

Review Article

VITILIGO: A COMPREHENSIVE REVIEW OF ETIOLOGY, PATHOGENESIS, AND TREATMENT APPROACHES

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Abstract

The loss of skin pigmentation in vitiligo patients results in depigmented patches that can significantly lower their quality of life. Vitiligo is a chronic skin illness. Although there isn't a single treatment that will completely cure vitiligo, there has been a lot of advancement in the formation of more focused and efficient treatment alternatives in recent years. An overview of the most recent advancements in the treatment of vitiligo is given in this abstract, which includes novel treatments utilizing JAK inhibitors and regenerative therapies, topical corticosteroids and calcineurin inhibitors, and improvements in phototherapy techniques. Biologics, topical vitamin D analogues, and immunomodulatory treatments are also investigated as possible means of addressing the autoimmune components of the illness. Clinical trials and continuous research are helping the area of vitiligo therapy advance, giving patients with this difficult skin condition hope for better results and a higher quality of life. It is recommended that dermatologists and other healthcare professionals remain current on these novel treatments and engage in patient consultations to customize treatment regimens according to each patient's unique needs and the severity of their illness.

Keywords: Vitiligo; Pathology; Recent treatment; Autoimmune disease.

Introduction

The integumentary system is made up of skin and its by-products [hair, nails, sweat, and oil glands]. The body's largest organ is the skin [1]. It safeguards against damage to the underlying structures. Skin has a role in controlling body temperature. It controls how much water is released into the environment as well. The epidermis, hypodermis, and dermis are the three layers that comprise the skin. An extensive network makes up the skin's structure, which acts as the body's first line of defence against viruses, UV rays, chemicals, and mechanical harm [2].

The skin plays a crucial role in maintaining overall health and well-being, and any damage or disease affecting it can have significant consequences. Therefore, proper skin care is essential to keep the skin healthy and prevent various skin conditions. The layers of the skin are described through the diagram [3].

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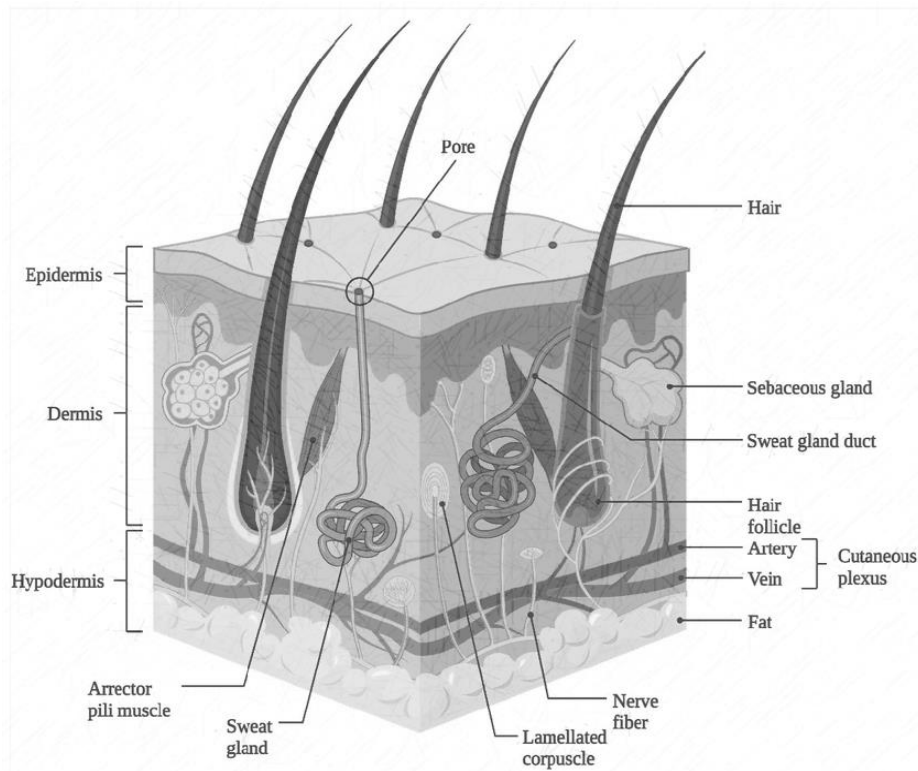


Fig. 1: Human skin anatomy showing different skin layers [4]

The thickness of the skin varies depending on the area of the body and each layer is unique. The skin is composed of three primary layers, each with its unique structure and function. These layers, from outermost to innermost, are shown in the flowchart. The epidermal and dermal regions have different thicknesses. Certain areas of skin lack hair, such as the soles of the feet and palms of the hand [5].

