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Phototherapy in Pediatric Patients: Choosing the Appropriate Treatment Option

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Phototherapeutic modalities, including narrowband-UVB, broadband-UVB, PUVA photochemotherapy, and excimer laser therapy are valuable tools that can be used for photoresponsive dermatoses in children. As a systematically safer alternative compared with internal agents, including the prebiologic and biological therapies, phototherapy should be considered a possible treatment option for children with diseases including psoriasis, atopic dermatitis, pityriasis lichenoides chronica, and vitiligo.
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When choosing appropriate therapies for dermatologic conditions in the pediatric population, clinicians must not only consider disease severity and morphology but also the general systemic safety profile of the treatment. Fortunately, many diseases, including psoriasis, atopic dermatitis, vitiligo, and pityriasis lichenoides, are photoresponsive dermatoses for which phototherapy represents an especially valuable treatment option. The pediatric population is a special population for whom it is important to avoid systemic agents and their associated potential risks whenever possible. Phototherapy represents a safe alternative for appropriately selected cases. There are 4 phototherapeutic options: narrowband-UVB (NBUVB), broadband-UVB (BBUVB), psoralen-UVA photochemotherapy (PUVA), and excimer laser therapy. This article aims to review which therapeutic modalities may be preferred for which light-responsive conditions in the pediatric population. Phototherapeutic modalities will be discussed in the following order: NBUVB, BBUVB, PUVA, and monochromatic excimer laser.

NBUVB

NBUVB, ranging from 311 to 313 nm, is a safe and efficacious treatment option for several photoresponsive conditions in adults. NBUVB represents a notable advance in phototherapy and is considered more efficacious than BBUVB in the treatment of psoriasis, mycosis fungoides (MF), and vitiligo. NBUVB also has been increasingly tested in the pediatric population as a therapy for diseases, including psoriasis, vitiligo, pityriasis lichenoides, MF, and atopic dermatitis.

Psoriasis

Psoriasis is a chronic inflammatory skin disease that can begin at any age and accounts for approximately 2% of visits to pediatric dermatologists. Most cases of childhood psoriasis can be controlled with topical regimens, including emollients, corticosteroids, coal tar, and vitamin D agents. However, some patients with a larger percentage of body surface area (BSA) involvement or more severe disease will require other therapeutic options, including phototherapy. Furthermore, children with extensive BSA involvement may not be good candidates for topical therapy because of the associated potential systemic risks of applying topical steroids and other agents to such extensive surfaces. In general, UVB phototherapy in combination with topical agents is the recommended treatment option before systemic therapy, including retinoids, methotrexate, cyclosporine, and biological agents.

The optimal wavelength for the treatment of psoriasis has been found to be approximately 313 nm, leading to the development of NBUVB phototherapy that emits a distinct band of high-intensity UVB light at 311 to 313 nm.[1] Although PUVA still appears to be more efficacious than NBUVB for psoriasis in head-to-head large comparison studies, especially with respect to duration of treatment effect, NBUVB is much simpler to apply and perhaps more practical for use in the pediatric population.[2] In general, NBUVB has proved to be more efficacious than BBUVB phototherapy, leading to faster clearance of psoriatic plaques and inducing

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longer remission periods.[3] The mechanism of action of UVB light is multifaceted, including the ability to induce T-lymphocyte apoptosis, increase secretion of interleukin-10, and diminish antigen presentation.[4]

The authors of one study[5] treated 20 children who had psoriasis unresponsive to topical therapy with NBUVB 3 times per week. The NBUVB dose was increased by 10% to 20% per session; the dose was maintained and not increased if any erythema was detected. In this population, the median age was 13 years, with 80% of patients having plaque psoriasis and 20% guttate psoriasis. Altogether, 69% of patients reached PASI 75 response (75% improvement in Psoriasis Area and Severity Index) and 52% of patients achieved PASI 90 response after an average of 32 phototherapy treatment sessions. In most patients studied (70%), the remission period was approximately 8 months. The major adverse event observed was erythema, which did not lead to discontinuation of therapy. Thus, most children had at least 75% improvement in their psoriasis after 32 treatments; this number would represent approximately 11 weeks of treatment at a phototherapy center.

