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# HEREDITARY SKIN DISORDERS: A COMPREHENSIVE REVIEW

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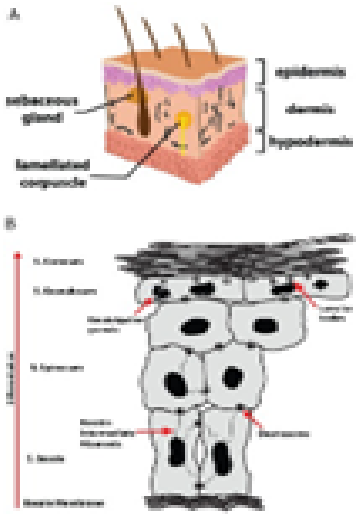
***Abstract:*** The skin consists of different cell types that express certain molecules and have different properties, and provides the interaction and intercellular communication that is important for the continuity of the skin. Additionally, a change in one of the molecules can affect the entire organization and function of these important networks, causing cell detachment, blistering, and other conditions in the skin. Phenotypes will emerge. Over the past few decades, the genetic basis of various monogenic skin diseases has been elucidated using classical genetic methods. More importantly, the results of these studies demonstrate the importance of different types of molecules and genetic and molecular interactions that lead to irreversible changes in the skin. With the advent of the Human Genome Project, next-generation sequencing technologies, and several other recent advances, progress has been made in reducing genetic variation rather than the Mendelian gene behind the monster patterns of genetic diseases. Over the past few years, progress has been made in uncovering the genes underlying various skin diseases and various phenotypes. Many molecules are directly involved in the pathogenesis of these diseases, many of which have been discovered through genetics and are discussed in detail in this chapter. These techniques help determine the genetics of monogenic skin diseases. Recently, the genetic basis of non-Mendelian dermatoses has begun to emerge, with many regions involved in their pathogenesis.

***Index Terms*** – Hereditary skin disorders, Skin. Phenotypes, Patterns of genetic diseases.

## I. INTRODUCTION

Skin is a soft, elastic layer of tissue that normally covers vertebrates and has three main functions: protection, control, and emotion. The adjective "leather" means "of the skin" (from the Latin word "cutis", "skin"). Animal skin; It is part of a complex system that includes skin, bones, ligaments, and the ectodermal tissue layer that protects the body. The skin of amphibians, reptiles and birds has different properties. [1] It also provides support and energy to the body [adipocytes allow triglyceride (TAG) production during lipogenesis] (2,3). The dermis is involved in the immune system; It gives elasticity and moisture to the skin (4) and nourishes and supports the epidermis (2,4,5). The dermo-epidermal junction (DEJ) is the connection between the dermis and epidermis. DEJ is involved in the adhesion process at the dermal-epidermal junction. YEJ works to promote the connection between epidermis and dermis and regulate metabolite exchange. It also plays a role in the migration of keratinocytes during wound healing (2,4,5). The epidermis, the outer layer of the skin, is the barrier between the body and the environment. Lipids are an important part of the skin. Many hydrophobic molecules play an

important role in the function of the skin, preventing excessive water loss (TEWL) and preventing the penetration of bacteria, allergens and other foreign substances. The lipophilicity of the skin prevents the diffusion of hydrophilic molecules. Various lipid subclasses, including sphingosine in the skin, have anti-inflammatory properties [6] (Becam et al., 2017). [7] The structure of the skin shows the epidermis, dermis and subcutaneous tissue. B. Epidermal structure showing four sublayers – stratum corneum (SC), stratum granulosum (SG), stratum spinosum (SS) and stratum basale (SB). Adjacent keratinocytes are connected by desmosomes. Keratin hyaline granules contain profilaggrin, which recruits keratin in the SC. Lamellar bodies contain lipids transported to the SG and SC regions. [8]

