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Review Article

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IMMUNOPATHOGENIC CAUSE OF PSORIASIS

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ABSTRACT

Psoriasis is a prevalent auto immune disease that affects the skin and joints, mostly affecting T cells and resulting in inflammation. It is an autoimmune-based, long-term inflammatory skin illness associated with psoriatic arthritis, mental, cardiovascular, and hepatic issues. Ten percent of patients have preventable psoriasis vulgaris, a condition with a superposed clinical makeup that comprises chronic plaque lesions. These people also get arthritis. In the bone marrow,T-lympocytes arises from a common lymphoid progenitor that also gives rise to B lymphocytes. Following that, T cells leave the bone marrow and travel to the thymus gland to begin developing; it is at the thymus where T cells acquire their moniker. When cytokines released by T cells were examined on the skin (epidermal specimen) of psoriatic patients, it was found that only a small percentage of cells secreted Th-2 related cytokines (IL-4 and IL-10). Whereas TNF-α, IL-2 and IFN-γ are Th1-related cytokines that are produced by almost all T cells.It is further suggested that through a complicated interaction between CD4+, CD8+T cells, and cross-presenting dendritic cells, CD8+ T cells are involved in the regulation of the Th1 polarization that is seen in psoriasis lesions.when a hyperactive immune system that targets healthy cells while attacking and producing an excessive number of skin cells is the cause ofpsoriasis. Genetics is important when one parent has psoriasis.Based on the information currently available, psoriasis mayrun in families and maybe influenced bygenetics. However, getting psoriasis is not a given just because a family member has it.People with psoriasis often develop the condition between the ages of 15 and 30, according to the National Psoriasis Foundation (NFP).Additionally, if you have a parent with psoriasis, your chances of getting the condition are increased by 28%.If one or both of your parents have the condition, your risk rises to 65%.Heart disease, metabolic syndrome, and dyslipidemia are prevalent health problems that impact the heart and blood vessels. Heart and blood vessel issues may be apparent since birth, including irregular heart rhythms and abnormalities in heart valves. Metabolic syndrome is a cluster of five disorders that may result in cardiovascular issues, stroke, and various health complications. Psoriasis, a condition linked to type 2 diabetes, is more prevalent among individuals with type 2 diabetes, leading to difficulties in insulin hormone production and utilization by the body. Diabetes is a multifactorial disease caused by a combination of genetic and environmental factors. Psoriasis involves inflammation in the gastrointestinal lining, which results in higher absorption of fats. The severity and location of skin affected determine the treatment for psoriasis.

INTRODUCTION

One common autoimmune condition affecting the joints and skin is psoriasis. That is dependent on T cells and causes inflammation.Disease manifestation is orchestrated by pro inflammatory CD4-positive T helper cells that generate either interleukin (IL)-17 (Th17) or interferon-γ (Th1).[7]

It is a chronic inflammatory skin condition caused by the immune system that is linked to psoriatic arthropathy as well as psychiatric, cardiovascular, and hepatic disorders.Numerous other conditions like arthritis, high blood pressure,depression, cardiovascular disease, obesity, diabetes mellitus, and decreased quality of life are all linked to psoriasis. Psoriasis vulgaris, a disease with a superposed clinical composition that includes chronic plaque lesions, is prevent in 10% of patients. These individuals also develop arthritis.[4] T lymphocytes are imapcted by the illness and target healthy skin cells. These T cells produce signals that cause the skin to become inflamed.[1,2] Additionally, the body produces more afflicted skin cells than it requires, which results in the psoriaisis specific plaques. For light skin tone, these plaques are usually red or pink; for deeper skin tones, they are usually light to dark brown, purple, or gray.[1]

