



Phototherapy for atopic dermatitis

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Abstract Phototherapy is a second-line treatment for moderate to severe atopic dermatitis (AD) that effectively decreases cutaneous inflammation with minimal or no systemic side effects. Children in grade school, adolescents, and adults may benefit from phototherapy, when they have chronic AD refractory to first-line topical treatments. This review focuses on six approaches for phototherapy in AD: (1) broadband ultraviolet B (UVB), (2) Goeckerman regimen (coal tar + broadband UVB), (3) narrowband UVB, (4) excimer lasers for targeted areas, (5) combination UVA/UVB, and (6) UVA-1. Phototherapy can be very effective in some individuals, but it is limited by inconvenience and adverse effects, including limited access to in-office treatment, difficulty adhering to thrice-weekly schedule, flaring from excessive heat, and increased risk of skin cancer. Dosing regimen and treatment concerns are reviewed.

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Introduction

Atopic dermatitis (AD) is a chronic, relapsing and remitting, inflammatory skin disease that is intensely pruritic. AD occurs most frequently in children, and childhood disease may persist into adulthood in up to 85% of cases.¹ AD is characterized by immune system activation² and defective skin barrier function, resulting in increased susceptibility to pathogens and allergens.³

Management of AD

Most patients with mild AD can achieve clinical improvement and short-term control of acute symptoms with topical emollients and anti-inflammatory agents, such as topical corticosteroids and calcineurin inhibitors, along with avoidance of triggers (eg, irritants and excess heat). Although these are effective in controlling mild AD, they are usually insufficient for inducing remission in more severe disease.

Limited options are currently available for the treatment of moderate to severe AD. These consist of phototherapy and systemic immunosuppressive agents, such as systemic corticosteroids, cyclosporine A, methotrexate, and azathioprine; however, systemic corticosteroids, cyclosporine A, and other immunosuppressive agents all have major side effects limiting

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long-term use. Although frequently used in clinical practice, oral antihistamines and systemic antimicrobials have scant scientific data supporting their efficacy.⁴ Due to its efficacy and low side-effect profile, phototherapy is considered second-line treatment in children and adults with refractory AD.⁵

Phototherapy was first reported as a dermatologic treatment in 1925, when William Goeckerman (1884-1954) of the May Clinic formulated a regimen consisting of applying crude coal tar followed by exposure to broadband ultraviolet light B (BBUVB) for the treatment of refractory or severe psoriasis.⁶ In the 1920s, it was also observed that AD improved in sea-air climates during the summer season; however, it was not until 1948 that the efficacy of BBUVB light with carbon arc lamps was found to be an effective treatment for AD.⁷ Morison, Parrish, and Fitzpatrick from the Massachusetts General Hospital published a trial in 1978 that jumpstarted the study of phototherapy as a treatment for AD. They reported clearing of refractory AD in 15 patients with oral administration of 8-methoxypsoralen followed by exposure to long-wave ultraviolet A irradiation (PUVA).^{5,8} It is now believed that the primary mechanisms of UV irradiation in AD and other inflammatory skin diseases are via photoimmunosuppression and immunomodulation.

Multiple forms of light therapy have been reported to be effective in AD. This review focuses on six modalities of phototherapy:

1. BBUVB
2. Goeckerman regimen
3. Narrow-band UVB (NBUVB)
4. Excimer lasers for targeted areas
5. Combination UVA/UVB
6. UVA-1, which has limited availability in the United States (Table 1).

Psoralens and UVA (PUVA) is a type of photochemotherapy and is beyond the scope of this review.

Guidelines

The American Academy of Dermatology Guidelines of Care for the Management of AD assessed the evidence for

Table 1 Phototherapy modalities for the treatment of atopic dermatitis

UVB
Broadband UVB (290-320 nm)
Goeckerman regimen: coal tar and broadband UVB
Narrowband UVB (311-313 nm)
Excimer laser (308 nm)
UVA
UVA-1 (340-400 nm)
Psoralens and UVA (PUVA)
Combined UVA/UVB (280-400 nm)

Table 2 Recommendations for the use of phototherapy

- Phototherapy is a second-line treatment, after failure of first-line treatment (emollients, topical corticosteroids, 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, and patient use of photosensitizing medications.
- The dosing and scheduling of light should be based on minimal erythema dose 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.

