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Vitiligo updates: Pathophysiology, diagnosis and stability evaluation

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Abstract
Skin patches with reduced pigmentation are the hallmark of the acquired idiopathic illness vitiligo. Vitiligo was present in 0.5% to 2% of the world's population, with an increase reaching 1.22% in Egypt. The loss of melanocytes, which produce the melanin pigment in the skin, hair, mucous membranes, and retina, leads to skin depigmentation in this illness.
Numerous hypotheses contend that genetics, environmental factors, and autoimmune play a part in the development of vitiligo. Other autoimmune diseases including thyroiditis, rheumatoid arthritis (RA), and diabetes mellitus are also linked to vitiligo. Vitiligo's aetiology may be influenced by the imbalance of the innate and adaptive immune systems.

Keywords: Polythene utilization, adults

Introduction
Due to the gradual loss of functional melanocytes in the epidermis over time, vitiligo is an acquired, multifactorial, depigmenting condition that manifests as confined white macules on the skin [1, 2].

Prevalence of vitiligo
About 1% of the world's population suffers with vitiligo, which has no preference for any race or sexual orientation [3, 4]. In Egypt, the reported prevalence is 1.22% in the overall population [5].
The age during which vitiligo first emerges varies. Although it can show up at any age, vitiligo often starts in childhood or young adulthood and peaks between the ages of 10 and 30. Nearly half of vitiligo sufferers acquire the ailment before age 20 [6].
Vitiligo has an unpredictable, yet often progressive, course. Few people (10–20%), mostly youngsters, may experience spontaneous regimentation, however it usually only affects a portion of the body's exposed skin [7].

Pathogenesis of vitiligo
A complex illness, vitiligo is influenced by both hereditary and non-genetic causes. It seems that the aetiology of vitiligo may differ across patients as a consequence of the observed variance in the disease's manifestations [8].
The vast majority of vitiligo sufferers blame certain life events (physical damage, sunburn, mental harm, sickness, or pregnancy) for the disease's start [9].
Some medications, including infliximab, anticonvulsants (carbamazepine), antimalarials (Chloroquine and quinine), Parkinson's disease medications (levodopa), external alopecia medications (Diphencyprone), and other medications (clofazimine, dopamine, hydroquinone monobenzylether ester, ganciclovir, and beta blockers), have been linked to the development of vitiligo [10].
To shed light on the cause of vitiligo, several theories have been put out, including those relating to genetics, cytology, immunity, neurological issues, inadequate antioxidative defence, and environmental melanocyte death [11]. But there is substantial evidence that vitiligo is primarily an autoimmune condition [12].

Autoimmune hypothesis

- The cellular and humoral aspects of the innate and adaptive immune systems are involved in generalized vitiligo, which is usually regarded as an autoimmune disease. The following proof reinforces up this assertion:
- Similar to other autoimmune illnesses, it has a chronic relapsing-and-remitting course [13].
- The potential outcome of immunosuppressive treatments such as UV phototherapy, topical and oral corticosteroids, and topical calcineurin inhibitors [14].
- T cell infiltration and circulating anti-melanocyte antibodies in perilesional skin [15].
- A connection to other autoimmune illnesses, such as systemic lupus erythematosus [20], autoimmune thyroid diseases [16], alopecia areata [17], Addison's disease [18], psoriasis, and insulin-dependent diabetic mellitus [19].

A. Innate immunity

Vitiligo patients' skin exhibits abnormal innate immune cell activation, which involves the recruitment of natural killer cells and inflammatory dendritic cells [21].

Additionally, cytokines generated by innate immune cells such as IL-1, IL-6, and IL-8 constitute the initial signal to attract and activate autoreactive T cells, which then directly destroy melanocytes [22]. Dendritic cells transport and deliver melanocyte-specific antigens to T cells (22). Monocytes generate the proinflammatory cytokines IL-6 and IL-8, were found to be increased in lesional vitiliginous skin. IL-6 and IL-8 can induce macrophages migration and they also cause B-cell activation [23].

B. Adaptive immunity

1. Humoral immunity

Specific autoantibodies and antigens

Anti-tyrosine hydroxylase (TH), anti-melanin-concentrating hormone receptor 1, and anti-tyrosinase-related protein 1 (TRP1) antibodies have all been identified in the blood of vitiligo patients [24]. Additionally, vitiligo activity and autoantibody levels are correlated [25]. Additionally, the presence of B-cell infiltration next to depigmented zones lends credence to the theory that a humoral mediator mediates the autoimmune phenomena [26].

