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REVIEW

Phototherapy with Narrowband UVB

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Phototherapy with ultraviolet (UV) radiation of wavelengths between 280 and 320 nm (UVB) is a safe and effective treatment for a variety of diseases. In addition to standard broadband UVB (bUVB), narrowband phototherapy with fluorescent bulbs emitting near monochromatic UV around 311 nm (nUVB) has become an important treatment for diseases such as psoriasis, atopic dermatitis and vitiligo. In addition to these indications, the number of diseases for which nUVB phototherapy is reported to be effective is continuously growing. The differential effects of nUVB phototherapy in comparison to other UV wavelengths as well as established and new indications for this treatment modality are reviewed.
Key words: broadband UVB; narrowband UVB; phototherapy; psoriasis; skin cancer; ultraviolet light.

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While it has been known for more than 2000 years that several skin diseases improve upon exposure to the sun (heliotherapy), the systematic investigation of phototherapeutic modalities did not start until the beginning of the twentieth century. In 1903, Niels Finsen received the Nobel Prize for developing phototherapy as a treatment for tuberculosis of the skin and 23 years later Goeckerman (1) showed the beneficial effect of natural sunlight in combination with tar for psoriasis vulgaris. In 1953, Ingram (2) initiated the combination of UVB radiation, dithranol and tar-bathing for psoriasis (2). Data from Fischer & Alsins (3) and Parrish & Jaenicke (4) subsequently showed that wavelengths around 311 nm provoke fewest erythema while being most effective for clearing psoriasis. According to these results a fluorescent bulb was developed (TL-01), emitting a major peak at 311 ($\pm$ 2 nm) and a minor peak at 305 nm. This treatment was later called narrowband UVB (nUVB) and following its introduction several studies were published on its superior efficacy in phototherapy of psoriasis (5–7).

PHOTOBIOLOGY

Interaction between UV radiation and the skin

UV radiation that reaches the skin is either reflected or absorbed by structures of the skin. While UVC ($<$280 nm) is mostly absorbed in the stratum corneum, UVA (320–400 nm) shows deeper penetration than UVB (280–320 nm) (8–12). Thus UVB is mainly absorbed by epidermal components, including keratinocytes, melanin and Langerhans cells (13). Biological effects of UV radiation are generated through interaction with absorbing molecules called chromophores. In the case of UVB the most important chromophores are proteins such as keratin, melanin, collagen and elastin, urocanic acid and DNA (14–16). Ultimately, the interaction of UV with chromophores can lead to a multitude of effects such as induction of oxidative stress and activation of transcription factors, as well as induction of damage to the cell membrane and DNA mutations.

Induction of DNA damage

UVB radiation leads directly to the generation of premutagenic lesions, so-called photoproducts. Among others, the most prevalent photoproducts induced by UV are cyclobutane pyrimidine dimers (CPD), pyrimidin-(6-4)-photoproducts (6-4PP) and Dewar isomers. Normally these lesions are repaired by a highly conserved repair mechanism called nucleotide excision repair (NER). This mechanism acts in a tightly regulated fashion including recognition and processing of DNA damage, unwinding of DNA by helicases, excision of the damage-containing fragment and re-synthesis by DNA polymerase (17). If UVB-induced lesions are not repaired, C$\rightarrow$T and CC$\rightarrow$TT transitions can occur as DNA mutations (18) representing initial events of multi-step carcinogenesis. These mutations are characteristic for UV exposure, in potentially relevant genes such as tumour suppressor genes or oncogenes (19). The fact that defective NER in the autosomal recessive disease xeroderma pigmentosum is associated with a strong increase of DNA mutations, photosensitivity and development of skin cancer further underscores the central role of DNA damage and its repair in the process of multi-step photocarcinogenesis (20, 21).

UV radiation and its effects on the immune system

UV radiation alters immunological function (22) and UVB can increase the production of pro-inflammatory substances like prostaglandins (PG) or tumour necrosis factor (TNF), as well as the production of anti-inflammatory factors like interleukin (IL)-10,

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Table I. *Recent studies (published since 1999) involving narrowband UVB (nUVB) shown with regard to patient number (n), study design and response rate (in some cases descriptive values in results have been calculated from the studies original data to facilitate comparison between studies)*

Study	Therapy regimen	Study design (*n*)	Response	Remarks
Psoriasis				
Pasic (42)	nUVB	Open trial (20)	≥90% PASI reduction: 45%	Children
Gordon (48)	nUVB vs PUVA	Randomized (100)	84% (PUVA), 63% (nUVB); 6 month remission: 35% (PUVA), 12% (nUVB)	
Tanew (45)	nUVB vs PUVA	Half-side, open, non-randomized (25)	PASI-reduction: 84% (nUVB); 89% (PUVA)	No significant differences
Dawe (41)	nUVB vs TMP-bath-PUVA	Half-side, randomized, observer-blinded, controlled (10)	100% (nUVB), 70% (bath-PUVA)	
Snellman (44)	nUVB vs TMP-bath-PUVA	Half-side, randomized (18)	PASI-reduction: 77% (nUVB); 45% (bath-PUVA)	
Markham (47)	nUVB vs bath-PUVA	Open, randomized, controlled (54)	Treatments to clear: 25; days to clear: 67 (nUVB), 66 (PUVA)	Remission: no difference
Calzavara-Pinton (85)	nUVB+ bath-PUVA	Half-side, open (12)	PASI-reduction: 67.8% (nUVB), 92.4% (PUVA)	
Schiffner (75)	nUVB+Dead Sea salt	Multicentre (280)	71.4% improvement	
Carrozza (52)	nUVB+dithranol	Open pilot (13)	PASI reduction: 83.9 ± 15.6%	
Woo (59)	nUVB+calcipotriol	Prospective, randomized, controlled (50)	Significant higher PASI reduction with calcipotriol	
Rim (61)	nUVB+calcipotriol	Randomized (28)	>95% response: 90.0% (with calcipotriol), 61.1% (no calcipotriol)	
Hofmann (66)	nUVB+dithranol vs calcitriol	Half-side, controlled (10)	CR: 100% both groups	PASI only on arms
Behrens (68)	nUVB+tazarotene	Half-side, open (10)	PASI reduction: 64% (nUVB/tazarotene), 48% (nUVB)	
Schiener (71)	nUVB+calcipotriol vs tazarotene	Half-side (10)	CR: after 19 treatments on both sides	No difference
Messer (65)	nUVB+tacalcitol	Half-side (24)	>50% response: 86% (tacalcitol/nUVB), 38% (tacalcitol)	After 6 weeks equal response
Spuls (77)	nUVB+acitretin	Retrospective (40)	>75% response: 72.5%	Recalcitrant psoriasis
Atopic dermatitis				
Pasic (42)	nUVB+UVA	Open trial (21)	≥90% SCORAD reduction: 45.4%; 70–90% reduction: 22.7%	Children
Hudson-Peacock (87)	nUVB	Open trial (37)	Response: 81%; CR: 43%,	
Reynolds (89)	nUVB vs UVA vs visible light	Randomized, controlled (72)	Reduction of total disease activity: 83% (nUVB), 47% (UVA), 47% (Visible light)	
Hjerppe (148)	nUVB vs bUVB/UVA	Half-side (10)	Pruritus reduction: significant effect of nUVB	No difference in SCORAD
Legat (90)	nUVB vs UVA1	Half-side, open (9)	Reduction of Costa and Leister score: 40% and 50% (nUVB), 33% and 30% (UVA1); pruritus: 67% (nUVB), 34% (UVA1)	
Der-Petrossian (88)	nUVB vs bath-PUVA	Half-side, randomized, investigator-blinded (12)	SCORAD reduction: 65.7% (bath-PUVA), 64.1% (nUVB);	
Brazzelli (91)	Cyclosporin A followed by nUVB	Open trial (7)	SCORAD reduction: 63.3% (CsA); relapses treated with nUVB led to further SCORAD-reduction (total 59.9%)	
Mycosis fungoides (MF) and parapsoriasis				
Gathers (93)	nUVB	Retrospective (24)	CR: 54.2%; PR: 29.2%; no response 16.7%; 30% of CR relapse after 12.5 weeks	Stage IA, IB
Clark (96)	nUVB	Open trial (8)	CR: 75%; relapse after 20 months	Patch-stage MF;
Hofer (92)	nUVB	Open trial (20)	CR: 95%; relapses: 100% within a mean of 6 months	SPP and early-stage MF

