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PSORIASIS DIGNOSIS AND ITS TREATMENT BY TOPICAL FORMULATION

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ABSTRACT

Plaque psoriasis is the most common variant of psoriasis. The most rapid advancements addressing plaque psoriasis have been in its pathogenesis, genetics, comorbidities, and biologic treatments. Biologics that inhibit TNF-α, p40IL-12/23, and IL-17 are also approved for the treatment of psoriatic arthritis. The most commonly prescribed light therapy used to treat plaque psoriasis is narrowband UV-B phototherapy. Fumaric acid esters (FAEs) like dimethylfumarate (DMF) are used for the treatment of adults with moderate to severe psoriasis. the molecular mechanisms by which DMF and its active metabolite monomethylfumarate (MMF) exert their anti-inflammatory and immune modulatory effects. Biological therapy became available for psoriasis with the introduction of alefacept at the beginning of this century. Up to then, systemic treatment options comprised small molecule drugs, targeting the immune system in a non-specific manner. This review offers an overview of biologics developed for psoriasis and illustrate a historical progress in the treatment of this common chronic inflammatory skin condition. Psoriasis is an ancient, universal chronic skin disease with a significant geographical variability, with the lowest incidence rate at the equator, increasing towards the poles. We discuss the strengths and limitations of the various models and the lessons learned. We conclude that, so far, there is no one model that can meet all of the research needs. Therefore, the choice model system will depend on the questions being addressed. Psoriasis is a chronic inflammatory disease that is characterized by plaque, inverse, guttate, pustular, and erythrodermic variants. This review focuses on the epidemiology, diagnosis, and treatment of cutaneous psoriasis. Other related topics discussed include peristomal psoriasis, the Koebner phenomenon, and the relationship

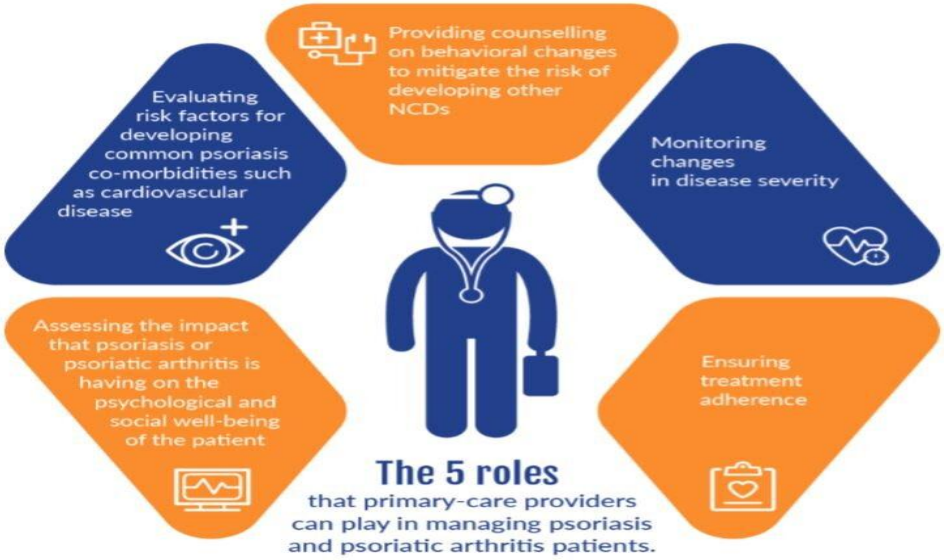
between biologic therapy and wound complications. The pathogenesis of psoriasis is complex and the exact mechanism remains elusive. There is no cure for psoriasis at the present time, and much of the treatment involves managing the symptoms. The biologics, while lacking the adverse effects associated with some of the traditional medications such as corticosteroids and methotrexate, have their own set of side effects, which may include reactivation of latent infections. Significant challenges remain in developing safe and efficacious novel targeted therapies that depend on a better understanding of the immunological dysfunction in psoriasis. Generalized pustular psoriasis (GPP) is a subtype of pustular psoriasis characterized by painful and occasionally disfiguring cutaneous manifestations with sepsis-like systemic symptoms. Affecting any age and race, GPP can occur with other forms of psoriasis or by itself. Treatment is not well established, but includes the use of retinoids, methotrexate, cyclosporine, corticosteroids, TNF-alpha inhibitors, topical therapy and phototherapy. The use of TNF-alpha inhibitors may result in the formation of antidrug antibodies and should be administered with methotrexate.