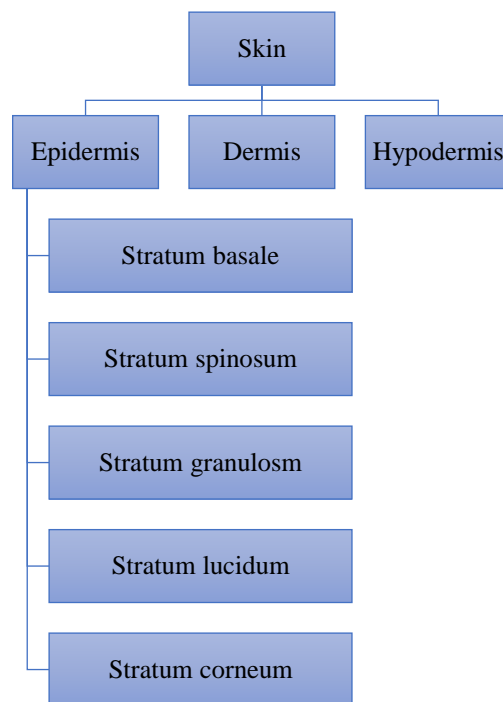


Fig. 2: Flowchart showing the different layers of the skin

The epidermis is the topmost layer of the skin, which acts as a protective barrier between the body and the external environment. It is composed of multiple layers of epithelial cells and is responsible for several important functions [6]. It comprises of-

Stratum basale: It is the deepest layer of the epidermis. The cells are cuboidal to columnar in shape. Melanocytes are also present in this layer [7].

Stratum spinosum: This layer is also known as the prickle cell layer. It contains irregular, polyhedral cells. Dendritic cells are also found [6].

Stratum granulosum: It is generally a 3-5 cell layer. Keratin precursors are found in keratohyalin granules, where they eventually gather, crosslink, and form bundles. The glycolipids that are released to the surface of the cells and serve as a glue to hold the cells together are found in the lamellar granules [6].

Stratum lucidum: Eleidin, a transformation product of keratohyalin, is present in a thin, transparent layer between 2-3 cell layers of the thicker skin seen on the palms and soles [8].

Stratum corneum: The top layer. 20–30 cell layers. It is composed of keratin and horny scales comprised of defunct keratinocytes, or anucleate squamous cells. This is the layer which changes most in thickness, especially in callused skin. The dead keratinocytes in this layer secrete defensins, which are a component of our first line of immunological defence [7, 9].

Dermis is deeper, thicker, and less cellular is called the reticular layer, and it is made up of dense connective tissue and bundles of collagen fibres. The sweat glands, hair, hair follicles, muscles, sensory neurons, and blood arteries are all located in the dermis. Meissner's corpuscles, Pascinian corpuscles and Ruffini's corpuscles are present in the encapsulated nerve ending [6, 10].

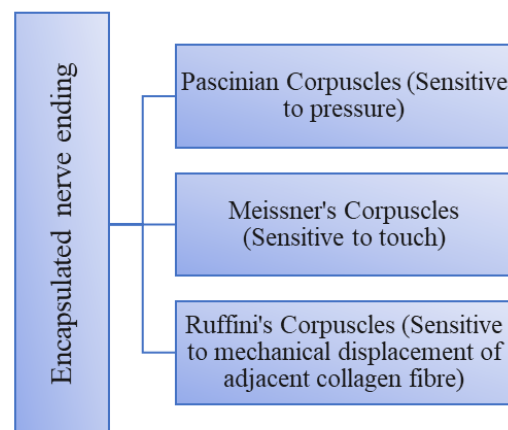


Fig. 3: Diagram of different corpuscles present in the dermis layer of the skin

Hypodermis is also known as subcutaneous fascia. It is located close to the dermis. Adipose lobules, some skin appendages including hair follicles, sensory neurons, and blood arteries are all present in this layer of skin, which is the skin's thickest layer [11].

There are many functions of the skin. It acts as a defense against water intrusion, microbial invasion, mechanical and chemical assault, and UV light damage. By controlling temperature and water loss and performing endocrine and exocrine tasks, the skin protects the body's homeostasis [3]. The functions of the skin are shown below:

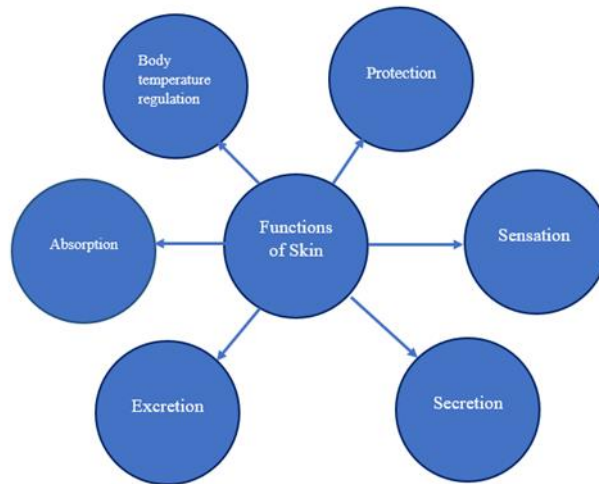


Fig. 4: Different functions of the skin

“Dermatosis” or skin diseases are a broad range of condition that affects the skin. Skin diseases are common diseases caused by bacteria, fungi or other micro-organisms. Skin diseases such as acne, eczema, psoriasis, and dandruff may be affecting both life-style and self-esteem. Dermatitis may cause rashes, inflammation, itchiness or other skin changes. Some of the common dermatoses are Acne, Psoriasis, Eczema, Cold sore, Lupus, Ringworm, Vitiligo, Leishmaniasis, Dandruff, Alopecia, etc [12].

