Clinical Cases in Dermatology
Series Editor: Robert A. Norman

John Koo · Mio Nakamura

Clinical Cases in Phototherapy

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Foreword

Phototherapy is as much an art as science. Protocols that are available here in this book and elsewhere are only rough guidelines. It is important to know various protocols when a clinician is starting out in phototherapy practice, but what is more essential is to pay attention to the variations in patients' responses to light therapy, which, not infrequently, defy the established protocols.

Phototherapy is also an art because there are numerous things the provider can do for the patient beyond the basic application of light. The rich choice of actions ranges from two-step phototherapy to optimize response in more difficult to treat areas such as the extremities, to phototherapy in combination with topical and/or internal medications. As such, this book contains many pearls but also warnings which need to be heeded when a more sophisticated regimen is brought to bear to improve recalcitrant conditions. In short, phototherapy starts scientifically with a more simple, basic regimen, but then the provider can go way beyond the basics through the "art" of this practice.

One disclaimer the authors would like to explicitly state at the beginning is the fact that much of this art comes from a mixture of clinical research data, collective practitioners' experiences over decades, and personal experience of the authors. As such, not every recommendation articulated in this book has the highest evidence-based support such as with worldwide, double-blind, placebo-controlled, randomized clinical trials involving a comparator group. Therefore, knowing that every phototherapy practitioner has his or her own unique demography of patients, geographic locations,

and other peculiarities, it is important to take the recommendations in this book with a "grain of salt" and adapt it to the reader's own unique situation.

Furthermore, this book is not a comprehensive coverage of all photo-responsive dermatologic conditions and mostly focuses on inflammatory skin conditions such as psoriasis and atopic dermatitis, as well as vitiligo, pruritus, and prurigo nodularis. Therefore, the phototherapy modalities covered here are limited to narrowband ultraviolet B, broadband ultraviolet B, the 308-nm excimer laser, and PUVA (psoralen plus UVA).

Phototherapy continues to be a very effective therapeutic modality for many skin conditions, and it is certainly one of the safest options for long-term control of chronic, potentially debilitating dermatologic diseases. If this book can be of assistance to practicing phototherapists anywhere in the world, the authors would be very fulfilled.

San Francisco, California, USA John Koo

Acknowledgments

This book would not be possible without the current and previous phototherapy and Goeckerman nurses at the University of California San Francisco (UCSF) Psoriasis, Phototherapy, and Skin Treatment Center. Our nurses work tirelessly for hundreds of patients who come to our center for treatments. It is an inspiration observing how our nurses truly care for our patients. Through their mastery of the art of phototherapy, which they have graciously shared with us, they have touched and improved the lives of so many of our patients who suffer from chronic, debilitating skin diseases.

This book is a constellation of experiences that has been documented over more than 30 years at the UCSF Psoriasis, Phototherapy, and Skin Treatment Center. It would not be possible without the hard work of current and previous fellows and medical students who have written manuscripts, taken photographs, and passed on their experiences and knowledge for years to come.

Lastly, it is the patience, flexibility, and openness of our patients who share their experiences that have allowed us to practice the art of phototherapy. None of this would be possible without the generosity of our patients.

It is an absolute honor for us to write this "memoir," on behalf of all that has been a part of the UCSF Psoriasis, Phototherapy, and Skin Treatment Center.

Contents

Chapter 1
Ultraviolet B Phototherapy for the Treatment of Moderate to Severe Psoriasis

Case

A 36-year-old male presents to your office for follow up for generalized psoriasis diagnosed 3 months ago. He has tried various topical corticosteroids and topical calcipotriene without much improvement. Not only is the topical regimen very time consuming and not very effective, but it has been nearly impossible for him to apply the topical medication to his entire body alone. He is otherwise healthy and denies history of photosensitizing disorders. He lives and works only a few blocks away from your office, which offers phototherapy.

On examination, the patient has well-demarcated, mildly erythematous and slightly indurated plaques with fine silvery scale scattered over his trunk and extremities consistent with partially-treated psoriasis (Fig. 1.1). He is Fitzpatrick skin type II. You discuss the option of starting phototherapy, including the fact that he would need to come to the office 3 times per week for at least 3 months initially, followed by potential ongoing maintenance treatments once or twice weekly. You also discuss potential side effects of phototherapy including burning or erythema. After the discussion, the patient states he is ready to commit to phototherapy.

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Discussion

Phototherapy involves repeated exposure of the skin to ultraviolet (UV) light to treat various inflammatory skin conditions such as psoriasis, atopic dermatitis, and vitiligo. This practice is one of the oldest treatment modalities in dermatology, dating back to the ancient Egyptians who used natural light in combination with herbal extracts to treat skin disease [1]. Phototherapy continues to be a highly preferred treatment by dermatologists [2]. The most commonly utilized phototherapy is ultraviolet B (UVB) phototherapy. There are two types of UVB. Broadband UVB (BB-UVB) was the first to be developed in the early 1900s and emits wavelengths of light between 290 and 313 nm. Narrowband UVB (NB-UVB), which emits wavelengths between 308 and 313 nm, was developed in the late 1980s and became standard of care for psoriasis after studies demonstrated that psoriasis is more responsive to wavelengths of around 312 nm [3].

For psoriasis, phototherapy is indicated for patients whose disease does not adequately respond to topical medications or those who have generalized involvement that is not amenable to topical treatment alone (Fig. 1.1). The patient must also be available to commit time and effort and present to the office 2 to 3 times per week for at least 3 months. Given that psoriasis is a chronic dermatologic condition, patients often need to continue phototherapy treatments long-term as maintenance, which are typically once or twice weekly sessions. It is therefore important to consider the patient's schedule, location, mode of transportation, overall convenience, and other logistics before choosing phototherapy as a treatment option. Furthermore, the issue of increasing costs of phototherapy treatments and decreasing reimbursement rates from insurance companies should also be considered [4].

Phototherapy is most commonly administered in the office setting in stand-up light booths (Fig. 1.2). The starting dose of

Figure 1.1 Patient with generalized psoriasis who is a candidate for phototherapy

UV light is determined by the individual patient's minimal erythema dose (MED) or Fitzpatrick skin type (Tables 1.1 and 1.2). MED is defined as the lowest dose of light that turns the skin erythematous or pink. In a busy phototherapy practice with a high volume of patients, formal MED testing can be cumbersome, labor intensive, and time consuming. Therefore, it may be more convenient to determine the starting dose from the patient's skin type. Subsequent dosing is then increased as tolerated (Tables 1.1 and 1.2). It is important for the patient not to miss more than 1 week of treatment, as subsequent dosing should not be increased if the patient misses more than 7 days of treatment (Table 1.3). The face and genitals should be covered and protected from the UV irradiation unless there is significant disease present in these areas. Typically, the face is wrapped with a towel. If the face needs to be treated and is exposed, proper eye goggles should be worn or the eyes should be closed. Male genitals are shielded with a towel or cone. The typical flow of a phototherapy treatment session at the University of California San Francisco (UCSF) Phototherapy Unit is out-

FIGURE 1.2 A stand-up UVB phototherapy booth in the office setting

Table 1.1 University of California San Francisco Psoriasis and Skin Treatment Center NB-UVB initial dosing protocol

Skin type	Dose (mJ/cm^2)	Subsequent increase (mJ/cm^2)
I	130	15–50
II	220	15–75
III	260	15–100
IV	330	15–150
V	350	15–200
VI	400	15–200

Table 1.2 University of California San Francisco Psoriasis and Skin Treatment Center BB-UVB initial dosing protocol

Skin type	Dose (mJ/cm^2)	Subsequent increase (mJ/cm^2)
I	10	10–50
II	20	10–50
III	30	10–50
IIII	40	10–50
V	50	10–75
VI	60	10–75

Table 1.3 Missed treatment protocol for both NB-UVB and BB-UVB

Missed visit	Action (for all skin types)
1–7 days	Increase dose per protocol
8–11 days	Hold dose constant
12–20 days	Decrease by 25%
21–27 days	Decrease by 50%
28 or more days	Restart with initial dose

lined in Fig. 1.3 [5]. Furthermore, a proper gentle skin care regimen, which is shown in Table 1.4, is important to avoid skin dryness and tightening post-phototherapy [5].

When patients present for phototherapy 3 times per week, approximately 60–75% of patients with moderate to severe psoriasis achieve at least 75% improvement in the Psoriasis Area and Severity Index (PASI-75) by week 12 [6]. There appears not to be a clear difference in efficacy between NB-UVB and BB-UVB [7], although some patients tolerate NB-UVB better than BB-UVB and vice versa (see Chap. 9). The most common side effects of phototherapy (Table 1.5) include erythema and burning. Management of phototherapy burn is discussed in Chaps. 7 and 8. Blistering is possible with more severe burns [3]. Photoaging and tanning are also possible side effects. There is no clear evidence for increased risk of melanoma or non-melanoma skin cancers in patients who receive UVB both short term and long term [8] (also see Chap. 27).

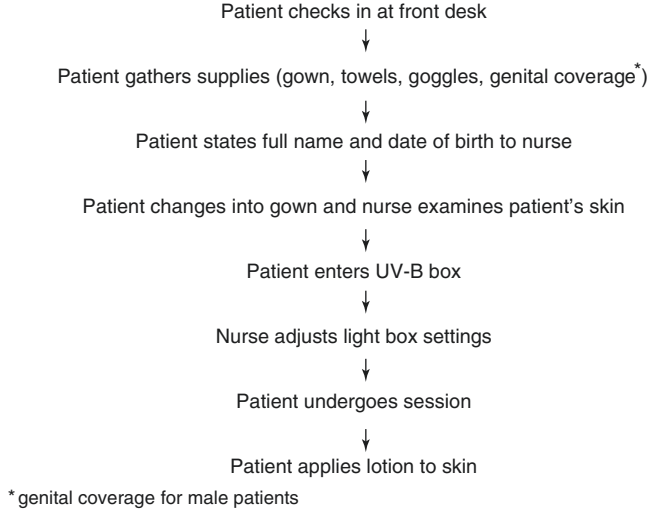

Figure 1.3 Flow of treatment for UVB phototherapy at the UCSF Phototherapy Unit

Table 1.4 Post-phototherapy skin care regimen

Bathe with mild soap or cleanser
Shorten shower times
Limit to one shower per day
Use warm (not hot) water only
Moisturize skin twice daily[a]

[a]Best time to moisturize is immediately after bathing and immediately after phototherapy session

Phototherapy is contraindicated in patients with photosensitizing diseases including systemic lupus erythematosus and xeroderma pigmentosum [9]. The patient's medication list should also be reviewed for photosensitizing agents and the dose adjusted properly (see Chap. 13). Phototherapy should also be avoided in patients with erythroderma in need of a "cool down" as UV light can worsen such patients (see Chaps. 11 and 19). Phototherapy is generally safe to use during pregnancy [9]. Monitoring of patients on phototherapy include baseline full body skin check, followed by regularly scheduled full skin examination to monitor signs of

Table 1.5 Side effects of UVB phototherapy

Side effect	Signs/symptoms
Burning	Redness, tenderness, pain, tightness, itching, rarely blistering noticeable 4–6 h after treatment
Photoaging	Coarseness, wrinkling, laxity, increased fragility, mottled pigmentation, telangiectasias, atrophic or fibrotic areas
Tanning	Skin darkening

photoaging, pigmentation, and cutaneous malignancies [9] (Table 1.6).

In the current patient with generalized psoriasis who is resistant to topical corticosteroids and topical calcipotriene, and given that the patient's schedule and other logistics are feasible with 3-times per week phototherapy sessions, he is an excellent candidate for UVB phototherapy. Since the patient is skin type II, he should be started at a dose of 220 mJ/cm^2 of NB-UVB (or 20 mJ/cm^2 BB-UVB) and the dose should be increased by 15–75 mJ/cm^2 (or 10–50 mJ/cm^2 for BB-UVB) for subsequent sessions. Prior to each phototherapy session, in order to accurately determine the subsequent dose, the patient should be asked about any symptoms consistent with the side effect of burning, including skin pain, itching, or tightness. The skin should also be examined carefully for erythema, peeling, or blistering, in addition to assessment of disease improvement.

The patient can continue to use topical corticosteroids and topical calcipotriene at home, but the application of any topical medications or emollients should be avoided immediately prior to phototherapy treatment sessions as the penetrance of UV light can be altered by the presence of topical substances on the skin. Furthermore, topical calcipotriene, topical retinoids, and other non-steroid topical medications can irritate the skin if burned during phototherapy, so caution is advised (see Chap. 7). It is also very important to discuss with the patient that it can take several weeks to see the results of phototherapy and maximum effectiveness will not be observed until at least 12 weeks or more after the treatment is initiated. This type of expectation management is important so that the

Table 1.6 Recommended monitoring of patients undergoing UVB phototherapy

Baseline monitoring	Full body skin check before initiation of therapy
Ongoing monitoring	Regular full skin examinations every 3–6 months to monitor for signs of photoaging, pigmentation, and cutaneous malignancies

patient is not discouraged by the potential slow onset of action of phototherapy.

Table 1.7 Summary of recommendations for UVB phototherapy for psoriasis from the American Academy of Dermatology, adapted from Menter et al. [9]

Indication	Generalized psoriasis (including guttate) unresponsive to topicals
Dosing	
BB-UVB	Initial dosing according to skin type (20–60 mJ/cm^2) or MED (50% of MED) Subsequent dosage increase by 5–30 mJ/cm^2 or ≤25% of initial MED Treatment 3–5×/week * Advise use of protective goggles and genital shields during treatment
NB-UVB	Initial dosing according to skin type (130–400 mJ/cm^2) or MED (50% of MED) Subsequent dosage increase by 15–65 mJ/cm^2 or ≤10% of initial MED Treatment 3–5×/week * Advise use of protective goggles and genital shields during treatment
Duration of treatment	
BB-UVB	Initial improvement often occurs within 4 weeks of therapy Single course is 20–25 treatments Maintenance therapy may prolong remission
NB-UVB	Response observed at 8–10 treatments Single course is 15–20 treatments Maintenance therapy may prolong remission
Short-term results (clearance)	
BB-UVB	Average of 20–25 treatments to induce clearance

(continued)

Table 1.7 (continued)

NB-UVB	More effective than BB-UVB, clearance within 2 weeks may be seen Average of 15–20 treatments to achieve clearance
Long-term results (remission)	
BB-UVB	Remission rate of 5% after 1 year
NB-UVB	Remission rate of 38% after 1 year
Contraindications	Patients with known lupus erythematosus or xeroderma pigmentosum
Caution should be exercised in	Patients with skin types I and II who tend to burn easily History of arsenic intake or previous treatment with ionizing radiation therapy History of melanoma or multiple nonmelanoma skin cancers Any medical condition that is severe enough that patient cannot tolerate heat or prolonged standing in light box
Toxicity	
Acute	Erythema Pruritus Burning
Long term	Photoaging Lentigines Telangiectasias Theoretical risk of photocarcinogenesis
Drug interactions	Cautious use with other photosensitizing medications When used in conjunction with systemic retinoids, dose of both retinoids and UVB may need to be lowered
Baseline monitoring	Full body skin check before initiation of therapy

Table 1.7 (continued)

Ongoing monitoring	Regular full skin examination to monitor signs of photoaging, pigmentation, and cutaneous malignancies
Pregnancy	Generally considered safe (expert opinion)
Nursing	Generally considered safe (expert opinion)
Pediatric use	No adequate study; may be used with caution in individuals aged <18 years
Psoriatic arthritis	No studies

The summary of recommendations for UVB phototherapy for psoriasis according to the American Academy of Dermatology is shown in Table 1.7 [9].

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Chapter 2
PUVA for the Treatment of Moderate to Severe Psoriasis

Case

A 53-year-old Asian female presents with generalized psoriasis. She is currently undergoing NB-UVB phototherapy. Despite treatments 3 times weekly for the past 6 months, she continues to have thick psoriasis plaques that cover her trunk and extremities. She is also using topical therapies without much added benefit. She has no history of photosensitizing diseases or other skin conditions. She has no personal or family history of melanoma or non-melanoma skin cancers. On examination, the patient is found to have very thick, micaceous, silvery-white scale overlying erythematous plaques covering approximately 15% of her trunk and extremities. She has Fitzpatrick skin type III and weighs 160 lbs.

You discuss with the patient the option of switching from NB-UVB to PUVA (psoralen plus ultraviolet A) phototherapy. You explain that given her thick plaques, PUVA may work better as UVA penetrates deeper into the surface and has been shown to be more effective than NB-UVB in some patients. You explain that she must continue to come in 3 times per week for at least 10 weeks or more, followed by potential long-term maintenance treatments of once or twice weekly. The risks and benefits of PUVA are discussed, and the patient agrees to start. Given that she comes in for her phototherapy treatments during her lunch break at work and

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would not be able to spend more than 30 min per treatment, you decide on systemic PUVA instead of bath PUVA, which would take much longer per treatment session. Lastly, you ask her to have an eye exam prior to starting systemic PUVA treatments to rule out existing cataracts.

Discussion

PUVA has been used to treat moderate to severe psoriasis for nearly four decades [1]. PUVA is photochemotherapy, which combines psoralens, a group of plant-derived compounds that make the skin more sensitive to light, with exposure of skin to a source of high-intensity, long-wavelength, ultraviolet A (UVA) light. The psoralen is either ingested orally in systemic PUVA or applied to the skin in soak, bath, or topical PUVA. After ingestion or application of the psoralen, the patient is subsequently exposed to an artificial source of UVA radiation. UVA radiation includes light between 320 and 400 nm, and due to the longer wavelength of light, UVA penetrates deeper than UVB [2].

PUVA is indicated for patients with moderate to severe psoriasis who have failed topical therapies. It is also used to treat eczema, vitiligo, mycosis fungoides, prurigo nodularis, and graft vs. host disease [3]. PUVA has been found to be more effective than UVB phototherapy in most patients with moderate to severe psoriasis [4] (Fig. 2.1). Patients who have failed UVB or have thicker lesions (Fig. 2.2) may do better with PUVA due to the deeper penetration of UVA. For the same reason, patients with involvement of the palms and soles (Fig. 2.3), as well as nail disease, may benefit from PUVA. On the other hand, skin type I patients are typically better candidates for UVB as the risk of burning is greater with PUVA. Patients with photosensitizing conditions including lupus erythematosus, porphyria, and xeroderma pigmentosus should not be treated with PUVA [5]. Furthermore, PUVA should be avoided in patients with personal history of melanoma or nonmelanoma skin cancer, if possible. PUVA is not recommended during pregnancy as psoralen is pregnancy category C [5].

FIGURE 2.1 PUVA is an effective treatment for moderate to severe psoriasis and palmoplantar psoriasis

FIGURE 2.1 (continued)

Figure 2.2 Patient with thick psoriasis plaques who has failed topical therapies and UVB phototherapy and is a good candidate for PUVA

The psoralen that is used in the United States is 8-methoxypsoralen called methoxsalen. Oxsoralen Ultra® (Valeant Pharmaceuticals North America LLC, Bridgewater, NJ, USA) is the recommended brand as it appears to have the best bioavailability when taken orally and also easily dissolves in water for soak/bath PUVA.

In systemic PUVA, the patient takes methoxsalen at a dose of 0.4–0.6 mg/kg (Table 2.1) 75 min prior to the exposure of UVA radiation. Nausea is the most common side effect unique to systemic PUVA and may be reduced by taking methoxsalen with protein, milk, or a full meal [6]. The flow of treatment for systemic PUVA at the UCSF Phototherapy Unit is shown in Fig. 2.4.

Soak PUVA is used to treat disease on the hands and feet. First, 10 mg of methoxsalen is mixed with 2 quarts of warm water for just hands or feet, or 20 mg of methoxsalen with 4 quarts of warm water for both hands and feet (Table 2.2). Water can come from a warm water sink or can be

FIGURE 2.3 Patient with palmar pustular psoriasis, a good candidate for soak PUVA

TABLE 2.1 Dosing of methoxsalen (Oxsoralen Ultra®) by weight for systemic PUVA

lbs	kg	Drug dose (mg)
<66	<30	10
66–143	30–65	20
144–200	66–91	30
>200	>91	40

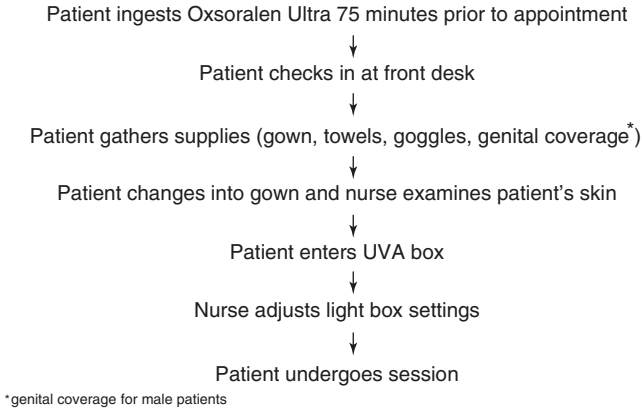

Figure 2.4 Flow of treatment for systemic PUVA phototherapy at the UCSF Phototherapy Unit

Table 2.2 Methoxsalen (Oxsoralen Ultra®) for topical PUVA

Whole body bath PUVA	Dissolve five capsules (50 mg) in three cups of warm water and add to 100 L of bath water (final concentration of 0.5%)
Hand/foot soak PUVA	Dissolve one capsule (10 mg) in 2 quarts of water for hand or foot. Dissolve two capsules (20 mg) in 4 quarts of water for hand and foot.
Cream or gel PUVA	Apply to affected area and remove immediately prior to UVA irradiation (effectiveness is lost within 2 h)

microwaved. Mixing the methoxsalen with warm water will cause the pill to dissolve and the solution will turn into a light aquamarine color. After making the solution, the affected areas on the hands and/or feet will be soaked within the solution for 30 min prior to light exposure (Figs. 2.5 and 2.6). After soaking, the hands and/or feet should be dried, not rinsed off. The flow of treatment for hand/foot PUVA at the UCSF Phototherapy Unit is shown in Fig. 2.6.

FIGURE 2.5 A UVA hand/foot phototherapy booth

Methoxsalen also comes in a topical gel or cream that can be applied to the affected skin surface immediately prior to light exposure (Table 2.2).

Similarly, in bath PUVA, which is used to treat the entire body, 50 mg of methoxsalen is dissolved in warm water and put into a bathtub containing 100 L of warm water (Table 2.2, Fig. 2.7). After bathing for 30 min, the patient will be exposed to UVA. The flow for bath PUVA at the UCSF Phototherapy Unit is shown in Figs. 2.8 and 2.9.