Pasic et al[6] and Jury et al[7] also studied the efficacy and safety of NBUVB in pediatric psoriasis patients with similarly small sample sizes of 20 and 35 patients, respectively. Pasic et al reported a PASI 70 response rate of 65% and a PASI 90 response rate of 45%, after a mean number of 19 phototherapy treatments; the PASI 75 response was not assessed.[6] Jury et al reported a PASI 90 response rate of 63%.[7] In another small study, Kumar et al[8] treated 20 pediatric psoriasis patients with NBUVB. Approximately 60% of patients obtained a PASI 90 response, and no improvement was seen in 10% of patients after a median number of 24 sessions.[8] In another group of children with median age 12 years, NBUVB was used to treat 28 pediatric patients with generalized guttate-type psoriasis.[9] Response was defined as a greater than 75% improvement in psoriasis (although PASI was not used to measure response). Patients were treated 3 times per week, which was reduced to twice or once weekly once response was reached. Altogether, 93% of patients responded. In general, plaque-type psoriasis required more treatment sessions compared with guttate psoriasis; the mean number of treatments required for response was 36 in plaque-type psoriasis compared with 16 treatments in guttate psoriasis. It is not clear, but perhaps the more indurated psoriatic plaques required more UVB irradiation compared with thinner, less scaly guttate plaques.

As an adjunct to treatment with NBUVB for psoriasis, mineral oil can be used before irradiation to enhance the therapeutic efficacy of UVB light and shorten treatment periods. Although thick petrolatum or tar preparations can potentially block UVB rays, mineral oil is not thought to reduce transmission or erythemogenicity of UVB light; it is thought to enhance transmission by changing the refractive index of the skin.[10] Pretreatment with mineral oil before NBUVB phototherapy has been tested in children with psoriasis.[11] In a study of 20 children ages 5 to 14 years, mineral oil was applied to half the body before phototherapy which was administered twice weekly. After 3 months, there was significantly greater improvement ($P < 0.05$) in scaling, induration, and clearance on the side of the body that was pretreated with mineral oil. Furthermore, the cumulative dosage needed for clearance of psoriatic plaques was significantly lower on the side pretreated with emollients. No adverse effects were noted with respect to mineral oil or NBUVB phototherapy; however, it should be noted that this study was conducted in India and all patients treated were Fitzpatrick skin type IV. Thus, there may be potential risk of mineral oil-associated burns in patients with fairer skin types.

The long-term risk of NBUVB light in children has yet to be determined. Although it is clear that NBUVB can be an efficacious and safe short-term treatment option in children with severe psoriasis, further prospective studies must be performed to evaluate the long-term risks of this therapy in children.

Vitiligo

Vitiligo can be a challenging condition to treat in children because of a lack of markedly efficacious treatments and limited available data in pediatric patients. NBUVB may be a safe and preferred treatment option for children with vitiligo because it is generally well-tolerated with minimal side effects. As discussed below in the PUVA section, PUVA is also a treatment option for vitiligo but may be considered second-line to NBUVB because of the concern regarding potential increased skin cancer risks, especially in fair-skinned patients.

In 20 children treated with NBUVB for vitiligo, 75% of patients achieved marked or complete repigmentation after an average 34 phototherapy treatments.[12] In another study, NBUVB was used to treat 9 pediatric patients with either localized or generalized vitiligo.[9] Response, which was defined as greater than 50% repigmentation, was achieved in 44% of those patients. The median number of treatments required for response was 14 but ranged widely among patients from 9 to 107 treatments. Thus, NBUVB can represent a preferred treatment option for children with vitiligo.

Pityriasis lichenoides

Pityriasis lichenoides is an acquired disorder affecting both children and young adults. Classification of this disease may be controversial, and it may be considered on a spectrum ranging from pityriasis lichenoides chronica to pityriasis lichenoides et varioliformis acuta.[13] In general, children with pityriasis lichenoides may have greater lesional body involvement compared with adults, as well as increased facial involvement. Additionally, pityriasis lichenoides in children may result in more dyspigmentation and have a poorer response to conventional treatment modalities, such as topical corticosteroids and oral erythromycin. Children are thought to have a more chronic and relapsing course of pityriasis lichenoides in comparison with adults. One study demonstrated that children had a median active disease duration of 30 months compared with 23.5 months in adults.[14]

