

How do acute and chronic inflammatory skin diseases arise? A brief review

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ABSTRACT

Inflammation is a condition in which the component of the body becomes red, sore, and swollen due to infection or injury. Inflammation of the skin is a symptom of the body's immunological reaction. Redness, heat, irritation, sensitivity, and swelling are all possible symptoms. Skin immune responses are critical for the host's defense against harmful germs. Deregulated immunological responses, on the other hand, may result in chronic inflammatory skin disorders. Local immune responses are regulated by extensive interaction in diverse cellular and microbial components of the skin to guarantee effective host defense, preserve and restore homeostasis, and avoid chronic illness. Inflammation of skin may be acute, such as from a skin infection, or persistent, such as from an autoimmune disorder. Skin inflammation usually presents as a rash that may be raised, red, or warm. Some inflammatory rashes cause blister or pimple and some may burn, sting, or itch. There are the evidences for the potential role of DNA methylation within the development of chronic inflammatory skin conditions that are limited. Atopic dermatitis, psoriasis, rosacea, leprosy, chronic pruritus, Hidradenitis suppurativa, and chronic urticarial are some skin inflammatory conditions caused due to bacteria, irritants, and allergens; however, the causes and symptom of all these diseases are different and somewhat similar also as all these are inflammatory diseases. In this review, we discuss some skin inflammatory diseases to understand its pathophysiology in better way.

Keywords: Inflammation, Skin, Pathogenesis, Immunological factors, Pain, Pathophysiology

Introduction

The skin, as the exterior barrier, is the organ that is most exposed to a variety of external stressors, resulting in frequent cell and barrier damage.^[1] As a consequence, skin has evolved a complicated set of mechanisms to defend itself and restore tissue integrity without causing septicemia.^[2] Skin is one of the greatest organs to research response mechanisms to tissue injury and healing experimentally because of its accessibility. Skin research has aided in the discovery of new basic concepts in regenerative biology that are relevant to the function of other epithelial mesenchymal tissues such as the gut, lung, and liver.^[3] We will concentrate on skin research here, but we will discuss the ramifications for other organ systems as well. Whenever host body get attacked by any foreign matter capable to activate host

immune system, our primary line of defense that is skin produces inflammatory symptoms to through the foreign matter out of the body or as the effect of fight of immune system with that foreign body.^[4]

However, sometimes inflammation lasts long and these are nothing but the skin diseases such as atopic dermatitis (AD), psoriasis, rosacea, leprosy, chronic pruritus, Hidradenitis suppurativa, and chronic urticarial; these skin problems are discussed in the current article.^[5]

AD

The number of resident and infiltrating immune cells in inflammatory AD skin is high. LCs, inflammatory dendritic cells (IDECs), macrophages, mast cells, and other cells are examples. The growth of atopic dermatitis relies heavily on the functional interaction of cutaneous immune cells.^{[6],[7]} In AD, an inadequate epidermal barrier enables possible allergens, irritants, and pathogens, such as *Staphylococcus aureus*, to penetrate the skin and activate keratinocytes' immune systems.^[8] Long and hot showers or baths; bath; cold and dry weather; detergents, heat,

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and rubbing cleansers; wool, soap, and artificial textiles; stress; allergens; dirt, sand, and smoke are some of the causes of AD.^[9]

Symptoms of AD include dry skin and itching, raw, sensitive, and swollen skin from scratching and rashes that appear on the arms and behind the knee. Severe AD has widespread of affected areas that is difficult to treat.^[10]

For treatment of AD topical preparations of antibiotic, corticosteroid and emollients are used.^[11] About 90% of AD patients have *S. aureus* colonization, which increases their risk of cutaneous infections.^[12] The inflammatory immune response is reduced by topical corticosteroids, which is the first-line therapy in AD flare-ups.^[13] Emollients having a high lipid (oil) content and a low water content are suggested for their ability to keep skin hydrated.^[14]

Psoriasis

Psoriasis is a long-term inflammatory skin disease which may have systemic signs. Psoriasis may affect people of any age, although it is most frequent in those between the ages of 15 and 30. The clinical outcome is unpredictably unexpected. Individualized and closely monitored treatment has been shown to reduce morbidity and enhance quality of life.^[15]

Although psoriasis is an immune-mediated disease with a hereditary tendency, no specific immunogenic factor has been discovered. Because of the presence of dendritic cells, cytokines, and T lymphocytes in psoriatic lesions, biologic treatments have been developed. Guttate, pustular, plaque, inverse, and erythrodermic psoriasis are the five forms.^[16]

Guttate psoriasis

Guttate psoriasis attacks about 8% of people with psoriasis. Guttate psoriasis is characterized by small, circular, and red patches causing inflammation. Guttate psoriasis is most often seen on the forearms, thighs, and breast, although it may appear anywhere on the body.