A skin condition known as vitiligo causes patches of skin to lose their pigment, leaving behind white or light-coloured patches. Melanocytes, the skin's pigment-producing cells, are destroyed or cease to function when it happens. Vitiligo is thought to be an autoimmune condition in which the body's immune system targets and kills melanocytes, while its specific etiology is yet unknown [13].

Although vitiligo can affect any part of the body, the face, hands, feet, and genital regions are the most frequently affected. The patches may change in size and shape over time, and they could also spread. Although vitiligo is not communicable and does not hurt the body, it can negatively affect a person's sense of self-esteem and quality of life [14].

Types of Vitiligo

There are different types of vitiligo based on the distribution and location of the depigmented patches on the skin. Vitiligo classification is crucial for evaluating prognosis and directing therapy approaches. The main types of vitiligo include:

1. Generalized or non-segmental vitiligo: This form makes up around 90% of instances of vitiligo and is the most prevalent. Depigmented patches of this kind typically develop symmetrically on both sides of the body and on sun-exposed parts like the face, hands, and feet [14].
2. Segmental vitiligo: This kind of vitiligo only affects a particular region of the body, typically on one side. In contrast to generalized vitiligo, it typically manifests earlier in life and advances more quickly. There may be connections between various autoimmune diseases and segmental vitiligo [13].
3. Mixed vitiligo: Patches of this type of vitiligo can appear on both sides of the body as well as in a localised location, and it combines characteristics of both generalised and segmental vitiligo [15].

4. Universal vitiligo: It is a rare type of vitiligo in which the face, trunk, and limbs are all covered in depigmented patches [16].

5. Acrofacial vitiligo: This type of vitiligo affects the face, the area around the mouth, the fingers, and the toes [17].

6. Mucosal vitiligo: This kind of vitiligo affects the mucous membranes, including the genitalia and the inside of the mouth and nose [17].

Types of vitiligo have been enlisted in the diagram given below:



Fig. 5: Types of vitiligo

Epidemiology

Skin diseases like vitiligo, can affect people of all racial and ethnic backgrounds, and are somewhat prevalent. It is predicted to impact 0.5% to 2% of the world's population, with no appreciable gender differences. Although vitiligo can develop at any age, the most frequent age range for onset is between 10 and 30 years old [18]. Various nations and ethnic groupings have quite diverse vitiligo prevalence rates. The country with the highest prevalence is India, where it affects about 8.8% of the population with a high incidence of melanoma, followed by Mexico and Japan, where it affects about 3% of people with lower rates of melanoma [19]. Between 0.5% and 1% of the population in the United States are thought to have vitiligo. In 1977, Denmark published one of the oldest and largest epidemiological studies on vitiligo. According to reports, 0.38 percent of the population as a whole was impacted. It is also more dominant in individuals with African, Middle Eastern, and South Asian ancestry [20].

People who have specific autoimmune conditions, such as thyroid disease, type 1 diabetes, and alopecia areata, are more likely to develop vitiligo. Additionally, the disease has a tendency to occur in families, pointing to a hereditary component [21]. Vitiligo is not transmissible and does not pose a significant health risk, but it can have a significant influence on a person's quality of life. People with vitiligo may experience communal stigma and discrimination, particularly in societies where fair skin is cherished. The psychological impact of vitiligo can be significant, and many people with the ailment experience mental health issues such as anxiety and depression [22].

Clinical Features:

The presence of clearly defined, depigmented or hypopigmented patches of skin is the primary clinical characteristic of vitiligo. These patches can appear anywhere on the body, including the face, hands, feet, and genital region, and they can vary in size and shape. The depigmented skin patches are typically symmetrical and may have wavy edges [23].

Other vitiligo clinical characteristics include:

- Hair pigment loss: In rare situations, the affected area's hair may also begin to lose its colour, turning white or grey [24].
- Koebner phenomenon: Some vitiligo patients may acquire fresh patches of depigmented skin in regions that have had trauma or injury. This condition is referred to as the Koebner phenomenon [25].
- Sun sensitivity: The depigmented areas of skin may be more prone to sunburn and other sun-related damage [23].
- Mucosal involvement: The mucous membranes, including those in the mouth, nose, and genitalia, can also be impacted by vitiligo [13].

Pathophysiology

Vitiligo has a complicated and multifaceted pathophysiology that is influenced by both hereditary and environmental factors. The eradication of melanocytes, the skin's pigment-producing cells, by autoreactive T lymphocytes, is one potential process. It is thought that melanocytes may be destroyed by the immune system as a result of genetic predisposition and environmental triggers like sunburn or chemical exposure. Another suggested process includes the buildup of harmful metabolites in the melanocytes, such as hydrogen peroxide. The melanocytes may be destroyed as a result of oxidative stress and damage brought on by this buildup. There is additional evidence to show that vitiligo development may be influenced by changes in the melanin synthesis pathway, including variations in the expression of genes related to melanogenesis [26-28].