KEYWORDS: retinoids, methotrexate, cyclosporine, corticosteroids.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease characterized by sharply demarcated erythematous plaques with whitish scale.[1,2] Psoriasis is one of the most frequent chronic inflammatory skin diseases. The prevalence of psoriasis varies with the country, and psoriasis can appear at any age.[3,4] Psoriatic lesions can be itchy and painful, and may cause extreme physical and emotional discomfort and reduce patients' quality of life.[5,6] In the most severe cases, patients with psoriasis have an increased risk of developing serious comorbidities.[7,8] Psoriasis is present worldwide, but with varying prevalence (e.g., 0.24% in Taiwan vs. 8.5% in certain areas of Norway).[9,10] Psoriasis susceptibility 1(PSORS1), which lies within an approximately 220 kb segment of the major histocompatibility complex on chromosome 6p21, is a major susceptibility locus for psoriasis.[11,12] HLA-Cw6 is the susceptibility allele within PSORS1; it is associated with early onset and severe and unstable disease.[13,14] In genetically predisposed individuals, various triggering factors can elicit the disease. In past surveys from 1982 to 2012, the exacerbating factors for the Japanese population were observed to be stress (6.4% to 16.6%), seasonal factors (9.7% to 13.3%), infection (3.5% to 8.3%), sun exposure (1.3% to 3.5%), and _-blockers (0.9% to 2.3%).[15,16] The risk factors for

psoriasis can be divided into two groups, namely, extrinsic and intrinsic risk factors (Figure 1).



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While the etiology of psoriasis remains to be fully elucidated, it is considered an immune-mediated disorder. A combination of genetic, immunological and environmental factors contributes to the phenotype of psoriasis[17,18,19,20] Histologically, psoriatic skin is infiltrated by T cells.[21,22,23,24] and neutrophils, which form Munro's microabscesses in the epidermis.[25]

Recently, it has been shown that the formation of cytosolic RNA:DNA complexes in keratinocytes within psoriatic lesions can also activate the production of inflammatory cytokines.[26]

TYPES OF PSORASIS

Plaque psoriasis: This type of psoriasis is by far the most common type, about 90% of patients suffer plaque psoriasis. Plaque psoriasis is phenotypically characterized by red scaly plaques with a diameter about 0.5 cm, and the distinction between plaques and normal skin is usually easy.[27] These plaques are often symmetrically distributed over the body, and this distribution differ between patients. However, there are some areas in various patients that are more likely to be affected, such as elbows, knees and scalp, than others, like the face. Based on these affected areas, a sub-classification of plaque psoriasis exists, e.g., nail, flexural, palmoplantar, scalp, and sebopsoriasis psoriasis. These divisions allow clinicians to

achieve the diagnosis and select the most appropriate treatment for each sub-classification through their specifications.[28]

Guttate psoriasis: Guttate psoriasis is an acute from of psoriasis, usually triggered by a bacterial infection, such as steptococcal infection, viral or bacterial. In this type of psoriasis, small papules erupt on the limbs, trunk or face. It often appears quite suddenly and it is common to start in childhood or during young adulthood. It manifests itself by spots on skin and itching. The spots on skin can be covered with flaky skin. Guttate psoriasis is easily identified through the spots on skin that are water-drop-shaped on the arms, trunk and legs.[29]