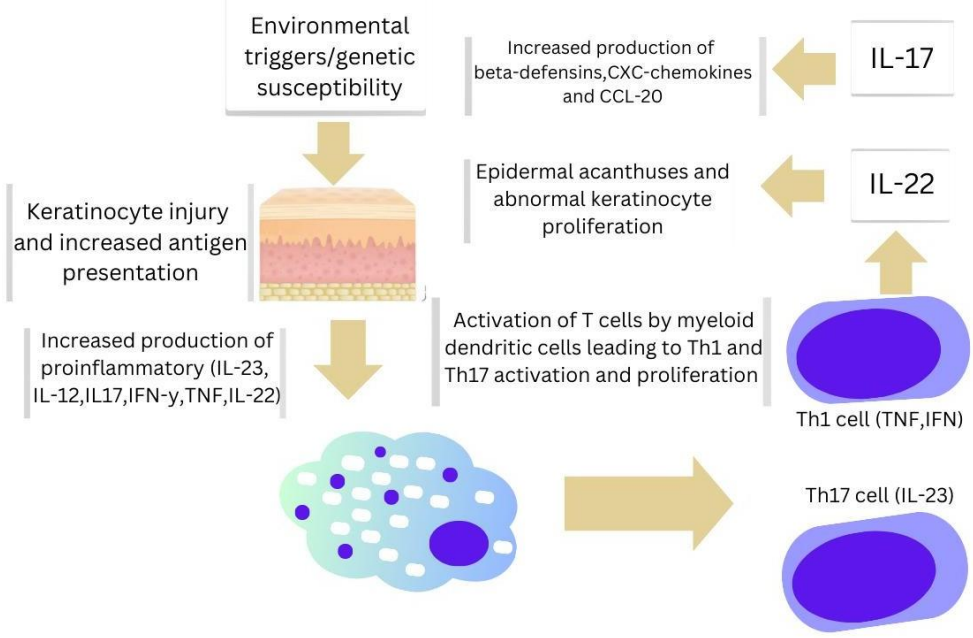
Involvement of cytokines in Psoriasis

Robert Willian, an English physician, first described psoriasis in 1809 as a straight forward diagnostic word for a number of skin disorders. He used the name lepra vulgaris in his description. Wilson et al. identified the involvement of T cells and T helper cells in psoriasis in 2007. In the bone marrow, T-lymphocytes arise from a common lymphoid progenitor that also gives rise to B

lymphocytes. Following that, T cells travel from the bone marrow to the thymus gland where they grow.It is the thymus that gives T cells their moniker.As precursor cells move to the thymus, they split into several kinds of T-lymphocytes.[23,24] T cell differentiation proceeds after exiting the thymus.Several subgroups of developed T cells are essential for controlling and shaping the immune response.[20] When cytokines by T cells were examined on the skin (epidermal specimens) of psoriatic patients, it was found that only a small percentage of cells secreted Th-2 related cytokines (IL- 4 and IL-10).[7,17] Additionally, IL-4, which is produced by activated CD4+ T cells, has anti- inflammatory properties and can enhance allergic reactions (20, 22, 23).[14] Furthermore, the cytokine IL-10 (interleukin) has strong anti-inflammatory qualities that shield the host and preserve normal tissue homeostasis.[17] Nearly all T cells produce Th1-related cytokines, such as IFN-γ, TNF-α, and IL-2.[23] Consequently, IFN-γ and TNF-α can stimulate keratinocytes to produce a variety of cytokines and growth factors, such as TNF-α, IL-6, IL-7, IL-8, IL-12, IL-15, and IL-18.[1,7,13] These cytokines belong to the BAFF (TNF) family.In the bone marrow, T-lymphocytes arise from a shared lymphoid progenitor that also gives rise to B lymphocytes. Research has indicated that TNF family member BAFF is essential for the development of aggressive B cells and autoimmune diseases.[14] A multitude of autoimmune disorders would arise if serum levels of BAFF (B cell activating factor) were to deregulate. Increased BAFF levels have been linked to organ specific autoimmune disease such as bollous pemphigoid and localised scleroderma.[23] iSince INF-γ injections intradermally can cause lesions,INF-γ may play a fundamental role in psoriasis. CD4+ and CD8+ cells both produce IFN-γ.[7,8]

