Vitiligo (1 of 9)

Patient presents w/ patches of hypopigmented skin

1.
DIAGNOSIS
Does clinical presentation confirm vitiligo?

[Diagram]

2.
ASSESSMENT
Classify & evaluate severity of vitiligo

NONSEGMENTAL VITILIGO

A. Non-pharmacological therapy
   • Patient education
   • Sunscreens
   • Camouflage cosmetics
   • Phototherapy

B. Pharmacological therapy
   Repigmentation therapy
   • Calcineurin inhibitor
   • Corticosteroid (Topical)
   • Photochemotherapy

FOLLOW-UP

Stable w/ repigmentation

A. Non-pharmacological therapy
   • Phototherapy
   • Narrowband UVB

SEGMENTAL VITILIGO

TREATMENT
See next page

B. Pharmacological therapy
   Repigmentation therapy
   • Corticosteroid (Systemic)
   • Depigmentation therapy

C. Surgical therapy

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Specific prescribing information may be found in the latest MIMS.
VITILIGO

SEGMENTAL VITILIGO

A Non-pharmacological therapy
• Patient education
• Sunscreens
• Camouflage cosmetics

B Pharmacological therapy
Repigmentation therapy
• Calcineurin inhibitor
• Corticosteroid

FOLLOW-UP

Stable w/ repigmentation
CONTINUE TREATMENT AS REQUIRED

Disease progression

Stable w/o repigmentation

A Non-pharmacological therapy
• Patient education
• Sunscreens
• Camouflage cosmetics

B Pharmacological therapy
Repigmentation therapy
• Calcineurin inhibitor
• Corticosteroid

C Surgical therapy

DIAGNOSIS

Vitiligo: An acquired, often familial, melanocytic disorder that produces focal depigmentation of the skin
• Diagnosis is usually confirmed based on the history & physical exam

History
• Onset of the lesion: 50% of patients first present before the age of 20
• Course of the disease: Usually progressive
  - Spontaneous repigmentation may occur in 25-40% of patients w/in 6 mth
• Precipitating factors: Eg emotional stress, sunburn, chemical exposure, skin trauma, inflammation, irritation or rash may precede lesions by 2-3 mth
• Family history of vitiligo or premature graying of the hair
• History of associated conditions (patient & patient’s family)
  - Eg thyroid disorders, alopecia areata, DM, pernicious anemia, collagen vascular diseases, Addison’s disease, melanoma, etc
• History of ocular (eg loss of visual acuity, poor night vision, or photophobia) or auditory (eg deafness) disorders

Physical Exam
Morphology of the Lesions
• Asymptomatic white colored macules or patches, w/ well-defined borders & otherwise normal skin surface
  - Occasionally, patients present w/ patches that have inflamed or hyperpigmented borders

Site of Distribution
• Hypopigmented areas usually appear on exposed areas eg the dorsal surface of the hands & feet, the arms, face (lips & around mouth, nose & eyes), hyperpigmented areas (eg axilla, genital, around nipples), umbilicus, anus & at sites of trauma (Koebner’s phenomenon) & bony prominences (eg knee & elbow)

Other Important Physical Findings:
• Depigmented hairs w/in vitiligious areas & on the head (including eyelashes, beard, etc)
• Changes in the choroid & retinal pigment epithelium
• Uveitis

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### ASSESSMENT

#### Classification

**Nonsegmental (bilateral) vitiligo (NSV)**
- Also known as vitiligo vulgaris, generalized vitiligo
- Chronic symmetrical depigmentation w/ an on-off cycle
- Depigmentation starts then stops for some time, w/ progressive expansion of affected area
- Usually starts on hands, feet or mouth

**Segmental (unilateral) vitiligo**
- Asymmetrical depigmentation w/ c usually begins in childhood
- Remains stable after 1 yr of onset
- Lesion follows a dermatomal pattern; may also have leaf-like or checkerboard pattern