Pustular psoriasis: Pustular psoriasis is the occurrence of small pustules at the edge or in the middle of inflammatory plaque, in hands, fingertips or feet. Less than 5% of psoriatic patients suffer from pustular psoriasis, which is characterized by reddening of the skin and subsequent formation of pustules and scaling that promotes severe irritation. The main causes of this type of psoriasis are systemic steroids, overexposure to ultraviolet light, stress, and pregnancy.[30]

Erythrodermic psoriasis: Erythrodermic psoriasis is an inflammatory form of the disease that affects most of the body surface (90% or more), characterized by periodic, widespread, fiery redness of the skin and the shedding of scales in sheets. Worldwide, about 1%_6% of psoriatic patients have erythrodermic psoriasis. This type has some characteristic symptoms, such as heart rate increase, fluctuating body temperature, reddening, and shedding of the skin. Severe sun burn, emotional stress, alcoholism, infection, and allergy, are the main causes of the erythrodermic psoriasis. Patients that suffer from erythrodermic psoriasis have fewer plaques and those will not be as thick when compared to plaque psoriasis which are larger and very thick.[31]

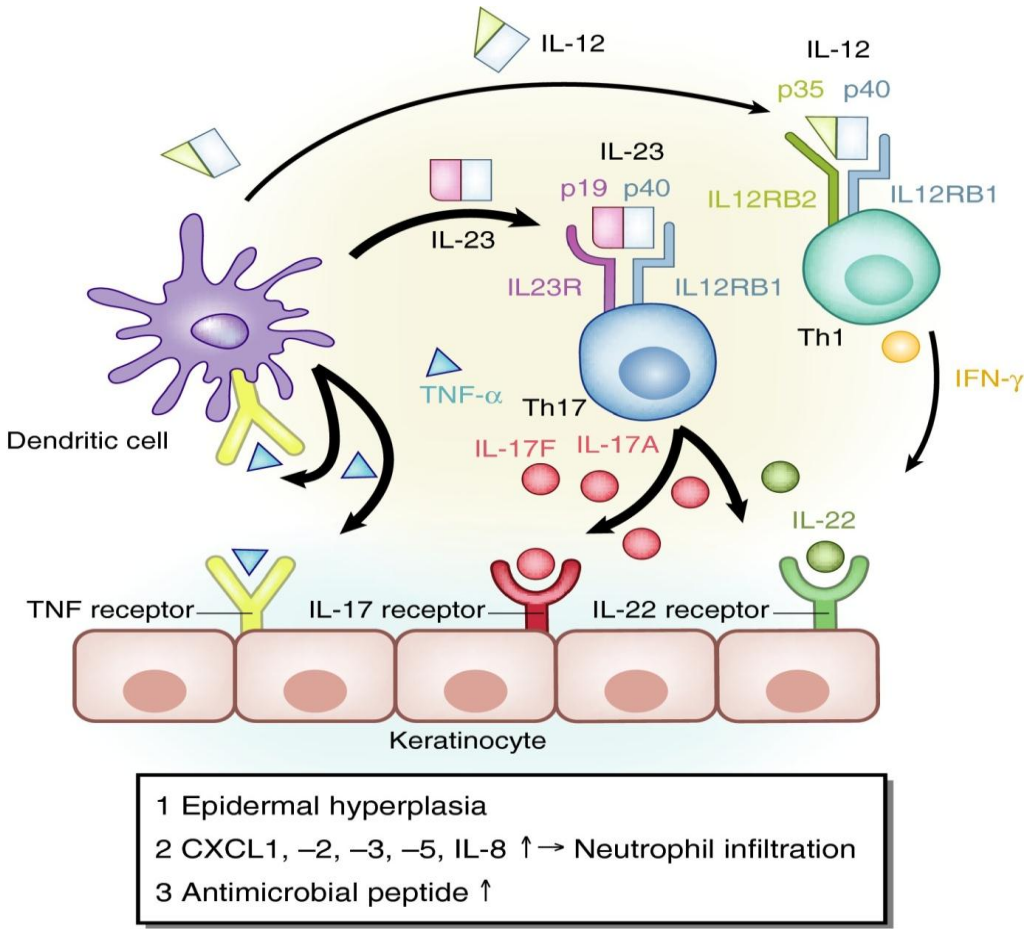
Flexural psoriasis: Flexural psoriasis is also known as inverse psoriasis and is frequently found in the armpits, groin, under the breasts, and in other skin folds around the genitals and the buttocks. Worldwide, about 18% of psoriatic patients have the flexural type. Irritation from rubbing and sweating, and red lesions that are characterized by smooth shape and shiny, are the main symptoms. Consequently, the high sensitivity to friction or sweating are the leading causes of flexural psoriasis.[32]