Pustular psoriasis

Pustular psoriasis affects around 3% of people with psoriasis. Pustules (inflamed or colored skin) might be accompanied by pustules (white, pus-filled, and painful lumps). Pustular psoriasis may affect just a few body areas, like the feet and hands, or it can affect the whole body.

Plaque psoriasis

Plaque psoriasis is the most common type, force increases to 80% of people with psoriasis. Plaques are raised areas of inflammatory, irritating, and uncomfortable skin with scales that may appear anywhere on the body. A few people's skin may also be red with silvery white scales. Some individuals may see plaques as purple. Plaques most often appear on the head, knees, elbows, and in and around the navel and lower back. However, it may affect any area of the body.

Inverse psoriasis

Inverse psoriasis affects one-quarter of psoriasis patients. The skin of people with inverse psoriasis is inflammatory, deep red, smooth, and non-scaly. Inverse psoriasis affects skin folds such as the arm pits, under breasts, vaginal area, and buttocks. It may cause agonizing itching as well as pain, which can be made worse by sweating and clawing in the afflicted areas.

Erythrodermic psoriasis

Erythrodermic psoriasis is a rare condition that affects only about 2% of people with psoriasis. This type of psoriasis may cause extensive redness and skin loss in large sheets. It often infects the entire body and might be deadly. Other symptoms include severe itching and pain, alterations in heart and temperature, dehydration, and nail irregularities. It is vital to get medical help as soon as possible if you are experiencing an erythrodermic flare.

Dry and cracked skin; tiny and scaly areas; red, itchy, and scaly patches; itching; swollen and stiff joints; and so on are all symptoms of psoriasis. Psoriasis patches may vary in size from a few spots of dandruff-like scaling to large-scale outbreaks.^[17] Cold and dry weather, stress, smoke, alcohol consumption, several medications, etc. may cause psoriasis. Viral infections such as cold sore and HIV worsen the symptoms of psoriasis. Psoriasis is a scaly and inflammatory skin condition that affects 1–3% of the world's population. It is a chronic, genetically driven, remitting, and relapsing illness. A combination of glucocorticoids, Vitamin D analogs, retinoid, salicylic acid, and phototherapy was utilized to treat psoriasis.^[18]

Rosacea

Rosacea (*L. rosaceus*, rosy) may be a chronic inflammatory dermatitis. It affects only 10% of the people.^[19] Rosacea is sometimes diagnosed after the age of 30. Kind of recent case study associated with this disease, patients plagued by rosacea have allergies, respiratory disorders gastrointestinal disease metabolic dysfunction, urogenital disorders, even have imbalance of female hormone composed to their age, sex, etc. Patients with moderate-to-severe Rosacea suffer having high lipid, high BP, digestion disease, heart diseases, and gastrointestinal disease. There are four kinds of Rosacea as Erythematotelangiectatic Rosacea, Papulopustular Rosacea, Phymatous Rosacea, and Ocular Rosacea.^[20]

The symptom of rosacea includes facial blushing or flushing, visible veins, swollen palms, burning sensation, eye problem, and enlarged nose. Rosacea can be reason for a continue blushing or flushing within the central a part of your face.^[21]

The causes of Rosacea include hot drinking and spiced food, red wine, alcoholic drinks, sun or wind, temperature extremes, and emotions also exercise. The reason of rosacea is unknown, but it may be because of an overactive immune system, environmental factors, and heredity.^[22]

Low-dose doxycycline is the only oral treatment for rosacea that has been authorized. Antibiotics and anti-acne medications may help manage and alleviate symptoms. It tends to become worse over time if left untreated. For moderate-to-severe rosacea with bumps and pimples, an oral antibiotic such as doxycycline (Rosacea and others) was given.^[23]

Leprosy

Leprosy, referred to as Hansen's disease, it is chronic disease which is produced by the microorganism referred as *Mycobacterium leprae*. This

Table 1: Diseases and their symptoms

Sr. No	Disease	Symptoms	Reference
1	Atopic dermatitis	Dry skin and itching, raw, sensitive, swollen skin from scratching, and rashes that appears on the arms and behind the knee	[6-14]
2	Psoriasis	Small, round, and red spots caused by inflammation dry and cracked skin; small and scaly spots; red and itchy scaly patches	[15-18]
3	Rosacea	Facial blushing or flushing, visible veins, swollen palms, burning sensation, eye problem, and enlarged nose	[19-23]
4	Leprosy	Nodules on the skin, discolored areas of skin, generally flat, that are numb and seem faded; Skin that is thick, stiff, or dry; Ulcers on the soles of the feet that are not painful; Swelling or lumps on the cheeks or earlobes that are not painful; Loss of eyelashes or brows	[24-27]
5	Chronic pruritus	Dry and cracked skin, leathery or scaly areas, redness, scratch marks, lumps, spots, or blisters skin that is itchy	[28-31]
6	Hidradenitis suppurativa	Blackheads occur in little pitted patches of skin, frequently in pairs, and cause abscesses and scarring	[32-34]
7	Chronic urticaria	Batches of red or skin-colored welts, itching, and painful swelling	[28,35-37]

