

Review

Not peer-reviewed version

# How Hormonal Balance Changes Lives in Women with Psoriasis

<u>Fortunato Cassalia</u>\*, Anna Lunardon , <u>Giovanni Frattin</u> , Andrea Danese , <u>Francesca Caroppo</u> , <u>Anna Belloni Fortina</u>

Posted Date: 7 November 2024

doi: 10.20944/preprints202411.0496.v1

Keywords:

psoriasis; hormonal balance; estrogen; menstrual cycle; pregnancy; menopause; women's health; quality of



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Review

# How Hormonal Balance Changes Lives in Women with Psoriasis

Fortunato Cassalia <sup>1,\*</sup>, Anna Lunardon <sup>1</sup>, Giovanni Frattin <sup>1</sup>, Andrea Danese <sup>2</sup>, Francesca Caroppo <sup>1,2</sup> and Anna Belloni Fortina <sup>1,3</sup>

- Dermatology Unit, Department of Medicine (DIMED), University of Padua, Padua; fortunato.cassalia@studenti.unipd.it, anna.lunardon@studenti.unipd.it, Giovanni.frattin@studenti.unipd.it, Francesca.caroppo@unipd.it
- <sup>2</sup> Section of Dermatology and Venereology, Department of Medicine, University of Verona, Verona; andrea.danese\_02@studenti.univr.it
- Pediatric Dermatology Regional Center, Department of Women's and Children's Health (SDB), University of Padua, Padua, Italy; anna.bellonifortina@unipd.it
- \* Correspondence: Fortunato.cassalia@studenti.unipd.it, +39 049 821207

Abstract: Psoriasis is a chronic, immune-mediated skin disease significantly impacting women, with disease severity often modulated by hormonal fluctuations. This review examines the influence of hormonal changes on the course of psoriasis in women, focusing on key life stages - including the menstrual cycle, pregnancy, postpartum, and menopause-and their impact on disease progression and symptomatology. Estrogen, the principal female sex hormone, plays a critical role in immune modulation. Variations in estrogen levels, which occur naturally throughout a woman's life, are associated with fluctuations in psoriasis severity. Low estrogen levels, as seen during menstruation or menopause, are linked to symptom exacerbation, while elevated levels during pregnancy may reduce symptoms in some women. However, responses are variable, with others experiencing no change or worsening during pregnancy. Postpartum, the rapid decline in estrogen often triggers severe flare-ups, while menopause, marked by a sustained estrogen reduction, frequently correlates with increased disease severity and flare frequency. The review also addresses the profound impact of psoriasis on women's quality of life, including physical discomfort, psychological distress, and social stigma. Additionally, fertility concerns are discussed, as severe psoriasis and associated treatments may increase the risk of adverse pregnancy outcomes. Consideration is given to hormonal therapies, lifestyle modifications, and their effects on psoriasis, underscoring the need for personalized treatment approaches that account for hormonal influences. Understanding these hormonal dynamics is essential for developing targeted, effective management strategies that enhance quality of life for women affected by psoriasis.

**Keywords:** psoriasis; hormonal balance; estrogen; menstrual cycle; pregnancy; menopause; women's health; quality of life

#### Introduction

Psoriasis is a chronic, immune-mediated dermatologic condition characterized by hyperproliferation of keratinocytes, leading to erythematous, scaly plaques on the skin's surface.[1,2] Affecting an estimated 125 million individuals globally, psoriasis is far more than a cosmetic issue; it imposes a substantial burden on physical health, mental well-being, and quality of life.[3,4] While both genders are susceptible to psoriasis, recent research highlights the profound influence of hormonal balance on disease manifestation and progression in women, adding complexity to its clinical management.[5,6] Hormonal fluctuations throughout the menstrual cycle, pregnancy, postpartum period, and menopause play a significant role in modulating immune responses and impacting psoriasis severity in women.[7,8] Estrogen and progesterone, among other hormones, interact with immune cells to influence cytokine production, altering inflammatory pathways central to psoriasis pathogenesis.[6,9] High estrogen levels, for example, are typically associated with anti-

inflammatory effects, which may alleviate symptoms, while reduced estrogen or elevated prolactin during certain life stages can exacerbate disease activity.[5,6] These hormonal dynamics not only influence the immune milieu but also impact various aspects of a woman's life, including her emotional health, reproductive decisions, and social relationships.[5,6,7,8,9] This paper investigates the nuanced relationship between hormonal changes and psoriasis in women, examining how estrogen, progesterone, and other hormones modulate immune function, affect disease severity, and alter life quality. By exploring these mechanisms, it offers a basis for personalized therapeutic strategies that address the unique hormonal context of female patients. Tailored management approaches can significantly improve treatment outcomes and quality of life for women with psoriasis, providing a holistic framework that encompasses hormonal influences, psychological support, and patient-centered care. Enhanced understanding of these interactions not only supports clinical advancements but also empowers women with strategies to navigate the complexities of living with chronic autoimmune disease.

#### 1. The Role of Hormones in Psoriasis (Table 1)

Psoriasis is a chronic, immune-mediated disorder characterized by dysregulation of immune responses, leading to persistent inflammation and hyperproliferation of keratinocytes.[1,2] Hormonal factors, particularly estrogen and progesterone, exert considerable influence on immune modulation and can significantly affect the course of psoriasis in women.[5,6] This review explores the mechanisms through which these hormones impact immune function and psoriasis severity.

**Table 1.** Role of hormones in immune modulation.

Estrogen	- Suppress production of pro-inflammatory	[5,6,11,12]
	cytokines: tumor necrosis factor-alpha (TNF- $\alpha$ ),	
	interleukin-6 (IL-6), and interferon-gamma (IFN-γ).	
	- Promotes the production of anti-inflammatory	[6,13,14,15]
	cytokines: interleukin-10 (IL-10) and transforming	
	growth factor-beta (TGF- $\beta$ ).	
	- Switches the balance from a pro-inflammatory Th1	[16]
	and Th17 response to a more anti-inflammatory Th2	
	response.	
	- Enhances Treg function.	[17]
Progesterone	- Inhibits proliferation of T cells	[0]
	- Reduces production of pro-inflammatory	[9]
	cytokines	[9]
	- Promotes keratinocyte proliferation.	[22]
Prolactin	- Promotes production of pro-inflammatory	[23]
	cytokines.	[22,23,24]
Cortisol	- Acute cortisol release has immunosuppressive	
	effects.	
	- Chronic stress can lead to dysregulation of cortisol	[25,26]
	production and promotes a pro-inflammatory state with	[25,26,27,28]
	an increase in production of pro-inflammatory	
	cytokines, worsening psoriasis symptoms.	

Estrogen and Immune Modulation

Estrogen, the primary female sex hormone, regulates not only the reproductive system and secondary sexual characteristics but also plays a critical role in modulating both innate and adaptive immunity.[10] The immunomodulatory properties of estrogen are multifaceted, involving various immune cells and signaling pathways that influence inflammation levels in psoriasis.[6,10]

# Anti-inflammatory Effects of Estrogen

Elevated estrogen levels are generally associated with anti-inflammatory effects.[6] Estrogen interacts with estrogen receptors (ER $\alpha$  and ER $\beta$ ) on multiple immune cells, including T cells, B cells, dendritic cells, and macrophages.[11] Through these receptors, estrogen can downregulate the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6), and interferon-gamma (IFN- $\gamma$ ), all of which are central to the pathogenesis of psoriasis. By inhibiting these cytokines, estrogen reduces inflammatory responses and may ameliorate psoriasis symptoms.[5,6,11,12]

Additionally, estrogen promotes the secretion of anti-inflammatory cytokines, including interleukin-10 (IL-10) and transforming growth factor-beta (TGF- $\beta$ ). These cytokines modulate immune responses by restricting the activity of pro-inflammatory cells and promoting immune tolerance, which is essential in mitigating autoimmune responses associated with psoriasis.[6,13,14,15]

#### Influence on Immune Cell Function

Estrogen also plays a role in altering the balance of T helper (Th) cell subsets. It can shift the immune response from a Th1 and Th17 profile, which is pro-inflammatory and prevalent in psoriasis, to a more anti-inflammatory Th2 profile.[16] This shift reduces the production of inflammatory mediators, subsequently decreasing skin lesions.[6,16] Furthermore, estrogen enhances the activity of regulatory T cells (Tregs), which are pivotal in maintaining immune tolerance and preventing autoimmunity. By enhancing Treg function, estrogen contributes to the suppression of autoimmune processes involved in psoriasis pathogenesis.[15,16,17]