Similar to UVB phototherapy, the dose of UVA is determined by the patient's skin type and increased as tolerated. In the U.S, PUVA is most commonly administered 2 to 3 times per week with at least 48 h in between treatments (Table 2.3). This allows for assessment of any erythemal reaction from the last treatment [7]. If no erythema is observed, the UVA dose should be increased. If erythema occurs but clears before the next session, then the dose should be maintained. If the erythema is persistent, the treatment should be skipped unless the area is very localized and can be shielded from UV light. The 4 times per week treatment regimen is more commonly performed in Europe and requires treatments on Mondays, Tuesdays, Thursdays, and Fridays (Table 2.4). This schedule may be more effective but can be associated with more

FIGURE 2.6 Hand and Foot Soak PUVA: A patient soaks her hands (**a**) and feet (**b**) in water containing methoxsalen for 30 min, then is exposed to UVA light (**c**)

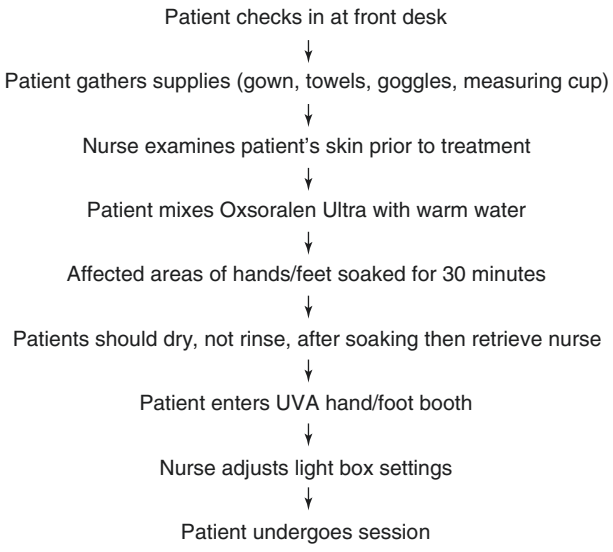

FIGURE 2.7 Flow of treatment for hand/foot soak PUVA phototherapy at the UCSF Phototherapy Unit

phototoxicity [1]. The patient must be able to commit to PUVA therapy long term. Patients are expected to present to the office 2 to 4 times per week for at least 30 treatments in the clearing phase. Given the chronic nature of psoriasis and other skin conditions as above, most patients require an ongoing maintenance regimen beyond the 30 treatments to prevent relapse.

As with UVB phototherapy, the face and genitals should be covered and protected from the UV irradiation unless there is significant disease present in theses areas. Typically, the face is wrapped with a towel. If the face needs to be treated and is exposed, proper eye goggles should be worn. Male genitals are shielded with a towel or cone. Proper post-treatment skin care guidelines, including avoidance of sunlight and wearing sunscreen for 24 h after treatments, are summarized in Table 2.5.

Potential short-term side effects of PUVA include burning, itching, and pigmentation of the skin. Burns, which often

Figure 2.8 Bath PUVA: a patient is mixing methoxsalen into a warm bathtub to soak her body prior to UVA exposure

appear as redness, tenderness, and blistering, may start 24–72 h after treatment in up to 10% of patients during the clearance phase [8]. For mild burns, a topical corticosteroid cream or ointment should be applied (see Chap. 7). Mild itching is common and can usually be relieved with topical emollients. A moderate-to-deep tan may develop while on treatment, but often fades 6 to 8 weeks after stopping treatment. Potential long-term risks of PUVA treatment include cataracts, skin aging, and non-melanoma skin cancer. Cataracts are considered a theoretical risk, as studies on

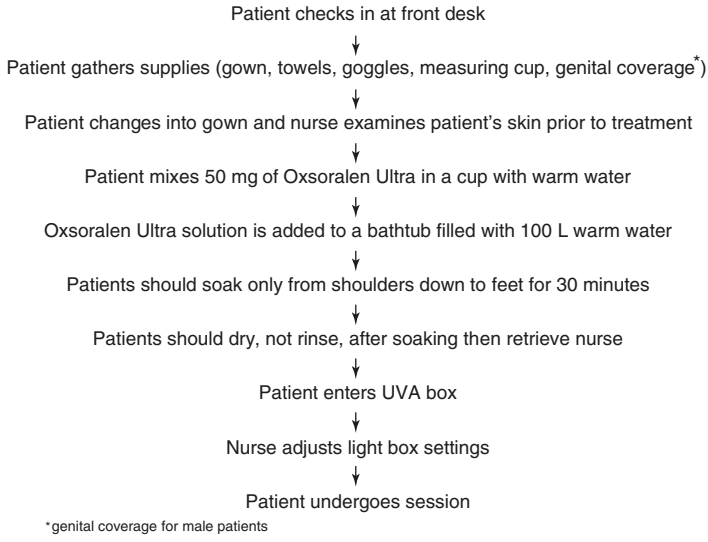

FIGURE 2.9 Flow of treatment for bath PUVA phototherapy at the UCSF Phototherapy Unit

TABLE 2.3 Dosage of ultraviolet A radiation (J/cm^2) for 2 to 3 times per week schedules

Skin type	Initial	Increments	Final
I	1.5	0.5	5
II	2.5	0.5	8
III	3.5	0.5–1.0	12
IIII	4.5	1.0	14
V	5.5	1.0	16
VI	6.5	1.0–1.5	20

humans with proper eye protection have not confirmed an increase in the risk of cataracts with UVA exposure [9]. Skin aging changes may include dryness, wrinkling, and freckling, which may disappear after treatment is stopped, though

Table 2.4 Dosage of ultraviolet A radiation (J/cm^2) for 4 times per week (Monday, Tuesday, Thursday, Friday) schedules

Skin type	Initial	Increments
I	0.5	0.5
II	1.5	0.5
III	2.5	0.5
IIII	3.5	1.0
V	4.5	1.0
VI	5.5	1.5

Table 2.5 Proper post-PUVA phototherapy skin care

Avoid exposure to sunlight and use sunscreen of SPF 15 or higher for at least 24 h after PUVA
Moisturize skin twice daily and frequently in between treatments
Avoid scrubbing skin hard or tearing off skin
Limit nail polish and makeup on areas receiving treatment
Avoid perfumes and colognes directly on skin
Avoid sunbathing during clearing stage of PUVA treatment

freckling may persist indefinitely. PUVA can lead to an increased risk of non-melanoma skin cancers, particularly among light-skinned individuals who have had more than 250 treatments [10]. The risk of genital skin cancer may also be increased, but may be prevented with proper shielding [11] (see Chap. 27). Table 2.6 summarizes the short-term and long-term side effects of PUVA. Monitoring of patients undergoing PUVA should include a full body skin exam and an eye exam to rule out cataracts prior to initiation of treatment, as well as regular skin checks every 3 to 6 months during treatments (Table 2.7).

In the current patient who has severe generalized psoriasis recalcitrant to topical therapies and NB-UVB, she is a good

Table 2.6 Side effects of PUVA phototherapy

Side effect	Signs/symptoms
Short term	
Burning	Redness, tenderness, tightness, blistering noticeable 24–72 h after treatment
Itching	Usually mild and relieved with emollients
Nausea (oral systemic PUVA only)	Reduced by consuming methoxsalen with protein, milk, or full meal.
Tanning	Skin darkening
Long term	
Photoaging	Coarseness, wrinkling, laxity, increased fragility, freckling
Cataracts[a]	Blurry vision, as though looking through frosted glass.
Nonmelanoma skin cancers	Unusual shaped growths may appear and grow quickly over time. Genital skin cancer is possible, but prevented with shielding

[a]Theoretical risk that has not been confirmed in humans with proper eye protection

Table 2.7 Recommended monitoring of patients undergoing PUVA phototherapy

Baseline monitoring	Full body skin check before initiation of therapy Eye exam to rule out cataracts before initiation of therapy
Ongoing monitoring	Regular full skin examinations every 3–6 months to monitor for signs of photoaging, pigmentation, and cutaneous malignancies

candidate for PUVA as she is Asian (skin type III) and has no personal or family history of skin cancer. Systemic PUVA is chosen due to her schedule, as bath PUVA will take over 1 hour each session when considering the preparation of the

bath, followed by soaking, and lastly the light exposure. Once she obtains a clearance eye exam, she can start treatments. She would be instructed to come in 3 times per week and take 30 mg of methoxsalen (according to body weight of 160 lbs) 75 min prior to arriving. She would be started at a dose of 3.5 J/cm^2 and increased by 0.5–1.0 J/cm^2 until reaching approximately 12 J/cm^2.

Table 2.8 The summary of recommendations for systemic PUVA for psoriasis according to the American Academy of Dermatology, adapted from Menter et al. [5]

Indication	Adults with generalized psoriasis who are resistant to topical therapy
Dosing	8-Methoxypsoralen (Oxsoralen Ultra), 0.4–0.6 mg/kg, taken 1–2 h before exposure to UVA Other available forms of psoralen include 5-methoxypsoralen and trimethylpsoralen Treatment 2–3x/week *UV protective eye wear should be worn when outdoors for 12 h post-ingestion
Duration of treatment	Initial improvement frequently seen within 1 month of therapy Single course is 20–25 treatments May be repeated as indicated
Short-term results (clearance)	89% Clearing with average of 25 treatments in US and 20 treatments in Europe 11.6 weeks to Clear in US studies compared with 5.3 weeks to clear in European studies
Long-term results (remission)	Once clearance has been achieved, maintenance treatment may or may not be used Remission times: 3–12 months
Contraindications	Patients with known lupus erythematosus, porphyria, or xeroderma pigmentosum

(continued)

Table 2.8 (continued)

Caution should be exercised in	Patients with skin types I and II who tend to burn easily History of arsenic intake or previous treatment with ionizing radiation therapy History of melanoma or multiple nonmelanoma skin cancers Any medical condition that is severe enough that patient cannot tolerate heat or prolonged standing in light box Severe liver disease that could lead to toxic levels of psoralens Possibly treatment with cyclosporine or methotrexate Pregnant or nursing
Toxicity	
Acute	Nausea and vomiting are common Dizziness and headache are rare Erythema: peaks at 48–96 h Pruritus Tanning: starts 1 week after PUVA Blisters, photo-onycholysis, melanonychia
Long term	Photocarcinogenesis (SCC, BCC, and possible melanoma): Increased risk of photocarcinogenesis in Caucasians with skin types I-III after 200 treatments; this risk not present for non-Caucasians Photoaging and lentigines are common, especially in patients of skin types I-III and are cumulative UVA dose dependent
Drug interactions	Caution when patient is taking other photosensitizing medication Should decrease UVA dose by one-third if oral retinoids are started while patient is receiving PUVA

Table 2.8 (continued)

Baseline monitoring	Skin cancer screening Eye examination; however, recent evidence demonstrates no increased risk of cataract in patients who receive PUVA If indicated by history: ANA panels (anti-Ro/La antibodies) Liver enzymes
Ongoing monitoring	Regular full skin examination because of potential increased risk of photocarcinogenesis in Caucasians In patients who are noncompliant with eye protection, yearly eye examination
Pregnancy	Category C
Nursing	Contraindicated for period of 24 h after ingesting psoralen
Pediatric use	No adequate study; may be used with caution in individuals aged e<18 y
Psoriatic arthritis	No studies

Table 2.9 The summary of recommendations for topical/bath PUVA for psoriasis according to the American Academy of Dermatology, adapted from Menter et al. [5]

Indication	
Topical PUVA	Adults with psoriasis of palms and soles
Bath PUVA	Adults and children with generalized psoriasis
Dosing	
Topical PUVA	Use 0.1% 8-methoxypsoralen in emollient and treat 2–3×/week Apply 30 min before UVA Start at 0.25–0.5 J/cm^2, increase by 0.25–0.5 J/cm^2
Bath PUVA	50 mg of 8-Methoxypsoralen (Oxsoralen Ultra) in 100 L of water 20–30 min pre-exposure Schedule similar to oral PUVA

(continued)

TABLE 2.9 (continued)

Duration of treatment	May take 30 treatments to have noticeable response Single course usually is 30–40 treatments May be repeated as indicated
Short-term results (clearance)	Clinically beneficial
Long-term results (remission)	Once clearance has been achieved, maintenance treatment may be used Remission times: 3–12 months
Contraindications	Patients with known lupus erythematosus, porphyria, or xeroderma pigmentosum
Caution should be exercised in	Patients with skin types I and II who tend to burn easily History of arsenic intake or previous treatment with ionizing radiation therapy History of melanoma or multiple nonmelanoma skin cancers Pregnant or nursing
Toxicity	
Acute	Erythema Blistering Hyperpigmentation
Long term	No increased risk of skin cancer demonstrated
Drug interactions	None
Baseline monitoring	None
Ongoing monitoring	For efficacy and monitor for burning
Pregnancy	Category C
Nursing	No data available
Pediatric use	Safe provided patient can follow instructions; however, no systemic absorption studies have been performed
Psoriatic arthritis	No studies

The summary of recommendations for systemic and topical/bath PUVA phototherapy for psoriasis according to the American Academy of Dermatology is shown in Tables 2.8 and 2.9 [5].

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Chapter 3
Excimer Laser for the Treatment of Mild to Moderate Psoriasis

Case

A 46-year-old female presents to clinic with a 3-year history of mild to moderate psoriasis on the elbows and knees. She has tried superpotent topical corticosteroids consistently for the past 1 year but continues to have resistant, stubborn plaques. She is getting tired of having to apply topical medicines twice daily and would like to discuss other treatment options for her localized disease.

On examination, you observe erythematous, moderately indurated plaques with some remaining white to silver scale on the bilateral elbows and knees (Fig. 3.1). The patient has Fitzpatrick skin type II. You discuss the option of the 308 nm excimer laser with her. She states that she would be able to come into your office twice weekly for treatments and is willing to try this treatment.

The patient is started on treatments per dosing protocol based her skin type and plaque thickness. The dose is increased at each visit until mild to moderate erythema is observed after each treatment, at which time the dose is kept constant. After 10 treatments, significant improvement is observed. After most of the lesions were cleared with the laser, the patient continued on topical therapies as needed and remained clear for a few months.

J. Koo, M. Nakamura, *Clinical Cases in Phototherapy*,
Clinical Cases in Dermatology, DOI 10.1007/978-3-319-51599-1_3,

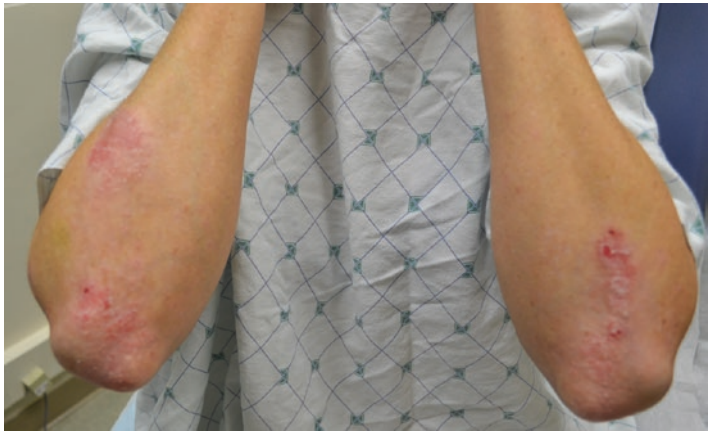

FIGURE 3.1 Patient with localized psoriasis amenable to treatment with the excimer laser

Discussion

The 308 nm excimer laser (Fig. 3.2) is a widely used device in dermatology that is FDA-approved for the treatment of psoriasis, atopic dermatitis, and vitiligo, but can also be used for various other diseases such as hypopigmented disorders, alopecia areata, cutaneous T cell lymphoma, granuloma annulare, Langerhans cell histiocytosis, lichen planus, and localized scleroderma [1]. For psoriasis, the excimer laser is currently indicated for patients with mild to moderate psoriasis with <10% body surface area (BSA) involvement. Excimer laser is particularly useful in localized lesions, in small children, in non-exposed sites (such as the scalp, ears, axillae, groin, and intergluteal cleft), in resistant sites (such as the elbows, knees, lower legs, and ankles), the palms, and in situations in which more accurate dosimetry is important [2]. Patients with a larger surface area involvement can also be treated with the excimer laser (Fig. 3.3); however, treatments can become time consuming and may be difficult in an office with limited time, staffing, or other logistical issues.

The term *excimer* is derived from "excited dimer", which describes the mixture of the noble gas xenon and the halogen chloride gas (XeCl), which when dissociated

Figure 3.2 The Xtrac® excimer laser

produces a 308 nm ultraviolet (UV) monochromatic coherent wavelength, which lies within the UVB spectrum [3]. The excimer laser is effective for the treatment of psoriasis by inducing apoptosis in keratinocytes and T-lymphocytes

FIGURE 3.3 Excimer laser can also be use for generalized psoriasis

through DNA breakage, upregulation of the tumor suppressor gene p53, and subsequent reduction of protooncogene bcl-2, leading to cell cycle arrest in keratinocytes and T-lymphocytes [1].

The 308 nm excimer laser was developed in 1997 as a targeted NB-UVB source for the treatment of psoriasis [4] (Fig. 3.4). The advantage of using the excimer laser is that because psoriasis plaques can take higher doses of light compared to normal skin, targeted treatment of psoriasis

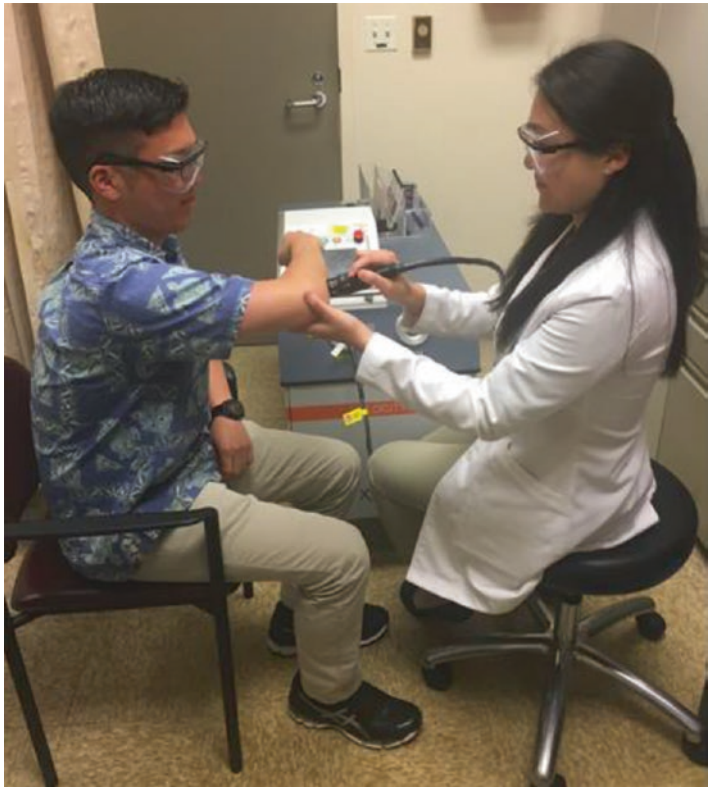

FIGURE 3.4 The excimer laser is a targeted phototherapy modality

lesions allows for use of higher doses of UVB. Higher doses of light permit quicker time to clearance of psoriasis lesions.

Currently, there are 2 available protocols used to determine the starting dose of the excimer laser: the induration protocol (Table 3.1) and the minimal erythema dose (MED) protocol (Table 3.2). In the induration protocol, the starting dose is based on the level of the plaque induration and the patient's Fitzpatrick skin type [5]. In the MED protocol, the

Table 3.1 Determining initial dose for XTRAC® ultra and XTRAC® velocity excimer lasers by plaque thickness

Plaque thickness	Induration score	Fitzpatrick I–III	Fitzpatrick IV–VI
Mild	1	300 mJ/cm^2	400 mJ/cm^2
Moderate	2	500 mJ/cm^2	600 mJ/cm^2
Severe	3	700 mJ/cm^2	900 mJ/cm^2

Table 3.2 Determining initial dose for XTRAC® ultra and XTRAC® velocity excimer lasers by minimum erythema dose (MED) and plaque characteristics

Plaque location	Plaque thickness	Plaque tan	Multiplier for initial dose
Knees, elbows, hands, feet	Thick, tough	Tanned	4 (400%)
Knees, elbows, hands, feet	Thick, tough	Not tanned	3 (300%)
Knees, elbows, hands, feet	Thick, moderate	Tanned	3 (300%)
Knees, elbows, hands, feet	Thick, moderate	Not tanned	2 (200%)
All other locations	Thick, tough	Tanned	3 (300%)
All other locations	Thick, tough	Not tanned	2 (200%)
Knees, elbows, hands, feet	Thick, tough	Tanned	4 (400%)

MED is established by first testing healthy, non-psoriatic skin and determining the minimal dose (in mJ/cm^2) that causes a well-demarcated, minimally erythematous or pink patch [6]. The initial dose is a multiplier of the MED depending on plaque characteristics. For both protocols, subsequent dosing is determined by clinical observation for erythema

Table 3.3. Determining subsequent doses for XTRAC® ultra and XTRAC® velocity excimer lasers

Outcome	Clinical observation	Dose change
No effect	No erythema at 12–24 h and no plaque improvement	Increase by 25%
Minimal effect	Slight erythema at 12–24 h but no significant improvement	Increase by 15%
Good effect	Mild to moderate erythema response at 12–24 h	Maintain dose
Considerable improvement	Significant improvement with plaque thinning and/or reduced scaliness or pigmentation has occurred	Maintain or reduce by 15% (to minimize hyperpigmentation and erythema)
Moderate/severe erythema	With or without blistering	Reduce dose by 25% (okay to treat around blistered area)

and overall improvement of the plaque (Table 3.3). Subsequent treatments should be at least 24–48 h apart as laser erythema is typically observed 12–24 h following the treatment session.

The excimer laser is quite effective for the treatment of psoriasis. In a multicenter open-label trial, 72% of patients with mild to moderate psoriasis achieved at least 75% improvement of the target plaque in an average of 6.2 treatments [7]. Compared with traditional whole-body

phototherapy, the excimer laser required fewer visits [7]. In another study, 13 out of 26 patients with plaque-type psoriasis had continued clearance or long-term improvement after 1 year [8]. The excimer laser is generally well tolerated with only a few adverse reactions including erythema, blistering, hyperpigmentation, hypopigmentation, and tanning (Table 3.4 and Fig. 3.5). Skin cancer has not been found to be associated with excimer laser use.

TABLE 3.4 Common side effects of the 308 nm excimer laser

Side effect	Signs/symptoms
Burning	Redness, tenderness, pain, tightness, itching, rarely blistering Noticeable 12–24 h after treatment
Hyper/Hypo-pigmentation	Post-inflammatory
Tanning	Skin darkening due to high dose of UVB

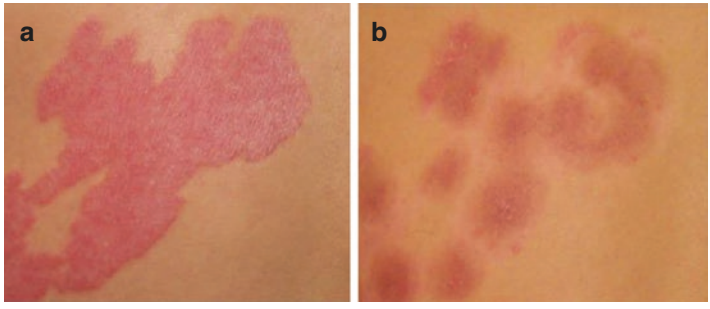

FIGURE 3.5 The side effects of the excimer laser include erythema and tanning, which fade over time. (**a**) A psoriasis plaque before excimer laser treatments. (**b**) After treatments with the excimer laser, erythema and hyperpigmentation (tanning) are observed but minimal psoriasis remains

The excimer laser can safely and effectively be combined with other treatments including topical therapies and phototherapy [2]. In one study, patients were treated with the excimer laser for 12 weeks in combination with clobetasol 0.05% spray for 4 weeks followed by calcitriol ointment thereafter. At 12 weeks, 83% of patients achieved PASI-75 (75% improvement or better in the Psoriasis Area and Severity Index compared to baseline) [9]. In another randomized prospective study, 256 patients were selected for PUVA monotherapy or PUVA plus excimer laser. Patients treated with the combination method were found to be in remission in half the treatment time (15 ± 6 vs 27 ± 7 days) and with half the cumulative UVA dose (22.9 ± 5.8 vs 53.2 ± 26.3) [10]. The excimer laser may be administered 2 to 3 times per week immediately preceding or following whole-body PUVA or NB-UVB therapy [2].

