COMMON HYPOPIGMENTATION DISORDERS

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ISCoD and 5th APMED Jan 31th – Feb 2nd, Jakarta, Indonesia

Introduction

- Hypopigmentation is the loss of skin color due to a reduction in melanin content. Although most often asymptomatic and benign, hypopigmented disorders can have significant cosmetic, psychological, economical, and societal consequences.
- Early diagnosis and appropriate management of these disorder can improve a patient quality of life, halt disease progression and prevent irreversible disability.

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Outline

- Idiopathic guttate hypomelanosis
- Progressive macular hypomelanosis
- Post-inflammatory hypopigmentation
- Pityriasis alba
- Vitiligo

IDIOPATHIC GUTTATE HYPOMELANOSIS

- A pigmentary disorder of unknown pathogenesis
- It does not appear to result from reduction in the number of epidermal and/or follicular melanocytes, but rather from an :
  - Impaired synthesis of melanin
  - Decreased size and poor melanization of melanosomes
  - Inadequate transfer of melanosomes from melanocytes to surrounding keratinocytes.

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016

Etiology

- The exact etiology remains unclear
- Several factors have been proposed such as **senile degeneration**, **chronic UV exposure**, **genetics**, **trauma**, **autoimmunity** and local inhibition of **melanogenesis**
- showing increasing prevalence with advancing age, and is rarely seen in children and young adults
- The hair is not involved

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016

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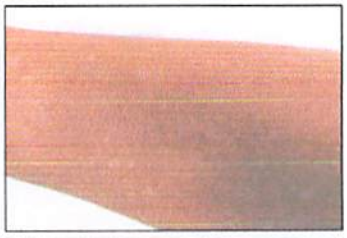
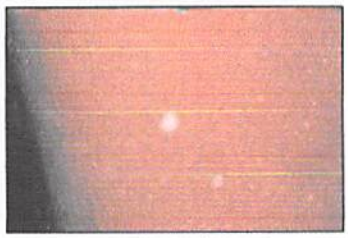
Clinical Manifestation





- Characterized by asymptomatic well-defined oval-to-round hypopigmented to depigmented porcelain white macules of sizes ranging from 0.5 to 6 mm
- The common sites on the sun-exposed areas of the body include the arms and the shins, but sometimes are widespread.

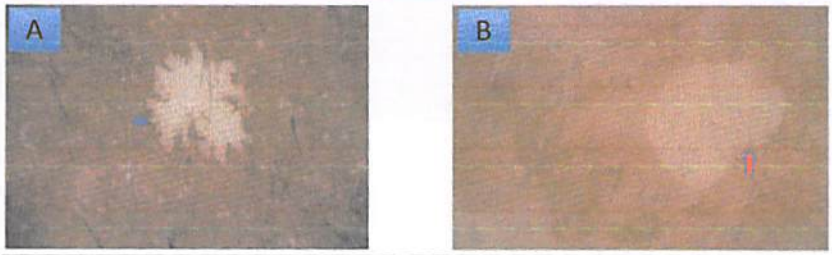
Kumarasinghe P, Uprety S, Sarkar R. Hypopigmentary disorders in Asian patients. Pigment International. 2017:13-20.

Classification of IGH

1. Solitary or multiple hypopigmented macules on a background of sun-damaged skin in sun-exposed areas
2. Solitary ivory white, stellate, well-circumscribed, sclerotic macules related to sun exposure, which can be seen on both sun-exposed and non-sun-exposed areas
3. Small well-circumscribed hypopigmented macules with keratotic flat crust and a scalloped border.

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016

Dermoscopy



A. Ameboid pattern (blue arrow). B. Petaloid pattern (red arrow). Lesional margins are distinct in contrast to vitiligo where margins are blurred.

Chatterjee M, Neema S. Dermoscopy of Pigmentary Disorders in Brown Skin. Dermatol Clin. 2018:36:473–485

Differential diagnosis

- Clinically, IGH lesions must be distinguished from several hypopigmented conditions.
- **Macular hypomelanosis.** It can be differentiated from IGH by its reduced depigmentation and less sharply demarcated border.
- **Vitiligo** can be distinguished by its age of inception, size, and distribution of lesions.
- **Pityriasis versicolor** might look like IGH. Nevertheless, it usually has a fine scale and it is frequently found on the upper trunk and shoulder.

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016

Treatment

- IGH may not be a significant problem in fair skin; however, it leads to **cosmetic concerns** and **psychological impacts** in patients with darker-skin types. Consequently, many patients seek medical care despite the benign course of disease progression.
- Currently, no standard treatment for IGH has been established, although many medical and surgical options have been studied.

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016

Topical

Surgery

Table 1 Medical and surgical therapies for idiopathic guttate hypomelanosis

First author	Treatment	Dosage or method	Results	Adverse effects
Medical treatment				
Falabella [2]	Intralesional corticosteroids	Intralesional triamcinolone monthly for 3 months	46.67 % (7/15) of the patients achieved a good response	
Pagnoni [35]	Topical retinoids	0.025 % tretinoin once nightly for 1 week, then 0.05 % tretinoin for 3 week, and 0.1 % tretinoin until completing the 4-month period	100 % (40/40) of the lesions clinically disappeared after 4 months	
Asawanonda [20]	1 % pimecrolimus cream	1 % pimecrolimus cream twice daily for 8 weeks	75 % (3/4) of the subjects demonstrated 25–75 % clinical improvement	
Roriaureir [21]	0.1 % tacrolimus ointment	0.1 % tacrolimus ointment twice daily for 6 months	11 % (3/26) of the patients demonstrated some degree of repigmentation	Transient skin burning
Ruvinskas [24]	88 % phenol peeling	Cotton-tipped application of 88 % phenol monthly for 2 sessions	64 % (89/139) of the lesions showed repigmentation, which in almost half of the lesions showed more than 75 % improvement	Persistent crust, PIH, ulceration, secondary infection, and scarring
Surgical treatment				
Phoenigam [17]	10 s cryotherapy	Single application of a 10-s cryogen	90.8 % (79/87) of the treated lesions reached complete repigmentation	Blisters on all lesions
Kumarasinghe [18]	3–5 s cryotherapy	Single application of a 3- to 5-s cryogen	All treated lesions showed good repigmentation	Blisters, slight hyperpigmentation
Hexsel [29]	Superficial dermabrasion	Single session of dermabrader	80 % (16/20) of the patients showed repigmentation	Erythema for up to 90 days
Shim [36]	Fractional CO_2 laser	Single session of fractional CO_2 laser	62.7 % (117/40) of the patients showed more than 75 % clinical improvement	Burning sensation, erythema, PIH
Goldwyn [37]	Fractional CO_2 laser	Single session of fractional CO_2 laser	47.9 % (115/240) of the patients showed more than 75 % clinical improvement	Pain, burning sensation, erythema, PIH
Roriaureir [28]	Non-ablative fractional photothermolysis	Four sessions of fractional 1550-nm erbium:glass laser monthly	60 % (72/120) of the lesions showed more than 50 % clinical improvement	Mild erythema, edema, and bronzing
Falabella [2]	Skin grafting	Normal autologous skin graft on depigmented lesions	6.66 % (1/15) of the patients showed repigmentation	