#### Progesterone's role in Psoriasis

Progesterone, another critical female hormone, plays a vital role in immune regulation by fostering an anti-inflammatory environment, particularly within the context of autoimmune diseases like psoriasis. It achieves this by inhibiting the proliferation of T cells—immune cells that are heavily involved in the inflammatory cascade of psoriasis.[9] T cells, especially T helper (Th1 and Th17) cells, are known for driving pro-inflammatory responses in psoriasis by releasing cytokines such as IL-17, IL-22, and TNF- $\alpha$ , which stimulate keratinocyte hyperproliferation and sustain the characteristic plaques and scaling of psoriatic skin.[18] Progesterone dampens this activity by reducing the production of these pro-inflammatory cytokines, thereby directly countering immune responses that exacerbate psoriasis.[9]

In addition to its impact on T cell function, progesterone modulates immune responses through its influence on other cytokines and immune cells. For instance, it enhances the production of anti-inflammatory cytokines like IL-10, which helps to limit the activity of pro-inflammatory cells, promoting a more regulated immune environment.[15,19] By reducing the expression of inflammatory mediators, progesterone helps restore balance in the immune system, creating conditions that are less favorable for psoriatic inflammation.[9,15,19]

The immunosuppressive effects of progesterone may also explain the symptomatic changes often observed in women with psoriasis during different stages of the menstrual cycle and pregnancy.[19] During the luteal phase of the menstrual cycle, progesterone levels rise, which may contribute to a reduction in psoriatic inflammation and an improvement in symptoms for some women.[19,20,21] In pregnancy, progesterone levels increase significantly, especially in the second and third trimesters, creating an anti-inflammatory state that can lead to symptomatic relief for many women with psoriasis.[7] However, in the postpartum period, when progesterone levels drop sharply, a rebound increase in inflammation may occur, often leading to psoriasis flare-ups.[19,20,21]

Understanding these cyclical changes in progesterone and their effects on immune regulation is crucial in managing psoriasis in women, particularly those with hormone-sensitive disease patterns.

This insight suggests that hormonal fluctuations are a significant factor in disease severity and may offer a basis for exploring hormone-based therapeutic approaches to modulate immune responses and improve patient outcomes in women with psoriasis.

#### Prolactin's Role in Psoriasis

Prolactin, a polypeptide hormone primarily associated with lactation, is increasingly recognized for its role in immune regulation. Prolactin is produced not only by the pituitary gland but also by various immune cells, including T and B lymphocytes, under certain conditions.[22] This hormone has pro-inflammatory properties that may exacerbate autoimmune conditions like psoriasis.[22,23]

In psoriasis, elevated prolactin levels have been linked to an increase in keratinocyte proliferation—a hallmark feature of the disease.[23] Prolactin promotes the expression of proinflammatory cytokines, such as TNF- $\alpha$ , IL-6, and IL-17, in keratinocytes and immune cells. These cytokines drive inflammatory processes in the skin, leading to the formation and maintenance of psoriatic plaques. Prolactin can also stimulate lymphocyte activity, enhancing the immune response and potentially worsening psoriasis symptoms.[22,23,24] Understanding prolactin's role in psoriasis underscores the need for therapies that modulate this hormone in patients who show elevated levels, especially during times of physiological stress or lactation.

#### Cortisol and Stress Response

Cortisol is a glucocorticoid hormone synthesized by the adrenal glands in response to stress through the hypothalamic-pituitary-adrenal (HPA) axis. It plays a complex role in immune regulation and inflammation. Acute increases in cortisol typically exert immunosuppressive effects by inhibiting the release of pro-inflammatory cytokines and reducing lymphocyte proliferation, which is beneficial for transient inflammatory responses. However, chronic stress leads to dysregulation of cortisol production, often resulting in a "flattened" diurnal rhythm where cortisol levels are abnormally low in the morning and elevated at night.[25,26]

This cortisol dysregulation can shift the immune system into a chronic pro-inflammatory state, exacerbating autoimmune conditions like psoriasis. When cortisol is persistently low or irregular, the body's natural anti-inflammatory response weakens, allowing inflammatory pathways, particularly those involving IL-17 and TNF- $\alpha$ , to persist unchecked.[27,28] This heightened inflammatory response in the skin leads to increased keratinocyte activity and further contributes to plaque formation and scaling in psoriasis.[27,28] The relationship between cortisol levels, stress, and psoriasis suggests that stress management strategies—such as mindfulness-based interventions, cognitive-behavioral therapy, and, in some cases, pharmacological support—could play a supportive role in managing psoriasis.[29]

#### Hormonal Imbalance and Psoriasis Severity

The delicate balance between hormones such as estrogen, progesterone, prolactin, and cortisol is crucial for immune homeostasis, and disruptions in this balance are known to influence psoriasis severity. [5,6,18,22,23,28] Estrogen generally promotes anti-inflammatory effects, while progesterone supports immune tolerance; together, they create a protective hormonal environment against autoimmune inflammation. [6,9] However, when estrogen levels are low (e.g., during the luteal phase of the menstrual cycle or post-menopause), or when there is an imbalance between estrogen and progesterone, the risk of immune dysregulation increases. [6,10] This imbalance can shift the immune response towards a pro-inflammatory state, marked by an increase in Th1 and Th17 activity, both of which are associated with psoriasis pathogenesis. [16] In clinical practice, understanding these hormonal interdependencies underscores the importance of a personalized approach to psoriasis treatment in women. Comprehensive management strategies that address hormonal balance, stress reduction, and lifestyle modifications hold promise for improving quality of life and reducing disease severity in women affected by psoriasis. [30]

# 2. Hormonal Fluctuations Across Life Stages (Table 2)

Hormonal fluctuations throughout a woman's life can influence the severity and progression of psoriasis due to their immunomodulatory effects. Key hormonal events—including the menstrual cycle, pregnancy, the postpartum period, and menopause—induce shifts in estrogen and progesterone levels, which can impact psoriasis symptoms differently.[7] Understanding these influences is essential for tailoring treatment approaches to optimize care at each life stage.

**Table 2.** Hormonal fluctuation across women's life stages.

Women's life stages	Effect on estrogen and progesterone levels	Effect on psoriasis symptoms	Ref
Menstrual cycle (luteal phase and menstruation)	Decline in estrogen and progesterone levels.	Increased inflammation and exacerbation of psoriasis symptoms.	[31]
Pregnancy	Elevated levels of estrogen and progesterone.	Improvement in psoriasis symptoms. Sometimes complete remission.	[6,8,9,32]
Postpartum Period	Rapid decline in estrogen and progesterone levels.	Rebound effect with flare- ups and worsening of psoriasis, sometimes more severe than before pregnancy.	[7,8,9,19]
Menopause	Decline in estrogen and progesterone production.	Increased psoriasis activity with more frequent and severe flare-ups during and after menopause.	[7,8,10]

# Menstrual Cycle

The menstrual cycle is a monthly series of hormonal changes, particularly involving estrogen and progesterone, which influence immune responses and inflammation. Many women with psoriasis report symptom variation during different phases of their cycle.[31]

- Symptom Worsening During Luteal Phase and Menstruation
  - In the luteal phase (post-ovulation) and menstruation, estrogen and progesterone levels decline significantly, reducing their anti-inflammatory effects. This hormonal drop is linked to increased inflammation, often exacerbating psoriasis symptoms such as itching, redness, and scaling.[31] Research suggests that low estrogen levels may increase pro-inflammatory cytokine activity, such as TNF- $\alpha$  and IL-6, which are key players in psoriasis pathogenesis.[11,12]
- Clinical Implications
  - Recognizing this cyclical pattern enables healthcare providers to implement proactive strategies, such as temporary increases in topical treatments or lifestyle adjustments, to mitigate flare-ups during high-risk phases of the menstrual cycle. Lifestyle modifications and stress management may also enhance symptom control and quality of life.[7,19,32]

# Pregnancy

Pregnancy induces substantial hormonal shifts, with estrogen and progesterone levels rising progressively to maintain the pregnancy and promote fetal development. These elevated hormone levels can profoundly impact immune function and psoriasis symptoms.[6,9,19]