Although IgA anti-melanocyte antibodies have also been found, these anti-melanocyte antibodies are of the immunoglobulin G (IgG) class [27], which includes the subclasses IgG1, IgG2, and IgG3 [28-29]. Melanocytes are the preferred site of expression for the 35 and 90 kDa proteins [30]. Other researchers have found melanocyte-specific vitiligo antibody targets at 45, 65, 70, 88, and 110 kDa [31].

Non-Specific autoantibodies and antigens

Antibodies in vitiligo patients are typically directed to antigens with molecular weights of 35, 40–45, 75, 90, and 150 kDa, which are located on the cell surface, according to immunoprecipitation investigations utilising melanocyte protein extracts [32]. These proteins, which range in size from 40 to 45 kDa to 75 and 150 kDa, appear to represent widespread tissue antigens [30]. Patients with vitiligo may have a wide range of circulating organ-specific antibodies, such as thyroid gland antibodies [33]. It was established that six thyroid conditions had varying degrees of occurrence in vitiligo. Subclinical hypothyroidism had the highest frequency, while Graves' illness or subclinical hyperthyroidism had the lowest prevalence [34]. Additionally, it was revealed that some individuals with vitiligo had anti-thyroid peroxidase and anti-thyroglobulin antibodies that were positive. The researchers came to the conclusion that thyroid dysfunction testing should be done on vitiligo patients [35].

Cell-mediated immunity

Inflammatory infiltrates in the skin of perilesional vitiligo patients show cell-mediated immunity in this condition (36) and autoreactive CD8+ T lymphocytes may directly cause melanocyte death [37].

Compared to stable vitiligo, lesional, marginal, and nonlesional active vitiligo skin have more CD4+ and CD8+ cells [38].

T cytotoxic cell participation

Patients with vitiligo have higher levels of cytotoxic CD8+ T lymphocytes that are autoreactive to melanocytes in both their blood and skin, and these cells may be detected entering the epidermis in the afflicted skin. In fact, the severity of the illness is correlated with the level of CD8+ cellular infiltration [39].

Through particular antigens made up of melanogenic pathway proteins including gp-100, MART-1, tyrosinase and tyrosinase related proteins 1 and 2, epidermal melanocytes have been identified as the autoimmune cellular targets [40].

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Patients' blood levels of IFN-induced chemokines such CXCL9 are said to have risen [44]. One of the chemokines that draws cytotoxic T lymphocytes to the epidermis' melanocytes is CXCL9 [45].

Furthermore, the IFN-induced chemokine CXCL10 and its receptor CXCR3, which are found on autoreactive CD8+ T cells in the blood and lesional skin of vitiligo patients, appear to be essential for T cell recruitment in vitiligo [46].

T helper cell participation

It has been demonstrated that naive CD4+ T cells may divide into the Th1, Th2, Th17, and regulatory T cells (Tregs) cell types. IFN and TNF are mostly produced by Th1 cells, whereas IL-4, IL-5, and IL-13 are made by Th2 cells, IL-17, IL-22, and IL-6 are made by Th17 cells, and IL-10 and TGF- (transforming growth factor-) are made by T regs [47].

Follicular Helper CD4+ T (TFH) cells are specialised B cell suppliers that support the generation of antibodies and have been demonstrated to be crucial in the development of auto-immune illnesses such systemic lupus disease. Patients with active vitiligo had more active TFH cells than stable patients or healthy controls. Vitiligo sera had higher levels of IL-21, which is primarily generated by TFH cells and is positively linked with disease activity [48].

T regulatory cell participation

T regulatory cells (Tregs) are crucial in the avoidance and handling of illness. Patients who lack Tregs and have immunological polyendocrinopathy or X-linked disease are more likely to develop vitiligo [49].

Tregs are crucial for deleting self-reactive T cells that have eluded the thymus' clonal deletion process [50].

In cases with active vitiligo, Treg function is diminished. Patients with active vitiligo had lower levels of TGF-1 generated by Tregs than do those with stable disease [51]. Additionally, Treg function may be hampered by the elevated levels of IL-6 detected in lesional vitiliginous skin, which might activate the immune response against melanocytes farther from the initial afflicted locations [52].