In the current patient with localized psoriasis on the elbows and knees who has failed superpotent topical corticosteroids despite good compliance, the excimer laser is an excellent option. The patient is also available to present to the office at least twice weekly, which is an important consideration in order to achieve maximum benefit. In this patient who has moderately indurated plaques (induration score of 2) and has skin type II, the starting dose would be 500 mJ/cm^2. The dose would then be increased as tolerated as judged by erythema. Concomitant continued use of topical corticosteroids is recommended for added benefit, as well as to treat potential side effects of erythema or burning due to the laser. At least 10 treatments or approximately 6 weeks of consecutive treatments are required to see the positive effects of the excimer laser.

The summary of recommendations for targeted phototherapy for psoriasis according to the American Academy of Dermatology is shown in Table 3.5 [11].

Table 3.5 The summary of recommendations for targeted phototherapy for psoriasis according to the American Academy of Dermatology, adapted from Menter et al. [11]

Indications	Adult and pediatric patients with mild, moderate, or severe psoriasis with <10% BSA involvement
Dosage	Initial dose depends on individual's skin type (including formal MED testing), plaque characteristics, and thickness (500–900 mJ/cm^2 for XTRAC) Subsequent doses adjusted according to clinical response and/or side effects
Duration of treatment	Dosing 2–3×/week until patient is clear, usually average of 10–12 treatments are needed
Short-term results	Initial response within 8–10 treatments; depends on multiple factors such as device used, protocol used, lesion characteristics, and site
Long-term results	Mean remission times of 3.5–6 months
Caution should be exercised in	In patients with photosensitivity disorders
Toxicity	Erythema Hyperpigmentation Blistering, particularly with higher doses
Drug interactions	May need to lower dosing based on presence of photosensitizing medications *Note: action spectrum of most photosensitizing medications is in UVA range
Baseline monitoring	None
Ongoing monitoring	For efficacy and for burning
Pregnancy	No studies in pregnancy have been performed but expert opinion is that it is safe

Table 3.5 (continued)

Nursing	No studies in nursing mothers have been performed but expert opinion is that it is safe
Pediatric use	No large-scale studies in children have been performed but expert opinion is that it is safe
Psoriatic arthritis	No studies

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Chapter 4
Goeckerman Therapy for the Treatment of Severe Generalized Psoriasis

Case

A 63-year-old male presents with severe generalized psoriasis covering most of his scalp, trunk, and extremities. His psoriasis has been untreated for the past few months. He reports severe discomfort due to tightness and cracking of his thickened skin, as well as unbearable skin flaking. He has never tried any systemic treatments for psoriasis. He suffers from active hepatitis C and hepatocellular carcinoma and is currently undergoing chemotherapy. He is on disability and is not employed. Due to his multiple medical problems, you deduce that he is not a candidate for any systemic or biologic treatments for psoriasis but is a candidate for the Goeckerman day treatment program.

The patient is referred to a Goeckerman treatment center. Each day he undergoes NB-UVB phototherapy followed by topical coal tar under plastic occlusion. He is treated 5 days per week for 4–5 h per day. He returns for follow up 6 weeks later after completing the Goeckerman regimen and is almost clear with only residual post-inflammatory hyperpigmentation. He states that the treatment quickly worked to clear his psoriasis without any adverse effects. After 6 weeks of Goeckerman, he continues to receive three times per week NB-UVB phototherapy with topical gold tar and/or corticosteroid at home with continued remission of his severe psoriasis.

J. Koo, M. Nakamura, *Clinical Cases in Phototherapy*,
Clinical Cases in Dermatology, DOI 10.1007/978-3-319-51599-1_4,

Discussion

The Goeckerman regimen is a unique combination therapy of UVB light and application of crude coal tar for the treatment of psoriasis, eczema, prurigo nodularis, and chronic pruritus [1–4]. First introduced in 1925, the Goeckerman regimen remains one of the oldest, yet most effective and reliable treatment options for patients with moderate to severe psoriasis [5] (Fig. 4.1). Although the exact mechanism of action of the combination of tar and phototherapy is unknown, it is speculated that tar is anti-inflammatory and is also a photosensitizer that can increase the effectiveness of phototherapy [6].

In the Goeckerman regimen, NB-UVB or BB-UVB is administered per protocol (see Chap. 1). Following light exposure, coal tar is applied to the entire body (Fig. 4.2a). Coal tar is available in two forms: crude coal tar and liquor carbonis detergens (LCD). Crude coal tar, commonly referred to as "black tar," is compounded in white petrolatum ointment or Cetaphil® cream (Galderma Laboratories, L.P.) in concentrations of 2%, 5%, and 10%. LCD, commonly referred to as "gold tar," is compounded in Aquaphor® ointment (Beiersdorf, Inc.), Cetaphil cream, or Vanicream™ lotion (Pharmaceutical Specialties, Inc.) as 20% concentration. The patient's body is then wrapped and the patient stays in the occlusive plastic wrap for approximately 4–5 h (Fig. 4.2b). The tar is washed off with mineral oil. In cases of severe psoriasis that is very erythematous and inflamed (Fig. 4.3), it is recommended that the patient undergo a cool down period during which topical corticosteroids are applied to the affected areas and occluded with plastic wrap until the erythema is greatly reduced. The cool down period can range from 3 to 14 days [7].

The supplies required for conducting the Goeckerman regimen is shown in Table 4.1 and Fig. 4.4. The flow of the Goeckerman day treatment program at the UCSF Phototherapy and Skin Treatment Center is shown in Fig. 4.5.

The treatment is administered daily, 5 days a week, for approximately 6 weeks for a total of 30 sessions. Individual patient's length of treatment can vary depending on severity of disease and response to therapy. Each day, the patient

FIGURE 4.1 A patient with severe generalize psoriasis with multiple co-morbid medical problems who is a candidate for the Goeckerman day treatment program

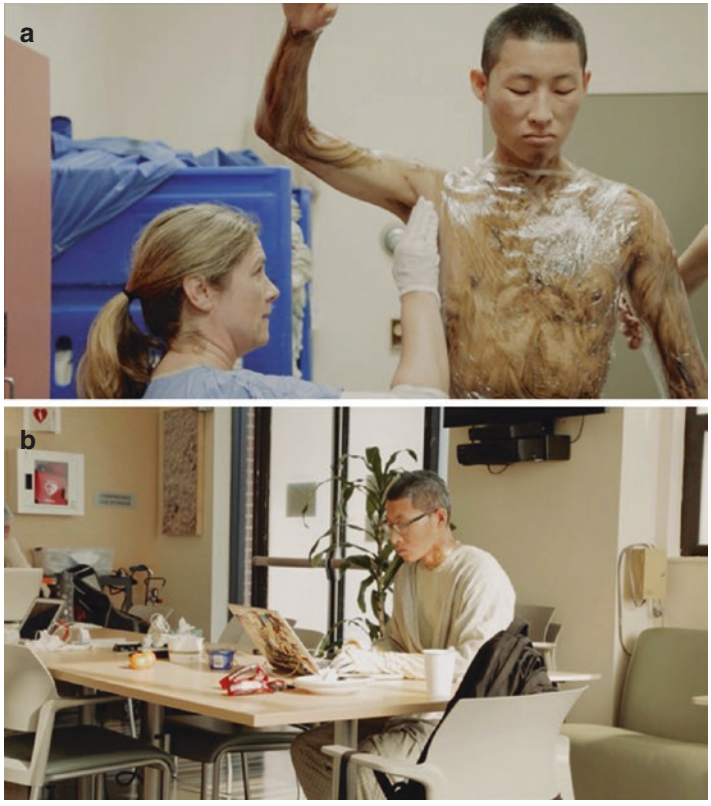

FIGURE 4.2 A patient undergoing Goeckerman therapy: (**a**) following treatment with UVB phototherapy, topical coal tar is applied to the skin and the body is wrapped with plastic occlusive wrap. (**b**) The patient remains in the occlusive wrap for 4–5 h

should be assessed by the nurse and doctors for response to treatment, as well as possible side effects including itching and burning. When leaving the Goeckerman regimen, the patient is discharged with a maintenance phototherapy and topical regimen to prevent relapse [7].

Although novel internal agents such as biologics have advanced psoriasis treatment, Goeckerman therapy remains an extremely effective treatment with a quick onset of action

and dramatic improvement in psoriasis severity. Studies have shown that 100% of patients on Goeckerman therapy achieve PASI-75 (75% improvement or better in the Psoriasis Assessment of Severity Index from baseline) by 12 weeks [8],

Figure 4.3 Severely inflamed and erythematous skin requires a "cool down" with topical corticosteroids prior to phototherapy and application of coal tar in the Goeckerman regimen.

FIGURE 4.3 (continued)

which far exceeds the average improvement for many currently available biologic agents [9]. Goeckerman is also successful in patients with psoriasis refractory to phototherapy or internal medications [1]. Even more impressive are the sustained effects of Goeckerman therapy; following treatment, 90% of patients maintain PASI-75 at 8 months and

Table 4.1 Supplies used for the Goeckerman regimen at the UCSF Phototherapy and Skin Treatment Center

Crude coal tar 2%, 5%, 10% ("black tar")	White petrolatum ointment Cetaphil cream
Liquor carbonis detergens 20% (LCD or "gold tar")	Aquaphor ointment Cetaphil cream Vanicream lotion
Topical corticosteroids (when cool down is needed)	Clobetasol propionate 0.05% ointment Triamcinolone 0.01% ointment Desonide 0.05% ointment etc.
Tar removal	Mineral oil Soap
Emollients (post-therapy and at home)	Aquaphilic ointment Vanicream
Occlusion	Industrial-size plastic wrap
Miscellaneous	Gown Gloves Socks Shower cap

73% at 1 year or longer [10]. Goeckerman therapy is also shown to significantly improve quality of life [11]. Similarly, Goeckerman is effective in treating severe eczema [2] and prurigo nodularis [3].

The safety profile of Goeckerman therapy is excellent. Unlike biologic and systemic agents, there are no systemic or internal side effects, and therefore, Goeckerman therapy can be administered to patients with multiple co-morbid medical problems including infection and malignancy. Goeckerman therapy is entirely topical and has limited internal absorption. It also has relatively few external side effects. The most commonly observed side effects (Table 4.2) include those of phototherapy such as erythema and burning, in addition to mild itching or irritation from tar and folliculitis due to occlusive

FIGURE 4.4 The supplies required for conducting the Goeckerman regimen

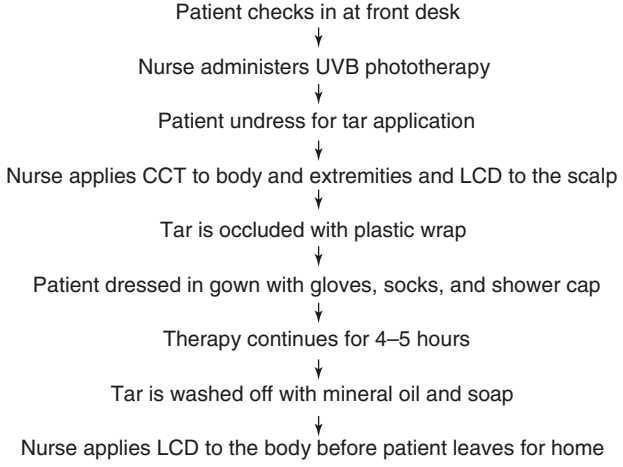

FIGURE 4.5 The flow of the Goeckerman day treatment program at the UCSF Phototherapy and Skin Treatment Center

Table 4.2 Common side effects of the Goeckerman regimen

Side effect	Signs/symptoms
Burning	Redness, tenderness, pain, tightness, itching, rarely blistering noticeable 4–6 h after UVB phototherapy
Tanning	Skin darkening
Itching/irritation	Due to tar
Folliculitis	Due to occlusion of ointments

application of ointments. Patients should also be advised to avoid sun exposure while the tar is applied as it can cause the skin to burn easily. One of the main concerns regarding coal tar is the theoretical carcinogenic potential. However, many studies including a review of 13,200 patients undergoing Goeckerman regimen for psoriasis and eczema showed that there is no increased risk of cancer with tar therapy compared to topical corticosteroids [12].

The efficacy and safety of the Goeckerman therapy makes it an excellent treatment for patients who may have previously failed multiple therapies, the elderly, pregnant patients, children, and the immunosuppressed. Nevertheless, there are few disadvantages. The first is the commitment required to present to the treatment center daily for at least 6 weeks consecutively. Employment/school and transportation issues are common patient barriers to enrolling in the Goeckerman program. Many patients who are able to undergo Goeckerman therapy are often retired or on disability. However, it is possible for patients who are employed to go on temporary disability with the help of the provider in order to undergo this treatment. Children often enroll during the summer months when they do not have school. Another disadvantage to Goeckerman therapy is that there are currently only a few centers in the U.S. that conduct Goeckerman therapy. This is due to limited resources and high cost of the Goeckerman regimen.

For the current patient who presents with severe generalized psoriasis recalcitrant to topical treatments and phototherapy, and who has active hepatitis C and hepatocellular

carcinoma, treatment options are limited. Systemic therapies (such as methotrexate, acitretin, and cyclosporine) and biologic agents are not options due to active hepatitis C and malignancy. One treatment option that is not immunosuppressive and does not have internal toxicity is the Goeckerman regimen. Given that the patient is motivated, willing to be compliant, is able to present for daily treatments, and can continue to present for maintenance phototherapy, he is an excellent candidate for the Goeckerman program.

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Chapter 5
Avoiding Undertreatment with Phototherapy

Case

A 23-year-old female presents with generalized plaque-type psoriasis involving the trunk and all extremities. Scalp and intertriginous areas are spared. She has used various topical corticosteroids without relief. The patient strongly prefers to avoid internal therapies such as oral agents or biologics because she is afraid of even the remote possibility of internal side effects. Because she has generalized psoriasis and prefers an external approach, therapy with UVB is recommended. However, she promptly states that she has failed UVB phototherapy, which was conducted by another dermatologist. She reports having faithfully gone for treatments 3 times per week for 4 months and yet observed no obvious improvement. She denies ever experiencing sunburn-type of symptoms such as tingling, burning, skin peeling, or skin tightness. She also states that she never observed her skin turning red during the 4 months of phototherapy. The previous dermatologist reportedly told her that she has failed UVB phototherapy and therefore she has no choice but to take internal mediations unless she wants to continue using only topical treatments. She was not happy with this pronouncement and comes to your office seeking a second opinion.

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Discussion

If the patient undergoing UVB or PUVA phototherapy observes no improvement, and at the same time no hint of erythema or even the faintest signs and symptoms of phototoxic reaction (sunburn) are noted, there is high probability that the patient is undertreated. Undertreatment is most commonly due to the administration of inadequate doses of light.

Every patient has his/her own unique dosimetry threshold, which is the amount of light that is required to be administered before any improvement is observed. Even though erythema or phototoxic reaction is not a requirement for inducing clinical improvement in most patients, it is also known that the optimal dose of light for maximal efficacy lies close to or at the individual's minimal erythema dose (MED) [1–4]. MED is the lowest dose of light at which the skin turns erythematous or pink (Fig. 5.1).

Unfortunately, there are many practitioners who are quite risk averse and will not administer appropriately aggressive doses of light. Some practitioners are also known to "cap" the dosimetry used in their practice. "Capping" the dosimetry means that the practitioner specifies a maximum dose of light

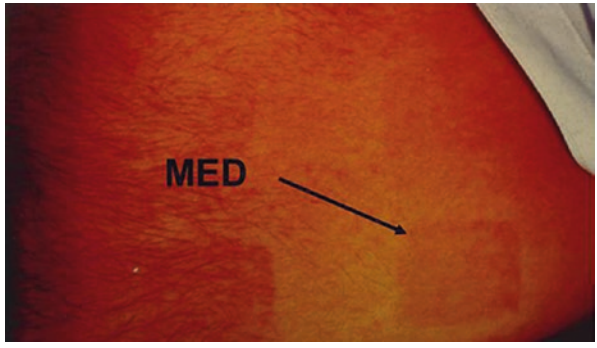

Figure 5.1 Minimal erythema dose (*MED*) is the dose at which the skin turns erythematous or pink

that can be administered to any one patient in their practice; the phototherapy technician, nurse, or other supporting staff are not allowed to go beyond this dose even if the patient is not showing any benefit. The amount of light that is required to lead to clinical improvement, as well as tolerance, varies tremendously among individuals, and they do not always correlate with skin color or Fitzpatrick skin type [5]. Therefore, it is important not to arbitrary limit the amount of light exposure, especially if the patient is showing no benefit and no side effects.

In addition to inadequate dosimetry of phototherapy, patients may also be undertreated in terms of frequency of treatment sessions and the overall duration of phototherapy. Patients should initially start with 3 times per week treatments to allow for rapid up titration to the optimal dose of light. At least 4 to 6 weeks is commonly required to see the initial positive effects of phototherapy. Drastic improvement will likely take approximately 30 treatments or 10–12 weeks. It is important for the practitioner and patient not to give up on phototherapy too early in the course of treatment. The practitioner should provide the patient with appropriate expectations and encouragement regarding the potential slow onset and even slower time to maximum improvement seen with phototherapy.

Undertreatment can waste patients' time and effort and can lead to the patients being erroneously labeled as "phototherapy failure" when in fact they were simply not given adequate dosimetry for improvement. Therefore, it is critically important to push the dosimetry gradually until the patient starts showing improvement, the MED is reached (the skin turns slightly erythematous or pink), or the patient reports signs and symptoms of burning. Furthermore, before the patient is labeled as "phototherapy failure", he/she should have an adequate trial of phototherapy with regard to frequency and total number of treatments. Table 5.1 outlines the tips for avoiding undertreatment with phototherapy.

Table 5.1 Tips for avoiding undertreatment with phototherapy

Increase the dose at subsequent visits until: The MED is reached (when the skin turns erythematous or pink) The patient reports signs and symptoms of burning Significant improvement in the disease is observed
Avoid "capping" the dosimetry (arbitrary specifying a maximum dose of light that can be administered to any one patient)
Do not assume an optimal dose of light based only on skin color or Fitzpatrick skin type
Treatments should be initiated at a frequency of 3 times per week
Wait at least 20–30 treatments to assess overall effectiveness of phototherapy

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Chapter 6
"Erythemogenic" Phototherapy for Select Patients Who Need It

Case

A 33-year-old male comes to your office for treatment of generalized psoriasis. He is started on UVB phototherapy. He presents for treatment sessions diligently 3 times per week. Initially, he does well and shows steady progress with decreasing scale, erythema, and induration of psoriatic plaques. However, after several months of progress, the improvement plateaus and the patient is left with resistant plaques on the extremities. After seeing no improvement for another 2 months, the patient asks you to increase the amount of light so he can be slightly sunburned. He states that the previous dermatologist that he did phototherapy with purposefully used high doses of light that would turn his skin pink. He also reports that mild erythema all over his body, for him, is mostly asymptomatic and leads to much better clinical improvement.

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Discussion

According to the medical literature, it appears that for many patients, the optimal amount of light is near the minimal erythema dose (MED), which is the dose at which the skin turns slightly erythematous or pink [1–4]. Deliberately administering a dose of light consistent with the patient's MED is called "erythemogenic" phototherapy. Erythemogenic phototherapy can be tricky because it can cause discomfort in some patients. In addition to the erythematous appearance of the skin, some patients also experience uncomfortable symptoms of burning, stinging, itching, or skin tightness. This can happen as soon as the MED is reached. Therefore, consistent treatment at the MED is not possible in all patients but only practical if the patient does not experience discomfort in terms of both appearance and symptoms.

For those patients who can tolerate induction of mild erythema (i.e. treatment at the MED), the erythemogenic phototherapy strategy is an option in order to maximize the speed of improvement and overall efficacy, although this may be controversial [1–3]. This strategy can also be used if the sub-erythemogenic dosimetry strategy leads to "stalemate" at a point of improvement that is less than satisfactory for the patient. Unfortunately, many patients cannot tolerate erythemogenic phototherapy. Furthermore, it may be preferable to have some margin of safety in patients who may be exposed to extra sunlight outside of the therapeutic setting. In such cases, "sub-erythemogenic" phototherapy, in which the dose of light is deliberately kept just below the MED, is the preferred strategy.

One situation in which erythemogenic phototherapy is almost always preferred is when using the excimer laser. The excimer laser dosimetry protocol calls for observation of mild erythema of the psoriasis plaque for the treatment response to be considered "good effect", and the dose is kept stable once this is reached (Table 3.3 and Fig. 6.1). In most cases, this optimal dose of excimer laser is actually a "supra-erythemogenic" dose, which is well beyond the MED of non-involved skin [5].

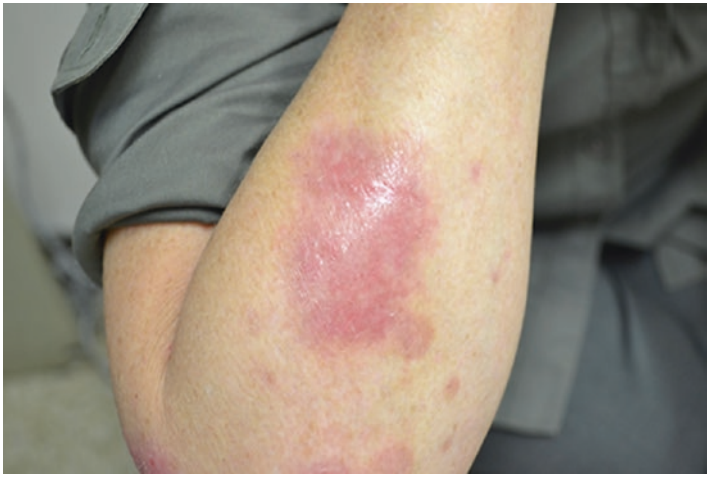

FIGURE 6.1 "Erythemogenic" phototherapy (treating up to the dose at which the skin turns erythematous to pink) is the preferred method for treatment with the excimer laser

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Chapter 7
Recognizing and Managing Initiation Burn

Case

A 17-year-old male with generalized atopic dermatitis was referred for UVB phototherapy. The patient is started on 130 mJ/cm^2 of NB-UVB per protocol, but as soon as phototherapy is initiated, the patient reports experiencing burning sensation. On examination, increased erythema is noted on his chest and back. The patient looks disappointed and says, "I burned with such little amount of light. I guess this means that I cannot do phototherapy. Maybe I have to take internal steroids again."

Instead of labeling the patient a "phototherapy failure", he is asked to apply liberal amounts of topical corticosteroids to the body and return for his next treatment in 2 days. When he arrives for his treatment, his skin is no longer erythematous and appears calm. At this time, he is given a very small dose of NB-UVB at 30 mJ/cm^2, which he tolerates well without any burning sensations. He is kept at this dose for the next 3 treatment sessions. At the subsequent visit, he is challenged with 50 mJ/cm^2 of UVB, which he again tolerates without any problems. Eventually, the patient is able to withstand dosimetry consistent with the standard protocol, and his atopic dermatitis gradually improved over time.