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phototherapy.⁴ Evidence level assigned to in-office phototherapy for AD was IIB, whereas home phototherapy was assigned only IIIC. These indicate that the utility has not been demonstrated in larger, more rigorous studies. Recommendations included supervision by an experienced physician and usage of phototherapy as a *second-line* therapy in AD, after failure of first-line treatment with emollients, topical corticosteroids, and/or topical calcineurin inhibitors (Table 2). Phototherapy can be administered as monotherapy or combination therapy with emollients and topical corticosteroids. The steroid-sparing effect of phototherapy is considered a beneficial feature of therapy. Combination therapy with phototherapy and topical calcineurin inhibitors should be avoided due to the theoretical cancer risk cited in the black box warning on the topical calcineurin inhibitor labels.

Phototherapy can be used in short courses for clearance or longer courses with variable scheduling for maintenance in patients with chronic disease. A minimum 3-month trial is usually undertaken, provided the patient can access and tolerate therapy. Major barriers to patient access for phototherapy include local availability, travel time, missed school or work, coverage by insurers, out-of-pocket costs, patient skin type, skin cancer history, and use of photosensitizing medications. Dosing is guided by Fitzpatrick phototype as per the American Academy of Dermatology guidelines (Tables 3 and 4). Home phototherapy under physician supervision is recommended as backup for patients, who are unable to access in-office phototherapy twice or thrice weekly.⁹

NBUVB was cited as the most commonly used wavelength and modality of light-based therapy for AD. NBUVB and combination UVA/UVB have largely replaced older modalities, such as BBUVB and UVA-1. The guidelines also address pediatric usage and comment on good data to support efficacy and tolerability but not on long-term data on carcinogenicity. Neither localized laser light such as pulsed dye, excimer, and diode, nor systemic extracorporeal photochemotherapy has been endorsed based on more limited evidence.

Table 3 Dosing guidelines for broadband ultraviolet B

According to skin type		
Skin type	Initial UVB dose, mJ/cm ²	UVB increase after each treatment, mJ/cm ²
I	20	5
II	25	10
III	30	15
IV	40	20
V	50	25
VI	60	30
According to MED		
Treatment	Initial UVB dose, mJ/cm ²	UVB increase after each treatment, mJ/cm ²
Initial	50% of MED	—
2-10	—	Increase by 25% of initial MED
11-20	—	Increase by 10% of initial MED
≥ 21	—	As ordered by physician
If subsequent treatments are missed for		
Prior treatment	Dose adjustment	
4-7 days	Keep dose same	
1-2 weeks	Decrease dose by 50%	
2-3 weeks	Decrease dose by 75%	
3-4 weeks	Start over	

MED, minimal erythema dose; UV, ultraviolet.

Administered 3-5 times/week.

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NBUVB can be administered initially based on phototypes; however, minimal erythema dose (MED) testing is preferred. Ongoing monitoring of bulb emission and UV output are needed to maintain precise delivery of UV therapy. Therapy can be administered once to three times weekly, with weekly long-term maintenance required in some patients with chronic disease.

Broadband UVB (290-320 nm)

Broadband UVB (BBUVB) phototherapy began with the use of carbon arc lamps in 1948¹⁰ and has since been used successfully for many years as a treatment for AD. BBUVB with a dosing of .5-1.0 MED was significantly more effective than visible light, with complete healing of lesions in most patients. The same study showed no significant differences in efficacy between .8 versus .4 MED doses of BBUVB in 25 patients.¹¹ This supports a regimen in which providers begin BBUVB therapy with lower dosing and incrementally increase when disease is refractory.