CO_2 carbon dioxide, *PIH* postinflammatory hyperpigmentation

Juntongjin P, Laosakul K. Idiopathic Guttate Hypomelanosis: A Review of Its Etiology, Pathogenesis, Findings, and Treatments. Am J Clin Dermatol. 2016.

PROGRESSIVE MACULAR HYPOMELANOSIS (PMH)

- PMH is a primary, acquired, non-scaly macular hypopigmentation, mostly observed in adolescents and young adults between the ages of 13 and 45 years.
- The disorder is mostly seen in patients with darker skin types (III–VI)
- In lighter skin types, the hypopigmented macules are much less obvious, and therefore patients often do not notice the lesions or do not find it worth visiting a doctor.

Hassan AM, El-Badawi MA, Abd-Rabou FA, Gamei MM, Moustafa KA, Almokadem AH. Progressive macular hypomelanosis pathogenesis and treatment: a randomized clinical trial. Journal of Microscopy and Ultrastructure. 2014;205–216.

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Etiopathogenesis

A clear etiology has not been found

Propionibacterium acnes type III is involved in the formation of PMH. The mechanism are:

- **First**, the production of bacterial enzymes with degradative properties that target the integrity of epidermal skin cells and the barrier function of sebaceous follicles.
- **Second**, *P. acnes* might be involved in triggering inflammation by constitutively produced factors such as porphyrins, surface determinants like a glycocalyx polymer or stress proteins, an acid shift, or heat shock.
- **Last,** *P. acnes* contain genes encode CAMP factor homologs that act as pore-forming toxins, which may affect the function of melanocyte.

Relyveld GN, Westerhof W, Woudenberg J, Kingswijk M, Langenberg M, Vandenbroucke-Grauls CM, et al. Progressive macular hypomelanosis is associated with a putative Propionibacterium species. J Invest Dermatol. 2010;130:1182-1184.

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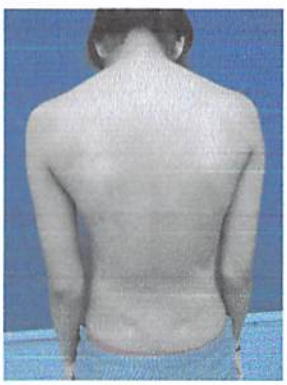
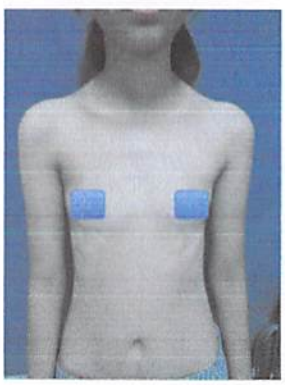
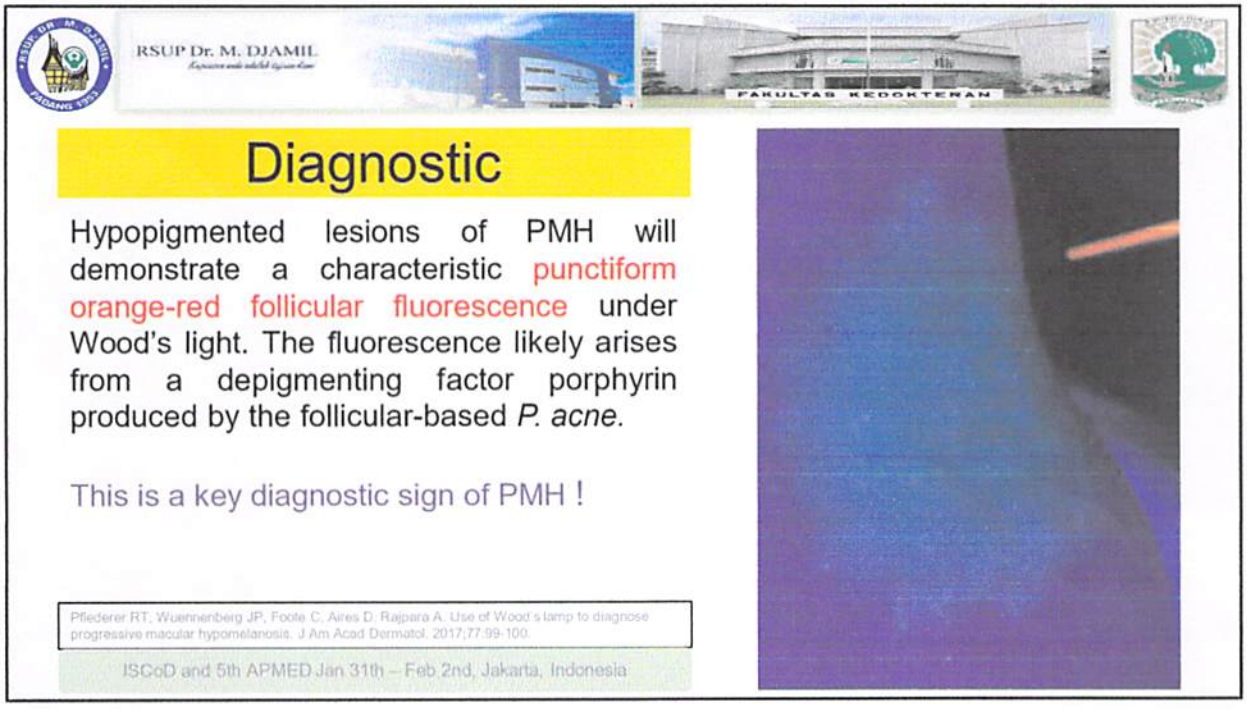
Clinical manifestation

- Asymptomatic
- presenting as symmetric, hypopigmented, poorly demarcated, smooth macules and/or patches.
- localized predominantly on the trunk.,the mid lumbar region and abdominal involvement is present in 40% of cases; rarely is the face
- The lesions are distributed in areas with a known high density of sebaceous glands. invo.





