Definition of Vitiligo

Vitiligo is an acquired pigmentary disorder of the skin in which the pigment cells of the skin (melanocytes), mucous membranes, and sometimes the hair are affected. Symptoms and signs of vitiligo include a focal or disseminated depigmentation and hypopigmentation of the skin (white patches). For this reason, it is also known as leukoderma.

It is a progressive disorder in which some or all of the melanocytes in the affected skin are selectively destroyed. The usual type of vitiligo is called ‘Vitiligo Vulgaris’ (means: common vitiligo). Variant types include linear, segmental, trichrome and inflammatory vitiligo.

While vitiligo may be more obvious in patients with darker skin, this disorder does not have a racial or ethnic predilection. It is an acquired pigmentary disorder of the skin.
condition is frequently associated with disorders of autoimmune origin, with thyroid abnormalities being the most common.

Melanocytes are destroyed in the process of focal apoptosis. There is no resultant structural or functional loss of the affected areas of the body.

Epidemiology of Vitiligo

Vitiligo is not infectious, and it equally affects males and females without racial, ethnic or socio-economic predilections. However, it is more common before the age of 20 in more than 50% of the time. The worldwide prevalence of this disease is 0.5 %, and in India, it rises in some regions up to 10-20%.

Note: The substantial psychological and social consequences of this condition are often underestimated!

Patterns / Classification of Vitiligo

Types of vitiligo can be differentiated by their clinical distribution and localization.

1) Non-segmental vitiligo (NSV)

NSV includes the generalized, acrofacial or acral, mucosal, and universal subtypes. Generalized and acral or acrofacial vitiligo are most common.

Generalized: characterized by bilateral, often symmetrical, depigmented macules or patches occurring in a random distribution over multiple areas of the body surface. Generalized vitiligo may begin in childhood or early adulthood and often occurs at sites subjected to pressure, friction, and/or trauma. Depigmented patches are common on the face, trunk, and extremities.

Acral or acrofacial: consists of depigmented macules confined to the distal extremities and/or the face. It may later include other body sites, resulting in typical generalized vitiligo.
Mucosal: typically involves the oral and/or genital mucosa. It may occur in the context of generalized vitiligo or as an isolated manifestation. Isolated mucosal vitiligo that has not changed its characteristics after at least two years is defined as an undetermined or unclassified type.

Universal: complete or nearly complete depigmentation of the skin. Some skin areas and hairs may be partially spared. Universal vitiligo usually results from progression of generalized vitiligo.

2) Segmental vitiligo

- Unilateral, asymmetric distribution of white macules that match a cutaneous segment (dermatomal distribution)
- Monosegmental is most common
- Early age of onset, during childhood
- Rapid stabilization

3) Mixed:

- Combination of nonsegmental and segmental vitiligo

Pathogenesis of Vitiligo
Although several theories have been proposed regarding the pathogenesis of loss of epidermal melanocytes in vitiligo, still the precise cause is not known. The frequent association of the disease with other several autoimmune diseases would suggest possible HLA associations in vitiligo, such as: A2, DR4, DR7, and Cw6. The most convincing evidence of autoimmune pathogenesis is the demonstration of circulating autoantibodies in patients with vitiligo.

Autoimmune diseases that well established in association with vitiligo are:

- Thyroid disorders, particularly Hashimoto thyroiditis and Graves disease.
- Endocrinopathies such as Addison disease and diabetes mellitus.
- Alopecia areata
- Pernicious anemia

**Cellular immune theory:**

Melanocytes destruction can be directly mediated by autoreactive cytologic T-cells. An increased number of CD8 cytotoxic lymphocytes reactive to MelanA/Mart1 (melanoma antigen recognized by T cells), tyrosinase and glycoprotein 100 has been seen in patients with vitiligo.

**Oxidant stress theory:**

Oxidant stress theory suggests that the accumulation of free radicals are toxic to the melanocytes and may lead to their destruction.

A further possible cause is metabolic genesis. Due to defective tetrahydrobiopterin and catalase activity, oxidative processes are disrupted and oxidative stress occurs. Neurogenic processes also appear to play a role. In this case, stress-induced mediators
could be responsible for the activation of the immune system. 
The primary manifestation of the disease often occurs after strong UV exposure or mechanical skin damage.

**Note:** Vitiligo is often associated with other autoimmune diseases such as: alopecia areata, hashimoto thyroiditis, or diabetes mellitus!

### Symptoms of Vitiligo

Vitiligo signs include:

- The lesions are depigmented, sharp and there is irregularly circumscribed maculae.
- Vitiligo lesion are usually white, well-demarcated, round, oval, or linear in shape with convex borders in range from millimeters to centimeters in size.
- It enlarges centrifugally over time at an unpredictable rate.
- Initial lesions occur most frequently on the hands, forearms, feet, and face, favoring a perioral and periocular distribution.
- Poliosis (depigmentation or whitening of the hair) can occur.
- Follicular repigmentation occurs by spreading from the periphery.

**Note:** The Koebner phenomenon (also called isomorphic response) can occur due to mechanical irritations!

Vitiligo is either chronic and progressive, or it can manifest in periodic exacerbations. In rare cases, spontaneous remission can occur.

### Diagnosis of Vitiligo

- Vitiligo is a clinical diagnosis.
- The histology is unremarkable, with the exception of the lack of melanocytes.
- **Wood’s lamp** (364 nm) displays a white fluorescence of the hypopigmented maculae.
- Other autoimmune diseases should be ruled out in the diagnosis.

