the powdered seeds with less than 1g of a pellittar root and honey, and take it by mouth." After this the patient had to expose the affected parts of the skin to sunlight for one to two hours until they began to perspire. After this treatment blisters would form, but not on the healthy skin. Under the burst blisters the skin would soon regain its normal color.

The Egyptian Discovery

Not content with these past discoveries, El Mofty persuaded the Egyptian pharmacologists Fahmy and Abou Shady to examine the *Ammi majus* seeds. They succeeded in the same year, 1947, in isolating three crystalline substances from the powdered seeds. (1, 15, 17) They had different chemical structures and, in connection with the name of the plant, they were called ammoidin, ammidin, and majudin or bergapten. (16)

El Mofty's publication about a new treatment of "white-spot disease" in 1948 in Egypt (49) and in the following years in many dermatological journals (50–55) was a medical sensation, and because there was no known cure for vitiligo it was checked in many places. (10–12, 29) Then followed an intense preoccupation with these substances from the plant *Ammi majus* Linn., (21, 47) firmly based on the analytical work of Fahmy (15–17) and Abou Shady. (1) El Mofty writes later about this race for new discoveries in dermatological research: "There have been more publications about light and its effect on the skin in the past 15 years than in the previous 50 years." (55) The American authors, especially Fitzpatrick, Fulton, Lerner and Pathaks (18, 19, 23, 47, 77, 79, 80) worked on this problem, basing their efforts on previous research. The Swiss dermatologist Kuske (44) was the first to recognize in 1938 that the group of drugs of furocoumarins produced an increased photosensitivity of the skin. The three substances of the plant *Ammi majus* Linn. belong to this group. Independently, El Mofty found (56) that brown patches appeared on the hands and face of an assistant who was occupied with the preparation of these plant extracts. This proved to be a stimulus for him to try topical treatment with these vegetable substances. Everywhere in dermatology, interest was concentrated on the treatment of vitiligo and similar lesions of pigment formation, (40, 41, 47, 94) but eventually hope of finding an effective treatment had to be abandoned. The findings of El Mofty were not fully confirmed in the northern, less sunny countries. The number of treatment failures was much higher than in the Egyptian series. After a relatively short time, two reasons were found for this: the lower intensity of the sunlight in northern latitudes, which did not produce a full effect of 8-methoxypsoralen, and the lighter skin of the Middle and North Europeans and North Americans, where the treatment produced an unexpectedly violent reaction in the healthy skin. In other words, the light skin of Europeans is more sensitive to the effect of 8-methoxypsoralen and sunlight, and therefore the recommended treatment for vitiligo must be interrupted, or even discontinued, with the result that the full therapeutic effect cannot be achieved.

The American Discovery

The impossibility of standardizing the vitiligo treatment because of regional differences of sun intensity, as well as the frequent treatment failures, led to a loss of interest by many dermatologists. Fortunately, basic research was not affected by this negative attitude. The search continued for a specific light source that would produce the optimal effect of the photochemical reaction of 8-methoxypsoralen. For this purpose, artificial and therefore standardizable light sources of different wavelengths and intensities were examined. The Americans Fulton, Leyden and Papa (23) were the first to be successful in 1968. In a fluorescent tube whose light was called "black-light-blue" they found a light source that corresponded well in its wavelength to 8-methoxypsoralen to produce an optimal effect on the pigment-forming cells of the skin. These years of expensive experiments only confirmed what El Mofty had discovered in the space of a few months with limited scientific resources. The therapeutic results were not essentially improved by the black light lamp. The treatment of vitiligo was successful in less than 40% of patients. The great advantage of the black light lamp was not only that the serious side effects of natural sunlight could be avoided, but that years later it provided the opening for the enormous possibilities of photochemotherapy.

