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Psoriasis: A comprehensive review

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Abstract

Psoriasis is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyperproliferation affecting 2-3 % of world's population. Pathophysiology of the disease includes mainly the activation and migration of T cells to the dermis triggering the release of cytokines (tumor necrosis factor-alpha TNF-alpha, in particular) which lead to the inflammation and the rapid production of skin cells. The possible factors and triggers causing psoriasis include emotional stress, skin injury, systemic infections, certain medications and intestinal upsets. Various types of psoriasis have been reported such as plaque psoriasis, psoriatic arthritis, scalp psoriasis, flexural psoriasis, guttate psoriasis, pustular psoriasis, nail psoriasis, erythrodermic psoriasis which can be diagnosed by clinical findings such as skin biopsies etc. Therapeutic agents that either modulate the immune system or normalize the differentiation program of psoriatic keratinocytes are suggested for treating psoriasis. Based on the type of psoriasis, its location, extent and severity there are various treatment regimens available for psoriasis such as topical agents, phototherapy, systemic agents, and homeopathic approach which can help to control the symptoms. This review aims to cover each and every aspect of the disorder Psoriasis and details of particularly plaque psoriasis as about 80% of people who develop psoriasis have plaque psoriasis.

Key-Words: Psoriasis, Plaque psoriasis, Psoriatic arthritis, Phototherapy, Topical steroids.

Introduction

Psoriasis is regarded as an autoimmune disease in which genetic and environmental factors have a significant role. The name of the disease is derived from Greek word 'psora' which means 'itch'. Psoriasis is a non-contagious, dry, inflammatory and ugly skin disorder, which can involve entire system of person[1]. It is mostly inherited and mainly characterized by sharply marginated scaly, erythematous plaques that develop in a relatively symmetrical distribution. The most commonly affected sites are the scalp, tips of fingers and toes, palms, soles, umbilicus, gluteus, under the breasts and genitals, elbows, knees, shins and sacrum[2]. This disease is chronic in nature with a tendency to relapse. In this disease, the skin keeps scaling as flakes called psoriatic plaques due to rapid and excessive multiplication of epidermis cells which look like fishy skin & finally peels off as exfoliation.

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The silvery-white plaques are caused by accelerated regeneration and accumulation of skin on sites of predilection due to rapid destruction process. Plaques may range in size from a few millimetres to a large part of the trunk or limb. Plaques frequently appear on skin of the elbows and knees, but can affect any area including the scalp and genitals. Fingernails and toenails are frequently affected (psoriaticnail dystrophy) and can be seen as an isolated finding[3]. Psoriasis can also cause inflammation of the joints, which is known as psoriatic arthritis. Psoriasis is linked to dandruff and unfortunately to some forms of arthritis. It is also believed that there is also a link between psoriasis and the HIV virus. Psoriasis is one of the most maltreated diseases from olden days, which continues now with the search of a good remedy[4]. This review is a compilation of all the aspects regarding psoriasis.

Epidemiology

Psoriasis affects both sexes equally and can occur at any age, although it most commonly appears for the first time between the ages of 15 and 25 years. The

prevalence of psoriasis in western populations is estimated to be around 2-3%. The prevalence of psoriasis among 7.5 million patients who were registered with a general practitioner in the United Kingdom was 1.5%[5]. A survey conducted by the national psoriasis found a prevalence of 2.1% among adult Americans. The study found that 25% of people with psoriasis could be classified as having moderate to severe psoriasis[6]. Around one-third of people with psoriasis report a family history of the disease, and researchers have identified genetic loci associated with the condition[7]. Studies of monozygotic twins suggest a 70% chance of a twin developing psoriasis if the other twin has psoriasis. The concordance is around 20% for dizygotic twins. These findings suggest both a genetic predisposition and an environmental response in developing psoriasis. Onset before age 4 usually indicates a greater genetic susceptibility and a more severe or recurrent course of psoriasis[8]. Psoriasis does not spread from one person to another by contact but can be transmitted genetically [25%][9]. Psoriasis occurs most commonly in the third decade of life. It has higher incidence in females than males. Children are rarely affected. Whites suffer more than blacks. Nearly 30% of psoriasis patients have arthritis problems. The onset of the disease occurs most commonly at about the age of 20 years. 10 to 15 % of people have psoriatic arthritis. In the United States, about 7 million people (2%-3% of people) have psoriasis. About 150,000-260,000 new cases are diagnosed each year[10]. Most people who have psoriasis of the nails also have skin psoriasis (cutaneous psoriasis). Only 5% of people with psoriasis of the nails do not have skin psoriasis. In people who have skin psoriasis, 10%-55% have psoriasis of the nails (also called psoriatic nail disease). About 10%-20% of people who have skin psoriasis also have psoriatic arthritis, a specific condition in which people have symptoms of both arthritis and psoriasis. Of people with psoriatic arthritis, 53%-86% have affected nails, often with pitting. Psoriasis tends to run in families[11]. If you have a parent or a sibling who has psoriasis, you have a 16%-25% chance of having psoriasis, too. If both of your parents have psoriasis, your risk is 75%. Males and females are equally likely to have psoriasis. Psoriasis can occur in people of all races[12].