- Improvement of Symptoms
  - During pregnancy, many women with psoriasis experience symptom relief due to the antiinflammatory effects of high estrogen and progesterone.[6,8,9] Estrogen has been shown to

modulate immune responses by promoting an anti-inflammatory environment, decreasing levels of pro-inflammatory cytokines like TNF- $\alpha$  and IL-6, and fostering regulatory T cell activity.[11,12] Research indicates that up to 60% of pregnant women with psoriasis may see an improvement or even achieve remission.[32]

## • Variability in Response

Despite the general trend of symptom improvement, a subset of women may experience no change or worsening symptoms. This variability could be due to genetic factors, environmental influences, and individual differences in immune system sensitivity.[32]

#### • Immune System Shift

Pregnancy involves a shift toward a Th2 immune response, which is less inflammatory and beneficial for psoriasis. This shift decreases Th1 and Th17 responses—typically dominant in psoriasis—and helps prevent excessive inflammation, contributing to symptom improvement.[33]

# • Clinical Management

Managing psoriasis in pregnant women requires a careful balance between effective symptom control and fetal safety. Topical therapies are generally preferred, while systemic treatments are used cautiously due to potential risks. Collaboration between dermatologists and obstetricians is vital for optimal care, as psoriasis treatment must be tailored to minimize risks to the mother and baby.[9,31,32]

## Postpartum Period

The postpartum period involves a sudden decline in estrogen and progesterone levels as the body returns to its pre-pregnancy state. This sharp hormonal drop can trigger a "rebound effect," which may lead to significant symptom flare-ups.

## Rebound Effect and Symptom Flare-ups

This hormonal shift is associated with increased production of pro-inflammatory cytokines, leading to heightened immune activity. Many women experience more severe psoriasis symptoms post-delivery, sometimes presenting with new lesions or more extensive skin involvement. This period is challenging as women balance new motherhood responsibilities while managing their health.[7,8,9,19]

## • Contributing Factors

In addition to hormonal fluctuations, factors like sleep deprivation, physical recovery from childbirth, and postpartum stress can exacerbate psoriasis. Psychological aspects, including postpartum depression and anxiety, may also worsen disease severity, emphasizing the need for mental health support.[34]

# • Treatment Considerations

Postpartum psoriasis management should take a holistic approach, focusing on physical and emotional health, breastfeeding considerations, and social support. Topical therapies are generally preferred for their safety profile in breastfeeding mothers. If systemic treatments are required, healthcare providers must carefully weigh the benefits against potential risks for both mother and infant.[34]

## Menopause

Menopause signifies the end of reproductive years and brings a permanent reduction in estrogen and progesterone levels. These hormonal declines can have significant implications for psoriasis severity and symptom management. [7,8,10]

#### • Increased Disease Activity

With the loss of estrogen's anti-inflammatory properties, many women experience more frequent or severe psoriasis flare-ups during menopause. Estrogen deficiency is linked to

increased production of pro-inflammatory cytokines and decreased regulatory T cell function, creating an immune environment conducive to psoriasis exacerbation. Lesions may become more extensive or resistant to previously effective treatments.[7,8,10]

# Skin Changes and Sensitivity

Menopause also induces changes in skin texture, such as dryness, thinning, and reduced elasticity. These alterations can worsen psoriasis symptoms by making the skin more susceptible to irritation, discomfort, and heightened sensitivity to treatments. Reduced skin barrier function in menopausal women with psoriasis may lead to an increased risk of injury or infection.[7]

# • Hormone Replacement Therapy (HRT)

Hormone replacement therapy (HRT) may offer symptom relief by restoring estrogen levels, potentially mitigating psoriasis severity. Some studies indicate that HRT may alleviate menopausal symptoms and improve psoriasis outcomes. However, the effects of HRT on psoriasis vary among individuals, and HRT carries potential risks, including an increased risk of cardiovascular disease and breast cancer. A comprehensive evaluation of HRT's benefits and risks is essential in managing menopausal women with psoriasis.[34]

#### • Clinical Recommendations

In postmenopausal women with psoriasis, healthcare providers should consider revising treatment strategies to account for hormonal changes and skin sensitivities. Adjustments may involve optimizing topical treatments, emphasizing skincare to address dryness and sensitivity, and evaluating the potential role of HRT in symptom management.[7,34,35]

## 4. Impact on Quality of Life

Psoriasis significantly affects women's quality of life by influencing physical health, emotional well-being, social interactions, and professional activities. Hormonal fluctuations often intensify these challenges, particularly during life stages such as menstruation, pregnancy, postpartum, and menopause, which can exacerbate symptoms.[30,36]

# **Physical Effects**

Psoriasis is associated with several physical symptoms that can impair day-to-day functioning:

#### • Discomfort and Pain

Women with psoriasis frequently experience persistent itching, pain, and skin tightness, which can worsen during hormonal fluctuations. Lesions in sensitive areas such as the scalp, nails, genitals, and skin folds can interfere with routine activities like dressing, grooming, and hygiene. Discomfort can disrupt sleep, leading to fatigue, which further diminishes quality of life. Sleep deprivation can exacerbate both physical symptoms and psychological distress, creating a cycle that compounds disease burden.[37]

# • Functional Impairment

Psoriasis can affect fine motor skills, particularly if lesions are present on the hands or if psoriatic arthritis is involved. Nail psoriasis, for instance, may impair tasks such as typing, writing, or buttoning clothes. Joint pain and stiffness, characteristic of psoriatic arthritis, can limit mobility and make simple movements painful. This functional impairment impacts independence and productivity in both personal and professional contexts.[38,39]

#### Psychological and Emotional Well-being

Psoriasis has profound effects on mental health and self-perception:

#### Self-esteem and Body Image

The visibility of psoriatic lesions can cause psychological distress and impact body image. Women with psoriasis may feel embarrassed, self-conscious, and stigmatized, affecting their confidence in social, professional, and intimate settings. This can result in social withdrawal and

reluctance to engage in activities that reveal affected skin, such as swimming or exercising in public spaces.[40]

#### • Mental Health Disorders

Women with psoriasis are at an increased risk of mental health conditions, particularly depression and anxiety. The chronic nature of psoriasis, combined with hormonal imbalances and the unpredictability of symptom flare-ups, can exacerbate these mental health challenges. Depression and anxiety are not only consequences of physical symptoms but also contribute to a cycle that can worsen psoriasis severity due to stress and emotional strain.[41]

# • Coping Mechanisms

Some women may develop maladaptive coping mechanisms in response to psoriasis, such as social withdrawal, substance use, or disordered eating. These behaviors can provide temporary relief from emotional pain but ultimately worsen physical health and mental well-being. Access to mental health support and counseling is crucial for promoting adaptive coping strategies and breaking this cycle.[42]

#### Social and Interpersonal Relationships

The social implications of psoriasis extend beyond self-perception, affecting relationships and interactions with others:

#### Social Isolation

Due to the visibility of lesions and the fear of judgment or misunderstanding, many women with psoriasis withdraw from social activities. Misconceptions about psoriasis being contagious can amplify feelings of isolation, as friends, colleagues, or even strangers may avoid physical contact. This isolation can deepen psychological distress and reinforce negative self-image.[43]

#### • Intimate Relationships

Psoriasis can affect intimate relationships on both physical and emotional levels. Concerns about appearance, physical discomfort during sexual activity, and decreased libido (influenced by hormonal changes and psychological distress) can impact intimacy. Open communication with partners is essential for managing expectations and providing reassurance. Educating partners about psoriasis's non-contagious nature can also foster understanding and empathy, strengthening relationships.[43,44,45]

# • Communication and Education

Educating close contacts about psoriasis and its impact can dispel misconceptions and improve social support. Friends and family who understand the chronic, non-contagious nature of psoriasis are better equipped to provide meaningful support, reducing the emotional burden and promoting acceptance.[46]

#### Professional and Educational Impact

Psoriasis also affects women's professional lives and educational pursuits, presenting barriers to productivity, acceptance, and advancement:

#### Work Productivity

Physical symptoms such as pain and fatigue, combined with psychological distress, can reduce productivity, increase absenteeism, and limit career opportunities. Psoriatic arthritis may further hinder workplace performance by restricting mobility and causing joint pain, especially in physically demanding jobs. Visible lesions can be particularly challenging in professions that emphasize appearance or require public interaction, as stigma and discomfort can affect performance and self-confidence.[43,47,48]