- Desai SR, Owen JL. Progressive macular hypomelanosis: An update. Pigment Int 2014;1:52-5.
- Pictures is private document.

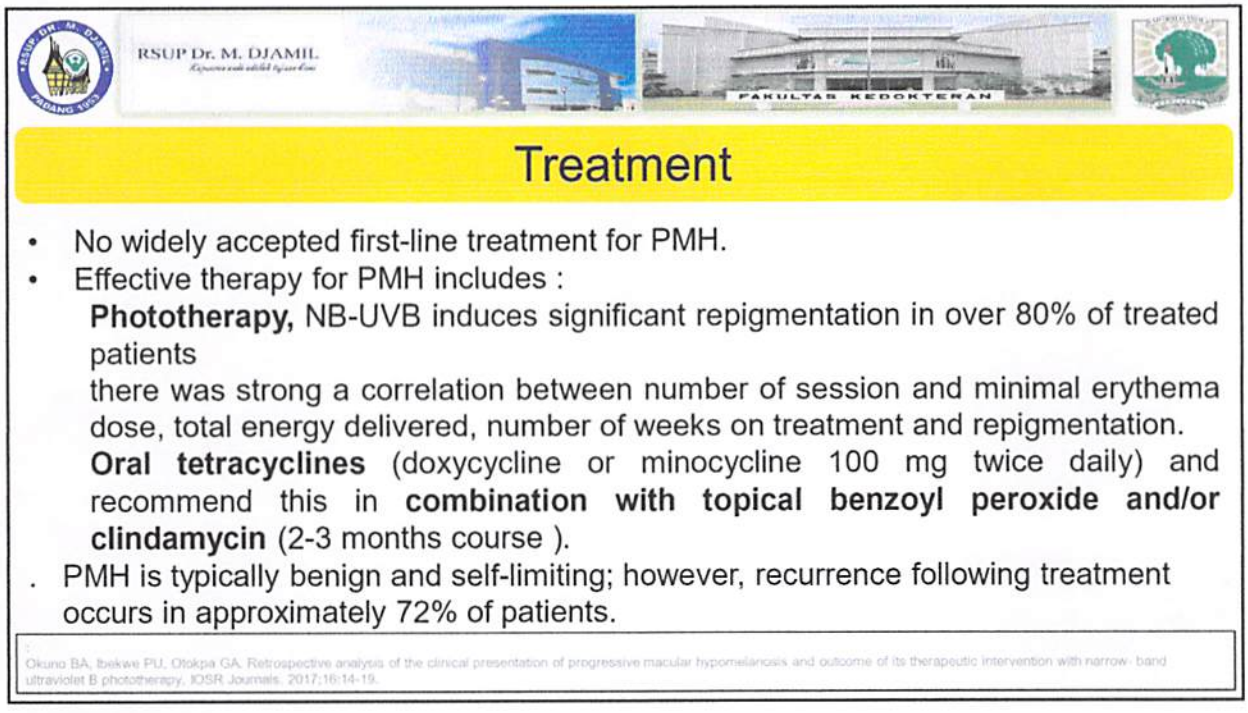


Diagnostic

Hypopigmented lesions of PMH will demonstrate a characteristic punctiform orange-red follicular fluorescence under Wood's light. The fluorescence likely arises from a depigmenting factor porphyrin produced by the follicular-based *P. acne*.

This is a key diagnostic sign of PMH !

Pfiederer RT, Wuennenberg JP, Foote C, Aires D, Rajpara A. Use of Wood's lamp to diagnose progressive macular hypomelanosis. J Am Acad Dermatol. 2017;77:99-100.



Treatment

- No widely accepted first-line treatment for PMH.
- Effective therapy for PMH includes :

  Phototherapy, NB-UVB induces significant repigmentation in over 80% of treated patients

  there was strong a correlation between number of session and minimal erythema dose, total energy delivered, number of weeks on treatment and repigmentation.

  Oral tetracyclines (doxycycline or minocycline 100 mg twice daily) and recommend this in **combination with topical benzoyl peroxide and/or clindamycin** (2-3 months course).

. PMH is typically benign and self-limiting; however, recurrence following treatment occurs in approximately 72% of patients.

Okuno BA, Ibekwe PU, Otokpa GA. Retrospective analysis of the clinical presentation of progressive macular hypomelanosis and outcome of its therapeutic intervention with narrow- band ultraviolet B phototherapy. IOSR Journals. 2017;16:14-19.

Diagnostic

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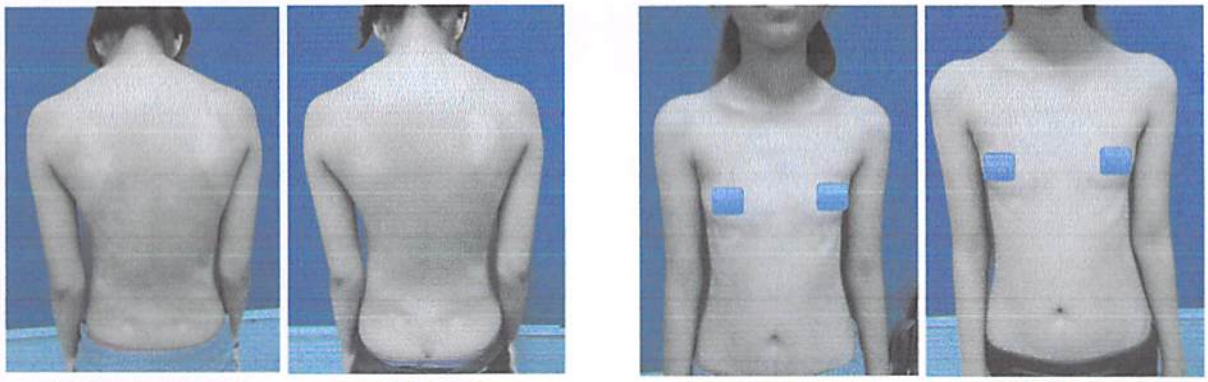
Combination Benzoyl peroxide 5%, clindamycin phosphate 1,2% and NB-UVB for 3 months.