TNF-α exerts pleiotropic effects on diverse cell types and plays a role in the pathogenesis of some autoimmune and inflammatory disorders. Psoriasis lesions are brought on by an increase in T lymphocytes.DCs and macrophages produce a lot of IL-23 in situ in psoriasis lesions (32,62). With a subgroup including the activation markers CD25, HLADR, and CD27, the majority of T lymphocytes linked to psoriasis are CD3+ CD2+CLA+.[7] The combination between these and other cytokines and growth factors produced in psoriasis lesions can account for most of the clinical features of psoriasis, including increased inflammation and neovascularization.Many diseases are primarily caused by these cytokines and chemokines, and finding potential therapeutic targets for them in the future is a constant problem.[13]

Links of cytokines in psoriasis



How autoimmune disease affect skin

The body's largest and most important protective organ is the skin. It acts as a physical hedge against the surroundings while covering the entire body.It aids in controlling body temperature and securities the organ from damage, ultraviolet (UV) shafts, bacteria, contagions, and toxins.[16] It has varying density and performs distinct places at colorful fleshly locations. The skin is composed of three primary layers. The top subcaste is the epidermis, the second subcaste is the dermis, and the third and deepest subcaste is the subcutaneous towel. The remotest subcaste of epithelial towel that shields the body from the outside world is called the skin epidermis. The epidermis is composed of stratified and keratinized squamous epithelium.[3] The number of layers of epithelial cells in it varies based on the part of the body it resides in. It is devoid of any blood vessels. The four layers that comprise the epidermis are the stratum corneum, stratum granulosum, stratum basale, and stratum spinosum. Skin that is thin indicates

that it is mature. The soles of the bases and the triumphs of the hands are the only ones with "thick skin." Its fifth subcaste, the stratum lucidum, is located between the stratum corneum and the stratum granulosum. Keratinocytes, melanocytes, Langerhans and Merkel cells are among the epidermal cells. The maturity of the epidermis's cells, or keratinocytes, come from the rudimentary subcaste.[1,3,4] The lipids and keratin produced by these cells are necessary for the conformation of the epidermal water hedge. also, keratinocytes help control calcium situations by easing the skin's immersion of UVB light, which is necessary for the activation of vitaminD. Grainy subcaste keratinocytes express several molecules associated with ingrain impunity, such as antimicrobial peptides (1, 2), lipocalin 2, β-defensin, cathelicidin (CAMP/ LL- 37), psoriasin (S100A7), calgranulin A (S100A8), and calgranulin B (S100A9).[16,28] When psoriasis is caused by an hyperactive vulnerable system that attacks and produces an inordinate number of skin cells while targeting healthy cells. The following are the main cells that beget psoriasis

1. Keratinocytes are cells set up in the skin's remotest subcaste, the epidermis. In psoriasis, keratinocytes gain exorbitantly presto. The skin develops red spots (shrine) and thick, argentine scales as a result of this fast cell development.
2. Important seditious vulnerable cells, similar as T cells(T lymphocytes), are hyperactive and attack healthy skin cells in psoriasis victims.[28] These cytokines TNF-α, interleukins, and excrescence necrosis factor-α increase keratinocyte proliferation and foster inflammation.Cognitive goods of ReTinoic acid supporter pull out do in layers.[7]
3. Dendritic cells When T cells encounter antigens(damaged or alien accoutrements), these antigen presenting cells stimulate T cells. Dendritic cells are hypothecated to be involved in the inauguration and conservation of the seditious response in the skin in psoriasis.
4. White blood cells known as neutrophils are drawn to the area of inflammation in psoriasis. They've a part in the towel damage and inflammation that the tormented skin displays. Because the immune system misidentifies healthy tissues in this case, skin cells as alien invaders, psoriasis is classified as an autoimmune disease.[22] Itching, occasionally pain, and red areas coated with silvery scales are the hallmark signs of psoriasis, which are caused by an interaction between these immune cells and the skin cells. The following are some typical ways that autoimmune disorders may affect the skin

