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TREATMENT TRENDS OF PSORIASIS-AN OVERVIEW

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ABSTRACT

Chronic inflammatory psoriasis is a skin disorder that frequently manifests systemically. Environmental and genetic variables are part of the etiology. The diagnosis is made on the basis of the characteristic scaly, erythematous skin lesions, which frequently have extra joint and nail presentations. This type of psoriasis is more common in plaque. Guttate, pustular, erythrodermic, and inverse psoriasis are examples of atypical types. A new thorough global systematic review of the epidemiology of psoriasis was conducted in order to provide information for the WHO Global Report on Psoriasis. This study set out to conduct a thorough evaluation of the global literature on the epidemiology of psoriasis. Dermatology's understanding of psoriasis illness and its treatment options is constantly improving. Research is being conducted to develop the most effective interventions for the current situation.

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INTRODUCTION

The skin is the largest sense organ in the human body. It serves as the body's first line of defense and carries out a number of vital tasks. It supplies about 10% of the body's total mass and has an area of 1.7 m on average. Because skin can also absorb substances applied topically, it is becoming more widely accepted that skin is the best route for delivering a range of pharmacological compounds. The structure of the skin facilitates the penetration of topically applied substances into the different layers of the skin and into the systemic circulation.

The majority of the components enter the skin via the sebaceous follicle, sweat ducts, and stratum corneum, which are the three main entry points.Over the last few years, a new method for managing a number of major issues has emerged using topical medication delivery. Because of its special advantages, the topical drug delivery system is used when other drug delivery methods are unable to produce the best possible therapeutic outcome. Furthermore, the topical method is also the best way to treat localized skin illnesses like bacterial or fungal infections[1].

The basic way to categorize topical drug delivery methods is by consistencies; these consistencies include semi-solids, liquids, solids, and other preparations. The drug's characteristics and the intended site must be taken into consideration while choosing a dose form. In addition, a number of physiochemical parameters, such as skin thickness, pH, hydration, lipid content, blood flow, hair follicle density, sweat gland density, partition coefficients, molecular weight, etc., also affect how permeable the medication is[1].

STRUCTURE OF SKIN

The three main layers of skin are the dermis, the epidermis, and the subcutaneous tissues. The outermost layer is called the epidermis, while the layer beneath it is called the dermis. The tissues and cells that make up the subcutaneous layer are fatty[1].

EPIDERMIS

It is the skin's outermost layer, which is non-vascular in nature and comes into direct touch with substances applied topically. The epidermis, which is composed of stratified squamous epithelial cells, serves as a barrier and creates a protective layer. The stratum corneum, stratum lucidum, stratum granulosam, stratum spinosum, and stratum basale are the five layers that make up the epidermis. The innermost layer is called stratum basale, while the outermost layer is called stratum corneum, which is the thickest layer (20–30 cells)[1].

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DERMIS

Its primary functions include feeding the cells of the epidermis and supporting it physically. The dermis is made up of two layers: the reticular layer and the papillary layer. Elastic, fibrillin, and collagen are found in both layers. Moreover, the dermis contains blood vessels, nerve endings,

hair follicles, and certain important glands including sweat and sebaceous glands. This layer also contains a few tiny blood veins that give the epidermis flexibility, nutrition, and oxygen[1].

SUBCUTANEOUS LAYER

It is made up of fatty tissues and cells that act as a cushion to protect the body and act as insulation [1].