The Iranian-German Discovery

This was the position of research and black light treatment with 8-methoxypsoralen in dermatology in the early seventies, when all biologists, physicists and dermatologists who had worked on these problems, or at least were interested in them, met at the International Congress in Tokyo in 1972. Excellent lectures were given about physical questions, microscopic findings and problems of chemistry and molecular biology that occurred in connection with the two special factors: light and photosensitizing substances; however, the use of this therapy for any disease other than vitiligo was not mentioned. Chance again selected an Oriental, the Iranian doctor Seyed Abdol Madjid Mortazawi, to prove the real value of the black light and 8-methoxypsoralen treatment and to show the many situations where its use would prove successful.

Mortazawi, assistant chief of the Department of Dermatology of the Municipal Hospital, Wuppertal, was interested in the treatment of vitiligo, since this condition was considered in his country to be leprous. This is probably because the appearance of vitiligo was mistaken for the skin lesions of leprosy. When searching for a better therapy, he came across the work of Fulton, Leyden and Papa, (23) and with the help of his chief, Professor Harald Oberste-Lehn, he used their method on a Turkish patient with extensive vitiligo. He treated his patient with a home-

made version of the American irradiation equipment and 8-methoxypsoralen, according to the instructions of Fulton, Leyden and Papa. (23) The vitiligo improved so quickly and so thoroughly that he could demonstrate it with photographic documentation at the Congress of the German Dermatological Society in 1971 in Berlin. For the Iranian, the result was so encouraging that he decided to try this treatment on other skin conditions.

During his training in the skin department at the Municipal Hospital in Wuppertal he had learned that irradiation with sunlight and ultraviolet light constitutes an old and well known method of dermatological therapy. Of course, heliotherapy or irradiation with ultraviolet light had lost some of its importance in the previous 20 years when different steroid preparations had in rapid succession come onto the market. But two diseases were not much influenced by this: acne and psoriasis. While heliotherapy is used only as supplementary treatment of acne, the importance of phototherapy for psoriasis has never been underestimated or ignored. Every patient knows that his psoriasis can often be improved or cleared up by intensive exposure to the sun. This may be the main reason for the popularity of the Dead Sea as a tourist attraction. Sufferers from psoriasis come to this inland sea in the desert because of the high intensity of the sunlight and the desquamatory effect of its salt water. However, every psoriatic patient also knows that this treatment will produce only temporary clearing. Thus a high price has to be paid for a cure of short duration.

Aware of the advantages and disadvantages of heliotherapy, Mortazawi decided to try the 8-methoxypsoralen (8-MOP)–black light combination in the treatment of psoriasis, hoping that the effect of the photochemical process would be at least equal to, if not better than, sunlight or ultraviolet light. In collaboration with Oberste-Lehn, he started to treat psoriasis with 8-methoxypsoralen and black light. They used five black light tubes, which, according to instructions (23), were mounted side by side on a board and fitted to a support. (59, 70) Mortazawi then painted the lesions of psoriatic patients with a solution of 8-methoxypsoralen and exposed them to black light. These doctors determined the optimal concentration of the medication and period of irradiation (still valid today), as well as the almost ideal incubation time, i.e., the interval needed between the application of 8-methoxypsoralen and the beginning of black light irradiation (57, 60–62). With this primitive apparatus they succeeded in becoming the first men in the history of dermatology to clear up psoriasis with the combination of black light and 8-methoxypsoralen.

When asked to cooperate, I immediately introduced the method in the skin department in Nuremberg. Within three weeks I had designed and constructed a cylindrical black light cabin. It was the first unit of this type, consisting of a 2-m-high vertical metal cylinder that ran on castors. A

hinge made it possible to open the cabin, so that the patient could enter and stand in the center for his treatment. The horizontal diameter of the cabin was 1.5 m. The inside was covered with aluminum foil to reflect the radiation and on it were mounted symmetrically 30 black light tubes of the type Sylvania F20T 12-BLD “black-light-blue.” (117, 118) I had deliberately used a cylindrical shape for the cabin in order to produce a homogeneous, uniform irradiation of the body surface. Within a few months I treated 74 patients with psoriasis in this black light cabin, usually with surprisingly good results. (118)

The year 1972 came to an end. In the meantime, Mortazawi and Oberste-Lehn, impressed by the original success, had worked out instructions for the irradiation dose, the necessary number of exposures and the suitable concentration of the 8-methoxypsoralen solution; in addition, they had discovered the reaction of both diseased and healthy skin to black light irradiation.(62, 71)