Causes

The cause of psoriasis is not fully understood, but it is generally believed to have a genetic component. Also in psoriasis, factors in the immune systems and other biochemical substances that normally regulate orderly proliferation and maturation of epidermal cells are impaired. These cause inflammation and increased proliferation of skin cells leading to the characteristic clinical features of scaling and redness[13]. Several factors are thought to aggravate psoriasis. These include stress, excessive alcohol consumption, and smoking. Individuals with psoriasis may suffer from depression and loss self-esteem. As such, quality of life is an important factor in evaluating the severity of the disease. Certain medicines, including lithium salt and beta blockers, have been reported to trigger or aggravate the disease. Excessive alcohol consumption, smoking and obesity may exacerbate psoriasis or make the management of the condition difficult. Individuals suffering from the advanced effects of the human immunodeficiency virus, or HIV, often exhibit psoriasis[14]. Psoriasis is a fairly idiosyncratic disease. The majority of people's experience of psoriasis is one in which it may worsen or improve for no apparent reason. Studies of the factors associated with psoriasis tend to be based on small (usually hospital based) samples of individuals. These studies tend to suffer from representative issues, and an inability to tease out causal associations in the face of other (possibly unknown) intervening factors. Conflicting findings are often reported. Nevertheless, the first outbreak is sometimes reported following stress (physical and mental), skin injury, and streptococcal infection[15]. Conditions that have been reported as accompanying a worsening of the disease include infections, stress, and changes in season and climate. Researches show that whether a person develops psoriasis or not may depend on a 'trigger'. Possible psoriasis triggers include emotional stress, skin injury, systemic infections, certain medications and intestinal upsets. Studies have also indicated that a person is born genetically predisposed to psoriasis and multiple genes have been discovered[16]. According to Ayurveda when all these factors combine with change in life style, constipation, indigestion, stress that leads to psoriasis[17]. Stress, skin injuries, a streptococcal infection, certain medications and sunburn are some of the known potential triggers[15]. Medications that can trigger psoriasis are anti-malarial drugs, beta-blockers and lithium[18]. Dermatologists have seen psoriasis suddenly appear after a person takes one of these medications, gets a streptococcal infection, or experiences another triggers. Sometimes food can also trigger the disease process. For e.g. citrus fruits, sour foods, sauces, coffee, tea, alcohol and soft drinks[19].

Pathophysiology

Psoriasis is immune mediated condition which is caused by faulty signals in the body's immune system. It is believed that psoriasis develops when the immune system tells the body to over-react and accelerate the

growth of skin cells. Normally the skin cells mature and are shed from the skin's surface every 28 to 30 days[20]. When psoriasis develops, the skin cells mature in 3 to 6 days and move to skin surface. Instead of being shed, the skin cells pile up, causing the visible lesions. It is also found that genes that cause psoriasis can determine how a person's immune system reacts. These genes can cause psoriasis or other immune-mediated conditions such as rheumatoid arthritis or Type-I Diabetes[21].