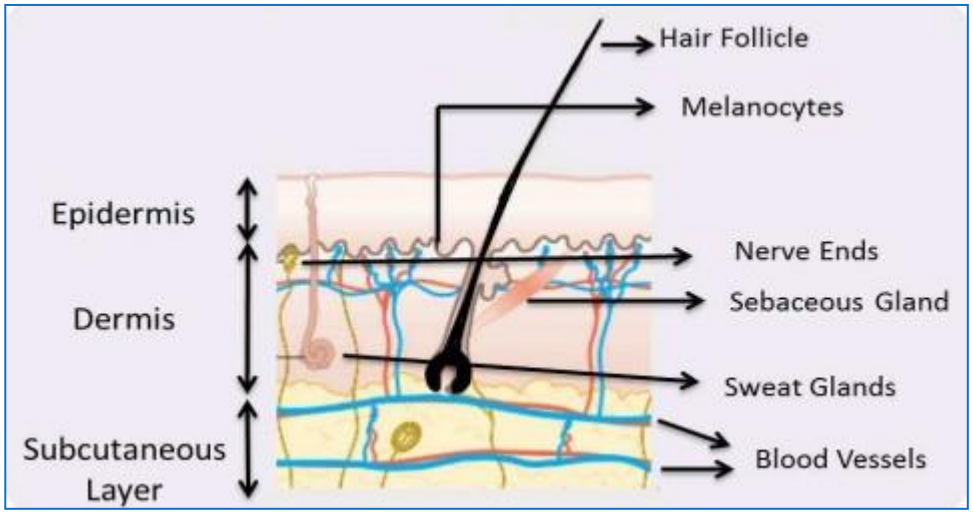

Figure 1:Strucutre of skin

PENETRABILITY OF THE SKIN

The topically applied active component must penetrate all layers of skin in order to reach the systemic circulation and produce the desired local effects. The three main routes of skin penetration are intercellular, follicular, and transcellular. Drugs are transported through the interface between epithelial cells during intercellular penetration. Transcellular penetration refers to the drug's ability to pass through epithelial cells. When a medication undergoes follicular penetration, it crosses the skin barriers with the hair follicles[1].

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Factors influencing the items administered topically in terms of penetration and absorption

1) Hydration of the skin
2) Vacularity
3) Lipid content;
4) Skin pH
5) Density of hair follicles
6) Sweat gland density
7) Skin inflammation
8) Diminished contents
9) Coefficient of partition
10) The molecular weight
11) Ionization degree[1].

Methods to increase the rate of penetration and absorption
1) Chemical Boosting
2) Improvement of the Body
3) Improvement of Biochemistry
4) Enhancement of Supersaturation[1].

PSORIASIS

Psoriasis is a long-term skin disorder that frequently has systemic symptoms, particularly arthritis. The estimated prevalence is roughly equal for men and women, affecting % of adult U.S. population. Although psoriasis can occur at any age, it usually first manifests between the ages of 15 and 30. The course of the clinical manifestation is uncertain. Therapy that is tailored to each patient and closely watched can reduce morbidity and improve quality of life[2].

RISK FACTORS AND ETHIOLOGY

A first-degree relative with psoriasis affects about one-third of psoriasis patients. A multifactorial mode of inheritance is suggested by research. The beginning and progression of the illness are linked to numerous stressful physiological, psychological, and environmental occurrences. Psoriasis can be brought on by direct skin damage (Koebner phenomenon). Additionally, a streptococcal throat infection can cause the illness or make pre-existing psoriasis worse. Although it hasn't been demonstrated that human immunodeficiency virus infection causes psoriasis, it can make the condition worse already. Psoriasis frequently gets worse as the infection spreads.

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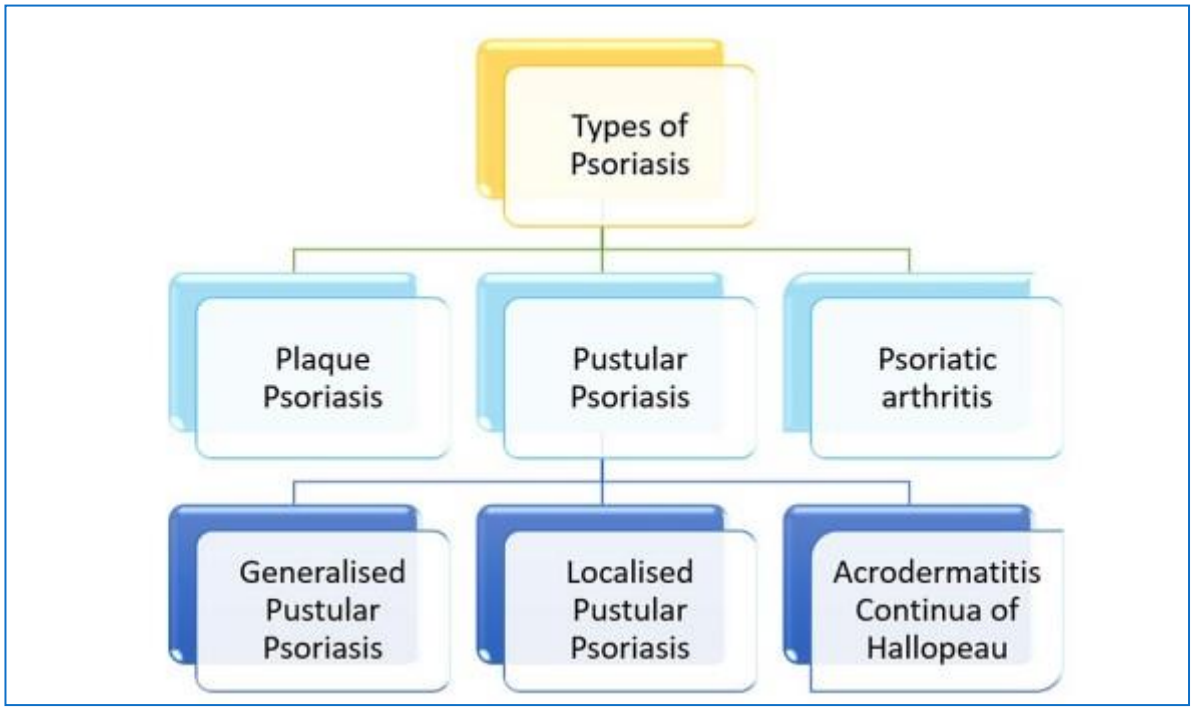
Both the incidence and severity of psoriasis are increased by smoking. Psoriasis is also linked to obesity and alcohol consumption and misuse. Patients with psoriasis may be more prone to harmful habits, but these connections may not be causal[2].