Nail psoriasis: Nail psoriasis affects fingernails and toenails, causing pitting, abnormal nail growth, and discoloration. Worldwide, about 50%_80% of psoriatic patients have nail

psoriasis. Patients will note changes in the nail color, little pits in nails, lines across nails, loosening of nail and thickening of skin under nail. This type of the disease may be caused by environmental causes, combined with genetic and immune causes.[33]

Psoriatic arthritis: Psoriatic arthritis is an inflammatory disease which affects the joints of children and adults that suffer from psoriasis. Worldwide, about a third of psoriatic patients have psoriatic arthritis. The red, swollen, tender, warm and stiff joints, arthrosclerosis, stroke, and myocardial infarction are the characterized symptoms of this type of psoriasis. Psoriatic arthritis is usually caused by trauma or injury on skin, like cuts or burns, medicines, alcohol, skin irritants, and smoking.[34]

The pathogenesis of psoriasis; The pathogenesis of psoriasis is complex and not fully elucidated. Excessive activation of parts of the adaptive immune system is thought to be central to the pathogenesis of psoriasis.[35] In the initial steps of psoriasis pathogenesis, a variety of cell types, including plasmacytoid dendritic cells, keratinocytes, natural killer T cells, and macrophages, secrete cytokines that activatemyeloid dendritic cells(Figure 2).



In the initial steps of psoriasis pathogenesis, a variety of cell types, including plasmacytoid dendritic cells, keratinocytes, natural killer T cells, and macrophages, secrete cytokines that activate myeloid dendritic cells (Figure 1).

For example, DNA-LL37 complexes stimulate plasmacytoid dendritic cells to secrete interferon alfa (IFN-α) which, in turn, activates myeloid dendritic cells. Once activated, myeloid dendritic cells secrete IL-12 and IL-23. IL-12 induces differentiation of naive T cells to TH1 cells. IL-23 is central to the survival and proliferation ofTH17andTH22cells.TH1 cells secrete interferongamma(IFN-γ) and TNF-α;TH22cells secrete IL-22;andTH17 cells secrete IL-17, IL-22, as 8% in Norway.[36,37.38] In most regions, women and men are affected equally.[39] While psoriasis can manifest at any age, a bimodal age distribution exists for psoriasis presentation at ages 18 to 39 years and also at ages50to69years.[39] Genetic and environmental factors may influence the age at onset of psoriasis. For example, the presence of the human leukocyte antigen (HLA)-C*06 allele is associated with earlier-onset age of psoriasis.[40]

Epidemiology: Biologics are the proof-of-concept for the significant progress that has been achieved in understanding the complex pathogenesis of psoriasis. The specific targets of biologics have out-pointed crucial cytokines, including tumor-necrosis-factor (TNF)-_, interleukin (IL)-23 and IL-17, for the development and maintenance of the skin changes in psoriasis. The sequences of cellular events involved in IL-23 and Th17 signalling are referred to as the IL-23/Th17 signalling pathway, and is one of the most studied in psoriasis.[41]