Goeckerman regimen (coal tar + BBUVB)

Today, many centers still use the Goeckerman regimen in combination with topical corticosteroids, oral antihistamines, emollient baths, and/or systemic agents.¹² Although the

Goeckerman regimen is used worldwide to treat AD,^{13,14} evidence for its efficacy in AD is limited to a few retrospective studies.^{10,12,15} Despite its efficacy and relatively safety, Goeckerman therapy is not commonly used in AD. This is largely due to concerns about carcinogenicity from tar, as well as increased cost to payers for inpatient care, and replacement with NBUVB and other outpatient newer phototherapy modalities.

Narrowband UVB (311-313 nm)

NBUVB is indicated for treating moderate to severe AD. NBUVB offers several benefits, including being steroid sparing, longer lasting, and less erythemogenic than BBUVB.¹⁶ NBUVB is often considered the first-line phototherapy among providers owing to its efficacy, availability, ease of administration, and minimal side-effect profile.¹⁷ Tolerability of NBUVB for AD can be limited by overheating and perspiration, both of which may trigger AD flares. Air-conditioned NBUVB regimens can overcome these problems and have been shown to be quite effective.¹⁸ NBUVB has been shown to be as or more effective than visible light, UVA, medium dose UVA-1, and PUVA.^{17,19-23}

NBUVB combined with other therapies has also been reported to be effective. In a trial of 7 adults aged 28-40 years, an 8-week neoadjuvant course of oral cyclosporine A (4-5 mg/kg/day until clinical improvement was achieved [average ~4 weeks],

Table 4 Dosing guidelines for narrowband ultraviolet B

According to skin type			
Skin type	Initial UVB dose, mJ/cm ²	UVB increase after each treatment, mJ/cm ²	Maximum dose, mJ/cm ²
I	130	15	2000
II	220	25	2000
III	260	40	3000
IV	330	45	3000
V	350	60	5000
VI	400	65	5000
According to MED			
Treatment	Initial UVB dose, mJ/cm ²	UVB increase after each treatment, mJ/cm ²	
Initial	50% of MED	—	
2-20	—	Increase by 10% of initial MED	
≥ 21	—	Increase as ordered by physician	
If subsequent treatments are missed for			
Prior treatment	Dose adjustment		
4-7 days	Keep dose same		
1-2 weeks	Decrease dose by 25%		
2-3 weeks	Decrease dose by 50% or start over		
3-4 weeks	Start over		
Maintenance therapy for NBUVB after >95% clearance			
Interval between doses	Duration	Dose adjustment	
1 week	4 weeks	Keep dose same	
2 weeks	4 weeks	Decrease dose by 25%	
4 weeks	Ongoing	50% of highest dose	

MED, minimal erythema dose; NB, narrowband; UV, ultraviolet.
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then decreased to 2-3 mg/kg/day for 4 weeks) followed by a wash-out phase of 4-6 weeks and consecutive NBUVB therapy (3 times weekly for 2-3 months), demonstrated a sustained improvement in the scoring of atopic dermatitis index of 50% or more, relative to baseline.²⁴ The scoring of atopic dermatitis index is a validated scoring system in AD that evaluates six items: erythema, edema, excoriations, lichenification, oozing/crusts, and dryness. NBUVB can be beneficial in pediatric AD, but it is limited by age, compliance, and maturity.²⁵⁻²⁸

Few studies have examined the mechanism(s) of action of NBUVB in AD. A trial of 12 adults with moderate to severe chronic AD found that NBUVB 3 times weekly either until clearance or 12 weeks reversed epidermal dysfunction and immune activation, suppressed Th2 and Th22 axes, eliminated inflammatory leukocytes, and normalized epidermal hyperplasia and differentiation.²⁹

Excimer laser (308 nm)

Monochromatic excimer light (MEL) came into usage in the late 1990s. MEL provides a convenient source of targeted

phototherapy, requiring sessions only every 7-15 days, which may improve patient compliance and quality of life.³⁰ With a maximum irradiating area of 504 cm², excimer laser also offers the option of treatment targeted to only affected areas, thereby reducing potential risk for adverse events. MEL was found to be more effective than NBUVB in psoriasis.^{31,32} Several small studies showed the efficacy of MEL in AD. Despite promising results, the recent American Academy of Dermatology guidelines did not endorse MEL for AD at this time. Therefore, usage should be decided on a case-by-case basis.

