Last Section Update: 01/2016

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1 Overview

Summary and Quick Facts for Psoriasis

- Psoriasis is an inflammatory condition that causes patches of dry, flaking and itchy skin. The inflammation associated with psoriasis is systemic in many cases, and people with psoriasis are at increased risk of cardiovascular disease and diabetes.
- This protocol will teach you about the causes of psoriasis and what treatments are available. Learn about supplements and dietary and lifestyle changes that may help ease the inflammation that contributes to psoriasis.
- Supplementation with omega-3 fatty acids from fish oil has been shown in clinical studies to improve several aspects of psoriasis.

Psoriasis is a systemic inflammatory disorder that generally comprises excessive production of skin cells leading to patches of thick, scaly, inflamed, often itchy skin. The systemic inflammation underlying psoriasis can also manifest as psoriatic arthritis, a potentially severe arthritic joint condition. About 7.4 million US adults aged 20 or older have psoriasis.

Those with psoriasis have a markedly increased risk of developing other major inflammatory disorders, particularly:

- cardiovascular disease
- diabetes
- metabolic syndrome
- stroke

Note: This link between psoriasis and systemic health is underscored by a 5-year diminished life expectancy among those with the disease, largely attributable to increased cardiovascular disease risk. All people with moderate-to-severe psoriasis should review Life Extension's protocols on **atherosclerosis and cardiovascular disease** and **chronic inflammation**, and be screened for cardiovascular risk factors.

Integrative interventions like fish oil, vitamin D, and pycnogenol have potent anti-inflammatory properties and have been shown to alleviate symptoms of psoriasis.

Causes and Risk Factors

- Genetics is an important contributor in up to 90% of cases, with a variant gene HLA-Cw6 conferring the greatest risk
- There are also many triggers including injury, sunburn, infection, obesity, certain medications, emotional stress, alcohol, and tobacco

Signs and Symptoms

While psoriasis can appear anywhere on the skin, it most often affects the elbows, knees, scalp, lower back, and genitals. Potential signs and symptoms include:

Skin

- Raised, reddish patches covered with thick, silvery-white, shiny scales, which may be itchy
- Pinpoint bleeding spots appear when scales are scraped off (Auspitz sign)

Systemic

- Fever, dehydration, and elevated white blood cell count may occur in severe cases

Other

- Joint stiffness or pain, including inflammation or damage in psoriatic arthritis

Diagnosis

The diagnosis of psoriasis is based on a physical examination of the skin, scalp, and nails. Skin biopsy and blood testing are rarely necessary.

Conventional Treatment

- Topical (eg, corticosteroids and vitamin D analogs): first-line treatment for mild psoriasis
- Systemic medications: affect the whole body; used for more severe forms of psoriasis
- Phototherapy: light therapy for moderate-to-severe psoriasis

Novel and Emerging Strategies

- Fumaric acid esters, which have been shown to lead to complete clinical remission in up to 82.5% of participants, may also ameliorate cardiovascular risk by improving endothelial function.
- Several small molecule drugs and biologics are emerging as therapeutic options for treating psoriasis.

Dietary and Lifestyle Considerations

- A Mediterranean-style diet reduces the severity of psoriasis, with higher consumption of olive oil and fish associated with lower psoriasis severity.
- Climatotherapy and balneotherapy, the medical use of mineral water and mud baths, are shown to be beneficial in psoriasis.
- Good sleep hygiene is helpful, as nighttime melatonin levels are significantly lower in psoriasis patients.

Integrative Interventions

- **Fish oil:** Fish oil supplements given to psoriasis patients for up to six months resulted in clinical improvement in skin redness, hardening, scaling, and itching.
- **Vitamin D:** In a 2013 study, psoriasis symptoms significantly improved in patients receiving high daily doses of vitamin D3 in combination with a low-calcium diet.
- **Pycnogenol**: In a study in psoriasis patients, the addition of pycnogenol to standard treatment resulted in significant improvement in skin redness, hardening, and scaling compared with standard treatment alone.
- **White peony extract:** A 2014 study showed substantial clinical improvement, along with a significant drop in inflammatory cytokines, in 32% of patients treated exclusively with peony glucosides.
- **Whey protein:** In one study, administration of whey protein isolate resulted in clinical improvement in patients with psoriasis, regardless of whether the whey protein was given alone or in addition to topical or light therapies.

2 Introduction

Psoriasis is a ***systemic inflammatory disorder*** that generally comprises excessive production of skin cells leading to patches of thick, scaly, inflamed, often itchy skin. The systemic inflammation underlying psoriasis can also manifest as ***psoriatic arthritis*** , a potentially severe arthritic joint condition. About 7.4 million US adults aged 20 or older have psoriasis (Rachakonda 2014; Mayo Clinic 2015; Sen 2014; Parisi 2013; Schalock 2014; Bowcock 2005; Traub 2007; Kurd 2010; Pirro 2015; Elsevier BV 2015).

Psoriasis can be both physically and psychologically debilitating. Those with psoriasis have a markedly increased risk of developing other major inflammatory disorders, particularly ***atherosclerosis and cardiovascular disease***, ***obesity***, ***diabetes***, *metabolic syndrome*, and ***stroke*** (Ni 2014; McDonald 2012; Tobin 2011; Yeung 2013; Benson 2015). The emotional burden of severe psoriasis, historically termed the “heartbreak of psoriasis,” can increase the risk of psychological disorders (Parisi 2013; Schalock 2014; Kurd 2010).

The inflammatory link between psoriasis and systemic health is underscored by **reduced lifespan** among those afflicted with this disease: moderate-to-severe psoriasis patients have a 5-year diminished life expectancy. This reduced lifespan is largely attributable to increased cardiovascular disease (Ryan 2015; Ni 2014; Reich 2012; Grozdev 2014), so it is crucial that people with psoriasis also review Life Extension’s protocols on **atherosclerosis and cardiovascular disease** and **chronic inflammation**.

Conventional psoriasis therapy has considerable limitations including variable treatment response and serious side effects such as potential liver toxicity, as well as increased risk of cancer and infection due to immunosuppressive drugs (Jani 2015; Garcia-Pérez 2013; Grozdev 2014; Lee 2012; Kamangar 2012; Stern 2012; Sivamani 2010).

Fortunately, a number of *natural* compounds such as ***omega-3 fatty acids***, ***vitamin D***, ***pycnogenol,*** and ***peony extract*** may confer benefits for psoriasis patients, protect against adverse effects of some psoriasis treatments, and reduce the risk of cardiovascular and other chronic diseases often associated with psoriasis (Millsop 2014; Balbas 2011; Kamangar 2013; Gulati 2015; Wang, Zhang 2014).

A healthful eating pattern—such as the **Mediterranean diet**—can also help reduce the severity of psoriasis. ***Weight loss*** in obese patients can reduce systemic inflammation associated with psoriasis and lead to clinical

improvement. Sun exposure and topical moisturizers can help as well (Heier 2011; UMMC 2014a; Barrea 2015; Bhatia 2014; Upala 2015; Millsop 2014).

