# Vitiligo in children

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***Background:*** **Vitiligo is an acquired depigmentary disorder affecting around 1% of the world's population. In 25% of cases it has its onset prior to the age of 14 years.**

***Data sources:*** **Articles on vitiligo in children published after 1995 were retrieved from PubMed. The prevalence, etiology, clinical presentation, differential diagnosis, treatment and management of vitiligo in children were summarized.**

***Results:*** **Vitiligo is characterized by acquired, sharply demarcated depigmented macules or patches on the skin, the mucous membranes and/or white hair and it is mainly differentiated from congenital achromic skin lesions. It is frequently associated with various autoimmune diseases. Hashimoto's thyroiditis is the most common association in children. Information on the nature, possible causes and course of the disease leads to acceptance of the disorder and higher compliance with the treatment. The choice of medical treatment depends on the type, location and duration of lesions as well as the eagerness of the child and his/her parents to pursue therapy.**

***Conclusion:*** **The management of childhood vitiligo includes information and reassurance of young patients and their parents on the disease, thyroid investigation, avoidance of trigger factors, topical treatment and proper follow-up.**

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## Introduction

Vitiligo is an acquired depigmentary disorder affecting around 1% of the world's population. Approximately 50% of the cases have the onset of their disease prior to the age of 20 years and 25% prior to the age of 14 years.[1,2] Vitiligo is characterized by selective destruction of melanocytes of the basal layer of the epidermis and/or occasionally the hair follicle resulting in white patches on the skin, the mucous membranes and/or white hair.

## Etiology

Various theories have been proposed for the etiology of vitiligo, including genetic, neural, autocytotoxic/metabolic and autoimmune theories, all of which have been encompassed in the convergence theory. It seems that vitiligo has a multifactorial etiology, where genetic factors, various kinds of stress (emotional stress, oxidative stress with the accumulation of free radicals), accumulation of toxic melanin precursors in melanocyte (e.g., DOPA dopachrome, 5, 6-dihydroxyindole), disturbance of melanocyte homeostasis (e.g., impaired intracellular and extracellular calcium), and autoimmunity can all contribute to the development of the disorder.[3-5]

Vitiligo is frequently associated with various organ specific autoimmune diseases, e.g., Hashimoto's thyroiditis, Addison's disease, diabetes mellitus type 1, and pernicious anemia.[3] Hashimoto's thyroiditis is the most common association in children. In a group of 54 Greek children and adolescents with known vitiligo, Hashimoto's thyroiditis was found to be 2.5 times and hypothyroidism 10 times more frequent than in a healthy age- and sex-matched population.[6] It must be noted that in only 2 out of 13 patients with vitiligo and Hashimoto's disease, thyroiditis with overt hypothyroidism preceded vitiligo by one year while in the remaining 11 patients Hashimoto's thyroiditis with subclinical hypothyroidism was revealed by laboratory investigation after the onset of vitiligo.[6] This finding is important as far as the management of children with vitiligo is concerned.

## Clinical presentation

Vitiligo is characterized by acquired, sharply demarcated

depigmented macules or patches that can appear anywhere on the skin though there is a predilection for orifices and bony prominences. The disease is classified according to the distribution and extent of depigmentation as follows:

Generalized vitiligo is the most common type in both children and adults and consists of scattered macules over the entire body, usually in a symmetrical distribution;

Acrofacial vitiligo affects facial orifices and distal fingers;

Segmental vitiligo occurs in a dermatomal or quasidermatomal region (It is more common in children than in adults. It tends to spread rapidly over the affected area, although activity usually ceases after a short period and the involvement of other body sites is unusual);

Focal vitiligo with one or more macules in the same area but not segmentally distributed;

Universal vitiligo is characterized by a complete or nearly complete depigmentation of the body (>80% of surface area).[1,3]

## Differential diagnosis

The diagnosis of vitiligo is based on the patient's history and clinical presentation. The doctors should keep in mind that vitiligo lesions are acquired, show complete depigmentation, and have well demarcated sometimes hyperpigmented borders and normal skin texture. The disease can be easily differentiated from achromic nevus (congenital lesion with irregular non-hyperpigmented borders), albinism or piebaldism (The lesions are present at birth and in piebaldism are usually confined to the head and upper trunk), morphea or lichen sclerosus (abnormal skin texture), and post infectious/post inflammatory hypopigmentation (e.g., tinea versicolor, varicella, pityriasis alba) where the lesions are hypopigmented rather than depigmented. It must be noted that examination under Wood's light is helpful in discriminating between partial versus complete depigmentation.

