Protocol of Kasr Al-Ainy's Phototherapy Unit-Cairo University for the management of photo-responsive skin diseases-part 2: protocol of phototherapeutic management of diseases

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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 the authors believe that 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 2, the specific measures of the protocol for phototherapeutic management of different skin diseases will be discussed.

Keywords:
alopecia areata, management, mycosis fungoides, phototherapy, pityriasis lichenoides chronica, protocol, pruritus, psoriasis, scleroderma, vitiligo

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Introduction

The specific measures of the Kasr Al-Ainy Phototherapy Unit protocol for phototherapeutic management of different skin diseases will be discussed as follows.

Protocol of phototherapeutic management of diseases

Protocol for vitiligo

Combination of phototherapy with other therapeutic measures is the rule.

Phototherapy

(1) **Narrow-band ultraviolet light B (NB-UVB) (311 nm):**
When it comes to repigmentation of vitiligo, NB-UVB stands as the main tool in this regards [1]; hence, it is used constantly in combination with all other therapeutic measures.
Phototherapy recommendations modified from The Vitiligo Working Group phototherapy recommendations [2]:
   (a) **Frequency of administration:**
   Optimal: 3 times per week.
   Acceptable: 2 times per week.
   (b) **Fixed dosing based on skin phototype (SPT):**
   Initiate dose at 500 mJ/cm2 for SPTs III–V, 300 mJ/cm2 for SPTs I and II [2].
   (c) **Maximum acceptable dose:**
   Face: 2500 mJ/cm2.
   Body: 5000 mJ/cm2.
   (d) **Non-photoadapted:**
   Use nonsteroidal anti-inflammatory drugs (ibuprofen 400 mg) before session [3].
   (e) **Maximum number of exposures:** 500 for type I–III and unlimited for darker [4].
   (f) **Course of NB-UVB:**
   Assess treatment response after 18–36 exposures.
   Minimum number of doses needed to determine lack of response: 48 exposures [2].

Because of the existence of slow responders, 70 exposures may be needed to determine lack of response to phototherapy.

(g) **Dose adjustment based on degree of erythema:**
No erythema: increase 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 affected areas become light pink, then resume at 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 last tolerated dose.

(h) **Device calibration or bulb replacement:**
Device calibration is done every 1–3 months or 100 working hours and the dose is readjusted according to the manufacturer attached sheet.

(i) **Outcome measures to evaluate response:**
Serial photography to establish baseline severity, disease stability, and response to treatment. Validated scoring systems, such as vitiligo area severity index (VASI) or vitiligo extent score (VES)-plus, to quantify degree of response.

(j) **Posttreatment recommendations:**
Application of sunscreen and avoidance of sunlight.

(k) **Topical products before phototherapy:**
Avoid all topical products for 4 h except mineral oil.
Mineral oil can be used to enhance light penetration in areas of dry, thickened skin, such as the elbows and knees.

(l) **Tapering NB-UVB after successful repigmentation (>80) has been achieved [5]:**
First month: phototherapy twice weekly.
Second month: phototherapy once weekly.
Third and fourth months: phototherapy every other week.
After 4 months: discontinue phototherapy [2].

(m) **Follow-up:**
SPTs I–III: yearly follow-up for total body skin examination to monitor for adverse effects of phototherapy, including cutaneous malignancy.
SPTs IV–VI: no need to return for safety monitoring as no reports of malignancy exist with this group.
All patients: return upon relapse for treatment.

(n) **Minimum age for NB-UVB in children:**
Minimum age is when children are able to reliably stand in the booth with either their eyes closed or wearing goggles.
Typically around 7–10 years of age depending on the child.

(o) **Eyelid lesions:**
Keep eyes closed during treatment.

(p) **Sites of special importance:**
Cover face during phototherapy if uninvolved.
Shield male genitalia.
Protect female areola with sunscreen prior to treatment, especially in SPTs I–III.
Acral lesions may require higher doses or combination with topical photo-chemotherapy ultraviolet A (PUVA).

(q) **Combination treatment for stabilization:**
Oral antioxidants.
Topical treatments.
Oral minipulse corticosteroids.

(r) **Treatment of NB-UVB induced skin changes:**
Xerosis: emollient or mineral oil.
Skin thickening: topical corticosteroids or keratolytics [2].