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Discussion

Even though the phenomenon called "initiation burn" may not be well documented in the medical literature, it is not uncommon. Initiation burn is a phenomenon in which the patient unexpectedly experiences burn very early in the course of phototherapy at very low dosimetry. In other words, the patient appears to be photosensitive without any underlying cause [1]. This phenomenon may be more commonly experienced by patients with atopic dermatitis and other forms of eczema compared to patients with psoriasis. Although the exact cause and underlying pathophysiologic mechanism of this phenomenon are not well understood, it may be due to the hypersensitive nature of the skin to UV light in a certain subset atopic dermatitis patients [2] or due to heat-induced flare [3]. In patients with psoriasis, the prevalence of photosensitivity is estimated to be 5.5% [4] and is associated with skin type I, a heredity of photosensitivity, advanced age, and psoriasis affecting the hands [5].

When initiation burn occurs, it is important not to jump to the conclusion that the patient is not a candidate for phototherapy or has "failed" phototherapy. Instead, it is recommended to deliberately continue phototherapy with the highest amount of light the patient can tolerate, even if this is a very low dose. This allows the skin to desensitize, harden, or get used to the light [1]. After the patient tolerates several treatment sessions at low dosimetry, a very small incremental increase can be attempted. If the patient tolerates the slightly higher dose, further increase in dosimetry can be tried again in small increments. The practitioner should be very careful and aware of any erythema on the skin or any reports by the patient of burning symptoms, in which case the dose should be kept stable or lowered accordingly. The suggested dosimetry protocol for a patient with initiation burn is shown in Table 7.1.

Table 7.1 Suggested dosing protocol for a patient with initiation burn

	Initial dose (mJ/cm^2)	Subsequent dose increments (mJ/cm^2)[a]
NB-UVB	30	10–30
BB-UVB	5	5–10
PUVA	0.25	0.5

[a]Maintain tolerable initial dose for approximately 2 to 5 treatments before attempting subsequent dose increments to allow time for photohardening. Subsequent dose should only be increased if there is no erythema and symptoms of burning after the previous treatment session

Eventually, through photohardening, many of these patients are able to get used to the light and overcome this phenomenon of initiation burn. It is not unusual for these patients to eventually tolerate much higher doses of light than that which caused the initial initiation burn. Of course, the patient will eventually reach his/her true MED which then needs to be respected.

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Chapter 8
Managing Phototherapy-Induced Burn

Case

A 66-year-old female with generalized psoriasis experiences uncomfortable phototoxic reaction of burning and redness on the breasts and abdomen following UVB phototherapy. She had received a phototherapy treatment yesterday afternoon. This morning she woke up with significant discomfort. She promptly reports this episode to the phototherapy staff by phone. She was calm and collected because she was already told beforehand that this sunburn type reaction can happen during the course of phototherapy. After notifying the clinic staff, she applies generous amounts of clobetasol ointment over the red areas and takes ibuprofen according to the recommended dosage on the bottle. The phototherapy nurse tells the patient not come in for her next session of phototherapy until the redness and discomfort completely subside. The patient continues to apply clobetasol twice daily and takes ibuprofen around the clock for the next couple of days. A week later, the patient is much improved without any signs of symptoms of a phototoxic reaction. Phototherapy is restarted at a dose lower than the dose that led to the phototoxic reaction and this was well tolerated.

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Discussion

The optimal management of a phototoxic reaction should take place long before such a reaction happens. This means that every patient who starts phototherapy should be told ahead of time that he/she might eventually experience a "sunburn" type reaction as a natural consequence of dosimetry titration [1]. As the dose of light is gradually increased to find the patient's individual optimal dose for improvement, it is possible that the patient experiences burn. With NB-UVB therapy, there have also been reports of rare blistering strictly at the site of psoriatic lesions while the surrounding skin remains unaffected [2–4]. Some have speculated that due to rapid clearance by NB-UVB, psoriatic plaques may not gain the same photoprotection as normal skin, exposing them to a burning dose midway through treatment [4].

It is helpful to let the patient know that phototoxic reaction from UVB does not happen while the patient is getting treatment in the light box; it happens at least a few hours after but less than 24 h from the last UVB light exposure [5]. With PUVA, the burning is experienced 6–36 h following the treatment [5]. This way, the patient is not shocked or surprised when a phototoxic reaction does happen hours following the actual treatment session. Furthermore, the areas that are at highest risk of burn are parts of the body that are closest to the light bulbs within the walls of the phototherapy booth. This can include parts that naturally protrude, such as the breasts in women, abdomen in overweight or obese patients, and buttocks (Fig. 8.1).

A very effective way to minimize the discomfort of phototoxic reaction is to apply a superpotent topical steroid such as clobetasol at the earliest sign or symptom of skin burn noted by the patient. For this reason, it is recommended that adult phototherapy patients be prescribed a superpotent topical steroid to have available at home to use in case this adverse effect occurs. Ointment formulation is most recommended since it is least irritating and most efficacious. The risk of

FIGURE 8.1 Phototherapy-induced burn often occurs in areas of the body that naturally protrude, such as the breasts in women, abdomen in overweight or obese patients, and buttocks. In severe cases, blistering and desquamation can be observed.

applying clobetasol ointment for a few days is minimal if sensitive skin such as the face, groin, or skin folds is avoided because the topical therapy is used only for a few days until the phototoxicity subsides. Therefore, the patient can be recommended to apply it as soon as he/she suspects that burn may be developing. If the erythema noted or symptom experienced turns out to be a "false alarm", no harm is done with only a few days application of clobetasol to non-sensitive skin. It is important to remember that the sooner it is treated, the less the symptoms. In addition, ibuprofen or other anti-inflammatory medications can be helpful in decreasing the phototoxic reaction and symptoms.

Table 8.1 Keys to management of phototherapy-induced burn

1. Tell every patient ahead of time that he/she might eventually experience a "sunburn" type reaction as a natural consequence of dosimetry titration. The burn most commonly occurs 4–6 h after a treatment
2. Every patient undergoing phototherapy should be prescribed a topical corticosteroid to use at home in case a phototoxic reaction occurs
3. Topical corticosteroid (superpotent when appropriate) should be applied at the earliest sign or symptom of skin burn noted by the patient
4. Ibuprofen can help decrease the phototoxic reaction and symptoms
5. Restart phototherapy only when both the last of the erythema and symptoms disappear. Resume at a dose that is lower than the highest dose previously tolerated, as there can be residual excitability of the skin after a phototoxic reaction

Lastly, it is important to hold phototherapy treatments until the phototoxic reaction is completely resolved. This means that phototherapy may have to be held for a few days, even up to a week, until both the last of the erythema and symptoms disappear. This is because the excitability of the recently burned skin can persist beyond the time visible erythema completely resolves. For localized burn, the region of the burn can be covered until it resolves, and the rest of the body can continue to be treated. When restarting, the dose should be reduced to the highest dose tolerated that did not produce the phototoxic reaction [5]. The above recommendations are summarized in Table 8.1.

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Chapter 9
When Patients Cannot Tolerate Narrowband-UVB

Case

A 51-year-old male with generalized psoriasis starts NB-UVB phototherapy. NB-UVB dosimetry is initiated per protocol. However, within 1–2 weeks of starting, the patient complains that his skin feels quite irritated following each treatment. Initially, he was thought to have "initiation burn" (see Chap. 7) and lower dosimetry with careful titration was attempted. However, despite the most careful dosimetry modulation, the patient still complained of irritation after each NB-UVB exposure. He denies past medical history of photosensitizing diseases such as systemic lupus erythematosus. You examine the skin to find only lesions consistent with partially-treated psoriasis and no additional primary skin findings to explain the patient's skin irritation.

Discussion

NB-UVB phototherapy, which emits wavelengths of light between 308 and 313 nm, was purposely designed to optimize the treatment of psoriasis after early studies showed that psoriasis responds better to wavelengths of light closer to 310 nm [1]. However, rarely, there are patients with psoriasis who cannot tolerate NB-UVB due to the skin becoming irritated from the light [2, 3]. The exact cause of this is unclear.

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Although some studies point that NB-UVB may be more effective than BB-UVB [4], when a patient cannot tolerate NB-UVB, BB-UVB is a good alternative treatment option [5]. PUVA phototherapy may also be tolerated as the therapeutic light spectrum of PUVA is completely different from that of UVB. If neither BB-UVB nor PUVA are available, heliotherapy utilizing natural sunlight may be an effective and safe therapeutic option provided that it is done in the correct manner (see Chap. 10).

Similarly, there are patients who cannot tolerate BB-UVB but can tolerate NB-UVB. BB-UVB is more commonly used for patients with atopic dermatitis, prurigo nodularis, and chronic pruritus, as it appears to have less irritating effects compared to NB-UVB and is better tolerated [5]; however, this, of course, can vary depending on the individual. Therefore, at the UCSF Phototherapy Unit, there are psoriasis patients who might be categorized as NB-UVB intolerant who are doing very well with BB-UVB. On the other hand, there are patients with atopic dermatitis, other eczema, and chronic pruritus who are intolerant of BB-UVB but do much better with NB-UVB. This is another reiteration of the importance of individualizing treatments to each patient when practicing phototherapy.

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Chapter 10
Heliotherapy

Case

A 47-year-old female with a long history of localized psoriasis presents to the office after experiencing severe work-related distress, which has now caused her psoriasis to generalize over the trunk and extremities. On physical examination, the patient is noted to have many plaques of psoriasis scattered widely over the body. Scaling and induration of the plaques are mild to moderate in severity. The patient expresses her wish to be treated from outside rather than take medications that are internal.

Due to the fact that she has relatively thin plaques with only mild to moderate scaling, she is a good candidate for phototherapy and office-based phototherapy is suggested. Unfortunately, the patient is not able to present to the office 3 times per week due to her busy work schedule. She also lives very far away from any office that offers phototherapy. Given that the patient is highly reliable and motivated, heliotherapy is suggested. Her past medical history is reviewed for any photosensitizing disorders, and her medication list including herbal supplements is reviewed to make sure she is not on any photosensitizers. She is recommended to expose her affected skin to natural sunlight during lunchtime at her office and at home on weekends daily.

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After 2 months of heliotherapy, the patient presents for follow up. She reports that she was able to get sunlight to her psoriasis around noontime for approximately 10 min on most weekdays and on the weekends. She presents with overall improvement of her psoriasis in most areas of the body. She is asked to continue every 3 to 6 month follow up for evaluation of treatment response and routine skin examinations.

Discussion

The use of natural sunlight for therapeutic purpose, called heliotherapy, is an under-utilized therapeutic option today. This treatment method dates back to the Ancient Egyptians, who used natural light in combination with herbal extracts to treat skin disease [1]. In the nineteenth century sunbathing was recognized as a basic part of psoriasis therapy that resulted in appearance of health centers in the seaside resorts across England and Germany [2]. However, overtime, misconceptions have developed that manufactured phototherapy equipment is far superior to sunlight for the treatment of various skin diseases such as psoriasis and atopic dermatitis. This is actually not entirely true because no matter how fancy or expensive the phototherapy equipment may be, the amount of light that the patient can tolerate is still limited by the individual's minimum erythema dose (MED) or the sunburn threshold. Most patients are capable of experiencing sunburn from natural sunlight. This means that, if sunlight is used properly and carefully, the patient theoretically can be treated as aggressively as with a phototherapy booth available in a dermatology office [2, 3]. One study has shown that clinical improvement of psoriasis following sun exposure is preceded by a rapid reduction in local and systemic inflammatory markers, strongly suggesting that immune modulation mediates the observed clinical effect [4].

Prior to initiating heliotherapy, the patient should be asked about any history of photosensitivity. The patient's medication list should be reviewed for any photosensitizing

medications (see Chap. 13). This should include any vitamins or herbal supplements, which can often have photosensitizing properties. The patient should report to the dermatologist any new medications or supplements that are initiated while practicing heliotherapy. Furthermore, the patient should be asked about personal history of skin cancer and be advised to be cognizant of any new skin lesions that appear or change and report such findings to the dermatologist as soon as possible. Unlike UVB phototherapy, heliotherapy may be associated with an increased risk of skin cancer.

Heliotherapy should be conducted in a way to maximize benefit. UVB rays from the sun are the strongest around noontime during the summer months. Since UVB light, especially near 310 nm, is found to be optimal for the treatment of psoriasis, it is important to tell the patient to conduct heliotherapy using the midday sun so that they do not waste time early in the morning or late in the afternoon and become disappointed when they do not see adequate results. Even though there is plenty of visible light at those times, it is UVB that is mainly responsible for the therapeutic effect of sunlight, and therefore heliotherapy that is not conducted with midday sunlight, especially in the summer, is likely to fail [5].

The patient can be instructed to expose the affected skin to natural sunlight for "as long as possible without getting sunburned". The skin should initially be exposed to sunlight for a duration of time that the patient knows he/she can tolerate well without burning. The duration should be increased gradually until either obvious improvement is seen or the MED is reached (the skin appears slightly erythematous or pink). The optimal method of conducting heliotherapy is summarized in Table 10.1.

Lastly, it is critical to instruct all patients to protect the face from sun exposure especially if they have no lesions on the face. This is because the risk of skin cancer is the greatest on the face. Fortunately, psoriasis tends to spare the face. Similarly, the genitals and other sensitive areas should also be protected from sunlight. Furthermore, the patient should continue to be monitored by the dermatologist on a regular basis to assess treatment response, as well as to conduct skin examinations.

Table 10.1 The optimal method of conducting heliotherapy

Time	Around noontime during summer months when UVB is the strongest (depends on location)
Duration	For as long as possible without getting sunburned and until the skin appears slightly erythematous or pink (MED)
Frequency	Every other day
Exposure	Only affected areas (protect the face, genitals, and other sensitive areas from sunlight)
Monitoring	Baseline skin examination, followed by regular follow up with dermatologist to assess treatment response and conduct skin examinations

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Chapter 11
Cool Down Before Initiation of Phototherapy

Case

A 69-year-old Caucasian female with longstanding history of psoriasis presents with an erythrodermic flare in which nearly all skin surfaces are bright red with only the face spared. Her past medical history is significant for HIV, currently under well control on anti-retroviral therapies, as well as hepatitis C. Due to her comorbid medical conditions, the decision is made to start the patient on phototherapy. However, before she can safely start phototherapy of any kind, the patient is "cooled down".

The "cool down" procedure is initiated by applying liberal amounts of triamcinolone 0.01% ointment, dispensed from one pound jars, to the whole body (except the face). For sensitive areas such as the axilla, intertriginous, and groin regions, desonide 0.05% ointment is used twice daily. After applying the topical corticosteroids, the skin is covered with large sheets of saran wrap, which sticks well to the ointment without the use of adhesive tape.

After 1 week of the above procedure all day each day, the intense inflammation begins to resolve and the skin is no longer red and only pink. At this time, NB-UVB is initiated at 30 mJ/cm^2. The first 3 phototherapy sessions are kept stable at 30 mJ/cm^2 and is tolerated by the patient without any burning symptoms or other signs that the light is aggravating the

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inflammation. The dose is then gradually increased very cautiously by 10–30 mJ/cm^2 as tolerated, which is at a rate that is much slower than the usual dosing increment schedule. At the same time, the above cooling procedure is continued only at home. It is made sure that topical agents are not present on the skin at the time of the actual phototherapy session to ensure reasonably constant penetration of the light into the skin.

After 2 weeks, the erythema becomes very mild and she is able to stop the "cool down" procedure at home and instead use topical corticosteroids as needed to the affected areas. NB-UVB is continued at a frequency of 3 times per week, which is tolerated well. At 8 week follow up, the patient is tolerating NB-UVB per the usual protocol and is almost completely clear.

Discussion

It is critical for every phototherapy provider to know that extremely intense erythema, such as in this case of erythroderma (Fig. 11.1), is a contraindication to any type of phototherapy, be it NB-UVB, BB-UVB, PUVA, or excimer laser [1]. Phototherapy, in reality, is a "double-edged sword" as it can either help or aggravate inflammation. This is easily observable by the fact that natural sunlight generally helps patients with psoriasis by decreasing skin inflammation but not if the patient gets sunburned. In fact, serious sunburn can cause Koebnerization and result in worsening of psoriasis [2]. This implies that light therapy helps decrease inflammatory intensity until a threshold dose is reached when it turns into a pro-inflammatory force (i.e. sunburn).

The pro-inflammatory potential of phototherapy is most concerning if the patient is already extremely intensely inflamed at the time of presentation. Clinically, this "over the top" intensity can be readily identified by the "bright red" or "beefy red" coloration of the erythema (Fig. 11.2). If such a patient were to receive phototherapy by error, the intensity

FIGURE 11.1 Patient with erythrodermic psoriasis requiring a "cool down" procedure prior to starting any kind of phototherapy

of inflammation can become so severe to the point that the patient may have to be hospitalized with whole body edema, pain, and other complications. Therefore, it is crucial not to rush into phototherapy if the patient appears erythrodermic or near erythrodermic. It is worth emphasizing that "erythrodermic" psoriasis needs not involve 100% of the body surface area. Since psoriasis tends to spare the face, it is not unusual for a patient to present with nearly whole body erythroderma but sparing the face and possible a few other locations.

The above phenomenon whereby the most intensely erythematous skin can be made more inflammatory by phototherapy also applies to patient who have localized but bright red lesions; the intensity of the inflammation is key, not the amount of body surface area involved. Therefore, if a patient were to present with the most unusually intense inflammation

FIGURE 11.2 Patient with severely inflamed, "beefy" and bright red psoriasis requiring "cool down" prior to starting phototherapy

of, for example, hand and foot psoriasis or eczema, it is still necessary to "cool down" the skin down before starting hand/foot PUVA or other light treatments. Another type of intensely inflamed psoriasis requiring "cool down" or avoidance of phototherapy all together is pustular psoriasis [3].

The "cool down" procedure can be conducted by using liberal amounts of topical corticosteroids as explained above. Triamcinolone 0.01% ointment is most commonly used at the UCSF Phototherapy Unit as it can be dispensed in one-pound jars as opposed to tubes, which allows for easier and more generous application. Alternatively, "cool down" can be performed using a rapid-acting systemic mediation, namely cyclosporine, for both psoriasis and eczema (see Chap. 19) [4], or acitretin for pustular psoriasis [3]. Infliximab is a rapid-acting biologic agent that can also be used in the setting of erythrodermic psoriasis (Tables 11.1).

After beginning the "cool down", the patient is ready to start phototherapy once the skin is no longer red and only pink. Phototherapy is then added gingerly and increased very cautiously, especially at the beginning (Tables 11.2). At the UCSF Phototherapy Unit, patients with erythroderma is usually started at 30 mJ/cm^2 (NB-UVB) and if this is tolerated for at least several treatments, then the dose is increased by 10–30 mJ/cm^2. Ultimately, the timing and rate of subsequent

Table 11.1 Various "cool down" methods prior to initiating phototherapy for inflammatory skin conditions

"Cool down" method	Use
Topical corticosteroids under plastic occlusion	Any topical steroid-responsive inflammatory skin conditions including erythroderma
Cyclosporine	Severe psoriasis (any subtype including plaque, guttate, pustular, erythrodermic, palmoplantar), severe atopic dermatitis/eczema
Acitretin	Pustular psoriasis, erythrodermic psoriasis
Infliximab	Erythrodermic psoriasis, severe plaque psoriasis

Table 11.2 An example of a conservative phototherapy protocol for patients who present with erythroderma after proper "cool down" is completed

	Initial dose (mJ/cm^2)	**Subsequent dose increments (mJ/cm^2)**
NB-UVB	30	10–30
BB-UVB	5	5–10
PUVA	0.25	0.5

dose increments are up to the phototherapy practitioner's assessment of each individual patient's disease state and predicted response to UV light. The patient is instructed to continue the "cool down" at home until the erythema is only mildly pink. It is important that the patient does not apply any topical corticosteroids to the skin immediately prior to a treatment session as this can alter the penetration of light into the skin.

For most patients who present erythrodermic but undergo "cool down", followed by phototherapy, they are eventually able to tolerate doses of light close to that of the usual protocol.

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Chapter 12
Two-Step Phototherapy for Patients with Resistant Disease

Case

A 27-year-old male with generalized plaque psoriasis worst on the lower legs presents for follow up. He has been doing NB-UVB phototherapy 3 times per week in the office for the past year with great improvement of psoriasis on his trunk. However, he continues to have stubborn plaques on both of his shins. In addition to regular phototherapy, he uses topical corticosteroids to these stubborn areas with minimal additional improvement. He is very bothered by the appearance of his lower legs and the fact that he cannot wear shorts or go to the beach without being embarrassed. The patient states that the 3 times per week phototherapy regimen has been manageable with his schedule and he can continue treatments; however, he would like these resistant plaques to go away. One examination, he has well-demarcated, thick erythematous plaques with minimal scale on the bilateral shins and ankles. His chest, abdomen, and back are clear of psoriasis.

In order to further improve the psoriasis on his lower legs, the patient is started on a two-step phototherapy regimen. During each treatment session, the trunk and extremities are first treated as per protocol. Then all of his skin except for the lower legs is covered with a gown and towels, and he is again exposed to light, starting at a low dose and increasing per

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protocol. He is also instructed to step on a stool in the phototherapy booth to improve irradiation to the lower legs. With this two-step regimen, the patient returns 3 months later with near clearance of the stubborn plaques on his lower legs.

Discussion

It is not uncommon for patients to have only a partial response to UVB phototherapy. Typically, adequate improvement of disease is seen on the trunk, but treatment response may be poor on the distal extremities (Fig. 12.1). In such cases, instead of declaring that these patients have "failed" UVB, the two-step approach can be utilized [1].

In the two-step approach, patients will first receive phototherapy as usual to the whole body for overall exposure (the face and genitals should be covered if there is no disease in these areas). After completing this portion of the treatment session, the patient will come out of the booth and cover areas of the body with lower MED such as the trunk. Since the extremities can generally tolerate more light than the trunk, the patient will then re-enter the phototherapy booth to receive an additional dose of the light to the extremities [2] (Fig. 12.2). The second step of this two-step regimen should

FIGURE 12.1 A patient with recalcitrant psoriasis on the lower legs who would benefit from two-step phototherapy, which allows for higher doses of additional light to be given to the legs

FIGURE 12.2 The two-step phototherapy allows for higher doses of light to be delivered to resistant areas such as the extremities

be started at low dose and increased as tolerated per protocol. Examples of how this two-step phototherapy can be effectively documented in the patients' medical records are illustrated in Table 12.1.