Healthy patients' melanocyte-specific autoreactive CD8+ T cells display a profile that implies continuing Treg-mediated regulation, but the cells from vitiligo patients seem more activated and lack this feature [53].

Oxidative stress hypothesis

Reactive oxygen species (ROS) levels are enhanced in cultivated cells *in vitro* and in both lesional and non-lesional skin, which is evidence of the melanocytes' heightened oxidative stress in vitiligo [54].

Highly reactive oxygen free radicals, or ROS, are produced by a variety of processes, including as cellular metabolism normally, other enzymatic activities, disruption of ER homeostasis, inflammatory cytokines, environmental toxins, and light or ionising radiation [55].

Patients with active vitiligo have peripheral blood mononuclear cells that produce more reactive oxygen species (ROS) and have diminished antioxidant defences, including elevated superoxide dismutase activity, decreased catalase activity, and decreased vitamin E levels. This imbalance makes melanocytes more vulnerable to oxidative stress, which results in cellular death [56]. Additionally, there is an increase in cholesterol and a decrease in cardiolipin (CL) in the mitochondrial inner membrane [57].

Additionally, it has been proposed that elevated ROS and high levels of cellular stress are what initially activate the innate immune system in vitiligo [58].

Neural hypothesis

Melanocytes are neural crest-derived cells having a connection to the neurological system throughout development. According to neural hypothesis, the neurochemical mediators released by nerve terminals, such as acetylcholine, are toxic to melanocytes and cause their demise. Thus, cholinergic sympathetic nerve dysfunction may be related to segmental vitiligo [59-60].

In addition, lesional segmental vitiligo skin showed physiologic abnormalities linked to sympathetic nerve function such as acetylcholine activity, neuropeptide distribution, and catecholamine metabolism [61]. Segmental vitiligo lesions also appeared in areas corresponding to local neurologic damage such as subacute encephalitis, spinal cord tumours, or following trauma [61].

There may be a connection between stress and the formation of vitiligo since generalised vitiligo typically appears after emotional stress, anxiety, depression, adjustment difficulties, and obsessive symptoms [62, 63]. These stresses cause the condition by producing high levels of neuropeptides like Neuropeptide Y (NPY). A diverse array of soluble substances called neuropeptides (NPs) and neurotransmitters connect the immunological, neuroendocrine, and endocrine systems [64].

Genetic hypothesis

The polygenic pattern of vitiligo inheritance implies that numerous alleles contribute to the genetic risk for illness. The majority of the discovered genes produce proteins that are involved in melanocyte development, apoptosis, and immune control [65].

Numerous studies have found that 6.25-38% of individuals with vitiligo had a favourable family history [22], with a concordance rate of 23% in monozygotic twins [66].

About 50 susceptibility loci encoding for immune system components have been discovered through genome-wide association analyses. These loci demonstrate that the immune system plays a significant role in the pathogenesis of vitiligo by involving both the innate immune system (NLRP1, CASP7, C1QTNF6, TRIF) and the adaptive immune system (FOXP3, BACH2, CCR6, PTPN22, HLA class I and II) [67].

Environmental hypothesis

The presence of mono benzyl ether of hydroquinone in factory workers' gloves caused depigmentation on their hands and in remote areas, which was the first environmental exposure linked to vitiligo. A second "outbreak" of vitiligo cases (16,000 cases) was reported in the summer of 2013 in Japan and was subsequently attributed to the use of skin-lightening products that contained rhododendron as the activator [68].

All of these substances have the property of being phenols, which have benzene rings with hydroxyl groups attached that resemble the amino acid tyrosine. They function as tyrosine analogues, interfering with the manufacture of melanin and the tyrosinase enzyme, stressing melanocytes, and causing the release of inflammatory factors that trigger an autoimmune assault on the melanocytes. Additionally, vitiligo melanocytes are far more susceptible to phenolic compounds than normal melanocytes are, and when exposed to these chemicals, they readily undergo apoptosis [69].

In India, a crimson dye solution known as Alta (henna) is applied to the feet to colour them cosmetically. The dye has been known to cause vitiligo where it was applied, contact dermatitis preceding depigmentation, and distant depigmentation on the hand [70-72].

Melanocytorrhagy hypothesis

It is a belief that vitiligo is brought on by the persistent detachment and transepidermal loss of melanocytes, which may be connected to melanocytes' higher vulnerability to mechanical and other local stresses [73]. About half of vitiligo patients experience mechanical stress and related koebnerization [74].