Table I. *(Continued.)*

Study	Therapy regimen	Study design (*n*)	Response	Remarks
Diederen (94)	nUVB vs PUVA	Retrospective (56)	CR: 81% (nUVB), 71% (PUVA); remission in months: 24.5 (nUVB), 22.8 (PUVA)	Early-stage MF
Vitiligo				
Scherschun (99)	nUVB	Retrospective (7)	75% response: 71.4%; rest: 50–40% response	Response depended on duration
Njoo (102)	nUVB	Open trial (51)	75% response: 53%; stable disease: 80%;	Children; localization dependence
Tjioe (100)	nUVB+folic acid+vitamin B12	Randomized, controlled (27)	$\leqslant$100% repigmentation: 92%; equal response with FA and vitamin B12	Localization dependence
Pruritus				
Baldo (107)	nUVB	Open trial (10)	CR: 80%	Polycythaemia+pruritus
Polymorphous light eruption				
Dummer (113)	nUVB and UVA/bUVB	Open trial (25)	Response: 80% (nUVB), 66.6% (UVA/UVB)	nUVB effective after ineffective UVA/UVB
Gupta (111)	nUVB in hidroa vacciniforme	Retrospective (5)	Response: 60%	Spontaneous clearing: 60%
Graft-versus-host disease				
Grundmann-Kollmann (114)	nUVB	Open trial (10)	CR: 70%; significant improvement: 30%	Recalcitrant
Rare cases				
Pityriasis lichenoides				
Pasic (42)	nUVB	Open trial (9)	$\geqslant$90% reduction: 33.3%; 70–90% reduction: 33.3%	Children
Lichen planus				
Saricaoglu (123)	nUVB	Open trial (10)	CR: 100% (30–51 radiations)	
Taneja (122)	nUVB	Open trial (5)	CR: 100%; Remission: $\geqslant$5–21 months	Oral lesions: no response
Seborrhoeic dermatitis				
Pirkhammer (124)	nUVB	Open trial (18)	CR: 33.3%, PR: 66.6%; pruritus: 100%	100% relapse after 21 days

CR, complete remission; PR, partial remission; SPP, small plaque parapsoriasis; SCORAD, Severity Scoring of Atopic Dermatitis; PUVA, psoralen with UVA; PASI, Psoriasis Area and Severity Index.

alpha-melanocyte stimulating hormone (MSH) and PGE2. UVB down-regulates the expression of intercellular adhesion molecule (ICAM)-1 (13). With regard to wavelength, reduction of the density and function of Langerhans cells in the skin and their migration to the draining lymph nodes is more pronounced with bUVB than with nUVB (23). Infiltrating epidermal T cells as well as mast cells are susceptible to UVB-induced apoptosis (24–26) and depletion of T lymphocytes from psoriatic lesions seems to be greater after nUVB than after bUVB irradiation (27). Moreover, nUVB appears to have a more immunosuppressive effect than bUVB on natural killer cell activity, cytokine responses and lymphoproliferative responses of peripheral blood mononuclear cells (23, 28) and photo-isomerization of trans- to cis-urocanic acid is more effective with nUVB than with bUVB (23), with urocanic acid photoconversion being mainly induced by wavelengths between 310 and 340 nm (29). Therefore, the immunomodulatory effects of nUVB appear to be more pronounced than bUVB.

nUVB suppresses the production of interferon (INF)-γ, IL-2 and IL-12 and increases that of IL-4 and IL-10, which together could account for a shift of the immune response in the direction of T-helper (Th)2-like responses (30–32). The shift from an IFN-γ-dominated Th1 to an IL-4 dominated Th2 response appears to be one of the major factors determining the therapeutic efficacy of nUVB phototherapy as well as that of many systemic treatments such as IL-4 (33), not altering plasma antibody concentrations (34).

In the case of psoriasis, nUVB seems to clear plaques through local rather than systemic effects, as unexposed plaques cleared significantly less than directly exposed plaques (35). However, it has also been hypothesized that clearing of psoriasis is a combination of local and systemic effects (36).

INDICATIONS FOR NARROWBAND UVB

Phototherapy with bUVB or nUVB has been reported to be effective and safe for the treatment of a large number of skin diseases. In addition to psoriasis, atopic dermatitis and vitiligo, various other skin diseases can be treated successfully with nUVB phototherapy, like parapsoriasis, initial mycosis fungoides, graft-versus-host disease and pruritus, as well as acquired perforating dermatosis, lichen planus, lichen simplex chronicus,

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lymphomatoid papulosis, generalized granuloma anulare, nummular dermatitis, pityriasis lichenoides chronica, pityriasis rosea, pityriasis rubra pilaris, pruritic folliculitis of pregnancy, seborrhoeic dermatitis, Schnitzler's syndrome and Sneddon-Wilkinson disease (as reviewed in refs 37, 38). Table I depicts newer studies reporting efficacy and possible combinations of nUVB phototherapy with other treatment modalities. The most important indications will be discussed in detail below.

Psoriasis

Monotherapy with nUVB. According to Feldman et al. (39), with regard to efficacy, safety and cost-effectiveness, UVB phototherapy appears to be the best first-line treatment for the control of generalized psoriasis and there is a large body of evidence indicating that nUVB is more effective than bUVB as a monotherapeutic agent in the treatment of psoriasis even in children (5, 40–42). Whereas bUVB is considered to be most effective close to the minimal erythematous dose (MED), nUVB has also been shown to be effective in sub-erythemogenic doses (27). However, Diffey (43) could show in a mathematical model that clearance of psoriasis plaques is achieved faster with higher MED rates.

Furthermore, nUVB has been shown to be more effective than bath-PUVA with trimethoxsalen (41, 44), and according to some studies it was as effective as systemic PUVA therapy (45–47), although this evaluation was dependent on the type of psoriasis. In a study by van Weelden et al. (46), the therapeutic result differed depending on the treated body site, with lesions on the trunk responding better to nUVB and lesions on the extremities responding better to PUVA. Other studies showed that PUVA is more effective for psoriasis than nUVB alone (48) and systemic PUVA remains an important therapeutic modality for patients with high PASI scores, especially those who do not respond adequately to nUVB.

For treatment of psoriasis with nUVB, three rather than two or five radiations a week are effective (49, 50) and low incremental regimens are sufficient according to Wainwright et al. (51), who showed this regimen to be as effective as high incremental regimens but less erythemogenic.

Combination therapies for psoriasis. In order to reduce cumulative UV doses and to enhance clearance of psoriasis lesions, combination therapies with topical as well as systemic agents have been established.

nUVB plus dithranol (Ingram): In many studies the efficacy of dithranol combined with UVB (broadband or narrowband) could be shown (7, 52, 53). As dithranol is difficult to handle this therapy is mainly reserved for hospital settings.