Before | After | Before | After

Photo is private document

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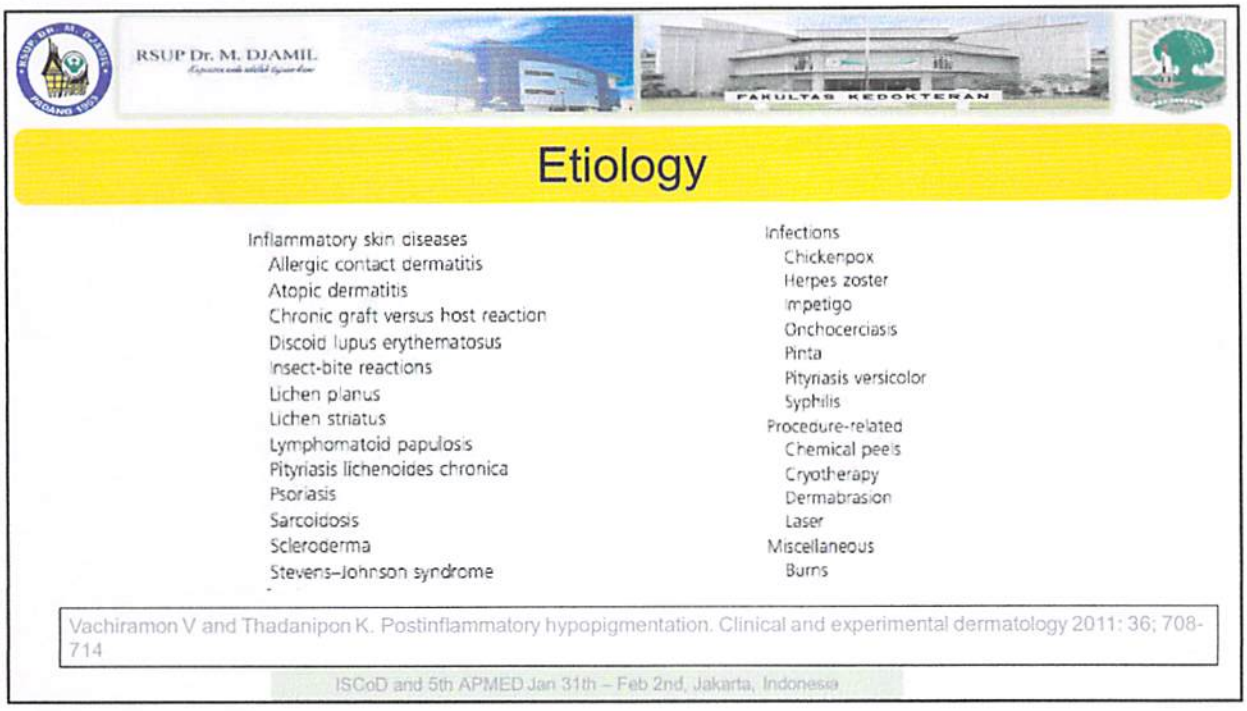
POST INFLAMMATORY HIPOPIGMENTATION

Post inflammatory hyperpigmentation (PIH) is a common, acquired pigmentary disorder caused by cutaneous endogenous inflammation, external injury, or cutaneous procedures.

The primary morphology of the underlying inflammatory disease often provides a straightforward diagnosis; however, low-grade inflammation may occasionally be clinically undetectable, especially in dark-colored skin

Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011: 36; 708-714



Etiology

Inflammatory skin diseases
- Allergic contact dermatitis
- Atopic dermatitis
- Chronic graft versus host reaction
- Discoid lupus erythematosus
- Insect-bite reactions
- Lichen planus
- Lichen striatus
- Lymphomatoid papulosis
- Pityriasis lichenoides chronica
- Psoriasis
- Sarcoidosis
- Scleroderma
- Stevens–Johnson syndrome

Infections
- Chickenpox
- Herpes zoster
- Impetigo
- Onchocerciasis
- Pinta
- Pityriasis versicolor
- Syphilis

Procedure-related
- Chemical peels
- Cryotherapy
- Dermabrasion
- Laser

Miscellaneous
- Burns

Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011: 36; 708-714

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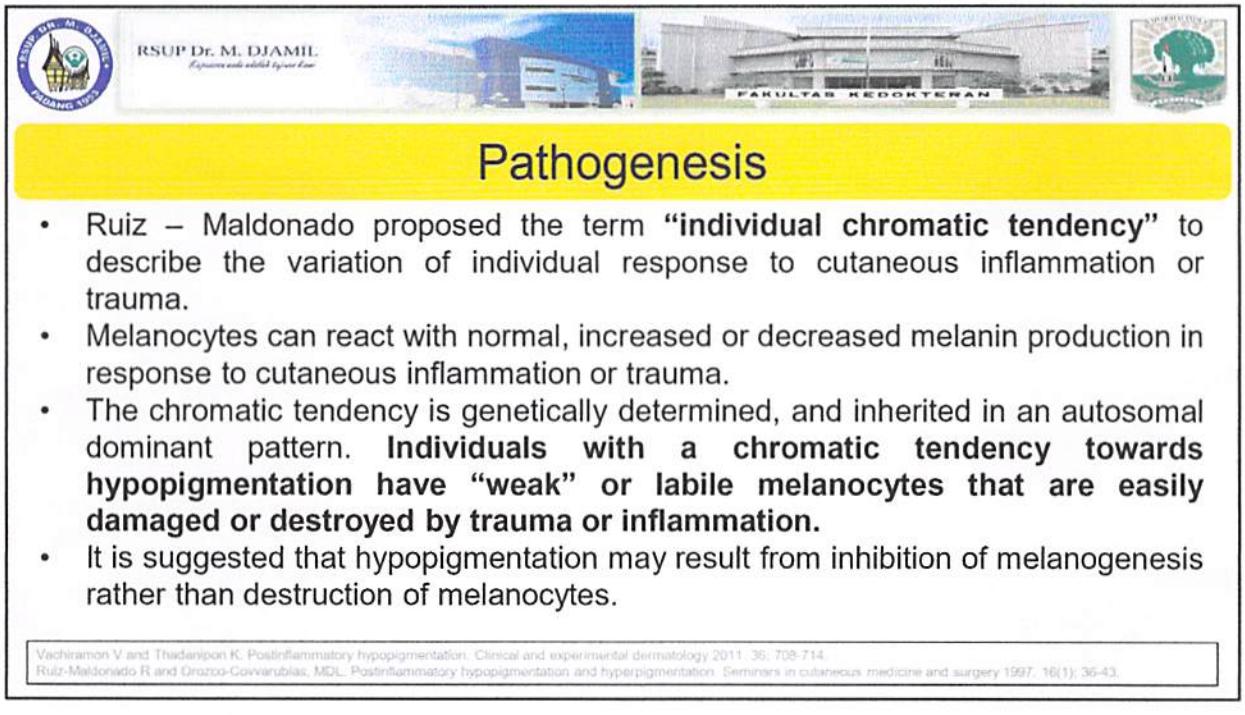