Rashes and Lesions: Skin rashes and lesions are common manifestations of autoimmune disorders. As an illustration

Systemic lupus erythematosus (SLE): Frequently presents as various skin lesions on sun exposed parts of the skin, as well as a butterfly-shaped rash on the face.[2]

Blistering and Ulceration: Antibodies directed against proteins that maintain the integrity of skin layers can result in blistering of the skin in certain autoimmune diseases.[22]

Hair and Nail Changes: Autoimmune diseases can affect hair and nails:

Alopecia areata: Causes patches of hair loss on the scalp and occasionally on other body parts.[29]

Psoriasis: Can affect the nails, causing pitting, discoloration, and crumbling.

Changes in Pigmentation: Some autoimmune conditions affect pigment-producing cells (melanocytes), leading to changes in skin color[29,22]

Vitiligo: Results in depigmented patches of skin due to destruction of melanocytes.

Raynaud's Phenomenon: While primarily a vascular disorder, Raynaud's phenomenon often accompanies autoimmune diseases and can cause changes in skin color (white, blue, or red) due to blood vessel spasms triggered by cold or stress.[2]

Maintaining immune monitoring and reacting to infections, allergies, and other skin- related problems depend on the SALT system. It is crucial in the setting of autoimmune skin illnesses because dysregulation of the skin's immune system can result in tissue damage and chronic inflammation.

Genetic links of Psoriasis

Psoriasisin one parent makes geneticssignificant.Psoriasis mayrunin familiesandmay be influenced by genetics, according to available data. But having a family member with psoriasis does not guarantee that one will get it.The National Psoriasis Foundation (NFP) states that psoriasis often develops in people between the ages of 15 and 30.You also have a 28% probability of developing psoriasis if you have a parent who has the ailment.[11] Your risk increases to 65% if one or both of your parents have the illness.[5] Every cell in your body has genes, which are similar to blueprints. That is rarely the result of a single faulty gene.[8] One of the genes most frequently linked to psoriasis is HLA-Cw6. However, the majority of the time, a combination of many genes and environmental factors including stress, pollutionexposure, and food havea role. Psoriasis can, albeit rarely, develop in people without a familial history, but only in a small percentage of cases. This individual has spontaneous gene alterations that, in the presence of environmental triggers, can result in psoriasis.[11]

Psoriasis seems to be an example of such. Over two dozen genes have been found by researchers thus far that may be involved with the illness. Researchers have even been able to connect certain genes to other forms of psoriasis, such as pustular, guttate, and plaque.

Even if you have any of these genes, your chances of getting psoriasis are quite low. At least half of the population carries the genes associated with a higher risk of psoriasis.[5]

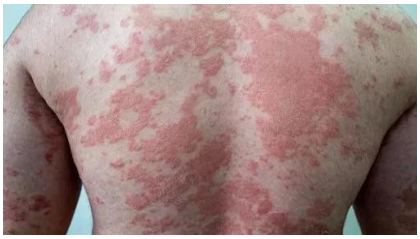


Figure 2: Scaly patches on Skin.

However, only 2% of the population suffers from the condition. However, psoriasis can still develop even if you do not inherit the genes that may cause it.

Other diseases caused Psoriasis

In addition to these conditions, people with psoriasis may also be at higher risk for developing osteoporosis, liver disease, renal disease, Crohn's disease, diabetes, metabolic syndrome, obesity, and uveitis, an inflammation of the center part of the eye.