UVB plus vitamin D3 analogues: Vitamin D3 analogues inhibit proliferation, induce terminal differentiation of human keratinocytes and exhibit immunomodulating properties (54). Several studies showed that calcipotriol as well as calcitriol and tacalcitol are efficacious, safe and can be used on a long-term basis for psoriasis (55–58). Vitamin D3 analogues, when used after nUVB irradiation, reduce the nUVB dose necessary. Furthermore, clearing of plaques occurs faster if vitamin D is applied (59–61). Vitamin D3 derivatives may be used up to 2 h before phototherapy (62, 63) or after UV application, as they are unstable under UV irradiation (64). One study showed that pretreatment with tacalcitol accelerated the response to nUVB (65).

Hofmann et al. (66) found no difference in the efficacy of the combination of nUVB with dithranol versus nUVB with calcipotriol in a half-side trial. However, studies with higher patient numbers are necessary to confirm this finding.

UVB plus topical retinoids: In clinical studies, tazarotene 0.1% gel in combination with nUVB showed faster and significantly greater reduction of psoriasis plaques with significantly lower median cumulative UV exposure than UVB alone (67, 68). Mild irritations like erythema, peeling, dryness, burning and pruritus do occur but photosensitivity is not observed (69, 70). Comparison of tazarotene plus nUVB versus calcipotriol plus nUVB in clinical studies revealed no significant therapeutic difference (71). However, reduction of stratum corneum by retinoids increases UV erythemogenicity and a more cautious increment of UV is recommended when combined with tazarotene (72).

UVB plus salt: Balneophototherapy is a widely applied treatment modality in combination with bUVB or nUVB (73, 74). A multicentre study with 280 psoriasis patients describes a PASI reduction of 71.4% when patients are irradiated with nUVB in the presence of Dead Sea salt solution (75). These are encouraging data, but controlled comparative trials are needed to support these results.

Combination of UVB and systemic therapy: UVB plus systemic retinoids (isotretinoin and acitretin) both can improve the efficacy of nUVB, almost reaching the effectiveness of PUVA (76). In patients refractory to other treatments, the combination of low-dose acitretin and nUVB results in greater improvement than monotherapy with either acitretin or nUVB (77) and retinoids may protect against development of squamous skin cancer (78–81). Thus combination of nUVB with systemic retinoids is a possible alternative to avoid large cumulative PUVA doses.

UVB plus psoralen: Psoralen is normally combined with UVA (PUVA). Anecdotal reports describe equal efficacy of psoralens in combination with nUVB when

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compared to PUVA, although it is unclear to what extent improvement was due to nUVB radiation alone (82–84). The combination of bath-PUVA plus additional nUVB has also been described with nUVB enhancing the phototoxic and therapeutic activities of bath-PUVA (85).

Atopic dermatitis (AD)

There is a large body of evidence indicating that nUVB is effective in the treatment of atopic dermatitis (86). In a recent study, Pasic et al. (42) combined nUVB with UVA for atopic dermatitis in children and showed ⩾90% reduction of the SCORAD index in 45.4% and 70–90% reduction in another 22.7% of patients. Hudson-Peacock et al. (87) described a response rate of 81% with complete clearance in 43% for nUVB twice weekly. The first randomized investigator-blinded, half-side comparison study on the efficacy of 8-methoxypsoralen bath-PUVA versus nUVB in patients with severe chronic atopic dermatitis found equal effectiveness after a mean duration of 40 days when used three times a week in equi-erythemogenic doses (88). Another randomized, controlled, double-blind study with 73 patients treated with nUVB, bUVB/UVA or visible light twice a week showed nUVB to be most effective with respect to the following end points: disease activity and ability to sleep for up to 3 months after cessation of therapy (89). Furthermore, nUVB was shown to be as effective as medium-dose UVA1 in clearing chronic AD and better in reducing pruritus (90).

Combination of nUVB phototherapy with cyclosporin A (CsA) has been reported to be effective in the treatment of atopic dermatitis. Patients with severe atopic dermatitis were treated with oral short-term CsA for 4 weeks. Then CsA was washed out for 4–6 weeks followed by nUVB phototherapy applied three times a week for up to 2 months. This regimen showed good clinical response. However, the study did not investigate long-term effects of this protocol (91) and this combination has to be viewed critically.

Early stage mycosis fungoides (MF) and parapsoriasis en plaques

Several studies indicate the beneficial effect of nUVB for patch-stage mycosis fungoides (Ia/Ib) and parapsoriasis (92, 93). Times to reach complete remissions range from 6 weeks (92) up to 66 months (94). The time to relapse after complete responses after photochemotherapy with PUVA ranges between 6 and 43 months (95). For nUVB prolonged remission up to 20 months has been described (96). Diederen et al. (94) describes even higher complete remissions rates and longer mean relapse-free intervals when comparing nUVB with PUVA (81% vs 71% resp. 24.5 vs 22.8 months). Some authors propose a maintenance phototherapy once a week after complete clearing of mycosis fungoides. As p53 mutations were described in tumour stage MF with a mutation spectrum strikingly similar to that reported in non-melanoma skin cancer and characteristic for DNA damage caused by UVB radiation, precautions regarding long-term phototherapy have to be taken (97). Even though treatment of MF with UVB still raises the issue of carcinogenicity, until now there has been no clinical evidence suggesting that UVB treatment promotes progression of MF.

Vitiligo

No randomized controlled trials investigating the efficacy of nUVB in the treatment of vitiligo have been published so far. However, several clinical studies report that nUVB can achieve up to >75% repigmentation in about two-thirds of patients after at least 1 year of treatment (98, 99). Repigmentation >90% can even be observed (100). nUVB seems to be more effective than bUVB, local steroids or PUVA (101) and this wavelength also appears to be effective in children (102). Body areas with good responses (>75%) include face, neck, trunk and proximal extremities, whereas distal extremities as well as genital areas respond very modestly (<25%) or not at all. nUVB seems to be safe as regards photocarcinogenicity, as up to now only two patients with vitiligo have been reported to develop squamous cell carcinoma after prolonged PUVA therapy (103, 104).

Pruritus

Phototherapy of pruritus can be effective due to treatment of the underlying disease, such as atopic dermatitis, lichen planus or lymphoma. Symptomatic improvement can also be achieved by phototherapy in pruritus associated with uraemia, primary biliary cirrhosis, macular amyloidosis and Hodgkin's lymphoma (105). According to Hsu & Yang (106) uraemic pruritus responds only to bUVB but not to nUVB. Baldo et al. (107) showed nUVB to be effective for treatment of pruritus associated with polycythaemia vera. One open trial study showed that the combination of initial thalidomide followed by nUVB for prurigo nodularis leads to an excellent response after an average of 12 weeks (108).

Polymorphous light eruption (PLE)

PLE is mainly provoked by UVA and to a lesser extent by a combination of UVA/UVB or UVB alone and a light-hardening effect can be seen. For patients with severe forms of PLE effective photo-hardening in spring with nUVB has been described as equally effective as with PUVA, UVA1 or bUVB (109, 110). Photohardening with nUVB has also been used for actinic prurigo, idiopathic solar urticaria, erythropoietic protoporphyria, amiodarone photosensitivity, congenital erythropoietic protoporphyria, homozygous variegate porphyria or hydroa vacciniforme, even when patients

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showed abnormal photosensitivity in the UVB spectrum (86, 111, 112). PLE lesions provoked by UVA and UVB may respond to photohardening with nUVB, even in patients where UVA/UVB treatment was inefficient. On the other hand, if PLE lesions are induced by bUVB, correct application of nUVB might be impossible. In these very rare cases PUVA therapy has been reported to be a valid alternative (113).