**Mixed vitiligo**
- NSV w/ segmental vitiligo

**Unclassified vitiligo**
- Focal at onset, then progresses as multifocal w/ segmental & nonsegmental features
- Serves as a diagnostic point until disease can be classified as NSV, segmental, or mixed

#### Scoring Systems

**Vitiligo Area Scoring Index (VASI)**
- Quantifies total extent of depigmentation based on 5 sites: upper extremities, hands, trunk, lower extremities, feet
- Uses a percentage scale to visually assess involvement & degree of skin pigmentation

**Vitiligo European Task Force (VETF) System**
- Analyzes disease extent, stage, & disease progression
  - Extent - uses rule of nines
  - Stage - based on pigmentation of skin & hair

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pigmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>normal (no depigmentation)</td>
</tr>
<tr>
<td>1</td>
<td>incomplete depigmentation (includes spotty depigmentation, trichrome, light homogenous pigmentation)</td>
</tr>
<tr>
<td>2</td>
<td>complete (hair whitening included &lt;30%)</td>
</tr>
<tr>
<td>3</td>
<td>complete w/ significant hair whitening (&gt;30%)</td>
</tr>
</tbody>
</table>

- Disease progression - assesses degree of spreading based on Wood’s lamp & electric light exams

**Vitiligo Extent Tensity Index (VETI)**
- A recently formulated scoring system that produces a constant number based on the extent & severity of vitiligo
- Uses the rule of nines; disease tensity is stages according to the affected area (head, upper extremities, trunk, lower extremities, genital area)
- Further studies are needed to prove its potential in accurately diagnosing vitiligo

#### Diagnostic Examinations

**Wood’s Lamp Examination**
- In patients w/ fair skin, it is used to detect vitiliginous lesions & in patients w/ darker skin, it is used to assess the degree of vitiligo lesions
- May also be used to detect vitiligo lesions on the axillae, anus & genitalia which are often clinically inapparent

**Other Exams**
- Additional laboratory exams may be needed for patients w/ history of autoimmune disorders
  - Anti-thyroid peroxidase, antithyroglobulin antibodies, thyroid function tests
  - Punch biopsy is suggested to differentiate vitiligo from other dermatoses

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### NON-PHARMACOLOGICAL THERAPY

#### Patient Education
- Educate patient, friends & relatives about the disease
  - It is important for them to overcome any stigmas they may have about vitiligo
- Explain the nature of the disease to the patient
  - Vitiligo does not affect the patient’s health directly, but is a cosmetic issue
  - Spontaneous recovery may occur
- Treatment options should be discussed
  - Treatment may be long & difficult, & the results are often unpredictable
  - Review the risks vs benefits along w/ expected outcomes of the treatment options

#### Sunscreens
- Patient should use sunscreen w/ SPF >15 that protects against both UVA & UVB rays on all exposed skin
  - Vitiliginous areas are easily sunburned
  - Sunburn can cause the depigmentation area to extend
- Patient should avoid outdoor activities from 11 am-3 pm or use appropriate clothing for sun protection

#### Camouflage Cosmetics
- Eg Stains/dyes, self-tanning products, whitening lotions, tinted cover creams, foundations, colorants/dyes for white hair
  - Quick-tanning preparations that contain dihydroxyacetone (DHA) may be used
    - These preparations are esp useful on areas, eg the eyelids, where potent topical corticosteroids or photochemotherapy should not be used

#### Phototherapy
- Eg UVB, narrow band UVB, excimer laser
- New onset, facial & neck lesions (except eyelids) tend to have the best results
- Vitiligo of the hands, feet & over bony prominences respond poorly to treatment
- Effects: Causes inflammation that promotes activation & migration of melanocytes from a melanocytic reservoir (eg hair follicles) causing repigmentation
  - At least 2-3 mth are needed to see the results & therapy should be continued for at least 1 yr to gain maximum results
- If there is no effect after 6 mth of therapy or new/enlarged macules appear, treatment should be discontinued
- Photographs may assist in evaluating therapy