In the present patient who has recalcitrant psoriasis plaques on the lower legs, in addition to the above two-step approach whereby he receives additional dosage of light to the legs, it may also be helpful for the patient to step on a stool to elevate himself while in the booth (Table 12.1 and Fig. 12.3). This is because the top and bottom of the UV

a

Phototherapy	10/4/2016	10/6/2016
Phototherapy treatment #	415	416
UV type	nbUVB	nbUVB
Patient report	No problems; Other	Other
Patient report comments	Let's go up on both parts	"I got a little bit pink and still pink, I think we should probably stay the same"
Erythema asmt of unaffected skin	None	None
Erythema comments		
Physical exam comments	Lower legs and eyebrows with scale and induration	Slight erythema to legs, indurated, scale to lower legs, left> right
Lesion erythema	1 (pink)	1 (pink)
Lesion induration	1 (slight)	1 (slight)
Lesion scale	1 (slight)	1 (slight)
Comments		
Phototheraphy box - UVB	NB2	NB1
Face plus total body (mJ UVB)	385	385
Additional body (mJ UVB)	0	0
Additional arms/legs (mJ UVB)	700	700

10/11/2016	10/13/2016	10/18/2016
417	418	419
nbUVB	nbUVB	nbUVB
Itch	Other	No problems
"LITTLE MORE ITCHY - NOT FROM LIGHT."	"Itching, not so much, its OK"	"Let's go up today"
None	None	None
NO NEW SCALE LEGS	Scale to left lower leg	Elbows pink with minimal scale and legs with large pink slight
1 (pink)	1 (pink)	1 (pink)
1 (slight)	1 (slight)	1 (slight)
1 (slight)	1 (slight)	1 (slight)
NB1	NB2	NB2
410	410	435
	0	0
735	735	770

b

Phototherapy	10/13/2016	10/17/2016
Phototherapy treatment #	402	403
UV type	bbUVB	bbUVB
Patient report	Other	No problems
Patient report comments		
Erythema asmt of unaffected skin	None	None
Erythema comments	DECREASED FACIAL AND NECK ERYTHEMA	
Physical exam comments		Decreased neck erythema, new fissures to fingers
Lesion erythema	1 (pink)	1 (pink)
Lesion induration	1 (slight)	1 (slight)
Lesion scale	1 (slight)	1 (slight)
Comments		
Phototheraphy box - UVB	BB	BB
Face plus total body (mJ UVB)	70	80
Additional body (mJ UVB)	125	125
Additional arms/legs (mJ UVB)	220	240

10/24/2016	10/27/2016
404	405
bbUVB	bbUVB
No problems	No problems
"I was away last week"	"We can go up"
None	None
New thumb fissures, neck remains erythematous	New fissures to right thumb, erythema to anterior neck, right side>left
1 (pink)	1 (pink)
1 (slight)	1 (slight)
1 (slight)	1 (slight)
BB	BB
80	90
125	125
240	260

TABLE 12.1 Examples of how to document the two-step phototherapy regimen effectively into the patients' medical records: (**a**) a patient with psoriasis on NB-UVB, (**b**) a patient with atopic dermatitis on BB-UVB

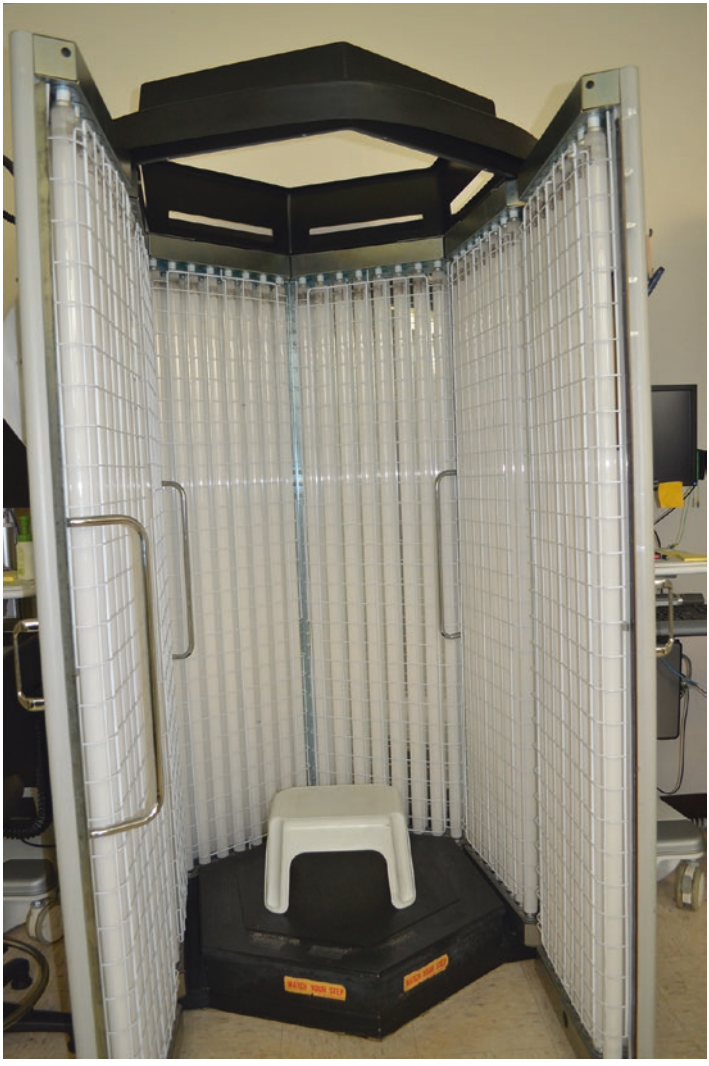

FIGURE 12.3 It can be beneficial for the patient to elevate oneself on a step-stool to increase the dose of light received on the lower legs, as the intensity of radiation is less at the top and bottom of the UV lamps

lamps have much lower intensity of radiation compared to the middle [3]. Ironically, patients end up receiving less UV exposure in precisely the areas that need it the most. By elevating the patient within the booth, the amount of irradiation to the legs may improve, leading to better outcomes.

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Chapter 13
Phototherapy in the Setting of Photosensitizing Medications

Case

A 59-year-old female with generalized psoriasis is very interested in undergoing UVB phototherapy. She clearly prefers an external method of treatment and is very much afraid of internal therapeutic options even after long counseling sessions on her concerns. Her past medical history is significant for hypertension for which she takes hydrochlorothiazide. Several other anti-hypertensive medications were tried by her primary care physician, but either they did not work or she could not tolerate them due to side effects.

To make phototherapy safe while continuing a potential photosensitizing medication, she is asked to take her once daily dose of thiazide diuretic as far away in time from the next phototherapy session. In another words, she is asked to maximize the time between her medication dose and the next phototherapy session to minimize the blood level of the photosensitizing medication at the time she goes into the light box. She is asked to keep this consistent every day, especially on days she is receiving phototherapy.

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NB-UVB phototherapy is initiated cautiously at 130 mJ/cm^2, which is the protocol for one skin type below her own skin type; the patient has skin type II, but she is treated as skin type I. The subsequent dose is increased per protocol for skin type I which is 15–50 mJ/cm^2 per treatment. With these precautions, the patient does not experience any phototoxic reaction, eventually tolerating a dose that is as high as the average patient not on photosensitizing medication. Her psoriasis mostly cleared over several months.

Discussion

Some medications are known to cause photosensitivity, and these medications are routinely avoided in phototherapy practice if possible (Table 13.1) [1]. However, just because a medication is on this list does not mean that it causes photosensitivity in everyone. In fact, when precautions are taken as described above, most patients on a photosensitizing medication can still successfully undergo phototherapy. Furthermore, many of these medications are shown to only be photosensitizing with UVA [1], and therefore, there is less

Table 13.1 Medications known to have photosensitizing potential, adapted from Glatz and Hofbauer [1]

Antimicrobials	**NSAIDS**	**Anti-hypertensives**
Doxycycline	Naproxen	Furosemide
Minocycline	Ketoprofen	Hydrochlorothiazide
Ciprofloxacin		Calcium-channel blockers
Levofloxacin		
Voriconazole		
Antimalarials	**Retinoids**	**Other**
Chloroquine	Acitretin	Psoralens
Hydroxychloroquine	Isotretinoin	Chlorpromazine
Quinidine	Targretin	

concern when the patient is undergoing UVB phototherapy. However, caution should still be exercised.

Prior to beginning phototherapy, all patients should be asked to bring in their complete medication list. Patients should also disclose any vitamin or herbal supplements, as well as alternative treatments that they are receiving for any indication. It is also important that the patient promptly reports any changes to medications or supplements during the course of phototherapy treatments. If the patient is found to be on a potential photosensitizing agent, then there are several keys to conducting phototherapy in this setting.

First, maximum time should be given between medication dosing and the next phototherapy session in order to minimize blood levels of the medication [2]. Stern et al. showed that the worst time to take a photosensitizing medication is shortly before the next phototherapy session. In this study, rates of phototoxic side effects were compared between patients who took the photosensitizing medication as far away as possible from the phototherapy session and those who took the photosensitizing medication fairly close to the time of phototherapy. Not surprisingly, the patients who deliberately allowed for maximum time between the medication dosing and phototherapy experienced much less phototoxic reaction.

Second, phototherapy should be initiated conservatively. Patients who are on a photosensitizing medication should follow the dosimetry protocol per one skin type lower than the patient's actual skin type. For example, for the above case illustration, given that the patient has skin type II and is on a photosensitizing medication, she should be treated per protocol of a patient with skin type I. The subsequent dose increase is also based on the skin type I protocol. Alternatively, if a patient is inevitably started on a photosensitizing medication during the course of phototherapy treatments, the dose of light at the subsequent visit should be decreased by 50% [3]. The above recommendations are summarized in Tables 13.2 and 13.3.

Table 13.2 Recommended assessments and precautions regarding the use of photosensitizing medication during the course of phototherapy

Prior to initiating phototherapy	Patient to disclose active medication list, including any vitamin or herbal supplements and alternative treatments
During course of phototherapy	Patient to promptly report to practitioner any new or changes to existing medications/ supplements If on a photosensitizing agent, give maximum time between medication dosing and the next phototherapy session in order to minimize blood levels of the medication

Table 13.3 Recommended dose adjustments for patients on photosensitizing medications

Patients on a photosensitizing drug at the start of phototherapy	Treat per protocol of one skin type lower than the patient's actual skin type (i.e. if skin type II, treat per protocol of skin type I).
Patient starts a photosensitizing drug during course of phototherapy	Decrease dose by 50%, then proceed with subsequent dose increases per protocol for patient's actual skin type

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Chapter 14
Phototherapy-Induced Iatrogenic Polymorphous Light Eruption

Case

A 64-year-old male with a 5-year history of psoriasis vulgaris presents with a flare of his psoriasis. On examination, he has well-demarcated, erythematous plaques with silver-white scale covering approximately 20% of the trunk and extremities. 3 times per week treatment with NB-UVB phototherapy is initiated. The initial dose of NB-UVB is determined by his skin type and the dose is increased slowly as tolerated. Steady improvement is observed over the next few weeks with decreasing erythema, induration, and scale of the psoriatic plaques. However, when he presents for treatment day 15, he complains of itchy rash on the arms and back. On examination, he is noted to have new scattered pruritic papules and papulovesicles coalescing into plaques on the extensor surfaces of the forearms, chest, and back (Fig. 14.1). The records show that at the last phototherapy session, he was given the highest dose of NB-UVB to date at 1040 mJ/cm^2.

Given the history and morphology of the lesions, the patient is suspected to have polymorphous light eruption (PMLE) induced by phototherapy. Phototherapy treatment is held and the patient is instructed to apply liberal amounts of clobetasol to the new rash and avoid the sunlight as much as possible. A few days later, he reports significant improvement of the itching and rash (Fig. 14.2). One week later, phototherapy

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FIGURE 14.1. Patient with a new pruritic eruption of erythematous papules, papulovesicles, and plaques that developed on treatment day 15 of NB-UVB consistent with phototherapy-induced, iatrogenic PMLE

FIGURE 14.2 After holding phototherapy treatments and treating with topical corticosteroids for 7 days, the eruption resolved and phototherapy was restarted at low dose with no return of PMLE lesions

is restarted at 330 mJ/cm^2 (the starting dose for his skin type) and slowly increased as tolerated. The patient returns to your clinic 4 weeks later with no evidence of PMLE and continued improvement of his psoriasis.

Discussion

PMLE affects up to 20% of the population and is most commonly characterized by pruritic lesions, which appear a few hours to days following light exposure [1]. Lesions vary from papules to papulovesicles to plaques, and insect-bite like strophulus forms have also been reported. Naturally, PMLE most commonly occurs in the spring and summer months when one is exposed to more sunlight. One study has found that approximately 5.5% of patients with psoriasis have photosensitivity, with approximately half of these patients having a diagnosis of PMLE [2].

PMLE can be induced by various wavelengths of light. Although most patients with PMLE are sensitive to UVA light only, others are sensitive to only UVB or both UVA and UVB [3, 4]. It has been shown that repetitive exposure to suberythemogenic doses of UV light to the same skin area is necessary to provoke lesions of PMLE, which is the basis of the current diagnostic method called photoprovocation [5]. Although the exact pathogenic mechanisms of PMLE remain unknown, partial failure of UV-induced immunosuppression and subsequent delayed-type hypersensitivity response to a UV-modified skin antigen is likely a key factor. Whereas UV rays induce Langerhans cell migration out of the epidermis in healthy skin, Langerhans cells of PMLE patients are resistant to this effect [6]. Furthermore, this resistance to UV-induced immunosuppression is only observed in a narrow UV-dose response window of 1 minimal erythema dose (MED) of solar simulated UV radiation, but not 0.6 or 2 MED [7]. Treatment of PMLE includes photo-hardening, a method by which the skin is exposed to small, incremental doses of light to allow the skin to desensitize. This is thought to provide immunosuppression without inducing delayed-type hypersensitivity [1]. Management of PMLE also includes preventative photo-protective measures.

Phototherapy is effective in the treatment of psoriasis through its immunosuppressive mechanisms. It has been shown that UVB produces maximal results when used at or near the patient's MED [8]. In the present case, the patient tolerated up to 1030 mJ/cm^2 of NB-UVB, which is likely near the his MED, before PMLE lesions were induced (Fig. 14.1). For this patient and others who develop phototherapy-induced iatrogenic PMLE, phototherapy should be held and PMLE should be treated appropriately, such as with topical corticosteroids, until the lesions completely improve (Fig. 14.2). The patient can then be restarted on NB-UVB at a significantly lower dose than the threshold dose that induced the PMLE or down to the starting dose per skin type. The dose of light should then be increased cautiously as tolerated while observing for signs of recurring PMLE [9] (Fig. 14.2).

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Chapter 15
Herpes Zoster During Phototherapy

Case

A 72-year-old female with generalized pruritus presents for her scheduled session of phototherapy. She has been presenting for BB-UVB phototherapy twice weekly for the past year with overall improvement in her pruritus. Her last treatment was 2 days ago. When she arrives, the phototherapy nurse asks her about any symptoms she has had since her last phototherapy session. The patient reports a new sensation of burning pain and tingling on the left side of her mid back. Her pruritus continues to be under good control but with occasional scattered itchy spots on the back. As usual, the nurse has her change into a gown so that her skin can be examined prior to her treatment. The nurse then calls you into the room, as she is concerned about a red rash on the left side of the patient's back.

On examination, you see grouped erythematous papules and papulovesicles in a dermatomal distribution on the left mid back consistent with herpes zoster (HZ). You examine the rest of the body and only find mild excoriations on the back where the patient reports pruritus. You ask the nurse to please cover the region that is affected by HZ with a towel and continue to treat the rest of the skin per protocol. You discuss with the patient her diagnosis of shingles and give her a prescription for anti-viral therapy. For the next several

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treatments, the left side of the back is covered during phototherapy treatments until all of the lesions crust, heal, and disappear completely. Because there was no lapse in treatment sessions, the patient's pruritus continued to be under good control during her HZ outbreak.

Discussion

Herpes zoster (HZ) is a sporadic disease caused by reactivation of latent varicella-zoster virus (VZV) from the dorsal root ganglia. It is characterized by a unilateral vesicular rash in a dermatomal distribution often associated with severe pain. HZ can occur at all ages but is most common in older patients. Declining cellular immunity because of increasing age or immunosuppression are known risk factors for reactivation of VZV. HZ is relatively common, and the lifetime risk of HZ is estimated at 10–20% [1]. A certain subset of patients, such as those with rheumatoid arthritis, appears to be at increased risk of HZ [2]; however, the risk in patients with various dermatologic conditions, such as psoriasis, atopic dermatitis, and chronic pruritus, is not well delineated.

Although phototherapy calms inflammation and may have an effect to reduce immune activity in the skin, studies have not shown an increased risk of developing HZ during phototherapy [3]. Patients on certain biologic agents for the treatment of psoriasis may be at increased risk of HZ; however, this has not been shown to be the case with phototherapy [3]. As HZ is a relatively common occurrence in the general population, it is important to know how to approach a patient undergoing phototherapy who presents with an outbreak of HZ.

At the UCSF Phototherapy Unit, patients typically continue phototherapy treatments despite HZ outbreak, especially if their primary disease (such as psoriasis, atopic dermatitis, pruritus, etc.) are symptomatic and need continued treatment for disease control. In such a case, the general region of the HZ lesions should be covered with a gown or

towel. In the current case in which the patient had HZ lesions on the left mid back, the left side of the back was covered while scheduled phototherapy sessions were continued; the rest of the exposed skin is treated per protocol. The area should be covered until all of the lesions have resolved and the skin is back to the patient's normal state. Proper contact precautions are advised for staff who are treating patients with HZ. Phototherapy can be continued in the setting of post-herpetic neuralgia without any adverse consequences.

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Chapter 16
Enhancing Phototherapy with Topical Agents

Case

A 58-year-old female with generalized plaque-type psoriasis undergoes NB-UVB phototherapy with marked improvement over the first 3 months. However, despite clearing or near clearing of most of her plaques, some recalcitrant ones still remain, especially on the extremities. Two-step phototherapy, in which the whole body is treated followed by an extra dose to the extremities after covering the trunk (face is covered from the start), is initiated and the dosing is maximized to her tolerance. Despite this, several of the recalcitrant lesions still remain moderately scaly and indurated.

Options of adding acitretin or switching to a biologic agent are discussed, but the patient adamantly prefers to keep away from internal medications. In view of this, tazoratene (Tazorac®) 0.05% cream is initiated only to these stubborn plaques. The patient is asked to start with only 3 times per week, once daily applications to the affected areas. She is instructed not to apply tazoratene or any other topicals for at least a few hours before the phototherapy session, as doing so may change the reflective index of light penetrating the skin.

Tazoratene 0.05% cream is tolerated on these indurated plaques without any irritation. After several weeks, the concentration of tazoratene is increased to 0.1% cream. The patient notes "peeling" on the surface of these plaques

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without any irritation. Over the next few weeks, the plaques become thinner and start to improve again even though the dosimetry of the phototherapy could not be increased since it was already maximized before tazoratene cream was started. In time, the recalcitrant plaques gradually dissolved with the combination of tazoratene cream daily, 3 times per week, with NB-UVB phototherapy 3 times per week.

Discussion

It is well known that the oral retinoid acitretin can significantly enhance the efficacy of phototherapy whether it is used in conjunction with NB-UVB, BB-UVB, or PUVA (see Chap. 17) [1]. It is less well known that a topical retinoid can do the same. Tazoratene is a topical retinoid that is FDA-approved for the treatment of psoriasis. Compared with twice-daily fluocinonide 0.05% cream, once-daily tazarotene 0.05 and 0.1% gels show similar efficacy in reducing plaque elevation. Studies have also shown that tazoratene has a more prolonged therapeutic effect after discontinuation than twice-daily fluocinonide cream [2]. Furthermore, the phototherapy enhancing effects of tazoratene is well-documented in the literature [3–5]. Topical retinoids can enhance phototherapy when there are resistant plaques with thick scale and the UV rays cannot penetrate effectively.

There are several factors to be aware of when a topical vitamin A agent is used. Topical vitamin A is significantly more likely to cause irritation to the skin than topical vitamin D and certainly more than any topical steroids [6, 7]. Therefore, the provider should be cautious and start with the lower concentration (0.05%) to make sure that no irritation occurs before increasing to the higher concentration of tazoratene (0.1%). Thicker, more treatment resistant psoriasis may be less prone to irritation by tazoratene as compared to thinner plaques. In addition, it is important to instruct the patient to do his/her best to only put tazoratene on the plaque and avoid exposure to normal skin. This is because

Table 16.1 Topical therapies to enhance effectiveness of phototherapy

Topical retinoids	**Topical keratolytics**
Tazoratene 0.05 or 0.1% in cream or gel	Salicylic acid 6% in ointment, cream, gel, lotion, etc. Lactic acid 5 or 12% cream/lotion
Topical coal tar	**Anthralin/dithranol**
Crude coal tar 2%, 5%, 10% in petrolatum LCD 20% in petrolatum	Up to 10% in paste, ointment, cream

normal appearing skin is much more prone to topical retinoid irritation than psoriasis plaques.

Other topical agents that can be helpful in making phototherapy more effective include keratolytics such as salicylic acid and lactic acid, and tar products such as crude coal tar in the Goeckerman regimen (see Chap. 4), liquor carbonis detergens (LCD) or gold tar, and anthralin (Table 16.1).

Salicylic acid, in concentrations of 5% and above, exerts an increasingly potent, rapid, and deep keratolytic effect on the stratum corneum. Salicylic acid is thought to reduce intercellular cohesion between keratinocytes by dissolving the intercellular cement material and reducing the pH of the stratum corneum, thereby increasing hydration and softening [8]. Salicylic acid is most beneficial in extremely thick or scaly psoriatic plaques. It also promotes skin availability of other topical therapies by allowing better penetration of topical medications. While salicylic acid is commonly effective when used as a pretreatment before initiation of phototherapy, topically administered salicylic acid in concentrations of 0.1% and greater, is actually photoprotective [8]. Thus, application of salicylic acid immediately before UVB phototherapy is not recommended. Local irritation such as stinging, burning, dry skin, peeling, scaling, or contact dermatitis are potential side effects of salicylic acid.

Lactic acid or alpha-hydroxy acids (AHAs), which is available in various concentrations such as 5 or 12% (LacHydrin),

also helps remove scale. Lactic acid penetrate the epidermis, inducing an increase in stratum corneum turnover, leading to desquamation of the outermost layer without impairing barrier function [9]. Lactic acid can also work as an emollient at the same time it helps remove scale to enhance UV penetration.

Coal tar products have been widely used in the past to enhance UVB phototherapy. In the Goeckerman regimen, crude coal tar or black tar (2%, 5% or 10%) in petrolatum is commonly used (see Chap. 4); however, it is very difficult to use black tar at home as it can stain clothes, sheets, furniture, etc. LCD or gold tar is a little easier to use at home as it is less messy. When the intensity of the UVB therapy is titrated to a sub-erythemogenic level (see Chap. 6), tar preparations provide additional therapeutic benefit [10]; tar is thought to enhance the effects of phototherapy. It is important to remember that topical coal tar agents can also impede the penetration of UVB light if present on the skin, especially if thickly applied just before UVB phototherapy. In addition, when topical tar agents are used consistently such as in the Goeckerman therapy, it is important for the patient to avoid inadvertent ambient sunlight exposure, such as exposure to the left arm through the open car window, because even that can lead to sunburn due to the phototherapy-enhancing effect of the tar products.