## • Discrimination and Stigma

Women with psoriasis may encounter discrimination or harassment in the workplace or educational settings due to misconceptions about their condition. Psoriasis is often misunderstood, with some perceiving it as contagious or reflective of poor hygiene, leading to

prejudice. Legal protections may be necessary to address workplace discrimination, ensure fair treatment, and promote an inclusive environment.[49,50]

# • Academic Challenges

Managing psoriasis symptoms and treatment regimens can interfere with academic responsibilities, impacting performance and opportunities for advancement. For students with psoriasis, navigating treatment schedules alongside coursework and social obligations may be challenging. Educators and academic institutions that are informed about psoriasis can help provide support and accommodations, such as flexibility with assignments or exams, allowing students to manage their health without compromising their education. [51,52]

# 2. Fertility and Reproductive Health

Although psoriasis itself does not directly lead to infertility, several factors associated with the condition can influence reproductive health, including the impact of systemic inflammation, medications, stress, and lifestyle factors. Here's how each of these elements may affect fertility:

Disease Severity and Systemic Inflammation

Psoriasis is an inflammatory disease that, in severe cases, can lead to systemic inflammation beyond the skin. This widespread inflammation can disrupt reproductive function by influencing hormonal regulation, ovulation, and even implantation:[53,54]

- Hormonal Disruption: Chronic inflammation can interfere with the hypothalamic-pituitary-ovarian (HPO) axis, which is crucial for regulating reproductive hormones like estrogen, progesterone, and luteinizing hormone (LH). Disruptions in this axis can lead to irregular menstrual cycles, affecting fertility by making it harder for ovulation to occur predictably.[6,8,9,25,53,54]
- Impact on Ovulation and Implantation: Inflammation may also affect the uterus and ovaries directly, impairing ovulation or creating a less hospitable environment for implantation. Studies have shown that elevated inflammatory markers (e.g., TNF-alpha, IL-6) can influence the reproductive environment, potentially lowering conception rates or increasing the risk of early miscarriage in women with chronic inflammatory conditions.[12,54,56]

## Medication Effects

Some medications used to treat moderate to severe psoriasis have known teratogenic effects, meaning they can cause birth defects and are generally unsafe during pregnancy. This is particularly true for medications such as methotrexate and retinoids:[57]

- Methotrexate: Methotrexate is a systemic immunosuppressive drug that is often used to treat severe psoriasis but is highly teratogenic. It interferes with folate metabolism, which is crucial for DNA synthesis and cell division, affecting both male and female fertility. Women planning a pregnancy are advised to discontinue methotrexate for at least 3 months prior to conception.[57]
- Retinoids (e.g., acitretin): Retinoids are derivatives of vitamin A that are used in psoriasis management but can cause severe birth defects if used during pregnancy. Women on retinoids are usually advised to wait at least 3 years after stopping treatment before attempting to conceive due to the drug's long half-life.[57]
- Other Immunosuppressants: Some other medications, like cyclosporine, may be used in specific
  cases but require close monitoring due to potential risks to the developing fetus and possible
  impacts on fertility.[57] Biologic drugs such as TNF inhibitors are generally considered safer for
  use during pregnancy, but each case should be evaluated individually.[57]

# Psychological Stress and Hormonal Balance

The stress of living with a chronic condition like psoriasis can also play a role in reproductive health:

ç

- Stress and the HPO Axis: Psychological stress can lead to changes in the HPO axis, impacting
  hormone release and potentially leading to menstrual irregularities, anovulation (absence of
  ovulation), or luteal phase defects (which can hinder implantation). Chronic stress activates the
  hypothalamic-pituitary-adrenal (HPA) axis, increasing cortisol levels. Elevated cortisol can
  disrupt the delicate balance of reproductive hormones, further complicating fertility.[25,53,54]
- Cyclical Impact of Flare-Ups: Psoriasis symptoms often fluctuate with hormonal changes, and flare-ups may exacerbate stress levels, creating a cyclical problem. The additional stress during flare-ups may impact reproductive hormones, increasing the likelihood of irregular periods and complicating timing for conception.[31,53]

#### Lifestyle Factors

Psoriasis is associated with certain lifestyle factors, including higher rates of obesity, smoking, and alcohol consumption, which can adversely impact reproductive health:

- Obesity and Insulin Resistance: Obesity is prevalent among individuals with psoriasis and is a
  known risk factor for insulin resistance, which can contribute to polycystic ovary syndrome
  (PCOS). PCOS is a common endocrine disorder that can cause irregular menstrual cycles and
  anovulation, both of which can negatively impact fertility.[57,58]
- Smoking and Alcohol: Smoking and excessive alcohol use are also more common in individuals with psoriasis and have both been linked to decreased fertility. Smoking can lead to premature ovarian failure, reduced egg quality, and increased risk of early pregnancy loss. Alcohol, on the other hand, can interfere with hormone levels and reduce the likelihood of conception.[59,60]
- Metabolic Syndrome: Psoriasis is also linked to metabolic syndrome, which is a combination of
  conditions including hypertension, hyperglycemia, and abnormal cholesterol levels. Metabolic
  syndrome can contribute to inflammation and hormonal dysregulation, further complicating
  fertility and reproductive health.[57,61]

#### Pregnancy Planning and Management

For women with psoriasis, careful planning is essential for a healthy pregnancy. This includes consulting healthcare providers about safe medication use, managing disease activity, and addressing any lifestyle modifications that could improve fertility outcomes:

- Preconception Counseling: Women with psoriasis should consult with healthcare providers before trying to conceive to discuss medication adjustments and other preparation steps.
   Discontinuing certain medications, switching to safer alternatives, or modifying the dosage under medical supervision may be necessary to ensure a safe pregnancy.[57,62]
- Management During Pregnancy: In some cases, pregnancy can improve psoriasis symptoms due
  to hormonal changes that favor an anti-inflammatory state. However, managing psoriasis
  during pregnancy can be challenging because options for systemic treatments are limited.
  Topical treatments are generally safer and are often preferred for controlling symptoms.[7,57,62]
- Lifestyle Adjustments: For women planning pregnancy, addressing lifestyle factors such as weight management, smoking cessation, and alcohol reduction is critical. Optimizing these aspects can improve fertility, reduce inflammation, and enhance overall reproductive outcomes.[57,59,60]

## 6. Management Strategies

Effective psoriasis management in women requires a personalized treatment approach that considers unique factors, such as hormonal fluctuations, disease severity, comorbidities, and life stages. Here's a breakdown of scientifically-supported approaches in managing psoriasis:

## 2. Personalized Treatment Approaches

**Topical Therapies** 

doi:10.20944/preprints202411.0496.v1

11

- Corticosteroids: Topical corticosteroids are often the first-line treatment for mild to moderate
  psoriasis. They help reduce inflammation and slow cell turnover. However, long-term use
  should be monitored to prevent skin thinning, especially in sensitive areas.[8,63]
- Calcineurin Inhibitors (e.g., Tacrolimus): Effective for delicate skin areas like the face and genitals, these agents modulate immune response without the same side effects as steroids, although they are usually used as second-line treatments.[57]
- Emollients and Moisturizers: Regular use of emollients helps keep the skin hydrated, reducing scaling and discomfort. Studies show that well-hydrated skin can improve the efficacy of other topical treatments.[64]

# Systemic Treatments

- Methotrexate and Cyclosporine: These immunosuppressants are often used for moderate to severe cases of psoriasis but can have significant side effects, including liver and kidney toxicity.
   For women planning pregnancy, methotrexate is contraindicated due to its teratogenic effects.[57]
- Acitretin: A retinoid used in psoriasis treatment, acitretin is effective but also teratogenic, with pregnancy avoidance recommended for 3 years post-treatment.[57]
- Biologic Agents: Biologics, including TNF-α inhibitors (e.g., infliximab), IL-17 inhibitors (e.g., secukinumab), and IL-23 inhibitors (e.g., guselkumab), target specific immune pathways involved in psoriasis and offer targeted, effective control with fewer systemic effects. Biologics are generally considered safe but must be evaluated on an individual basis, especially for pregnant or breastfeeding women.[57]