The pathophysiology of psoriasis must be understood in terms of the prominent pathologies occuring in both major components of the skin the epidermis and the dermis. There are two main hypotheses about the process that occurs in the development of the disease. The first considers psoriasis as primarily a disorder of excessive growth and reproduction of skin cells. The problem is simply seen as a fault of the epidermis and its keratinocytes. The second hypothesis sees the disease as being an immune-mediated disorder in which the excessive reproduction of skin cells is secondary to factors produced by the immune system[22,23]. Current research suggests that the inflammatory mechanisms are immune based and most likely initiated and maintained primarily by T cells in the dermis[24]. Antigen-presenting cells in the skin, such as Langerhans cells, are believed to migrate from the skin to regional lymph nodes, where they interact with T cells. Presentation of an as yet unidentified antigen to the T cells, as well as a number of co-stimulatory signals, triggers an immune response, leading to T cell activation and the release of cytokines. Co-stimulatory signals are initiated via the interaction of adhesion molecules on the antigen-presenting cells, such as lymphocyte function-associated antigen (LFA)-3 and intercellular adhesion molecule, with their respective receptors CD2 and LFA-1 on T cells. These T cells are released into the circulation and traffic back into the skin. Reactivation of T cells in the dermis and epidermis and the local effects of cytokines such as tumor necrosis factor lead to the inflammation, cell mediated immune responses, and epidermal hyperproliferation observed in persons with psoriasis. The immune-mediated model of psoriasis has been supported by the observation that immunosuppresant medications can clear psoriasis plaques. However, the role of the immune system is not fully understood, and it has recently reported that an animal model of psoriasis can be triggered in mice lacking T cells. This presents a paradox to researchers as traditional therapies that reduce T-cell counts generally cause psoriasis to improve[25,26]. Yet, as CD4-T-cell counts decrease with the progression of HIV, psoriasis worsens. In addition, HIV is typically characterized by a strong Th2 cytokine profile, whereas psoriasis vulgaris is characterized by strong Th1 secretion pattern. It is also hypothesized that the diminished CD4-T-cell presence causes an over-activation of CD8-T-cells, which are responsible for the exacerbation of psoriasis in HIV positive patients[27].

Diagnosis

The diagnosis of psoriasis is usually based on the appearance of the skin. There are no special blood tests or diagnostic procedures for psoriasis. Sometimes a skin biopsy, or scraping may be needed to rule out other disorders and to confirm the diagnosis. Skin from a biopsy will show clubbed Rete pegs if positive for psoriasis. Another sign of psoriasis is that when the plaques are scraped, one can see pinpoint bleeding from the skin below. Diagnosis of psoriasis is made easily by clinical examination. Usually no tests are required to diagnose psoriasis, but to rule out other complications blood tests, urine test and imaging studies are often performed. Sometimes biopsy may be necessary to differentiate it from fungal infection. Blood tests are done for total count, ESSR, RA factor, ASO titre, serum uric acid level, T-cells etc. leucocytosis and increased T-cells lymphocytes are often noted. The microscopic examination of the discharges or blister fluid shows only lymphocytes infiltration. Imaging studies like X-ray or bone scan can help in diagnosing the case with joint pain[28].

One should look into the history of ingestion of drug application of streptococcal infection. It is necessary to give special attention and avoidance of irritant agents. One should asses the degree of metabolic derangement by appropriate tests in the erythrodermic disease. Assessment of the degree and extent of joint damage by radiography when appropriate is necessary. Increased nucleic acid turnover due to prolific epidermal cell division may lead to increased blood uric acid level thus is asymptomatic and rarely merits attention. Assessment of the degree of social and emotional disability caused by the disfigurement is needed. Some patients may also require treatment for psychological upsets[29].

Severity

Psoriasis is usually greded as mild (affecting less than 3% of the body), moderate (affecting 3-10% of the body) or severe. Several scales exist for measuring the severity of psoriasis. The degree of severity is generally based on the following factors: the proportion of body surface area affected; disease activity (degree of plaque redness, thickness and scaling); response o previous therapies; and the impact of the disease on the person[5].

Prognosis

Psoriasis is a lifelong condition. There is currently no cure but various treatments can help to control the symptoms. Many of the most effective agents used to treat severe psoriasis carry an increased risk of significant morbidity including skin cancers, lymphoma and liver disease. However, the majority of people's experience of psoriasis is that of minor localized patches, particularly on the elbows and knees, which can be treated with topical medication. Psoriasis does get worse over time but it is not possible to predict who will go on to develop extensive psoriasis or those in whom the disease may appear to vanish. Individuals will often experience flares and remissions throughout their lives. Controlling the signs and symptoms typically requires lifelong therapy[30].

According to one study, psoriasis is linked to 2.5 fold increased risk for non-melanoma skin cancer in men and women, with no preponderence of any specific histologic subtype of cancer. This however could be linked to antisporiatic treatment[31].

