User:Sonia Kulycky/Drafts/Vitiligo (Disease)

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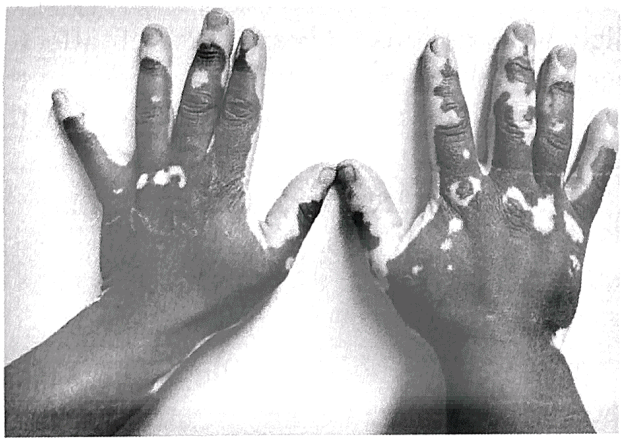
Vitiligo is a chronic, non-contagious autoimmune disease characterized by a selective loss of melanocytes, which results in hypopigmented or even white macules of variable shape and size on the skin or mucous membranes. These macules have clearly defined borders [1] [2] .



Vitiligo

Disease	
Features	
signs	Hypopigmented skin macules
Symptoms	
Differential diagnosis	Differential diagnosis
Information	
Speciality	Dermatology

? Unrevised page

1 Epidemiology

Vitiligo has an estimated prevalence of 0.5-2% at the global population level, with some regional variability [3] [4] . The severity of the disease is inversely proportional to the distance from the equator [3] . The majority of studies show a slightly increased prevalence in women [3] . About 50% of vitiligo cases present in childhood or adolescence [3] . Infantile vitiligo is associated with atopic diathesis, halo nevus, as well as a family history of vitiligo or other autoimmune diseases [3]. Vitiligo that develops after puberty is associated with acrofacial disease or diseases of

Summary

the thyroid gland, and some studies show a reduced risk of melanoma and other skin cancers [3] . Between 10-15% of patients with generalized vitiligo also have autoimmune diseases [1] , such as thyroid disease, anemia, certain endocrine diseases such as Addison's disease, and other skin diseases [1] .

2 Etiologies

Vitiligo is caused by the destruction and/or death of certain clustered melanocytes in the epidermis, which leads to the loss of melanin in the form of spots on the skin. Vitiligo is recognized as an autoimmune disease associated with metabolism and oxidative stress, cell detachment diseases, as well as hereditary diseases and environmental factors [5] .

3 Pathophysiology

Vitiligo develops from a coexistence of several factors such as genetic, immunological, and environmental factors [2] .

The 4 main theories are:

1 - Vitiligo is hereditary, and develops from mutated genes [6] .

Several epidemiological studies strongly suggest that vitiligo is hereditary. About 20% of affected patients report at least one affected first-degree family member. Several genes have been identified in the role of the development of vitiligo. Their mutation, over or under-activation can contribute to the development of vitiligo. Here are some examples [6] :

- FOXD3, when mutated, impairs melanoblast differentiation [6] .
- NLRP1 leads to the activation of the inflammatory response, especially in the skin, in response to certain triggers [6] .
- PDGFRA plays an essential role in the differentiation and survival of melanocytes during embryonic development as well as in the regulation of skin pigmentation [6] .
- HLA - this may not be specific to vitiligo [6] .
- XBP1 is a transcription factor. Its interaction with HLA-DR molecules can promote the development of vitiligo [6] .

2 - Some melanocytes are destroyed by the immune system for any reason [2] .

This can be explained by the presence of certain intrinsic abnormalities in certain melanocytes of patients with vitiligo [7] . Consequently, under IFN-γ stimulation, the affected melanocytes present their own antigens, which triggers the proliferation of T cells, and thus the adaptive response of lymphocytes [7] . This results in the apoptosis of the "diseased" melanocytes and the manifests by the de-pigmentation characteristic of the disease [7] .

melanocytes are destroyed by toxic substances produced during the normal formation of ..., or by physical stress. This in turn can cause the immune system to attack and destroy certain ...anocytes, as mentioned above [2].

These toxic substances are called free radicals, or reactive oxygen species (ROS, or ROS) which cause oxidative stress. An elevation in ROS can be explained by exposure of the skin to UV radiation, skin contact with certain cytotoxic chemical agents, trauma, pregnancy, or other physical stress [8].

Second, the production of melanin requires energy, ie large amounts of adenosine triphosphate (ATP). ATP biosynthesis produces a lot of ROS by mitochondria. This overproduction of ROS by the mitochondria can also contribute to the destruction of melanocytes [8].