#### Narrow band UVB (NBUVB)
- Recommended 1st line treatment for patients w/ active &/or widespread vitiligo
- W/ lesser adverse effects & more efficacious compared to PUVA & other phototherapies
- NBUVB is a fairly effective treatment for symmetrical vitiligo esp on the face, trunk & proximal extremities

#### 308-nm Excimer Laser
- Targeted phototherapy w/ excimer laser may be an option for patients w/ chronic stable vitiligo
- More prospective studies are needed to further evaluate this treatment modality

#### Depigmentation
- Eg Q-switched ruby/alexandrite lasers, cryotherapy
- Q-switched lasers are indicated for recalcitrant cases, patients w/ Koebner phenomenon
  - May be used w/ Methoxyphenol
- Cryotherapy may be used for recalcitrant cases
  - May be given w/ or w/o Methoxyphenol

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### PHARMACOLOGICAL THERAPY

#### Repigmentation Therapy

**Calcineurin Inhibitors**
- Eg Pimecrolimus, Tacrolimus
- **Mode of action:** inhibits cytokines production & enhances melanocyte migration
- Causes less skin atrophy compared to steroids
- Should only be used as 2nd line treatment because of increased incidence of lymphoma & skin cancer
- **Pimecrolimus**
  - Alternative therapy to Clobetasol
- **Tacrolimus (Topical)**
  - Preferred agent for treating vitiligo in younger patients & in skin-sensitive areas eg eyelids
  - Several studies have shown repigmentation in localized vitiligo
  - One small study showed that topical Tacrolimus was almost as effective as topical Clobetasol in treating localized vitiligo in children

**Corticosteroid (Topical)**
- Eg Clobetasol, Desonide, Fluocinolone, Mometasone, Methylprednisone aceponate
- May be useful for localized vitiligo
- Lower-potency corticosteroids may be used for children <2 yr who are not candidates for topical PUVA
- **Effects:** May be effective repigmenting agents
  - 3-4 mth are needed to see optimal results
  - Clobetasol propionate may result in better repigmentation when other topical steroids have failed
- Application is only once daily
- Use of mid- or lower-potency corticosteroids are preferable considering side effects of long-term high-potency corticosteroids
  - Use caution when applying to the face & flexors
  - Should not be applied to eyelids or periorbital areas due to the risk of steroid-induced glaucoma & cataracts
  - Monitor response w/ Wood’s lamp exam at 6-wk intervals & examine for possible side effects
  - Photographs may assist in evaluating therapy
- Stop treatment if no response after 3 mth
- Treatment is continued if repigmentation occurs

**Corticosteroid (Systemic)**
- Eg Betamethasone, Dexamethasone
- Studies using pulse therapy w/ systemic steroids showed significant efficacy against unstable vitiligo by slowing disease activity

#### Photochemotherapy
- In approximately 70-80% of patients, repigmentation occurs following Psoralens + UVA (PUVA) treatment
- 20% of patients achieve complete repigmentation
- **Topical PUVA**
  - Considered for patients w/ localized vitiligo (<20% of the BSA) or for child >5 yr old w/ localized vitiligo
  - Psoralens lotion is diluted to a 0.01-0.1% soln & is applied to affected skin prior to UVA exposure
- **Oral PUVA**
  - Considered for patients w/ more extensive vitiligo (>20% of body involvement) & for persons recalcitrant to topical therapy
  - Not recommended for children <12 yr
  - Oral Psoralen is taken 90-120 min prior to UVA exposure
- **Heliotherapy/Psoralens & sunlight (PUVASOL)**
  - Trioxsalen is taken 2-4 hr prior to outdoor sunlight exposure (11 am-3 pm; may start at 10 am in tropical areas)
  - Photographs may assist in evaluating therapy

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1Many low-high potency topical corticosteroids are available. Please see prescribing information for specific formulations in the latest MIMS. For potency listing, please refer to the Dosage Guideline section in the Atopic Dermatitis or Psoriasis Treatment Plan.
B PHARMACOLOGICAL THERAPY (CONT’D)