Treatment

Treatment can be topical (emollients, dithranol, tar, deltanoids, corticoids, tacrolimus), systemic (methotrexate, cyclosporin, acitrecin, hydroxyurea, fumarates) or with ultraviolet light. Phototherapy and systemic agents should be used only when topical treatments are inadequate. Novel systemic treatments for psoriasis include a rapidly expanding range of biological therapies. These are proteins (usually antibodies) with highly specific actions. Severe forms of psoriasis such as erythrodermic and generalized pustular psoriasis can be life-threatening and may require urgent treatment in hospital[32,33].

There can be substantial variation between individuals in the effectiveness of specific psoriasis treatments. Because of this, dermatologists often use a trial-and-error approach for finding the most appropriate treatment for their patient. The decision to employ a particular treatment is based on the type of psoriasis, its location, extent and severity. The patient's age, sex, quality of life, comorbidities, and attitude toward risks associated with the treatment are also taken into consideration[34,35]. Medications with the least potential adverse reactions are preferentially employed. If the treatment goal is not achieved then therapies with greater potential toxicity may be used. Medications with significant toxicity are reserved for severe unresponsive psoriasis. This is called as psoriasis treatment ladder. As a first step, medicated ointments or creams, called topical treatments, are applied to the skin. If topical treatment fails to achieve the desired goal then the next step would be to expose the skin to ultraviolet (UV) radiation. This type of treatment is called phototherapy. The third step involves the use of medications which are taken internally by pill or injection. This approach is called systemic treatment[36-39].

Diet

The first step is reducing the severity of your psoriasis is "Drink lots of water." Drink at least 2 liters a day. The second step is to "Improve your diet" and eat lots of green leafy vegetables. This will not cure your psoriasis, but it may dramatically reduce it. The following foods are popular triggers; Coke-a-cola, red meat, MSG, chili, hot spices, junk foods, oily foods, berries (such as strawberries) tomato, most acidic food and Vita-C so their consumption needs to be controlled. People with poor diets will likely have much worse psoriasis[40,41].

It has been proved that a good diet (less of food mentioned above) lots of water and lots of vegetables, a good multi vitamin tablet and also zinc tablets daily can help to reduce psoriasis, it is not a recognized treatment, nor a cure. Any results from a diet are probably due to increased general health and the removal of unhealthy foods. Acidic foods in particular have been proven to worsen psoriasis, so simply eliminating these from your existing diet will improve your psoriasis as much as any 'wonder diet' could[42,43].

Ingestion of alcohol has been reported to be a risk factor for psoriasis in men but not in women. It would be prudent for men with psoriasis to restrict their intake of alcohol or avoid it entirely.

Suggestion is given that people with psoriasis may improve on a hypoallergenic diet. It have been reported that eliminating gluten (found in wheat, rye and barley) improved psoriasis for some people. So that a doctor can help people with psoriasis determine whether gluten or other foods are contributing to their skin condition[44-46]. Fumaric acids, fish oil, triglycerides, folic acid, flaxseed oil, Vita-D are found to be effective against psoriasis. Thus eating well will better prepare your body to respond to any recurring medical condition e.g. if you are taking methotrexate, be sure to get enough folate, an important Vita-B[47-49]. **(Resources healthnotes NEWSWIRE – a weekly news service)** Guidelines of care for Psoriasis Andrew IB, Richard AB ; Lebwhol M

Topical Agents:

Topical treatments are usually the first to be tried when fighting psoriasis. They involve applying lotions or moisturizers to the skin that can help to reduce the accelerated production of skin cells and reduce inflammation. There are vast ranges of topical treatments available. Varieties of externally applied

preparations used are petroleum jelly, liquid paraffin, tar, ointment, psoralen (photosensitive drug), salicylic acid, steroid ointment, & creams etc to care for skin dryness and infection[50,51].