In the same year, 1972, Professor Hagen Tronnier, a member of our team, examined the effect of 8-methoxypsoralen and black light on psoriasis and other skin diseases (110) at the skin department of Tübingen University. As a well-known photobiologist, he was able, when he became director of the Municipal Skin Clinic in Dortmund, to devote himself intensively to the new therapeutic principle. Our consistently positive results with psoriasis were also confirmed in the treatment of other skin diseases. Professor Günter Stüttgen, director of the University Skin Clinic of the Rudolf Virchow Hospital in Berlin, began with his associates to examine clinically and experimentally the pharmacodynamic effect of 8-methoxypsoralen on the human skin. (39, 86, 87)

The first publications, in 1972, by Mortazawi about the treatment of “vitiligo, psoriasis, parapsoriasis and acne vulgaris with 8-methoxypsoralen and UVA” (57) did not create much excitement in the world of dermatology. But international interest was stimulated instantly when at the beginning of 1974, my paper appeared in the British Journal of Dermatology (118) on 78 psoriasis patients who had been treated successfully with black light and 8-methoxypsoralen. The numerous requests for information, mainly from the United States, were the best indication of the importance of the newest form of dermatotherapy. The year 1974 saw further development of the method in Wuppertal, Nuremberg and Dortmund. In Nuremberg alone, 500 patients had been treated. Relapses and improvements had appeared. The success was unquestionable. Television and radio reported our success and many patients came to the three centers for the new treatment. The first trials were started in the clinics and in private practice.

The scene changed quickly when, at the end of 1974, the Americans Parrish, Fitzpatrick, Tannenbaum and Pathak (76) reported in the New En-

gland Journal of Medicine that they had treated 21 patients with psoriasis with black light and 8-methoxypsoralen. The results were the same as those reported several times by us in the previous two years in lectures and publications. Our American colleagues had been motivated to try this treatment as a result of their visit to the Photobiological Congress in Bochum in 1972, where Tronnier and Schüle (110) had reported their results with topical black light 8-methoxypsoralen treatment of psoriasis. Mortazawi (59) confirmed the results of Tronnier et al. (110) with reference to his own psoriasis patients where 8-methoxypsoralen had been used either orally or topically before the black light irradiation.

Instead of the topical application of 8-methoxypsoralen, which we normally use, Parrish et al. (76) had given their psoriasis patients 8-methoxypsoralen orally in tablet form before the irradiation. Because the American authors did not mention the originators of the oral therapy, i.e., Od-doze et al. (73) and Mortazawi, (59) the lay press in Europe accepted the "new" therapy of psoriasis as a revolutionary discovery. At this time, over 1000 patients had been treated in the black light centers in Wuppertal, Nuremberg and Dortmund. (70, 82, 106) As a result of the press reports, many of them became insecure and asked if they could receive the "new American treatment." Although the American publication did not contain any new discoveries, it was nevertheless of great value. The method was brought to the attention of the public, and doctors and patients could work more effectively for its general acceptance. The number of scientists and doctors interested in photochemotherapy increased, and interest grew to the extent that prejudices were refuted. In 1975 and 1976 photochemotherapy was introduced, apart from West Germany, into Scandinavia, East Germany, Poland, Hungary, Austria, Switzerland, Italy, Yugoslavia, Bulgaria, Holland, Belgium, France, Great Britain, the United States and Canada, both systematically and experimentally. The number of publications was augmented by new reports. What yesterday was a vague hope is today a reality. Whether the result is successful or otherwise depends not only on the type of skin disease being treated, but mainly on two conditions: first on the cooperation of the patients, which was mentioned earlier, and second on the technical performance of the photochemotherapy. Published instructions failed to prevent repeated mistakes by doctors and patients, as a result of which undesirable side effects or insufficient clearing occurred and so discredited the method. Therefore it is my purpose to describe in detail the important conditions, the necessary "tricks" and typical mistakes, and to keep the doctor and his patients as completely informed as possible.