

Protocol of Kasr Al-Ainy's phototherapy unit – Cairo University for the management of photoresponsive skin diseases – part 1: general protocol

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Received: 23 October 2021

Revised: 4 February 2022

Accepted: 9 February 2022

Published: 1 September 2022

Journal of the Egyptian Women's Dermatologic Society 2022, 19:145–151

One of the most commonly used and effective lines of treatment in chronic skin diseases is phototherapy. A protocol of the Kasr Al-Ainy Phototherapy Unit has been proposed for the treatment of different dermatological diseases such as psoriasis, mycosis fungoides, and vitiligo based on the best current research-based guidelines and the experience of the phototherapy team. This protocol is the cornerstone of the everyday practice in Kasr Al-Ainy Phototherapy Unit and we believe dermatologists dealing with such diseases in their hospitals or clinics, can find it helpful and applicable to get better results with their patients. In part 1, the general measures of the protocol will be discussed.

Keywords:

excimer, minimal erythema dose, minimal phototoxic dose, NB-UVB, phototherapy, protocol, PUVA, skin diseases, management

J Egypt Women's Dermatol Soc 19:145–151

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1687-1537

Introduction

Kasr Al-Ainy's phototherapy unit is one of the premier phototherapy units founded in Egypt in 1990. The unit includes four (ultraviolet A) UVA devices, five (narrowband ultraviolet B) NB-UVB devices, one (broadband ultraviolet B) BB-UVB device, two hands-and-feet UVA devices, one scalp UVA device, and one excimer-light device, as well as targeted NB-UVB and targeted UVA1 devices. The unit works 6 days/week with six daily working hours. The number of patients attending the unit includes nearly 150 patients/day. The unit served around 7000 patients since it was founded till now and it receives 300–350 new admissions/year. The total number of patients receiving sessions include ~150 vitiligo, ~40 psoriasis, ~80 mycosis fungoides (MF) patients, and ~35 patients with other dermatoses.

Protocol for phototherapy and photochemotherapy (by consensus).

Steps of patients admission and discharge in the phototherapy unit are shown in Table 1.

General protocol

Patients

- (1) Age of patient: more than or equal to 12 years for oral psoralen therapy. NB-UVB and topical

(psoralen plus ultraviolet A) PUVA may be used for younger age (≥ 6 years where children are able to reliably stand in the booth with either their eyes closed or wearing goggles).

- (2) Extent of disease: more than 10% of body-surface area (according to the rule of nine) [1], except in MF, any extent for cabinet devices [2], palmoplantar affection alone for the hands-and-feet devices, as well as localized skin affection for targeted devices and excimer light.
- (3) Tapering of steroids: both oral and potent topical steroids in psoriatic patients already taking steroids (except for topical steroids in palmoplantar lesions); use weaker steroids and taper gradually till they are stopped (possible rebound), tapering can go hand-in-hand with the start of phototherapy.
- (4) Face: cover with a sunscreen (e.g. zinc oxide) if free. While, if few lesions are present, give 25% of the total body dose (maximum dose is 1 J/cm^2) [1].
- (5) Extremities: could be given an extra dose.
- (6) Advise patients to use emollients after and in-between the sessions to avoid dryness of the skin (not before the session).

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Table 1 Steps of patients' admission and discharge in the phototherapy unit

Steps	Mission
1	Deciding if the patient is a candidate for phototherapy by examination, and explaining regulations with patients, until they understand the system with proper history taking
2	Determining the appropriate line of therapy, either: A – phototherapy as monotherapy B – phototherapy as combination therapy
3	Ordering investigations for the patient and ophthalmology examination
4	Writing a sheet, and determining the days and time of receiving the sessions
5	If the patient is retreated, add previous cumulative dose
6	At sessions, patients are to be properly examined, evaluated, dose adjusted, side effects noted, and all remarks written in the phototherapy follow-up sheet
7	Cumulative dose must be recorded clearly both in computer file and on patients' sheet, whether as final response or on total discharge from the unit

(7) Oral psoralen: 0.5–0.7 mg/kg bodyweight of 8-methoxypsoralen or 0.3–0.5 mg/kg of oxypsoralen as a single dose taken 1½–2 h before irradiation. It is ingested immediately after a nonfatty meal.