- **Topical steroids:** These are principal topical agents used for psoriasis and are very effective in clearing mild to moderate disease. They may be used as single agents or in combination with other agents in moderate to serious disease. They at by their antimitotic, immunosuppressant and anti-inflammatory effects. Therapy is usually started with a potent steroid (clobetasol propionate or belathasone dipropionate) applied once or twice daily. On improvement, maintenance therapy may be done with application on weekends or substitution with mid-potency low-potency steroids. Application under occlusion with plastic sheets or intra-lesional may rapidly clear lesions. Low or mid potency steroids are used for lesions on face, neck, flexures and genitalia in preference to tar, salicylic acid and anthralin which may act as irritants. Prolonged topical steroids use can cause skin atrophy, hair growth and hypo pigmentation[37].
- **Coal tar:** The benefits of coal tar have been known for many years. It has declined however with the availability of other topical agents. Coal tar is used in many forms of treatment and can be purchased in crude or refined form for treating all levels of psoriasis. Coal tar (crude) contain thousands of chemicals, hence standardization is impossible. Some of the components have anti-mitotic properties. They may also inhibit enzymes that contribute the pathogenesis of psoriasis. Coal tar is often combined with ultraviolet B phototheraphy. Coal tar solution in a concentration of 2-10% in various vehicles is used. Coal tar produces are such as lotions, bath additives, soap blocks and moisturizers. Drawbacks include its strong smell, irritation, staining of clothes and potential for causing photosensitivity. Coal tar only treats the inflammation, not the cause, and will do nothing to prevent your psoriasis occurring. Coal tar should relieve the itchiness, swelling and some flaking, but it only offers temporary relief. The FDA says a coal tar solution of between 1-5% has been proven as a safe product[52,53].
- **Salicylic acid:** It helps to remove scales and crusts (keratolytic). In a concentration of 2-10%, it is usually combined with coal tar, steroids and dithranol[54].
- **Dithranol:** It is an effective agent for treating thick plaques of psoriasis. It is a derivative of a traditional medicine chrysarobin and has been in use for a century. Dithranol causes skin irritation and brownish discoloration of skin. It is best used as 'short contact therapy' to avoid these side effects. In a concentration of 0.1-1%, it is applied once a day and washed off thoroughly after a contact period of 10 minutes to one hour. It may stain clothing[52].
- **Topical vitamin D3 analogs:** Calcipotriol, a synthetic Vita-D3 analog, is both safe and effective. It blocks epidermal proliferation, enhances maturity of cells, and has anti-inflammatory effects. It is no more effective than the moderately potent topical steroids, but combination of calcipotriol with topical steroids is more effective than either agent alone. Combination with phototherapy or oral agents is used. Unlike topical steroids, skin atrophy or tolerance is not problem, but irritation may occur on application particularly on areas like face. Calcipotriol is very expensive. Vita-D helps to regulate calcium and phosphorus in the body and can also be produced by the skin when exposed to UVB light[55,56].
- **Tazarotene:** Tazarotene is a synthetic retinoid with properties similar to that of Vita-A. Tazarotene is available as a gel. In the treatment of psoriasis, it may be used as a single agent or in combination with a corticosteriod cream or ointment, calcipotriol or phototherapy. Irritation is common with tazarotene, which can be minimized by applying a thin layer of medication only to the patches and avoiding the uninvolved surrounding skin. It should not be used on the genitals or in the skin folds. It is contraindicated in pregnancy[57].
- **Tacrolimus:** It is immunosuppressant that is very useful in the management of atopic dermatis, can also benefit psoriasis. It may be beneficial over sensitive areas like the face where topical steroid application may have troublesome side effects[54].

Bath solutions and moisturizers help soothe affected skin and reduce the dryness which accompanies the build-up of skin on psoriatic plaques. Medicated

creams and ointments applied directly to psoriatic plaques can help reduce inflammation, remove built-up scale, reduce skin turn over, and clear affected skin of plaques. Ointment and creams containing coal tar, dithranol (anthralin), corticosteroids like desoximetasone (Topicort), vitamin D3 analogues (for example, calcipotriol), and retinoids are routinely used. The mechanism of action of each is probably different but they all help to normalise skin cell production and reduce inflammation. Activated vitamin D and its analogues are effective inhibitors of skin cell proliferation. The disadvantage of topical agents are variably that they can often irritate normal skin, can be time consuming and awkward to apply, cannot be used for long periods, can stain clothing or have strong odour. As a result, it is sometimes difficult for people to maintain the regular application of these medications. Abrupt withdrawl of some topical agents, particularly corticosteroids, can cause an aggressive recurrence of the condition. This is known as a rebound of the condition. Topical agents are available as creams, ointments, lotions, gels and shampoos. These agents are useful for mild to moderate psoriasis of limited involvement[37,51,52].

Phototherapy

It has long been recognized that daily, short, non-burning exposure to sunlight helped to clear or improve psoriasis. Niels Finsen was the first physician to investigate the therapeutic effects of sunlight scientifically and to use sunlight in clinical practice. This became known as phototherapy. Sunlight contains many different wavelengths of light. It was during the early part of the 20th century that it was recognized that for psoriasis the therapeutic property of sunlight was due to the wavelengths classified as ultraviolet (UV) light[58].