Aside from overproduction of ROS, there may also be a lack of ROS housekeeping, such as a lack of the enzyme catalase, which normally assists in neutralizing ROS [9]. Deficiencies in vitamins A or C as well as glutathione peroxidase can also ~~be involved.~~ contribute to increase in ROS. (which also normally assist in neutralizing ROS)

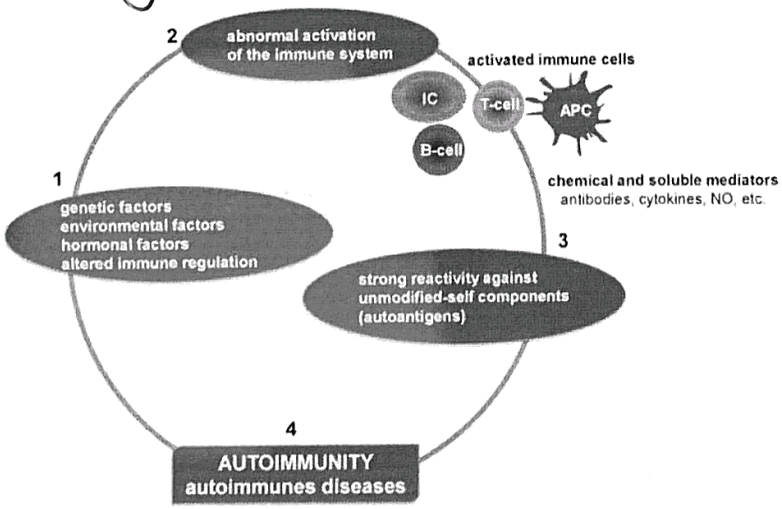
Finally, the production of ROS by the lesional skin of patients with vitiligo has been linked to an activation of adaptive immunity, especially CD8+ T lymphocytes via the JAK-STAT pathway [10].

4 - There may be an interaction between certain melanocytes and neurons, which could explain a subtype of vitiligo, segmental vitiligo [2].

This is possibly explained by the fact that melanocytes have the same embryological origin as neurons [11]

clearly in science

explaining short segmental



4 Clinical presentation

The classic presentation of vitiligo is as follows:

- **Hypopigmented skin** macules, ~~see white~~, with a diameter between 5mm and 5cm or more, of variable shape [2].
- One or more macules in a single place (localized type), or several macules on several areas of the body (generalized type) [2].

well demarcated

lost patchy

or depigmented (white)

- These macules can be found anywhere on the body, most often on the face, armpits, knees, and feet as well as the parts of the body most exposed to the sun [2] [12] .
- It is possible to find premature gray or white hairs in the center of the macules [2] [12] .
- Conversely, the follicles that are found in the center of the macules may remain pigmented, which means partial re-pigmentation [2] .

There are 2 forms of vitiligo: **generalized** and **localized.**

Generalized vitiligo can be divided into 3 subtypes:

1) *Common* : macules are found around the eyes, mouth, armpits, elbows, on the fingers and backs of the hands, on the genitals, knees, on the backs of the feet/ankles, and/or toes [1] .

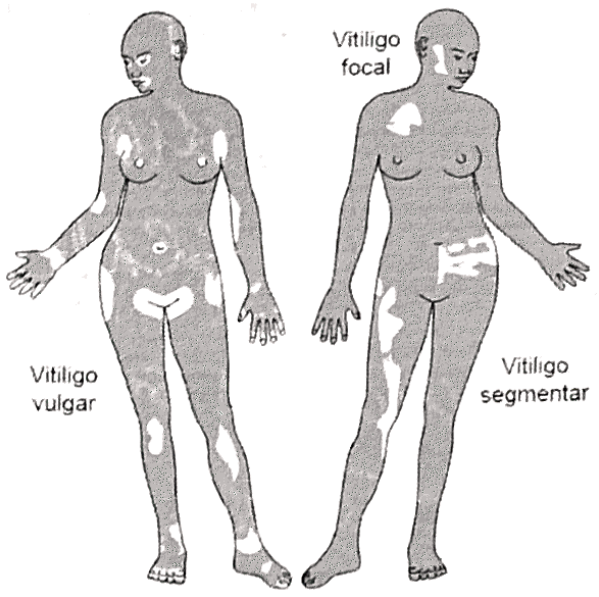
2) *Acrofacial* : the macules are located around the eyes and the mouth, as well as on the hands and feet [1] .

3) *Universal:* the body is almost, or completely amelanic with only a few pigmented regions remaining [1] .