The exact mechanisms that lead to the development of vitiligo are not fully understood, but there are several theories [28-30]:

1. Autoimmune theory: This is the most extensively accepted theory for the progress of vitiligo. It proposes that the body's immune system erroneously attacks and destroys the melanocytes, which are the cells that produce the pigment melanin. This can be activated by factors such as exposure to certain chemicals, stress or viral infections.
2. Genetic theory: Vitiligo has been found to track in families, indicating that there may be a genetic factor in its development. Several genes have been recognized that may be involved in the progress of vitiligo.
3. Neural theory: This theory recommends that changes in the nerve cells that supply the skin may subsidize to the development of vitiligo. This could be due to factors such as exposure to certain chemicals or trauma.
4. Oxidative stress theory: This theory proposes that oxidative stress, which happens when free radicals and antioxidants are unequally distributed in the body, may contribute to vitiligo development.

Autoimmune theory: Currently, the most widely accepted theory explaining how vitiligo develops is the autoimmune theory. According to this idea, the melanocytes—the cells that make the pigment melanin, which gives colour to the skin, hair, and eyes—are attacked and destroyed by the body's immune system. Normally, the immune system protects the body from outside invaders like viruses and bacteria, but in the case of vitiligo, it wrongly views melanocytes as alien and begins to fight them. Genetics, environmental circumstances, viral infections, and other causes can all lead to this attack [31]. White patches of skin come from the loss of pigmentation brought on by the demise of melanocytes. Though the precise cause of the autoimmune reaction is not yet known, it is thought to be caused by a complicated interaction between the immune system and melanocytes [32]. Numerous pieces of data back up the autoimmune idea. For instance, people who have vitiligo frequently also have thyroid disease, rheumatoid arthritis, or type 1 diabetes. Additionally, it has been discovered that people with vitiligo have higher prevalence levels of a few immune system-related genes [33]. Immunomodulatory treatments, such as topical corticosteroids, are frequently used in the treatment of vitiligo to reduce the autoimmune response and stop the loss of melanocytes [27].

Genetic theory: There is an indication to suggest that genetics play a vital role in the development of vitiligo. The genetic theory suggests that certain genes that are responsible for regulating immune function and melanocyte activity may increase the vulnerability to vitiligo. Several genes, including immune system-regulating genes like NLRP1, PTPN22, and CTLA4, have been discovered that may contribute to the vitiligo formation process. In addition, it has been discovered that vitiligo is connected to genes that control the activity of melanocytes, including TYR, TYRP1, and OCA2 [34, 35]. It's crucial to remember that not everyone with these genetic variants will get vitiligo. It is thought that vitiligo may only occur if a combination of genetic and environmental variables, such as exposure to specific chemicals or viral infections, are present. According to studies, vitiligo frequently runs in families, indicating that the condition may have a genetic component. The likelihood of acquiring vitiligo is higher in people with a family history than in people without one [36]. The research and development of novel medications and treatments may be aided by understanding the genetic underpinnings of vitiligo. For instance, scientists are right now looking into the use of gene therapy to help vitiligo patients' melanocytes operate again [37].

Neural theory: The neural theory proposes that alterations in the nerve cells that supply the skin may subsidize the process of development of vitiligo. According to this theory, damage or dysfunction in the nerves that supply the skin can disrupt the normal communication between melanocytes and nerves, leading to damage to skin coloration [38]. Numerous factors have been recognized that can damage or dysfunction the nerves supplying the skin, including physical trauma, exposure to certain chemicals, and psychological stress. These factors can cause changes in the nerve cells, including altered neurotransmitter levels and changes in the growth and survival of nerve cells [39]. According to studies, vitiligo patients have altered neural activity and decreased nerve density in the affected skin regions. Additionally, it has been discovered that areas of vitiligo have an augmented number of dysfunctional cells known as substance P-positive nerve fibres, raising the possibility that they may be involved in the progression of the condition [40]. The precise mechanisms governing the interaction between nerve cells and melanocytes in vitiligo are not entirely understood, and the neurological hypothesis is still under investigation. However, addressing issues like physical trauma and exposure to specific chemicals that can harm or malfunction the nerves supplying the skin may help to lower the chance of developing vitiligo [41, 42]. Treatment options for vitiligo that target the neural theory include phototherapy, which uses light to stimulate nerve and melanocyte function, and nerve growth factor therapy, which involves the use of growth factors to promote the growth and survival of nerve cells [43].

Oxidative stress theory: The oxidative stress theory proposes that the disproportion between free radicals and antioxidants in the body may contribute to the development of vitiligo. Free radicals are molecules that are unstable and reactive due to the presence of unpaired electrons. They can cause damage to cells, including melanocytes, by attacking their DNA and other cellular components. Antioxidants are molecules that can counteract free radicals and prevent or repair the damage they cause [44]. In vitiligo, it is supposed that the formation of free radicals is increased, while the antioxidant defenses of the body are diminished. This can lead to oxidative stress, which can contribute to the melanocytes destruction and the loss of skin pigmentation [41]. Several factors have been identified that can upsurge oxidative stress in the body and contribute to vitiligo formation. Exposure to ultraviolet [UV] radiation, which can generate free radicals in the skin, as well as exposure to certain chemicals, such as phenols and quinones are some of the factors which can also cause oxidative stress [45]. Studies that have discovered higher levels of oxidative stress indicators in those with vitiligo compared to those without the illness offer evidence to support the oxidative stress theory. Additionally, some research shows that antioxidant supplements like vitamins C and E may lower oxidative stress and help with vitiligo symptoms [46]. Oxidative stress can lead to cellular damage and dysfunction even if the oxidative stress theory is currently under investigation. Vitiligo and other health disorders may be less likely to occur if oxidative stress is addressed with a healthy lifestyle with a balanced diet rich in antioxidants and limiting exposure to environmental pollutants [47].