Graft-versus-host disease (GvHD)

The first-line treatment for GvHD is photochemotherapy (PUVA), especially when the skin involvement is severe. Moreover, Grundmann-Kollmann et al. (114) reported 10 patients, resistant to combinations of immunosuppressive drugs, of which seven patients showed complete clearance after treatment with nUVB five times a week over 3–5 weeks. After clearing of cutaneous GvHD, radiation was continued as maintenance therapy for at least 4 weeks and no patient relapsed during a follow-up of 4–18 months. As nUVB phototherapy is a non-aggressive treatment that may be of benefit for patients who are receiving higher doses of immunosuppressive drugs, including CsA or FK506, this form of phototherapy may be an alternative to systemic and topical PUVA in mild cases or during onset of the disease (115).

Rare diseases and other indications

There are anecdotal reports of using nUVB in various other diseases. Thus nUVB has been successfully used for subcorneal pustular dermatosis (Sneddon-Wilkinson disease) (116, 117), acquired perforating dermatosis (118) and pruritic folliculitis of pregnancy (119).

For classical juvenile pityriasis rubra pilaris (PRP), a good clinical result was observed with nUVB in combination with acitretin (120). Notably, PRP can be provoked by UV irradiation and painful and tense lesional blistering has been described under nUVB. Thus, phototesting prior to initiation of nUVB as well as discrete dose increments are mandatory (121). Patients with lichen planus have successfully been treated with nUVB: pruritus responded early and a complete flattening occurred within 30–51 radiations and no relapse was seen during follow-up of 20 months. Again, photoaggravated lichen planus should be kept in mind (122, 123).

Other diseases responding to treatment with nUVB include chronic pityriasis lichenoides in children, but not pityriasis lichenoides et varioliformis acuta (42) and seborrhoeic dermatitis (124).

ADVERSE EFFECTS OF NUVB

Early side effects

Early side effects of nUVB include erythema and dryness of the skin. The maximum erythema occurs 8–24 h after irradiation (125, 126). As patients over 70 years show a prolonged nUVB-induced erythema, a more cautious approach to dose increases is recommended in the elderly (127).

Late side effects

Chronic exposure to UV radiation induces premature aging (photoaging) of the skin, showing typical clinical signs of leathery appearance, wrinkling, reduced recoil capacity and increased fragility of the skin (128, 129). Both wavelengths UVA and UVB are capable of inducing the different metabolic changes that result in enhanced skin aging (128, 130). The relative influence of nUVB in comparison to UVA or bUVB has not yet been investigated.

More important than photoaging after chronic UVB exposure is the risk of skin tumour induction. While the role of PUVA in the induction of skin tumours is undisputed, in humans the role of UVB phototherapy in skin carcinogenesis is less clear. No significant increase in the risk of developing squamous cell carcinoma or basal cell carcinoma has been associated with long-term exposure of patients with psoriasis to bUVB phototherapy in older and recent studies (131–133), even in combination with crude coal tar over 25 years (134). At present it is not clear whether nUVB or bUVB is more carcinogenic. Several animal studies found that nUVB has a higher carcinogenic potency than bUVB (135–137), while others did not confirm this (4, 5, 138–140). Macve & Norval (141) showed that tumour outgrowth is enhanced by bUVB, but not by nUVB or UVA1. Remarkably, cis-urocanic acid seemed not to be important for tumour induction, although it is recognized as an initiator of UV-induced immunosuppression.

Throughout the UVB spectrum, the first DNA lesions induced are pyrimidine dimers, but the number of dimers produced decreases dramatically with longer UV wavelengths. For example, irradiation of human fibroblasts with equal UVB energy produces 100 pyrimidine dimers at 302 nm, but only 1 dimer at 312 nm. Similarly, 60 functional mutations of the hypoxanthine phosphoribosyltransferase gene are produced at 302 nm, but only one is produced at 312 nm (142). These data were confirmed by Tzung & Runger (143) and Budiyano et al. (144), who showed 10-fold higher doses of nUVB yielding a similar amount of CPD and also a 1.5–3 times higher amount of oxidative DNA damage compared with bUVB.

Data investigating the carcinogenic risks of nUVB and bUVB are limited. When used in humans nUVB seems not to be associated with a higher carcinogenic risk when compared with bUVB, but a significantly reduced risk compared with PUVA (145, 146). A first long-term retrospective study by Weischer et al. (147) during a follow-up of 10 years further supports the view that neither nUVB nor bUVB significantly increase the

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risk of skin cancer. Nevertheless, phototherapy must be applied with due caution and patients possibly receiving long-term phototherapy should be followed up by a dermatologist on a regular basis.

CONCLUSION

Phototherapy with nUVB is a safe and effective treatment modality for a continuously increasing number of skin diseases. In addition to its low erythemogenicity and high therapeutic efficacy, its major advantages are possible combination with other topical or systemic treatment modalities and cost-effectiveness. More clinical trials are needed to investigate important issues such as carcinogenicity and effectiveness in skin diseases other than psoriasis.