Psoriatic Arthritis

Your joints may hurt, swell, and become stiff if you have psoriaticarthritis. Approximately 1 in 4 persons who already have psoriasis are affected by it. areas of red, flaky skin coated with silvery areas are the result of psoriasis. Before they even have psoriasis, some people may develop psoriatic arthritis. Rarely, persons with psoriatic arthritis may never have any discernible psoriasis patches. Both psoriasis and psoriatic arthritis are autoimmune diseases brought on by immune system flaws.[25]

Cardiovascular Disease

Heart and blood vessel problems are grouped together as cardiovascular ailments. One or more cardiac and/or blood vascular components may be affected by these disorders. A person with the condition may exhibit no symptoms at all or symptoms in the form of bodily symptoms.[18,32]

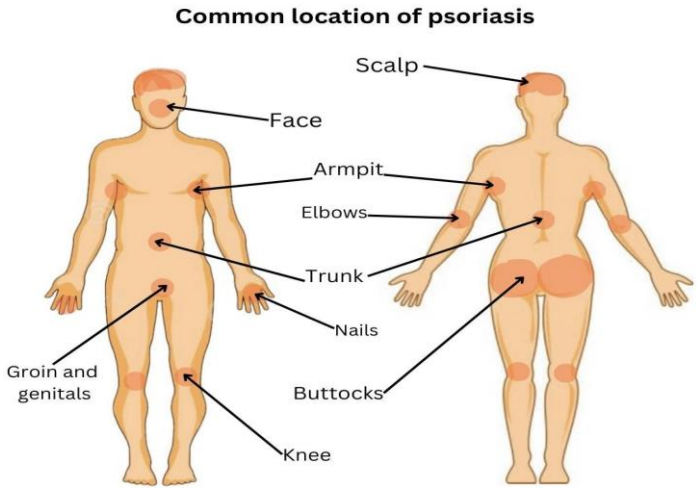


Figure 3: Skin Lesions on different parts.

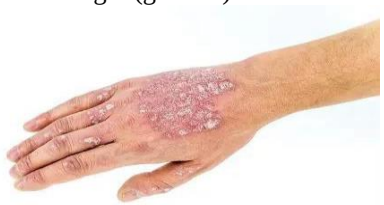
Heart and blood vessel issues, such as constriction of blood vessels in the heart, other organs, or the body at large, are referred to as cardiovascular disease.

Heart and blood vascular problems are present from birth.[32] Heart valves not operating correctly. Abnormal heartbeats.

Metabolic Syndrome

Diabetes mellitus, heart disease, stroke, and other health problems can be brought on by a group of five conditions known as metabolic syndrome.[21] A person is diagnosed with metabolic syndrome if they have three or more of these risk factors

High levels of blood sugar (glucose)



Decrease the good cholesterol levels in the blood (HDL) High blood triglyceride levels.

Hypertension

The National Psoriasis Foundation partially financed a recent study that found uncon- trolled blood pressure was more common in persons with severe psoriasis. One well-known cardiovascular risk factor that raises the possibility of myocardial ischemia and infarction, stroke, and cardiovascular mortality is hypertension.[27] Psoriasis and hypertension have been proven to positively correlate in numerous research. Moreover, the majority of research indicates that psoriasis sufferers are more likely to develop hypertension. Nonetheless, there aren't many prospective studies looking at the relationship between psoriasis risk and hypertension. People with severe psoriasis had a 48% increased risk of hypertension, the study found.[27] Compared to those without psoriasis, those with moderate psoriasis (3–10% of their body surface area) had a 20% higher risk of uncontrolled blood pressure.