PATHOPHSYIOLOGY

Despite a genetic propensity, psoriasis is an immune-mediated illness for which no specific immunogen has been found. Biologic therapy have been developed as a result of the identification of T lymphocytes, dendritic cells, and cytokines in psoriatic lesions[2].

TYPES OF PSORIASIS



PLAQUE PSORIASIS

The cutaneous disorder known as plaque psoriasis is caused by the development and differentiation of keratinocytes, which results in dry, itchy, red, erythematous, elevated skin areas. The start and maintenance phases of psoriasis are when the entire mechanism takes place. The main adenosine monophosphate involved in the initiation phase is LL37, which starts the process by interacting with either ribonucleic acid (DNA or RNA) or deoxyribonucleic acid [3].

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PUSTULAR PSORIASIS

The most common disease subgroups in this set of varied therapeutically unique subgroups include palmoplantar psoriasis and generalized pustular psoriasis. Although phenotypically and genetically distinct from psoriasis vulgaris, these variants may be associated with symptoms of plaque psoriasis, supporting their inclusion in the dermatitis spectrum. Aseptic pustules are the most typical form in which it manifests[3].

PSORIATIC ARTHRITIS

One kind of inflammatory arthritis is psoriatic arthritis.Joint pain, stiffness, and swelling are among the symptoms, which might flare up and then go away. Morning stiffness is a common symptom of the illness. Significant arthritis can develop from even modest skin psoriasis[3].

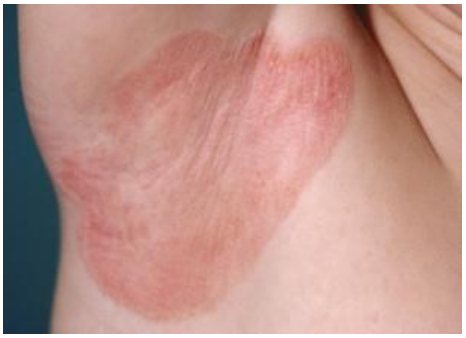

Figure 2: Erythematous plaque in an inverse pattern in the axilla

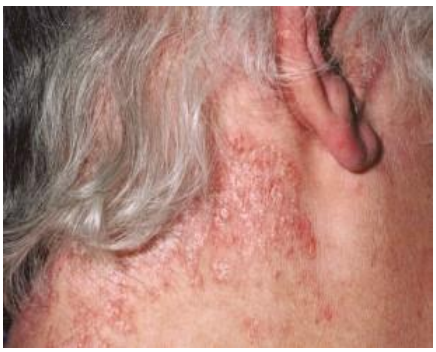

Figure 3: Scaling plaque in psoriasis

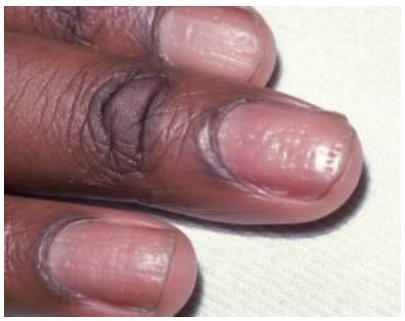

Figure 4: Classic nail pitting in a patient with psoriasis.