Phototherapy involves exposure to ultraviolet radiations by means of special equipment using fluorescent light source emitting specific wavelength of radiation. Natural sunlight may be used as a source of UV, but exposure becomes imprecise. UV acts by reducing cellular proliferation and modifying the immune response. Psoriasis responds to ultraviolet rays. Regular exposure to sun or artificial UV lights can cause the symptoms to subside. Approaches include UVB i.e. exposure to ultraviolet B light and PUVA i.e. exposure to UV rays combined with the drug psoralen, which increases the light sensitivity of skin. New techniques include lasers, which can focus the beneficial effects of light especially on psoriatic lesions. UV phototherapy is the simplest and easiest treatment with the best general results for clearing psoriasis[59].

- **UVB therapy:** Ultraviolet B is widely used as broadband therapy (290-320nm). Now-a-days narrow band UVB (310-312nm) has become more popular either as a sole agent or in combination with topical calcipotriol or tazarotene, or systemic agents like acetretin or methotrexate. Narrow band UVB therapy is a relatively safe and effective therapy for moderate to severe psoriasis. **(Bulletin)** UVB treatment initially takes place with a doctor, but UVB units are also available for use in the home. UVB works by stimulating a chemical reaction in the skin cells to stop them reproducing so quickly.[47]
- **PUVA therapy:** Ultraviolet A (320-400nm) is used in combination with a photosensitizing agent. A psoralen compound (usually 8-methoxy psoralen i.e., 8MOP) is taken orally followed by exposure to UVA (PUVA therapy = Psoralen + UVA). The usual dose is 0.6mg/kg taken two hours before exposure. Exposure time is gradually increased till adequate response is obtained. Two or three treatments are given per week. Protective sunglasses should be worn during exposure and for the remainder of the day. After significant clearance of the lesions, frequency of administration is reduced and maintenance treatments continued for a variable period. Precisely how PUVA works is not known. The mechanism of action probably involves activation of psoralen by UVA light which inhibits the abnormally rapid production of the cells in psoriatic skin. There are multiple mechanisms of action associated with PUVA, including effects on the skin immune system. PUVA is associated with nausea, headache, fatigue, burning, and itching. Long-term treatment is associated with squamous-cell and melanoma skin cancers. PUVA therapy should be avoided in children, pregnancy, lactation and patients with hepatic, renal and severe cardiovascular disease. Cataract formation and diseases aggravated by ultraviolet radiation are other contraindication. Side effects include erythema, sunburn and cutaneous pigmentation. Nausea and headache is frequently complained off[49,50].

Systemic treatment

Psoriasis which is resistant to topical treatment and phototherapy is treated by medications that are taken internally by pill or injection. This is called systemic treatment. Patients undergoing systemic tratment are

required to have regular blood and liver function tests because of the toxicity of the medication. Pregnancy must be avoided for the majority of these treatments. Most people experience a recurrence of psoriasis after systemic treatment is discontinued. The three main traditional systemic treatments are methotrexate, cyclosporine and retinoids[54]. Methotrexate and cyclosporine are immunosuppressant drugs; retinoids are synthetic forms of vitamin A. other additional drugs, not specifically licensed for psoriasis, have been found effective. These include the antimetabolite tioguanine, the cytotoxic agent hydroxyurea, sulfasalazine, the immunosuppresants mycophenolate mofetil, azathioprine and tacrolimus. These have all been used effectively to treat psoriasis when other treatments have failed. Although not licensed in many countries fumaric acid esters have also been used to treat severe psoriasis in germany for over 20 years[49]. Various oral and injectable drugs are used in severe disease not responding to topical agents. Generally, these drugs have potential for serious adverse effects. Oral medications such as methotrexate and cyclosporine may help. Systematic therapy as a variety of oral or injectable medications is used in severe recalcitrant psoriasis in adults. Some of them may be combined for better efficacy. All these agents are potent medicines with potential for serious toxicities. They should be used in only extreme situations in childhood psoriasis. Many of these drugs have potentially severe side effects. You will need to be monitored closely when using them[47].