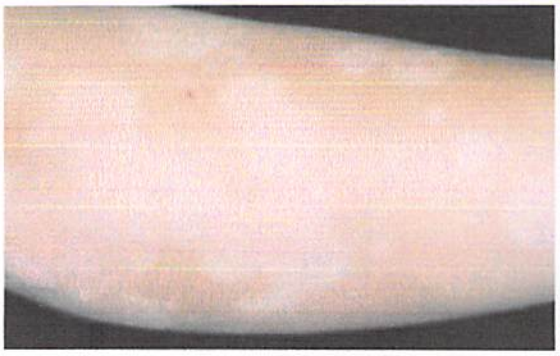
Pathogenesis

- Ruiz – Maldonado proposed the term **"individual chromatic tendency"** to describe the variation of individual response to cutaneous inflammation or trauma.
- Melanocytes can react with normal, increased or decreased melanin production in response to cutaneous inflammation or trauma.
- The chromatic tendency is genetically determined, and inherited in an autosomal dominant pattern. **Individuals with a chromatic tendency towards hypopigmentation have "weak" or labile melanocytes that are easily damaged or destroyed by trauma or inflammation.**
- It is suggested that hypopigmentation may result from inhibition of melanogenesis rather than destruction of melanocytes.

Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011: 36; 708-714.
Ruiz-Maldonado R and Orozco-Covvarubias, MDL. Postinflammatory hypopigmentation and hyperpigmentation. Seminars in cutaneous medicine and surgery 1997; 16(1): 36-43.

Clinical Manifestation

Usually appear as **hypochromic** or **achromic** macules or patches, often asymptomatic and correlate with the configuration and distribution of the original inflammatory dermatosis.



- Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011.

Post-inflammatory hypopigmentation after treatment for psoriasis

Dermoscopy

- Examination under Wood's lamp and dermoscopy accentuates the lesion, and helps distinguish between hypopigmented and depigmented lesions.
- Confocal laser scanning microscopy may allow distinction between different hypomelanotic conditions, based on the melanin content and distribution patterns.
- Biopsy is rarely diagnostic, but useful in ruling out infectious or malignant mimickers.
- Histopathology of postinflammatory hypopigmentation shows nonspecific findings, including decreased epidermal melanin, variable degrees of superficial lymphohistiocytic infiltration, and presence of melanophages in the upper dermis.

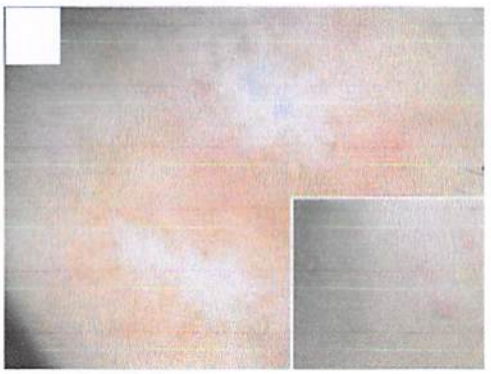
Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011: 36; 708-714

Treatment

- Identifying the underlying etiology and controlling inflammation is the first step in management.
- Most important management → **identify the cause.**
- Medium-potency topical steroid in combination with a tar-based preparation → twice daily.
- Topical pimecrolimus 1% cream twice daily.
- Topical photochemotherapy → topical application of 0.001 – 0.5% 8–methoxypsoralen in aquaphor or hydrophilic ointment to the affected area for 20–30 min, followed by UVA exposure 1–3 times per week at an initial dose of 0.2– 0.5 J/cm2, increasing by 0.2–0.5 J/cm2 weekly.
- Extensive area → Nb-UVB or oral PUVA may be used 2–3 times weekly.
- Ablative fractional CO_2

Vachiramon V and Thadanipon K. Postinflammatory hypopigmentation. Clinical and experimental dermatology 2011; 36: 708-714.

Dermoscopy



Whilst post-inflammatory hypopigmentation often presents with some dermoscopic findings typical of the original lesions (in this case, the star-like arrangment typical of prurigo nodularis).