## Treatment

The goal of treatment is to suppress depigmentation and stimulate repigmentation. This is achieved by suppression of inflammation (e.g., topical corticosteroids, immunomodulators) or oxidation (e.g., vitamin D3 analogues, pseudocatalase) in early active lesions and/or stimulation of melanocyte division and migration (e.g., phototherapy [PUVA, narrowband UVB, 308 nm excimer laser, heliotherapy] and vitamin D3 analogues). It must be noted that the melanocytes that migrate into the basal layer of the depigmented skin come from contiguous pigmented skin (Melanocytes migrate about 2-3 mm into the depigmented skin) and from the hair follicle of the lesion.[7] Therefore, early small lesions have a better response to treatment than the long-standing larger ones. Besides, lesions on the face and neck respond better to treatment than those located on the trunk and especially on the distal extremities and bony prominences with a low density of hair follicles or without hair follicles. Since vitiligo skin is slow to respond to treatment, topical preparation should be applied for at least 4 months and ultraviolet light exposure continued for 6 months[8,9] prior to discontinuation for lack of response.

Studies showed that only 16%-36% of dermatologists actively treat vitiligo for a better recovery.[10,11] The following is a brief review of treatment of childhood vitiligo, suggesting that this is an unjustifiably pessimistic attitude toward the disease management.

### Topical corticosteroids

Among the various therapeutic regimens proposed for vitiligo the most widely prescribed treatment in children is the application of topical corticosteroids. A prospective study[12] showed that: a) 13 of 23 children (57%) with vitiligo (mean age: 7.9 years, mean duration of vitiligo 1.3 years) treated with a medium strength topical steroid (prednicarbate 0.25%) twice a day for at least four months had 50% or greater repigmentation to all involved skin areas and b) children with non-segmental vitiligo had a better response than those with segmental vitiligo (71.4% vs 33.3%). Topical corticosteroids, however, have local (e.g., atrophy, striae, telangiectasia) and systemic side-effects.[13]

### Calcineurin inhibitors

Following the introduction of topical immuno-modulators, several studies have shown their equal or near equal efficacy on topical corticosteroids.[14-18] In a retrospective study,[16] 57 children with vitiligo (mean age: 9.2 years; mean duration of vitiligo 2.9 years) were treated with 0.03% tacrolimus or 0.1% ointment once or twice daily for at least 3 months. As a result, ≥50% regimentation was achieved in 67% of patients with vitiligo on the head and neck including the segmental type and 41% of patients with vitiligo on the trunk/extremities. The authors noted that the overall response rates were not significantly different based on concentration and that the response to tacrolimus twice daily was greater than once daily. They concluded that tacrolimus ointment should be used as the treatment of choice for vitiligo of the head and neck, including segmental vitiligo, in pediatric patients and as an alternative to topical corticosteroids for patients with vitiligo involving the trunk and extremities.

### Vitamin D3 analogues

Vitamin D3 analogues have also been used effectively in the treatment of vitiligo as monotherapy[19] or combined with exposure to NB-UVB phototherapy,[20] sunlight[21] or topical corticosteroids.[22] A prospective study[22] of 12 children with vitiligo (mean age: 13.1 years) showed that 10 children had a mean of 95% repigmentation after a combined treatment of topical corticosteroids in the morning and calcipotriene ointment in the afternoon for an average of 4.5 months (range: 2-7 months). Since 4 of the 10 children had previously failed trials of topical corticosteroids alone, the combination of the two agents might be more efficacious than the use of topical corticosteroids as monotherapy.