Photochemotherapy
- Khellin + UVA (KUVA)
  - Less phototoxic & mutagenic compared to PUVA
  - Topical administration of Khellin is preferred; oral Khellin administration is discouraged because of increased incidence of liver toxicity
  - Further studies are needed to establish efficacy of outdoor sunlight exposure w/ KUVA treatment

Depigmentation therapy
- Considered for patients w/ extensive & refractory vitiligo, who are willing to undergo irreversible depigmentation
  - May also be used in patients who have facial vitiligo & are unwilling to attempt repigmentation
- Monobenzyl ethyl ester, a Hydroquinone derivative, a bleaching agent, is used
  - Effects: Remaining pigment is removed from normal skin by destroying the melanocytes
    - Results are usually evident w/in 1 mth of therapy & complete depigmentation takes 6-12 mth
  - Patients must understand that this is a permanent & irreversible procedure
    - Permanent photosensitivity results from treatment
  - Other depigmenting agents: Methoxyphenol (Mequinol), 88% Phenol, Imatinib, Imiquimod, Diphencyprone
    - Further studies are needed to prove the efficacy of these agents for depigmentation therapy in vitiligo

C SURGICAL THERAPY

Should only be used in non-progressive, small areas of inactive vitiligo
- Eg epidermal blister grafting, autologous mini punch grafting, ultrathin epidermal sheet grafting, micropigmentation (tattooing), etc
- May be an option if topical steroids or photochemotherapy fail to repigment
  - Surgery is usually limited to patients who have segmented or localized disease
  - May be used in some generalized patients
- The following areas tend not to repigment well:
  - Forehead, hairline, dorsal fingers & ankles
- Follow surgery w/ phototherapy

D FOLLOW-UP

Nonsegmental Vitiligo
- NSV patients on narrowband UVB therapy should be reassessed on the 3rd & 6th mth of therapy
  - If still w/ disease progression after 3 mth of narrowband UVB therapy w/ topical steroid/calcineurin inhibitor therapy, consider switching to systemic corticosteroid therapy
    - After 3-6 mth, consider surgical interventions if disease is stable but w/o repigmentation, or depigmentation therapy if w/o repigmentation & w/ Koebner phenomenon
    - After 9 mth of narrowband UVB treatment, consider surgical interventions if disease is stable but repigmentation stopped

Segmental Vitiligo
- Reassess patients on topical steroids & calcineurin inhibitors on the 6th mth of therapy

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## Other Dermatologicals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Available Strength</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monobenzone</td>
<td>20% cream</td>
<td>Apply 12 hrly to areas w/ unwanted pigmentation</td>
<td>Adverse Reactions: Skin irritation &amp; sensitization, may be transient. Excessive depigmentation beyond treated area may occur which may result in unsightly patches. Depigmentation is irreversible. Special Instructions: Preliminary trial on a small area is recommended. Patient must avoid direct skin contact w/ others for 1-2 hr after application. Must use sun protection measures because of permanent photosensitivity. Discontinue after 4 mth if no improvement.</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>0.03%, 0.1% oint</td>
<td>Apply 0.1% oint 12 hrly x 6 mth</td>
<td>In one small study 0.1% oint was used in children. Application: Apply a thin layer to affected skin &amp; rub-in gently &amp; completely. Adverse Reactions: Local effects: Burning, stinging, soreness, pruritus which usually decreases w/ continued use. Less common: Bacterial &amp; viral infections. If lymphadenopathy occurs, cause should be investigated &amp; if no clear cause, Tacrolimus should be discontinued. Shortened time to skin tumor formation in animal photo-carcinogenicity study. Special Instructions: Do not apply to areas of acute cutaneous viral infections. Clinical cutaneous infections should be cleared before application of Tacrolimus. Should not be used w/ occlusive dressing. Patients should minimize or avoid natural or artificial sunlight.</td>
</tr>
</tbody>
</table>