This protocol will examine the underappreciated link between psoriasis and other serious inflammatory conditions, most notably cardiovascular disease. The causes and triggers of psoriasis, its conventional treatments, and exciting new therapies will be reviewed. Dietary and lifestyle factors along with state-of-the-art natural compounds targeting both the skin manifestations and systemic inflammation of psoriasis will be discussed as well.

3 Background

Psoriasis results from a complex interaction of the immune cells, skin cells, and inflammatory messengers called cytokines, resulting in an inflammatory cascade that affects not only the skin but tissues throughout the body (Monteleone 2011; Traub 2007; Jariwala 2007; Cai 2012). The skin lesions typical of psoriasis arise when this inflammatory cascade causes skin cells to multiply too quickly. The new skin cells move to the outermost layer of skin in only a few days rather than weeks. Older skin cells cannot be shed fast enough, so they pile up on the surface as thick, silvery, flaky areas of dead skin. Redness and swelling develop as a result of increased blood flow from newly formed capillary blood vessels. This formation of new blood vessels is called *angiogenesis* and is an important contributor to psoriasis (Liew 2012; AAD 2015; NIH 2013; Das 2009).

Psoriasis Subtypes

There are several subtypes of psoriasis, and an individual can have more than one subtype.

Table 1: Subtypes of Psoriasis

Subtypes	Description
Plaque psoriasis	Most common form; red plaques covered by thick, silvery, shiny scales
Guttate psoriasis	Drop-shaped lesions on the trunk, limbs, and scalp; often triggered by streptococcal sore throat (pharyngitis)
Pustular psoriasis	Characterized by uninfected pus blisters on the palms and soles; may be prompted by medication, stress, infection, or certain chemicals
Inverse psoriasis	Smooth red lesions located in the armpits, groin, under the breasts and in other skin folds; often occurs in obese patients and aggravated by friction and sweating
Erythrodermic psoriasis	Reddening and scaling of

	skin over large area of the body; may be a reaction to severe sunburn, corticosteroid treatment, or poorly controlled psoriasis

(NIH 2013; Usatine 2013; Schalock 2014; Hall 2015; Armstrong 2014)

Psoriatic Arthritis

Up to 30% of psoriasis patients are diagnosed with an inflammatory joint disease called **psoriatic arthritis**, though many remain undiagnosed. The pathophysiology of psoriatic arthritis is complex and not completely understood. Scientists suspect that autoimmunity underlies this condition, and an autoantibody correlating with psoriatic arthritis (anti-carbamylated protein) has recently been described (Chimenti 2015). In 10–15% of psoriatic arthritis cases, joint disease develops before skin symptoms (Villani 2015; Goldman 2016; Hall 2015). Psoriatic arthritis can affect any joint in the body, and can range from mild to severe; frequent flare-ups and remissions are common (Lee 2010; NLM 2015; Girolomoni 2009; Traub 2007). A severe, destructive form of psoriatic arthritis known as arthritis mutilans afflicts a subset of patients. Large prospective studies suggest obesity is a significant risk factor for psoriatic arthritis (Love 2012; Li 2012; Elsevier BV 2015; Goldman 2016).

Psoriatic skin lesions can appear as much as two decades before the onset of arthritis. The severity of skin disease and joint inflammation are not related (Elsevier BV 2015; Hall 2015). Psoriasis of the skin and psoriatic arthritis may be different manifestations of the same underlying inflammatory disease (Hebert 2012; Traub 2007).

Psoriasis and Cardiovascular Disease

The link between psoriasis and cardiovascular disease is especially strong (Gelfand 2006; Ryan 2015; Ni 2014; Girolomoni 2009; Siegel 2013; Spah 2008). In an observational study involving more than half a million subjects, 30-year-old male patients with severe psoriasis were more than three times as likely to have a heart attack over an average of more than five years of follow-up compared with controls without psoriasis (Gelfand 2006). Cardiovascular disease also contributes to a 5-year reduction in life expectancy among individuals with moderate-to-severe psoriasis (Ryan 2015).

In one study, patients with severe plaque psoriasis were found to have significantly greater arterial stiffness compared with healthy controls (Gisondi 2009). In a separate controlled study, coronary artery calcification—another indicator of cardiovascular disease—was more prevalent in psoriasis patients (Ludwig 2007).

According to a consensus statement issued by the National Psoriasis Foundation, patients with psoriasis represent a high-risk cardiovascular disease population. Screening for cardiovascular risk factors in patients with moderate-to-severe psoriasis is strongly advised (Doukaki 2013).

4 Causes and Risk Factors

The precise cause of psoriasis is unknown. While there is a strong genetic component, psoriasis also has many environmental and lifestyle triggers including injury, sunburn, infection, obesity, certain medications, emotional stress, alcohol, and tobacco (Monteleone 2011; Traub 2007; Jariwala 2007; Cai 2012), which interact with the immune system, causing inflammation and rapid proliferation of skin cells (Siegel 2013; Armstrong 2014; NIH 2013; UMMC 2014a).

Genetics

Psoriasis is a highly heritable disorder, with genetics believed to be an important contributor in up to 90% of cases, and a markedly increased risk in those with a first- or second-degree relative with the condition. The risk of developing psoriasis is 60% in those with two affected parents (Gupta 2014; Eder 2015; Usatine 2013; Hall 2015).

While psoriasis involves multiple genes, a variant gene called HLA-Cw6 appears to confer the greatest risk. This

gene is part of a family of genes, referred to as the HLA complex, that is strongly associated with common autoimmune diseases including type 1 diabetes, celiac disease, and multiple sclerosis (Kaukinen 2002; Bahcetepe 2013; Gupta 2014; Delves 2014).

Streptococcal Infection

A streptococcal infection of the throat and tonsils often precedes guttate psoriasis, and streptococcal infections may also exacerbate other types of psoriasis (Armstrong 2014; NIH 2013; Mallbris 2009). The association between streptococcal infection and guttate psoriasis has been known for decades, and is quite strong (Telfer 1992; Leung 1995; Whyte 1964). In one study, psoriasis patients had approximately 10-fold higher frequency of strep throat than healthy controls (Gudjonsson 2003). Also, tonsillectomy has been shown to substantially reduce the severity of psoriasis (Thorleifsdottir 2012).