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REFERENCES

1. Goeckerman WH. The treatment of psoriasis. Northwest Med 1925; 24: 229–231.
2. Ingram JT. The approach to psoriasis. Br J Dermatol 1953; 2: 591–594.
3. Fischer T, Alsins J. Treatment of psoriasis with trioxsalen baths and dysprosium lamps. Acta Derm Venereol 1976; 56: 383–390.
4. Parrish JA, Jaenicke KF. Action spectrum for phototherapy of psoriasis. J Invest Dermatol 1981; 76: 359–362.
5. van Weelden H, De La Faille HB, Young E, van der Leun JC. A new development in UVB phototherapy of psoriasis. Br J Dermatol 1988; 119: 11–19.
6. Green C, Ferguson J, Lakshmipathi T, Johnson BE. 311 nm UVB phototherapy – an effective treatment for psoriasis. Br J Dermatol 1988; 119: 691–696.
7. Karvonen J, Kokkonen EL, Ruotsalainen E. 311 nm UVB lamps in the treatment of psoriasis with the Ingram regimen. Acta Derm Venereol 1989; 69: 82–85.
8. Hoffmann K, Kaspar K, Altmeyer P, Gambichler T. UV transmission measurements of small skin specimens with special quartz cuvettes. Dermatology 2000; 201: 307–311.
9. Chadwick CA, Potten CS, Nikaido O, Matsunaga T, Proby C, Young AR. The detection of cyclobutane thymine dimers, (6-4) photolesions and the Dewar photoisomers in sections of UV-irradiated human skin using specific antibodies, and the demonstration of depth penetration effects. J Photochem Photobiol B 1995; 28: 163–170.
10. Campbell C, Quinn AG, Angus B, Farr PM, Rees JL. Wavelength specific patterns of p53 induction in human skin following exposure to UV radiation. Cancer Res 1993; 53: 2697–2699.
11. Farr PM, Diffey BL, Steele MC. A preliminary study on the in vivo transmission of light through psoriatic plaques. Photodermatology 1984; 1: 87–90.
12. Wassberg C, Backvall H, Diffey B, Ponten F, Berne B. Enhanced epidermal ultraviolet responses in chronically sun-exposed skin are dependent on previous sun exposure. Acta Derm Venereol 2003; 83: 254–261.
13. Krutmann J, Morita A, Elmets A. Mechanisms of photo(chemo)therapy. In: Krutmann J, Honigsmann H, Elmets CA, Bergstresser PR, eds. Dermatological phototherapy and photodiagnostic methods. Berlin: Springer, 2001: 56–59.
14. Clingen PH, Arlett CF, Cole J, Waugh AP, Lowe JE, Harcourt SA, et al. Correlation of UVC and UVB cytotoxicity with the induction of specific photoproducts in T-lymphocytes and fibroblasts from normal human donors. Photochem Photobiol 1995; 61: 163–170.
15. Trautinger F. Mechanisms of photodamage of the skin and its functional consequences for skin ageing. Clin Exp Dermatol 2001; 26: 573–577.
16. Dalziel KL. Aspects of cutaneous ageing. Clin Exp Dermatol 1991; 16: 315–323.
17. Berneburg M, Krutmann J. Photoimmunology, DNA repair and photocarcinogenesis. J Photochem Photobiol B 2000; 54: 87–93.
18. Berneburg M, Lowe JE, Nardo T, Araujo S, Fousteri MI, Green MH, et al. UV damage causes uncontrolled DNA breakage in cells from patients with combined features of XP-D and Cockayne syndrome. EMBO J 2000; 19: 1157–1166.
19. Mathonnet G, Leger C, Desnoyers J, Drouin R, Therrien JP, Drobetsky EA. UV wavelength-dependent regulation of transcription-coupled nucleotide excision repair in p53-deficient human cells. Proc Natl Acad Sci U S A 2003; 100: 7219–7224.
20. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol 1987; 123: 241–250.
21. Berneburg M, Lehmann AR. Xeroderma pigmentosum and related disorders: defects in DNA repair and transcription. Adv Genet 2001; 43: 71–102.
22. Duthie MS, Kimber I, Norval M. The effects of ultraviolet radiation on the human immune system. Br J Dermatol 1999; 140: 995–1009.
23. El Ghorr AA, Norval M. Biological effects of narrow-band (311 nm TL01) UVB irradiation: a review. J Photochem Photobiol B 1997; 38: 99–106.
24. Krueger JG, Wolfe JT, Nabeya RT, Vallat VP, Gilleaudeau P, Heftler NS, et al. Successful ultraviolet B treatment of psoriasis is accompanied by a reversal of keratinocyte pathology and by selective depletion of intraepidermal T cells. J Exp Med 1995; 182: 2057–2068.
25. Ozawa M, Ferenczi K, Kikuchi T, Cardinale I, Austin LM, Coven TR, et al. 312-nanometer ultraviolet B light (narrow-band UVB) induces apoptosis of T cells within psoriatic lesions. J Exp Med 1999; 189: 711–718.
26. Szepietowski JC, Morita A, Tsuji T. Ultraviolet B induces mast cell apoptosis: a hypothetical mechanism of ultraviolet B treatment for uraemic pruritus. Med Hypotheses 2002; 58: 167–170.
27. Walters IB, Burack LH, Coven TR, Gilleaudeau P, Krueger JG. Suberythemogenic narrow-band UVB is markedly more effective than conventional UVB in treatment of psoriasis vulgaris. J Am Acad Dermatol 1999; 40: 893–900.
28. Guckian M, Jones CD, Vestey JP, Cooper EJ, Dawe R, Gibbs NK, et al. Immunomodulation at the initiation of phototherapy and photochemotherapy. Photodermatol Photoimmunol Photomed 1995; 11: 163–169.
29. Laihia JK, Jansen CT. Urocanic acid photoconversion in relation to erythematogenicity of radiation from different types of phototherapy equipment. Photodermatol Photoimmunol Photomed 1994; 10: 13–16.

Acta Dermato-Venereologica adv51356.3d 11/11/04 18:25:49
The Charlesworth Group, Wakefield +44(0)1924 369598 - Rev 7.51n/W (Jan 20 2003)

30. Barr RM, Walker SL, Tsang W, Harrison GI, Ettehadi P, Greaves MW, et al. Suppressed alloantigen presentation, increased TNF-alpha, IL-1, IL-1Ra, IL-10, and modulation of TNF-R in UV-irradiated human skin. J Invest Dermatol 1999; 112: 692–698.
31. Enk CD, Sredni D, Blauvelt A, Katz SI. Induction of IL-10 gene expression in human keratinocytes by UVB exposure in vivo and in vitro. J Immunol 1995; 154: 4851–4856.