Chatterjee M, Neema S. Dermoscopy of Pigmentary Disorders in Brown Skin. Dermatol Clin. 2018:36:473–485

PITYRIASIS ALBA

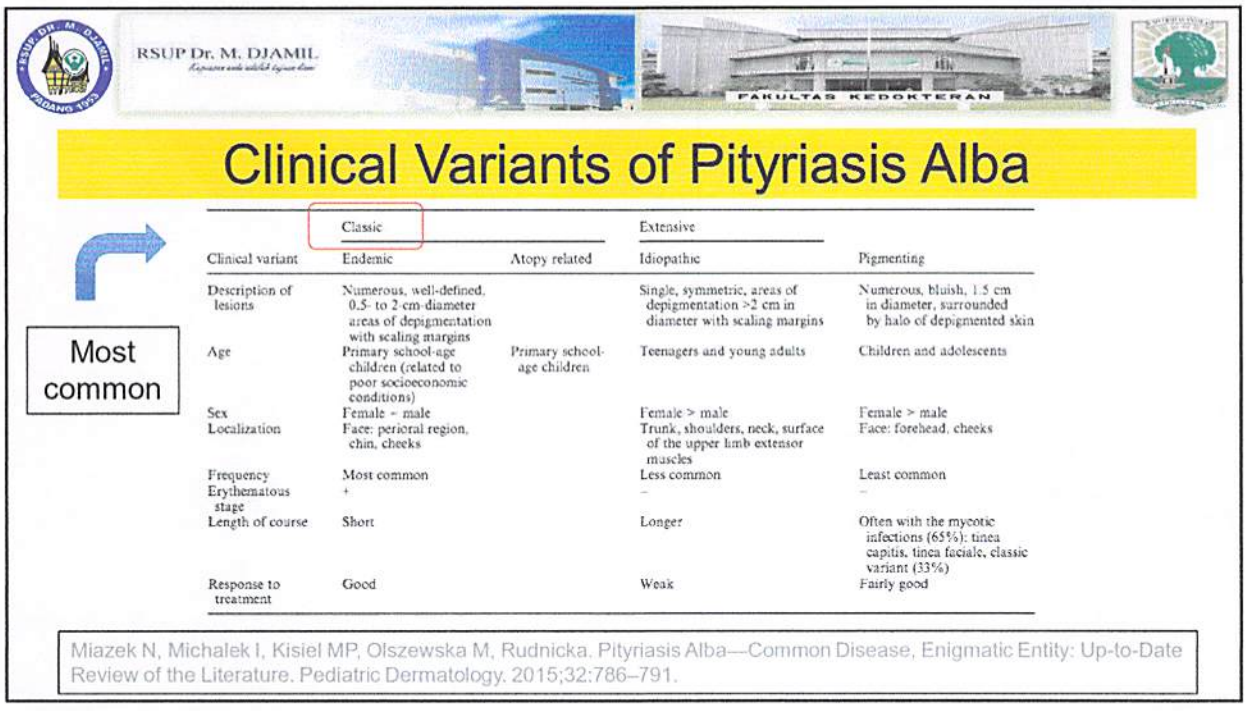
- Pityriasis alba (PA) is a common benign condition mainly affecting the head and neck regions of preadolescent children, more noticeable in darker skin types and there is no gender or skin type predilection
- Occurs predominantly in children between the ages of 3 and 16 years.

Miazek N, Michalek I, Kisiel MP, Olszewska M, Rudnicka. Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatric Dermatology. 2015;32:786–791.

Etiology

- The etiology remains not well elucidated but pityriasis alba has been commonly characterized as a mild form of atopic dermatitis.
- Excessive, unprotected sun exposure as well as hygienic habits (frequent bathing and hot baths) are strongly related to the development of pityriasis alba. All these conditions present as whitish scaly patches with ill-defined border

Miazek N, Michalek I, Kisiel MP, Olszewska M, Rudnicka. Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatric Dermatology. 2015;32:786–791.

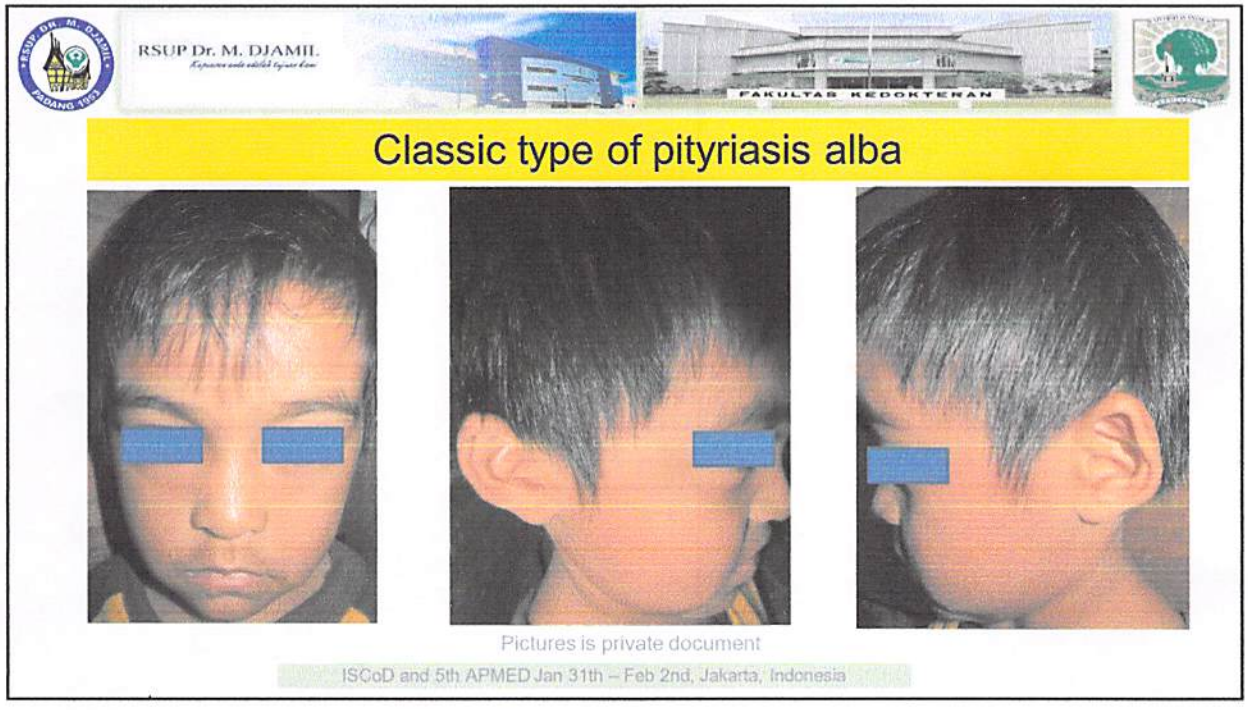


Clinical Variants of Pityriasis Alba

Most common

	Classic		Extensive	
Clinical variant	Endemic	Atopy related	Idiopathic	Pigmenting
Description of lesions	Numerous, well-defined, 0.5- to 2-cm-diameter areas of depigmentation with scaling margins		Single, symmetric, areas of depigmentation >2 cm in diameter with scaling margins	Numerous, bluish, 1.5 cm in diameter, surrounded by halo of depigmented skin
Age	Primary school-age children (related to poor socioeconomic conditions)	Primary school-age children	Teenagers and young adults	Children and adolescents
Sex	Female = male		Female > male	Female > male
Localization	Face: perioral region, chin, cheeks		Trunk, shoulders, neck, surface of the upper limb extensor muscles	Face: forehead, cheeks
Frequency	Most common		Less common	Least common
Erythematous stage	+		–	–
Length of course	Short		Longer	Often with the mycotic infections (65%): tinea capitis, tinea faciale, classic variant (33%)
Response to treatment	Good		Weak	Fairly good

Miazek N, Michalek I, Kisiel MP, Olszewska M, Rudnicka. Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatric Dermatology. 2015;32:786–791.