Table 2: Environmental and Lifestyle Risk Factors for Psoriasis

Risk Factors	Description
Injury (Koebner phenomenon)	Response to skin trauma, including surgical scars, injection sites, abrasions, sunburn, allergic reactions, or other rashes
Infection (bacterial, viral)	Streptococcal infection in the upper respiratory tract is strongly associated with guttate psoriasis and may worsen plaque psoriasis; human immunodeficiency virus (HIV); EV-HPV, a strain of human papillomavirus (HPV)
Medications	Certain drugs can trigger an outbreak or worsen the condition, including beta-blockers, ACE inhibitors, lithium, chloroquine, and indomethacin; withdrawal of systemic steroids
Weather	Cold, dry air can be a trigger; some patients improve in spring
Stress	Stressful events or chronic stress can exacerbate psoriasis and contribute to flare-ups; **stress reduction techniques** may help control the condition
Obesity	A review of studies involving nearly 135000 psoriasis patients showed a positive association between body mass index and the severity of psoriasis
Tobacco smoking	Smokers have an increased risk of psoriasis; the risk of pustular

	psoriasis is 5.3 times greater
Alcohol abuse	Excessive alcohol consumption is associated with psoriasis
Poor sleep hygiene	Sleep deprivation and shift work appear to intensify psoriatic skin inflammation and increase the risk of developing psoriasis

(Fleming 2015; Adamzik 2013; Armstrong 2014; UMMC 2014a; Schalock 2014; Gudjonsson 2003; Majewski 2002; Majewski 2003; Boyd 1999; Ferri 2015; Usatine 2013; Hirotsu 2012; Li, Qureshi 2013)

Associated Diseases

Systemic inflammation increases risk for several other diseases among psoriasis patients (Ni 2014; Ryan 2015; Siegel 2013; Padhi 2013; Dowlatshahi 2013; McDonald 2012; Tobin 2011):

- **cardiovascular disease**
- **obesity**
- **diabetes**
- **high blood pressure**
- **abnormal blood lipids**
- metabolic syndrome
- **non-alcoholic fatty liver disease**
- cancer
- **anxiety** and **depression**
- **inflammatory bowel disease**
- **elevated homocysteine**

5 Signs and Symptoms

Symptoms of psoriasis can vary from person to person depending on the type and severity. While psoriasis can appear anywhere on the skin, it most often affects the elbows, knees, scalp, lower back, and genitals. Potential signs and symptoms include (Schett 2011; Liu 2014; Thomson 1990; Usatine 2013; UMMC 2014a; AAD 2015; NIH 2013; Schalock 2014):

- Skin
  - Raised, reddish patches covered with thick, silvery-white, shiny scales
  - Reddening of skin can also be diffuse and widespread
  - Pinpoint bleeding spots appear when scales are scraped off (Auspitz sign)
  - Appearance of plaques at site of skin injury or infection (Koebner phenomenon)
  - Teardrop-shaped lesions on trunk, limbs, and scalp after viral or bacterial (usually streptococcal) infection
  - Pus-filled bumps or blisters on palms and soles
  - Skin lesions may be itchy
- Systemic

- Fever, dehydration, and elevated white blood cell count may occur in severe cases
- muscle weakness
- uveitis (inflammation of part of the eye called the uvea)

- Other
  - Nail changes – pitting, discoloration, thickening, separation from nail bed
  - Joint stiffness or pain, including inflammation or damage in psoriatic arthritis

6 Diagnosis

The diagnosis of psoriasis is based on a physical examination of the skin, scalp, and nails. Skin biopsy and blood testing are rarely necessary (UMMC 2014a; Usatine 2013).

Other skin diseases with a similar appearance are ruled out by differential diagnosis. These include eczema, dermatitis (contact, atopic, seborrheic, nummular), tinea, lichen planus, lichen simplex, pityriasis rosea, cutaneous lupus erythematosus, syphilis, drug reactions, squamous cell carcinoma in situ, and mycosis fungoides (cutaneous T-cell lymphoma) (Armstrong 2014; Usatine 2013; Schalock 2014). If psoriatic arthritis is suspected, rheumatoid arthritis and gout are screened for using laboratory tests and x-rays (Bosmansky 1983; Sankowski 2013; Busse 2010).

7 Conventional Treatment

An integrated approach to the diagnosis and treatment of psoriasis, with emphasis on comprehensive screening and aggressive treatment of associated conditions (particularly cardiovascular), is important (Ryan 2015; Ni 2014; Padhi 2013; Siegel 2013; Spah 2008). Combining various treatments—topical, phototherapy, systemic drugs—allows lower dosages of each and can improve treatment effectiveness (NIH 2013; UMMC 2014a).

The goals of treatment are to minimize psoriasis symptoms, improve the patient's quality of life, and achieve and maintain remission with minimal adverse effects (Usatine 2013; Armstrong 2014; AAD 2015).

Typically, treatment options fall into one of three categories (Armstrong 2014; Usatine 2013):

- Topical: first-line treatment for mild-to-moderate psoriasis
- Systemic medications: affect the whole body; used for more severe forms of psoriasis
- Phototherapy: light therapy for moderate-to-severe psoriasis

Topical Therapy

Topical treatments applied directly to plaques include medicated creams, ointments, and lotions. They are usually the first treatment given when psoriasis is diagnosed, and are often combined with stronger therapies (NIH 2013; UMMC 2014a). Topical therapies include:

Table 3: Topical Therapies

Topical Therapies	Description
Corticosteroids	Cornerstone of psoriasis treatment, especially for mild disease; examples are hydrocortisone and betamethasone; reduce inflammation, slow cell growth, and relieve itching; often combined with other medications, especially vitamin

	D analogs
Vitamin D analogs	Synthetic forms of vitamin D such as calcipotriene induce normal growth of skin cells; more effective for body and scalp psoriasis when combined with topical corticosteroids
Tar products (including Goeckerman regimen)	Reduces inflammation and slows cell growth; most effective when combined with UVB light; use has declined in part due to historical and disputed safety concerns about cancer, and the time and labor-intensive nature of treatment
Anthralin	Anti-inflammatory, slows cell growth; rarely used due to skin irritation and staining, but may be useful when combined with phototherapy
Tazarotene	Synthetic form of vitamin A for mild psoriasis; more effective when combined with corticosteroids or other treatments
Calcineurin inhibitors	Alternative to topical steroids for face and other sensitive regions such as the genitals because they do not cause skin atrophy, but less effective; examples are tacrolimus and pimecrolimus; may be associated with increased risk of skin cancer and lymphoma
Occlusive tapes or dressings	Some topical medications, especially corticosteroids, may be applied by means of a tape or dressing that is often left on overnight
Keratolytic agents	Examples include salicylic acid, alpha-hydroxy acids; mechanisms not completely understood, but may modulate pH of outer layer of skin (stratum corneum) and reduce keratinocyte-keratinocyte

	adhesion, helping facilitate natural cell shedding; extensive use can cause side effects as a consequence of systemic absorption (eg, ringing in the ears, headache, dizziness); should not be applied to more than 20% of body surface area; sometimes combined with topical steroids

(Dawn 2006; Pearce 2006; Usatine 2013; UMMC 2014a; NIH 2013; Schalock 2014; Ferri 2015; Roelofzen 2010; Armstrong 2014; Wang, Lin 2014; Federman 1999; Chiricozzi 2012; Pittelkow 1981; Menter 1983; Stern 1980)

Phototherapy

Phototherapy, or light therapy, is a commonly used and effective psoriasis treatment generally reserved for patients with moderate-to-severe psoriasis (Armstrong 2014). Exposing the skin to ultraviolet light helps control psoriasis by several mechanisms, including destruction of skin-infiltrating T cells, suppression of elevated inflammatory cytokines, and alteration of gene expression (Wong 2013; Furuhashi 2013). Phototherapy can be administered as ultraviolet A (UVA) light in combination with medications, or as variations of ultraviolet B (UVB) light with or without medications (Koo 2000; NIH 2013; UMMC 2014a; Luftl 1998; Schalock 2014).