32. Walters IB, Ozawa M, Cardinale I, Gilleaudeau P, Trepicchio WL, Bliss J, et al. Narrowband (312-nm) UV-B suppresses interferon gamma and interleukin (IL) 12 and increases IL-4 transcripts: differential regulation of cytokines at the single-cell level. Arch Dermatol 2003; 139: 155–161.
33. Ghoreschi K, Thomas P, Breit S, Dugas M, Mailhammer R, van Eden W, et al. Interleukin-4 therapy of psoriasis induces Th2 responses and improves human autoimmune disease. Nat Med 2003; 9: 40–46.
34. Jones CD, Guckian M, El Ghorr AA, Gibbs NK, Norval M. Effects of phototherapy on the production of cytokines by peripheral blood mononuclear cells and on systemic antibody responses in patients with psoriasis. Photodermatol Photoimmunol Photomed 1996; 12: 204–210.
35. Dawe RS, Cameron H, Yule S, Man I, Ibbotson SH, Ferguson J. UV-B phototherapy clears psoriasis through local effects. Arch Dermatol 2002; 138: 1071–1076.
36. Gibbs NK. Narrowband UV-B phototherapy clears psoriasis through a combination of local and systemic effects. Arch Dermatol 2003; 139: 665–666.
37. Samson YS, Gielczyk R, Scherschun L, Lim HW. Narrow-band ultraviolet B treatment for vitiligo, pruritus, and inflammatory dermatoses. Photodermatol Photoimmunol Photomed 2003; 19: 164–168.
38. Lebwohl M. Should we switch from combination UVA/UVB phototherapy units to narrowband UVB? Photodermatol Photoimmunol Photomed 2002; 18: 44–46.
39. Feldman SR, Garton R, Averett W, Balkrishnan R, Vallee J. Strategy to manage the treatment of severe psoriasis: considerations of efficacy, safety and cost. Expert Opin Pharmacother 2003; 4: 1525–1533.
40. Coven TR, Burack LH, Gilleaudeau R, Keogh M, Ozawa M, Krueger JG. Narrowband UV-B produces superior clinical and histopathological resolution of moderate-to-severe psoriasis in patients compared with broadband UV-B. Arch Dermatol 1997; 133: 1514–1522.
41. Dawe RS, Cameron H, Yule S, Man I, Wainwright NJ, Ibbotson SH, et al. A randomized controlled trial of narrowband ultraviolet B vs bath-psoralen plus ultraviolet A photochemotherapy for psoriasis. Br J Dermatol 2003; 148: 1194–1204.
42. Pasic A, Ceovic R, Lipozencic J, Husar K, Susic SM, Skerlev M, et al. Phototherapy in pediatric patients. Pediatr Dermatol 2003; 20: 71–77.
43. Diffey B. Towards optimal regimens for the UVB phototherapy of psoriasis: a mathematical model. Acta Derm Venereol 2004; 84: 259–264.
44. Snellman E, Klimenko T, Rantanen T. Randomized half-side comparison of narrowband UVB and trimethylpsoralen bath plus UVA treatments for psoriasis. Acta Derm Venereol 2004; 84: 132–137.
45. Tanew A, Radakovic-Fijan S, Schemper M, Honigsmann H. Narrowband UV-B phototherapy vs photochemotherapy in the treatment of chronic plaque-type psoriasis: a paired comparison study. Arch Dermatol 1999; 135: 519–524.
46. van Weelden H, Baart dlF, Young E, van der Leun JC. Comparison of narrow-band UV-B phototherapy and PUVA photochemotherapy in the treatment of psoriasis. Acta Derm Venereol 1990; 70: 212–215.
47. Markham T, Rogers S, Collins P. Narrowband UV-B (TL-01) phototherapy vs oral 8-methoxypsoralen psoralen-UV-A for the treatment of chronic plaque psoriasis. Arch Dermatol 2003; 139: 325–328.
48. Gordon PM, Diffey BL, Matthews JN, Farr PM. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999; 41: 728–732.
49. Cameron H, Dawe RS, Yule S, Murphy J, Ibbotson SH, Ferguson J. A randomized, observer-blinded trial of twice vs. three times weekly narrowband ultraviolet B phototherapy for chronic plaque psoriasis. Br J Dermatol 2002; 147: 973–978.
50. Dawe RS, Wainwright NJ, Cameron H, Ferguson J. Narrow-band (TL-01) ultraviolet B phototherapy for chronic plaque psoriasis: three times or five times weekly treatment? Br J Dermatol 1998; 138: 833–839.
51. Wainwright NJ, Dawe RS, Ferguson J. Narrowband ultraviolet B (TL-01) phototherapy for psoriasis: which incremental regimen? Br J Dermatol 1998; 139: 410–414.
52. Carrozza P, Hausermann P, Nestle FO, Burg G, Boni R. Clinical efficacy of narrow-band UVB (311 nm) combined with dithranol in psoriasis. An open pilot study. Dermatology 2000; 200: 35–39.
53. Storbeck K, Holzle E, Schurer N, Lehmann P, Plewig G. Narrow-band UVB (311 nm) versus conventional broad-band UVB with and without dithranol in phototherapy for psoriasis. J Am Acad Dermatol 1993; 28: 227–231.
54. van der Vleuten CJ, Gerritsen MJ, Steijlen PM, de Jong EM, van de Kerkhof PC. A therapeutic approach to erythrodermic psoriasis: report of a case and a discussion of therapeutic options. Acta Derm Venereol 1996; 76: 65–67.
55. Langner A, Ashton P, van de Kerkhof PC, Verjans H. A long-term multicentre assessment of the safety and tolerability of calcitriol ointment in the treatment of chronic plaque psoriasis. Br J Dermatol 1996; 135: 385–389.
56. van de Kerkhof PC, Berth-Jones J, Griffiths CE, Harrison PV, Honigsmann H, Marks R, et al. Long-term efficacy and safety of tacalcitol ointment in patients with chronic plaque psoriasis. Br J Dermatol 2002; 146: 414–422.
57. Fogh K, Kragballe K. Recent developments in vitamin D analogs. Curr Pharm Des 2000; 6: 961–972.
58. Bourke JF, Iqbal SJ, Hutchinson PE. The effects of UVB plus calcipotriol on systemic calcium homeostasis in patients with chronic plaque psoriasis. Clin Exp Dermatol 1997; 22: 259–261.
59. Woo WK, McKenna KE. Combination TL01 ultraviolet B phototherapy and topical calcipotriol for psoriasis: a prospective randomized placebo-controlled clinical trial. Br J Dermatol 2003; 149: 146–150.
60. Kerscher M, Volkenandt M, Plewig G, Lehmann P. Combination phototherapy of psoriasis with calcipotriol and narrow-band UVB. Lancet 1993; 342: 923.
61. Rim JH, Choe YB, Youn JI. Positive effect of using calcipotriol ointment with narrow-band ultraviolet B phototherapy in psoriatic patients. Photodermatol Photoimmunol Photomed 2002; 18: 131–134.