There is limited data on the use of NBUVB for pityriasis lichenoides in children, but it is known to be an efficacious

therapy and well-tolerated treatment for young adults.[13] NBUVB light was used to treat pityriasis lichenoides chronica in 5 pediatric patients, ages 3 to 16 years. All 5 children responded to NBUVB treatment (with >75% improvement in lesions) after an average number of 22 treatments.[9]

Mycosis Fungoides

Mycosis fungoides (MF) is a cutaneous T-cell lymphoma that is rare in children. When presenting in childhood, MF is usually limited to early patch-stage disease without lymph node enlargement or histologically positive lymph nodes.[15] In 1 case report, a 4-year-old female patient with patch-stage MF received NBUVB 3 times weekly and had histologic remission after 30 treatment sessions.[16] She then underwent maintenance therapy for 5 months. There is no particular established treatment protocol designed for children, and both PUVA and UVB phototherapy have been used. NBUVB is considered more effective than BBUVB for MF and is considered an appropriate treatment for managing MF in both children and young adults.[17]

Atopic Dermatitis

Atopic dermatitis is an inflammatory, pruritic skin condition typically involving a chronic relapsing course in children and young adults. Topical emollients, topical corticosteroids and calcineurin inhibitors represent the mainstay of therapy for atopic dermatitis. However, children and young adults with severe disease may require further therapy. Many phototherapy centers use NBUVB as a useful therapeutic modality to enhance clearance and decrease pruritus for children with moderate and severe atopic eczema. As in the treatment of psoriasis, there are several mechanisms by which UVB treats atopic dermatitis. Suppression of proinflammatory cytokines, such as interleukin (IL)-12, suppression of tumor necrosis factor-α, induction of IL-10, modulation of immune activation and reduction of skin surface bacteria are just some of the implicated mechanisms.[18,19]

In a study by Jury et al[7] of 25 children with atopic dermatitis, 68% of children achieved minimal residual disease after treatment with NBUVB. However, the severity of atopic dermatitis and length of remission were not discussed. In a retrospective review of children with severe eczema, 40% of children who had at least 10 treatments with NBUVB achieved complete clearance or minimal residual activity of their atopic dermatitis.[18] Good or moderate improvement was achieved in another 49% of children in the study. Phototherapy was well tolerated, and median remission was 3 months long. Of note, children in this study continued to use emollients and topical steroids, which reduced the potency of medication throughout the NBUVB treatment course. This is akin to real clinical practice, where patients will likely be using a combination of phototherapy and topicals. Additionally, children in this study with higher minimal erythema doses (MEDs) greater than 390 mJ/cm^2 were more likely to achieve clearance compared with those with lower MEDs. The authors suggested that perhaps children with greater MEDs experienced less erythema, which could lead to worsening of atopic dermatitis and postponement of NBUVB treatments. The most common adverse event was erythema, which was usually transient. NBUVB can thus be considered a useful adjunct in managing atopic dermatitis, with as few as 10 treatment sessions required to observe an effect.

Cutaneous microbiota has been examined in both control and atopic dermatitis patients who underwent treatment with NBUVB phototherapy.[19] After phototherapy, cutaneous staphylococcal microbial levels are decreased in atopic dermatitis patients. In fact, after phototherapy the microbial population in atopic dermatitis patients is similar to control patients. Thus, NBUVB phototherapy can reduce skin surface bacteria and suppress superantigen production from *Staphylococcus aureus* in children with atopic dermatitis. However, it is unclear whether this reduction in skin surface bacteria translates clinically into reduced skin infections requiring antibiotics or decreased pruritus.

BBUVB

BBUVB light (280-320 nm) may be a useful treatment for pediatric psoriasis, pityriasis lichenoides chronica, pruritus, and atopic dermatitis. In a study of pediatric psoriasis patients ranging from 5 to 17 years of age, UVB phototherapy was used to treat 30 patients with guttate and/or plaque psoriasis.[9] Response, defined as greater than 75% improvement in psoriasis was achieved in 93% of patients after less than 20 BBUVB treatments.