Lastly, in certain parts of the world (especially England), anthralin or dithranol is also used to enhance UVB phototherapy in a treatment that is called the Ingram regimen [11]. Anthralin is especially effective for thick, scaly psoriasis plaques. However, the use of anthralin has not been popular in the United States due to the skin staining effect of this compound, although the stain wears off the skin in approximately 10 days (Fig. 16.1). Anthralin is applied for short period of time ranging from 5 to 30 min. Anthralin is still commercially available in the U.S. in concentrations ranging from less than 1% to up to 10%. Therefore, for truly recalcitrant plaques of psoriasis that have defied all other therapeutic options, compounded anthralin in high

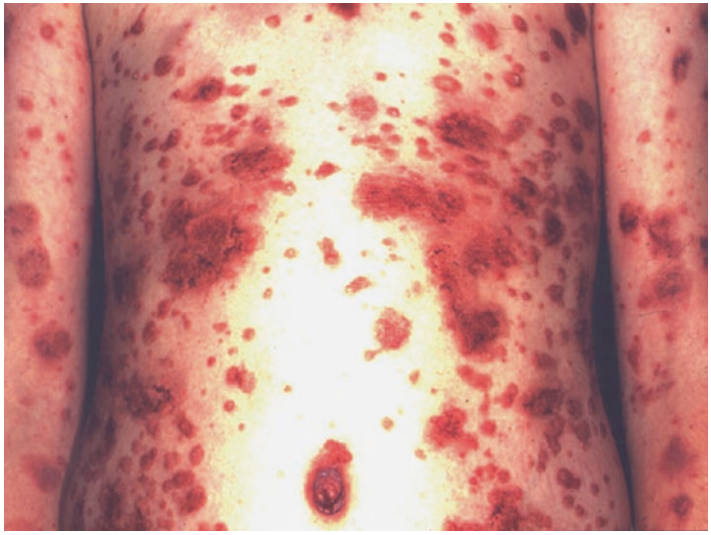

Figure 16.1 Skin staining from anthralin, which wears off the skin after approximately 10 days (From http://www.health.auckland.ac.nz/).

concentrations may prove efficacious provided that the patient does not get irritated by the high concentration that is needed to clear such plaques.

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Chapter 17
Combing Phototherapy with Acitretin: Re-PUVA and Re-UVB

Case

A 62-year-old Asian male presents for follow up of severe generalized psoriasis. He has been doing PUVA 3 times per week for the past 6 months with stubborn lesions on the trunk and extremities. He has been using topical corticosteroids in the morning and a topical retinoid tazoratene at night with minimal added benefit. The patient has history of lung cancer, and therefore, systemic immunosuppressive therapies should be avoided if possible.

On review of the PUVA phototherapy records, it is clear that the patient's dose of UVA is quite high and the dose of light appears to be optimized. On examination, you notice indurated plaques with very thick, micaceous scale on the trunk and extremities. You suspect that UV light is not able to penetrate through such hyperkeratotic scale. Therefore, after discussing the risks and benefits, including required laboratory monitoring, the patient is stared on acitretin 25 mg per day. At the subsequent phototherapy session, the patient reports to the nurse that he has started a new medication called acitretin. Given that acitretin is photosensitizing, the phototherapy nurse decreases the dose of PUVA by 50% in order to avoid burn.

Over the next several weeks, the patient tolerates acitretin well with only mild dry lips and dry skin and no laboratory

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abnormalities. His psoriasis plaques slowly thin out. He continues PUVA treatments 3 times per week and notices overall improvement of his psoriasis. Interestingly, his dose of PUVA is much less than it was prior to starting acitretin but appears to be working much better.

Discussion

PUVA is often combined with another treatment to achieve more rapid clearance at a lower dose of UVA radiation. When the disease is clear, the second therapy is usually discontinued and the control of psoriasis can be maintained by PUVA alone [1]. The effectiveness of retinoid plus PUVA ("re-PUVA") using acitretin has been well studied [2, 3]. In a randomized, double blind comparative study of 60 patients with severe, widespread psoriasis treated with PUVA, marked or complete clearing of psoriasis occurred in 80% of the patients (20 of 25) without acitretin and in 96% of the patients (22 of 23) with acitretin. The mean cumulative UVA dose given to patients in the acitretin-PUVA group was 42% less than that required for patients in the placebo-PUVA group, implying that acitretin substantially augments the efficacy of PUVA in the treatment of severe psoriasis [2]. Another study has shown the superiority of re-PUVA in decreasing lesional scores after 6 weeks of therapy and having fewer number of PUVA exposures and less total dose of UVA until remission [3].

Similarly, retinoids can enhance UVB phototherapy in "re-UVB" (retinoid plus UVB) [4, 5]. Acitretin has been shown to enhance the efficacy of UVB phototherapy in an 8-week, randomized, comparator study, which found that more than twice the number of patients in the combined BB-UVB and acitretin cohort reached PASI-75 as compared to the BB-UVB only cohort [4]. Acitretin can be used at a dose as low as 10 mg per day to as high as 50 mg per day [5]. The addition of acitretin is especially useful for patients with extremely indurated and hyperkeratotic lesions that do not

Figure 17.1 Psoriasis patients with thick, micaceous scale may benefit from combination treatment of acitretin and phototherapy

allow for effective UV penetration (Fig. 17.1). The addition of a retinoid can help thin the lesions to enhance the effects of phototherapy.

There are 2 approaches when using acitretin to enhance phototherapy (Table 17.1). The first approach is to start the patient on acitretin 2 weeks before starting phototherapy to prepare the skin for phototherapy. In this case, phototherapy can be started per standard protocol and increased as tolerated. The standard protocols are described in Chap. 1 for UVB and Chap. 2 for PUVA. The second approach is to add acitretin to an already maximized phototherapy regimen that is not yielding satisfactory results. In this case, acitretin can be added at a low dose (10–25 mg per day) and at the same time, the dose of phototherapy should be reduced by 50%. This is important in order to avoid a "delayed retinoid burn" [6] (Fig. 17.2). This phenomenon occurs when a severe phototoxic reaction is experienced as a result of adding acitretin to a previously tolerated phototherapy dose. Because acitretin induces cell differentiation and leads to sloughing of

Table 17.1 Combining acitretin and UVB (Re-UVB) or acitretin and UVA (Re-PUVA)

	Patient has not yet started acitretin or phototherapy	**Patient's phototherapy is already maximized**
Acitretin	Start acitretin at appropriate dose (10–25 mg/day)	Add acitretin at appropriate dose (10 or 25 mg/day)
UVB	After approximately 2 weeks, start UVB per standard protocol and increase as tolerated (see Table 1.1)	Reduce UVB dose by 50% and increase per as tolerated (see Table 1.1)
PUVA	After approximately 2 weeks, start PUVA per standard protocol and increase as tolerated (see Table 2.3)	Reduce UVA dose by 50% and increase per as tolerated (see Table 2.3)

Figure 17.2 Retinoid-induced burn: phototoxicity specifically on the psoriasis plaque during phototherapy in combination with a systemic retinoid

Table 17.2 Common side effects of acitretin, which are dose dependent (data on file with connetics pharmaceuticals corp.)

Adverse event	Acitretin > 25 mg/day (%)	≤ 25 mg/day (%)
Cheilitis	> 75	70
Skin peeling	50–75	30
Alopecia	50–75	13
Pruritus	25–50	26
Dry skin	25–50	4
Nail disorder	25–50	0
Arthralgia	10–25	4
Headache	1–10	13
Myalgia	1–10	0
Depression	1–10	0

keratinocytes from psoriatic plaques, this leads to excessive light penetration and results in phototoxicity specifically on the psoriasis plaque. To prevent this adverse event, it is suggested that the UV dose is decreased by 50% when an oral retinoid is initiated.

The current patient who has very thick, micaceous scale was not able to achieve satisfactory results with PUVA alone, likely due to the fact that the UV light could not effectively penetrate through his thick, hyperkeratotic lesions. In such a case, the addition of acitretin will likely thin the plaque and enhance the effectiveness of phototherapy. In this patient who was already tolerating a high dose of PUVA, the dose should be halved once acitretin is initiated.

Of note, when using acitretin, patients should be counseled on common side effects such as cheilitis, dry mouth, and dry skin. These unpleasant side effects are dose dependent, and therefore, the lowest effective dose of acitretin should be used (Table 17.2). Furthermore, acitretin should not be used in females of reproductive potential as it is teratogenic

(pregnancy category X) and pregnancy should be avoided for at least 3 years after discontinuing acitretin. Proper laboratory monitoring should be conducted, initially every 4–6 weeks, then at least every 3 months thereafter. Laboratory monitoring includes liver function tests and fasting lipids. Despite the required monitoring, acitretin can be a very safe long-term option and a good combination agent, as there is no immune-suppressive potential and has a unique mechanism of action from many other psoriasis therapies.

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Chapter 18
Combining Phototherapy with Methotrexate

Case

A 48-year-old Hispanic male with long history of generalized psoriasis presents for options beyond topical therapies. He is currently on topical corticosteroids and topical vitamin D, which have been optimized but have resulted in inadequate response. The patient is interested in phototherapy for its lack of concern for internal side effects. He is started on NB-UVB phototherapy.

Over several weeks, his psoriasis largely improves, but a fair amount of resistant lesions remain, especially on the extremities. At this time, the patient is open to starting an internal agent. However, unfortunately, all biologics, as well as apremilast, are not covered by his insurance. Acitretin is covered but with an extremely high copay that the patient cannot not afford. Methotrexate is then discussed including its various side effects and risk profile. The patient is agreeable to frequent laboratory tests to monitor for side effects. In addition, he already has several children and has no plans to father any more children. The use of proper measures to avoid pregnancy during his methotrexate therapy is discussed. After tolerating the test dose, the patient is started on methotrexate 15 mg weekly. Very importantly, he is asked to take his methotrexate dose every Friday night. He is instructed to continue NB-UVB 3 times per week.

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Several weeks later, the patient presents for follow up. He has been doing well with the weekly dose of methotrexate in combination with NB-UVB phototherapy. Methotrexate is tolerated without nausea, fatigue, or laboratory abnormalities. The dose of phototherapy has been maximized for his tolerance, and his psoriasis is almost clear.

Discussion

When phototherapy alone or methotrexate alone results in inadequate response for a patient with psoriasis, the two therapies can be combined safely and effectively [1–3]. If the patient is a candidate for and can tolerate methotrexate, then this combination therapy could be both a very convenient and affordable way to enhance phototherapy.

Although the following phenomenon may not be well documented in the literature, one important thing to note regarding the combination of phototherapy and methotrexate is that extremely rarely, methotrexate can induce an acute phototoxic reaction [4] or even more rarely a delayed phototoxic reaction [5–7] following phototherapy. Therefore, patients should take the complete dose of their weekly methotrexate on Friday night if possible. Provided that the patient does not receive phototherapy on the weekends, this gives maximum amount of time between the dose of methotrexate and the next phototherapy session. Just like with other photosensitizing medications as discussed in Chap. 13, minimizing blood levels of the medication at the time of phototherapy results in the lowest risk of phototoxicity [8].

It is also important to discuss the various risks associated with methotrexate therapy, including bone marrow suppression and hepatotoxicity, which should be monitored with frequent laboratory testing [7]. For the above patient, given that he is of reproductive age, the reproductive warning of methotrexate, which applies to both men and women, is discussed. Men are not to father any children during methotrexate therapy and for at least 3 months afterwards. This warning came about because of documented negative effects of

methotrexate on sperm samples [9], although to date, there have not been any significant reports of birth defects as a result of the father being on methotrexate [10].

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Chapter 19
Combining Phototherapy with Cyclosporine "Cool Down"

Case

A 38-year-old female presents with erythrodermic psoriasis. The patient is bright red from head to toe. The patient has no systemic symptoms and vital signs are within normal. Due to the intensity of erythema, prior to initiating phototherapy, she is started on a "cool down" procedure with topical corticosteroids. Triamcinolone 0.1% ointment is applied liberally all over the body and occluded with plastic wrap. This application of topical steroids under occlusion is repeated daily for 2 weeks.

At this time, although the patient feels much more comfortable with less skin irritation and itching, the erythema remains with diffuse red and pink coloration over the entire body. The experienced phototherapy nurse is uncomfortable initiating even the lowest dose of NB-UVB for this patient since, in her experience, there is still substantial risk of light aggravating inflammation at this intensity of erythema.

Since the patient is relatively young and generally healthy, the decision is made to augment the cooling procedure with cyclosporine. After discussing the side effects and risk profile, two sets of blood tests, including creatinine, and blood pressure are checked at least 1 day apart and found to be within acceptable limits. Cyclosporine at the dose of 5 mg/kg per 24 h is then prescribed in BID divided doses.

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On follow up 2 weeks later, the patient reports tolerating the cyclosporine well and denies side effects including gastrointestinal upset, headache, and paresthesia. Along with the continuation of the topical "cooling" regimen, the erythema has steadily decreased. On examination, the patient is only pink with no residual areas of bright redness. At this point, NB-UVB is started at a very low dose of 30 mJ/cm^2 and increased by 10–30 mJ/cm^2 as tolerated. With this regimen, the patient's psoriasis significantly improves. On follow up a few months later, cyclosporine begins to be tapered off as NB-UVB is continued.

Discussion

Cyclosporine is one of the most powerful and quick acting therapeutic options when it comes to decreasing the intensity of skin inflammation [1]. As discussed in Chap. 11, "cooling down" severely inflamed skin is necessary prior to initiation phototherapy (Fig. 19.1). When erythrodermic patients cannot be "cooled down" with topical corticosteroids alone, cyclosporine is an excellent option provided that the patient is generally healthy and does not have any contraindications to cyclosporine therapy including serious infection, immune suppression, and uncontrolled or severe hypertension [2]. Because cyclosporine is much less expensive than biologic agents, it is generally easier to access and can be initiated promptly. This is extremely advantageous in erythrodermic patients, as therapy should be started as soon as possible. Prior to starting cyclosporine, baseline laboratory tests should be performed which include complete blood count, liver function tests, serum bilirubin, magnesium, potassium, uric acid, lipids, blood urea nitrogen, and two sets of creatinine levels at least 24 h apart. Two sets of blood pressures should also be obtained at least 24 h apart. The diastolic blood pressure should consistently be 90 or less [2] (Table 19.1).

In this case of erythrodermic psoriasis resistant to topical occlusive therapy, cyclosporine is key. However, the topical

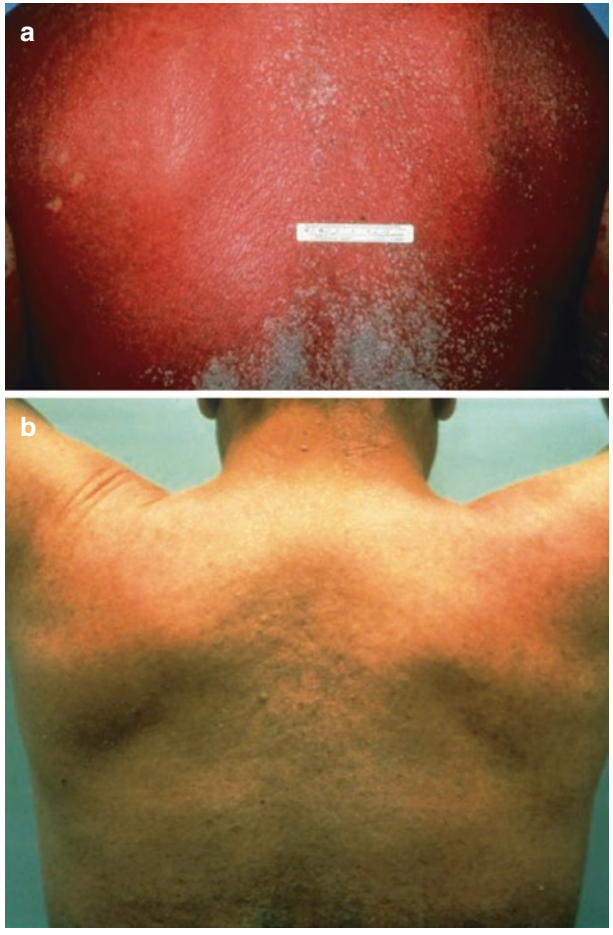

FIGURE 19.1 A patent with erythrodermic psoriasis requiring cyclosporine "cool down" prior to initiation of phototherapy (**a** before initiation of cyclosporine, **b** after cyclosporine "cool down")

cooling regimen should still be continued since simultaneously therapy from both inside and outside is likely more efficacious than just doing one or the other. In addition, patients with intense skin inflammation sometimes

Table 19.1 Pre-cyclosporine work up and laboratory assessments

Crucial	Important
Creatinine[a]	Potassium level
Blood pressure (≤ 90 diastolic)[a]	Magnesium level
	Triglycerides
	Liver function tests
	Uric acid

[a]Obtain at least two values more than 24 h apart

experience uncomfortable skin irritation and tightening due to dryness on the surface of the skin. Because of this, liberal application of triamcinolone ointment should be continued not only for its anti-inflammatory effect but also to relieve symptoms maintain lubrication of the skin surface.

Providers may be concerned about the concomitant use of cyclosporine and phototherapy in the same patient. The Food and Drug Administration (FDA) does recommend against the combined use of cyclosporine and phototherapy due to the possibility of an increased risk of skin cancer [3]. This concern arises from the fact that phototherapy may increase the risk of skin cancer, and since cyclosporine is immunosuppressive, their combined use may increase this risk further. This is a reasonable concern for long-term combination especially in fair-skinned, Caucasian patients. However, it is a very different situation when cyclosporine is used for a short period of time to cool the skin down so that a very safe, long-term treatment such as UVB can be initiated. To date, there is no evidence showing increased risk of skin cancer with short-term use of cyclosporine (typically 1 to 2 months) according to dermatology guidelines concomitantly with phototherapy [4, 5]. Some patients require several months of combined use of cyclosporine with phototherapy, but in the authors' experience, increased risk of skin cancer in these patients has not been observed.

For this case, it is important to note that the cyclosporine that was prescribed to the patient was *cyclosporine modified* or Neoral. This is because only Neoral® is FDA-approved for use in psoriasis, not the old formulation Sandimmune.

Sandimmune has unreliable and erratic absorption as compared to Neoral [6]. Each patient who is prescribed cyclosporine for psoriasis should be aware that Sandimmune is not the same as Neoral and the patient may experience relapse if sudden switch is made by pharmacy error.

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Chapter 20
Combining Phototherapy with Apremilast

Case

A 51-year-old female with moderate to severe chronic plaque psoriasis presents for follow up. She is currently using topical treatments only with gradual worsening of her psoriasis to the point that it now covers most of her trunk, elbows, and knees. She is interested in starting apremilast (Otezla®) as she recently saw a commercial on TV and heard from others that "it does not cause infections or cancers like biologics do". Furthermore, she is extremely needle phobic and does not want to try any biologic agents. After discussing the risks and benefits of apremilast, she is prescribed the starter titration pack.

The patient returns for follow up 2 month later. She states that she experienced some nausea and diarrhea for the first few weeks, but this has now subsided and she is tolerating the full dose. She has noticed some improvement of her psoriasis with less scaling and redness; however, she continues to have generalized involvement. You discuss with the patient that apremilast can take 4 to 6 months to reach maximum effectiveness and encourage her to continue apremilast while also maximizing her topical regimen.

The patient again returns for follow up 3 months later. It has been almost 6 months since starting apremilast, and she continues to have stubborn psoriasis plaques on the trunk and extremities despite also using topical treatments as

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instructed, although much improved. She would like to discuss if there are any additional treatments she can do at this time. She is still opposed to biologic injectable medications. After discussion, the decision is made to start NB-UVB phototherapy in combination with apremilast. After starting phototherapy, the patient does not experience any negative photosensitivity reactions. On the combined therapy of apremilast and phototherapy, her psoriasis eventually starts to improve further, and she is almost clear after a few months.

Discussion

Apremilast (Otelza®) is a phosphodiesterase-4 inhibitor that is FDA-approved for the treatment of moderate to severe psoriasis and psoriatic arthritis. In phase 3 trials, approximately 33% of patients on apremilast achieved 75% improvement of greater in the psoriasis area and severity index (PASI-75) at week 16 [1]. Because the efficacy is generally lower compared to most biologic agents such as adalimumab, ustekinumab, secukinumab, and ixekizumab, it is not uncommon for a patient on apremilast to require an additional therapeutic modality such as phototherapy. Furthermore, due to the low side effect profile, apremilast can be safely added as a combination regimen to phototherapy, other oral systemic agents, or biologics [2–5]. However, it is important to be patient and wait at least 4 to 6 months to see the maximum effect of apremilast before declaring that the patient has failed monotherapy with apremilast.

The combination use of apremilast with UVB phototherapy was officially tested in the phase 3 U.S. wide clinical trial, which led to the FDA approval of apremilast for moderate to severe psoriasis [6]. In this official combination trial, photosensitivity reaction was not noted and the combination appeared safe. Although the data regarding the additional therapeutic benefit of adding phototherapy to apremilast has yet to be made public, in clinical practice this combination is not uncommon and there may be synergistic benefit.

Table 20.1 Common side effects of apremilast (30 mg BID) [1]

Adverse event	Occurrence (%)
Diarrhea	19
Nausea	15
Upper respiratory infection	10–18
Tension headache	7–10
Other headache	6

Since apremilast is considered one of the safer internal therapeutic options where the FDA package insert wording does not describe it as an immunosuppressant [7], and since UVB phototherapy is also one of the safest treatment options available with no convincing increased risk of skin cancer after more than a century of use [8], this combination is one of the safest that can be offered to the patient that needs more than one therapeutic modality to clear generalized psoriasis. The most common side effects of apremilast include nausea, diarrhea, and headache, which usually resolve within the first one to 2 months of use [1, 6] (Table 20.1).

In the current case in which the patient was unable to see satisfactory results after 6 months of apremilast even with maximum use of topical therapies, a safe and effective option is to add phototherapy to the current regimen.

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Chapter 21
Combining Phototherapy with Biologic Agents

Case

A 32-year-old male with a 10-year history of chronic plaque psoriasis presents for follow up. He has been taking etanercept 50 mg weekly for the past 3 years. It was initially working well and his skin was almost clear for the first 2 years. However, in the past year, his psoriasis has worsened slowly. He has been using clobetasol ointment twice daily to the affected areas without much additional improvement. He complains of itching and discomfort, as well as dissatisfaction with the current treatment. On examination, he is noted to have well-demarcated, erythematous, indurated plaques with silver scale on the elbows and knees. He also has similar but smaller plaques scattered on the chest, abdomen, and trunk. The patient is tolerating etanercept with no side effects. He asks what more can be done for his psoriasis. The patient denies personal history of melanoma or non-melanoma skin cancers.

The decision is made for the patient to add NB-UVB treatments at a frequency of 3 times per week. He is treated as per protocol. He returns to your clinic 3 months later with marked improvement of the psoriasis on his trunk and extremities. At this time, you conduct a thorough full body skin check and ascertain no new suspicious skin lesions and only a few psoriasis plaques. Given the positive outcome, the

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patient is able to decrease the frequency of phototherapy down to twice weekly, followed by once weekly a few months later with maintenance of near clear skin. He continues to take etanercept once weekly and applies topical corticosteroids as needed.