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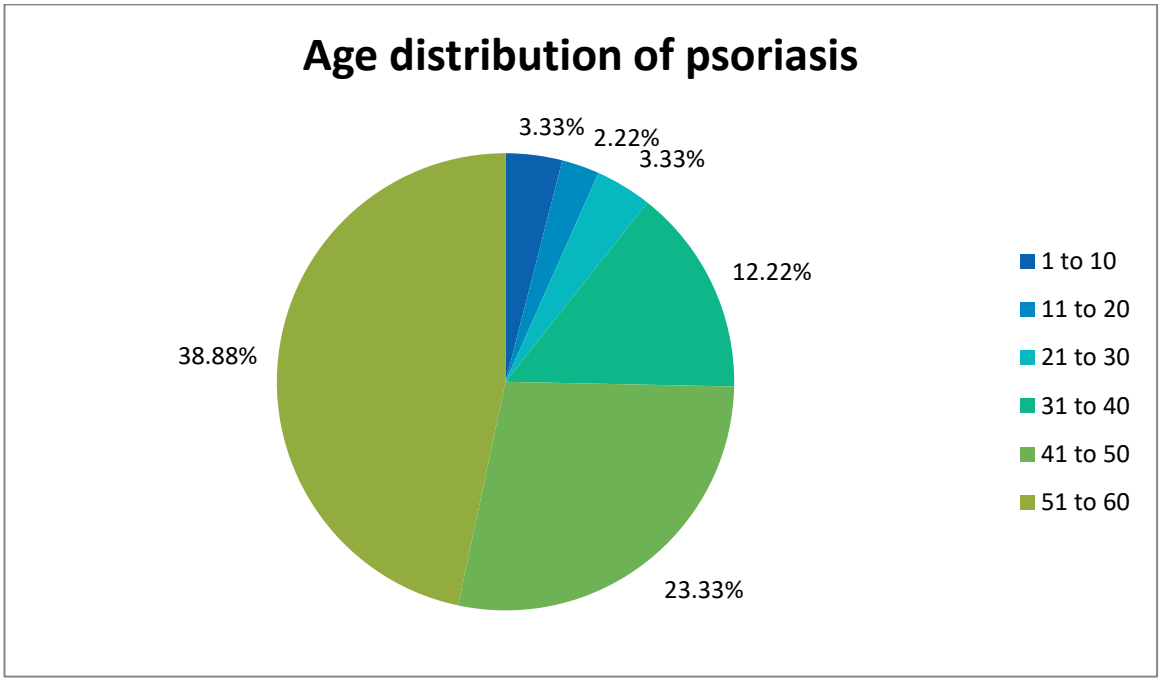
EPIDEMIOLOGY

It is believed that psoriasis affects 2-3% of people worldwide. It is well known that the disease is more common in the world's polar areas, but the impact it has on a tropical or subtropical nation like India cannot be understated. Due to varying environmental and genetic factors, the prevalence of psoriasis can differ from region to region in a country as diverse as India. Psoriatic arthritis can develop at any age between 35 and 50, with no discernible sex bias. There has been evidence of a higher incidence in men, with a peak age at onset in the third and fourth decades of life. The estimated point prevalence of pediatric psoriasis in one of the major studies conducted in Northern India was 0.0002%[4].



PREVIOUS TREATMENT FOR PSORIASIS

Treatment was thought to be a transient, recurrent skin condition that might be partially but not totally cured. Psoriasis is no longer appropriately treated as a separate skin disorder, according to popular belief. Depending on how severely the dermis is involved, additional choices should be considered when selecting a course of treatment. Among them are the presence of PsA and risk factors, clinical and social impacts, co-occurring medications, planned pregnancies, individual preferences, and treatment goals. m. The evolution of more precise psoriasis medication targeting over the past century serves as an example of effective transferable research. Progress in understanding the biology of the

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condition has made this feasible. Many topical and systemic psoriasis treatments were available even a century ago, such as salicylic acid, coal tar, and dithranol preparations. The first medication to be documented as being taken by psoriasis patients is topical steroids. In today's modern medication development process, biologics serve as the proof of concept for patient treatment. It could have been the case that there was no noticeable effect because of its low potency. Prednisolone and triamcinolone taken orally both work well. Vitamin D analogs were studied for a variety of dermatoses in the 1980s. It has been shown that calcipotriol, administered topically to treat psoriasis, can slow the growth of epidermal keratinocytes. As additional systemic therapies were established, it became evident that psoriasis needed an impartial and trustworthy way to evaluate the severity and response to treatment[5].