#### Phototherapy

Narrowband UVB and PUVA Therapy: Phototherapy is effective for moderate to severe
psoriasis and is considered safe during pregnancy, making it a valuable option for women
needing more than topical treatments. Narrowband UVB therapy has been shown to reduce
flare-ups without systemic side effects, making it suitable for long-term management.[65]

#### Hormone-Based Therapies

• Hormone Replacement Therapy (HRT): Postmenopausal women may see some improvement in psoriasis symptoms with HRT, as estrogen can have anti-inflammatory effects. However, HRT carries risks (e.g., cardiovascular disease, breast cancer), and its impact on psoriasis varies; thorough risk assessment is essential before initiation.[34]

#### 2. Lifestyle Modifications

Stress Management

- Mindfulness, Relaxation and Meditation: These techniques help manage psychological stress, which can trigger or exacerbate psoriasis flares. Stress management has been shown to positively impact immune function and hormonal balance, potentially reducing symptom severity. [66,67]
- Cognitive-Behavioral Therapy (CBT): CBT helps women develop effective coping mechanisms and reduces psoriasis-related anxiety and depression. Studies have found CBT beneficial in reducing stress-related flare-ups.[66,67]

#### Healthy Diet

 Anti-Inflammatory Diet: Diets rich in antioxidants, omega-3 fatty acids, and anti-inflammatory foods, such as fruits, vegetables and whole grains, have been associated with reduced psoriasis symptoms. Omega-3 fatty acids, found in fish and flaxseeds, have been shown to reduce systemic inflammation.[68,69] • Avoiding Processed Foods and Alcohol: Alcohol, processed foods, and high sugar intake are linked to increased inflammation and can exacerbate psoriasis. A healthy diet supports overall immune function and may reduce the frequency of flares.[59,60,70]

#### Regular Exercise

 Physical Activity: Regular exercise improves cardiovascular health, reduces obesity risk, lowers stress levels, and improves psoriasis severity. Exercise also reduces pro-inflammatory markers, aiding in better disease management.[71]

# Avoiding Triggers

Personal Triggers: Common triggers include smoking, alcohol, allergens, and certain foods.
 Keeping a symptom diary to identify triggers can help in managing flare-ups more effectively.
 Smoking, for instance, is associated with higher psoriasis risk and severity, making cessation highly beneficial. [59,60,70,72]

# 2. Multidisciplinary Care

# Collaborative Approach

• Team-Based Care: A multidisciplinary approach involving dermatologists, rheumatologists, gynecologists, mental health professionals, and primary care providers offers comprehensive care. This collaborative care model is critical for women with psoriasis, addressing physical symptoms, emotional challenges, hormonal influences, and reproductive health needs.[62,73,74,75]

#### Patient Education

Self-Management Education: Educating women about how hormonal changes impact
psoriasis empowers them to manage their condition proactively. Support groups, counseling,
and access to educational resources can improve self-management and treatment adherence,
particularly during life stages associated with hormonal changes, such as pregnancy or
menopause.[46,62]

#### Psychological Support

 Mental Health Access: Psychological support is crucial for managing psoriasis, as the visible nature of the disease can lead to anxiety, depression, and social withdrawal. Access to mental health resources like counseling and support groups can help women manage the emotional aspects of living with a chronic skin condition.[75]

# Family Planning Services

Safe Contraception and Preconception Counseling: For women of reproductive age, coordinated
care is essential to address contraception choices, preconception counseling, and pregnancy
management. Many psoriasis medications are contraindicated during pregnancy, so advance
planning with a healthcare provider can optimize reproductive outcomes and minimize disease
activity during pregnancy.[57,62]

## 7. Future Directions and Research

Recent research highlights the complexity of psoriasis, a chronic inflammatory disease that appears to be influenced by various factors, including immune function, hormonal balance, genetics, and psychological aspects.[1,5,6,75] Below are key areas for further investigation:

## Estrogen Receptor Studies

doi:10.20944/preprints202411.0496.v1

- Role of Estrogen Receptors in Psoriasis Pathogenesis: Estrogen has been shown to influence immune function, but the exact mechanisms remain unclear. [6,10] Estrogen receptors (ERs), specifically  $\text{Er}\alpha$  and  $\text{Er}\beta$ , are expressed on immune cells and play roles in immune regulation. Research suggests that  $\text{Er}\alpha$  activation might have pro-inflammatory effects, while  $\text{Er}\beta$  activation could be anti-inflammatory, potentially impacting psoriasis severity. [11,76]
- Targeting Estrogen Receptor Pathways: By investigating how different estrogen receptors
  influence immune cells, scientists may uncover specific pathways that could be modulated for
  therapeutic purposes. For example, selective estrogen receptor modulators (SERMs) might offer
  ways to manage inflammation in psoriasis without the side effects associated with broad
  hormone replacement therapies.[77]

# Genetic and Epigenetic Factors

- Genetic Variations and Psoriasis Susceptibility: Studies have identified several genetic loci associated with psoriasis, particularly in genes related to immune responses, such as IL-23 and TNF-α pathways.[78] Research into how these genetic variations interact with hormonal changes could explain why psoriasis severity fluctuates with life stages (e.g., puberty, pregnancy, menopause).[7,9,19,78]
- Epigenetic Modifications and Hormone Sensitivity: Epigenetic changes, such as DNA methylation and histone modifications, influence gene expression without altering DNA sequences.[79] Hormones like estrogen can impact these epigenetic mechanisms, potentially affecting psoriasis severity and treatment responses.[16,80,81] Investigating how epigenetic factors modify hormonal sensitivity in individuals with psoriasis may provide insights into why some patients experience more severe symptoms and aid in the development of personalized therapies.
- Personalized Medicine: Identifying genetic and epigenetic markers linked to psoriasis severity
  and treatment response could facilitate personalized medicine.[81] By tailoring treatment
  approaches based on genetic profiles, healthcare providers may be able to optimize therapies
  and reduce side effects.

#### Longitudinal Studies

- Natural History of Psoriasis Through Life Stages: Longitudinal studies that follow women through hormonal transitions (e.g., puberty, pregnancy, menopause) are essential for understanding how hormonal fluctuations impact psoriasis.[7] Such studies can clarify if specific life stages exacerbate or alleviate symptoms, informing the timing and types of intervention strategies.
- Tracking Disease Progression and Triggers: By monitoring psoriasis progression and flare-up
  patterns in relation to hormonal changes, researchers can gather insights into which
  interventions are most effective at different life stages. For instance, such studies could identify
  whether hormone fluctuations are linked to periods of remission or exacerbation, guiding both
  timing and choice of treatments.
- Evidence-Based Treatment Timelines: Long-term data can help identify optimal treatment windows and strategies for managing psoriasis, potentially leading to interventions that are timed to life-stage transitions, such as beginning hormone-based treatments at menopause if appropriate.

# Hormone-Based Treatments

- Selective Estrogen Receptor Modulators (SERMs): SERMs, which are already used in conditions
  like osteoporosis and breast cancer, may represent a promising area for psoriasis
  treatment.[77,82] These drugs selectively stimulate or block estrogen receptors, which could
  allow for modulation of immune responses related to psoriasis without widespread hormonal
  effects.[77] Trials are needed to determine the efficacy and safety of SERMs for psoriasis.
- Progesterone Analog Research: Progesterone, another key hormone, may have immunomodulatory effects that could impact psoriasis.[9] Progesterone analogs could be

- explored for their potential in modulating immune function, particularly during life stages where progesterone naturally fluctuates (e.g., pregnancy). Current research is limited, but understanding how progesterone and its receptors impact psoriasis could open new therapeutic options.
- Clinical Trials for Hormone-Based Therapies: Clinical trials investigating hormone-based therapies, including estrogen and progesterone treatments, are essential for understanding their effects on psoriasis.[6,9] Such trials can assess the safety, efficacy, and optimal dosing regimens of hormone therapies for patients with psoriasis, especially for women undergoing hormonal changes.