All dosage recommendations are for non-pregnant & non-breastfeeding women, & non-elderly adults w/ normal renal & hepatic function unless otherwise stated. Not all products are available or approved for above use in all countries. Products listed above may not be mentioned in the disease management chart but have been placed here based on indications listed in regional manufacturers’ product information. Specific prescribing information may be found in the latest MIMS.
# Dosage Guidelines

## PSORALENS (ORAL)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
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| Methoxsalen      | Adult & Childn  
>12 yr: 20 mg PO 2-4 hr prior to UVA  
Usually given 2-3x/wk (w/ ≥48 hr between treatments) depending on UVA schedule  
**Max dose:** 600 mcg/kg | **Adverse Reactions**  
• Nausea, insomnia, nervousness, depression  
• When combined w/ UVA may cause pruritus & mild transient erythema, headache, vesiculation, bulla formation, dizziness, edema, onycholysis, acne, severe skin pain, severe burns, premature aging, hypertrichosis  
• Severe burns may result from inadvertent sunlight/UV light exposure post-treatment  
• Increased risk of malignant neoplasms  
**Special Instructions**  
• Dose of UVA should be adjusted based on patient response  
• Avoid in patients w/ aphakia, melanoma, patients w/ diseases associated w/ light sensitivity  
• Use w/ caution in patients w/ hepatic insufficiency  
• Protect genitalia & eyes during therapy  
• Avoid sunlight even through glass for >8 hr after Methoxsalen ingestion & avoid excessive sunlight for 24-48 hr after PUVA treatment  
• Wear suitable eye protection for 12-24 hr after therapy  
• Patients should undergo ophtha exams & regular exams to look for signs of malignant or premalignant skin lesions |
| Trioxsalen (Trioxysalen) | 0.3 mg/kg PO 2-4 hr prior to sunlight exposure  
Usually given 2-3x/wk w/ ≥48 hr between doses depending on PUVASOL schedule | **Adverse Reactions**  
• Nausea, pruritus, erythema, skin pain, edema, headache, dizziness, depression, premature aging of the skin  
• Increased risk of melanomas  
**Special Instruction**  
• Initial sun exposure is up to 15 min between 11 am-3 pm (May start at 10 am in tropical areas)  
  - Increase exposure by 5 min/treatment based on patient response up to 2 hr/treatment  
• Wear suitable eye protection & protect lips during & for 12-24 hr after therapy  
• Protect skin from sunlight for up to ≥48 hr  
• Avoid in patients w/ hepatic dysfunction & in patients w/ diseases associated w/ photosensitivity  
• Eye exams should be performed regularly |

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### Dosage Guidelines

#### PSORALEN (TOPICAL)

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<th>Dosage</th>
<th>Remarks</th>
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</thead>
</table>
| Methoxsalen | 1% lotion, topical soln | Apply 0.1-0.01% diluted solution to lesion prior to UVA. Usually given 1x/wk (w/ ≥48 hr between treatments) depending on UVA schedule | Application  
- Affected area only should be painted with solution which has been diluted in ethanol, petrolatum or hydrophilic petrolatum  
- Test doses using diluted 0.01-0.1% lotion should be performed  
- Exposure to UVA may begin immediately after application to up to 2 hr after application  
- Time exposed to UVA light & concentration of lotion should be increased gradually as per patient response  
**Adverse Reactions**  
- Pruritus & mild transient erythema, headache, vesiculation, bulla formation, dizziness, edema, onycholysis, acne, severe skin pain, severe burns, premature aging, hypertrichosis  
- Increased risk of malignant neoplasms  
**Special Instructions**  
- Avoid in patients w/ aphakia, melanoma, patients w/ diseases associated w/ light sensitivity  
- Protect genitalia & eyes during therapy  
- Unaffected skin should be protected w/ opaque sunscreen  
- After UVA exposure, wash lotion off & protect areas from sunlight for ≥48 hr  
- Wear suitable eye protection for 12-24 hr after therapy  
- Patients should undergo ophtha exams & regular exams to look for signs of malignant or premalignant skin lesions |

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Please see the end of this section for reference list.