UVA/UVB

Combination UVA/UVB phototherapy (280-400 nm) can be administered by tubes whose emission irradiation spectrum includes both wavelengths (eg, Metec Helarium), or by combining UVA and UVB tubes simultaneously or in tandem. The combined spectrum tubes have the disadvantage of being unable to dose UVA and UVB separately. UVA/UVB therapy grew in popularity as a treatment for AD when it was shown to

Table 5 Side effects of phototherapy

Common
Actinic damage
Increased skin aging
Local erythema and tenderness
Pruritus
Burning
Stinging
Dyspigmentation (especially early on in patients of color)
Heat-induced flares
Claustrophobia (especially in children)
Uncommon
Nonmelanoma skin cancer
Melanoma (especially with PUVA)
Lentigines
Photosensitive eruptions
Polymorphous light eruption
Lupus flare
B6 deficiency
Folliculitis
Folic acid depletion
Photo-onycholysis (especially PUVA)
Herpes simplex virus (HSV) reactivation
Facial hypertrichosis
Cataract formation (especially with PUVA)
Headaches, nausea, vomiting with PUVA
Hepatotoxicity (PUVA)
Ocular toxicity (especially psoralens)

be more effective than BBUVB.^{33–35} Efficacy of UVA/UVB has also been demonstrated in children.³⁶

UVA-1

UVA-1 (340–400 nm) was initially developed to avoid the adverse effects, that is, risk of sunburn higher-energy, lower wavelength, irradiation of UVA-2 (320–340 nm) and UVB (290–320 nm).^{37–40} Higher doses of UVA-1 penetrate deeper into the dermis and superficial vessels than UVB and UVA-2.^{41,42} Unlike most other phototherapies, UVA-1 is also effective in the treatment of acute AD flares.^{43–45}

High-dose UVA-1 treatment may be limited by intolerance to heat and intense sweating in patients. In response, “UVA1 cold light,” from lamps that filtered the infrared rays, was created and found to have greater improvement than conventional UVA-1 or UVA/UVB.³⁹ In two dose-comparison studies, there was no significant difference between high-dose (130 J/cm²) and medium-dose (65 J/cm²) UVA-1 at improving AD,^{46,47} although medium-dose was more effective than low-dose UVA-1 (20 J/cm²).⁴⁶ Medium-dose was better tolerated than high-dose UVA-1.⁴⁶ Medium-dose UVA-1 appears to have similar efficacy to NBUVB^{19,21} and topical tacrolimus for treatment of AD.⁴⁸

Tanning beds

There have not been any studies directly investigating the efficacy of tanning beds as a treatment of AD. One study of Swedish teenagers reported that 66% of patients with AD used tanning beds to treat their AD.⁴⁹ Tanning beds may offer a convenient and cost-effective alternative for patients who find in-office phototherapy cumbersome from expense or inconvenience; however, the light used in tanning beds is poorly defined, with a variable spectral distribution of UV output.⁵⁰ Previous studies found that tanning beds cause dramatically higher rates of melanoma and nonmelanoma skin cancer.^{51,52} Risk of skin cancer with tanning beds outweighs the potential benefits, which are not well defined at this point. Due to lack of tanning-bed-specific literature, use of this modality is not recommended.

Safety and limitations

The incidence of adverse effects of phototherapy is unknown, but it is believed to be low.⁴ Common and uncommon adverse effects are listed in Table 5. Some adverse effects are distinct to the mode of therapy, including cataract formation in UVA therapy.⁴ Due to potential long-term effects of UV irradiation, phototherapy is a second-line AD treatment. Finally, age-specific psychosocial factors must be considered in children, including intimidation of devices and concerns of caregivers.