(s) **Patient monitoring:**
Weekly: clinical assessment.
Monthly: clinical, photographing, vitiligo (VSAS) signs activity score, and vitiligo disease activity (VIDA).
Every 3 months: photography and evaluation of extent (VASI and VES) and activity (VIDA and VES).
Evaluation at session 48: stop treatment sessions if no response at all.
Evaluation at session 70: if repigmentation reaches 25% or less phototherapy is discontinued.
Phototherapy is to be continued so long there is ongoing repigmentation confirmed by photos.

(2) **Photo-chemotherapy ultraviolet A (PUVA):**

(a) Systemic PUVA:
- Oral PUVA is now considered the second-line therapy due to lower efficacy compared with NB-UVB and more long- as well as short-term side effects [2,6].

(b) Topical PUVA/PUVAsol (recommended for localized disease):
- Different topical photosensitizers including 8-methoxypsoralen (MOP) at very low concentrations starting at 0.001%, Khelin 2%, or oil of bergamot starting at 25% concentration can be applied for 30 min

followed by exposure to solar light (if machines are not available) (PUVAsol) [6,7] or UVA (Topical PUVA) [6,8].
- Topical PUVA has the advantage of being safe, with lower cumulative dose and negligible systemic side effects compared with oral PUVA [6,9]. Nevertheless, it lacks systemic stabilizing effect on active vitiligo as well as causing perilesional hyperpigmentation and more likely blistering reactions [6].
- Initial dose: sessions are started at 0.5 J/cm^2[10].
- Follow the same guidelines as NB-UVB, apart from maximum dose of up to 10 J/cm^2 per session.
  (i) Regarding PUVAsol, patients are taught about gradual increase in the duration of UV exposure and to tailor their exposure to development of faint erythema lasting ≤48 h.

(c) **Excimer light/laser** (recommended for localized disease):
- Monochromatic 308 nm high-fluence light or laser targeted devices have been developed, offering the advantage of more rapid response with fewer sessions [11,12]. However, being targeted, they lack stabilizing effect on active vitiligo and are suitable only for localized vitiligo [6]

All targeted light therapies lack the ability of stabilization of the total body unlike NB-UVB; therefore, they cannot be considered as monotherapy in active disease.

Protocol for psoriasis

Patient approach according to whether it is mild psoriasis or moderate to severe psoriasis [13]:

(1) Mild psoriasis: body surface area (BSA) of up to 10%, the Psoriasis Area and Severity Index (PASI) of up to 10, and the Dermatology Life Quality Index (DLQI) of up to 10.
(2) Moderate to severe psoriasis: BSA greater than 10% or PASI greater than 10 and DLQI greater than 10 [13].

Patients' criteria for admission to phototherapy

(1) Psoriasis vulgaris involving >10% of surface area.
(2) Guttate psoriasis.
(3) Localized pustular psoriasis of the palms and soles (topical or systemic PUVA is preferred/NB-UVB).
(4) For maintenance of pustular or erythrodermic psoriasis after being controlled by systemic medications:
  (a) Initially control these patients until partial remission using systemic medications [14].
  (b) Introduce phototherapy as a combination with the systemic drug; methotrexate or retinoid for a short period till disease control. Gradually withdraw the systemic methotrexate or retinoid.
  (c) Continue phototherapy alone.
  (d) The use of potent topical corticosteroids should be limited to a short period (by consensus):
    - 4 weeks with gradual weaning to 1–2 times/week until adequate control is obtained with phototherapy.
    - 10 Subsequently, potent topical steroids are replaced by vaseline for long-term safe control [15].