### UV therapy

Narroband UVB (NB-UVB) phototherapy is considered as a safe and effective therapeutic option in the treatment of vitiligo in children. Studies[8,9,23,24] have shown that exposure to NB-UVB 2-3 times a week on nonconsecutive days for 6-12 months resulted in >75% repigmentation in at least 50%-75% of children. The response to treatment depends on the location, extent and duration of vitiligo as well as the duration of treatment. Children affected by recent vitiligo and/or with lesions located on the face and neck had a better response to the therapy.[8,9,23,24] Unlike NB-UVB phototherapy, the 308 nm excimer laser device delivers radiation to vitiligo skin only, so it is indicated for localized vitiligo.[25-27] Exposure to artificial UV light, however, is time-consuming and interferes with childhood activities including school attendance; it can lead to the loss of many school hours. Heliotherapy (exposure to natural UV light) is an alternative although care must be taken to avoid sunburns.[28] The common perception that vitiliginous skin is at increased risk for cancer from UV is not based on epidemiological studies. It seems that mechanisms other than that offered by melanin pigmentation, for example, the antioxidant status may also play a protective role.[29] Carefully controlled exposure to sunlight may therefore be beneficial.

### Pseudocatalase

Topically applied pseudocatalase PC-KUS activated by a low-dose NB-UVB phototherapy has recently been used in the treatment of vitiligo in children. Schallreuter et al[30] in a retrospective study of 71 children with vitiligo (mean age: 10.3 years) found that more than 75% repigmentation was achieved in 66 of the 71 children on the face/neck, 48 of 61 children on the trunk, and 40 of 55 children on the extremities after NB-UVB activated pseudocatalase daily treatment for 8-12 months. The total dose of NB-UVB per annum for each child was in the range of 42-60 mJ/cm$^2$, which is equivalent to approximately 5.6 hours of sun exposure per annum. The therapy had no side-effects.

## Management of vitiligo in children

After the diagnosis is established, information on the nature of the disease, treatment options, expected results and reassurance on the benign course of vitiligo leads to acceptance of the disorder and higher compliance with the treatment. Emotional stress may induce and/or exacerbate vitiligo and vice versa.[31] One of the most important goals in the management of vitiligo, therefore, is for the child to not loose his/her self-esteem and confidence. Young patients should be referred to a specialist for psychological support if necessary.

The medical record form includes the age, sex, personal and family history of thyroid disorder/autoimmune diseases, age at onset, potential precipitating events including emotional stress, physical illness, skin trauma occurring 2 to 3 months before the onset of pigment loss, duration, location, type, extent and activity of vitiligo as well as previously used treatments. The above parameters are important for the choice of therapy.

The percentage of depigmentation in relation to the total body surface is estimated by using the hand-palm rule, i.e., a lesion the size of the patient's palm equals 1% of his/her total body surface.[32] The activity of vitiligo is estimated by the vitiligo disease activity (VIDA) score which is a useful scoring system of the patient's own opinion of the present disease activity (Table).[32] Using the VIDA score, children are actively involved in the assessment and management of their disorder. Photographs are taken for all or some representative lesions.

Thyroid dysfunction is screened annually in all children with vitiligo. In the presence of positive antithyroid antibodies with normal thyroid function, thyroid ultrasonography is given by an experienced radiologist. If echographic findings are compatible with autoimmune thyroiditis, the patient is referred to an endocrinologist for monitoring and possible replacement therapy. In the presence of positive antithyroid antibodies and an elevated thyroid stimulating hormone level, confirmed by two tests four weeks apart, the patient is referred promptly to an endocrinologist for monitoring and therapy. These patients have the highest rates of

**Table.** Vitiligo disease activity (VIDA) score on a six-point scale[32]

| VIDA score | Disease activity |
|---|---|
| +4 | Active in the past 6 weeks |
| +3 | Active in the past 3 months |
| +2 | Active in the past 6 months |
| +1 | Active in the past year |
| 0 | Stable for at least one year |
| -1 | Spontaneous repigmentation |

Active: appearance of new lesions or expansion of existing lesions.

progression to overt hypothyroidism and L-thyroxine treatment should be started.[6]

Vitiligo lesions frequently appear at sites of microtraumas (Köbner phenomenon). Therefore, proper skin care and avoidance of microtraumas is of great importance. The choice of medical treatment depends on the type, location and duration of lesions as well as the eagerness of the child and his/her parents to pursue therapy.

In conclusion, vitiligo is not an uncommon disease in children and it is frequently associated with Hashimoto's thyroiditis. It can respond to therapy and this should, therefore, always be offered. Finally, appropriate information and psychological support of the patient and his/her parents is of utmost importance.

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