BBUVB was also used to treat 12 pediatric patients (mean age 10 years) with diffuse, central or peripheral lesions of pityriasis lichenoides chronica.[9] The average duration of treatment was 3.7 months, or approximately 18 treatments. More than 80% of patients responded to treatment with >75% improvement in their lesions. In another study, BBUVB was used to treat 8 pediatric patients with pityriasis lichenoides chronica, of whom 7 patients completely or almost cleared after a median of 18 treatments.[14] However, one half of the patients subsequently relapsed within 3 months. BBUVB represents a useful treatment tool for children with pityriasis lichenoides, but repeat treatment periods may be necessary because of the chronic and relapsing nature of this disease.

For many conditions, including plaque and guttate psoriasis, NBUVB is replacing BBUVB as the first-line therapeutic option. Coven et al[1] have demonstrated that NBUVB leads to more rapid clearance of psoriatic plaques in fewer treatment sessions compared with BBUVB. Additionally, a systematic review by Gambichler et al[20] concluded that NBUVB should be considered the first-line phototherapeutic option for moderate-to-severe atopic dermatitis on the basis of efficacy, cost, and risk-benefit profile. However, for a small proportion of patients with atopic dermatitis, NBUVB can actually be more irritating and less effective compared with BBUVB. NBUVB requires 5- to 10-fold greater doses than BBUVB to achieve minimal erythema, requiring greater doses to induce lymphocyte apoptosis.[21,22] It may be possible that the greater doses needed when using NBUVB phototherapy result in burning or cutaneous sensitivity for some patients (who may

not experience the same irritation with the lower doses used from BBUVB light). BBUVB is not only efficacious for the treatment of both psoriasis and mild to moderate atopic eczema, but can also be less irritating for patients. Thus, BBUVB phototherapy may still represent a valuable treatment choice for a pediatric patient who cannot tolerate or does not achieve adequate clinical response to NBUVB.

PUVA Photochemotherapy

Photochemotherapy (ie, PUVA) is a treatment modality used with either oral or topical psoralen, a photosensitizing agent that enhances the efficacy of UVA light (320-400 nm). PUVA with oral psoralen is generally not preferred in children younger than 12 years of age because of the potential side effects, including nausea, vomiting, cataracts and ocular toxicity, and phototoxic reactions. The major disadvantage of PUVA is the risk of cutaneous carcinogenesis. The increased risk of squamous cell carcinoma in white patients treated with PUVA is well documented.[23] However, it is important to note that PUVA is still a useful therapeutic modality for plaque psoriasis, vitiligo, and MF, among other conditions. It is generally more effective than UVB phototherapy in treating thicker, indurated lesions of hand and foot psoriasis and hand and foot eczema, because UVA wavelengths penetrate deeper compared with UVB wavelengths. Furthermore, when choosing a particular phototherapy, PUVA might be considered in the nonwhite pediatric population, as the increased lifetime risk of skin cancer has been demonstrated only in fair-skinned Caucasian patients.

Psoriasis

Although NBUVB is still the recommended first-line phototherapeutic modality, PUVA can be a treatment option for pediatric patients with psoriasis. In 1 study, PUVA was used to treat 7 patients with guttate and/or plaque-type psoriasis.[9] Patients were selected for treatment with PUVA if they were older children (>12 years) or if their psoriatic plaques were resistant to both NBUVB and BBUVB phototherapy. Greater than 75% improvement in psoriasis was achieved in 83% of patients with an average of 28 PUVA treatments required.

Vitiligo

PUVA is an efficacious treatment modality for pediatric vitiligo and the psoralen can be delivered orally to children greater than 12 years or topically to children of any age. Eight patients with either localized or generalized vitiligo were treated with PUVA. Response was defined as >50% repigmentation and was achieved in greater than half (57%) of patients. The median number of necessary treatments was 25.[9] In young patients, a trial of PUVA for 2 to 3 months can be used to assess response.

Mycosis Fungoides

Although data in the pediatric population remains limited, PUVA can also be a treatment option for MF. In a 15-year-old patient with MF, PUVA treatment resulted in greater than 75% improvement after 30 treatment sessions.[9] The patient was given long-term maintenance therapy to prevent relapse. The patient received more than 300 PUVA treatments and was initially cleared of disease but relapsed 6 years later.