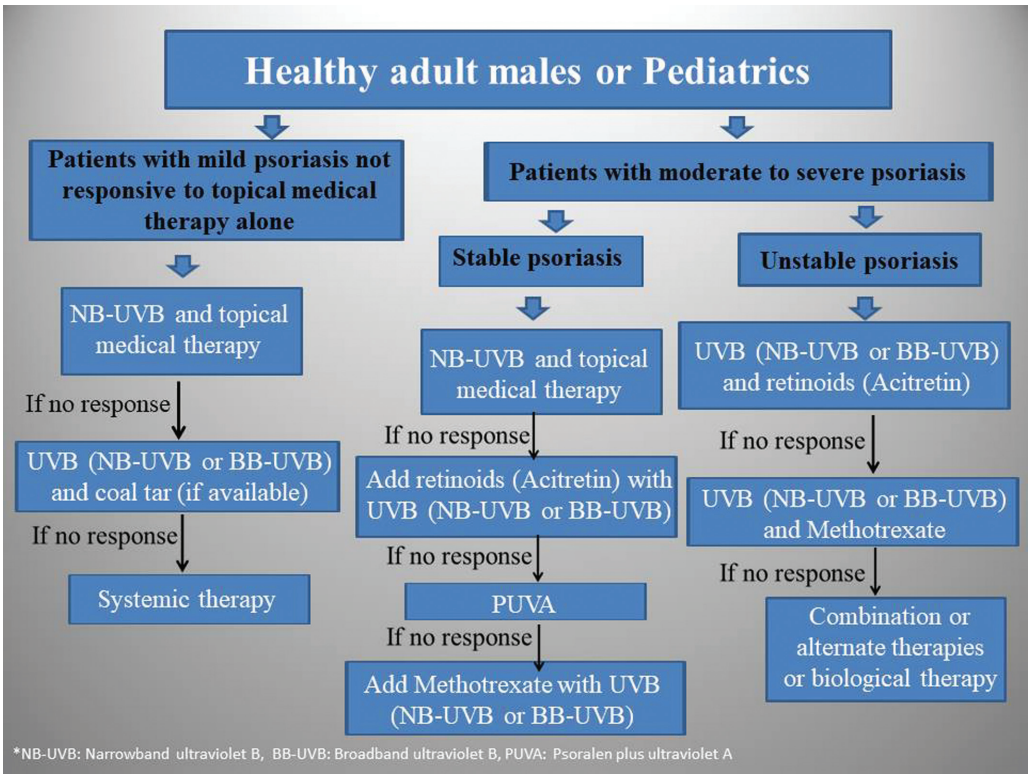
N.B.: patients with psoriatic arthritis alone are not candidate for phototherapy as a monotherapy.

Protocol according to patients' circumstances

(1) Healthy adult males or pediatrics (<18 years) with chronic plaque psoriasis:
Follow the algorithm shown in Fig. 1.
(2) Women of childbearing potential using appropriate contraception with chronic plaque psoriasis:
Same as adult males except for using isotretinoin (not acitretin as it is teratogenic potential: remains for 3 years after cessation of the drug) [16].
N.B.: in case of methotrexate (clears in 3 months) [17,18].
(3) Women trying to conceive or pregnant females with chronic plaque psoriasis, give NB-UVB (in addition to topical therapy and folate supplementation) [19]
(4) Adults with palmoplantar psoriasis (males or females not of childbearing potential)
- Topical photo/chemo/therapy
  (1) Targeted NB-UVB and Acitretin
  (2) Topical PUVA and Acitretin

(5) Approach to a patient with HCV after hepatologist consultation [20]:
Mild disease:
  (a) Topical therapy in addition to NB-UVB.
Moderate to severe disease:
  (b) Initially control these patients by systemic cyclosporine.

Figure 1



Algorithm of protocol for psoriasis management in healthy adult males or pediatrics.

(c) Gradually withdraw the drug.
(d) Introduce NB-UVB as a maintenance therapy.
(e) Continue NB-UVB alone.

Criteria of initial response to various therapies

(1) Diminished itching if present
(2) Decreased scaling.
(3) Decreased erythema.
(4) Decreased thickness of plaques or dryness of the pustules in pustular psoriasis with decreased appearance of new lesions.
(5) Disappearance of the lesions with residual hypo- or hyperpigmentation.

Rule of discharge of responding patients

Till patients reach PASI 75 (75% improvement of baseline PASI score).

Protocol of mycosis fungoides:

Main steps:

Mycosis fungoides (MF) stages IA, IB, and IIA are eligible for phototherapy/photochemotherapy:

(1) **Protocol for Stage IA:**
(a) If single or two patches, localized or well defined [21]:Targeted UVA1.If targeted UVA1 is not available, consider topical therapy such as betamethasone-17 valerate or tazarotene.
(b) For more widespread lesions but <10% BSA: monotherapy using NB-UVB, PUVA [22], or BB-UVA (20 J/cm2/session) [23] for 3 times/ week.