Classic type of pityriasis alba

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Treatment

- **The primary objective of treatment is to limit the potential triggering factor**. One needs to reduce exposure to sunlight, apply sunscreen daily, and in some patients decrease the frequency of baths or beauty treatments.
- The first attempts to treat PA were based on emollient creams. The effectiveness of emollient therapy is difficult to evaluate because of coexisting AD, for which PA is an identification criterion

Miazek N, Michalek I, Kisiel MP, Olszewska M, Rudnicka. Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatric Dermatology. 2015;32:786–791.

Treatment

Clinical Study

Double-Blind, Placebo-Controlled, Randomized Study Comparing 0.0003% Calcitriol with 0.1% Tacrolimus Ointments for the Treatment of Endemic Pityriasis Alba

Berenice Moreno-Cruz, Bertha Torres-Álvarez, Diana Hernández-Blanco, and Juan Pablo Castanedo-Cazares

Dermatology Department, Hospital Central "Dr. Ignacio Morones Prieto", Universidad Autónoma de San Luis Potosí, Avenida Carranza No. 2395, CP 78210, San Luis Potosí, Mexico

Based on the results of our study, we could suggest that calcitriol is at least as effective as tacrolimus, and superior to petrolatum in endemic PA, offering some clinical advantages to the pediatric population. Side effects such as skin burning sensation and immunosupression would be absent compared to tacrolimus, besides the potential of avoiding carcinogenic risk.

Cruz BM, Alvarez BT, Blanco DH, Cazares JPC. Double-Blind, Placebo-Controlled, Randomized Study Comparing 0.0003% Calcitriol with 0.1% Tacrolimus Ointments for the Treatment of Endemic Pityriasis Alba. Dermatology Research and Practice. 2012:1-6.

VITILIGO

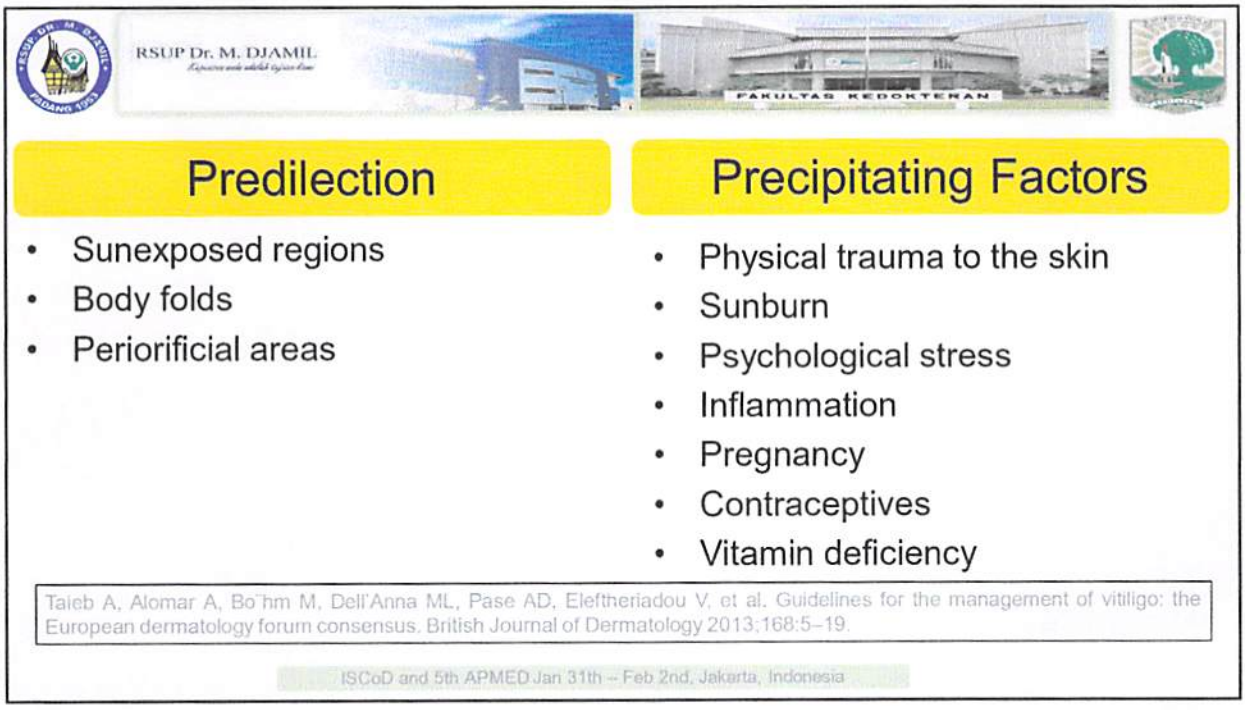
Vitiligo is acquired pigmentation disorder, characterized by **depigmented patches**, as a result of the **disappearance of functioning melanocytes from the epidermis,** commonly begins in **childhood or young adulthood**, with peak onset of 10–30 years, the **incidence decreases with increasing age.**

Yaghoobi R, Omidian M, Bagherani N. Vitiligo: A review of the published work. Journal of Dermatology 2011;38:419–31.

Pathogenesis

- Autoimmune destruction of melanocyte
- Defects of melanocyte adhesion
- Neurogenic damage
- Biochemical damage
- Autocytotoxicity
- and others

Taieb A, Alomar A, Bo¨hm M, Dell'Anna ML, Pase AD, Eleftheriadou V, et al. Guidelines for the management of vitiligo: the European dermatology forum consensus. British Journal of Dermatology 2013;168:5–19.