#### Psychoneuroimmunology Research

- Mind-Body Interactions in Psoriasis: The emerging field of psychoneuroimmunology (PNI) examines how psychological factors, neurological processes, and immune responses interact in disease contexts.[83] Stress, for example, can exacerbate psoriasis by stimulating the hypothalamic-pituitary-adrenal (HPA) axis, which releases cortisol and other stress hormones. Chronic stress also impacts immune function, leading to increased inflammatory cytokine production that can worsen psoriasis.[84]
- Role of Stress Hormones and Neurotransmitters: Research suggests that stress hormones like
  cortisol, as well as neurotransmitters such as serotonin and dopamine, may influence immune
  responses in psoriasis.[26,27] This connection indicates that stress reduction and psychological
  interventions may play important roles in managing psoriasis, especially given the skin-brain
  connection.[85] Investigating these pathways could lead to novel, holistic approaches that
  combine pharmacological and psychological therapies.
- Interdisciplinary Treatment Approaches: Given the complex interactions between the mind and immune function, interdisciplinary approaches that include mental health support alongside dermatologic treatment may improve outcomes. This approach might involve cognitive-behavioral therapy (CBT), mindfulness-based stress reduction, and other interventions aimed at reducing stress and improving mental well-being.[66,67,75]

# 8. Conclusion

Hormonal balance is a fundamental factor in the clinical course and management of psoriasis in women, significantly affecting disease severity, symptom fluctuation, and overall quality of life. Hormones such as estrogen, progesterone, prolactin, and cortisol interact with immune pathways critical to psoriasis pathogenesis, modulating cytokine profiles, T-cell activation, and keratinocyte activity. These hormonal influences highlight the need for individualized, adaptive management strategies that accommodate the unique physiological and immunological needs of each woman. Women face distinctive challenges as hormonal fluctuations during menstruation, pregnancy, postpartum, and menopause can exacerbate or mitigate psoriasis symptoms. Each life stage involves unique hormonal shifts that necessitate personalized treatment protocols, psychological support, and education. A comprehensive, multidisciplinary approach that includes dermatologists, endocrinologists, gynecologists, and mental health professionals offers a holistic framework to address not only the physical manifestations but also the psychosocial and emotional impacts of living with psoriasis. This integrated approach can significantly improve patient outcomes by targeting the diverse factors that influence disease progression. Healthcare providers must recognize and address the intricate interplay between hormonal dynamics and psoriasis to support women more effectively. Combining pharmacologic treatments with lifestyle interventions, stress management, and patient education empowers women to navigate the complexities of this chronic autoimmune disease. Continued interdisciplinary research and collaboration will deepen our understanding of hormonal impacts on psoriasis, facilitating innovative, patient-centered care and improved quality of life for women with this condition.

doi:10.20944/preprints202411.0496.v1

15

**Author Contributions:** For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, X.X. and Y.Y.; methodology, X.X.; software, X.X.; validation, X.X., Y.Y. and Z.Z.; formal analysis, X.X.; investigation, X.X.; resources, X.X.; data curation, X.X.; writing—original draft preparation, X.X.; writing—review and editing, X.X.; visualization, X.X.; supervision, X.X.; project administration, X.X.; funding acquisition, Y.Y. All authors have read and agreed to the published version of the manuscript." Please turn to the <u>CRediT taxonomy</u> for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Funding: This research received no external funding

**Informed Consent Statement:** Not applicable

**Conflicts of Interest:** The authors declare no conflicts of interest.

#### References

- Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013;133(2):377-385. https://doi.org/10.1038/jid.2012.339
- 2. Samarasekera EJ, Smith CH; National Institute of Health and Care Excellence; Royal College of Physicians. Psoriasis: guidance on assessment and referral. Clin Med (Lond). 2014;14(2):178-182. https://doi.org/10.7861/clinmedicine.14-2-178
- 3. Psoriasis statistics. 2020. National Psoariasis Foundation. Available at: https://www.psoriasis.org/psoriasis-statistics/[accessed 9 November 2020] [Epub ahead of print].
- 4. Blackstone B, Patel R, Bewley A. Assessing and Improving Psychological Well-Being in Psoriasis: Considerations for the Clinician. Psoriasis (Auckl). 2022;12:25-33. Published 2022 Mar 25. https://doi.org/10.2147/PTT.S328447
- Cassalia F, Belloni Fortina A. Psoriasis in women with psoriatic arthritis: hormonal effects, fertility, and considerations different Reumatismo. for management at stages of life. 2024;76(3):10.4081/reumatismo.2024.1775. Published 2024 11. Sep https://doi.org/10.4081/reumatismo.2024.1775
- 6. Adachi A, Honda T. Regulatory Roles of Estrogens in Psoriasis. J Clin Med. 2022;11(16):4890. Published 2022 Aug 20. https://doi.org/10.3390/jcm11164890
- 7. Ceovic R, Mance M, Bukvic Mokos Z, Svetec M, Kostovic K, Stulhofer Buzina D. Psoriasis: female skin changes in various hormonal stages throughout life--puberty, pregnancy, and menopause. Biomed Res Int. 2013;2013:571912. https://doi.org/10.1155/2013/571912
- 8. Vena GA, Cassano N, Bellia G, Colombo D. Psoriasis in pregnancy: challenges and solutions. Psoriasis (Auckl). 2015;5:83-95. Published 2015 May 18. https://doi.org/10.2147/PTT.S82975
- 9. Hellberg S, Raffetseder J, Rundquist O, et al. Progesterone Dampens Immune Responses in In Vitro Activated CD4+ T Cells and Affects Genes Associated With Autoimmune Diseases That Improve During Pregnancy. Front Immunol. 2021;12:672168. Published 2021 May 12. https://doi.org/10.3389/fimmu.2021.672168
- 10. Fuentes N, Silveyra P. Estrogen receptor signaling mechanisms. Adv Protein Chem Struct Biol. 2019;116:135-170. https://doi.org/10.1016/bs.apcsb.2019.01.001
- 11. Du P, Yuan B, Cao J, et al. Methyltransferase-like 17 physically and functionally interacts with estrogen receptors. IUBMB Life. 2015;67(11):861-868. https://doi.org/10.1002/iub.1444
- 12. Xu HT, Zheng Q, Tai ZG, et al. Formononetin attenuates psoriasiform inflammation by regulating interferon signaling pathway. Phytomedicine. 2024;128:155412. https://doi.org/10.1016/j.phymed.2024.155412
- 13. Brunsing RL, Prossnitz ER. Induction of interleukin-10 in the T helper type 17 effector population by the G protein coupled estrogen receptor (GPER) agonist G-1. Immunology. 2011;134(1):93-106. https://doi.org/10.1111/j.1365-2567.2011.03471.x
- 14. Qi Q, Liu X, Zhang Q, Guo SW. Platelets induce increased estrogen production through NF-κB and TGF-β1 signaling pathways in endometriotic stromal cells. Sci Rep. 2020;10(1):1281. Published 2020 Jan 28. https://doi.org/10.1038/s41598-020-57997-6
- 15. Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626-638. https://doi.org/10.1038/nri.2016.90
- 16. Danesh M, Murase JE. The immunologic effects of estrogen on psoriasis: A comprehensive review. Int J Womens Dermatol. 2015;1(2):104-107. Published 2015 May 14. https://doi.org/10.1016/j.ijwd.2015.03.001