(8) Topical psoralen (where ultrameladinine paint is applied to the skin):

(a) They are used in the following occasions:

- (1) When systemic psoralens are contraindicated.
- (2) Children less than 10 years [3].
- (3) Localized palmoplantar pustulosis [4] (if the cause is any disease other than pustular psoriasis).
- (4) Localized lesions of vitiligo or psoriasis.
- (5) Resistant patches of psoriasis or MF; topical psoralen is combined with systemic psoralens (that are used for at least 2 weeks before topical application of psoralen).
- (6) Alopecia areata.

(b) Types of preparations:

- (1) Oil of bergamot 25% in alcohol and Khellin 2% for face lesions.
- (2) Ultrameladinine paint 0.03% (8-methoxypsoralen) or meladinine paint 0.1%:
 - (1) Liquid formulas can be applied in serial dilutions.
 - (2) It should be applied 15–60 min before exposure to UVA.
 - (3) Starting dose is 0.5–1 J/cm² to be increased by 0.5 J/cm² every two sessions.

(9) Protection during PUVA therapy:

(a) In unit:

- (1) Use UV-opaque goggles for the eyes.
- (2) Sunscreens or white/thick fabrics for the face.
- (3) Protect male genitalia.

(b) After the session:

- (1) Use UV-opaque goggles for the eyes for 12 h.
- (2) Proper clothing and sunscreens for the skin.

(c) In-between sessions:

- (1) Avoid excessive sun exposure to the skin.
- (2) Avoid phototoxic drugs or those that increase photosensitivity.
- (3) Liberal amount of emollients.

Unit

A sheet for every patient must be done to record the duration of exposure and number of joules, to be able to calculate the total cumulative dose.

The lamps must be calibrated every 1–3 months or 100 h of working.

Indications of phototherapy (chemotherapy) [5]

- (1) Psoriasis.
- (2) MF.
- (3) Vitiligo.
- (4) Scleroderma.
- (5) Atopic dermatitis.
- (6) Alopecia areata.
- (7) Generalized lichen planus.
- (8) Mastocytosis.
- (9) Pityriasis rosea.
- (10) Pigmented purpuric eruptions.
- (11) Pityriasis lichenoides.
- (12) Lymphomatoid papulosis.
- (13) Pityriasis rubra pilaris.
- (14) Generalized pityriasis alba and post-pityriasis versicolor.
- (15) Palmoplantar vesiculopustular eruptions.
- (16) Lichen sclerosus et atrophicus.
- (17) Renal, hepatic, senile, and nonspecific pruritus.
- (18) Progressive macular hypomelanosis (previously known as acromia parasitica).

Indications of excimer light/laser

- (1) Vitiligo: excimer laser/light is of special value in localized vitiligo, requiring fewer number of sessions as compared with NB-UVB [6]. However, it lacks systemic stabilizing effect of NB-UVB [7].

- (2) Psoriasis: targeted excimer sessions for localized and resistant plaques have proven efficacy where dose can be adjusted according to thickness of each plaque and individual minimal erythema dose (MED) [8].
- (3) Other indications: excimer sessions have been suggested as a potential therapeutic modality in localized lesions of a number of dermatoses, for example, alopecia areata, atopic dermatitis, MF (early localized lesions), scleroderma, genital lichen sclerosis, prurigo nodularis, granuloma annulare, pityriasis alba, and palmoplantar pustulosis [9].

Contraindications of phototherapy (chemotherapy) [5]

Absolute

- (1) Pregnant and lactating females (phototherapy only is allowed).
- (2) Xeroderma pigmentosa, LE, or other photosensitive dermatoses, dermatomyositis.
- (3) History of skin cancer other than MF.
- (4) Previous radiograph treatment (for other malignancies, except MF).
- (5) Epilepsy.

Relative (weighing benefits vs. side effects)

- (1) Pemphigus and pemphigoid.
- (2) Immunosuppression (concomitant use of methotrexate and cyclosporine in PUVA therapy).
- (3) Renal and hepatic failure.
- (4) Myocardial disease or other chronic conditions.
- (5) Cataract and aphakia in PUVA therapy.
- (6) Claustrophobia.
- (7) High cumulative doses:
 - (a) PUVA: more than 1000–2000J, or 200–250 sessions.
 - (b) NB-UVB: more than 500 sessions for type I–III skin phototypes.

Investigations

- (1) For all patients:
 - (a) (Complete blood count) CBC.
 - (b) Liver-function tests.
 - (c) Urea and creatinine.
 - (d) (Antinuclear antibody) ANA for suspicious patients.
 - (e) Fasting and 2-h postprandial blood sugar.
 - (f) A skin biopsy once before admission.
- (2) Photography of patients:

Each patient should have a photograph once at admission and once at discharge.