Predilection

- Sunexposed regions
- Body folds
- Periorificial areas

Precipitating Factors

- Physical trauma to the skin
- Sunburn
- Psychological stress
- Inflammation
- Pregnancy
- Contraceptives
- Vitamin deficiency

Taieb A, Alomar A, Bo¨hm M, Dell'Anna ML, Pase AD, Eleftheriadou V, et al. Guidelines for the management of vitiligo: the European dermatology forum consensus. British Journal of Dermatology 2013;168:5–19.

Main types of vitiligo according to Vitiligo Global Issues Consensus Conference (VGICC) classification

- **Vitiligo/non-segmental vitiligo (NSV)**
  - Generalized
  - Acrofacial
  - Universal
  - Mucosal
  - Mixed
- **Segmental vitiligo (SV)**

Katsambas AD, Nicolaidou E. Vitiligo Classification and Clinical Presentations. In E.B. Handog, M.J. Enriquez-Macarayo (eds.) *Melasma and Vitiligo in Brown Skin*. Springer India;2017.

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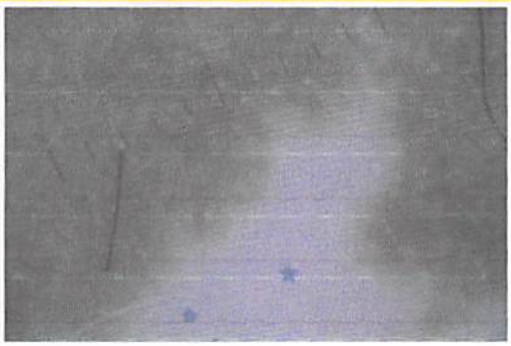
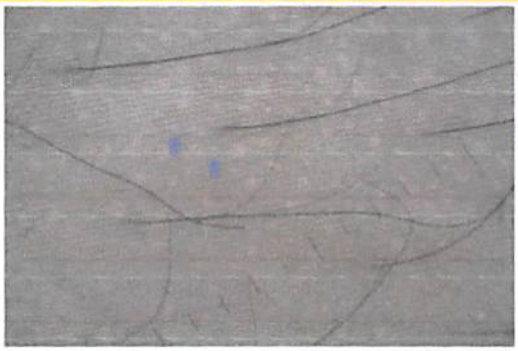
Dermoscopy



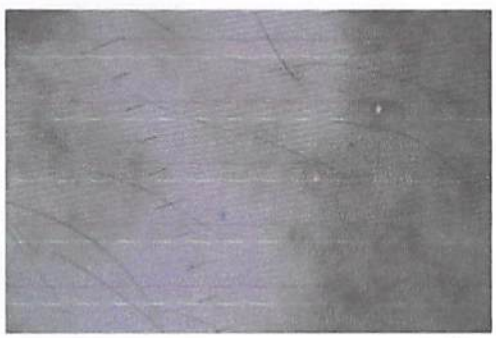
Dermoscopy of fully evolved vitiligo showing absence of pigment network (blue star), leukotrichia (blue arrow), and diffuse white glow.



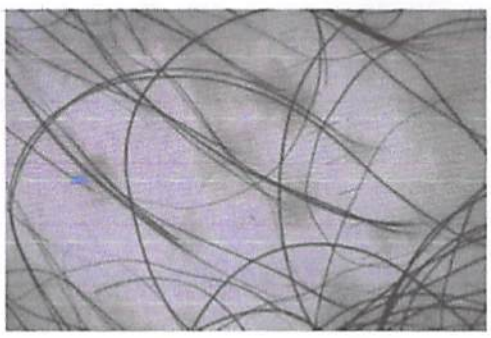
Dermoscopy of perilesional skin in unstable vitiligo showing tapioca or sago grain pattern (blue arrows).

RSUP Dr. M. DJAMIL

FAKULTAS KEDOKTERAN



Dermoscopy of unstable or progressive vitiligo showing a trichrome pattern. Depigmentation (blue star), hypopigmentation (orange star), and normal skin color (green star).



Dermoscopy of repigmenting or stable vitiligo showing perifollicular pigmentation and reticular pattern of pigmentation (blue arrow).

Chatterjee M, Neema S. Dermoscopy of Pigmentary Disorders in Brown Skin. Dermatol Clin. 2018;36:473–485

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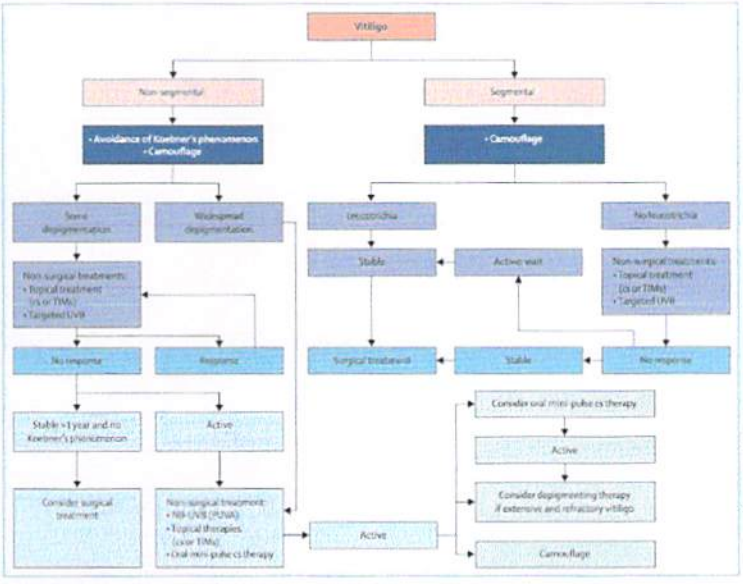
Therapeutic algorithm of vitiligo



Ezzedine K, Eleftheriadou V, Whitton M, Geel N. Vitiligo. The lancet. 2015:1-15,

Take home message

- The most important management is to identify the cause.
- A combination of conventional and newer treatments may work synergistically to provide additional improvement in patients' disease state and quality of life.

Thank you...

Thank you...

Terima kasih...

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