### Differential Diagnosis of Vitiligo

- Mycosis fungoides
- Albinism
- Leprosy
- Pityriasis versicolor

### Treatment of Vitiligo

Spontaneous remission is possible; however, it is uncommon. Typically, vitiligo is managed using phototherapy. This is then combined with other measures that can strengthen the melanogenic effect.

### Phototherapy
Psoralen has a photosensitizing effect. Before UV radiation, psoralen is either taken orally or applied topically. In a PUVA water bath, the patient lies in a bathtub filled with water containing psoralen. Radiation follows after immersion in the bath.

**Local Treatments**

Topical glucocorticoids are used for local treatment. These dermocorticoids have an anti-inflammatory and an immunosuppressive effect. Undesirable side effects include atrophy of the skin, telangiectasias, and intolerance reactions. For these reasons, topical glucocorticoids should not be applied extensively or for longer duration.

Tacrolimus and Pimecrolimus are topical calcineurin inhibitors. They are classified as immune modulators as they inhibit the activation and proliferation of T-cells. It should be taken into account that in the United States, these calcineurin inhibitors are only indicated for the treatment of atopic dermatitis, and the US Food and Drug Administration issued a **black box warning** for Tacrolimus and Pimecrolimus in 2005/2006, warning about a possible risk of cancer. Many scientific studies, however, dispute this fact and show very promising treatment results.

Vitamin D analogs such as calcipotriol also have an anti-inflammatory effect. In addition, they promote the differentiation of normal skin. The prescribed dosages should not be exceeded as this could lead to the development of systemic side effects such as hypercalcemia.

Laser therapy are effective on limited, stable patches of vitiligo. Depigmentation therapy may be indicated in carefully selected patients. Tattooing can be used in dark-skinned individuals to regiment the depigmented skin.

Excimer laser is combined with topical tacrolimus and corticosteroids in the treatment of segmental vitiligo. Also, the use of khellin 4% ointment in combined with monochromatic excimer light (MEL) at 308 nm is useful in providing valid therapeutic results in the treatment of vitiligo.

**Systemic treatments**

Glucocorticoids have an immunosuppressive effect. Oral administration of glucocorticoids can be used for short term therapy. Long-term treatment of this type is not recommended due to the side effects.

**Supporting measures**

Areas affected by vitiligo should be rigorously protected from sunlight. The skin is very
sensitive due to the lack of pigment. Vitamin D supplements should be taken, as a deficiency can occur due to a lack of exposure to natural sunlight.

Camouflage is a cosmetic concealer for the affected areas. It mimics the color of healthy skin. Additionally, self-tanning lotions may be utilized for a better cosmetic result. In extremely advanced cases of generalized vitiligo, depigmentation using bleaching agents can be considered.

Other treatments

In autologous melanocyte transplantation, pigment cells are harvested from the patient and re-implanted. These melanocytes are cultivated in vitro for several weeks. The epidermis of the areas affected by vitiligo is removed using laser. The colonies of cultured melanocytes are then applied on the skin.

Depigmentation therapy can be done using monobenzyl ether of hydroquinone, especially in very severe cases where patients have few areas of normal skin pigmentation. The depigmented areas must be protected aggressively to avoid spotty repigmentation.

Surgery

The basic types of repigmentation surgery include the following:

- Non-cultured epidermal suspensions
- Thin dermoeipidermal grafts
- Suction epidermal grafting
- Punch minigrafting
- Cultured epidermis with melanocytes or cultured melanocyte suspensions

Overview of treatment options

1. **Phototherapy**: UV-B 311 nm, Excimer laser, PUVA, KUVA
2. **Local Treatment**: Glucocorticoids, calcineurin inhibitors, vitamin-D analogs
3. **Systemic Treatment**:
   Glucocorticoids can be applied as short-term treatment.
4. **Supporting Measures**: UV protection and cosmetic treatments such as Camouflage
5. **Other Treatments**: Melanocyte transplants (very costly), split-skin graft

Prognosis

To this day, there is no cure for vitiligo. Treatment options can positively influence its development and possibly lead to repigmentation. In any case, sufficient protection from sunlight is necessary to prevent malignant skin diseases.

Review Questions

Solutions can be found below the references.

1. **At what age does vitiligo present itself in half of all cases?**
   A. At adolescence.
   B. Between 1 and 6 years old.
C. From the age of 50.
D. From birth onwards.
E. From the age of 60.

2. Which is the most common form of vitiligo?
   A. Localized vitiligo
   B. Acrofacial vitiligo
   C. Universal vitiligo
   D. Vitiligo vulgaris
   E. Segmental vitiligo

3. How can hypopigmented maculae be visualized during diagnosis?
   A. UV B 311nm
   B. Dermatoscope
   C. PUVA
   D. Wood’s lamp
   E. Contrast media

Patients frequently ask

What causes vitiligo?

The cause of vitiligo is not known. It can be assumed that this condition is an autoimmune reaction (melanocytes are either temporarily or permanently destroyed). Another possible cause of vitiligo is metabolic genesis. Neurogenic processes, if stress-induced mediators activate the immune system, also appear to play a role.

Is there a cure for vitiligo?

Vitiligo can be treated using steroids, calcineurin inhibitors, and narrow-band ultraviolet. The choice has to be based on a specific individual who needs to understand the risks associated with each type of treatment. Lighter skinned people may protect themselves from destructive rays of the sun and with time vitiligo may heal on its own in some patients.

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Correct answers: 1A, 2D, 3D

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