Ways of administration of phototherapy (by consensus)

Monotherapy

- (1) Advantages:
 - (a) Lower cost.
 - (b) Better compliance.
- (2) Disadvantages:
 - (a) Loss or limited efficacy.
 - (b) Side effects:
 - (1) Cumulative toxicity.
 - (2) Presence of resistant lesions.

Combination therapy

- (1) A safe and effective approach
- (2) Preferred in almost all patients.
- (3) It is the use of two or more agents with synergistic or complementary action concomitantly, which produces:
 - (a) Lower dose for each treatment line.
 - (b) Toxicity-sparing regimens for each of the agents.

When to switch to combination therapy?

- (1) If monotherapy is not or no longer effective.
- (2) To reduce cumulative and/or acute toxicity.
- (3) To reduce side effects.
- (4) To improve therapeutic outcome (less time, more efficacy).
- (5) Increased possibility of tailoring therapy to individual needs.

Common problems during therapy and their management

- (1) Gastric irritation or vomiting:
 - (a) Psoralen could be taken immediately after eating a nonfatty meal.
 - (b) Divide the dose with half an hour between the two doses (the patient should attend the session 90–120 min after the last dose) [5].
 - (c) Use an anti-emetic half an hour before eating.
 - (d) If all the above failed, calculate the dose as 0.5 mg/kg (in case of meladinine tablets or shift to meladinine capsules that are less-gastric irritants).
- (2) Itching [5]:
 - (a) It may be due to the disease itself, for example, MF or psoriasis (itching was there before starting therapy and is expected to improve with treatment) or

related to phototherapy (starts 24–48 h after the session).

- (1) If the skin is dry, make sure the patient is using emollients, if not, give liberal amounts.
 - (2) If no response to emollients, reduce the UV dose.
 - (3) If there is no response, give antihistamines and stop UV for few sessions.
 - (4) Omit any source of irritation.
 - (5) Stop diuretics if used, for example, for erythrodermic or pustular psoriasis (after initial control of the disease).
 - (6) If itching persists and becomes intractable in spite of the above measures, stop UV therapy totally.
- (3) Severe phototoxic reactions (marked erythema, edema, vesicles, or bullae):
- (a) Stop UVR until erythema subsides.
 - (b) Give cold compresses, rest, and antibiotics in case of blister formation due to UVA burn (manage as a burn in extensive lesions).
 - (c) Give acetyl-salicylic acid (aspirin twice daily) or any other NSAIDs.
 - (d) Topical or systemic steroids may be used.
 - (e) On resuming UVR, start with half the previous dose or the last dose before burning [10].
- (4) Thickening of the skin (especially in vitiligo):
- (a) Stop PUVA for 2–4 weeks with intralesional steroids or steroids under occlusion on the thickened skin.
 - (b) If only few patches, apply steroids under occlusion, cover during sessions, and continue sessions on the rest of the lesions.
 - (c) Proper increment from the start may decrease this problem.
- (5) Increased tanning of normal skin:
- (a) Reassure the patient that the tan will disappear spontaneously after stoppage of therapy.
 - (b) A sunscreen may be used to protect the sun-exposed normal skin (except in MF) [11].
- (6) Appearance of new lesions:
- (a) Continue therapy if they present disease progression and look for the criteria of response.
 - (b) Notice if the lesions represent Koebner's phenomenon, which might be due to itching or a phototoxic reaction, manage accordingly.

Important tasks that should be done in each phototherapy unit (by consensus)

- (1) Prepare patients' paper work if eligible for phototherapy:

- (a) Full laboratory investigations.
 - (b) Refer to the ophthalmology clinic for slit-lamp examination (once at admission).
- (2) If the patient is eligible for PUVA:
- (a) Calculate the dose of psoralen.
 - (b) Inform the patient about precautions.
 - (c) Sunglasses.
 - (d) Cover genitalia during sessions.
 - (e) Contraception.
- (3) Give out the instruction sheet attached to patient's card.
- (4) Examine the patients every session and increase the dose every two sessions for PUVA and every session for NB-UVB (according to the degree of erythema), until there is mild persistent erythema, then fix the dose (Tables 2 and 3).
- (a) Write any observation in the sheet.
 - (b) Check dropouts/month.