Melanin Biochemistry

Melanin; is a natural pigment that imparts colour to our skin, hair, and eyes. It is formed by specialized cells called melanocytes, which are found in the skin, hair follicles, and other parts of the body. Melanin plays a dynamic role in the protection of the skin and eyes from the harmful effects of ultraviolet [UV] radiation by absorbing and scattering the radiation before it can penetrate deeper into the skin layers [48]. Eumelanin and pheomelanin are the two main types of melanin found in the body. Eumelanin is responsible for brown and black pigmentation, while red and yellow pigmentation is caused by pheomelanin [49]. The amount and type of melanin formation from melanocytes are determined by a combination of genetic and environmental factors, such as exposure to UV radiation, hormones, and certain medications [50]. Melanin has important physiological functions rather than just a cosmetic pigment. Melanin, for instance, controls immunological responses, protects the skin from oxidative stress, and regulates body temperature. Additionally, antioxidant, anti-inflammatory, and antibacterial properties of melanin have been discovered [51]. A reduction or absence of melanin production is an indicator of some diseases, including vitiligo and albinism, which results in depigmentation of the skin, hair, and eyes. On the other hand, excessive melanin production is a feature of some illnesses, like hyperpigmentation and melanoma [52].

Due to the death or malfunction of melanocytes, the cells that produce melanin, vitiligo patients experience a loss of melanin pigmentation. This loss of melanocytes and alteration of the melanin manufacturing pathway affect the biochemistry of melanin in vitiligo [53]. A complex series of biochemical reactions that occur in melanocytes are involved in the synthesis of melanin. The crucial enzymes involved in melanin synthesis include tyrosinase, tyrosinase-related protein 1 [TRP-1], and tyrosinase-related protein 2 [TRP-2]. Tyrosine, an amino acid, is transformed by these enzymes into melanin pigments, such as eumelanin and pheomelanin [54], [55]. The formation of melanin is given in a simplified schematic flowchart:

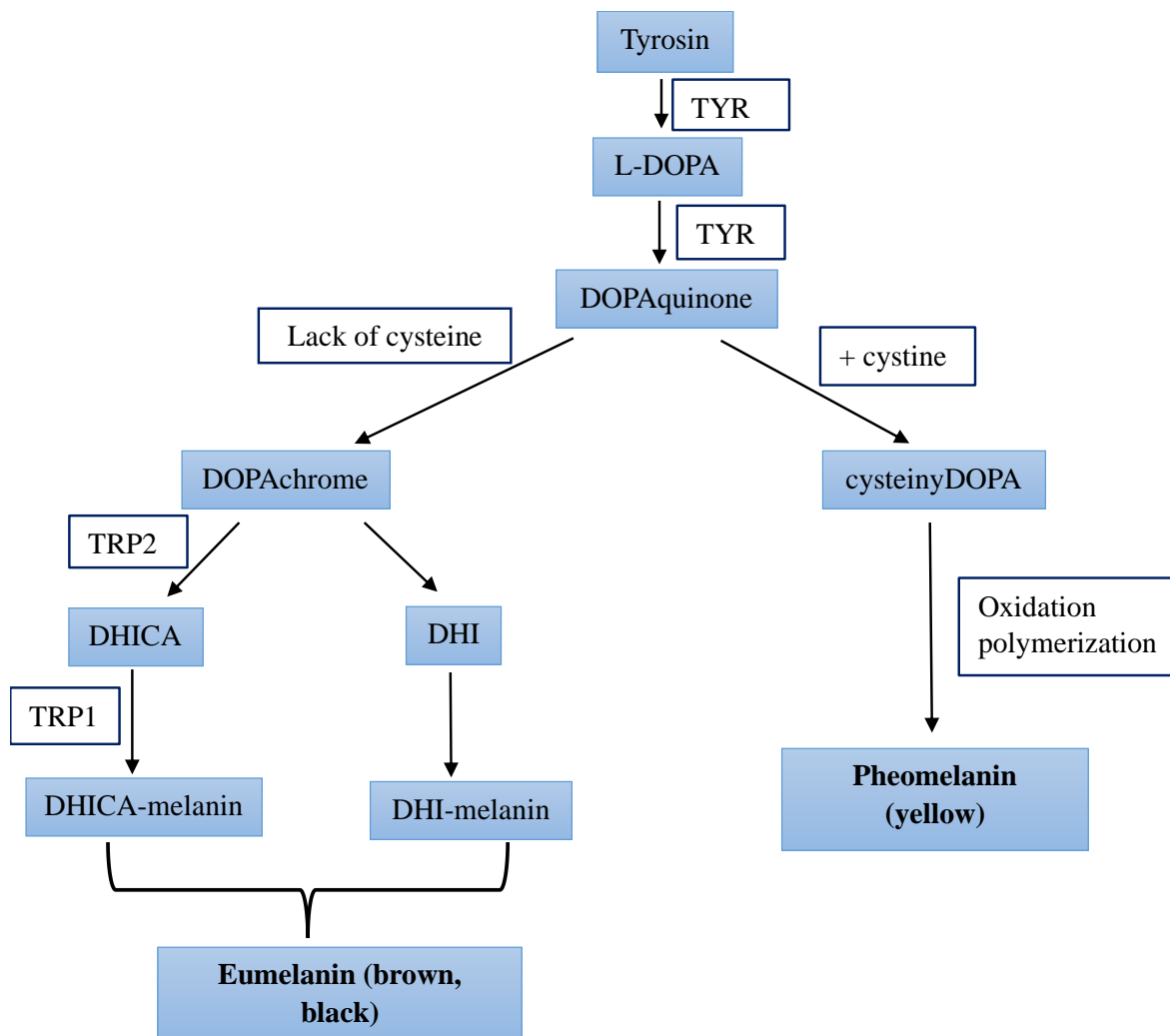


Fig. 6: Simplified schematic flowchart of melanin synthesis in melanocytes

In vitiligo, there is a reduction or absence of melanocytes, which consequences in decreased or absent tyrosinase activity. This leads to a decrease in melanin production and the distinctive depigmentation of the skin in vitiligo [56].

Additionally, research has indicated that people with vitiligo may have changes in the expression and activity of additional enzymes involved in the manufacture of melanin, namely TRP-1 and TRP-2 [57]. The kind and quantity of melanin generated as a result of these variations in enzyme activity may shift, which may be a factor in the depigmentation seen in vitiligo. Thus, the loss or malfunction of melanocytes and disturbance of the melanin manufacturing pathway cause the biochemistry of melanin in vitiligo to change [58]. Understanding these molecular alterations is crucial for creating new vitiligo treatments that attempt to boost melanin production and stop skin depigmentation [59], [57]. The flowchart of the melanin destruction has been shown below:

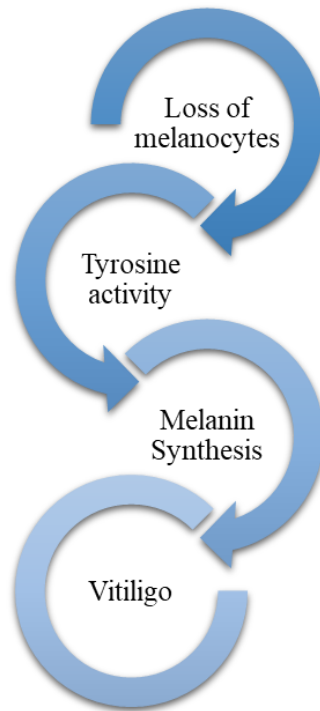


Fig. 7: Flowchart of formation of vitiligo through melanin destruction

Diagnosis

A dermatologist or other skilled healthcare provider will often combine a physical examination with a medical history to make the diagnosis of vitiligo [60].

The medical expert will search for areas of skin that have lost pigmentation while performing the physical examination [61]. To more thoroughly inspect the skin, they might use a special lamp called a Wood's lamp that emits ultraviolet light. A skin sample may occasionally be performed and analyzed under a microscope to confirm the diagnosis [62].

The medical practitioner may also inquire about any symptoms or medical disorders that may be causing the skin changes, as well as any family history of vitiligo.

If an analysis of vitiligo is established, the healthcare professional may suggest further testing or imaging to rule out other ailments that can cause loss of pigmentation, such as autoimmune disorders or skin cancer [63]. They may also discuss treatment choices with the patient, which can include topical medications, light therapy, or oral medications, depending on the severity and extent of the condition [64].

During a clinical investigation of vitiligo, dermatologist or other qualified healthcare personnel will examine the skin for characteristic patches of depigmentation. The examination may include the following table:

Table 1: Different clinical diagnoses of vitiligo

Sl. No.	Examination	Methodology
1.	Visual Examination	The medical expert will search for any white or depigmented spots of skin. To more thoroughly inspect the skin, they might use a Wood's lamp or a strong light [65, 66].
2.	Medical background	The healthcare provider will inquire about any symptoms or illnesses that might be causing the skin changes, as well as any vitiligo in the family history [67].
3.	Skin biopsy	To confirm the diagnosis of vitiligo, a tiny sample of skin may occasionally be taken and studied under a microscope [68].
4.	Eye examination	Because vitiligo can affect both the eyes and the skin, the medical practitioner may occasionally check the eyes for indications of irritation or pigment loss [69].
5.	Other tests	In some rare cases, blood tests or imaging tests may be suggested to rule out other conditions that can cause depigmentation of the skin [70].