- 17. Yang X, Tian Y, Zheng L, Luu T, Kwak-Kim J. The Update Immune-Regulatory Role of Pro- and Anti-Inflammatory Cytokines in Recurrent Pregnancy Losses. Int J Mol Sci. 2022;24(1):132. Published 2022 Dec 21. https://doi.org/10.3390/ijms24010132
- 18. Singh R, Koppu S, Perche PO, Feldman SR. The Cytokine Mediated Molecular Pathophysiology of Psoriasis and Its Clinical Implications. Int J Mol Sci. 2021;22(23):12793. Published 2021 Nov 26. https://doi.org/10.3390/ijms222312793
- 19. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and post partum. Arch Dermatol. 2005;141(5):601-606. https://doi.org/10.1001/archderm.141.5.601
- 20. Bouman A, Heineman MJ, Faas MM. Sex hormones and the immune response in humans. Hum Reprod Update. 2005;11(4):411-423. https://doi.org/10.1093/humupd/dmi008
- 21. Bouman A, Moes H, Heineman MJ, de Leij LF, Faas MM. The immune response during the luteal phase of the ovarian cycle: increasing sensitivity of human monocytes to endotoxin. Fertil Steril. 2001;76(3):555-559. https://doi.org/10.1016/s0015-0282(01)01971-9
- 22. Freeman ME, Kanyicska B, Lerant A, Nagy G. Prolactin: structure, function, and regulation of secretion. Physiol Rev. 2000;80(4):1523-1631. https://doi.org/10.1152/physrev.2000.80.4.1523
- 23. Botezatu D, Tovaru M, Georgescu SR, Leahu OD, Giurcaneanu C, Curici A. Interplay Between Prolactin and Pathogenesis of Psoriasis Vulgaris. Maedica (Bucur). 2016;11(3):232-240.
- 24. Lee YH, Song GG. Association between circulating prolactin levels and psoriasis and its correlation with disease severity: a meta-analysis. Clin Exp Dermatol. 2018;43(1):27-35. https://doi.org/10.1111/ced.13228
- 25. Straub RH, Cutolo M. Glucocorticoids and chronic inflammation. Rheumatology (Oxford). 2016;55(suppl 2):ii6-ii14. https://doi.org/10.1093/rheumatology/kew348
- 26. Yeager MP, Pioli PA, Guyre PM. Cortisol exerts bi-phasic regulation of inflammation in humans. Dose Response. 2011;9(3):332-347. https://doi.org/10.2203/dose-response.10-013.Yeager
- Slominski AT, Brożyna AA, Tuckey RC. Cutaneous Glucocorticoidogenesis and Cortisol Signaling Are Defective in Psoriasis. J Invest Dermatol. 2017;137(8):1609-1611. https://doi.org/10.1016/j.jid.2017.04.004
- 28. Repousi N, Fotiadou S, Chaireti E, et al. Circadian cortisol profiles and hair cortisol concentration in patients with psoriasis: associations with anxiety, depressive symptomatology and disease severity. Circadian cortisol profiles and hair cortisol concentration in patients with psoriasis: associations with anxiety, depressive symptomatology and disease severity. Eur J Dermatol. 2022;32(3):357-367. https://doi.org/10.1684/ejd.2022.4267
- 29. Graubard R, Perez-Sanchez A, Katta R. Stress and Skin: An Overview of Mind Body Therapies as a Treatment Strategy in Dermatology. Dermatol Pract Concept. 2021;11(4):e2021091. Published 2021 Sep 1. https://doi.org/10.5826/dpc.1104a91
- 30. Bilgiç Ö, Bilgiç A, Sivrikaya A, Selvi Y, Ünlü A, Altinyazar HC. Association between endocrinological, immunological and psychosocial variables in psoriasis patients. G Ital Dermatol Venereol. 2016;151(6):603-609
- 31. Bello GD, Maurelli M, Schena D, Gisondi P, Girolomoni G. Variations of symptoms of atopic dermatitis and psoriasis in relation to menstrual cycle. J Am Acad Dermatol. 2022;87(4):892-895. https://doi.org/10.1016/j.jaad.2021.12.014
- 32. Raychaudhuri SP, Navare T, Gross J, Raychaudhuri SK. Clinical course of psoriasis during pregnancy. Int J Dermatol. 2003;42(7):518-520. https://doi.org/10.1046/j.1365-4362.2003.01760.x
- 33. Østensen M, Villiger PM, Förger F. Interaction of pregnancy and autoimmune rheumatic disease. Autoimmun Rev. 2012;11(6-7):A437-A446. https://doi.org/10.1016/j.autrev.2011.11.013
- 34. Belinchón I, Velasco M, Ara-Martín M, et al. Management of Psoriasis During Preconception, Pregnancy, Postpartum, and Breastfeeding: A Consensus Statement. Consenso sobre las actuaciones a seguir durante la edad fértil, el embarazo, el posparto y la lactancia en pacientes con psoriasis. Actas Dermosifiliogr (Engl Ed). 2021;112(3):225-241. https://doi.org/10.1016/j.ad.2020.10.002
- 35. Cassalia F, Cazzaniga S, Ofenloch R, et al. Comparison of Perceptions of Skin Condition, Product Use and Allergen Reactivity Between People with Psoriasis and Controls in the European Dermato-Epidemiology Network (EDEN) Fragrance Study. Acta Derm Venereol. 2024;104:adv23513. Published 2024 Mar 4. https://doi.org/10.2340/actadv.v104.23513
- 36. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis. 2005;64 Suppl 2(Suppl 2):ii18-ii25. https://doi.org/10.1136/ard.2004.033217
- 37. Ljosaa TM, Mork C, Stubhaug A, Moum T, Wahl AK. Skin pain and skin discomfort is associated with quality of life in patients with psoriasis. J Eur Acad Dermatol Venereol. 2012;26(1):29-35. https://doi.org/10.1111/j.1468-3083.2011.04000.x
- 38. Kimball AB, Gieler U, Linder D, Sampogna F, Warren RB, Augustin M. Psoriasis: is the impairment to a patient's life cumulative?. J Eur Acad Dermatol Venereol. 2010;24(9):989-1004. https://doi.org/10.1111/j.1468-3083.2010.03705.x

- 39. Hawro M, Maurer M, Weller K, et al. Lesions on the back of hands and female gender predispose to stigmatization in patients with psoriasis. J Am Acad Dermatol. 2017;76(4):648-654.e2. https://doi.org/10.1016/j.jaad.2016.10.040
- 40. Nazik H, Nazik S, Gul FC. Body Image, Self-esteem, and Quality of Life in Patients with Psoriasis. Indian Dermatol Online J. 2017;8(5):343-346. https://doi.org/10.4103/idoj.IDOJ\_503\_15
- 41. Pollo CF, Miot HA, Matos TDS, et al. Prevalence and factors associated with depression and anxiety in patients with psoriasis. J Clin Nurs. 2021;30(3-4):572-580. https://doi.org/10.1111/jocn.15577
- 42. Kouris A, Platsidaki E, Kouskoukis C, Christodoulou C. Psychological parameters of psoriasis. Psychiatriki. 2017;28(1):54-59. https://doi.org/10.22365/jpsych.2017.281.54
- 43. Ghorbanibirgani A, Fallahi-Khoshknab M, Zarea K, Abedi H. The Lived Experience of Psoriasis Patients from Social Stigma and Rejection: A Qualitative Study. Iran Red Crescent Med J. 2016;18(7):e27893. Published 2016 May 21. https://doi.org/10.5812/ircmj.27893
- 44. Magin P, Heading G, Adams J, Pond D. Sex and the skin: a qualitative study of patients with acne, psoriasis and atopic eczema. Psychol Health Med. 2010;15(4):454-462. https://doi.org/10.1080/13548506.2010.484463
- 45. Salle R, Halioua B, Le Fur G, Aubert R, Shourick J, Taieb C. Psoriasis and sexuality: Patients express their feelings. Skin Health Dis. 2022;3(3):e199. Published 2022 Dec 28. https://doi.org/10.1002/ski2.199
- 46. Larsen MH, Strumse YS, Andersen MH, Borge CR, Wahl AK. Associations between disease education, self-management support, and health literacy in psoriasis. J Dermatolog Treat. 2021;32(6):603-609. https://doi.org/10.1080/09546634.2019.1688233
- 47. Snyder AM, Taliercio VL, Webber LB, et al. The Role of Pain in the Lives of Patients with Psoriasis: A Qualitative Study on an Inadequately Addressed Symptom. J Psoriasis Psoriatic Arthritis. 2022;7(1):29-34. https://doi.org/10.1177/24755303211066928
- 48. Assessing work-related productivity loss and indirect costs of psoriasis across six countries. Br J Dermatol. 2020;183(3):e65-e90. https://doi.org/10.1111/bjd.19351
- 49. Hrehorów E, Salomon J, Matusiak L, Reich A, Szepietowski JC. Patients with psoriasis feel stigmatized. Acta Derm Venereol. 2012;92(1):67-72. https://doi.org/10.2340/00015555-1193
- 50. Armstrong A, Bohannan B, Mburu S, et al. Impact of Psoriatic Disease on Quality of Life: Interim Results of a Global Survey. Dermatol Ther (Heidelb). 2022;12(4):1055-1064. https://doi.org/10.1007/s13555-022-00695-0
- 51. Bronckers IMGJ, van Geel MJ, van de Kerkhof PCM, de Jong EMGJ, Seyger MMB. A cross-sectional study in young adults with psoriasis: potential determining factors in quality of life, life course and work productivity. J Dermatolog Treat. 2019;30(3):208-215. https://doi.org/10.1080/09546634.2018.1506077
- 52. Napolitano M, Megna M, Patruno C, et al. Psoriasis and high school students: an educational approach. G Ital Dermatol Venereol. 2018;153(5):632-635. https://doi.org/10.23736/S0392-0488.17.05511-0
- 53. Lambe M, Bergstrom AV, Johansson ALV, Weibull CE. Reproductive patterns and maternal and pregnancy outcomes in women with psoriasis-A population-based study. J Am Acad Dermatol. 2020;82(5):1109-1116. https://doi.org/10.1016/j.jaad.2019.05.099
- 54. Chen TC, Iskandar IYK, Parisi R, et al. Fertility Trends and Adverse Pregnancy Outcomes in Female Patients With Psoriasis in the UK. JAMA Dermatol. 2023;159(7):736-744. https://doi.org/10.1001/jamadermatol.2023.1400
- 55. Tuğrul Ayanoğlu B, Özdemir ED, Türkoğlu O, Alhan A. Diminished ovarian reserve in patients with psoriasis. Taiwan J Obstet Gynecol. 2018;57(2):227-230. https://doi.org/10.1016/j.tjog.2018.02.010
- 56. Takeshita J, Grewal S, Langan SM, et al. Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol. 2017;76(3):377-390. https://doi.org/10.1016/j.jaad.2016.07.064
- 57. Balakirski G, Gerdes S, Beissert S, Ochsendorf F, von Kiedrowski R, Wilsmann-Theis D. Therapy of psoriasis during pregnancy and breast-feeding. J Dtsch Dermatol Ges. 2022;20(5):653-683. https://doi.org/10.1111/ddg.14789
- 58. Moro F, Tropea A, Scarinci E, et al. Psoriasis and polycystic ovary syndrome: a new link in different phenotypes. Eur J Obstet Gynecol Reprod Biol. 2015;191:101-105. https://doi.org/10.1016/j.ejogrb.2015.06.002
- 59. Wei J, Zhu J, Xu H, et al. Alcohol consumption and smoking in relation to psoriasis: a Mendelian randomization study. Br J Dermatol. 2022;187(5):684-691. https://doi.org/10.1111/bjd.21718
- 60. de Angelis C, Nardone A, Garifalos F, et al. Smoke, alcohol and drug addiction and female fertility. Reprod Biol Endocrinol. 2020;18(1):21. Published 2020 Mar 12. https://doi.org/10.1186/s12958-020-0567-7
- 61. He Y, Lu Y, Zhu Q, et al. Influence of metabolic syndrome on female fertility and in vitro fertilization outcomes in PCOS women. Am J Obstet Gynecol. 2019;221(2):138.e1-138.e12. https://doi.org/10.1016/j.ajog.2019.03.011
- 62. Rademaker M, Agnew K, Andrews M, et al. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration. Australas J Dermatol. 2018;59(2):86-100. https://doi.org/10.1111/ajd.12641