Before clinical lesions manifest, vitiligo patients' melanocyte membranes lack or have irregular distributions of E-cadherin (Ecad), which mediates the adhesion between melanocytes and keratinocytes in the epidermis. The epidermis's melanocytes' separation from the basal to suprabasal layers is linked to this anomaly [75].

Dendrites, They not only play crucial roles in the transfer of melanosomes between melanocytes and keratinocytes, but they also significantly boost melanocyte adhesion in the basal layer of the epidermis. Loss of dendricity may be another cause causing melanocyte loss since abnormal

dendrite shape of vitiligo melanocytes *in vitro* has been documented [76, 77].

DDR1 expression was shown to be lower in lesional vitiligo skin than in non-lesional skin, according to a research. In addition, lower levels of lesional and non-lesional DDR1 expression were discovered in vitiligo skin compared to controls. As a result, decreased DDR1 expression may be related to the aetiology of vitiligo's defective melanocyte adhesion process [78].

The convergence hypothesis

First, this hypothesis is explained [79]. It is based on the notion that vitiligo is caused by a confluence of many pathogenic pathways, including neurogenic dysregulation, oxidative stress, autoimmunity, and melanocytorrhagia. Additionally, vitiligo is seen as a condition rather than a unique entity by several writers [80].

This idea states that vitiligo is induced by a variety of etiologic variables that affect melanocyte survival, rather than only predisposing mutations, melanocytes reacting to chemical or radiation exposure, or hyperreactive T cells [81]. According to this view, NSV is a primary melanocytorrhagic illness in which the melanocytes' indolent detachment and subsequent transepidermal loss are caused by an altered melanocyte reaction to friction. If self-tolerance is compromised for whatever reason, damaged melanocytes produce melanosomal antigens during their transepidermal migration and may trigger an immune response [81].

The autoimmune hypothesis is regarded as and acknowledged as the dominant explanation among the other ideas produced, including autoimmunity, oxidative stress, melanocyte development and faulty melanocyte adhesion, viral infections, and neurological processes Figure (1) [82].

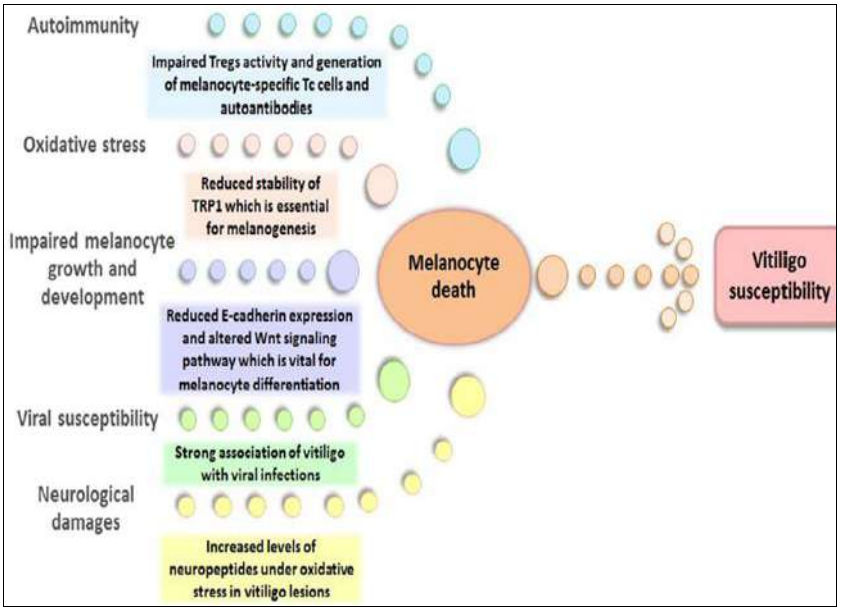

Fig 1: Principles governing the etiopathogenetic emergence of vitiligo [82].

Clinical picture

Asymptomatic yet visually deforming, vitiligo causes depigmented areas on the skin and/or mucous membranes that are milky white or chalky in colour. The lesions often have distinct borders and come in a range of shapes and sizes. Furthermore, the hair in the vitiliginous regions often becomes white [83]. Any location can develop lesions, which centrifugally increase at an unexpected rate and can manifest at traumatised sites like the elbows and knees. Additionally, vitiligo lesions are extremely susceptible to ultraviolet (UV) radiation and can burn when exposed to the sun [7].