(2) **Protocol of Stage IB-IIA**
(a) For patches and thin plaques [22]
PUVA for all adult patients unless there is contraindication.
NB-UVB for children, for adults if hypopigmented MF or superficial MF patches if there is contraindication to PUVA therapy.
BB-UVA could be used as PUVA if there is contraindication to PUVA or intolerance to oral psoralen in adult patients where UVA is not contraindicated and if the devices are available ± combination therapy [in this order]:
– Potent topical steroids.
– Oral acitretin (10 mg for children and 25 mg for adults).
– Systemic interferon (interferon-α2a, 3 million units 3 times/week or pegylated

Interferon alpha (IFNα) once weekly by intramuscular (IM) or subcutaneous (SC) route).

(b) Thick plaques: PUVA or BB-UVA (20 J/cm^2/session) + combination therapy (the aforementioned combinations in the same order) [23].
(c) For very thick plaques, adjuvant targeted UVA1±, topical psoralen or intralesional steroids could be used.
(d) For a single tumor in the context of MF patches and plaques, localized radiotherapy, adjuvant targeted UVA1, intralesional corticosteroids or IFNα are helpful in addition to total body phototherapy for the patches and plaques.
(e) Patients beyond stage IIA are not candidate to join the phototherapy unit, should be treated by the Hemato-Oncology Unit (except between courses of chemotherapy or electron beam to reduce the tumor burden).
(f) Methotrexate should not be used for early MF except in resistant nonresponding patients having a contraindication for the use of retinoids or interferon.
(g) Very thick plaques must be biopsied to confirm that they are still plaques and have not progressed to tumor stage [24].
   – Patient monitoring [24]:
     • At session 30 (to evaluate patient's response to phototherapy/photochemotherapy):
       Biopsy is performed
     • Assessment of efficacy of initial treatment regimen in the form of:
       Decreased itching
       Decreased scaling
       Decreased lesion thickness
       Complete disappearance of lesions
       Return of normal skin color in hypopigmented MF
   – If poor response is observed in the form of:
     Lack of clinical clearance.
     Progress of thickening and induration/infiltration of existent lesions.
     Appearance of new lesions after initial improvement.
     Then:
     – Change initial treatment regimen by one more line/add adjuvant if not used from the start or
     – Change NB-UVB + adjuvant to PUVA +adjuvant
     – At session 60: biopsy
     – Biopsy every 30 sessions so long as improvement continues (no limit for number of sessions) till complete clinical clearance is observed.
     – After initial clinical clearance (with or without pathological clearance) sessions are tapered as follows [24]:

2/week	2 months
1/week	2 months
1/2 weeks	2 months
1/month	maintain

     – If lesions recur (clinical recurrence) return to 3 sessions/week

Proper stage selection and proper combination therapy from the start improve therapeutic outcome.

Protocol for generalized scleroderma [25]

(1) Baseline and final ultrasound of the skin.
(2) Start with BB-UVA 15 J/cm^2 for 10 sessions ± topical steroid and vitamin D (combined), then reassess:
   (a) If no response: increase the dose to 20 J/cm^2 for another 20 sessions.
   (b) If good response assess on session 30.
   (c) If there is ongoing improvement/if the lesions are still responding, give 10–20 more sessions.
(3) Discharge maximally after 30 sessions if no or minimal response.
   (a) Patients of acrosclerosis are treated the same way or with targeted UVA1 or with PUVA.
   (b) Topical steroids, vitamin D derivatives, and calcineurin inhibitors could be added.
   (c) Systemic steroids and/or methotrexate may be added in generalized or active rapidly progressive localized scleroderma patients from the start.

Protocol for localized scleroderma

Treated by targeted UVA or targeted UVA1.

Protocol for alopecia areata (Topical PUVA)

(1) Dermoscopically guided biopsy before sessions.
(2) Start topical PUVA for (localized {25% or resistant}, totalis, and universalis) in skin types I–IV.
(3) Use UVA scalp device (a prerequisite before starting the treatment).
(4) Patient should keep the scalp protected from light in between sessions.
(5) Ultrameladinine paint (0.1% 8-MOP solution without dilution) will be applied 15–20 min before the session.