MANAGEMENT, BOTH CURRENT AND FUTURE

When systemic medication is ineffective for moderate-to-severe psoriasis, biologics are advised. This license is in favor of the current iterative approach to psoriasis treatment. Patients with limited or mild illness frequently get topical therapy initially. They are given a moderate-to-severe diagnosis if this is insufficient, and phototherapy or other conventional systemic therapies may be helpful. Certain medications such as TNF-α inhibitors (Infliximab, adalimumab, certolizumab pegol, etanercept), IL23 inhibitors (ustekinumab, guselkumab, risankizumab, and tildrakizumab), IL17 inhibitors (secukinumab, ixekinumab, brodalumab), IL36 receptor antagonist, and sphingosine one and the Janus kinase inhibitor (JAK) trofatinib)[5].

TNF-α inhibitor: It is recognized as an essential regulating cytokine in inflammatory conditions connected to the chronic immune system, such as psoriasis. Etanercept was the first TNF inhibitor approved for the treatment of psoriasis. For the treatment of psoriasis, TNF inhibitors, infliximab, adalimumab, and certolizumab pegol are currently available. TNF is abundant in skin lesions and plasma from psoriasis patients. It plays a major role in the induction and transmission of immunological activity by concentrating on an inflammatory response that penetrates the epidermis.Ustekinumab is the first inflammatory medication authorized for the treatment of psoriasis among IL23 inhibitors. It targets the interleukin 23 p40 subunit. Etanercept and placebo are significantly less effective than ustekinumab in the short term therapy of moderate to severe psoriasis[5].

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Guselkumab is a monoclonal antibody (mAb) that binds to the p19 component of IL23 and is composed entirely of human immunoglobulin G1 (IgG1). Given its clinical efficacy in treating plaque psoriasis, guselkumab has also been investigated for the treatment of other illnesses, such as erythrodermic psoriasis (EP), PsA, and generalized pustular psoriasis (GPP). As demonstrated by a meta-analysis of the case, risankizumab is more effective than adalimumab in treating the condition. Members of the IL-36 group of cytokines, inflammatory mediator agonists of IL36 include IL-36 and IL-36R, along with another receptor antagonist (IL-36Ra). These cytokines attach to and spread via IL-36R and the IL-1R accessory protein (IL-1RAcP), a heterodimeric transmitter. For the treatment of adult flare-ups of generalized pustular psoriasis (GPP), one of the IL36 receptor antagonists is spesolimab; the USA has approved spesolimab after the first dose. In the event that GPP flare symptoms persisted, a second dosage of 900 mg was administered for a week. Spesolimab is prescribed at a dose of 900 mg administered intravenously over a period of 90 minutes[5].

Rho-associated kinase inhibitor (ROCK2): The serine-threonine kinases ROCK1 and ROCK2, members of the rho family, are responsible for mediating the phosphorylation of downstream targets in cells [38]. The function of ROCK proteins in regulating the immune system varies depending on the state of the individual's illness[5].

CONCLUSION

Millions of people worldwide suffer with psoriasis, an inflammatory skin illness mediated by both genes and the immune system. The disease manifests clinically as erythematous, spherical plaques covered in salivary micaceous scale and epidermal hyperproliferation, which have a severe negative impact on the physical, social, and emotional health of the patient. A powerful group of autoinflammatory skin diseases with considerable clinical and genetic variation is pustular psoriasis. y. Understanding of physiology has grown, new medications and treatment techniques have been developed, and results and evaluations have improved. To give PsA patients the best care possible, doctors need to be aware of these important advances. Adequate actions can aid in the illness's treatment. Many researchers' current advancements in the disease's treatment techniques have a significant influence on our understanding of the problem.

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