The goal of the clinical examination for vitiligo is to identify distinctive depigmented patches and rule out any other potential causes of skin abnormalities. The medical expert may suggest additional tests or imaging and go over treatment options with the patient depending on the seriousness and scope of the condition. A non-invasive imaging method called dermoscopy can be used to more closely inspect the skin. Skin structures that are not apparent to the naked eye can be seen thanks to it [71]. Dermoscopy in vitiligo can show the existence of depigmented patches as well as characteristics including perifollicular hyperpigmentation and disruption of the pigment network [72]. A skin sample is examined microscopically as part of histopathology. It can be utilised to demonstrate the loss of melanocytes from the afflicted skin, supporting the diagnosis of vitiligo. In vitiligo, the dermis may exhibit an increase in lymphocytes and melanophages whereas the epidermis is typically thin and may exhibit a decrease in the number of keratinocytes [73].

Differential Diagnosis

Other skin conditions can be familiar with vitiligo, which makes differential diagnosis important to avoid misdiagnosis and ensure suitable treatments [74]. Here are some examples of skin conditions that can resemble vitiligo:

1. post-inflammatory hypopigmentation: This skin condition develops after the skin is inflamed, injured, or otherwise traumatized. Skin pigmentation is lost as a result, which can mimic vitiligo. Post-inflammatory hypopigmentation, however, typically affects a small area, and the skin may seem or feel different from unaffected skin [75, 76].

2. Pityriasis alba: It is a typical skin disorder that typically impacts kids and teenagers. Round, scaly, hypopigmented patches on the face, neck, and upper arms are its defining features. The skin may appear somewhat raised and scaly, and the patches may mimic vitiligo but are typically less well-defined [77].

3. Tinea versicolor: This is a fungal skin infection that can cause hypo- or hyperpigmentation of the skin. It commonly affects the trunk and upper arms and can resemble vitiligo [78]. However, tinea versicolor usually has a fine, powdery appearance, and may be more visible under UV light [79].

4. **Nevus depigmentosus:** This congenital skin disorder results in a localized loss of pigmentation. Although it may resemble vitiligo, it typically develops from birth and does not advance or spread [80, 81].

5. **Albinism:** This hereditary disorder causes the skin, hair, and eyes to completely or partially lack melanin. It can mimic vitiligo, although it often develops from birth, and the skin may look or feel different from unaffected skin [82].

These are only a few instances of skin disorders that can resemble vitiligo; other illnesses should also be taken into account when making a differential diagnosis. Therefore, it is crucial to seek medical help especially the advice of a dermatologist for a proper diagnosis and treatment care plan [83].

Current Therapies Available for Vitiligo

A persistent skin condition called vitiligo is characterized by a loss of skin pigmentation. Although there is no known therapy for vitiligo, there are several approaches that can help to improve skin quality and slow the disease's progression [84]. The following are some vitiligo treatment options:

1. **Topical corticosteroids:** These anti-inflammatory drugs can be administered topically to the skin to lessen inflammation and encourage repigmentation. They work best when applied in the early stages of vitiligo, but it may take several months before you see any improvement [85-87].

2. **Topical calcineurin inhibitors:** These are immunosuppressive drugs that can be used topically to treat skin irritation and encourage repigmentation. They are most effective when used in the early stages of vitiligo, and results may take several months to appear [88].

3. **Phototherapy:** Using UV light to encourage skin repigmentation is known as phototherapy. Either narrowband UVB or PUVA [psoralen plus UVA] therapy can be used to deliver it. Up to 70% of patients can benefit from phototherapy, although it takes several months of therapy and has potential drawbacks like sunburn and skin ageing [89].

4. **Excimer laser:** This UVB therapy type exposes the skin's afflicted regions to a high-intensity UVB beam. It is normally well tolerated and can cure minor patches of vitiligo, but it may take several months to see results [90].

5. **Skin grafting:** This procedure involves moving healthy skin from one part of the body to the section of the skin that is damaged. It can be effective in treating small areas of vitiligo, but it is invasive and may result in scarring or poor cosmetic outcomes [91].

6. **Micropigmentation:** This technique uses cosmetic tattooing to conceal the skin's depigmented spots. It may work well to improve the skin's appearance, but it is only a temporary fix and may need follow-up treatments [92, 93].

7. **Combination therapy:** To increase the efficacy of treatment, combination therapy combines two or more types of therapies. For instance, a combination of phototherapy and topical corticosteroids may be more efficient than either therapy alone [94, 95].

Herbal Treatments for Vitiligo

Traditional medicine has employed herbal vitiligo therapies for ages. It is crucial to remember that clinical trials have not been used to fully examine the efficacy and safety of these medicines, and some herbal remedies may interact negatively with other pharmaceuticals or cause side effects [96, 97]. Among them, some herbal treatments for vitiligo are:

1. *Psoralea corylifolia*: Also referred to as babchi, this herb is frequently used in Ayurvedic medicine to cure vitiligo [98]. It has been demonstrated that the psoralen component in *Psoralea corylifolia* increases the skin's production of melanin [99]. Psoralen, however, can also lead to photosensitivity, and up the danger of skin cancer and sunburn [100].

2. *Ginkgo biloba*: *Ginkgo biloba* is a popular herbal remedy that is believed to have antioxidant and immunomodulatory properties. Some studies have suggested that *Ginkgo biloba* may help to reduce inflammation and promote melanin production in the skin [101].