The benefits of phototherapy can also be obtained naturally through controlled exposure to sunlight, which contains both UVA and UVB (Brenner 2008; Søyland 2011) (see “Dietary and Lifestyle Considerations”).

Ultraviolet B (UVB) phototherapy. There are two types of UVB phototherapies: narrowband and broadband.

- *Narrowband UVB* is the most commonly used phototherapy for psoriasis as it has the best risk-benefit ratio compared with other types of light therapy (Usatine 2013; NIH 2013).
- *Broadband UVB* has been used for psoriasis for decades. However, it is not as potent as narrowband UVB or UVA, and is not typically helpful for chronic psoriasis (NIH 2013; Kirke 2007; Usatine 2013).

Psoralens and ultraviolet A (PUVA) phototherapy. PUVA therapy is a combination treatment of a medication called psoralen and UVA radiation. Psoralens (eg, 8-methoxypsoralen, or methoxsalen) are photosensitizing agents that make the skin more sensitive to light. These agents interact with DNA and reduce DNA synthesis upon exposure to UVA, leading to reduced proliferation of skin cells (Stern 2007). PUVA therapy is effective in clearing psoriasis in more than 85% of cases. However, long-term use may increase the risk of squamous cell skin cancer and melanoma (Archier 2012). PUVA usually requires a specialty clinic or hospital, and involves treatment two to three times per week. This treatment can lead to redness, burning and blistering, particularly if dosage is not correctly controlled; it also ages skin, termed “skin photoaging” (Naldi 2009; Tahir 2004; Schalock 2014; Armstrong 2014; NIH 2013; Ferri 2015; HQO 2009).

Goeckerman Therapy

Developed in 1925, the Goeckerman regimen consists of the application of crude coal tar combined with exposure to UVB light. The coal tar makes the skin more responsive to the UVB light (Dennis 2013; Gupta 2013; IFPMA 2015). It has been demonstrated in moderate-to-severe psoriasis to be as effective as conventional psoriasis therapy with lower expense, and to improve overall quality of life and reduce emotional distress (Chern 2011).

In one study, all 300 patients treated with the Goeckerman regimen reported 90% or more clearing of psoriatic lesions (Menter 1983). In another study, a 75% improvement in the Psoriasis Assessment Severity Index (PASI) was achieved in 25 patients receiving Goeckerman therapy over a 3-month period, with 95% of patients reaching this level of improvement after just two months. This compares favorably with the 67–68% reported efficacy of new biologic response modifiers (Lee 2005; Gupta 2013).

Efficacy of Goeckerman therapy tends to manifest rapidly, while the duration of remission experienced by patients is often quite long—anywhere from 9.5 months to over a year. Patients with recurrent psoriasis often repeat the regimen at yearly or longer intervals (Gupta 2013).

The Goeckerman regimen is somewhat controversial, however, as some evidence suggests this treatment may by genotoxic (Fiala 2006) and a 1980 study showed a small increase in skin cancer risk (though the authors themselves said the benefits outweighed the risks) (Stern 1980). On the other hand, multiple more-recent clinical studies did not show an increased risk of cancer from Goeckerman treatment, even in those using crude coal tar for long periods of time (van Schooten 1996; Pittelkow 1981; Roelofzen 2010). In fact, compared to oral systemic agents such as methotrexate and biologics, Goeckerman therapy may have a favorable safety profile, and side effects are generally minimal (Gupta 2013; Roelofzen 2010; Pittelkow 1981).

The long treatment time and labor-intensive nature of the Goeckerman regimen remain impediments to its widespread adoption (de Miguel 2009).

Systemic Medications

Systemic oral or injectable drugs may be prescribed for more severe forms of psoriasis (Armstrong 2014).

Methotrexate. Methotrexate (Trexall) is a first-line systemic drug used to treat adults with severe psoriasis and psoriatic arthritis whose condition has not responded to topical treatments or phototherapy. The drug slows turnover of skin cells by inhibiting the metabolism of folate, a B vitamin necessary for normal cell metabolism, differentiation, and division (Bailey 1999; Gold Standard 2015; Higdon 2014a). It also has immunosuppressive and anti-inflammatory properties. Methotrexate can cause liver damage and decrease production of red blood cells, white blood cells, and platelets (Kozub 2011; Schalock 2014; Armstrong 2014; NIH 2013).

Retinoids. Retinoids are related chemically to vitamin A. They help regulate growth of skin cells. Retinoid drugs include acitretin (Soriatane) and isotretinoin (Accutane). Retinoids can be effective in severe adult psoriasis that does not respond to other therapies, and are sometimes combined with other treatments. Oral retinoids should not be used by women who are pregnant or may become pregnant since they may cause birth defects (Schalock 2014; Armstrong 2014; NIH 2013).

Cyclosporine. Cyclosporine rapidly suppresses the immune system and slows the growth of skin cells. It powerfully suppresses the immune system and is often used to prevent graft rejection in organ transplant recipients. Cyclosporine is generally reserved for short-term “rescue” use to bring very severe and extensive psoriasis under control; long-term use can cause significant adverse effects including kidney problems, hypertension, and non-melanoma skin cancers (Paul 2003; Armstrong 2014; Schalock 2014; NIH 2013).

Apremilast. Apremilast (Otezla) is an oral anti-inflammatory drug that is approved by the Food and Drug Administration (FDA) for plaque psoriasis and psoriatic arthritis (FDA 2014; Fala 2015). Although the exact mechanism of apremilast’s anti-psoriasis activity remains unclear, this medication inhibits an enzyme called phosphodiesterase 4. By doing so, apremilast appears to interrupt the production of numerous proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), that are elevated in psoriasis. Apremilast was the subject of two randomized controlled trials in which it was superior to placebo for the treatment of psoriasis. Its side effect profile includes depression, suicidal thoughts, fatigue, and insomnia (Zerilli 2015; Paul 2015; Papp 2015).

Biologic response modifiers . Biologic response modifiers, or biologics, are protein-based drugs. They are given by subcutaneous injection or intravenous infusion. Unlike traditional systemic drugs that suppress the entire immune system, biologics target specific parts of the immune system. Biologics are highly effective in treating moderate-to-severe psoriasis, and are FDA approved for treating plaque psoriasis. These drugs can increase risk of serious infection and cancer (NIH 2013; UMMC 2014a; NPF 2015b), but they are less toxic than traditional systemic therapies (Declercq 2013; Mansouri 2015). Examples of biologics used in the treatment of psoriasis include adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade), ustekinumab (Stelara), and secukinumab (Cosentyx) (Armstrong 2014; Schalock 2014; NPF 2015b; Usatine 2013; Sanford 2015; FDA 2015; Bagel 2012).

8 Novel and Emerging Strategies

Systemic Medications

Fumaric acid esters. Fumaric acid is a naturally occurring acid first isolated in 1832 from *Fumaria officinalis L.*, a member of the poppy family. Plants in this family have been used medicinally since ancient times (European Commission 2003). More recently, fumaric acid esters, including dimethylfumarate and salts of monoethylfumarate, have shown promise in treating dermatologic conditions, including psoriasis. In 1994, a combination of dimethylfumarate and three salts of monoethylfumarate, Fumaderm, was approved in Germany for the treatment of psoriasis (Dunn 2013). Fumaric acid esters have been described as safe and effective for the treatment of psoriasis and other dermatologic diseases, and are used off-label to treat psoriasis in many countries (Wollina 2011; Atwan 2015).