The clinical sign of vitiligo is depigmentation of the skin and hair follicles. This causes white, generally symmetrical macules and patches that typically get bigger over time and appear more frequently in conspicuous places like the face and limbs. Due to the browning of unaffected skin, vitiligo is typically initially noticed in sun-exposed areas in people with fair skin [66].

Classification of vitiligo

Based on the location and degree of the depigmented area's involvement, not all cases of vitiligo act the same way. According to the Vitiligo Global Issues Consensus Conference (VGICC), which took place in 2011 in Bordeaux, vitiligo is divided into two primary groups. Table (1) [84].

Vitiligo non-segmental (NSV).

Vitiligo in segments (SV).

According to a 2012 worldwide consensus study, all types of vitiligo should be referred to as "vitiligo," with the exception of the segmental variation, which has to be classified differently due to its unique prognosis and therapeutic response [84].

Table 1: Classification of vitiligo [84]

Types	Subtypes
Non-segmental vitiligo	Acrofacial
	Mucosal (More than one affected)
	Generalized of common
	Universal
	Mixed (Associated with ssegmental vitiligo
	Rare forms
Segmental	Unisegmental, bisegmental or multisegmental
Unclassified or indeterminate	Focal
	Mucosal (Only one site affected

- Focal vitiligo is the name given to a tiny, isolated, depigmented patch (10–15 cm2) that lacks a clear, unilateral segmental distribution and does not advance for at least two years. Segmental vitiligo (SV), non-segmental vitiligo (NSV), or no classification at all, may develop from it [84].
- Mucosal vitiligo-This condition is referred to as mucosal vitiligo when it affects just one isolated spot in the oral or vaginal area [88].
- The head, hands, and feet are typically the only body parts to experience acrofacial vitiligo. The "lip-tip" vitiligo, which is frequently observed in South Asia and is resistant to therapy, typically involves distal finger, toe, and face orifice involvement [84].
- Achromatic macules or patches with varying distribution make up vitiligo vulgaris. They can affect any region of the trunk, hands, fingers, face, and trauma-exposed areas, and are frequently symmetrical [84].
- Mixed vitiligo, which results from the blending of two or more kinds. The segmental form often comes before NSV [84].
- Full or almost full depigmentation of the skin, which may or may not include body hair (>80% of BSA), is referred to as universal vitiligo [84].

Segmental vitiligo

It can be identified by the unilateral spread of one or more macules. This variety often manifests at a younger age, has a less correlation with autoimmune illnesses, and stabilises quickly [85]. Occuring in a small percentage of patients (5–16%) [7].

Segmental vitiligo generally affects the face, advances swiftly over 6 months to 2 years, and leukotrichia appears suddenly. However, the condition usually stabilises on its own without therapy. Early leukotrichia is a defining feature, and it is ten times less prevalent than other vitiligo forms [86].

Segmental vitiligo's distribution frequently, but not always, resembles a dermatome or other cutaneous segment. Other SV distribution patterns that span many dermatomes or match sizable regions bounded by Blaschko's lines can be found. Rapid onset and involvement of the hair follicle pigmentary system are two examples of particular traits. Most individuals only have one distinct segment affected, however in a small percentage of cases, there may be two or more segments with ipsilateral or contralateral distribution [87].

Clinical signs of active vitiligo

- In addition to typically coloured skin, trichrome vitiligo is distinguished by both depigmented and hypopigmented macules. The advancement of the hypopigmented patches to complete depigmentation is their natural evolution [7].
- The extra appearance of marginal or perifollicular hyperpigmentation is referred to as quadrichrome vitiligo. Darker skin types, especially those with repigmentation, seem to show this variety more frequently [7].
- Additional blue-gray hyperpigmented macules in pentachrome vitiligo are sites of cutaneous melanin incontinence.
- These individuals have the confetti kind, which includes several small, distinct hypomelanotic macule [7].
- Erythema around the edges of vitiligo macules is a clinical indicator of inflammatory vitiligo [7].
- The lack of epidermal melanocytes and the abundance of dermal melanophages give blue vitiligo its blue-grey colour [88].
- The Koebner phenomenon: Vitiligo has reportedly developed at burn, cut, or abrasion sites [88].
- The development of new lesions and the enlargement of existing ones [89].