3. *Curcuma longa*: Due to its anti-inflammatory and antioxidant characteristics, turmeric is a common spice in Indian food as well as being utilized in traditional medicine. According to some research, the turmeric ingredient curcumin may aid in lessening inflammation and encourage the formation of melanin in the skin [102].

4. Red clay: This form of clay is thought to have antioxidant properties and may aid in promoting the production of melanin in the skin. The use of red clay for the treatment of vitiligo is supported by a small body of scientific research, nonetheless [103].

It is crucial to remember that using herbal remedies for vitiligo should only be done with a doctor's approval. Some herbal treatments may not be suitable for use in some groups, such as pregnant women or people with specific medical conditions [104]. Herbal medicines may interact with other pharmaceuticals. When taking herbal treatments for vitiligo, it's also crucial to keep sun protection precautions because some of these treatments may make you more susceptible to sunburn and skin cancer [105].

Prognosis

The progress of the disease varies significantly between individuals, making the natural history of vitiligo somewhat unpredictable. While the depigmented patches may occasionally stay put and not expand over time, they may also do just the opposite and keep on growing. In addition, some people might naturally repigment the afflicted skin, whereas others might not [106]. Up to 30% of patients may experience spontaneous repigmentation, particularly young children and teenagers. Small areas or patches of repigmentation may appear, and it may only be transient or incomplete [107]. Though the exact causes of spontaneous repigmentation are unknown, it is suspected that they may involve the activation of melanocyte stem cells in hair follicles or the migration of melanocytes from the healthy skin around the affected area [108]. The psychological and quality of life of an individual may be significantly impacted by vitiligo. A person's self-esteem, body image, and confidence may be affected by the loss of pigmentation, which can cause social isolation, anxiety, and sadness. Since the disorder is apparent, stigmatisation and prejudice may result, particularly in cultures where fair skin is admired [109].

In addition, because of the absence of skin's protective melanin, those who have vitiligo may get skin cancer and sunburn [110]. As a result, it's critical for those who have vitiligo to practise sun protection techniques, such as using sunscreen and wearing protective clothing [111,112]. Thus, vitiligo is a difficult and unexpected disorder that can seriously affect a person's quality of life. Vitiligo patients should seek help and care from a dermatologist or mental health specialist to manage the physical and psychological effects of the disorder [113].

Future Aspects

The goal of continuous research is to create vitiligo treatments that are even more effective [113]. The following are a few of the research areas:

1. Stem cell therapy: Stem cells can develop into melanocytes, making them a potentially effective treatment for vitiligo repigmentation. The safety and efficacy of utilising stem cells to treat vitiligo are still being investigated [114].

2. Immunomodulators: Since the immune system is a major factor in the vitiligo development, immunomodulators including interleukin inhibitors and JAK inhibitors are being researched as potential vitiligo treatments [115].

3. Melanocyte transplantation: A promising method for treating vitiligo involves transferring melanocytes from healthy skin to the portions of the skin that have lost their colour. Researchers are examining several methods for transplanting melanocytes, including skin equivalents, epidermal cell suspensions, and cultured melanocyte suspensions [116].

4. Gene treatment: Genetic material is inserted into the body's cells through gene therapy to fix genetic flaws. Researchers are investigating the use of gene therapy to help vitiligo patients' melanocytes regain their functionality [117].

5. Combination therapy: Researchers are examining the use of medications that combine several mechanisms that contribute to the vitiligo onset, such as stem cell therapy and melanocyte transplantation or JAK inhibitors combined with phototherapy [118, 119].

6. New topical medications: To treat vitiligo, researchers are looking at the use of new topical medications that target the immune system or encourage melanocyte regeneration [120].

Looking at the research and development of certain medications and therapies, we can conclude that promising research is being done to provide more efficient vitiligo treatments. Before these medicines are generally accessible, though, it might take a few years, and further analysis is required to determine their efficacy and safety.

Conclusion

Melanocytes, the cells that produce the melanin that gives skin its colour, are lost in vitiligo, a skin condition. According to estimates, vitiligo affects about 1% of the world's inhabitants and can afflict persons of any race or ethnicity. Vitiligo is thought to be an autoimmune condition in which the body's immune system targets and kills melanocytes, while its specific causes are yet unknown. Genetics, environmental factors, and oxidative stress are further potential causes of vitiligo. There is currently no known treatment for vitiligo, however, there are a number of approaches that can assist to improve skin quality and reduce or stop the disease's progression. Topical corticosteroids, calcineurin inhibitors, phototherapy, and surgical procedures are some of these treatments. Living with vitiligo can be difficult because the condition can lead to serious psychological discomfort and have an impact on a person's quality of life and sense of self. Vitiligo sufferers can manage their illness and maintain happy lives, nevertheless, with the aid of encouraging friends and family, access to care, and self-care routines. In conclusion, it can be said that vitiligo is a chronic and difficult condition but can be managed with the right care, appropriate treatment, and encouraging people around the patients. As a result, patient can lead a happy and satisfying life.

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Conflict of Interest

The authors have no conflict of interest.

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