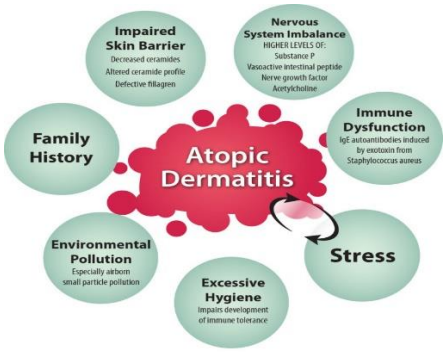


## II.TYPES

I. Type 1

The role of topical probiotics in skin conditions: A systematic review of animal and human studies and implications for future therapiesWhat is probioticsTo aid in the discussion of probiotics, certain definitions are re- quired. In 2001, the Expert Panel commissioned by the Food and Agriculture Organization of the United Nations and supported by the World Health Organization defined probiotics as “live microor- ganisms which when administered in adequate amounts confer a health benefit on the host”.[9] This differs from postbiotics, which are probiotic-derived effector molecules that are secreted by bac- teria or release after lysis that can exert properties similar to their parent probiotics.[10–18] Thus, postbiotics aim to recapitulate the beneficial effects of probiotics while avoiding the risk of adminis- tering live microorganisms. For example, one postbiotic, butyrate, a major energy source for the colon, is produced by many commensal bacteria and has important roles in intestinal growth and differen- tiation[19,20] and control of inflammation.[21–26] Heat-killed probiot- ics may also function as postbiotics.[27] Prebiotics are non-digestible dietary product that promotes the growth of commensal bacteria to encourage intestinal health.[28]4.1 Skin conditions in which topical probiotics have been explored 4.1.1 Atopic dermatitis Atopic dermatitis (AD) is a common disorder of this skin thought to be related to epidermal barrier defects and immune dysregula- tion.[35] Individuals with AD experience pruritus, erythema and der- matitis plaques that may weep, crust or scale.[36] While AD has a complex pathophysiology, it is thought to develop in individuals with a genetic predisposition who are acted on by exogenous factors.[37] The pathophysiology of AD is commonly linked to the loss of filag- grin and alterations in the skin barrier.[38] Patients with AD have a decreased capacity to express certain AMPs, such as cathelicidins and β-defensins.[39–43] However, other studies have demonstrated increased AMP expression in AD.[79–47] AD has also been shown to be associated with alterations in the skin microflora, such as an abundance of S aureus. [48,49] S aureus has been linked to T-cell dys- function,[50] reduced AMPs,[42,51] more severe allergic reactions[52,53] and disruptions in the skin barrier.[54] Additionally, it has been shown that the depth of penetration of S aureus is dependent on both anti- microbial and physical properties of the skin dermis, both of which are disrupted in AD.[55] This suggests an environmental milieu that is promoting a pathophysiological response. Thus, recent work has begun to explore how topical therapy could augment the microflora of AD patients and induce a positive biome balance by eliminating pathogenic bacteria and supporting beneficial bacteria. For example, commensal coagulase-negative staphylococci in human skin have been shown to prevent Staphylococcus aureus from producing AMP. [68] If this device works, it could be a way to treat Alzheimer's patients. For atopic dermatitis and seborrheic dermatitis, topical probiotics have been shown to increase skin ceramides, improve erythema, crusting, and itching, and reduce

Staphylococcus aureus concentrations. However, these studies used different probiotics, vehicles, and doses and investigated different end points. Probiotics include Streptococcus thermophilus, Vibrio filamentum, Streptococcus hominis, Streptococcus epidermidis and Lactobacillus johnsonii. Therefore, although it is known that all these diseases are beneficial, there is no clear concept explaining the recommended treatment. [33,58,34,67,68] The ability of probiotics to reduce the concentration of pathogenic bacteria depends on the type of resistance found in vitro. [31-32,56,57] Atopic dermatitis is directly related to fragility, as it is a skin disease caused by bacterial changes in the skin and an increase in Staphylococcus aureus. [39-43,48-51,54] Restoration of "normal" microbiota also improves skin symptoms, as does the temporary improvement achieved with short-term oral antibiotic therapy.