- 64. Fluhr JW, Cavallotti C, Berardesca E. Emollients, moisturizers, and keratolytic agents in psoriasis. Clin Dermatol. 2008;26(4):380-386. https://doi.org/10.1016/j.clindermatol.2008.01.015
- 65. Zhang P, Wu MX. A clinical review of phototherapy for psoriasis. Lasers Med Sci. 2018;33(1):173-180. https://doi.org/10.1007/s10103-017-2360-1
- 66. Rousset L, Halioua B. Stress and psoriasis. Int J Dermatol. 2018;57(10):1165-1172. https://doi.org/10.1111/ijd.14032
- 67. Mar K, Rivers JK. The Mind Body Connection in Dermatologic Conditions: A Literature Review. J Cutan Med Surg. 2023;27(6):628-640. https://doi.org/10.1177/12034754231204295
- 68. Katsimbri P, Korakas E, Kountouri A, et al. The Effect of Antioxidant and Anti-Inflammatory Capacity of Diet on Psoriasis and Psoriatic Arthritis Phenotype: Nutrition as Therapeutic Tool?. Antioxidants (Basel). 2021;10(2):157. Published 2021 Jan 22. https://doi.org/10.3390/antiox10020157
- 69. Pona A, Haidari W, Kolli SS, Feldman SR. Diet and psoriasis. Dermatol Online J. 2019;25(2):13030/qt1p37435s. Published 2019 Feb 15.
- 70. Ma X, Nan F, Liang H, et al. Excessive intake of sugar: An accomplice of inflammation. Front Immunol. 2022;13:988481. Published 2022 Aug 31. https://doi.org/10.3389/fimmu.2022.988481
- 71. Duchnik E, Kruk J, Tuchowska A, Marchlewicz M. The Impact of Diet and Physical Activity on Psoriasis: A Narrative Review of the Current Evidence. Nutrients. 2023;15(4):840. Published 2023 Feb 7. https://doi.org/10.3390/nu15040840
- 72. Rasool F, Akhtar S, Hassan I, Zeerak S, Mubashir S, Sheikh G. Common Contact Allergens in Patients with Palmoplantar and Scalp Psoriasis and Impact of their Avoidance on Dermatology Life Quality Index: A Hospital-Based Study. Indian J Dermatol. 2018;63(2):160-164. https://doi.org/10.4103/ijd.IJD\_760\_16
- 73. Cobo-Ibáñez T, Villaverde V, Seoane-Mato D, et al. Multidisciplinary dermatology-rheumatology management for patients with moderate-to-severe psoriasis and psoriatic arthritis: a systematic review. Rheumatol Int. 2016;36(2):221-229. https://doi.org/10.1007/s00296-015-3377-z
- 74. Costa-Silva M, Vide J, Lopes S, Azevedo F, Magina S. Psoriasis and comorbidities: general practitioners' awareness. Acta Dermatovenerol Alp Pannonica Adriat. 2018;27(1):5-7.
- 75. Makara-Studzińska M, Ziemecki P, Ziemecka A, Partyka I. Potrzeba psychologicznego i społecznego wsparcia osób chorych na łuszczyce [The psychological and social support in patients with psoriasis]. Pol Merkur Lekarski. 2013;35(207):171-174.
- 76. Chen P, Li B, Ou-Yang L. Role of estrogen receptors in health and disease. Front Endocrinol (Lausanne). 2022;13:839005. Published 2022 Aug 18. https://doi.org/10.3389/fendo.2022.839005
- 77. Lin X, Huang T. Impact of pregnancy and oestrogen on psoriasis and potential therapeutic use of selective oestrogen receptor modulators for psoriasis. J Eur Acad Dermatol Venereol. 2016;30(7):1085-1091. https://doi.org/10.1111/jdv.13661
- 78. Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of psoriasis. Annu Rev Immunol. 2014;32:227-255. https://doi.org/10.1146/annurev-immunol-032713-120225
- 79. Zhang L, Lu Q, Chang C. Epigenetics in Health and Disease. Adv Exp Med Biol. 2020;1253:3-55. https://doi.org/10.1007/978-981-15-3449-2\_1
- 80. Cignarella A, Boscaro C, Albiero M, Bolego C, Barton M. Post-Transcriptional and Epigenetic Regulation of Estrogen Signaling. J Pharmacol Exp Ther. 2023;386(3):288-297. https://doi.org/10.1124/jpet.123.001613
- 81. Olejnik-Wojciechowska J, Boboryko D, Bratborska AW, et al. The Role of Epigenetic Factors in the Pathogenesis of Psoriasis. Int J Mol Sci. 2024;25(7):3831. Published 2024 Mar 29. https://doi.org/10.3390/ijms25073831
- 82. Patel HK, Bihani T. Selective estrogen receptor modulators (SERMs) and selective estrogen receptor degraders (SERDs) in cancer treatment. Pharmacol Ther. 2018;186:1-24. https://doi.org/10.1016/j.pharmthera.2017.12.012
- 83. Tausk F, Elenkov I, Moynihan J. Psychoneuroimmunology. Dermatol Ther. 2008;21(1):22-31. https://doi.org/10.1111/j.1529-8019.2008.00166.x
- 84. Yang H, Zheng J. Influence of stress on the development of psoriasis. Clin Exp Dermatol. 2020;45(3):284-288. https://doi.org/10.1111/ced.14105
- 85. Wardhana M, Windari M, Puspasari N, Suryawati N. Role of Serotonin and Dopamine in Psoriasis: A Case-Control Study. Open Access Maced J Med Sci. 2019;7(7):1138-1142. Published 2019 Apr 14. https://doi.org/10.3889/oamjms.2019.267

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.