62. Kragballe K. Vitamin D and UVB radiation therapy. Cutis 2002; 70: 9–12.
63. De Rie MA, Di Nuzzo S, Brands S, Hansen AB, Bos JD. Calcipotriol ointment and cream or their vehicles applied immediately before irradiation inhibit ultraviolet B-induced erythema. Br J Dermatol 2000; 142: 1160–1165.
64. Lebwohl M, Quijije J, Gilliard J, Rollin T, Watts O. Topical calcitriol is degraded by ultraviolet light. J Invest Dermatol 2003; 121: 594–595.
65. Messer G, Degitz K, Plewig G, Rocken M. Pretreatment of psoriasis with the vitamin D3 derivative tacalcitol increases the responsiveness to 311-nm ultraviolet B: results of a controlled, right/left study. Br J Dermatol 2001; 144: 628–629.
66. Hofmann UB, Eggert AA, Brocker EB, Goebeler M. Calcitriol vs. dithranol in combination with narrow-band ultraviolet B (311 nm) in psoriasis. Br J Dermatol 2003; 148: 779–783.
67. Koo JY. Tazarotene in combination with phototherapy. J Am Acad Dermatol 1998; 39: S144–S148.
68. Behrens S, Grundmann-Kollmann M, Schiener R, Peter RU, Kerscher M. Combination phototherapy of psoriasis with narrow-band UVB irradiation and topical tazarotene gel. J Am Acad Dermatol 2000; 42: 493–495.
69. Guenther LC. Optimizing treatment with topical tazarotene. Am J Clin Dermatol 2003; 4: 197–202.
70. Koo JY, Lowe NJ, Lew-Kaya DA, Vasilopoulos AI, Lue JC, Sefton J, et al. Tazarotene plus UVB phototherapy in the treatment of psoriasis. J Am Acad Dermatol 2000; 43: 821–828.
71. Schiener R, Behrens-Williams SC, Pillekamp H, Kaskel P, Peter RU, Kerscher M. Calcipotriol vs. tazarotene as combination therapy with narrowband ultraviolet B (311 nm): efficacy in patients with severe psoriasis. Br J Dermatol 2000; 143: 1275–1278.
72. Lebwohl M, Drake L, Menter A, Koo J, Gottlieb AB, Zanolli M, et al. Consensus conference: acitretin in combination with UVB or PUVA in the treatment of psoriasis. J Am Acad Dermatol 2001; 45: 544–553.
73. Boer J, Schothorst AA, Boom B, Hermans J, Suurmond D. Influence of water and salt solutions on UVB irradiation of normal skin and psoriasis. Arch Dermatol Res 1982; 273: 247–259.
74. Gambichler T, Rapp S, Senger E, Altmeyer P, Hoffmann K. Balneophototherapy of psoriasis: highly concentrated salt water versus tap water – a randomized, one-blind, right/left comparative study. Photodermatol Photoimmunol Photomed 2001; 17: 22–25.
75. Schiffner R, Schiffner-Rohe J, Wolfl G, Landthaler M, Glassl A, Walther T, et al. Evaluation of a multicentre study of synchronous application of narrowband ultraviolet B phototherapy (TL-01) and bathing in Dead Sea salt solution for psoriasis vulgaris. Br J Dermatol 2000; 142: 740–747.
76. Green C, Lakshmipathi T, Johnson BE, Ferguson J. A comparison of the efficacy and relapse rates of narrow-band UVB (TL-01) monotherapy vs. etretinate (re-TL-01) vs. etretinate-PUVA (re-PUVA) in the treatment of psoriasis patients. Br J Dermatol 1992; 127: 5–9.
77. Spuls PI, Rozenblit M, Lebwohl M. Retrospective study of the efficacy of narrowband UVB and acitretin. J Dermatol Treat 2003; 14(Suppl 2): 17–20.
78. Bollag W, Holdener EE. Retinoids in cancer prevention and therapy. Ann Oncol 1992; 3: 513–526.
79. van de Kerkhof PC, de Rooij MJ. Multiple squamous cell carcinomas in a psoriatic patient following high-dose photochemotherapy and cyclosporin treatment: response to long-term acitretin maintenance. Br J Dermatol 1997; 136: 275–278.
80. Bavinck JN, Tieben LM, Van der Woude FJ, Tegzess AM, Hermans J, ter Schegget J, et al. Prevention of skin cancer and reduction of keratotic skin lesions during acitretin therapy in renal transplant recipients: a double-blind, placebo-controlled study. J Clin Oncol 1995; 13: 1933–2938.
81. Nijsten TE, Stern RS. Oral retinoid use reduces cutaneous squamous cell carcinoma risk in patients with psoriasis treated with psoralen-UVA: a nested cohort study. J Am Acad Dermatol 2003; 49: 644–650.
82. de Berker DA, Sakuntabhai A, Diffey BL, Matthews JN, Farr PM. Comparison of psoralen-UVB and psoralen-UVA photochemotherapy in the treatment of psoriasis. J Am Acad Dermatol 1997; 36: 577–581.
83. Ortel B, Perl S, Kinaciyan T, Calzavara-Pinton PG, Honigsmann H. Comparison of narrow-band (311 nm) UVB and broad-band UVA after oral or bath-water 8-methoxypsoralen in the treatment of psoriasis. J Am Acad Dermatol 1993; 29: 736–740.
84. Sakuntabhai A, Diffey BL, Farr PM. Response of psoriasis to psoralen-UVB photochemotherapy. Br J Dermatol 1993; 128: 296–300.
85. Calzavara-Pinton P. Narrow band UVB (311 nm) phototherapy and PUVA photochemotherapy: a combination. J Am Acad Dermatol 1998; 38: 687–690.
86. Collins P, Ferguson J. Narrow-band UVB (TL-01) phototherapy: an effective preventative treatment for the photodermatoses. Br J Dermatol 1995; 132: 956–963.
87. Hudson-Peacock MJ, Diffey BL, Farr PM. Narrow-band UVB phototherapy for severe atopic dermatitis. Br J Dermatol 1996; 135: 332.
88. Der-Petrossian M, Seeber A, Honigsmann H, Tanew A. 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.
89. Reynolds NJ, Franklin V, Gray JC, Diffey BL, Farr PM. Narrow-band ultraviolet B and broad-band ultraviolet A phototherapy in adult atopic eczema: a randomised controlled trial. Lancet 2001; 357: 2012–2016.
90. Legat FJ, Hofer A, Brabek E, Quehenberger F, Kerl H, Wolf P. Narrowband UV-B vs medium-dose UV-A1 phototherapy in chronic atopic dermatitis. Arch Dermatol 2003; 139: 223–224.
91. Brazzelli V, Prestinari F, Chiesa MG, Borroni RG, Ardigo M, Borroni G. Sequential treatment of severe atopic dermatitis with cyclosporin A and low-dose narrow-band UVB phototherapy. Dermatology 2002; 204: 252–254.
92. Hofer A, Cerroni L, Kerl H, Wolf P. Narrowband (311-nm) UV-B therapy for small plaque parapsoriasis and early-stage mycosis fungoides. Arch Dermatol 1999; 135: 1377–1380.
93. Gathers RC, Scherschun L, Malick F, Fivenson DP, Lim HW. Narrowband UVB phototherapy for early-stage mycosis fungoides. J Am Acad Dermatol 2002; 47: 191–197.
94. Diederen PV, van Weelden H, Sanders CJ, Toonstra J, van Vloten WA. Narrowband UVB and psoralen-UVA in the treatment of early-stage mycosis fungoides: a retrospective study. J Am Acad Dermatol 2003; 48: 215–219.
95. Herrmann JJ, Roenigk HHJr, Hurria A, Kuzel TM, Samuelson E, Rademaker AW, et al. Treatment of mycosis fungoides with photochemotherapy (PUVA):