In order to give a better understanding of where in the immune system the various biologics are targeting, an overview is given in the following, of the most important cells and cytokines involved in development of psoriasis. Psoriasis pathogenesis involves both the innate—and the adaptive immune response. Though, psoriasis is mainly considered a T-cell mediated disease, and the T-cell targeting biologics, alefacept and efalizumab substantiated the role of T-cells as primary modulators. The IL-23/Th17 pathway not only involves different subgroups of T-cells, but also include, e.g., dendritic cells, macrophages, neutrophils, and keratinocytes. The initiation of this inappropriate immune response is still being elucidated, but the combination of a predisposing genotype and external factors as skin trauma, known pharmaceuticals, bacterial and viral infections, and stress have been suggested as key triggers. Traditionally, pathogenesis of psoriasis is considered in two phases, the initiation phase and the maintenance phase. Some of the triggers of psoriasis are known to disrupt or

stress the keratinocytes in the epidermis which in turn release self-deoxyribonucleic acid.[42] (DNA) and the anti-microbial peptide LL-37 (cathelicidin). Besides self-DNA, pathogen-derived DNA is able to form a complex with LL-37. The complex binds to toll-like receptor 9 on plasmacytoid dendritic cells in the dermis. The plasmacytoid dendritic cell secretes type 1 interferons (IFN-_ and -_), TNF-_, IL-6, and IL-1_ that stimulate the local myeloid dendritic cells to migrate to the local draining lymph nodes. Upon contact with the resting naive T-cells, they secrete cytokines including TNF-_, IL-12 and IL-23, which induce the T-cell to differentiate into mature Th1-, Th17-, and Th22-cells. When returning to the skin, these specific T-cell linages release TNF-_, IFN-, IL-17A and -F, and IL-22 that stimulate keratinocytes to proliferate and leads to an altered differentiation. Erythema due to angiogenesis, dilated and tortuous vessels in the dermal papilla, thickening of the skin due to acanthosis, and scaling due to an accelerated proliferation and altered differentiation of keratinocytes develop. Around 10 years ago, the IL-17 producing subtype of T-cells, Th17-cells, was identified.[43] IL-17A has though been found not only to be linked to the cluster of differentiation (CD)4 + T-cells. CD8 + T-cells, _ T-cells, natural killer cells, mast cells and neutrophils are all sources of IL-17A.[44]

Diagnosis Psoriasis

Diagnosis is usually made on clinical findings; skin biopsy is rarely used to diagnose psoriasis. The Psoriasis Area and Severity Index (PASI) score has been used to quantify disease severity of erythema, infiltration or thickness, scaling and the extent of lesions in patients with widespread disease.[45] More recently ,easier-to-use scores, such as the psoriasis global assessment (PGA) or lattice system-physician's global assessment (LS-PGA) have been developed for routine clinical practice.[46] Clinical diagnosis of inverse psoriasis can be difficult, owing to secondary alterations such as friction. A full body examination, in particular the genitoanal, peri-umbilical, and retro-auricular areas, scalp, and nails, should be checked for psoriasis. Psoriasis shows characteristic histopathological changes in almost every cutaneous cell type (figure 2A–D). By contrast with normal skin (figure 2A, B), psoriatic hallmark features include epidermal acanthosis (thickening of viable layers), hyperkeratosis (thickened cornified layer), and parakeratosis (cell nuclei present in the cornifed layer; asterisk in figure 2D). Epidermal rete ridges (thickenings that extend down between dermal papillae) are markedly elongated. In the dermis, dilated and contorted blood vessels reach into the tips of the dermal papillae (arrows in figure 2C). An inflamatory infiltrate containing T-lymphocytes is notable within the dermis and epidermis (figure 2B,

D), and an increased number of macrophages, mast cells, and neutrophilic granulocytes. These cells accumulate within the epidermis (asterisk in figure 2B) forming so-called pustules of Kogoj or subcorneal microabscesses, also referred to as Munro's microabscesses.

The most common differential diagnoses of psoriasis include tinea capitis and tinea corporis, seborrheic dermatitis (scalp, face, and chest involvement) and eczema of several causes (atopic dermatitis, allergic, or irritant contact dermatitis). Less common differential diagnoses include lichen planus (mucosal involvement, scarring alopecia, and severe itch), pityriasis rosea (usually self-limiting within a few weeks), pityriasis rubra pilaris, secondary syphilis (especially in cases of guttate psoriasis), and cutaneous lymphoma.

