

# Research paper on an overview of psoriasis

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Psoriasis is a disease that is part of the broader group of disorders known as papulo-squamous disorders. It is one of the most common dermatological conditions in the world. According to the National Psoriasis Foundation its prevalence is nearly 2. 2% of the American population, and 2-3% of the worldwide population. It is clinically characterized by papules that are sharply demarcated from the normal skin and plaques, both covered by scaling skin (Harrison's, 2008). In the past, the studies on psoriasis focused on the hyper- proliferation of the skin cells; but recently, the focus has changed to study the defects in the immune system that are an important part for the development of the disease. These studies on the immune system have lead to the development of treatments that specifically target the dysregulation of the immune system.

## **Pathophysiology**

In leman's terms psoriasis is a condition wherein that the immune systems sends out erroneous information to the cells of the skin, which leads to an increased turnover of cells and the hyper-keratinization seen. The first studies on the immune effects associated with development of psoriasis

began when leukocyte infiltrates, which are component of the innate and adaptive immunity, were found in the skin cells of psoriatic skin (Blauvelt, Ehst, 2012). The following is an overview on the theorized sequence of immunological events that lead to the development of psoriasis. The first step in the process is the activation of dendritic cells and other cells in the skin that are part of the innate immune response. The cells of the innate immune response are namely the dendritic cells, which include plasmacytoid dendritic cells and myeloid dendritic cells, macrophages and neutrophils. The cytokines that are released from these cells include interferon-alpha (IFN- $\alpha$ ), tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin - 12 (IL-12) and -23 (IL-23) (Blauvelt, Ehst, 2012). The plasmacytoid dendritic cells are the ones that are primarily responsible for the secretion of IFN- $\alpha$ . IFN- $\alpha$  is one of the main cytokines that is involved in the beginning processes involved in autoimmune and antiviral immunity (Blauvelt, Ehst, 2012). Evidence to support the involvement of IFN- $\alpha$  in the pathogenesis of psoriasis, comes from studies that observed that systemic IFN- $\alpha$  treatment exacerbated psoriasis in affected patients.

TNF -  $\alpha$  is a pro-inflammatory cytokine that is found to be a primary cytokine involved in many inflammatory diseases, including psoriasis. Dendritic cells, T-helper cells, and keratinocytes in the skin are responsible for the secretion of TNF- $\alpha$ ; these cells also respond by activation in the presence of this cytokine(Blauvelt, Ehst, 2012).

Myeloid dendritic cells are antigen-presenting cells that are responsible for the secretion of many different types of cytokines that influences the activity of the T cells. The myeloid dendritic cells are also responsible for the

secretion of IL-12, which leads to the up-regulation of Th1 cells and CD8+ T cells; it also secretes IL-23, which differentiates CD4+ cells into Th17 cells. Finally the myeloid cells produce IL-20, which affects keratinocytes, and nitric oxide, which causes vasodilation (Blauvelt, Ehst, 2012).

The effects that T cells have on cytokines and their importance in psoriasis was discovered by the effect of cyclosporine, which is an inhibitor of T cell response, in the treatment of psoriasis. CD4+ cells are found in all biopsy skin samples in patients with psoriasis (Nikaeln, Phillips, Gilbert, Savino, Silverman, Stone, & Menter, 1991). Their importance in the pathophysiology in the development of psoriasis was deduced when CD 4+ T cells from patients that suffered from psoriasis, were injected into graft skin transplanted onto mice that suffered from SCID; this caused the graft skin to develop psoriatic changes. Th17 and Th1 cells are types of CD4+ cells; stimulation of Th17, by IL-23, leads to the activation of keratinocytes. Th1 cells like the myeloid dendritic cells produce a vast array of cytokines following stimulation. Examples of such cytokines include, interferon gamma (IFN -  $\gamma$ ), TNF -  $\alpha$ , and IL - 2; these cytokines, especially IFN- $\gamma$ , cause psoriatic changes in skin that is not affected by psoriasis. CD8+ cells have a less important roll in the development of psoriasis (Blauvelt, Ehst, 2012). Endothelial cells within psoriatic skin lesions express very high levels of vascular endothelial growth factor (VEGF (Blauvelt, Ehst, 2012)), leading to the dilated and torturous blood vessels found in psoriatic lesions. Besides our own individual biology, environmental factors may play a role in the development of autoimmune disease such as psoriasis. Certain types of

medication, trauma, infection, or any sort of stressor may influence the onset of an inflammatory response (Blauvelt, Ehst, 2012).