Dyslipidemia

Numerous studies on the connection between blood lipid levels and psoriasis have been published since the early 1900s.Boehncke and Boehncke's 2011 study examined the con- nection between the severity of psoriasis and cardiovascular morbidity. Thirteen Later, the dyslipidemia associated with this disease was found time and time again in a number of studies carried out in populations with varying racial and geographic origins.[30] Although there have been several instances of raised serum lipid levels in psoriasis, few studies have also shown normal values.[9,10] In most research, it has been found that blood cholesterol and triglycerides are much increased. It is believed that psoriasis is significantly influenced by aberrant fat metabolism. Numerous proinflammatory cytokines, such as TNF*κ*, INF-Gamma, and IL-1, work on the body to produce an environment that is pro-inflammatory6, 17.[7,10] Psoriasis is characterized by an inflammatory change in the gastrointestinal endothelium that leads to increased fat absorption. In addition, dyslipidemia is an adverse effect of a number of psoriasis drugs. In the current study, serum levels of triglycerides, LDL, and VLDL were greater in psoriatic patients and lower in controls, but HDL levels were lower in both groups.[9] Numerous studies have shown that dyslipidemia varies in severity among psoriasis patients.

Diabetes

People with type 2 diabetes are more likely to have psoriasis. It is a disorder that makes it more difficult for your body to produce and utilize the insulin hormone. Diabetes and psoriasis are prevalent illnesses that can have a number of serious repercussions.[21] Psoriasis and diabetes are common comorbidities, with the former being considered a risk factor for the latter. Diabetes mellitus is known to cause retinopathy, nephropathy, neuropathy, cancer, cardiovascular disease, metabolic illness, nonalcoholic fatty liver disease, and other side effects and comorbidities. Similar to psoriatic disease, diabetes has a complicated etiology, meaning that a variety of genes as well as external factors, such environmental circumstances, play a role.[21] We have control over some of the factors that are contributing to the increase in diabetes incidence, but not all of them.

Treatment and UV therapy

The kind and severity of your psoriasis, as well as the affected area of skin, will define the course of treatment. Your doctor will likely begin with a moderate treatment, such applying topical lotions to the skin, then progress to more potent ones if needed.[14,15]

The most common treatment used for psoriasis is topical

Lotions and ointments applied to the skin. Topical therapies are generally used first for mild to severe cases of psoriasis.

Steroids creams

A topical corticosteroid may be all the medication you need if you have mild to moderate psoriasis.[12] Applying this medication to psoriasis will help

1. Lessen redness, swelling, scaling, and itching; also, it can help clear up the psoriasis.
2. Reduce the rate of growth of your skin cells.[5,6]

Emollients

Emollients are topical moisturizers that are used directly on the skin to prevent moisture loss and coat it in a protective layer. Emollients moisturize the skin and lessen scaling and irritation, which is their primary effect. On skin that has been moisturized, several topical therapies are believed to perform better.[5,12]

Vitamin D analogues

If you have mild to moderate psoriasis on your scalp, trunk, or limbs, you may want to consider using vitamin D-like treatments in addition to or instead of steroid creams. They function by delaying the synthesis of new skin cells. Additionally, they have some other properties like anti-inflammatory Eg:calcitriol and calcipotriol.[15]

Coal tar

The thick, heavy oil known as coal tar is arguably the most traditional psoriasis treatment. Although its exact mechanism of action is unknown, it can lessen itching, irritation,and scales.It can be used to treat psoriasis of the scalp, trunk, or limbs when other topical treatments fail.[19]

Phototherapy is also a therapy to reduce psoriasis effect

One of the best ways to cure psoriasis is with phototherapy. Regularly exposing the skin to UV radiation while under medical care is known as phototherapy. UVB is a useful treatment for psoriasis which contained by Natural sunlight.[26,31] UVB rays alter resident immune cells and skin cells as they reach the skin's outermost layer. These modifications lessen the pro-psoriasis cytokines. In addition to its potent anti-inflammatory properties, UVB also lessens irritation and encourages regulatory T-cells, which thwart autoimmune reactions. The most popular type of light therapy is narrowband UVB since it is both extremely safe and effective. "The discomfort and length of the commute are the biggest downsides.[26] For around three months, patients usually require three treatments per week.

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