INTRODUCTION:

Skin is a complex layer composite of several tissues forming a barrier between our physical body and outside environment. However, this barrier remains open to the environment. The skin consists of three layers namely the epidermis, the dermis, and the subcutaneous layer. The epidermis, called stratum corneum, is the outer layer covering the whole body, which contains numerous nerve endings that makes the skin a large sense organ. The stratum corneum is the rate limiting barrier to percutaneous absorption and serves as a protective barrier. Drug should cross stratum corneum and enter into epidermal and dermal tissues.

Psoriasis is one of the most common human skin diseases. It occurs when the immune system mistakes the skin cells as a pathogen and sends out faulty signals that speed up the growth cycle of the skin. It leads to rapid accumulation of skin cells on the skin surface forming a thick silvery surface, dry red patches which may pain. This is a persistent and long-lasting disease. There are six types of psoriasis. Even though many people suffer from one type at a time, there are also chances that one type may manifest to another; usually, this occurs due to an external factor, like abruptly stopping a medicine.

Psoriasis- pathophysiology:

Skin is a primary lymphoid organ with an effective immunological surveillance system equipped with antigen presenting cells, cytokine synthesizing keratinocytes, epidermotropic T cells, dermal capillary endothelial cells, draining nodes, mast cells, tissue macrophages, granulocytes, fibroblasts, and non-Langerhans cells. Skin also has lymph nodes and circulating T lymphocytes. Together these cells communicate by means of cytokine secretion and respond accordingly via stimulation by bacteria, chemical, ultraviolet (UV) light and other irritating factors. The primary cytokine released in response to antigen presentation is tumor necrosis factor-alpha (TNF-α). Generally, this is a controlled process unless the insult to the skin is prolonged, in which case imbalanced cytokine production leads to a pathological state such as psoriasis (Krueger et. al 2005).

Initially, immature dendritic cells in the epidermis stimulate T-cells from lymph nodes in response to as yet unidentified antigen stimulation. The lymphocytic infiltrate in psoriasis is
predominately CD4 and CD8 T cells. Adhesion molecules that promote leukocyte adherence are highly expressed in psoriatic lesions. After T cells receive primary stimulation and activation, synthesis of mRNA for interleukin-2 (IL-2) occurs, resulting in a subsequent increase in IL-2 receptors. Psoriasis is considered a Th1-dominant disease due to the increase in cytokines of the Th1 pathway – interferon gamma (IFN-γ), IL-2, and interleukin 12 (IL-12) – found in psoriatic plaques. The increased IL-2 from activated T cells and IL-12 from Langerhans cells ultimately regulate genes that code for the transcription of cytokines such as IFN-γ, TNF-α, and IL-2, responsible for differentiation, maturation, and proliferation of T cells into memory effector cells. Ultimately, T cells migrate to the skin, where they accumulate around dermal blood vessels. These are the first in a series of immunologic changes that result in the formation of acute psoriatic lesions. Because the above-described immune response is a somewhat normal response to antigen stimulation, it remains unclear why the T-cell activation that occurs, followed by subsequent migration of leukocytes into the epidermis and dermis, creates accelerated cellular proliferation. Therefore any topical antipsoriatic drug must reach epidermis for site specific action. Upregulated gene regulation may be a causative factor. Vascular endothelial growth factor (VEGF) and interleukin-8 released from keratinocytes may contribute to the vascularization seen in psoriasis.

Dendritic cells appear to be involved in the pathogenesis of psoriasis. One type of dendritic cell involved is the Langerhans cells, the outermost sentinel of the immune system that recognizes and captures antigens, migrates to local lymph nodes, and presents them to T cells. The activation of T lymphocytes releases pro-inflammatory cytokines such as TNF-α that lead to keratinocyte proliferation. This hyperproliferative response decreases epidermal transit time (the approximate time it takes for normal maturation of skin cells) from 28 days to 2-4 days and produces the typical erythematous scaly plaques of psoriasis (Nestle et al 2007)

**Types of psoriasis:**
There are six different types of psoriasis and different treatment options available for the same. Typically topical agents are used for mild disease, phototherapy for moderate disease, and systemic agents for severe disease

i. Plaque psoriasis:

It is the most common type. It is also called psoriasis vulgaris. Nearly, 80% of patients suffering from psoriasis have plaque psoriasis. This condition is characterized by the red, hard and raised patches on skin which have silvery white and scaly patches. These patches are known as plaques and generally they like small red bumps. They may remain as isolated, separate areas or join together for forming large plagues. Often they develop on the lower back, elbows and knees, though they may appear on any part of the body, including scalp. However, this condition rarely appears on the face. Plaques may last for months to years and they appear and disappear for no proper reason.

ii. Guttate Psoriasis:

This is another most common type. This is characterized by small and red spots on the skin. This condition is seen in children and young adults. Guttate psoriasis spots appear suddenly, often after certain viral or bacterial infections and generally appear on the trunk and limbs. Sometimes, it can be severe and needs injections or oral medications. Mild cases can be cleared without any medications and will never recur.

iii. Pustular Psoriasis:

This is a very rare condition and is observed in less than 5% of people affected with psoriasis. Pustular psoriasis is characterized by fluid filled bumps on the skin. These pustules may appear in hours after the surface of the skin becomes itchy and red. These pustules develop as waves, waving and healing in a few days and recurring. It can be generalized and can spread across the body or localized to the palms of hands and soles of feet.

iv. Inverse Psoriasis:
This is also called flexural psoriasis. Inverse psoriasis develops in skin folds like those found under the breasts and in the groin and armpits. Nearly 2 – 6% of people suffering from psoriasis have inverse psoriasis. This condition is more prone in obese people and aggravates due to sweating and friction. It appears like smooth and sometimes shiny patches appear instead of scaly lesions. The areas afflicted with this condition are tender, red and inflamed. This is because the areas are prone to fungal and yeast infections, and this is sometimes confused with candida.

v. Erythrodermic Psoriasis:

People with condition are relatively less. Only 1 – 2% of people suffering from psoriasis have erythrodermic psoriasis. This condition may develop in conjunction with the pustular psoriasis or develop on its own. Erythrodermic psoriasis is characterized by the red, inflamed and scaly rashes on the entire body. This skin ailment is often itchy and extremely painful. Usually this condition is treated with systemic and topical medications.

vi. Nail Psoriasis

Psoriasis of the nails occurs in fewer than 5% of people who do not have skin psoriasis. In people who have skin psoriasis, 10%-55% have psoriasis of the nails Psoriasis of the nails involves any of a number of changes to the nail area. Clear yellow-red nail discoloring that looks like a drop of blood under the nail plate may occur. Little pits may form in the nails. These pits develop when cells are lost from the nail's surface

**Treatments available:**

**Topical treatment**

About 80% of patients with the psoriasis are treated topically. Different moisturizers, medicated gels, creams and ointments of vitamin D3 analogues, corticosteroids, anthralin, topical retinoids, calcinurin inhibitors and coal tar are available in the market

➢ Corticosteroids: These are the most commonly prescribed medicines for psoriasis. They work by reducing inflammation and slowing the growth and built-up of skin cells. e.g.
Betamethasone, Mometasone, Triamcinolone, prednicarbate etc. These are available in different forms i.e. creams, ointments, lotions etc.

- Retinoids: Tazarotene and other retinoids derived from vitamin A are also used in the treatment of psoriasis.
- Coal Tar: Tar shampoos are often used for the treatment of scalp psoriasis.
- Salaicylic Acid: It is used to remove the scales that appear on patches of psoriasis.
- Calcineurin inhibitors: Calcineurin is a protein phosphatase. It activates the T cells of the immune system and can be blocked by drugs e.g Tacrolimus and Pimecrolimus.
- Vitamin D analogues: Drugs belonging to this category treats psoriasis by slowing down the growth of skin e.g Calcitriol, Calcipotriol, Maxacalcitol, Tacacalcitol.
- Drugs of plant origin: Anthralin, works by affecting the growth cycle of skin cells in the patches of psoriasis.
- Bath solutions and moisturizers, mineral oil, and petroleum jelly may help soothe affected skin and reduce the dryness which accompanies the build-up of skin on psoriatic plaques.

Light Therapy:

- The phototherapy involves exposing the skin to controlled amounts of natural sunlight.
- Use of artificial ultraviolet A (UVA) or ultraviolet B (UVB) light either alone or in combination with medications.
- Excimer laser: The excimer laser—recently approved by the Food and Drug Administration (FDA) for treating chronic, localized psoriasis plaques—emits a high-intensity beam of ultraviolet light B (UVB). The two brands currently on the market are the Xtrac and the Xtrac Velocity.
- Pulsed dye laser: The pulsed dye laser is approved for treating chronic, localized plaques. Using a dye and different wavelength of light than the excimer laser or other UVB-based treatments, pulsed dye lasers destroy the tiny blood vessels that contribute to the formation of psoriasis lesions.

Oral medication:
- Retinoids, Methotrexate, Cyclosporine, hydroxyurea, Thiguanine are available as oral dosage forms
- Immunomodulator drugs like etanercept, infliximib are given as Intravenous infusion, intramuscular injections or as subcutaneous injections in the patients who have failed to respond to traditional therapy.

Although steroids may work very well at first, psoriasis may become resistant to them over time. Topical corticosteroids are now often used in combination with topical vitamin D analogs. The greatest limitation to the combined therapy is the inconvenience of administration. Formulation of vitamin D should be applied first to the skin, followed by corticosteroid formulation after determined duration. Topical pharmaceutical composition comprising a combination of vitamin D analogue and topical corticosteroid would likely result in better patient compliance.