Fumaric acid esters can be taken orally and have been shown to be mostly safe, with mild side effects such as flushing and gastrointestinal disturbance (Atwan 2015). A 2014 meta-analysis (pooled analysis of published data) showed fumaric acid treatment was as effective as methotrexate for the treatment of psoriasis (Schmitt 2014). Also, a 2004 trial on 40 psoriasis patients found that fumaric acid esters, particularly dimethylfumarate, led to complete clinical remission in 82.5% of participants at 6 months (Carboni 2004).

In a retrospective study of data from 127 adolescents treated with fumaric acid esters for up to 60 months, researchers found average improvements of up to 66% on standardized psoriasis severity scales. These results were achieved by 36 months, though significant improvements were observed by 6 months (Reich 2016). A trial on 13 psoriasis patients (10 of whom completed the trial) showed that fumaric acid ester treatment for 24 weeks led to significant improvements is psoriasis severity in 80% of participants. Two of three subjects who had insulin resistance at baseline showed normal insulin responsiveness at the end of the study, and highly sensitive C-reactive protein (hs-CRP, a marker of systemic inflammation) improved by a median of 25% among participants who showed clinical psoriasis improvement. The treatment also appeared to ameliorate cardiovascular risk, as endothelial function improved by the end of the treatment period. The researchers suggested future trials investigate the potential of fumaric acid esters to improve cardiovascular outcomes in psoriasis patients (Boehncke 2011).

A 13-week randomized controlled trial on 143 psoriasis patients showed that oral fumaric acid esters plus topical calcipotriol (a vitamin D analog) outperformed fumaric acid esters alone. The combination treatment was more effective and faster acting than standalone fumaric acid esters. Because the combination regimen allowed for a slightly lower dose of fumaric acid esters, the researchers concluded that the risk-benefit ratio favored calcipotriol plus fumaric acid esters over fumaric acid esters alone (Gollnick 2002).

Small molecules. Small molecule drugs such as tofacitinib (Xeljanz) and ruxolitinib (Jakafi) are emerging as therapeutic options for treating psoriasis. Whereas biologics are delivered by subcutaneous or intravenous injection, many small molecule drugs can be administered orally or topically. Also, unlike large, protein-based biologics, these small molecule drugs are less likely to provoke immune reactions (Bagel 2014; Gooderham 2013; Morrow 2004).

- **Tofacitinib.** Tofacitinib is an immunosuppressant approved for rheumatoid arthritis. This drug blocks enzymes called Janus kinases (JAKs), which is thought to result in suppression of the pro-inflammatory action of several interleukins, including interleukin-6 (IL-6) (Migita 2014; Garcia-Pérez 2013; Levy 2012; Bagel 2014; Patel 2012; Lundquist 2014).

  In a 2015 trial, oral tofacitinib was superior to placebo and as safe and effective as etanercept, one of the most widely used injectable biologics, for the treatment of moderate-to-severe plaque psoriasis. Long-term studies are ongoing to confirm efficacy and safety (Bachelez 2015).

- **Ruxolitinib.** Ruxolitinib is a JAK inhibitor that can be administered topically. In a clinical study, application of ruxolitinib cream for 28 days significantly decreased the extent and severity of psoriasis lesions compared with placebo, with only mild side effects reported. Ruxolitinib is currently under development as a treatment for psoriasis (Gooderham 2013; Garcia-Pérez 2013; Levy 2012; Punwani 2012).

Biologics. Several new biologics are under development for the treatment of psoriasis. These agents target various inflammatory cytokines and their receptors, including IL-17 and IL-12/23 (Garcia-Pérez 2013; Patel 2012).

- **Brodalumab.** Brodalumab is a human monoclonal antibody that blocks the action of IL-17 by binding to its receptor (Bagel 2014). In one clinical trial, brodalumab demonstrated clearance of nearly two-thirds of psoriasis lesions in patients with severe psoriasis within 12 weeks. Side effects such as upper respiratory infection, low white blood cell count, and suicidality necessitate more extensive trials to confirm safety (Papp 2012; Carroll 2015; Patel 2012).
- **Ixekizumab.** Ixekizumab is a humanized monoclonal antibody that blocks the actions of IL-17. In a clinical study, the highest injectable dose of ixekizumab (150 mg) completely cleared the skin of approximately 40% of psoriasis patients by 12 weeks, with no serious adverse effects reported. Ixekizumab is currently undergoing further clinical trials (Leonardi 2012; Declercq 2013; Patel 2012; Garcia-Pérez 2013).
- **Briakinumab.** Briakinumab is a human monoclonal antibody that inhibits the actions of IL-12/23 (Patel 2012; Garcia-Pérez 2013; Gordon 2012). In a large year-long clinical trial, briakinumab was effective in the treatment of moderate-to-severe psoriasis. This study confirmed a previous trial showing that briakinumab can provide considerable relief from psoriasis. Since some adverse effects such as serious infections and skin cancers were reported, additional evaluation of the safety profile of this drug is needed (Gordon 2012; Garcia-Pérez 2013; Patel 2012).

9 Dietary and Lifestyle Considerations

Diet and Exercise

Mediterranean diet. The Mediterranean diet is a healthy eating pattern characterized by generous amounts of fruits and vegetables, whole grains, legumes, fish, seafood, and nuts. Few dairy foods and little meat and meat products are consumed. The diet is rich in extra virgin olive oil, and also includes moderate alcohol intake in the form of wine with meals (Barrea 2015).

A 2015 study found strict adherence to a Mediterranean-style diet reduces severity of psoriasis. Notably, higher consumption of extra virgin olive oil and fish were independently associated with lower psoriasis severity (Barrea 2015; Steffen 2014).

Gluten-free diet. Compared with the general population, patients with psoriasis and psoriatic arthritis have a greater frequency of concurrent autoimmune diseases, including **celiac disease**. A 2014 review concluded that a gluten-free diet may benefit psoriasis patients who have elevated celiac disease antibodies. In some cases, complete clearance of psoriatic skin was reported following a gluten-free diet (Bhatia 2014; Wu 2012; Addolorato 2003).

Weight loss. A rigorous review and analysis of the medical literature determined that weight loss by means of diet and lifestyle interventions reduces the severity of psoriasis in overweight or obese patients (Upala 2015). Several healthy weight loss strategies are described in the **Weight Loss** protocol.

Environmental Therapies

Environmental therapy comprises the utilization of environmental factors (eg, sunlight, salt and mineral baths, unique properties of certain geographic regions and climates) to modify the course of a disease. These therapies have been in use for thousands of years, including by the ancient Greeks and Romans. *Climatotherapy* and *balneotherapy* are overlapping treatment strategies shown to be beneficial in psoriasis (Riyaz 2011; Kopel 2013; Klein 2011; Roos 2010; Harari 2012).