II. Type 2

**ACNE**

Dysregulation of the central and adaptive immune system plays a role in the pathogenesis of acne. Local upregulation of inflammatory cytokines such as TNF-α, IL-1B, and IL-8 has been found to promote acne development by activating toll-like receptors and CD14 of propionibacteria and lipopolysaccharides. Propionibacteria can also stimulate the immune system through Th1 cells and humoral immunity. [60,61] Although acne can be treated with antibiotics, this is not an effective treatment for every patient and may cause side effects. [62] -64] Although the bacteria that cause acne are generally thought to be Propionibacterium, it is a common bacterium in healthy patients and therefore a disease that cannot explain itself. Although most species of Propionibacterium are similar between people with acne and people without acne, rare species of Propionibacterium vary from person to person.Two types, type 4 and type 5 ribosomes, have been found to be present only in acne patients and may play a role in pathogenesis through mechanisms that are not yet understood. [65] The use of oral probiotics in the treatment of acne has been reported in only one prospective study, in which acne patients were treated with probiotics alone, antibiotics only, or not at all. This probiotic contains a combination of Lactobacillus acidophilus, Lactobacillus delbrueckii, and Bifidobacterium bifidum. The combination may reduce the number of lesions compared to both groups of patients. [66] Although their mechanism of action is not fully understood, it can be concluded that probiotics can improve the dysregulated innate and adaptive immune system. In acne patients treated with topical probiotics, skin swelling, erythema, and the underlying cause decreased and skin inflammation improved. The probiotics examined included cell-free supernatants of Lactobacillus plantarum and Enterococcus faecalis. For this reason, similar to AD studies, different probiotics and postbiotics were studied and different points were analyzed, making comparison impossible. Third, since acne is associated with the growth of pathogenic bacteria and the basis of treatment is often antibiotics, [68,69] topical probiotics may provide better microbial recovery in the community and thus reduce acne occurrence No side effects

III.Type3.

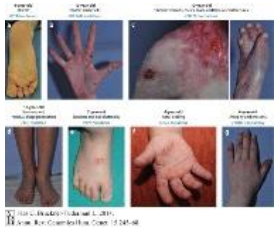
**GENETIC DIAGNOSIS OF MENDELIAN DERMATOSES.**

Recent advances in genomic association studies (GWAS) and next-generation sequencing (NGS) technologies have expanded their applications. Genomic research and clinical studies to identify genetic abnormalities that cause skin diseases. Because most mutations in human Mendelian dermatoses occur in protein genes, whole exome sequencing (WES) is often used to identify genes with atypical or specific phenotypes, including Mendelian dermatoses. Xu et al reported the use of WES to correct the c.2T>C (p.M1T) gene mutation of KLHL24 in Chinese twins with epidermolysis bullosa simplex. Similarly, Wang et al reported the use of WES to identify the c.823G>A (p.Ala351Thr) mutation in DKC1, which causes

mucocutaneous triangular dyskeratosis. In another article on this topic, WES analysis also identified a heterozygous missense mutation c.259G>A in GJB3, which is associated with erythrokeratosis multiforme, ichthyosis, and hearing loss. [70] Sensitive skin

IV.Type 4.

**GENETIC SKIN FRAGILITY**



Adhesive structures that provide stability to the skin include the basement membrane (BM) and desmosomes that support epidermal cells. Cell adhesion. Connect the epidermis and dermis (Figure 2). Both have supramolecular superstructures that interact in specific ways. One of the molecules in this structure is the target of pathogenic processes that cause skin diseases, including genetic changes and autoantibodies. According to the structure of the integumentary system, EB can be divided into four types: simple EB, borderline EB, dystrophic EB and Kindler syndrome [72]. Currently, 18 genes associated with EB are known, and most of them are proteins that play a role in epidermal and dermal adhesion [71]

V. Type 5

**PSORIASIS**

Psoriasis is a chronic disease. Skin disease that can also occur in patients with a genetic predisposition, affected by exogenous factors. While there are various subtypes of psoriasis, all are characterized by erythematic, and often pruritic, plaques.[73] Psoriasis is predominantly thought to be caused by an inappropriate activation of the cutaneous immune system against a perceived pathogen.[74,75] However, the local microflora has also been implicated as potential contributor. When compared to non-psoriasis patients, the skin flora of psoriasis patients dem- onstrates the same type of major species, but with less diversity and with alterations in the relative number of bacteria.[76,77] Propionibacterium and Actinobacteria species are present in lower concentrations in these patients, while Firmicutes, Proteobacteria, Acidobacteria, Schlegelella, Streptococcaceae, Rhodobacteraceae, Campylobacteraceae and Moraxellaceae species are present in higher concentrations compared with controls.[51,78,79] In addition, the decreased prevalence of bacteria such as Propionibacterium acnes can cause a shift towards a autoimmune response as the presence of these bacteria typically promotes a Th2-mediated response path- way, thereby downregulating the Th1 response that is associated with autoimmune activity.[80,81] In an animal model of psoriasis, an ethanol extract of L sakei demonstrated inhibition of inflammation as compared to clobetasol, the current high potency topical stand- ard of care.[82] Thus, while topical dysbiosis in psoriasis has been established, the utilization of topical probiotics for rosacea has yet to be explored