## **Epidemiology**

As mentioned earlier the worldwide prevalence of psoriasis is between 2-3%, and in the United States the prevalence around 2.2%; a population-based study found that Caucasians were affected at higher rate than African Americans with a prevalence of 2.5% and 1.3% respectively. It is seen in people of all races and affects both men and women nearly equally, which is different to many other autoimmune pathologies which are seen predominantly in women (Feldman, 2012). Psoriasis is found in two age groups; the first group of patients is between 20-30 years of age, and the second group is between 50-60 years old (Farber & Nall, 1974).

One study found that Norway had the highest prevalence rate of psoriasis in the population, but this study did not factor in confounding variables, as this study was done by questionnaire without having a positive follow up (Gudjonsson & Elder, 2007). Besides this study, other studies have shown that the highest prevalence in Europe is in Denmark and the Faeroe Islands, with 2.9% and 2.8% prevalence rates respectively (Gudjonsson & Elder, 2007). In the United States the prevalence rates appear to be low for the Asian population, at 0.3%. In Africa, while the evidence is limited to clinical based studies, the prevalence was higher in East Africans (2.0%) vs. West Africans (0.3%) (Gudjonsson & Elder, 2007).

The genetic aspect of psoriasis is one that has been known for nearly a century, and yet only about one-third of patients afflicted with this condition, have a first-degree relative that has it (Gudjonsson & Elder, 2007).

Analysis has identified several loci of different chromosomes that have associations with psoriasis; these loci are termed psoriasis susceptibility 1-9 (PSORS 1-9) (Nestle, Kaplan, & Barker, 2009). PSOR - 1 seems to be the major component in most cases of hereditary psoriasis. It is found on chromosome six of the Major Histocompatibility Complex (MHC), which is important in the hereditary component for the development of psoriasis, and is responsible for many components of the immune response.

## **Treatment**

Many treatment options exist for psoriatic disease. The decision to use oral agents, topical agents, or a combination of both, depends on many factors such as the extent of skin involvement, other health conditions, and evaluation of individual response to therapy. The decision to use topical or systemic agents should first begin with the evaluation of skin involvement. Mild -moderate involvement of the skin can usually be successfully treated with topical agents; while those patients with moderate - severe skin involvement may be required to use systemic treatment. Depending on the localization of the skin involvement, or the appearance of symptoms associated with psoriatic arthritis treatment options might change; for example lesions on the hand and foot might be extremely painful during normal activity, the social debilitation may also be a reason to seek a change in treatment options.

As mentioned previously, mild-moderate forms of psoriasis respond well to topical treatment with corticosteroids. Examples include topical retinoids such as tazarotene and vitamin D analogs such as calcitriol (Feldman, 2013). UVB therapy can also be beneficial therapy for this severity. UV radiation

appears to be beneficial because it has anti-proliferative in that it slows keratinization, and has anti-inflammatory effects (Feldman, 2013). Salt Severe disease requires the use of systemic corticosteroid treatment with a combination of phototherapy. Systemic corticoid treatment includes the use of retinoids, methotrexate, or cyclosporine. To specifically target the cells and signals of the immune system responsible for psoriasis, treatment involves the use of biological agents. These biological agents include, anti-TNF agents such as, adalimumab, entanercept, and infliximab, which work by preventing TNF- $\alpha$  from activating TNF receptors. Another biological agent, ustekinumab, is an anti-IL- 12/23 antibody (Feldman, 2013).

Psoriasis is a complex disease that we think develops from an improper immune response to the skin, but it has other factors that may also trigger it such as environmental or genetic factors. While a cure has not been discovered or created, proper treatment and regular follow ups by dermatologists can keep the immune reaction at bay.

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