The localized form is divided into 2 subtypes:

1) *Focal* : de-pigmented macules are found in one or a few areas only [1] .

2) *Segmental* : the macules are found on only one side of the body (unilateral), and do not ~~exceed~~ the midline [1] .

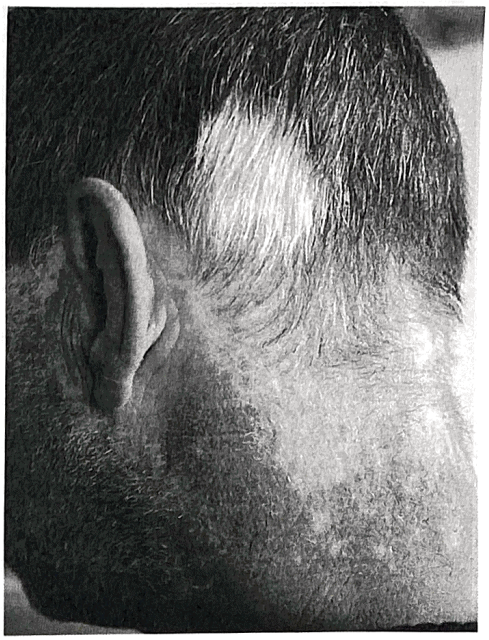


4.1 Risk factors

Since the pathogenesis of vitiligo is so complex and multifactorial, total prevention of vitiligo is not possible. There are, however, a few established risk factors:

- Skin contact with certain occupational chemicals such as tertiary 4-butyl phenol [2] .
- Family history of vitiligo [2] .
- Sometimes associated with certain autoimmune diseases such as thyroid, diabetes, anemia, lupus, Sjogren's syndrome, dermatomyositis, scleroderma, alopecia areata, inflammatory bowel disease,

tain endocrine diseases [2] [13] . * *It would be relevant investigate the possibility of the concomitant existence of these diseases according to the clinical judgment of the professional and the clinical presentation of the patient.*



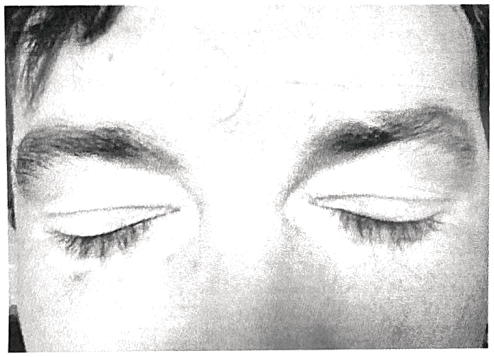
Loss of pigment from hair growing in the center of a de-pigmented site.

4.2 Clinical examination

A dermatological examination ~~will help to objectify~~ the following information:

- The location and distribution of macules [1] to help identify the subtype of the disease
- The degree of depigmentation of macules: hypopigmentation? Total depigmentation? [1]
- The size of macules [2]
- The presence or absence of inflammation [1]
- The stability of macules: do they grow or increase in number over time? Does the skin appearance remain stable over time? [1]
- The pigmentation of the hairs inside the plaques or macules [1]

It is advisable to perform this examination using Wood's lamp, especially in ~~paler~~ skin [1] . This will help visualize the contrast between affected and unaffected skin [1] . It would also be relevant to ask the patient the time of onset and the circumstances of onset. [1]



The Mandatory *Clinical Examination* section does not currently contain any information.

Any input would be appreciated.

Description:	This section discusses the signs to look for during the physical examination.
Sizes:	Bulleted list
Semantic tags:	Clinical examination , Clinical sign
Comments:	[display]
Example:	[display]

5 Paraclinical examinations

Paraclinical examinations are not always necessary for vitiligo, but the following are some possibilities:

- Blood sample to look for auto-antibodies that could demonstrate the presence of other autoimmune diseases [14] .

- TSH test to look for thyroid disease that may exist with vitiligo.
- Complete blood count and B12 assay to ~~look~~ for anemia as the cause.
- Biopsy to differentiate from certain other skin lesions such as onchocerciasis, or if there is prese of inflammation or sclerosis [1]

The mandatory section *Paraclinical examinations* does not currently contain any information.

Any input would be appreciated.

Description:	This section concerns the tests to order when the disease is suspected and the results expected in the presence of the disease.
Sizes:	Bulleted List, Table
Semantic tags:	Paraclinical examination , Paraclinical sign
Comments:	[display]
Example:	[display]

6 Clinical approach

It is very important to consider the psychological impact of vitiligo because it is a disease that can cause a loss of self-confidence in some patients [2] [15] . It would therefore be relevant to screen for depression, and even suicidal thoughts (which is rare), and to refer patients to support groups, or refer to a psychologist/psychiatrist if necessary.