(6) Sometimes before starting topical ultrameladinine, we can use systemic photo(chemo)therapy for 2 weeks (in patients >12 years old) to prepare the skin to topical psoralen and to avoid phototoxic reactions.

Another treatment option is the phototoxic dose regimen based on a study performed in our department that showed a good response in many patients [26]:

(1) Ultrameladinine paint (0.1% 8-MOP solution without dilution) will be applied 15–20 min before the session.
(2) Starting dose will be according to skin type:
  (a) 3 J/cm^2 for skin types (I, II, and III)
  (b) 6 J/cm^2 for skin type (IV)
(3) Assess the response every session and manage as follows:
  (a) If there is no or mild erythema increase the dose by:
    (1) 2–4 J/cm^2 in skin types (I, II, and III)
    (2) Double the dose in darker skin type (IV)
  (b) If there is severe erythema, oedema or blisters (burn):
    – Stop the sessions until complete recovery (7–12 days).
    – Add topical antibiotic and cold compresses. Try to postpone the use of topical steroids as possible.
    – On resuming the sessions, start with the last tolerated dose and then increase the dose in later sessions.
  (c) If the scalp skin becomes thickened or hyperpigmented or developed resistance following primary response:
    Rest until return to baseline (3–6 weeks), then restart the protocol, but with rapid increase in the dose.
  (d) Minoxidil topical lotion is used in-between sessions
(4) End point for treatment:
  (a) Partial response: <20% hair growth after 20 sessions
  (b) Good response: 50% or more hair growth
  (c) After 10 sessions, if there is no hair growth:
    Rest and start with:
    Minoxidil + Dermovate under occlusion if not tried before or
    Diphencyprone
(5) Topical PUVA may be used for few resistant patches.

Protocol for pityriasis lichenoides chronica [27]

(1) Give azithromycin 500 mg/day (250 mg for children) on empty stomach in a regimen of 3 days followed by 7 days' rest, to be repeated for 2 months:
  (a) If no response start phototherapy
  (b) If partial response, continue for 2 months.
(2) Four forms of photo/chemo/therapy could be applied:
  (a) PUVA (deep-seated lesions)
  (b) NB-UVB (superficial lesions)
  (c) BB-UVB (less commonly used)
  (d) BB-UVA (less commonly used)
(3) Sessions are 3/week for both Pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC)±moderate topical steroids until complete clearance (average 20–40 sessions). No maintenance is needed.
(4) In nonresponding lesions, add potent topical steroids, systemic methotrexate, or systemic steroids (in inflammatory lesions) with phototherapy.
  Discharge after 15 sessions if no or minimal response is obtained:
  (a) PLC + MF → manage as MF.
  (b) PLC after or during PUVA in a patient with MF → biopsy for chance of being a sign of clearance and do not increase the dose.

Protocol for atopic dermatitis [28]

(1) Photo/chemo/therapy could be used in the treatment of atopic dermatitis (AD); PUVA or NB-UVB.
(2) For mild-moderate AD: NB-UVB is moderately effective as an adjuvant to topical steroids or topical calcineurin inhibitors
(3) PUVA could be used instead of systemic steroids as monotherapy for severe AD.
(4) For all patients, topical emollients are the cornerstones of treatment.
(5) Sessions are 2–3 times/week.
(6) 20–30 sessions are needed.

Protocol for pruritus (NB-UVB, BB-UVB) [29]

(1) Emollients are a must
(2) Renal pruritus:
  – Effective within few sessions (8–12); however, further sessions on demand may be needed
(3) Hepatic pruritus: mildly effective with rapid relapse

(4) Senile and idiopathic pruritus: effective but dryness of the skin is a major problem (use emollients)

Protocol for lichen planus [30]

(1) NB-UVB or PUVA are effective options for extensive LP, with an average of 30 sessions are needed, 2–3 times weekly). However, postinflammatory hyperpigmentation is a major problem
(2) Topical or intralesional steroids can be added for hypertrophic lichen.

Protocol for mastocytosis [31]

(1) PUVA improves pruritus and Darier's sign but not the hyperpigmented lesions.
(2) It is advisable to start very gradual incremental regimen to avoid sudden mediator release.
(3) The response to PUVA is moderate and slow with early relapse, so, PUVA could be used as an adjuvant to medical treatment in severe mastocytosis.

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There are no conflicts of interest.

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