Phototherapy protocol [13]

- (1) Prior to phototherapy, the individual UV sensitivity of the patient should be evaluated. This is done by measuring the MED and Fitzpatrick skin-type dosing as shown in Table 3.
- (2) The initial dose lies at 75–100% of MED for NB-UVB and 30–50% MED for BB-UVB.
- (3) Treatments are given two to five times weekly.
- (4) As UVB erythema appears before 24 h, increments may be done at each session.
- (5) The aim of dose increments is to maintain a minimal erythema as a clinical indicator of optimal dosimetry.

Table 2 Minimal phototoxic dose

J/cm ²	Skin type
1–8	I
2–16	II–IV
10–24	V–VI

Table 3 Dose of UVA for induction phase (skin-type dependent) [12]

Maximum dose	Increments	Initial dose (J/cm ²)	History	Skin type
5	0.5	1.5	Always burn, never tan	I
8	0.5	2.5	Always burn, sometimes tan	II
12	0.5–1	3.5	Sometimes burn, always tan	III
14	1.0	4.5	Never burn, always tan	IV
16	1.0	5.5	Brown skin	V
20	1.0–1.5	6.5	Black skin	VI

- (6) Regarding NB-UVB, the rate of increase depends on treatment frequency, effect of preceding exposure.

For example,

No erythema: increase the next dose by 10–20%.

Pink asymptomatic erythema: hold at current dose, until erythema disappears, then increase by 10–20%.

Bright-red asymptomatic erythema: stop phototherapy until the affected areas become light pink, then resume at the last tolerated dose.

Symptomatic erythema (includes pain and blistering): stop phototherapy until the skin heals and erythema fades to a light pink, then resume at the last tolerated dose.

- (1) Treatment is given, until total remission is reached, few residual lesions or no further improvement can be obtained with continued treatment.
- (2) Some regimens use skin-type-dependent starting doses and fixed increments.
- (3) Dose adjustment following missed doses:

4–7 days between treatments: hold the dose constant.

8–14 days between treatments: decrease the dose by 25%.

15–21 days between treatments: decrease the dose by 50%.

Over 3 weeks between treatments: restart at the initial dose.

Some tests used in the unit

Procedure for determination of the minimal erythema dose for NB-UVB and BB-UVB [13].

Although measuring the MED is the most accurate way to determine the starting dose, it is not used now by most phototherapy centers.

- (1) Prior to the initiation of phototherapy treatments, the patient will be asked to attend the treatment center for two consecutive days.
- (2) The area to be tested is to be a sun-protected region on the hip or buttocks.
- (3) Other areas of the skin must be covered with layers of cloth over clothing or UV-protective material.

- (4) The parts to be irradiated should be uniform in size and at least 2 cm².
- (5) Specific garments for MED determinations with six or more exposure parts should be used for the phototesting.
- (6) A lateral ink mark or some other type of identification should identify the location of each tested area.
- (7) The dose for each part for routine UVB (NB-UVB and BB-UVB) phototesting is dependent on the skin type of the patient to be tested. The two dosage schedules [13] are shown in Table 4.
- (8) The patient has to wear eye protection during the delivery of the UV doses for the MED testing.
- (9) The dose delivery can best be done by beginning with all of the parts open for UV testing followed by closing the individual parts after a specific dose of UV light has been delivered.
- (10) At the completion of the phototesting, the special garments used in the testing should be removed and the areas rechecked to make sure adequate marking of the skin has been done to identify the actual ports tested.
- (11) The patient will be instructed not to receive any natural or artificial UV light to this region of the skin during the next 24 h.
- (12) The patient has to return to the phototherapy center after 24 h.
- (13) The area of the phototesting should be identified by the markings at the different dosage sites.