organism attacked skin and nerves.^[24] As per the history, this disease was originated in Egypt in early 2400 BC. *M. leprae*, was discovered by G. H. Armauer Hansen in Norway in 1873. *M. leprae* is acid fast bacillus is a major human pathogen.^[25] The route from which the *M. leprae* enters into the human body is also not known. The main risk factor associated with this disease is the people staying in the area with poor conditions like dirty water inadequate food or other illness ends up in the upper risk for gaining this infection. IT has been shown that *M. leprae* can invade SCs by specific laminibinding protein of 21 kda in additionally to PGL-1.^[26]

Leprosy is divided into two poles, with clinical manifestations transitioning between them. There are five types of leprosy based on clinical, histological, and immunological criteria: Tuberculoid polar leprosy (TT), borderline tuberculoid (BT), midborderline (BB), borderline lepromatous (BL), and lepromatous polar leprosy (LL).^[27] For treatment reasons, patients were split into two groups: Paucibacillary and multibacillary. Later, it was strongly suggested that the categorization be based on the number of skin lesions, but only up to five for paucibacillary (PB) and more than 5 for multibacillary.^[25-27]

The acid-fast, rod-shaped bacillus *M. leprae* causes leprosy, which is a persistent illness. Leprosy is a group of disorders that typically affect surface tissues, particularly the skin and peripheral nerves.^[24] A mycobacterial infection triggers a wide range of cellular immune responses at first.

Skin is discolored, flat, numb, and seems fading (lighter than the surrounding skin); nodules (growths) on the skin; skin is thick, stiff, or dry; sores on the bottom of the foot that are not painful; inflammation or bumps on the cheekbones or earlobes that are not painful; loss of eyelashes or brows.^[26]

The exact process by which leprosy spreads is uncertain. When a patient with leprosy sneezes or coughs, droplets containing *M. leprae*

bacteria are released into the atmosphere and inhaled by someone else. Leprosy is spread by intimate physical contaminated hands.^[27] Leprosy is treated with antibiotics, anti-inflammatory medicines, and steroids.^[24-27]

Chronic Pruritus

Chronic pruritus refers to almost daily itching, lasting for 6 weeks. Clinically, it has been described as the most frequent symptom in dermatological condition. Chronic pruritus is often seen in the patients littered with different syndromes.^[28] This number of diseases can include inflammatory skin disease metabolic disorder liver and kidney.^[28] Interleukin (IL)-31 has been linked with pruritus associated with AD, prurigo nodularis, and cutaneous T-cell lymphoma, among other pruritic skin conditions. In dermatomyositis, skin IL-31 and its receptor, IL-31 receptor alpha, were considerably deregulated, and IL-31 mRNA expression was strongly linked with the VAS itch score ($r = 0.67$), suggesting that IL-31 may play a role in dermatomyositis-related pruritus etiology. Other cell types expressing CD8, CD68, CD11b, or CD11c were also found to secrete IL-31 in dermatomyositis.^[29] CD4+ T cells were the most common IL-31-producing cell type, but other cell types expressing CD8, CD68, CD11b, or CD11c were also found to secrete IL-31 in dermatomyositis.^[29]

Redness, scratch marks, lumps, spots, blisters, rough, broken skin, brittle, or scaly patches are the most common signs of persistent pruritus. Itchy skin may affect just a small area of the body, like the head, one elbow or a thigh, or the entire body. Itchy skin might develop without any other visible changes on the surface of the skin. Itching may sometimes be severe and linger for a long period. It becomes itchier when the individual rubs or scratches that spot. Moreover, the more it itches, the more scratching the individual does. It might be tough to break the itch-scratch cycle.^[30]

The most prevalent causes of chronic pruritus include insect bites and hives, skin problems, internal maladies, nerve disorders, psychological issues, irritation, and allergic responses. Examples include xerosis (dry skin), dermatitis (dermatitis), eczema, lice, worms, wounds, scarring, bug bites, and hive. Itchiness all throughout the body might indicate a more severe condition, such as liver disease, renal illness, anemia, diabetes, thyroid problems, multiple myeloma, or lymphoma.