Discussion

Although several biologic agents showing excellent efficacy for the treatment of moderate to severe psoriasis have been developed in the last decade, phototherapy appears to play an important role in a subset of patients with severe, recalcitrant psoriasis despite treatment with a biologic agent. Several studies have demonstrated the efficacy of using etanercept and NB-UVB in combination [1–6]. These studies evaluated this combination therapy in patients who had not previously received treatment, patients who had an inadequate response with etanercept alone (50 mg once-weekly or 50 mg twice-weekly dosing), or patients who had an inadequate response to NB-UVB alone. Overall, combination therapy was superior and time to clearance was reduced. A study by Lynde et al. also demonstrated the importance of high adherence to the NB-UVB regimen in order to achieve significant clinical improvement [4]. High adherence to the NB-UVB regimen was defined as missing not more than 2 treatments in any 4-week period.

One study to date has failed to establish efficacy of combination therapy of etanercept and NB-UVB. This head-to-head pilot study by Park et al., who examined combination treatment with NB-UVB and etanercept 50 mg twice weekly compared with etanercept monotherapy, did not demonstrate significantly enhanced improvement with combination therapy [7]. However, this study was limited by a small sample size of 13 patients. Furthermore, the patients all had a body mass index (BMI) of greater than 30, and studies have reported a suboptimal response to etanercept in psoriasis patients with a BMI of greater than 30 [8, 9].

Adalimumab or ustekinumab in combination with NB-UVB has also been investigated in a limited number of studies. A study by Bagel et al. evaluated the combination of adalimumab and NB-UVB [10], and another study, by Wolf et al., evaluated adalimumab and the excimer laser [11]. Both studies demonstrated that phototherapy significantly accelerates therapeutic response and improves the clearance of psoriatic lesions in patients who received adalimumab treatment. One study to date has evaluated the combination of ustekinumab with the excimer laser [12]. This was an intra-individual, half-body comparison study in which PASI-75 was achieved significantly more often on the UV-irradiated half than on the non-irradiated half at week 6 in patients on ustekinumab.

In general, combination therapy involving a biologic agent with NB-UVB phototherapy is very well tolerated with the most common side effects being mild burning and erythema. Patients with recalcitrant disease despite being on a biologic, such as in this case in which the patient has active, symptomatic psoriasis causing dissatisfaction, may benefit from this combination therapy. In this case, the patient is a candidate for the addition of traditional phototherapy, rather than excimer laser, as he has many small, scattered psoriatic lesions on the trunk that would be difficult to treat with a targeted modality such as the excimer laser. Although increased risk of skin cancers have not been reported throughout the duration of the above-mentioned trials, long-term studies do not currently exist. Therefore, patients being treated with phototherapy while on a biologic agent should be monitored periodically for any new lesions suspicious for skin cancer.

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Chapter 22
Phototherapy for the Pediatric Population

Case

An 8-year-old female presents with atopic dermatitis since infancy. She presents with her mother who states that she has tried various topical corticosteroids and topical non-corticosteroids without relief. The child has severe itching that keeps her awake at night. She just started second grade, and it is apparent to the mother and her teacher that she is having an increasingly difficult time staying focused and awake in school as she is either scratching or falling asleep. Her mother would like her skin to improve so that she does not fall behind in school because, despite her atopic dermatitis, she has been doing very well in school so far. The child is otherwise healthy aside from mild asthma and has reached her developmental milestones to date. On examination, she is actively scratching but is overall attentive and conversational with you and the mother. She has scattered erythematous, excoriated papules and lichenified plaques on the posterior neck and in the bilateral antecubital and popliteal fossae. Her face is also affected with erythematous, xerotic patches on the bilateral cheeks. Her trunk and extremities appear mildly erythematous and xerotic diffusely.

Given that the child generally appears to be well behaved and the mother is very supportive and reliable, you discuss the possibility of starting phototherapy and its risks and

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benefits. The mother is agreeable 2 to 3 times per week commitments to bringing the child in for phototherapy treatments after school. The mother is also confident that her child can listen and follow all directions by the phototherapy nurses and doctors and understands that this is absolutely crucial to ensure safe treatments. The decision is made to start the patient on NB-UVB phototherapy twice weekly.

Before receiving the first treatment, the patient and her mother undergo an orientation session where the nurse gives full explanations of what to expect during each treatment session in a way that the child can understand. The patient is shown where to change into a gown. Then the nurse introduces the phototherapy booth and demonstrates how she steps into the box. Once she is standing in the booth, the nurse will ask if she is ready, and if she is, she will close the doors. She will then remove the gown and stand inside the booth very still. She must also wear eye goggles, and the goggles must stay on at all times while in the booth. Once she is ready, the nurse will count down "3…2…1". After "1", the lights will turn on inside the booth and it will make a loud whirling noise. The nurse will always tell the child how many seconds this will last for, and that they can count together up to that number, and when they get to the number, the lights will turn off. At that point, she can get dressed. Once she is ready, the door will open. The child is reassured that her mother is always outside the booth, and if she gets scared, she can always says so and her mother and the nurse can both hear her.

For the first session, given the patient is skin type II and there is a large amount of visible inflammation on the skin, the starting dose is decided to be very low, and only 6 sec of light administration is required. Although the child appears apprehensive at first, with the support of the mother and the nurse, she is able to step into the light booth, count to 6, and complete the treatment as instructed.

The patient and her mother return for follow up 4 weeks later with already some improvement of her atopic dermatitis. She has less itching and is sleeping and paying attention

better in school. The patient reports to you that she is up to one whole minute in the booth and she doesn't even get scared anymore.

Discussion

Treatment of inflammatory skin conditions such as psoriasis, atopic dermatitis, and vitiligo can be difficult for the pediatric patient. Many therapies available to adult patients are not FDA-approved for use in the pediatric population, especially systemic medications. Many systemic medications have not been officially tested in children, and therefore, possible risks such as organ toxicity and effects on proper development into adulthood are common concerns. On the other hand, when the patient has severe or generalized disease, relying only on large amounts of topical medications is also a concern, for example, due to local effects such as skin atrophy or striae formation and internal effects such as systemic absorption and adrenal suppression with topical steroids. Therefore, phototherapy is often a good second-line treatment option.

Unfortunately, randomized controlled trial data comparing the efficacy and safety of various phototherapy modalities against each other and against other standards of treatment is lacking. However, the current data suggest that phototherapy is an effective treatment for children and should be a therapeutic option when disease is widespread or refractory to topical therapies [1]. Currently, most of the available reports regarding pediatric phototherapy are based on psoriasis, atopic dermatitis, and vitiligo using, most commonly, NB-UVB, followed by PUVA, BB-UVB, and excimer laser. For all of these conditions, phototherapy is effective in inducing improvement in the majority of patients [2–7]. Goeckerman therapy is another option for pediatric patients, especially in the summer months when children are off of school. This day treatment therapy, consisting of phototherapy and topical tar, is extremely safe and effective in pediatric patients (see Chap. 4).

However, long-term safety data of phototherapy and photochemotherapy in children is lacking. Photoaging is a well-known side effect of phototherapy, but its relevance for children has not been established [8]. Risk of skin cancer in the pediatric population is also unknown. Although studies in adult patients have not shown a clear increased risk of skin cancer with use of UVB phototherapy, pediatric patients have a longer time period compared to adults in which skin cancers can arise following phototherapy. Furthermore, PUVA treatments should be used with caution in pediatric patients as studies in adult patients have shown that more than 250 treatments can lead to increased risk of skin cancer in Caucasian patients [9].

Another disadvantage to phototherapy is the time commitment required on the part of both the child's and the accompanying guardian's schedules. Appointments scheduled in the early mornings or late in the day will help to avoid school absences. To promote treatment adherence, patients and guardians must be carefully counseled before therapy on the duration and expectations of therapy. In general, for psoriasis and atopic dermatitis, treatments are held 2 to 3 times per week and significant improvement is expected in responders after 20–30 treatments. In many patients, ongoing maintenance with once weekly treatment session is required [10].

Finally, it is important to assess pediatric patients in terms of their maturity when attempting to decide whether or not phototherapy is a valid option. It is unsafe to treat patients who are not able to follow directions, such as standing still or keeping eye protection on during treatments. The nurse or other staff members who administer phototherapy should periodically check through the window in the phototherapy booth to verify that patients are complying with these measures. If the child is fearful of being inside the phototherapy booth alone, there are ways to make phototherapy "fun". In addition to the counting technique as outlined in the current case, singing a song or playing music during treatments can be helpful. The child can also bring toys such as stuffed animals into the booth, provided that patient is not actively playing with the toy or the toy is preventing proper light penetrance

to the skin. Despite these measures, if the patient is still apprehensive or the guardian and/or provider are uncomfortable with the patient being in the booth alone, the guardian can accompany the patient inside the booth. The accompanying person should cover their skin from light and should be positioned to minimize blocking of light to large areas of affected skin.

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Chapter 23
Phototherapy for the Elderly Population

Case

An 82-year-old female presents for evaluation of chronic, generalized, idiopathic pruritus. The patient is generally healthy aside of mild hypertension for which she takes metoprolol. Work up in the past has been negative for any underlying cause of itch. She has tried topical emollients and topical corticosteroids without any improvement. Antihistamines such as hydroxyzine and doxepin are not options due to her age. She is in a lot of distress as she has not been able to sleep well for the past several months since this itching started. The patient lives alone just a few blocks from your office. She is able to complete all activities of daily living independently and her memory is intact. She is very active and goes for 1 to 2 mile walks every day. Given that she is overall physically and mentally well, you discuss the option of starting phototherapy.

The patient states that she would be able to present to the office for treatments 2 or 3 times per week as she walks by the clinic every day for her walk anyway. You discuss the risks and benefits, and the patient is started on BB-UVB.

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Discussion

Phototherapy is an ideal treatment option for the elderly population for many conditions, such as psoriasis, eczema, and idiopathic pruritus, when topical medications have failed [1]. Topical corticosteroid use may be limited in the elderly population as there is higher risk of developing skin atrophy in patients who already have age-related skin thinning. Phototherapy is advantageous because it is an external treatment that has very limited external side effects (i.e. burning) and does not have any internal side effects. This is especially useful for the elderly population who may be more sensitive to or at risk for side effects of systemic medications such as organ toxicity. Many elderly patients also have co-morbid medical problems and take various medications. Therefore, adding a systemic medication for a dermatologic problem can be challenging in this population.

From a medical perspective, phototherapy is systemically safer; however, when considering phototherapy as a treatment option for an elderly patient, it is important to consider physical, logistical, and psychological limitations unique to the elderly [2]. First, the patient may have limitations in mobility. The ability to step into and stand steadily in the phototherapy booth is a prerequisite for phototherapy, which can be difficult for some elderly patients. Second, it is important to consider barriers to transportation in the elderly population, as they may not be able to present to the office multiple times per week if they are not able to walk or drive independently. Taking public transportation can also be a challenge due to limited endurance or cognitive disability. Lastly, isolation, depression, and anxiety, which are commonly experienced by the elderly, make it more difficult for geriatric patients to access care [3].

Cases of idiopathic pruritus such as the present case are common in the elderly population. Phototherapy is a safe and effective option provided that the patient is mobile and can reliably and safely present to the office for 2 to 3 times per week treatments. Goeckerman therapy is also a good

treatment option for elderly patients who do not have the above discussed barriers and can present for daily treatments. In the current case, the patient is a great candidate for phototherapy as she is generally healthy and has no barriers to mobility or transportation. Elderly patients are treated per protocol (see Chap. 1). It is very important that the patient applies liberal amounts of emollients after each phototherapy session as the skin can become dry and tight after light treatments, especially in the elderly. Goeckerman therapy may be considered if the patient fails outpatient phototherapy.

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Chapter 24
Phototherapy for Atopic Dermatitis

Case

A 15-year-old female with generalized atopic dermatitis is referred for phototherapy. In the past, her atopic dermatitis was manageable with topical agents alone, but recently, it has generalized to the trunk and all extremities and topical agents are no longer adequate to control her disease. Furthermore, the atopic dermatitis now also involves her face where mild topical steroids have also been inadequate. On examination, typical erythematous, eczematous lesions are observed scattered over the trunk and extremities. There are also patchy areas of excoriations and lichenification. The periorbital region, antecubital fossae and popliteal fossae are also involved. The patient reports that her skin is easily aggravated by various materials she comes in contact with such as wool clothing, soap, and even some moisturizing lotions.

Because of the chronic hyper-irritability of her skin, which is not at all unusual in the atopic dermatitis population, the patient is started on a conservative dose of BB-UVB phototherapy. Her face is also treated while wearing proper eye protection. Despite initiating phototherapy at low dose with precaution, she experiences of symptoms of mild sunburn, and therefore, the dose of BB-UVB is decreased further. After approximately 2 weeks, small increments in dosimetry are attempted and tolerated well. After 3 to 4 weeks, the

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patient is able to tolerate the usual dosing protocol per her skin type (see Chap. 1), and her skin greatly improves along with the pruritus. The patient is instructed to continue using topical steroids and non-steroids focally on the lesions while largely maintaining with BB-UVB phototherapy.

Discussion

Phototherapy is a second-line treatment option for atopic dermatitis recalcitrant to topical therapies (Fig. 24.1) [1]. Table 24.1 shows the recommended use of phototherapy for the treatment of atopic dermatitis per the American Academy of Dermatology. Phototherapy is advantageous in that there are no internal side effects as opposed to systemic treatments for atopic dermatitis such as prednisone, methotrexate, azathioprine, and mycophenolate mofetil. NB-UVB, BB-UVB, PUVA, and excimer laser can all be effective for treatment of atopic dermatitis [2, 3]. The recommended protocols to treat patients with atopic dermatitis are similar to that of psoriasis patients as discussed in Chap. 1 for UVB phototherapy, Chap. 2 for PUVA, and Chap. 3 for excimer laser, although atopic dermatitis patients can be treated slightly more conservatively due to the hyper-irritability of their skin (Tables 24.2–24.4). Furthermore, as discussed in Chap. 4, the Goeckerman regimen is also very effective for severe, recalcitrant, generalized atopic dermatitis [4].

Although there is no single phototherapy modality that is clearly superior in terms of efficacy, it has been shown that natural sunlight is likely less effective than artificial light sources [5]. In the authors' experience, BB-UVB appears to work notably better for patients with atopic dermatitis as BB-UVB appears to be less irritating as compared to NB-UVB in this patient population. Patients with idiopathic, generalized pruritus, many of who are elderly, also appear to tolerate BB-UVB better. Therefore, at the UCSF Phototherapy Unit, BB-UVB is recommended first for patients with atopic dermatitis or chronic idiopathic pruritus.

FIGURE 24.1 A patient with severe, generalized, recalcitrant atopic dermatitis who is a candidate for UVB phototherapy

As discussed on in Chap. 7 on "inititation burn", it is not uncommon for patients with atopic dermatitis to experience irritation and even frank sunburn from a very low dose of UV light. This is because the skin of atopic dermatitis patients is chronically hyper-irritable with or without obvious eczematoid lesions, that they can even be irritated initially by light. However, in most cases, unless it is a case of severe photosensitive eczema, the skin is capable of "getting used to" the light

Table 24.1 Recommended use of phototherapy for the treatment of atopic dermatitis per the American Academy of Dermatology [1]

Phototherapy is a second line treatment, after failure of first-line treatment (emollients, topical steroids, and topical calcineurin inhibitors).
Phototherapy can be used as maintenance therapy in patients with chronic disease.
Phototherapy treatment of all forms should be under the guidance and ongoing supervision of a physician knowledgeable in phototherapy techniques.
The light modality chosen should be guided by factors such as availability, cost, patient skin type, skin cancer history, patient use of photosensitizing medications, etc.
The dosing and scheduling of light should be based upon minimal erythema dose (MED) and/or Fitzpatrick skin type.
Home phototherapy under the direction of a physician may be considered for patients who are unable to receive phototherapy in an office setting.

Table 24.2 Treatment protocol for NB-UVB for atopic dermatitis at the UCSF Phototherapy Unit

Skin type	Dose (mJ/cm^2)	Subsequent increase (mJ/cm^2)
I	130	15–50
II	220	15–50
III	260	15–100
IV	330	15–100
V	350	15–150
VI	400	15–150

with persistence and gentle modulation of dosimetry [6]. Since UVB phototherapy is one of the safest therapeutic options available to help maintain atopic dermatitis skin under good control long term, it is a shame to give up on this modality as soon as the patient complains of initial irritation.

Table 24.3 Treatment protocol for BB-UVB for atopic dermatitis at the UCSF phototherapy unit

Skin type	Initial dose (mJ/cm^2)	Subsequent increase (mJ/cm^2)
I	10	10–50
II	20	10–50
III	30	10–50
IIII	40	10–50
V	50	10–75
VI	60	10–75

Table 24.4 Missed treatment protocol for both NB-UVB and BB-UVB for atopic dermatitis

Missed visit	Action (for all skin types)
1–7 days	Increase dose per protocol
8–11 days	Hold dose constant
12–20 days	Decrease by 25%
21–27 days	Decrease by 50%
28 or more days	Restart with initial dose

Therefore, it is important to be able to figure out how to make phototherapy work for atopic dermatitis patients who may have very sensitive skin.

In this patient with generalized atopic dermatitis uncontrolled on topical therapies, UVB phototherapy is a good option provided that it is started very carefully, monitoring for initiation burn or light-induced irritability. Due to involvement of her face, the face can be exposed during phototherapy, but proper precautions should be taken with eye protection (Fig. 24.2). The patient should commit to 3 times per week treatment sessions for at least 12 weeks, followed by ongoing treatments at least once weekly for maintenance therapy long-term. Concomitant use of topical therapies, including topical corticosteroids, non-steroid topical therapies

Figure 24.2 When the treating the face with phototherapy, proper eye protection should be worn by the patient

(tacrolimus, pimecrolimus), and topical tar, are encouraged (but not on the skin during actual phototherapy sessions) in addition to a gentle skin care regimen consisting of frequent moisturizing and avoidance of triggers.

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Chapter 25
Phototherapy for Vitiligo

Case

A 28-year-old male presents for a one-year history of vitiligo. The skin around his mouth, both hands, and scattered spots on the trunk are affected. He has tried topical corticosteroids, as well as tacrolimus ointment and pimecrolimus cream, without much improvement. He is very anxious, and he believes that his vitiligo is rapidly spreading up his hands to his wrists. He asks if there is anything other than topical medications that can help his vitiligo.

The patient is started on NB-UVB phototherapy twice weekly at 130 mJ/cm^2, which is increased as tolerated by approximately 20 mJ/cm^2 depending on the response to previous therapies. As the dosage is increased, the affected skin becomes erythematous and islands of re-pigmentation are observed. He continues to use topical medications at home. At his three-month follow up visit, the patient has significant visible repigmentation of his vitiligo, especially on his face and hands, which he is very happy about (Fig. 25.1). He is continued on twice weekly phototherapy treatments until the majority of his lesions are re-pigmented and then maintained on once weekly treatments.

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Figure 25.1 Islands of repigmentation observed after NB-UVB treatments

Discussion

Vitiligo is a dermatologic condition characterized by well-circumscribed white macules and patches due to destruction of melanocytes. The exact pathophysiologic mechanism is unknown. Vitiligo is estimated to affect up to 2% of the population [1]. The disfigurement caused by vitiligo has significant negative impact on quality of life [2].

Topical treatments for vitiligo include corticosteroids and calcineurin inhibitors. Traditionally, PUVA was considered mainstay treatment; however, in 1997, Westerhof and Nieuweboer-Krobotova reported the first use of NB-UVB for the treatment of vitiligo [3]. Since then, NB-UVB has become first-line therapy for generalized vitiligo in adults, and as an alternative therapy after class-III corticosteroids have failed for vitiligo in children [4].

A number of studies have reported effectiveness of NB-UVB alone or in combination with topical therapies for the treatment of vitiligo [5, 6]. Furthermore, NB-UVB has been shown to be comparable or have slightly better efficacy than PUVA [7, 8]. More recently, the excimer laser has become an effective and advantageous phototherapy modality for localized vitiligo as it can deliver targeted therapy directly

Table 25.1 Phototherapy dosimetry protocol for vitiligo used at UCSF Phototherapy Unit

	Initial dose (mJ/cm^2)	Subsequent dose increase[a] (mJ/cm^2)
NB-UVB	130	15–50
PUVA	0.25	0.25–0.5

[a]Dose is increased until mild erythema of the vitiligo patch is observed

Table 25.2 Missed treatment protocol for vitiligo at UCSF Phototherapy Unit

Missed visit	Action (for all skin types)
1–7 days	Increase dose per protocol
8–11 days	Hold dose constant
12–20 days	Decrease by 25%
21–27 days	Decrease by 50%
28 or more days	Restart with initial dose

to lesions [9]. Home phototherapy can also be utilized for treatment of vitiligo in selected patients [10]. Studies have shown that patients with skin that tans easily may respond more favorably to phototherapy, as well as lesions in certain locations such as the face [11]. Furthermore, it has been shown that a shorter period before initial repigmentation correlates with a higher percentage of final repigmentation [12].

The dosimetry for NB-UVB varies but typically started at 130 mJ/cm^2 for the initial dose irrespective of skin type, which is increased by 15–50 mJ/cm^2 at each subsequent session as tolerated [1]. The dose should be increased until mild erythema develops and then kept stable. The dosing protocol for vitiligo used at the UCSF Phototherapy Unit is shown in Table 25.1, along with the missed treatment protocol in Table 25.2. The excimer laser is also effective for localized vitiligo. The dosing is based on the location of the vitiligo and each laser manufacturer's recommendations. 2 or 3 times per week treatments over several months is necessary for adequate response, followed by a possible ongoing maintenance regimen

of once weekly. Side effects include burning and erythema, as well as photoaging and photodamage. Some patients may perceive initial worsening of their vitiligo due to tanning of surrounding skin and should be reassured accordingly.

The current patient who has widespread vitiligo affecting multiple locations such as the face, hands, and trunk, and has failed topical therapies, is a good candidate for NB-UVB phototherapy. If his lesions were more localized, excimer laser would be a good alternative. Before starting phototherapy, it is important to discuss with the patient the expectations that consistent treatments 2 to 3 times per week for several months is necessary to see good results. Furthermore, ongoing maintenance may be required in the long term. If the patient is found to respond well to office based NB-UVB, it may be beneficial to consider a home phototherapy unit for long-term management. As combination therapy with topical medications appears to be safe and effective, topical therapies should be continued along with phototherapy.

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Chapter 26
Phototherapy for Prurigo Nodularis

Case

A 61-year-old male presents to the clinic with complaints of severe itching and big round bumps on the skin. He states he has had this rash for almost 3 years. He has tried various topical corticosteroids including clobetasol, betamethasone diproprionate, fluocinonide, and triamcinolone without any improvement. He has also tried lidocaine and capsaicin creams without any relief of itching. Past medical history is significant for chronic hepatitis C and cirrhosis of the liver. On examination, he has numerous firm, round, excoriated nodules covering 50% of the trunk and extremities. Laboratory testing for pruritus is negative. He is diagnosed with generalized prurigo nodularis. Due to his co-morbid medical conditions, internal medications should be avoided. After discussion, the patient is started on BB-UVB.

Discussion

A debilitating disease characterized by hard, intensely pruritic nodules most commonly on the extensor surfaces of the extremities, prurigo nodularis (PN) was first noted to be responsive to large doses of X-rays in 1924 [1]. Almost a century later, little remains known regarding the etiology and

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pathophysiology, and given relatively low prevalence, no large randomized-control studies have been done to evaluate the various treatment options used today. Therapies such as superpotent topical corticosteroids, intralesional corticosteroids, topical vitamin D analogs, topical capsaicin, antihistamines, and phototherapy are generally accepted treatment options [2]. Systemic medications such as thalidomide [3], methotrexate [4], and cyclosporine [5] have also been shown to be effective in a small number of studies.