Other limitations of phototherapy include expense, logistical requirements, special equipment, trained staff, and limited efficacy in difficult-to-treat areas, such as hairy skin and skin folds. Dose-escalating regimens for UVB therapy typically take several weeks before an antiinflammatory dose is achieved and efficacy is noted. As a result, we recommend that patients being treated with NBUVB and BBUVB should also be treated with topical and/or other systemic agents during the first few weeks of UV therapy.

Conclusions

NBUVB and medium-dose UVA-1 phototherapy are the most effective phototherapy modalities in AD. NBUVB has been shown to be most effective in managing chronic AD, whereas UVA-1 may be used for acute flares. Modernized Goeckerman protocols are effective in severe AD; however, concern for malignancy from coal tar has limited its popularity. MEL may be a good option for localized refractory AD lesions. Safe use of NBUVB in children has been well documented; however, less literature exists regarding other modalities, and so caution must be used. Larger randomized controlled trials are needed to determine the most effective modalities, dosage protocols, and maintenance requirements. In summation, long-term studies for the safety of phototherapy are needed.

References

- Margolis JS, Abuabara K, Bilker W, et al. Persistence of mild to moderate atopic dermatitis. *JAMA Dermatol.* 2014;150:593-600.
- Guttman-Yassky E, Lowes MA, Fuentes-Duculan J, et al. Major differences in inflammatory dendritic cells and their products distinguish atopic dermatitis from psoriasis. *J Allergy Clin Immunol.* 2007;119:1210-1217.
- Elias PM, Hatano Y, Williams ML. Basis for the barrier abnormality in atopic dermatitis: outside-inside-outside pathogenic mechanisms. *J Allergy Clin Immunol.* 2008;121:1337-1343.
- Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol.* 2014;71:327-349.
- Patrizi A, Raone B, Ravioli GM. Management of atopic dermatitis: safety and efficacy of phototherapy. *Clin Cosmet Invest Dermatol.* 2015;8:511-520.
- Goeckerman W. Treatment of psoriasis. *Northwest Med.* 1925;24:229-231.
- Nexman P. Clinical Studies of Besnier's Prurigo. . DissertationDenmark: Copenhagen. 1948.
- Morison WL, Parrish J, Fitzpatrick TB. Oral psoralen photochemotherapy of atopic eczema. *Br J Dermatol.* 1978;98:25-30.
- Williams HC, Grindlay DJ. What's new in atopic eczema? An analysis of the clinical significance of systematic reviews on atopic eczema published in 2006 and 2007. *Clin Exp Dermatol.* 2008;33:685-688.
- Maughan WZ, Muller SA, Perry HO, et al. Incidence of skin cancers in patients with atopic dermatitis treated with ocal tar. A 25-year follow-up study. *J Am Acad Dermatol.* 1980;3:612-615.
- Jekler J, Larko O. UVA solarium versus UVB phototherapy of atopic dermatitis: a paired-comparison study. *Br J Dermatol.* 1991;125:569-572.
- Dennis M, Bhutani T, Koo J, et al. Goeckerman therapy for the treatment of eczema: a practical guide and review of efficacy. *J Dermatolog Treat.* 2013;24:2-6.
- Roelofzen JH, Aben KK, Oldenhof UT, et al. No increased risk of cancer after coal tar treatment in patients with psoriasis or eczema. *J Invest Dermatol.* 2010;130:953-961.
- Lee E, Koo J. Modern modified 'ultra' Goeckerman therapy: a PASI assessment of a very effective therapy for psoriasis resistant to both prebiologic and biologic therapies. *J Dermatol Treat.* 2005;16:102-107.
- Pittelkow MR, Perry HO, Muller SA, et al. Skin cancer in patients with psoriasis treated with coal tar. A 25-year follow-up study. *Arch Dermatol.* 1981;117:465-468.
- Grundmann SA, Beissert S. Modern aspects of phototherapy for atopic dermatitis. *J Allergy (Cairo).* 2012;2012:121797.
- Berth-Jones J, Graham-Brown RA. Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis. *Lancet.* 1993;341:1557-1560.
- George SA, Bilsland DJ, Johnson BE, et al. Narrow-band (TL-01) UVB air-conditioned phototherapy for chronic severe adult atopic dermatitis. *Br J Dermatol.* 1993;128:49-56.
- Gambichler T, Othlinghaus N, Tomi NS, et al. Medium-dose ultraviolet (UV) A1 vs. narrowband UVB phototherapy in atopic eczema: a randomized crossover study. *Br J Dermatol.* 2009;160:652-658.