- **Methotrexate:** This anti-metabolite is a very popular and effective agent for treating severe psoriasis. It is usually given in a weekly or occasionally fortnightly pulse of 15mg. Equivalent dosage may also be used by intra-muscular or intravenous route. Methotrexate is effective in psoriatic arthropathy also. A low dose of maintenance therapy may be continued for sometime before withdrawal of the drug. Methotrexate schedule, the drug is remarkably well tolerated. Common side effects include anorexia, nausea and epigastric pain[60-63].
- **Oral retinoids:** These are synthetic compounds having Vita-A like cellular activities. A number of retinoids are available for treatment of severe forms of acne or other disorders of keratinization. Among them, acetretin is useful in the management of psoriasis. Oral retinoids act by their anti-inflammatory actions as well as by regulation and maturation. Acetretin is most effective when combined with topical agents or phototherapy in the generalized pustular and erythrodermic varieties of psoriasis. All retinoids have potentially serious toxicities. The most important is the risk of birth defects. So pregnant women or women who intend to become pregnant should never receive oral retinoids. Strict contraceptive methods should be done. Skin and mucous membrane side effects are common in the form of dryness of skin, nose, eyes, chapped lips and peeling of palmoplanter skin. Regular monitoring of lipid profile is needed[57].
- **Cyclosporine:** It is a cyclic polypeptide widely used as an immunosuppressant in organ transplantation. It acts in psoriasis through its inhibitory effects on T-cells. Cyclosporine should be reserved for patients with severe psoriasis. The usual oral dose is 3-5mg/kg in two divided doses. Major side effects are nephrotoxocity and hypertension. It may increase the risk of malignancies. It is contraindicated in renal dysfunction, hypertension, past or present malignancies, pregnancy, lactation and concomitant therapy with immunosuppressive or nephrotoxic drugs, this agent, like oral retinoids should be administered by dermatologists having experience in its use[64].

Herbal medicines

Traditional medicines hold a great promice as source of easily available effective therapy for skin diseases to the people, particularly in tropical developing counties, including India. It is in this context that the people use several plant derived preparations to cure skin diseases. Herbal remedies for psoriasis are increasingly popular and mainstream[65].

- **Milk thistle:** Milk thistle is believed to help prevent psoriasis outbreaks by encouraging proper liver function. The liver neutralizes certain toxins associated with psoriasis. Antibiotics are not indicated in routine treatment of psoriasis. However, antibiotics may be employed when an infection, such as that caused by the bacteria Streptococcus, triggers an outbreak of psoriasis, as in certain cases of guttate psoriasis. Milk thistle has been shown to inhibit human T-cell activation, which occurs in psoriasis; however, no specific studies have been done with psoriasis patients. Milk thistle products can be purchased at health food stores in tablet or fluid extract form. The herb should not be

taken when a person is also taking antipsychotics or male hormones. Few adverse effects have been seen when patients take milk thistle supplements, except for brief gastrointestinal disturbances and mild allergic reactions[66].

- **Oregano oil:** Oregano is a commonly used spice for baking and cooking. It possesses antibacterial and antifungal properties, which may be helpful with some infections associated with psoriasis. Oregano oil can be purchased at most health food stores. Many people have contacted the Psoriasis Foundation to let them know that use of oregano oil, either orally or topically, has helped their psoriasis. Oregano oil has been known to cause allergic contact dermatitis when applied to the skin[65].
- **Turmeric:** Turmeric is a primary component of curry powders used in cooking. The spice has a long history of being used in traditional Chinese medicine. Turmeric can be found in capsules to be used as a dietary supplement; however, many people who call the Foundation use the powdered form of the spice and mix it in with their food. Turmeric has also been reported to help relieve the swelling, pain and inflammation associated with arthritis[66].
- **Aloe vera:** *Aloe vera* is a stemless, perennial, droughtresisting, succulent plant and has reportedly been used since ancient times for medicinal purposes). It belongs to the lily (Liliaceae) family, and has stiff grey to bright green lance-shaped leaves containing clear gel in a central mucilaginous pulp. Recent research has shown that the pharmacologically active agent is concentrated in both the gel and the rind of the *Aloe vera* leaf. The active agents have shown considerable analgesic, antipruritic, wound healing and anti-inflammatory properties, thus justifying consideration of *Aloe vera* as an effective remedy for the treatment of psoriasis[68,69].

Herbs for External Use in the Treatment of Psoriasis

- **Aloe vera:** Applied in gel form to reduces inflammation
- **Cayenne (capsaicin) cream:** Applied repeatedly to relieves pain.
- **Chamomile:** It is soothing and anti-inflammatory herb applied as a cream
- **Lavender:** It is analgesic and anti-inflammatory oil mixed with olive oil and applied liberally to the affected areas.
- **Licorice root:** Applied as a cream or extract. It is soothing and may potentiate effects of topical corticosteroids.
- **Yarrow:** Two ounces of the herb added to one quart boiling water, allowed to simmer 10 – 15 minutes, and added to bath water. It is astringent and soothing.
- **Oatmeal:** Placed in a cheesecloth bag and dipped in bathwater to relieve itching.
- **Almond oil:** Applied after using other herbs for soothing and pleasantly aromatic effect.