Climatotherapy. Climatotherapy is based on the healing capacities of environmental factors associated with certain climatic locations, including air, temperature, humidity, barometric pressure, and light. Climatotherapy at the Dead Sea in particular is an effective natural treatment for psoriasis. The low altitude of the Dead Sea—the lowest human-inhabited place on earth at 419 meters below sea level—results in lower-intensity ultraviolet radiation, reducing risks associated with greater exposure duration; also, the unique spectrum of radiation in this region may be particularly beneficial for skin diseases. Bathing in the Dead Sea, which is the saltiest sea in the world and has extremely high mineral concentration, may normalize skin cell proliferation rate (Kazandjieva 2008;

Riyaz 2011; Kopel 2013).

Studies of psoriasis patients undergoing Dead Sea climatotherapy have reported impressive results: high response rate, long periods of remission, and partial to complete plaque clearance (Kazandjieva 2008). In one study, Dead Sea climatotherapy improved plaque psoriasis disease severity by 95% in up to three-quarters of subjects. Patients with early-onset psoriasis responded better than late-onset patients (Harari 2012). In another study, Dead Sea therapy resulted in significant improvement in the quality of life of patients with psoriasis and psoriatic arthritis (Kopel 2013).

Balneotherapy. Balneotherapy is the medical use of mineral water and mud baths (Riyaz 2011). In a randomized clinical trial, *synchronous balneotherapy*—artificial balneotherapy that simulates conditions at the Dead Sea—was superior to UVB phototherapy after 35 treatment sessions and six months of follow-up (Klein 2011). A review of studies found positive clinical results and long remission periods for both natural and artificial balneotherapy (Roos 2010).

Moderate sun exposure (heliotherapy). Two studies, which included a total of 30 patients with moderate-to-severe psoriasis, demonstrated that exposure to sunlight resulted in substantial clinical improvement. All patients stopped taking psoriasis medication four weeks before beginning heliotherapy. The treatment began with 45 minutes of sun exposure on both front and back of the body, with a gradual increase in exposure over the following days. The trials lasted 16 days. No sunburn occurred in these studies. A dramatic reduction of inflammatory cell numbers preceded the skin improvements, suggesting sunlight may act through immune system modulation (Heier 2011; Søyland 2011).

It is important that sun exposure be limited to a duration that does not result in sunburn. While moderate sun exposure may be beneficial in psoriasis, skin damage caused by sunburn may be detrimental (PAPAA 2015).

Moisturizers

The American Academy of Dermatology has called the use of unmedicated topical moisturizers " *an internationally accepted standard adjunctive therapeutic approach to the treatment of psoriasis*." In fact, in controlled trials of corticosteroid topical treatments, in which placebo is essentially an unmedicated moisturizer, placebo response rates of up to 47% have been found, suggesting moisturizers alone have a beneficial effect in psoriasis (Menter 2009).

Various preparations can be used as moisturizers or emollients, including creams, ointments, and oils. Patients should incorporate topical moisturizers into their routines, with application twice daily and after bathing. Using fragrance-free products and washing with moisturizing soaps is also recommended (Schalock 2014; NPF 2015a). Moisturizers promote skin rehydration by reducing water loss through evaporation (Ferri 2015).

Sleep Hygiene

Chronic sleep deprivation impairs the skin's integrity, weakens its function as a protective barrier, and exacerbates the inflammation of psoriasis (Oyetakin-White 2015; Hirotsu 2012; Kahan 2010; Axelsson 2010).

Melatonin, a hormone produced mainly by the brain's pineal gland, may play a role in the increased risk of psoriasis associated with sleep disruption. Secreted only during darkness, melatonin regulates the circadian sleep-wake cycle, promotes sleep, and modulates inflammation and immune function (NIH 2015; Li, Qureshi 2013; Esposito 2010; Radogna 2010). Studies have shown that nighttime melatonin levels are significantly lower in psoriasis patients compared with controls (Li, Qureshi 2013; Kartha 2014; Esposito 2010; Mozzanica 1988). Some researchers propose that sleep loss and circadian rhythm disruption should be considered risk factors for the development of psoriasis (Hirotsu 2012; Ando 2015).

A number of strategies for improving sleep quality are described in Life Extension's **Insomnia** protocol.

Stress Management

Emotional stress is often a consequence of dealing with psoriasis, but increasing evidence suggests stress also contributes to the development and exacerbation of psoriasis (Ni 2014; Brunoni 2014; Hall 2012; Hunter 2013). Stressful life events have been reported to precede the onset of psoriasis in 44% of patients and trigger flare-ups in 88% of psoriasis patients (Hall 2012). Research suggests the body's stress response may be impaired in psoriasis (Richards 2005). Therefore **managing stress** is an important goal for psoriasis patients. More

information is available in Life Extension's **Stress Management** protocol.

10 Nutrients

Fish Oil

A thorough review and analysis of the medical literature found that fish oil supplementation is beneficial in psoriasis. Fish oil supplements (up to 13.5 g eicosapentaenoic acid [EPA] and 9 g docosahexaenoic acid [DHA] daily) given to psoriasis patients for up to six months resulted in clinical improvement in skin redness, hardening, and scaling, and some studies found a benefit for itching (Millsop 2014).

Fish oil may also be effective as a complement to other therapies. In one study in patients with plaque psoriasis, the combination of omega-3 fatty acids and tacalcitol, a topical form of vitamin D, resulted in significantly greater improvement than tacalcitol alone (Balbas 2011).

Fish oil is well-known for its potent anti-inflammatory properties. Elevated concentrations of the pro-inflammatory omega-6 fatty acid arachidonic acid and inflammatory compound leukotriene B4, derived from arachidonic acid, have been found in the skin and red blood cell membranes of psoriasis patients. By displacing arachidonic acid in cell membranes, the omega-3 fatty acids EPA and DHA suppress inflammation by inhibiting the production of pro-inflammatory compounds such as leukotriene B_4 (Surette 2008; Millsop 2014; Balbas 2011; Wolters 2005).

Vitamin D

While topical synthetic forms of vitamin D (analogs) are used in the conventional treatment of psoriasis, multiple studies have demonstrated that the natural form of vitamin D_3 (cholecalciferol), which can be taken orally, may be a safe and effective psoriasis treatment (Kim 2010; Finamor 2013; Millsop 2014).

Oral vitamin D has the important advantage of improving vitamin D status, which results in many health benefits (Higdon 2014b). A number of studies have shown that psoriasis is associated with low serum levels of 25-hydroxyvitamin D. Vitamin D acts as an immune-modulating hormone that can reduce rapid growth of skin cells and suppress inflammation. Higher levels of vitamin D are associated with lower risk of cardiovascular disease, diabetes, and metabolic syndrome—all associated with psoriasis (Chandrashekar 2015; Soleymani 2015; Hossein-nezhad 2013; Gisondi 2012; Vitezova 2015).

In a 2013 study, psoriasis symptoms significantly improved in patients receiving high daily doses of vitamin D_3 (35000 IU) for six months in combination with a low-calcium diet and aggressive hydration. Blood chemistry parameters remained within the normal range; the authors explained that restriction of dietary calcium likely played a key role in avoiding excess calcium levels in this trial of high dose vitamin D. Nevertheless, 35 000 IU is a much higher-than-usual daily dose of vitamin D, and anyone high-dose vitamin D should test their blood levels of 25-hydroxyvitamin D regularly and adjust their dosage as necessary to avoid excessive levels.