- Majoie IM, Oldhoff JM, van Weelden H, et al. Narrowband ultraviolet B and medium-dose ultraviolet A1 are equally effective in the treatment of moderate to severe atopic dermatitis. *J Am Acad Dermatol.* 2009;60:77-84.
- Legat FJ, Hofer A, Brabek E, et al. Narrowband UV-B vs medium-dose UV-A1 phototherapy in chronic atopic dermatitis. *Arch Dermatol.* 2003;139:223-224.
- Reynolds NJ, Franklin V, Gray JC, et al. Narrow-band ultraviolet B and broad-band ultraviolet A phototherapy in adult atopic eczema: a randomised controlled trial. *Lancet.* 2001;357:2012-2016.
- Der-Petrossian M, Seeber A, Honigsmann H, et al. Half-side comparison study on the efficacy of 8-methoxypsoralen bath-PUVA versus narrow-band ultraviolet B phototherapy in patients with severe chronic atopic dermatitis. *Br J Dermatol.* 2000;142:39-43.
- Brazzelli V, Prestinari F, Chiesa MG, et al. Sequential treatment of severe atopic dermatitis with cyclosporin A and low-dose narrow-band UVB phototherapy. *Dermatology.* 2002;204:252-254.
- Darne S, Leech SN, Taylor AE. Narrowband ultraviolet B phototherapy in children with moderate-to-severe eczema: a comparative cohort study. *Br J Dermatol.* 2014;170:150-156.
- Clayton TH, Clark SM, Turner D, et al. The treatment of severe atopic dermatitis in childhood with narrowband ultraviolet B phototherapy. *Clin Exp Dermatol.* 2007;32:28-33.
- Jury CS, McHenry P, Burden AD, et al. Narrowband ultraviolet B (UVB) phototherapy in children. *Clin Exp Dermatol.* 2006;31:196-199.
- Collins P, Ferguson J. Narrowband (TL-01) UVB air-conditioned phototherapy for atopic eczema in children. *Br J Dermatol.* 1995;133:653-655.
- Tintle S, Shemer A, Suarez-Farinas M, et al. Reversal of atopic dermatitis with narrow-band UVB phototherapy and biomarkers for therapeutic response. *J Allergy Clin Immunol.* 2011;128:583-593. [e581-584].
- Mavilia L, Mori M, Rossi R, et al. 308 nm monochromatic excimer light in dermatology: personal experience and review of the literature. *G Ital Dermatol Venereol.* 2008;143:329-337.
- Novak Z, Bonis B, Baltas E, et al. Xenon chloride ultraviolet B laser is more effective in treating psoriasis and in inducing T cell apoptosis than narrow-band ultraviolet B. *J Photochem Photobiol B.* 2002;67:32-38.
- Bonis B, Kemeny L, Dobozy A, et al. 308 nm UVB excimer laser for psoriasis. *Lancet.* 1997;350:1522.
- Jekler J, Larko O. Combined UVA-UVB versus UVB phototherapy for atopic dermatitis: a paired-comparison study. *J Am Acad Dermatol.* 1990;22:49-53.
- Midelfart K, Stenvold SE, Volden G. Combined UVB and UVA phototherapy of atopic eczema. *Dermatologica.* 1985;171:95-98.
- Hannuksela M, Karvonen J, Husa M, et al. Ultraviolet light therapy in atopic dermatitis. *Acta Derm Venereol Suppl (Stockh).* 1985;114:137-139.
- Pasic A, Ceovic R, Lipozencic J, et al. Phototherapy in pediatric patients. *Pediatr Dermatol.* 2003;20:71-77.
- Polderman MC, Wintzen M, le Cessie S, et al. UVA-1 cold light therapy in the treatment of atopic dermatitis: 61 patients treated in the Leiden University Medical Center. *Photodermatol Photoimmunol Photomed.* 2005;21:93-96.
- Dittmar HC, Pflieger D, Schopf E, et al. UVA1 phototherapy. Pilot study of dose finding in acute exacerbated atopic dermatitis. *Hautarzt.* 2001;52:423-427.
- von Kobyletzki G, Pieck C, Hoffmann K, et al. Medium-dose UVA1 cold-light phototherapy in the treatment of severe atopic dermatitis. *J Am Acad Dermatol.* 1999;41:931-937.
- Kowalzik L, Kleinheinz A, Weichenthal M, et al. Low dose versus medium dose UV-A1 treatment in severe atopic eczema. *Acta Derm Venereol.* 1995;75:43-45.
- Breuckmann F, von Kobyletzki G, Avermaete A, et al. Mononuclear cells in atopic dermatitis in vivo: immunomodulation of the cutaneous infiltrate by medium-dose UVA1 phototherapy. *Eur J Med Res.* 2002;7:315-322.
- Morita A, Werfel T, Stege H, et al. Evidence that singlet oxygen-induced human T helper cell apoptosis is the basic mechanism of ultraviolet-A radiation phototherapy. *J Exp Med.* 1997;186:1763-1768.
- Darsow U, Wollenberg A, Simon D, et al. ETFAD/EADV eczema task force 2009 position paper on diagnosis and treatment of atopic dermatitis. *J Eur Acad Dermatol Venereol.* 2010;24:317-328.
- Krutmman J, Diepgen TL, Luger TA, et al. High-dose UVA1 therapy for atopic dermatitis: results of a multicenter trial. *J Am Acad Dermatol.* 1998;38:589-593.