Histopathology

The change of melanocytes at the dermal-epidermal interface is the most noticeable characteristic of vitiligo histopathologically [7, 90]. It demonstrates the complete lack of functional melanocytes within the lesions, whereas CD4+ and CD8+ T lymphocytes are most frequently observed at the margins of the lesions [91].

There are still some dopa-positive melanocytes and basal layer melanin granules in the peripheries of growing lesions, which are hypopigmented rather than totally depigmented. In the skin that seems normal and is close to vitiliginous regions, Focused regions of vacuolar alteration at the dermal-epidermal interface have been seen, along with a modest mononuclear cell infiltration. Melanocytes are frequently prominent and exhibit lengthy dendritic processes loaded with melanin granules. Degenerative alterations in cutaneous nerves and adnexal structures as well as epidermal thinning and flattening of dermal papillae have been documented in long-lasting lesions [92-94].

Melanocytes are typically absent from vitiligo lesions when stained specifically, such as with the Masson-Fontana method for melanin or the dihydroxy phenyl alanine approach for tyrosinase. Additionally, totally vitiligo skin lacks any sign of melanocytes according to specific autoantibodies for the melanocytic lineage. As a result, electron microscopy, which is unable to distinguish melanocytic cells in vitiligo achromic patches, also supports these histological findings. Langerhans cells seem to have taken the position of the degenerating melanocytes (95, 96). Other stains, such as Mel-5 and HMB-45, which both identify active and inactive melanocytes, as well as DOPA, which identifies active melanocytes, may also be helpful [8].

Diagnosis of vitiligo

- **Clinical diagnosis:** The diagnosis of vitiligo is mainly clinical, but occasionally, skin biopsy is required for confirmation, melanocytes and melanin are absent. Examination of the affected areas with Wood's light can help in differentiation of active vitiligo from several disorders characterized by varying degrees of hypopigmentation [97-97].
- **Wood's light:** Wood's light is a handheld UV irradiation device emitting UVA waves at a wavelength of approximately 365 nm [99]. It is helpful in making a diagnosis of vitiligo [100] as the lesions appear bright blue white due to autofluorescence [101].
- **Dermoscopy:** Examination of affected area by dermoscopy showed reduced or absent pigmentary network, perifollicular hyperpigmentation, and perilesional hyperpigmentation in the evolving vitiligo lesions [102].

Dermoscopy can be used to differentiate vitiligo from other depigmenting disorders. Vitiligo typically shows residual

perifollicular pigmentation and telangiectasia, which are absent in other hypopigmentation disorders [103].

Dermoscopy also helps in differentiation between stable and active vitiligo

a. Dermoscopic features of stable vitiligo include marginal and perifollicular hyperpigmentation, reticular pigmentation (a well-defined pigment network within the depigmented macule), and marginal reticular pigmentation (a well-defined pigment network at the margins of the macule) [104] among other dermoscopic findings.
b. Dermoscopic findings linked to progressive vitiligo include polka dot or confetti-like (depigmented dots distributed in a polka dot pattern), comet tail (micro-Koebner phenomenon), starburst or nebulous, trichrome vitiligo (three zones, brown, tan, and white), and salt and pepper pattern [104].

Reflectance confocal microscopy (RCM)

RCM is a very useful tool helping to determine the stability levels of vitiligo lesions. Active stage of vitiligo had an apparent loss of melanin in lesional skin, disappearance, or loss of integrity of the bright dermal papillary rings normally seen at the dermo-epidermal junction level, unclear border between lesional and normal skin, and highly refractile inflammatory cell infiltration within the papillary dermis at the edge of the vitiligo lesions. The stable stage of vitiligo had a complete loss of melanin in lesional skin, a clear lesional-normal skin border, and no inflammatory cell infiltration at the edge of vitiligo lesion [105].

RCM could be used also to identify repigmentation of skin during treatment. RCM showed dendritic melanocytes at the basal layer after excimer laser treatment [106].

Skin biopsy

Skin biopsy gives accurate diagnosis, this is not routinely performed. It is used only when the diagnosis is unclear or suspecting infectious causes like leprosy, sarcoidosis, or malignancy (mycosis fungoides) [107].

Differential diagnosis of vitiligo

Differential diagnosis of non-segmental vitiligo (NSV)

The diagnosis of generalized vitiligo in a patient with progressive, acquired chalk-white macules in typical sites is normally straightforward. Few such acquired conditions are so, patterned and symmetric as vitiligo can be. Wood's lamp examination may be required to visualize macules in patients with lighter skin phototypes and to identify macules in areas away from sun. Generalised vitiligo's primary differential diagnosis comprises the following Table (2) [84].