When PN is generalized, the disadvantage to topical therapies is that it can be impractical and there may be noncompliance given the inconvenience of frequent application of medications to scattered lesions over a large affected body surface area (Fig. 26.1). Systemic agents have various potential internal side effects and the need for frequent laboratory monitoring and the presence of comorbid medical conditions limit their use.

Figure 26.1 Generalized prurigo nodularis that is not amenable to topical therapies and is a good candidate for phototherapy

Although large-scale, randomized controlled trials are lacking, phototherapy is a treatment option that can be both safe and efficacious, especially for generalized PN. Phototherapy is thought to work in the treatment of PN by decreasing the number of epidermal and dermal nerve fibers related to the calcitonin gene-related peptide (CGRP), which contribute to chronic itch [6]. CGRP and nerve growth factor (NGF) are associated with neural hyperplasia and neurogenic inflammation, which may explain the underlying pathophysiology of PN [7].

There are only a few small studies available on each of the phototherapy modalities used for the treatment of PN, including PUVA, BB-UVB, NB-UVB, excimer laser, and UVA [8]. All studies show that phototherapy is overall effective in the majority of patients with PN yielding partial, if not complete improvement in appearance of lesions and symptoms of pruritus. There is no clear evidence that one phototherapy modality is superior to another, as none of these had active comparators. Because UVA penetrates deep into the skin, it may be assumed that UVA is more efficacious than UVB in treating PN; however, according to the limited data available so far, UVB and UVA appear to have similar clinical outcomes [9]. Excimer laser does have an additional benefit given its ability to focus on specific resistant nodules. Importantly, various combination therapies including BB-UVB and PUVA, bath PUVA and excimer, excimer and potent topical steroid, and Goeckerman therapy (BB-UVB, coal tar, and topical steroid) appear safe and effective. Alone and in combination therapies, the only reported adverse events are erythema and pruritus.

For this patient with generalized PN recalcitrant to topical therapies, phototherapy should be considered alone or in combination as mentioned above. For example, phototherapy can be used to treat the entirety of involved areas followed by spot-treatment of stubborn lesions with superpotent topical or intralesional corticosteroids. Excimer laser can also be used as a focused treatment modality. Given difficulty in applying topical therapies to all involved body surfaces, this

combination approach using phototherapy as generalized therapy and topical medication to more localized, resistant areas may also encourage patient compliance.

At the UCSF Phototherapy Unit, patients with PN are usually treated with BB-UVB rather than NB-UVB or PUVA. This is based on the authors' experience that overall, patients respond better and tolerate BB-UVB better than NB-UVB or PUVA. BB-UVB, NB-UVB, and PUVA are all initiated and increased per protocol as outlined in Chaps. 1 and 2.

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Chapter 27
Addressing the Question: Phototherapy and the Risk of Skin Cancer

Case

A 52-year-old Caucasian female with moderate to severe chronic plaque psoriasis presents for follow up. She has been undergoing NB-UVB phototherapy 1 to 2 times per week for the past 5 years, which keeps her psoriasis under good control. She denies any problems with phototherapy including burning or itching; however, she has noticed a few new "moles" on her arms and back. She has no personal or family history of melanoma or non-melanoma skin cancer. She is fair skinned and burns after 15–20 min in the sun. She wears sunscreen daily and tries to stay out of the sun as much as possible. She asks if phototherapy increases the risk of developing skin cancer.

Discussion

Given that UVA and UVB from natural sunlight are known to be carcinogenic to the skin, the main safety question for dermatologists and patients alike is the risk of skin malignancy of phototherapy (Table 27.1)

A recent comprehensive review conducted by Wang et al. [1] found that long-term exposure to PUVA (>250 treatments) is associated with an increased risk of non-melanoma

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Table 27.1 Phototherapy and the risk of skin cancer [1, 10]

There is no clear evidence of an increased risk of skin cancer in patients who have undergone UVB phototherapy, even long-term.
There is evidence of an increased risk of developing non-melanoma skin cancer with more than 250 treatments of PUVA in fair-skinned Caucasian individuals.
The concern for increased risk of skin cancer appears to be very low in darker-skinned, non-Caucasian populations.
The risk of melanoma does not appear to be increased with any phototherapy modality (UVB or PUVA).
The risk of genital skin cancers with UVB and PUVA are unclear, and therefore, genital shielding should be routinely practiced.
The combination use of acitretin and UVB (re-UVB) is effective in reducing the required cumulative UV dose and retinoids are shown to have anti-carcinogenic effects.

skin cancer among Caucasians; however no increased risk was seen among non-Caucasians. In Caucasian psoriasis patients, the dose-dependent increased risk of squamous cell carcinoma with systemic PUVA is well documented in the literature [2–5]. This significant increased risk of SCC with PUVA appears to be strongly correlated with the cumulative treatment dose, with a threshold of greater than 250 treatments, and continues to persist after stopping treatment [4]. A significant, modest increased risk of BCC with PUVA in Caucasians has also been observed [5]. Currently, there is not sufficient evidence to clearly associate long-term PUVA exposure with an increased risk of melanoma. Furthermore, non-Caucasians populations treated with PUVA appear to have no increased risk of melanoma and non-melanoma skin cancers.

With regard to both NB-UVB and BB-UVB phototherapy, there is no evidence for increased risk of skin cancer in both Caucasians and non-Caucasians, and therefore, UVB phototherapy may be safely used long-term. However, this finding should be confirmed with additional studies. Furthermore, although UVB monotherapy has been shown to be safe to

date, one study has shown that high exposure to UVB with prior PUVA treatment may increase skin cancer risk [6]. Even after controlling for PUVA exposure, high doses of UVB (>300 treatments) may increase nonmelanoma skin cancer and genital tumor incidence [7, 8]. As a result, in patients previously treated with PUVA, clinicians may need to use caution with high doses of UVB and genital shielding should be practiced.

Although studies of UVB phototherapy have not shown evidence for increased risk of skin cancer, if a clinician is still worried about this risk, there is the potential to manage such a patient with Re-UVB (retinoid plus UVB). This combination therapy is clinically appealing because retinoids can reduce the cumulative dose of UVB required to treat psoriasis [9]. Furthermore, retinoids have the potential benefit of a long-term reduction in the risk of developing skin cancer. It is believed that retinoids prevent skin carcinomas through their ability to stimulate epithelial differentiation and restore normal growth. Therefore, re-UVB is beneficial to reduce UVB exposure and to obtain a possible anti-skin cancer effect by increasing the maturation of skin cells [10].

In the current patient who has been receiving only NB-UVB for her psoriasis for 5 years, it is safe to tell the patient that there is currently no evidence that she is at higher risk of developing skin cancer due to phototherapy. The patient should continue to use proper sun protection and undergo routine full-body skin examination.

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Chapter 28
Prescribing a Home Phototherapy Booth

Case

A 24-year-old female presents for follow up of moderate to severe psoriasis. She had been presenting to the office for phototherapy treatments since she was a teenager with very good control of her psoriasis. However, she recently graduated from nursing school and is now working at a local hospital. Due to her busy schedule, she has not been able to come in for regular phototherapy treatments. In addition, the stress of her new job as a nurse in the intensive care unit is causing her psoriasis to flare. She would like to discuss obtaining a home phototherapy unit as she knows she responds very well to NB-UVB treatments and has not had problems with burning or erythema in the past. She would like to avoid systemic immunosuppressant agents as she deals with all kinds of sick patients in the hospital.

On examination, the patient has scattered, thin, mildly erythematous papules and plaques with fine white scale scattered over her trunk and extremities. You also conduct a full body skin examination and do not identify any lesions suspicious for skin cancer. You review her previous phototherapy records and confirm that she responded well to office-based phototherapy in the past. Given her years of experience receiving phototherapy and the fact that she is a very responsible patient, you decide to prescribe a home phototherapy

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unit. You go over the various types of units with the patient and choose the most appropriate unit for her condition, her home, and insurance coverage. You also educate the patient on proper use of the phototherapy unit. The patient returns for her regular follow up 3 months later with good control of her psoriasis once again.

Discussion

Phototherapy in a hospital or office setting can be inconvenient and unfeasible for some patients, as effective phototherapy usually requires 2 to 3 times per week treatments for at least 12 weeks with likely ongoing maintenance treatments to maintain adequate disease control. Many patients have difficulty committing to outpatient phototherapy because of inconvenience, time restraints, transportation problems, and high insurance co-pays [1]. For the provider, phototherapy may not be economically viable. Insurance reimbursement rates are decreasing while the cost of new, more efficacious office phototherapy units are increasing. The resources needed to train phototherapy staff can also deter providers from having office-based phototherapy [2].

For these reasons, home phototherapy units have been developed. The use of home phototherapy for patients with psoriasis was first reported in 1979 in a study from Sweden in patients who lived in remote areas far from their nearest hospital phototherapy center [3]. In 2009, a multicenter, randomized, controlled noninferiority trial was performed to compare home NB-UVB to outpatient NB-UVB phototherapy for the treatment of mild to severe psoriasis. This study found home NB-UVB and outpatient NB-UVB to be equally effective [4]. Home phototherapy was also shown to have lower treatment burden and increased patient satisfaction [4]. Furthermore, in a survey of 25 subjects receiving home phototherapy, the main reasons for choosing home over outpatient phototherapy were time, travel expenses, and difficulty with work schedule [5].

A patient is a candidate for home phototherapy if he/she has had a successful trial of outpatient phototherapy and has had proper education for use of a phototherapy unit. Patients are often prescribed a 3 times per week or every other day treatment regimen. A dosing chart is usually provided by the home phototherapy supplier along with the unit, and the provider should assist the patient to specify the correct skin type and starting dose and individualize the treatments as necessary. The dose of light should be maintained at or just below the dose that causes a mild erythema. Therefore, the dose is increased at increments until the patient experiences mild erythema after the treatment, then that dose should be maintained or slightly decreased [6]. Patients should also be instructed to stand 12 inches from the UV bulbs to maintain accurate dosing, wear UV protective goggles, and cover the genitals for males.

Patients should also be trained to recognize and report to the physician when experiencing side effects such as severe erythema, burning sensation, or blistering. Fortunately, various features have been developed in recent years to increase safety of home phototherapy. Features such as an integrated timer and automated calibration can limit the length of time of treatment sessions and number of treatment sessions between follow-up visits with the physician [7]. However, proper screening of candidates and patient education continue to be important to ensure safety and compliance [8].

Before initiating home phototherapy, the patient should have a full body skin examination. Regular follow up visits with routine skin checks should be performed by the dermatologist to monitor response to therapy and any side effects of therapy [9]. Despite the above measures, there are still concerns for home administration of phototherapy, including patient adherence and the possibility of overuse, underuse, and inappropriate use [10]. The suggested follow up procedures for safe and effective management of patients with a home phototherapy device are outlined in Table 28.1 [6].

Today, various types of phototherapy units are available from numerous suppliers (Table 28.2). The unit can vary from

Table 28.1 Suggested follow up procedures for patients with a home phototherapy device [6]

Encourage patient to follow the treatment regimen
Remind the patient of the appropriate treatment regimen
Three times per week or every other day treatments
Increase dose until just under the dose at which the skin turns pink
Use of a log to record each treatment
Re-emphasize safety measures
Use safety goggles
Genital shielding for men
Report to doctor any adverse effects such as severe erythema, burning sensation, or blistering
Do not allow other individuals to use their phototherapy unit
Regular follow-up visits with the dermatologist
Approximately every 3 months
Assessment of treatment response
Skin check for any adverse events

Table 28.2. Home phototherapy units by supplier (not a complete list, see Table 29.1 for handheld devices) [10–14]

Product	Type of UV light	Description
Daavlin		
UV Series	NB-UVB, BB-UVB, UVA	Full-body surrounding, walk-in cabinet; 12, 16, or 24 lamps
7 Series	NB-UVB, BB-UVB, UVA	6-ft. Panel with 8, 10, or 12 lamps that come with side doors or 4 or 6 lamps with optional reflective panel doors
4 Series	NB-UVB, UVA, UVA1, Blue	4-ft. Panel with 10 or 20 lamps

TABLE 28.2. (continued)

Product	Type of UV light	Description
1 Series	NB-UVB, UVA, UVA1 Blue	Small, portable unit with 4 lamps and a 180-degree lamp design
M Series	NB-UVB, UVA	Cabinet style for treatment of hands and feet, in 10, 6, and 4 lamps
National Biological Corp		
Panasol 3D	NB-UVB, BB-UVB, UVA	3-panel unit with 10 lamps for full-body treatment
Panasol II	NB-UVB, BB-UVB, UVA	Single panel in 6- and 2-ft. heights with 6, 8, or 4 lamps
Foldalite III	NB-UVB	Full-body surrounding cabinet with 16 or 32 lamps
Handisol II	NB-UVB	Portable treatment unit with 4 lamps that can be used horizontally, vertically, or angled for treatment of different areas
Hand/Foot II	NB-UVB, BB-UVB, UVA	A single unit with a hood and 8 lamps; optional cart to house 2 units, 1 for hands and 1 for feet for simultaneous treatment
UV BioTek		
Single Panel (models 100B, 80B, 60B, 40B)	NB-UVB	Single panel with 10, 8, 6, or 4 lamps, with decorative doors to conceal the lamps
Multidirectional	NB-UVB	3-Panel unit with 10 lamps and decorative doors that conceal the lamps when not in use

(continued)

Table 28.2. (continued)

Product	Type of UV light	Description
Full Body (model 1600B and 800B)	NB-UVB, BB-UVB	4-Panel unit with 8 or 16 lamps, for a flexible configuration for full-body exposure
Mobile-Lite	NB-UVB	Flat, portable light panel with 6 lamps that comes with a UV shield to use specifically for hands and feet or use open for localized plaques
SolarC Systems, Inc.		
E-Series (720-UVBNB and 720A–UVBNB)	NB-UVB	Single panel (E720M, each with 2 lamps) with option to add additional panels for a multidirectional unit
SolRx 1000 Series	NB-UVB, BB-UVB	6-ft. panel with 10, 8, 6, and 4 lamp units for NB-UVB or 6 and 4 lamp units for BB-UVB
SolRx 500 Series	NB-UVB	Tabletop device with 5, 3, or 2 lamps for localized areas or hands/feet

a full body, six-foot, three-dimensional device, to a two-foot single panel, to a hand/foot booth, to a scalp comb (Fig. 28.1). The number of light bulbs within a unit varies for some of the devices. The more lamps a unit has, the shorter the treatment time, which is more convenient and may increase patient compliance. However, it is necessary for the patient to weigh the time required for treatments versus the cost.

For the physician, an increasing number of resources are now available to increase knowledge and ease of prescribing

FIGURE 28.1 (**a**) full body, six-foot, three-dimensional device; (**b**) a two-foot single panel (**c**) a hand/foot booth; (**d**) a scalp comb (From https://www.natbiocorp.com/)

FIGURE 28.1 (continued)

Figure 28.1 (continued)

home phototherapy units [6]. The National Psoriasis Foundation is also a good resource for both patients and providers for general information about home phototherapy and the various suppliers available in the U.S. Many of the

companies that provide home phototherapy equipment have personnel available, free of charge, to assist with obtaining insurance coverage for the prescribed home phototherapy unit. The necessary paperwork differs between each company, but overall it is similar and includes a completed prescription form (often found on the company's website) and a letter of medical necessity, as well as the patient's insurance information.

Most patients are able to receive at least some coverage for a home phototherapy equipment from their insurance. The home phototherapy companies will often work with the patient and the insurance company to find options to help make the unit more affordable. For example, if the original claim is denied, the home phototherapy supplier can contact the insurance company and ask if an alternate unit would be covered or assist in sending an appeal letter to the insurance company. The supplier may also work with the patient who is unable to obtain insurance coverage and offer a payment plan or a discounted price. If a patient does not have insurance but is interested in purchasing a home light unit, they can purchase one directly from any company as long as they have a prescription [6].

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Chapter 29
Handheld Phototherapy Unit for Treatment of Localized Psoriasis or Scalp Psoriasis

Case

A 27-year-old female presents with scalp psoriasis, which she developed in early adolescence. She has tried various topical medications including superpotent topical steroids in various forms (cream, ointment, lotion, foam, and solutions) without adequate disease control. She has most recently tried a combination topical formulation of corticosteroid and vitamin D (betamethasone-calcipotriene) scalp suspension without additional improvement. She has itching, as well as flaking of the scalp. She is distracted at work and is embarrassed to go out in public.

On examination, she has discrete erythematous plaques with white to silver scale on the occipital scalp, as well as behind the ears. She also has erythematous plaques with silver scale on the bilateral elbows. The patient is tired of using topical medications and would to know other options for treating her psoriasis.

Discussion

Whole-body phototherapy is limited in that there can be needless exposure of uninvolved skin and no benefit to unexposed skin (such as the hair-covered scalp) [1]. In the last

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decade, various portable and lightweight handheld phototherapy units have become available for the treatment of localized psoriasis in the office and at home (Table 29.1) [2, 3]. These handheld devices, as compared with full-body irradiance in a booth or by a panel, have the added benefit of limiting skin exposure to UV light. The handheld devices are useful for the treatment of scalp psoriasis, as well as recalcitrant localized psoriasis plaques.

For example, the Dermalight 90 by National Biological Corporation (Cleveland, OH, USA) and the DermaPal by Daavlin (Bryan, OH, USA) have a comb attachment that allows for direct application of light to scalp lesions (Fig. 29.1). Although large-scale clinical trials are lacking, such light combs appear to be efficacious with longer remission compared with topical treatments [4, 5]. The handheld devices typically deliver NB-UVB, but some devices use BB-UVB or UVA. The DuaLight by Theralight, Inc. (Carlsbad, CA, USA) and Psoria-Light by Psoria-Shield (Tampa, FL, USA) can deliver both UVB and UVA, but these devices are for use only in an office setting.

For this patient with scalp psoriasis, as well as localized psoriasis plaques on the elbows, which are recalcitrant to topical treatments, a handheld, targeted UV modality may provide additional benefit. Topical therapies should continue to be used in conjunction with phototherapy for maximum effects. As discussed in Chap. 28, concerns for home administration of phototherapy are patient adherence and the possibility of overuse, underuse, and inappropriate use [6, 7]. Therefore, proper screening of candidates and patient education for safe and effective use of a home phototherapy unit continue to be important, as well as frequent follow ups with the dermatologist to monitor for treatment response and adverse effects [7]. For the physician, an increasing number of resources are now available to increase knowledge and ease of prescribing home phototherapy units [3].

TABLE 29.1. Handheld phototherapy devices [1, 2, 3]

Product	UV Source	Treatment area, inches	Size, inches	Features
Dermalight 90 (National Biological Corporation)	NB-UVB (three lamps)	1.75 × 5	3.2 × 12.8 × 1.2	Comb attachment for scalp treatment Timer to monitor treatment length Alert when energy from lamps gets low
Dermalume 2x (National Biological Corporation)	NB-UVB (two lamps)	3.3 × 5.4	4.1 × 7.5 × 2.8 (folded)	Key lock Timer that automatically turns lamps on/off Emergency on/off switch
DermaPal (Daavlin)	NB-UVB UVA	8.25 × 1.75	2.75 × 9 × 5	High-output lamps shorten treatment times Highly accurate, integrated timer

(continued)

TABLE 29.1. (continued)

Product	UV Source	Treatment area, inches	Size, inches	Features
DuaLight (Theralight)[a]	NB-UVB BB-UVB UVA	0.75 × 0.75	6.5 × 16.5 × 11.5	Minimal erythema dose and minimal phototoxic dose phototest modes Built-in timer and calibrating port Square aperture handpiece provides unobstructed view Flexible liquid light guide provided Disposable tip for hygienic single-patient use prevents cross-contamination
Levia (Daavlin)	UVB	0.67 × 0.67	8 × 6 × 11.5	Touch-screen control panel Built-in calibration port LiteSpot and LiteBrush attachments Light administered in small squares that can be tiled to treat the entire surface

Psoria-Light (Psoria-Shield)[a]	NB-UVB, UVA	(0.45 square inches)	18 × 22 × 8.5	LED (light emitting diode) source Fast switching, on/off ability, not requiring a warm-up or cool-down period High-definition digital camera to capture before and after photos of treatment sites Touch technology to detect the patient's treatment site before enabling UV dosage administration
100 Series Handheld Phototherapy (SolarC Systems)	NB-UVB BB-UVB (two lamps)	2.5 × 5	3.5 × 7 × 2.25	Includes a carrying case Includes aperture plates for precise localized treatment Positioning arm and UV brush Acrylic panel covering lamps Timer with maximum 20 min Switch lock

[a]Office use only

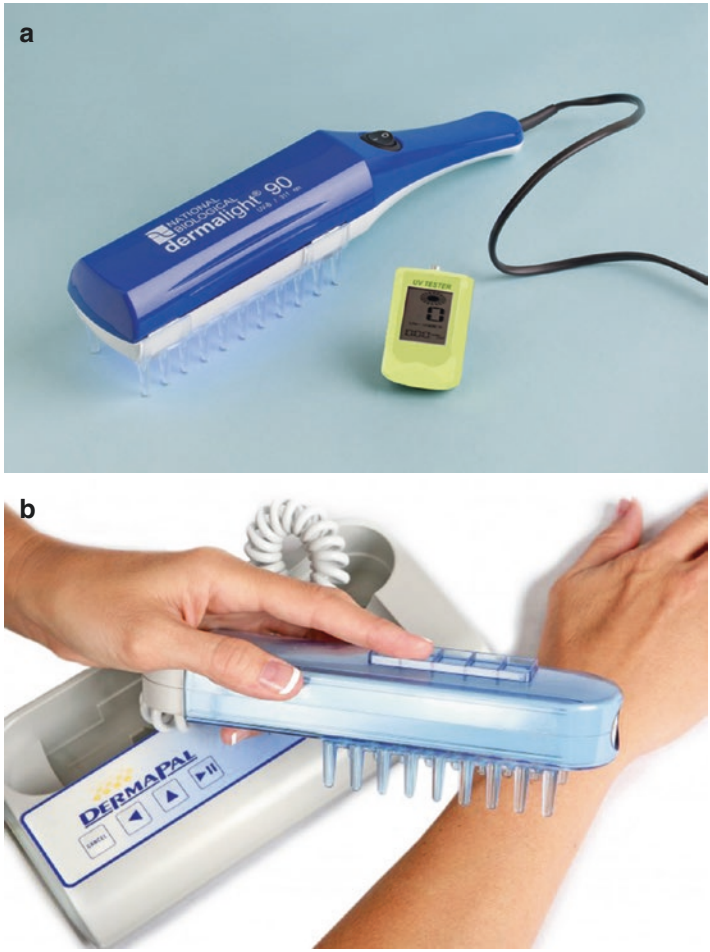

FIGURE 29.1 A comb attachment to a handheld phototherapy device allows for direct application of light to the scalp. (**a**) The Dermalight 90 by National Biological Corporation (Cleveland, OH, USA, https://www.natbiocorp.com/) (**b**) the DermaPal by Daavlin (Bryan, OH, USA, http://www.daavlin.com/)

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