Risk Factors for the Development of Psoriasis

Extrinsic Risk Factors

Mechanical Stress: In patients with psoriasis, skin lesions appear in uninvolved areas after various injuries.[49,50] This is known as the Koebner phenomenon. Radiotherapy, ultraviolet (UV) B, and even a slight skin irritation have been reported to trigger new lesions of psoriasis.[51,52] However, psoriatic lesions are not always observed in the uninvolved skin after injuries.[53,54] Type, site, depth, and degree of trauma may affect the pathogenesis of the Koebner phenomenon.[53] Under appropriate conditions, the Koebner phenomenon may occur, especially when there is dermal trauma with epidermal involvement. It is speculated that increased papillary dermis blood flow helps bring mediators that play a part in the pathogenesis of psoriasis.[53] However, the mechanisms underlying the Koebner phenomenon remain to be completely elucidated[53,54] Nerve growth factor (NGF) is a neurotrophic factor that is expressed in both the nervous system and peripheral organs. NGF is thought to be associated with the Koebner phenomenon.[55]

Air Pollutants and Sun Exposure: The increase in air pollution over the years has had major effects on the human skin, and various air pollutants such as polycyclic aromatic hydrocarbons, volatile organic compounds, oxides, particulate matter, ozone, heavy metals, and UV damage the skin by inducing oxidative stress.[56] Cadmium is one of the air pollutants which a_ect the pathogenesis of psoriasis. Patients with severe psoriasis had higher blood cadmium when compared with the general population.[57] This study suggests that environmental exposure to cadmium may compromise immunity, and micro environmental perturbation can predispose one to the worsening of psoriasis. The UV radiation that reaches the Earth's surface is divided into two subtypes: more than 95% UVA (315–400 nm) and

1%–5% UVB (280–315 nm). In the past several decades, phototherapy has been widely used to treat psoriasis.[58] Both narrowband UVB (311 nm) and excimer laser (308 nm) are currently used as the first-line therapy for psoriasis, and psoralen UVA (PUVA) is also used as the second-line therapy with preference to refractory psoriatic plaques.[58]

Drugs: Drug-related psoriasis is recognized as the onset and exacerbation of psoriasis which is associated with certain drugs. It is often difficult to identify drug-related causes of psoriasis in clinical situations. This is because the latency period between the start of the medication and the onset of psoriatic skin lesions can vary considerably between drugs.[59] In some cases, the psoriasis flare can persist even after the suspected drug has been discontinued. Moreover, there may be little difference between psoriasis and drug-related psoriasis in terms of the clinical and histopathological findings.[59] Drug-related psoriasis would manifest as plaque psoriasis, palmoplantar psoriasis, nail psoriasis, scalp psoriasis, pustular psoriasis, and erythrodermic psoriasis.[60]

Vaccination: Patients with psoriasis are at increased risk of infection, mostly because of treatment with immunomodulatory or immunosuppressive drugs.[61] Thus, vaccination is recommended to prevent specific infections.[61,62] However, vaccination can often trigger and exacerbate psoriasis. Several studies support the association between influenza vaccination and the exacerbation of psoriasis.[63,64] Influenza vaccination may also trigger the onset of psoriasis.[65]

Infection: The association between psoriasis and streptococcal infection is well established.[66] Psoriasis occurs after streptococcal infection, and the most common type is guttate psoriasis. Although the symptoms are self-limited, they can recur with the recurrence of streptococcal infection. Thus, tonsillectomy may be a potential treatment option for patients with recalcitrant psoriasis associated with episodes of tonsillitis.[67] Although prior infection with Streptococcus pyogenes is associated with guttate psoriasis, the ability to trigger guttate psoriasis is not serotype specific.[66] Candida species are a part of the normal human microbiota, and they were highly detected in either the skin or the mucosal membranes of patients with psoriasis.[68]