The high doses of vitamin D used in this study may have compensated for genetic variations (polymorphisms) related to vitamin D metabolism that are common in autoimmune conditions such as psoriasis. These inherited polymorphisms induce a relative resistance to vitamin D, necessitating higher doses to achieve optimal biologic effects (Finamor 2013).

Indeed, experimental research has shown that genetic variation in activity of 1-alpha-hydroxylase, the enzyme that converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D (the active form), strongly influences serum levels of active vitamin D (Vieth 1990). In fact, specific 1-alpha-hydroxylase mutations can cause vitamin D-specific rickets (Miller 2000). In mice prone to autoimmunity, upregulation of 1-alpha-hydroxylase activity in response to immune stimuli is dysfunctional. It has been proposed that 1-alpha-hydroxylase activity upregulation in immune cells during inflammatory stimuli serves as a guard against autoimmunity (Overbergh 2000). Thus, one factor contributing to autoimmune diseases could be defective 1-alpha-hydroxylase activity; taking high doses of vitamin D may help overcome this defect by providing abundant substrate upon which the suboptimally functioning 1-alpha-hydroxylase can act (Overbergh 2000).

Pycnogenol

Pycnogenol is an extract from the bark of the French maritime pine tree. It contains a range of polyphenolic compounds including proanthocyanidins, bioflavonoids, and catechins. Pycnogenol has strong anti-inflammatory,

anticlotting, and vasodilating properties (Belcaro 2013; Gulati 2015; Belcaro 2014; Grether-Beck 2016).

In a placebo-controlled clinical trial in psoriasis patients, the addition of 50 mg of pycnogenol three times daily to standard treatment resulted in significant improvement in skin redness, hardening, and scaling compared with standard treatment alone (Belcaro 2014).

Studies have also demonstrated that pycnogenol has beneficial effects in metabolic syndrome, which occurs frequently in patients with psoriasis (Gulati 2015; Belcaro 2013; Siegel 2013; Girolomoni 2009).

Polypodium leucotomos

Polypodium leucotomos is a tropical fern native to Central and South America where it has a long history of use as an herbal medicine for the treatment of inflammatory skin diseases. *Polypodium leucotomos* extract can help protect the skin from harmful effects of ultraviolet radiation, and can decrease the phototoxicity, pigmentation, and damage of human skin induced by PUVA (psoralen combined with UVA radiation) treatment. Because it also decreases DNA damage and immunosuppression induced by UV radiation, *Polypodium leucotomos* can slow premature skin aging and reduce the risk of skin cancers (Middelkamp-Hup 2004; Palomino 2015; Choudhry 2014).

While phototherapy—particularly PUVA—is a very effective treatment for psoriasis, it carries the risk of skin cancers, including melanoma. The photoprotective effects of *Polypodium leucotomos* make it a potential adjuvant to phototherapy used for psoriasis (Stern 2001; Nettelblad 1996; Middelkamp-Hup 2004; Gonzalez 2011; Palomino 2015; Choudhry 2014).

Peony Glucosides

Peony glucosides are extracted from the root of the peony plant, and have been shown to help restore immune system balance by decreasing the production of inflammatory cytokines. The peony plant has been widely used in traditional Asian medicine to treat autoimmune diseases (He 2011; Wang, Zhang 2014).

Findings from a 2014 study demonstrate potential benefits of peony glucosides in the treatment of psoriatic arthritis. Substantial clinical improvement, along with a significant drop in inflammatory cytokines, was observed in 32% of patients treated exclusively with peony glucosides. These results merit further investigation of peony glucosides as a safe and effective therapy for psoriatic arthritis (Wang, Zhang 2014).

Curcumin

The spice turmeric has been used as an herbal remedy in traditional Chinese and Ayurvedic medicine for thousands of years. Curcumin is generally considered to be the most active constituent in turmeric. Owing to its anti-inflammatory properties as well as its ability to inhibit excessive new growth of cells and blood vessels, curcumin has promise as a potential therapy in the treatment of psoriasis (Chen 2008; McFadden 2015; Antiga 2015; Sun 2013; UMMC 2014b).

In a clinical study, a combination of oral curcumin and topical steroids was superior to topical steroids plus placebo in treating psoriasis. These results suggest curcumin can be a safe and effective adjuvant therapy in psoriasis patients treated with topical steroids (Antiga 2015).

Probiotics

The trillions of bacteria present in and on the human body, called the microbiota, have a pronounced effect on our immune system. They have a direct effect in the digestive tract and act systemically as well, affecting distant sites including the skin and joints (Eppinga 2014; Geuking 2014; Ferreira 2014).

An altered microbiota is a factor in the initiation and promotion of immune-mediated inflammatory diseases, including inflammatory bowel disease. Both psoriasis and psoriatic arthritis have been associated with inflammatory bowel disease. It has been suggested that the microbiota may play a key regulatory role in the inflammatory pathways shared by these diseases (Li, Han 2013; Eppinga 2014; Geuking 2014; Ferreira 2014). In fact, emerging evidence suggests psoriasis may not strictly involve autoimmunity, but could be the consequence of interaction between the innate immune system and some bacteria of the human microbiota (Fry 2015).

In a 2013 study, administration of a probiotic called *Bifidobacterium infantis* significantly reduced plasma levels of the inflammatory biomarkers C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-α) in psoriasis

patients (Groeger 2013).

Whey Protein

Psoriasis is marked by an increase in oxidative stress and a decrease in levels of glutathione, the body's major scavenger of reactive free radicals. Whey protein effectively increases cellular glutathione levels because it is a rich source of the amino acid precursors of glutathione, particularly cysteine and related compounds (Prussick 2013; Kloek 2011; Balbis 2009; Zavorsky 2007).

In one study, administration of whey protein isolate over three months resulted in clinical improvement in patients with psoriasis, regardless of whether the whey protein was given alone or in addition to topical or light therapies (Prussick 2013).

Resveratrol

Resveratrol is a polyphenol found primarily in grapes, red wine, Japanese knotweed, and some berries. It effectively modulates inflammation, cell proliferation, and new blood vessel formation (OSU 2015; Kjaer 2015; Borriello 2014).

Resveratrol significantly improved the severity of skin inflammation in a mouse model of psoriasis. Skin thickness, redness, and scaling were all reduced in the resveratrol-treated group compared with the control group. Resveratrol decreased the production of the inflammatory cytokines IL-17 and IL-23, both significant contributing factors in the formation of psoriatic plaque (Kjaer 2015).

Zinc

The essential mineral zinc plays an important role in maintaining a healthy immune response. Zinc modulates production of inflammatory cytokines such as IL-2 and IL-6 (Foster 2012; OSU 2015). In a study in mice with induced psoriasis, injections of zinc into the abdominal cavity mitigated oxidative stress and caused a significant decrease in elevated serum levels of inflammatory IL-2 (Yin 2013).