Depending on the patient's clinical presentation, it could also be relevant to exclude the presence of other autoimmune diseases that sometimes present with vitiligo so as not to miss a serious and/or treatable diagnosis.

Finally, it is important to ~~reiterate~~ emphasize the importance of sun protection, ~~therefore the daily~~ wearing of sunscreen, ~~and~~ clothing ~~covering the skin. This is essential for any patient.~~

7 Differential diagnosis

There are a few differential diagnoses that may resemble vitiligo [1] :

- Depigmented nevus
- Halo-nevus (children)
- Piebaldism (children)
- Waardenburg syndrome (children)
- Albinism
- Chemical leucoderma
- Leucoderma associated with melanoma
- Scleroderma leucoderma
- Vogt-Koyanagi-Harada syndrome
- Onchocerciasis

Sun exposure may increase the risk of photo damage and skin cancer in hypo- or depigmented skin. Tanning of normal skin can increase the contrast with the lighter vitiligo spots. For these reasons

The mandatory *Differential Diagnosis* section does not currently contain any information.

Any input would be appreciated.

Description:	This section deals with the differential diagnosis of the disease, that is to say the other diagnoses to be considered when confronted with this diagnosis.
Sizes:	Bulleted list
Semantic tags:	Differential diagnosis
Comments:	[display]
Example:	[display]

The differential diagnosis of the disease is:

- differential diagnosis 1
- differential diagnosis 2
- differential diagnosis 3
- ...

8 ~~Processing~~ management

The treatment is aimed at partial or complete re-pigmentation of the skin, but there is no treatment that cures vitiligo definitively. Efficacy is influenced by the following factors [1] :

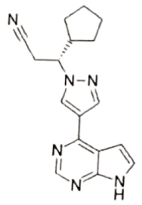
- Location: hairy areas are more likely to re-pigment versus hairless areas such as the mucous membranes, palms of the hands, soles of the feet, etc. [1] .
- Extent of disease: less expansive involvement is more successful than widespread involvement [1] .
- Stability: stable vitiligo that progresses little or not over time is more likely to re-pigment versus active vitiligo that progresses [1] .
- Pigmentation of hairs in macules: Presence of pigmented hairs is desirable for effective re-pigmentation [1] .

First-line treatments	**Topical treatments** (alone or in combination) ▪ Corticosteroids [12] [1] ▪ Vitamin D3 analogues [12] [1] (*in combination with another treatment)* ▪ Calcineurin inhibitors [12] [1] ▪ Self-tanning makeup (cosmetic camouflage) [16]
2nd line treatments	**Phototherapy** ▪ Narrowband UVB for example [12] [1]
Third-line treatments	**Surgery** (*only if vitiligo has been stable for 6 months and no Koebner phenomenon (https://dermnetnz.org/topics/the-koebner-phenomenon)*) ▪ Skin grafts [1] ▪ Suspension melanocyte transplantation [1]

Emergence of JAK inhibitors (JAKis)

Several new studies demonstrate the effectiveness of JAK inhibitors for the treatment of vitiligo. JAK/STAT pathway is implicated in several autoimmune diseases and its inhibition is increasingly (JAKis) as a treatment [17] [12] . JAK inhibitors block IFN-γ signaling, which helps with repigmentation [17] Ruxolitinib also inhibits the differentiation and migration of dendritic cells, thereby lowering the activation of CD8+ cells that participate in the pathogenesis of vitiligo. [17]Topical formulations demonstrate greater efficacy due to targeted delivery leading to greater concentration of the drug in the epidermis and dermis without the systemic adverse effects that can occur with the *per os formulation* [17] . According to the results of the ~~new~~ recent clinical trials, ruxolitinib caused significant re-pigmentation in the patient-subjects [17] . With the emergence of more and more clinical trials, JAK inhibitors could eventually become a treatment of choice for vitiligo.

The JAKs



The mandatory *Treatment* section does not currently contain any information.

Any input would be appreciated.

Description:	This section describes the treatment of the disease.
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Semantic tags:	Treatment , Pharmacological treatment
Comments:	[display]
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Additional pages

- Exercise program 1

Suggested treatments are:

- **exercise program** 1
  - Example of recommendation. [B, 2]
- non-pharmacological treatment **2**
- **Drug 80 mg PO TID x 7d**
- lack **of intervention**under the following circumstances...
- ...

9 Complications

Vitiligo usually does not cause complications in itself. However, a worrisome complication is the possibility of psychological distress as previously mentioned. On the other hand, with prompt support and appropriate follow-up, this can be managed very well.

10 Evolution