Lifestyle: Smoking and alcohol consumption have been associated with psoriasis. A systematic review and meta-analysis revealed that patients with psoriasis are more likely to be current or former smokers.[69] Smoking is associated with an increased risk of developing

psoriasis.[70] In addition, smoking is strongly associated with pustular lesions of psoriasis.[71] Alcohol consumption appears to be a risk factor for psoriasis. However, a past systematic review concluded that there was not enough evidence to establish whether the alcohol consumption was indeed a risk factor.[72]

Intrinsic Risk Factors

Obesity: Metabolic syndrome is common in patients with psoriasis[73,74] and obesity is strongly associated with the onset and exacerbation of psoriasis[75,76,77] A large prospective cohort study also showed a positive association between body mass index (BMI) and psoriasis.[78] Leptin is an adipose tissue hormone that functions as an afferent signal in a negative feedback loop that maintains homeostatic control of adipose tissue mass.[79]

Diabetes Mellitus; The prevalence of DM is generally influenced by ethnic origin and lifestyle factors. However, the prevalence of DM might be similar among diverse patient populations, ethnic backgrounds, and baseline therapy.[80] A meta-analysis revealed that psoriasis was associated with DM.[81] DM is divided into two groups, namely, type 2 and type 1 DM. Patients with psoriasis have a significantly higher risk of type 2 DM. However, the prevalence of type 2 DM does not correlate with patient age or severity of psoriasis[82] Psoriasis is a marker for increased risk of type 2 DM independent of its severity. It is unclear which disease comes first, psoriasis or type 2 DM.[82] As mentioned above, obesity is a risk factor for psoriasis. Obesity contributes to the onset and exacerbation of type 2 DM directly. Thus, obesity is associated with psoriasis as well as type 2 DM, and type 2 DM may not contribute to the pathogenesis of psoriasis directly. In contrast to type 2 DM, type 1 DM is a chronic disease characterized by insulin deficiency due to autoimmune destruction of insulin-producing pancreatic cells, leading to hyperglycemia.[83]

Hypertension: In a meta-analysis, patients with psoriasis showed greater prevalence and incidence of hypertension.[84] A multicenter non interventional observational study including 2210 patients with psoriasis revealed that 26% of patients with psoriasis had hypertension, and the incidence of hypertension was higher when compared with the general population.[85] Conversely, hypertension may be associated with the incidence of psoriasis.[86]

Mental Stress: Mental stress is a feeling of strain and pressure caused by internal perceptions which lead to anxiety or other negative emotions. Mental stress occurs when individuals think the demands exceed their ability to cope. Mental stress is commonly regarded as a well-

established trigger of psoriasis and many patients with psoriasis and physicians believe that mental stress exacerbates psoriasis. Although psoriasis leads to higher degree of distress as proved by measurements on Dermatology Life Quality Index scales, the relation between mental stress and psoriasis is complex. In a past systematic review including 39 studies (32,537 patients), 46% of patients believed their disease was stress reactive and 54% recalled preceding stressful events.[87] However, there was no high-quality evidence to support the notion that the preceding stress was strongly associated with the onset and exacerbation of psoriasis. The association was based primarily on retrospective studies with many limitations. It seems unclear whether mental stress a_ects the clinical course of psoriasis. In contrast, a prospective study concluded that cognitive and behavioral patterns of worrying and scratching were both independently related to an increase four weeks later in disease severity and itch, at moments when patients experienced a high level of daily stressors.[88]

Topical antipsoriatic medications

Corticosteroids: Topical corticosteroids, particularly high-potency corticosteroids, have been a mainstay in the topical treatment of psoriasis for decades.[89] Their efficacy can be attributed to multiple mechanisms of action, including their antiinflammatory, immunosuppressive and antiproliferative effects. Topical corticosteroids are classified into seven classes in the US shown good efficacy against chronic therapy-resistant psoriasis, including both progressive and stationary phases; and mometasone furoate.[90] Although topical corticosteroids are effective in maintenance of the disease, these therapies can cause many potential adverse effects, including cutaneous atrophy, formation of telangiectasia, development of striae, steroid rosacea, perioral dermatitis, hypothalamic-pituitary-adrenal (HPA) axis suppression, skin infections, and other effects.[91]