Alopecia Areata

PUVA has demonstrated only limited efficacy for pediatric patients with alopecia areata.[9] In 10 patients with alopecia areata, alopecia totalis, or alopecia universalis, only 2 patients responded with complete hair growth after an average of 56 PUVA sessions. However, Whitmont and Cooper[24] showed more promising results with 53% of alopecia totalis patients achieving complete hair regrowth.

Although practicing clinicians may be hesitant to use PUVA in the pediatric age group because of potential side effects and long-term increased risk of cutaneous carcinogenicity, it is important to remember that PUVA can be used for a large variety of skin conditions, including those discussed previously as well as palmoplantar pustulosis, morphea, cutaneous graft-versus-host disease, urticaria, pityriasis rosea, dyshidrotic eczema, histiocytosis, dermatitis herpetiformis, urticaria pigmentosa, lichen planus, mastocytosis, and granuloma annulare. Careful patient selection and individual consideration of risks versus benefits of the therapy will ensure safe and effective use of this modality.

Excimer Laser Targeted Phototherapy

The excimer laser is a 308-nm xenon-chloride monochromatic UVB light that can be used to treat localized lesions of atopic dermatitis, psoriasis and vitiligo in children. The excimer laser has shown to be safe and efficient in adults with localized plaque psoriasis, vitiligo, and early-stage MF.[25] Excimer laser therapy has been studied in adults, but the full range of potential uses of this medium in children has yet to be examined. The 308-nm laser offers an advantage in that a greater level of UVB radiation can be used to target lesional skin and spare unaffected skin, resulting in faster clearance after fewer treatments compared with traditional NBUVB or BBUVB phototherapy.[26]

In one study, 6 children with localized lesions of atopic dermatitis were treated with weekly sessions of excimer laser therapy.[27] Patients received between 6 and 12 treatments depending on skin type and treatment response. The initial dose ranged up to 1 MED and treatment was repeated weekly, with increased dosage depending on phototype and reduction in size or erythema of the skin lesion. Notably, this limited dose of 1 MED was likely used because atopic dermatitis was being treated; however, much greater doses, up to 16 MEDs have been used in the treatment of plaque psoriasis.[26] After treatment, 66% of patients achieved complete remission and another 16% achieved partial remission of atopic dermatitis lesions. Nearly one half of patients maintained their results at the 16-week follow-up visit.

In the treatment of psoriasis, this xenon-chloride laser delivers greater doses of UVB light to psoriatic plaques resulting

in a more rapid treatment response. In one study, 4 children had localized psoriatic plaques treated, resulting in a significant decrease in psoriasis severity scores.[28] Side effects were limited to blistering and hyperpigmentation. As opposed to traditional NBUVB phototherapy, which requires extensive exposure of uninvolved skin and an average of 20 to 30 treatments for significant improvement of psoriasis, the excimer laser can achieve similar endpoints to NBUVB phototherapy in approximately 10 treatment sessions without exposure of noninvolved skin to UVB irradiation.

Discussion

Multiple treatment options exist for photoresponsive diseases in the pediatric population, including both BBUVB and NBUVB, PUVA, and monochromatic excimer laser. It is important to avoid exposing children to the potential short- and long-term risks of prebiologic and biological systemic agents, including malignancy, infection, renal toxicity, hepatotoxicity, bone marrow suppression, and others. The systemic safety profile of phototherapeutic modalities makes them a preferred treatment option for children who require treatment beyond a topical regimen. Short-term side effects from all types of phototherapy can include burning, erythema, xerosis, and pruritus, which are usually transient, mild, and well-tolerated. The adverse effect that is of concern to most practicing dermatologists is the long-term increased potential risk of carcinogenesis, discussed later in this section.[29]

PUVA Photochemotherapy

There is an association of nonmelanoma skin cancers with PUVA treatment in adults.[30,31] The risk of squamous cell carcinoma is significantly increased in the white population for patients who receive more than 200 PUVA treatments.[23] However, so far there is no convincing evidence for an increased risk of skin cancer in nonwhite populations, such as Asian or Arabian–African populations, after long-term PUVA therapy.[32] Because the use of PUVA in children has remained somewhat limited, further data are needed to address the long-term risk of carcinogenesis in the pediatric population. However, clinicians considering PUVA phototherapy should be aware of the skin cancer risk in white patients. Thus, clinicians should pay careful attention to the pediatric patient's skin type or ethnic background; for instance, PUVA may be a more reasonable consideration for a dark-skinned child compared with a child with Fitzpatrick skin type I or II. Furthermore, such fairer skin types may potentially burn more easily.