According to one case report, supplementation with 50 mg zinc twice daily in a 67-year-old female with pustular psoriasis completely cleared skin lesions in 15 days. Zinc's anti-inflammatory and immune-modulating effects may explain its therapeutic efficacy in this case (Verma 2012). However, 100 mg of supplemental zinc daily is a relatively high dose and may not be suitable for everyone.

Vitamin E and Selenium

Selenium, a cofactor for enzymes such as glutathione peroxidase, and vitamin E are important contributors to the body's defenses against oxidative stress (NHMRC 2006). Concentrations of both vitamin E and selenium have been reported to be lower in psoriasis patients than in healthy subjects (Pujari 2014; Serwin 2003; Kharaeva 2009; Naziroglu 2012). Oral or topical administration of vitamin E and selenium may be beneficial in the treatment and prevention of psoriasis (Naziroglu 2012; Kokcam 1999).

In a double-blind placebo-controlled clinical trial in patients with erythrodermic psoriasis (a severe form of psoriasis that usually affects much of the body surface and causes marked inflammation and skin turnover) and psoriatic arthritis, supplementation with selenium and vitamin E, together with coenzyme Q_{10}, resulted in significant clinical improvement in disease severity (Kharaeva 2009).

Supplementation with selenium (200 mcg as sodium selenite) and vitamin E (10 mg as alpha-tocopheryl succinate) was demonstrated to increase low levels of glutathione peroxidase in 50 patients with various skin disorders, including psoriasis (Juhlin 1982). In another study, a measure of glutathione activity in psoriasis patients drinking selenium-rich water was found to be 50% higher than in healthy participants consuming low-selenium water (Shani 1985).

Many vitamin E formulations consist only of alpha-tocopherol. But mounting evidence suggests that other members of the vitamin E family, especially gamma-tocopherol, may be particularly integral to vitamin E's beneficial effects (Mathur 2015).

Folate

Levels of homocysteine—an independent risk factor for cardiovascular disease and possibly Alzheimer's disease—are often elevated in patients with psoriasis (Morris 2003; McDonald 2012; Tobin 2011; Malerba 2006).

Some studies have reported that psoriasis patients have lower levels of the B vitamin folate, which is essential in the breakdown of homocysteine. In one case-control study in patients with chronic plaque psoriasis, high plasma homocysteine correlated with increased disease severity and low levels of folate (Malerba 2006). Another study found decreased blood folate levels and increased plasma homocysteine levels in psoriasis patients who underwent UVB phototherapy (Juzeniene 2010).

Melatonin

Melatonin is a neurohormone secreted by the pineal gland in the brain. It regulates the 24-hour circadian rhythm, sleep, and inflammatory and immune processes. As an oral supplement, melatonin has been shown to be helpful in various sleep disorders such as insomnia and jet lag (NIH 2015; Kartha 2014; Radogna 2010).

Nighttime levels of melatonin have been demonstrated to be significantly lower in psoriasis patients than in matched control subjects without psoriasis (Kartha 2014; Mozzanica 1988). Shift workers with disrupted sleep-wake patterns also have low nighttime melatonin levels, along with an increased risk of psoriasis (Kartha 2014; Li, Qureshi 2013; Mozzanica 1988; Patel 2007; Yosipovitch 2000).

Given its complex and critical role in regulating a wide range of physiological functions, melatonin is being actively investigated for its importance to the major inflammatory diseases associated with psoriasis, including cardiovascular disease, type 2 diabetes, metabolic syndrome, and cancer (Sharma 2015; Zamfir Chiru 2014; Goyal 2014; Bonnefont-Rousselot 2014; Navarro-Alarcon 2014; Dominguez-Rodriguez 2012; Radogna 2010; Reiter 2010).

Topical Capsaicin

Capsaicin is a pungent compound present in various hot peppers including red chili peppers, jalapeños, and habaneros. Topical creams containing capsaicin have a long history of use as pain-relieving agents (Bode 2011; Chrubasik 2010).

In a double-blind study in which capsaicin cream was applied to only one side of the bodies of psoriasis patients, a significant reduction in scaling and redness was observed on the side of capsaicin application. While nearly half of the patients reported burning, stinging, itching, and redness upon initial application, these symptoms diminished or disappeared with continued treatment. The ability of capsaicin to inhibit dilation of blood vessels in the skin may have played a role in the therapeutic benefit (Bernstein 1986).

In another study in patients with pruritic (itchy) psoriasis, topically applied capsaicin was shown to significantly reduce itching and overall disease severity (Ellis 1993; Andoh 2003; Boca 2014).

Boswellia serrata

Commonly known as frankincense, *Boswellia serrata* gum resin extracts have been used in traditional Ayurvedic medicine, and are now being investigated and used for the treatment of chronic inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. Boswellic acids, the active components of the *Boswellia serrata* resin, exert anti-inflammatory effects primarily through inhibition of the proinflammatory enzyme 5-lipoxygenase (5-LOX) (Togni 2014; Wang 2009).

Topical *Boswellia* extracts may be promising for the treatment of psoriasis. In a double-blind placebo-controlled study, a topical formulation based on boswellic acids was shown to be effective in the treatment of psoriasis. Specifically, the boswellic acid formulation improved scales in 70% of subjects and skin reddening in 60% of subjects. None of the participants experienced an exacerbation of their condition (Togni 2014).

Previously, in a mouse model of psoriasis, a boswellic acid (3-O-acetyl-11-keto-beta-boswellic acid, or AKBA) injected systemically or under the skin, inhibited nuclear factor-kappa B (NF-κB)—a signaling molecule implicated in exacerbating psoriasis. This resulted in markedly decreased production of inflammatory cytokines such as TNF-α, along with a profound improvement in psoriasis-like skin inflammation (Wang 2009).

Update History

This information (and any accompanying material) is not intended to replace the attention or advice of a physician or other qualified health care professional. Anyone who wishes to embark on any dietary, drug, exercise, or other lifestyle change intended to prevent or treat a specific disease or condition should first consult with and seek clearance from a physician or other qualified health care professional. Pregnant women in particular should seek the advice of a physician before using any protocol listed on this website. The protocols described on this website are for adults only, unless otherwise specified. Product labels may contain important safety information and the most recent product information provided by the product manufacturers should be carefully reviewed prior to use to verify the dose, administration, and contraindications. National, state, and local laws may vary regarding the use and application of many of the therapies discussed. The reader assumes the risk of any injuries. The authors and publishers, their affiliates and assigns are not liable for any injury and/or damage to persons arising from this protocol and expressly disclaim responsibility for any adverse effects resulting from the use of the information contained herein.

The protocols raise many issues that are subject to change as new data emerge. None of our suggested protocol regimens can guarantee health benefits. Life Extension has not performed independent verification of the data contained in the referenced materials, and expressly disclaims responsibility for any error in the literature.

References

†Ratings based on results of the 2026 ConsumerLab.com Survey of Supplement Users. Omega-3 EPA/DHA ratings based on results of the 2025 ConsumerLab.com Survey of Supplement Users. Multivitamin rating based on results of the 2024 ConsumerLab.com Survey of Supplement Users. For more information, visit **www.consumerlab.com/survey**.

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