VI. Type 6

**ROSACEA**

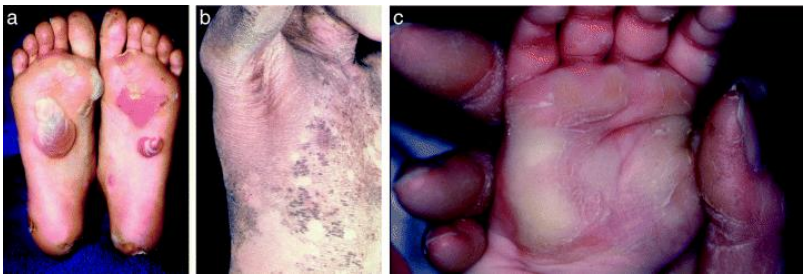
Rosacea is a chronic inflammatory skin condition that mainly affects the cheek, nose, chin and forehead. It is characterized by erythema, papules, pustules, telangiectasia, and discharge. The nose contains large sebaceous glands, often called sebaceous glands. Toll-like receptor 2 (TLR2) is overexpressed in the epidermis of rosacea patients and increases the inflammatory response. Expression of TLR2 induces abnormal expression of cathelicidin and increases the expression and activity of the serine protease kallikrein. These changes may be related to local changes caused by pro-inflammatory bacteria in the microbiome, but only in a positive direction. Relationships are established during this period. Rosacea is associated with mutations in Helicobacter pylori, Staphylococcus epidermidis, Chlamydia pneumoniae, Bacillus oleicum and Demodex, and recent studies have shown a link between gut bacteria and rosacea. There is only one report of the use of doxycycline and oral probiotics in the treatment of scalp and ocular rosacea. A good strategy is to target pathogenic bacteria with doxycycline while supporting commensal bacteria with probiotic therapy. Therefore,

although local dysbiosis in rosacea is well documented, the use of topical medications in rosacea should be evaluated. Human keratinopathy

VII. Type 7

**HUMAN KERATIN DISEASES**

The human disease associated with keratin replacement is the skin disease epidermolysis bullosa simplex (reviewed by Irvine and McLean, 1659). Ultrastructural analysis of skin from epidermolysis bullosa simplex patients revealed electron-dense cytoplasmic aggregates containing K5 and K14 keratin via immunolabeling ( Ishida-Yamamoto et al., 2017 ). (p. 1616)). Similarly, lesions in transgenic mice (K14 mutants) display intraepidermal cyst proteins histologically similar to cysts seen in patients with epidermolysis bullosa simplex (Vassar et al., 1616). Genetic linkage analysis shows a genetic link to epidermolysis bullosa simplex. Ib., 2016). 1616a), K14 and K5 mutations have been observed in many patients with epidermolysis bullosa simplex. . (Boniface et al. 1616b; ib.). . 1616; Lane et al Saib 1617) Shown here are blisters on the skin of a patient with epidermolysis bullosa simplex.




Clinical features of keratinopathy. (a) Weber-Cockayne is a patient with mild epidermolysis bullosa who develops blisters on his legs. (b) Diffuse epidermolytic keratosis in a patient with bullous congenital ichthyosis resembling erythroderma. (c) Prevention of epidermal parakeratosis occurring on the hands of mothers and children with epidermal parakeratosis.