Calcineurin inhibitors may be administered to the skin, such as tacrolimus (Protopic) and pimecrolimus (Elidel).^[31] Topical anesthetics, capsaicin, or doxepin are some of the medications that may help. Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac) and sertraline (Zoloft), and tricyclic antidepressants, such as doxepin, are examples of SSRIs.^[31]

Hidradenitis Suppurativa

Hidradenitis suppurativa is a painful and long-term skin disorder that results in abscesses and scars. Hidradenitis suppurativa has no known origin; however, it develops at sweat glands and hair follicles, most often around the grain, bottom, breast, and armpit.^[32] Chronic HS mainly

causes skin ulceration. Permanent trapping of foreign material and bacteria is done by the reepithelization. Deficient numbers of sebaceous gland, abnormal antimicrobial peptide, secretion of apocrine gland, or invaginations of epidermis are the possible contributors to pathology. A hallmark of disease is unrelenting cycles of relapses and remission. To assess the frequency of HS, using data estimations in the several studies, it comes to observation that difference setting (i.e., population vs. hospital), time period, or method of diagnosis (i.e., medically assessed vs. self-reported) are the estimations. According to recent research, HS is more of an auto-inflammatory condition. Although it has not been officially defined as an autoimmune illness, patients and physicians alike will often use the word “autoimmune” as a shorthand, leading to misunderstanding and controversy between the two.^[33]

Hidradenitis suppurativa might infect any area of the body. The below are some of the condition’s indications and symptoms: Blackheads form in little pitted areas of the skin and are frequently found in pairs. It usually starts with a single and painful lump under the skin that lasts weeks or months.^[34] Additional bumps may occur later, particularly in areas where the skin rubs against itself, such as the armpits, groin, buttocks, and breasts, where there are more sweat and oil glands. Some bumps or sores get larger, explode, and drain pus with an odor. Tunnels under the skin that link the lumps may form over time. These injuries leak blood and pus and, if they heal at all, do so slowly.^[34]

Although the actual etiology of Hidradenitis suppurativa is uncertain, the lumps are caused by clogged hair follicles. Obesity and smoking are both significantly linked to Hidradenitis suppurativa, and being fat and/or smoking will exacerbate the patient’s symptoms.^[32,33]

The tumor necrosis factor inhibitors adalimumab (Humira) and infliximab (Remicade) are two of the medications used to treat moderate-to-severe Hidradenitis suppurativa.^[32,33] For Hidradenitis suppurativa, several different biologics are being tested in clinical studies. Some persons with acne-like (acneiform) illness may benefit from oral retinoids. When a woman is pregnant, nursing, or planning to become pregnant, certain medicines are not suggested. If over-the-counter pain remedies do not work, a concentrated pain prescription or referral to a pain clinic may be prescribed.^[34]

Chronic Urticaria

Chronic urticaria is a skin allergy that may be quite distressing. Although it is usually innocuous, it may sometimes be a warning sign of a dangerous inside condition. Physical, infectious, vasculative physiological, and idiopathic etiologies have all been connected to the expansion of CU.^[28]

Chronic urticaria is a painful disorder that may have a negative impact on a patient’s quality of life. A rise in IL-4, IL-5, and interferon-gamma RNA characterizes the cytokine profile., connotative mix TH 1/ TH 2 response. Chronic urticaria is being due to the activation and degranulation of dermal mast cell.^[35]

The pathogenesis is based on the release of mediators, mostly histamine, by cutaneous mast cells. Specific immunoglobulin E,

components of complement activation, and non-specific compounds such as endogenous peptides, endorphins, and enkephalins may all cause release.^[36] According to studies, the products of an active immune system may reduce the cutaneous mast cell release threshold, potentially enabling endogenous substances to activate the cells. The resultant release of mediators results in repeated hives as a clinical manifestation. Despite the fact that the purpose of CU care is to identify a therapeutic cause, most CU patients, particularly adults, do not have one. Drugs, foods, infections, immune complex formation leading in urticarial vacuities, autoantibody generation, and underlying autoimmune illness, notably autoimmune thyroiditis, have all been identified as possible causes.^[37]

The following are signs and symptoms of chronic urticaria: Wheals are clusters of red or skin-colored welts that may develop anywhere on the body. As the response progresses, welts fluctuate in size, distort, and emerge and fade in and out. Itching, which may be very intense, angioedema is an unpleasant swell of the lips, eyelids, and neck that affects people of all ages. Signs and symptoms that flare up in reaction to stressors such as heat, exercise, or stress, as well as signs and symptoms that persist longer than 6 months and recur often and unpredictably, for sometimes months or years. Table 1 summarizes all the diseases discussed in study.

Prednisone and other oral corticosteroids may help reduce edema, redness, and itching. The cream version of the tricyclic antidepressant doxepin (Zonalon) may help alleviate itching.^[28,35-37]

Conclusion

Inflammation can be a condition in which an element of the body becomes red, sore, and swollen due to infection or injury. Skin inflammation could be a sign of an immune reaction within the body. The inflammatory skin diseases are AD, psoriasis, rosacea, leprosy, chronic pruritus, Hidradenitis suppurativa, chronic urticarial, and description of all these disorders explained in details in this review article.

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