Vitamin D3 analogues: The active form of vitamin D3 is known to play an important role in the regulation of intestinal calcium absorption, bone mineralization and the prevention of rickets. In addition to these actions, vitamin D3 has several more biological effects, including the stimulation of cellular differentiation, inhibition of proliferation and immunomodulation.[92] This makes vitamin D3 a potential candidate for treatment of psoriasis. However, parent vitamin D3 might not be suitable for treating psoriasis owing to potential for hypercalcemia. Hence, several vitamin D3 analogues have been developed for the treatment of psoriasis.[93] Vitamin D analogues bind to the vitamin D receptor, thus causing biological actions on both corneocytes and on immune-competent cells in the skin.

Analogues such as calcipotriol, tacalcitol and maxacalcitol inhibit corneocyte proliferation and stimulate corneocyte differentiation in vitro. In addition, these analogues have only minimal effects on with mild-to-moderate plaque psoriasis.[94]

Tacalcitol: Subsequent clinical studies have proved the efficacy and safety in the treatment of chronic plaque psoriasis, with no systemic side effects for up to 18 months.[95] The long-term safety and efficacy of tacalcitol ointment in patients with chronic plaque psoriasis, where up to 20% of the body surface was affected, was established in an open, multi-center, Phase IV study.[96]

Retinoids: Retinoids provide a distinct class of treatment and have a unique position within the armamentarium of antipsoriatic treatments, which are largely dominated by immunomodulatory approaches. The mechanism of action of retinoids in psoriasis may include direct suppression of inflammation as well as inhibition of proliferation and normalization of differentiation in the epidermal layer.[97] The cream formulations are being marketed as less irritating.[98] A recent improvement in tazarotene therapy was a reduction of skin irritation by short contact applications.[99]

Phosphodiesterase 4 inhibitors: Phosphodiesterase 4 (PDE4) is the predominant cyclic AMP degrading enzyme, present in a variety of inflammatory cells including eosinophils, neutrophils, macrophages, T cells and monocytes. In addition, this enzyme is expressed in nonimmune cells such as keratinocytes and fibroblasts. Owing to the broad anti inflammatory/immunomodulatory action of PDE4 inhibitors, it has been proposed that PDE4 inhibitors might also be efficacious for skin disorders such as psoriasis and atopic dermatitis.[100] These PDE4 inhibitors displayed strong anti-inflammatory action in models of allergic contact dermatitis in mice, in the arachidonic acidinduced skin inflammation in mice and in ovalbuminsensitized guinea-pigs. The determination of cytokines in skin homogenates revealed that both Th1 as well as Th2 cytokines are suppressed by PDE4 inhibitors, indicating an anti-inflammatory activity in both the Th2-dominated acute phase as well as the Th1-dominated chronic phase of atopic dermatitis. Owing to the suppression of Th1 cytokines, activity can also be expected in psoriasis.[100]

CONCLUSION

Psoriasis is a common, immune-mediated disease with associated arthritis, depression, and cardiovascular comor – bidities.[29–31] While no established diagnostic criteria exist for skin-

limited psoriasis, trained clinicians can often diagnose psoriasis based on clinical history and skin examination. In challenging cases, histopathology can be helpful in distinguishing psoriasis from other types of inflammatory skin diseases. In the current literature, there is a dearth of studies examining the sensitivity and specificity of clinical signs and symptoms for psoriasis. In this paper, we have provided diagnostic guidelines to aid the nondermatologist in recognizing and diagnosing psoriasis. Future studies are necessary to investigate and validate screening tools for diagnosing psoriasis.

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