45. Krutmann J, Czech W, Diepgen T, et al. High-dose UVA1 therapy in the treatment of patients with atopic dermatitis. *J Am Acad Dermatol*. 1992;26:225-230.
46. Mang R, Krutmann J. UVA-1 phototherapy. *Photodermatol Photoimmunol Photomed*. 2005;21:103-108.
47. Tzaneva S, Seeber A, Schwaiger M, et al. High-dose versus medium-dose UVA1 phototherapy for patients with severe generalized atopic dermatitis. *J Am Acad Dermatol*. 2001;45:503-507.
48. Osmola-Mankowska A, Polanska A, Silny W, et al. Topical tacrolimus vs medium-dose ultraviolet A1 phototherapy in the treatment of atopic dermatitis-a preliminary study in relation to parameters of the epidermal barrier function and high-frequency ultrasonography. *Eur Rev Med Pharmacol Sci*. 2014;18:3927-3934.
49. Boldeman C, Beitner H, Jansson B, et al. Sunbed use in relation to phenotype, erythema, sunscreen use and skin diseases. A questionnaire survey among Swedish adolescents. *Br J Dermatol*. 1996;135:712-716.
50. Radack KP, Farhangian ME, Anderson KL, et al. A review of the use of tanning beds as a dermatological treatment. *Dermatol Ther (Heidelb)*. 2015;5:37-51.
51. Ferrucci LM, Vogel RI, Cartmel B, et al. Indoor tanning in businesses and homes and risk of melanoma and nonmelanoma skin cancer in 2 US case-control studies. *J Am Acad Dermatol*. 2014;71:882-887.
52. Colantonio S, Bracken MB, Beecker J. The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. *J Am Acad Dermatol*. 2014;70:847-857.