In children younger than 12 years of age, oral PUVA is generally restricted to phototherapy centers where well-trained, experienced physicians and nurses are present. Some dermatologists consider oral psoralen to be relatively contraindicated in this age group and would first consider topical PUVA treatment. This is because the use of the photosensitizing agent psoralen may cause side effects, including nausea, cataracts, phototoxic reactions, hepatotoxicity, and headaches. Additionally, this generalized photosensitization requires 24 hours of photoprotection. Some children may have practical difficulty in avoiding sunlight after ingestion of psoralen. For instance, during school recess breaks children may be exposed to sunlight or could potentially be stigmatized by having to stay indoors alone. Bath PUVA may also be difficult in a pediatric population because it is time-consuming. In centers where oral PUVA is administered, psoralen is generally limited to children who weigh more than 100 lbs and is generally given 60 to 90 minutes before UVA exposure.[33] Additionally, it is best if children are given the final appointments of the day to provide a window of safety after UVA irradiation as the sun will be down sooner, therefore reducing the risk of inadvertent additional sunlight exposure.

UVB Phototherapy

A retrospective study of psoriasis patients who received UVB phototherapy from 1994 through 2000 showed no evidence for an increased risk of skin cancer associated with either NBUVB or BBUVB.[34] There was also no increase in skin cancer noted in a study of more than 4600 patients treated with NBUVB phototherapy between 1985 and 2002.[35] Clinicians may be concerned about a possible increased skin cancer risk secondary to repeated treatment courses and prolonged life expectancy in children. However, the use of phototherapy in the pediatric population has remained limited and studies are lacking which examine the long-term risk of phototherapy in children; therefore further data are needed in this population to address precisely the long-term risks.

NBUVB can be used to treat many photoresponsive dermatoses in children, across skin types I to V. Dosing can be established on the basis of a predetermined MED, or more commonly is determined on the basis of a standard protocol with Fitzpatrick skin type. Dosage increases are based on the protocol and also adjusted based on the patient's clinical response.[36]

For diseases, including psoriasis and vitiligo, it would be advisable to use NBUVB as a first-line phototherapeutic agent because of the potential short- and long-term toxicities of PUVA photochemotherapy. Additionally, when prescribing NBUVB for children with psoriasis, clinicians should also be aware that plaque psoriasis may require more phototherapy treatments to clear compared with guttate psoriasis. It is not clear why, but perhaps the more indurated psoriatic plaques require more UVB irradiation compared with thinner, less scaly guttate plaques.

Excimer Laser Targeted Phototherapy

Studies in which researchers used excimer laser in children with atopic dermatitis and psoriasis have thus far been limited to patients with Fitzpatrick skin types II and III; the authors cannot comment on whether this is a safe and efficacious treatment in children with skin types I or IV-VI. Side effects of excimer laser treatment include erythema, pruritus, vesiculation and edema, and hyperpigmentation. Localized blistering and erythema can be treated with potent topical corticosteroids. Although the optimal dosimetry and treatment protocol should be further defined in children, the

excimer laser is a novel treatment tool that can be used for localized atopic dermatitis lesions and psoriatic plaques in children. It can be used in conjunction with topical corticosteroids. With such machines becoming even more powerful soon, it may actually become feasible for the monochromatic excimer laser to be used in the treatment of generalized psoriasis and atopic dermatitis.

Conclusions

Phototherapy, including UVB, PUVA, and excimer laser treatment, should be considered as preferred treatment options for pediatric patients with photoresponsive dermatoses who require more than topical agents to control their disease. These phototherapeutic modalities can be used in conjunction with topical preparations, such as emollients, corticosteroids, vitamin D analogues, coal tar, and others. It is also important to consider the ethnicity and skin type of the patient because the potential risk of cutaneous carcinogenesis, which is perhaps the most concerning risk of phototherapy, varies tremendously between patients of different ethnic backgrounds and skin types. Finally, another important consideration when choosing a phototherapeutic regimen for pediatric patients is to select a phototherapy unit where physicians and nurses are very comfortable and experienced in managing children.

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