Initial studies of simple epidermal cleavages indicate that mutations in helical boundary motifs have a more severe impact than mutations in helical boundary motifs outside highly conserved regions. Here is a suggestion to follow the topic from beginning to end. Mutations in this region prevent filament elongation and have a greater impact on keratin formation (Steinert et al., 2017). For many years, changes associated with various types of epithelial fragility were found only in keratin 18 (see Ku et al., 1963, 2001; Irvine and McLean, 1659). Of these, 16 are epithelial keratins and 2 are sulfur keratins. Most keratin mutations are either bad mutations (replacement of one amino acid by another) or small changes/deletions that result in more defective proteins than just the native protein. Because keratin is a polymeric protein, these changes can be positive or negative, so most keratin diseases are inherited in an autosomal dominant form.

Keratins K5 and K14 are expressed in basal keratinocytes of all areas and other layers of the skin. Patients with ectopic mutations in the helix boundary motif, such as the Weber-Cockayne variant of epidermolysis bullosa simplex (Chan et al., 1619; Rugg et al., 1619), present a mild phenotype with relative differences in the two groups. . More bubbles. . . . Okay, his leg is hurt. Very sad [89]

VIII. Type 8:

**ECZEMA (DERMATITIS)**

• Types: atopic dermatitis, Ringer's dermatitis, coin dermatitis, seborrheic dermatitis.

• Symptoms: redness, itching, itchy skin. trash; Dry, flaky patches.

• WARNING: Avoid allergies (allergens, irritants), use moisturizer and follow instructions. [90] [90] American Academy of Dermatology (AAD), National Eczema Association. Vitiligo

IX. Type 9:

**VITILIGO**

Nonsegmental Vitiligo, Segmental Vitiligo.

• Symptoms: Change in skin color.

• Preventive measures: sun protection, makeup, phototherapy. [91] [91]

American Academy of Dermatology, International Vitiligo Support Group.

X. Type 10

**DERMATITIS HERPETIFORMIS (DH):**

• Symptoms: itching, rash.

• WARNING: Follow a gluten-free diet, take medications (Dapsone), and avoid skin irritants. [92]

Urticaria

XI. Type 11

**URTICARIA**

• Type of disease: acute urticaria, chronic urticaria.

• Symptoms: skin swelling, redness and itching.

• Prevention: Find the cause, treat and use antibiotics. [93]

| Genetic Skin Disorder | Symptoms | Treatments | Precautions |
|---|---|---|---|
| 1. Epidermolysis bullosa (EB) | - Blistered and brittle skin<br>- Wounds and scars<br>- Nail dystrophy | - Treatments and dressings<br>- Pain management<br>- Physical therapy | Use with caution<br>- Use soft cloths<br>- Get regular body checks |
| 2. Ichthyosis | - Thickened, scaly skin<br>- Dry and flaky<br>- Itching | - Moisturizers and emollients<br>- Topical tretinoin<br>- oral medications for severe diseases | - Avoid harsh soaps<br>- Keep your skin moist<br>- Protect from heat and cold |
| 3. Albinism | Deficiency Pigmentation<br>- Vision problems<br>- Sensitivity to light | - Sunscreen and protective clothing<br>- Visual aids for vision problems<br>- Genetic counseling | - Outdoors Sun wear glasses and a hat<br>- Get regular eye examinations<br>- Genetic counseling for home planners |
| 4. Xeroderma pigmentosum (XP) | Sensitivity to ultraviolet radiation<br>- Skin cancer<br>- Small freckle-like spot | - Preventing strict sun protection<br>- Regular skin examinations<br>- Genetic screening | - Avoid exposure to sunlight, especially during peak hours<br>- Wear protective clothing and sunscreen<br>- Approval Get attention to problems |
| 5. Neurofibromatosis type 1 (NF1) | - Café-au-lait spot<br>- Nerve Myomas ( nerve tumors)<br>- Learning disability | - Surgery to remove tumors<br>- Targeted medicine Symptoms<br>- Physical therapy | - Educational support for the disabled<br>- Genetic counseling<br>- Sun protection to prevent cancer |

| | | | |
|---|---|---|---|
| 6. Gorlin syndrome (silent basal cell carcinoma syndrome) | - Multiple basal cell carcinoma<br>- Jaw cysts<br>- Skeletal abnormalities | - Surgery to remove the tumor<br>- Medicines to control symptoms<br>- Genetic counseling | - Regular dental examination<br>- Genetic counseling for family planning |

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