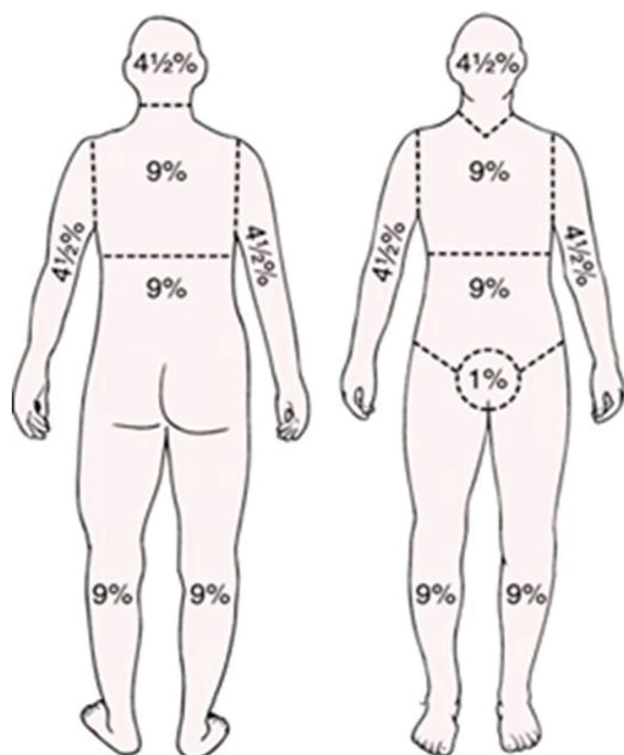
Positive reading is considered as identifiable faint erythema within the margins of the phototesting port
Rule of nines

- (1) A method of estimating the extent of burn or disease, expressed as a percentage of total body surface. In this method, the body is divided into sections of 9% or multiples of 9% each (Fig. 1):
- (2) Head and neck 9%.
- (3) Anterior trunk 18%.

Table 4 The dosage schedules of NB-UVB and BB-UVB according to skin phototype

NB-UVB		BB-UVB	
Skin type I–III	Skin type IV–V	Skin type I–III	Skin type IV–V
200 mJ/cm ²	400 mJ/cm ²	20 mJ/cm ²	60 mJ/cm ²
400 mJ/cm ²	600 mJ/cm ²	30 mJ/cm ²	70 mJ/cm ²
600 mJ/cm ²	800 mJ/cm ²	40 mJ/cm ²	80 mJ/cm ²
800 mJ/cm ²	1000 mJ/cm ²	50 mJ/cm ²	90 mJ/cm ²
1000 mJ/cm ²	1200 mJ/cm ²	60 mJ/cm ²	100 mJ/cm ²
1200 mJ/cm ²	1400 mJ/cm ²	80 mJ/cm ²	120 mJ/cm ²

Figure 1



Rule of nines.

- (4) Posterior trunk 18%.
- (5) Lower limbs 36%.
- (6) Genitals and perineum 1% [14].
- (7) The rule of nines [15] is fairly accurate for adults, but does not allow for differences in proportion in children. In Lurid–Browder classification [16], the percentages assigned to areas affected by growth are adjusted by age. The head decreases in relative size from infancy to adulthood, while the thigh and leg increase (Table 5) [14].

Photochemotherapy protocols

- (1) Two therapeutic concepts were used: the American and the European. Both are highly effective [12,17,18]. They are shown in Table 6. We use the American system in PUVA.

Minimal phototoxic dose

It is done by exposing eight, one-inch squares on the back to increasing doses of irradiation 1–2 h after ingestion of psoralen. Reading occurs 48–72 h later [19] (Table 2).

Dose of UVA for induction phase (skin-type dependent) [12,20] is shown in Table 3.

Table 5 The rule of nines [14,15]

Area	1 year	1–4 years	5–9 years	10–14 years	15 years	Adult
Head	19	17	13	11	9	7
Neck	2	2	2	2	2	2
Anterior trunk	13	13	13	13	13	18
Posterior trunk	13	13	13	13	13	13
R. buttock	2.5	2.5	2.5	2.5	2.5	2.5
L. buttock	2.5	2.5	2.5	2.5	2.5	2.5
Genitalia	1	1	1	1	1	1
R. U. arm	4	4	4	4	4	4
L. U. arm	4	4	4	4	4	4
R. L. arm	3	3	3	3	3	3
L. L. arm	3	3	3	3	3	3
R. hand	2.5	2.5	2.5	2.5	2.5	2
L. hand	2.5	2.5	2.5	2.5	2.5	2
R. thigh	5.5	6.5	8	8.5	9	9
L. thigh	5.5	6.5	8	8.5	9	9
R. leg	5	5	5.5	6	6.5	6
L. leg	5	5	5.5	6	6.5	6
R. foot	3.5	3.5	3.5	3.5	3.5	3
L. foot	3.5	3.5	3.5	3.5	3.5	3

Table 6 The American and the European photochemotherapy therapeutic concepts [12,17,18]

	European system	United States system
Starting dose	70–1 MPD	Skin-type dependent
Treatment/week	4	2–3
UVA dose increment	Individualized	Fixed

MPD, minimal phototoxic dose.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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