Acta Dermato-Venereologica adv51356.3d 11/11/04 18:25:49
The Charlesworth Group, Wakefield +44(0)1924 369598 - Rev 7.51n/W (Jan 20 2003)

long-term follow-up. J Am Acad Dermatol 1995; 33: 234–242.
96. Clark C, Dawe RS, Evans AT, Lowe G, Ferguson J. Narrowband TL-01 phototherapy for patch-stage mycosis fungoides. Arch Dermatol 2000; 136: 748–752.
97. McGregor JM, Crook T, Fraser-Andrews EA, Rozycka M, Crossland S, Brooks L, et al. Spectrum of p53 gene mutations suggests a possible role for ultraviolet radiation in the pathogenesis of advanced cutaneous lymphomas. J Invest Dermatol 1999; 112: 317–321.
98. Westerhof W, Nieuweboer-Krobotova L. Treatment of vitiligo with UV-B radiation vs topical psoralen plus UV-A. Arch Dermatol 1997; 133: 1525–1528.
99. Scherschun L, Kim JJ, Lim HW. Narrow-band ultraviolet B is a useful and well-tolerated treatment for vitiligo. J Am Acad Dermatol 2001; 44: 999–1003.
100. Tjioe M, Gerritsen MJ, Juhlin L, van de Kerkhof PC. Treatment of vitiligo vulgaris with narrow band UVB (311 nm) for one year and the effect of addition of folic acid and vitamin B12. Acta Derm Venereol 2002; 82: 369–372.
101. Njoo MD, Spuls PI, Bos JD, Westerhof W, Bossuyt PM. Nonsurgical repigmentation therapies in vitiligo. Meta-analysis of the literature. Arch Dermatol 1998; 134: 1532–1540.
102. Njoo MD, Bos JD, Westerhof W. Treatment of generalized vitiligo in children with narrow-band (TL-01) UVB radiation therapy. J Am Acad Dermatol 2000; 42: 245–253.
103. Buckley DA, Rogers S. Multiple keratoses and squamous carcinoma after PUVA treatment of vitiligo. Clin Exp Dermatol 1996; 21: 43–45.
104. Takeda H, Mitsuhashi Y, Kondo S. Multiple squamous cell carcinomas in situ in vitiligo lesions after long-term PUVA therapy. J Am Acad Dermatol 1998; 38: 268–270.
105. Kaptanoglu AF, Oskay T. Ultraviolet B treatment for pruritus in Hodgkin's lymphoma. J Eur Acad Dermatol Venereol 2003; 17: 489–490.
106. Hsu MM, Yang CC. Uraemic pruritus responsive to broadband ultraviolet (UV) B therapy does not readily respond to narrowband UVB therapy. Br J Dermatol 2003; 149: 888–889.
107. Baldo A, Sammarco E, Plaitano R, Martinelli V, Monfrecola G. Narrowband (TL-01) ultraviolet B phototherapy for pruritus in polycythaemia vera. Br J Dermatol 2002; 147: 979–981.
108. Ferrandiz C, Carrascosa JM, Just M, Bielsa I, Ribera M. Sequential combined therapy with thalidomide and narrow-band (TL01) UVB in the treatment of prurigo nodularis. Dermatology 1997; 195: 359–361.
109. Fesq H, Ring J, Abeck D. Management of polymorphous light eruption: clinical course, pathogenesis, diagnosis and intervention. Am J Clin Dermatol 2003; 4: 399–406.
110. Bilsland D, George SA, Gibbs NK, Aitchison T, Johnson BE, Ferguson J. A comparison of narrow band phototherapy (TL-01) and photochemotherapy (PUVA) in the management of polymorphic light eruption. Br J Dermatol 1993; 129: 708–712.
111. Gupta G, Man I, Kemmett D. Hydroa vacciniforme: a clinical and follow-up study of 17 cases. J Am Acad Dermatol 2000; 42: 208–213.
112. Warren LJ, George S. Erythropoietic protoporphyria treated with narrow-band (TL-01) UVB phototherapy. Australas J Dermatol 1998; 39: 179–182.
113. Dummer R, Ivanova K, Scheidegger EP, Burg G. Clinical and therapeutic aspects of polymorphous light eruption. Dermatology 2003; 207: 93–95.
114. Grundmann-Kollmann M, Martin H, Ludwig R, Klein S, Boehncke WH, Hoelzer D, et al. Narrowband UV-B phototherapy in the treatment of cutaneous graft versus host disease. Transplantation 2002; 74: 1631–1634.
115. Luftl M, Degitz K, Plewig G, Rocken M. Psoralen bath plus UV-A therapy. Possibilities and limitations. Arch Dermatol 1997; 133: 1597–1603.
116. Cameron H, Dawe RS. Subcorneal pustular dermatosis (Sneddon-Wilkinson disease) treated with narrowband (TL-01) UVB phototherapy. Br J Dermatol 1997; 137: 150–151.
117. Orton DI, George SA. Subcorneal pustular dermatosis responsive to narrowband (TL-01) UVB phototherapy. Br J Dermatol 1997; 137: 149–150.
118. Bayramgurler D, Apaydin R, Cetiner D, Zincirci C. Narrow-band ultraviolet B phototherapy for acquired perforating dermatosis. Australas J Dermatol 2003; 44: 76–78.
119. Reed J, George S. Pruritic folliculitis of pregnancy treated with narrowband (TL-01) ultraviolet B phototherapy. Br J Dermatol 1999; 141: 177–179.
120. Kirby B, Watson R. Pityriasis rubra pilaris treated with acitretin and narrow-band ultraviolet B (Re-TL-01). Br J Dermatol 2000; 142: 376–377.
121. Khoo L, Asawanonda P, Grevelink SA, Taylor CR. Narrow-band UVB-associated lesional blisters in pityriasis rubra pilaris. J Am Acad Dermatol 1999; 41: 803–804.
122. Taneja A, Taylor CR. Narrow-band UVB for lichen planus treatment. Int J Dermatol 2002; 41: 282–283.
123. Saricaoglu H, Karadogan SK, Baskan EB, Tunali S. Narrowband UVB therapy in the treatment of lichen planus. Photodermatol Photoimmunol Photomed 2003; 19: 265–267.
124. Pirkhammer D, Seeber A, Honigsmann H, Tanew A. Narrow-band ultraviolet B (ATL-01) phototherapy is an effective and safe treatment option for patients with severe seborrhoeic dermatitis. Br J Dermatol 2000; 143: 964–968.
125. Man I, Dawe RS, Ferguson J, Ibbotson SH. An intraindividual study of the characteristics of erythema induced by bath and oral methoxsalen photochemotherapy and narrowband ultraviolet B. Photochem Photobiol 2003; 78: 55–60.
126. Farr PM, Besag JE, Diffey BL. The time course of UVB and UVC erythema. J Invest Dermatol 1988; 91: 454–457.
127. Gloor M, Scherotzke A. Age dependence of ultraviolet light-induced erythema following narrow-band UVB exposure. Photodermatol Photoimmunol Photomed 2002; 18: 121–126.
128. Berneburg M, Plettenberg H, Krutmann J. Photoaging of human skin. Photodermatol Photoimmunol Photomed 2000; 16: 239–244.
129. Scharffetter-Kochanek K, Brenneisen P, Wenk J, Herrmann G, Ma W, Kuhr L, et al. Photoaging of the skin from phenotype to mechanisms. Exp Gerontol 2000; 35: 307–316.
130. Fisher GJ, Kang S, Varani J, Bata-Csorgo Z, Wan Y, Datta S, et al. Mechanisms of photoaging and chronological skin aging. Arch Dermatol 2002; 138: 1462–1470.
131. Stern RS, Laird N, Melski J, Parrish JA, Fitzpatrick TB, Bleich HL. Cutaneous squamous-cell carcinoma in patients treated with PUVA. N Engl J Med 1984; 310: 1156–1161.

132. Stern RS, Laird N. The carcinogenic risk of treatments for severe psoriasis. Photochemotherapy follow-up study. Cancer 1994; 73: 2759–2764.
133. Nijsten TE, Stern RS. The increased risk of skin cancer is persistent after discontinuation of psoralen+ultraviolet A: a cohort study. J Invest Dermatol 2003; 121: 252–258.
134. Pittelkow MR, Perry HO, Muller SA, Maughan WZ, O'Brien PC. Skin cancer in patients with psoriasis treated with coal tar. A 25-year follow-up study. Arch Dermatol 1981; 117: 465–468.
135. Wulf HC, Hansen AB, Bech-Thomsen N. Differences in narrow-band ultraviolet B and broad-spectrum ultraviolet photocarcinogenesis in lightly pigmented hairless mice. Photodermatol Photoimmunol Photomed 1994; 10: 192–197.
136. Gibbs NK, Traynor NJ, MacKie RM, Campbell I, Johnson BE, Ferguson J. The phototumorigenic potential of broad-band (270–350 nm) and narrow-band (311–313 nm) phototherapy sources cannot be predicted by their edematogenic potential in hairless mouse skin. J Invest Dermatol 1995; 104: 359–363.
137. Flindt-Hansen H, McFadden N, Eeg-Larsen T, Thune P. Effect of a new narrow-band UVB lamp on photocarcinogenesis in mice. Acta Derm Venereol 1991; 71: 245–248.
138. Fischer T, Alsins J, Berne B. Ultraviolet-action spectrum and evaluation of ultraviolet lamps for psoriasis healing. Int J Dermatol 1984; 23: 633–637.
139. Cole CA, Forbes PD, Davies RE. An action spectrum for UV photocarcinogenesis. Photochem Photobiol 1986; 43: 275–284.
140. Sterenborg HJ, van Weelden H, van der Leun JC. The dose-response relationship for tumourigenesis by UV radiation in the region 311–312 nm. J Photochem Photobiol B 1988; 2: 179–194.
141. Macve JC, Norval M. The effects of UV waveband and cis-urocanic acid on tumour outgrowth in mice. Photochem Photobiol Sci 2002; 1: 1006–1011.
142. Enninga IC, Groenendijk RT, Filon AR, van Zeeland AA, Simons JW. The wavelength dependence of u.v.-induced pyrimidine dimer formation, cell killing and mutation induction in human diploid skin fibroblasts. Carcinogenesis 1986; 7: 1829–3186.
143. Tzung TY, Runger TM. Assessment of DNA damage induced by broadband and narrowband UVB in cultured lymphoblasts and keratinocytes using the comet assay. Photochem Photobiol 1998; 67: 647–650.
144. Budiyanto A, Ueda M, Ueda T, Ichihashi M. Formation of cyclobutane pyrimidine dimers and 8-oxo-7,8-dihydro-2'-deoxyguanosine in mouse and organ-cultured human skin by irradiation with broadband or with narrowband UVB. Photochem Photobiol 2002; 76: 397–400.
145. An appraisal of narrowband (TL-01) UVB phototherapy, British Photodermatology Group Workshop Report (April 1996). Br J Dermatol 1997; 137: 327–330.
146. de Gruijl FR. Photobiology of photocarcinogenesis. Photochem Photobiol 1996; 63: 372–375.
147. Weischer M, Blum A, Eberhard F, Röcken M, Berneburg M. No evidence for increased skin cancer risk in psoriasis patients treated with broad band or narrow band UVB phototherapy: a first retrospective study. Acta Derm Venereol 2004; 84: 370–374.
148. Hjerppe M, Hasan T, Saksala I, Reunala T. Narrowband UVB treatment in atopic dermatitis. Acta Derm Venereol 2001; 81: 439–440.