Table 2: Non-segmental Vitiligo: Major Differential Diagnoses [84]

Diagnosis	Features
Inherited or genetically induced hypomelanoses	
Piebaldism	White forelock, midline depigmentation of anterior body, bilateral shin depigmentation; autosomal dominance
Tuberous sclerosis	Small or larger (ash-leaf) white spots, seizures, typically later appearance of other cutaneous symptoms (e.g., shagreen patches, angiofibromas); autosomal dominance
Ito's hypomelanosis	Linear distribution, unilateral or bilateral pattern of hypopigmented streaks; sporadic; chromosomal or genetic mosaicism (involving blood or skin cells)
Waardenburg's syndrome	White forelock, hypertelorism, deafness (variable degree); possible association with congenital megacolon (Hirschsprung's disease)
Postinflammatory hypopigmentation: Occurs in inflammatory disorders accompanied by increased epidermal turnover (e.g., psoriasis, atopic dermatitis), in lichenoid–cytotoxic infiltration of epidermal basal layer (e.g., lichen planus, toxic drug reactions), and in scleroderma; clinically distinguished by identification of the primary skin disease (e.g., scalp or plaque psoriasis, flexural dermatitis for atopic dermatitis, scleroderma plaques), but may coexist with primary disease; in genital areas, lichen sclerosus may resemble vitiligo or be associated with true vitiligo; biopsy is useful in cases that are difficult to diagnose	
Paramalignant hypomelanoses	
Mycosis fungoides	Patients with dark skin may exhibit skin depigmentation; nevertheless, a clinical diagnosis may be challenging without evidence of inflammation and skin infiltration. Biopsy results are diagnostic.
Melanoma	Under Wood's lamp, the margins of such vitiligoid lesions are typically less distinct than in common vitiligo, and depigmentation is typically incomplete. Vitiligoid changes range from the malignant Sutton's phenomenon, which is a halo of depigmentation around a cutaneous melanoma, to more widespread vitiligoid changes.
Parainfectious hypopigmentation	
Tinea versicolor	Can cause vitiligoid changes, generally after treatment in the absence of re-exposure to UV light; the distribution and shape of the lesions and the presence of scaling and yellow fluorescence of untreated lesions allow a definite diagnosis
Indeterminate leprosy	Manifested as hypochromic patches that are hypoesthetic to light touch
Progressive macular hypomelanosis: Seen in young adults and frequently referred to as a recalcitrant pityriasis versicolor; white macules are present on the trunk, with more marked involvement on the lower back and axillae Propionibacterium acnes is a suspected cause of depigmentation	
Post-traumatic leukoderma: May occur after deep burns or scarring in which hair follicles are removed entirely or in which the bulge area containing melanocyte precursors is destroyed; can be difficult to distinguish from true vitiligo when scarring is not obvious; may also occur after toxic epidermal necrolysis	
Occupational and drug-induced depigmentation	
Occupational	A subtype of vitiligo triggered by occupational exposure, which evolves from contact depigmentation (generally caused by a phenolic–catecholic derivative*) to a generalized phenomenon; may be difficult to distinguish from other cases of vitiligo
Drug-induced	Can result from use of systemic drugs (e.g. chloroquine, fluphenazine, physostigmine, imatinib) in rare cases topical imiquimod may also cause vitiligoid depigmentation

Differential diagnosis of segmental vitiligo (SV)

A congenital pigmentary condition called nevus depigmentosus is referred to as ND. Although there have been indications of a link between cerebral problems and limb enlargement, the condition is generally localised to the skin. The following are some of the most popular clinical diagnostic standards: Birth-present or early-onset leukoderma, no change in the leukoderma's distribution throughout time, no change in the texture or feel of the afflicted region, and no border of hyperpigmentation [108].

A uncommon neurocutaneous condition called hypomelanosis of Ito is characterised by hypopigmented skin lesions that have an odd pattern of streaks, whorls, swirls, and patches. The neurological and musculoskeletal systems are the most usually affected by the related systemic disorders, whereas the gastrointestinal, renal, and cardiac systems are less frequently affected [109].

Conclusion

The most commonly seen depigmenting skin illness, vitiligo, has a very complicated origin and continues to be one of the most challenging dermatological issues.

Conflict of Interest

Not available

Financial Support

Not available

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