Herbs to Take Internally for Psoriasis

- **Berberine (barberry, Oregon grape, goldenseal):** Use capsules, teas, or tinctures. Antioxidant, anti-inflammatory, and reputedly prevents toxin formation in the bowel.
- **Dong quai:** Capsules taken at the beginning of an outbreak will reduce inflammation.
- **Milk thistle:** Taken as a tea, tincture, or capsules. Anti-inflammatory; supports liver metabolism.
- **Psoralea, bishop's weed, or Angelica:** Taken as capsules, tincture, or tea. Contain psoralens; when combined with UV light, inhibits skin cell division. (Will sensitize the skin to UV light and increase the likelihood of sunburn).
- **Purslane:** Eat fresh or lightly steamed. Contains high quantities of vitamins A, C and E, as well as selenium and alpha-linolenic acid, all of which support skin health.

Treatment with Shark Cartilage

Studies have shown that shark cartilage extract prevents the formation of new blood vessels. The growth of new blood vessels is believed to play a role in the development and progression of psoriasis lesions. Shark cartilage is also known to have anti-inflammatory properties. AE-941 is a shark cartilage extract that has demonstrated some promising results in treating psoriasis. It is currently in clinical studies for treating psoriasis. It is taken by mouth once a day. Short-term side effects of AE-941 include nausea and skin rashes. Long-term side effects are not known at this time. Shark cartilage is normally taken in pill form as a food supplement and can be found at most health food stores.

Climatotherapy

Climatotherapy involves the notion that some diseases can be successfully treated by living in particular climate. Several psoriasis clinics are located throughout

the world based on this idea. The Dead Sea is one of the most popular locations for this type of treatment. In turkey & in Croatia (Altermedica), doctor fish which live in outdoor pools of spas, are encouraged to feed on the psoriatic skin of people with psoriasis. The fish only consume the affected areas of the skin. The outdoor location of the spa may also have a beneficial effect. This treatment can provide temporary relief of symptoms. A revisit to the spas every few months is often required. Treatment in the hot spring has been examined until now in two small clinical trials, with positive results[70].

Historical treatments

The history of psoriasis is littered with treatments of dubious effectiveness and high toxicity. These treatments received brief popularity at particular time periods or within certain geofraphical regions. The application of cat faeces to red lesions on the skin, for example, was one of the earliest topical treatments employed in ancient Egypt. Onions, sea salt and urine, goose oiland semen, wasp droppings in sycamore milk, and soup made from vipers have all been reported as being ancient treatments. In the more recent past, Fowler's solution, which contains poisonous and carcinogenic arsenic compound, was used by dermatologists as a treatment for psoriasis during the 18th and 19th centuries. Grenz rays (also called as ultrasoft X-rays or Bucky rays) was a popular treatment of psoriasis during the middle of the 20th century. This type of therapy was superseded by ultraviolet therapy. Undecylenic acid was investigated and used for psoriasis some 40 years ago[71].

Homeopathic Approach

The greatest joy for psoriasis patients is the disappearance of the rashes. The disappearances of the itch / scaly skin itself doesn't mean the disease is waning i.e., skin rash can be easily made to disappear with steroidal external applications which usually mask the complaint. Likewise, suppressive immune therapy with steroidal drugs will also mask the complaint, but very temporarily. Allopathic way of approach is usually against causative factor or disease. But Homeopathy treats the symptoms of patients rather than the diseases or its effects. Excellent results for one patients may have very little or no effect in another. This will make the patient feel frustrated, since he might have been referred by a patient who got better by going to the same doctor or by using the same medicines. It depends upon patient's symptoms. Homeopathy improves the general conditions of the patient to create an environment which is not favorable not disease. Also in other systems, the medicines are selected to stop proliferation of epidermis or infection. But Homeopathy aims at saving / making the skin healthy so that there won't be any need of production or proliferation of skin cells. It means that, if there is need, there will be excessive production. If there is no need, automatically, excessive exfoliation or scaling gets reduced. Homeopathic treatment should be followed for two winter seasons. Right treatment means improvement in the physical and mental state. Unlike other systems of other medicines, which are toxic during continuous usage, drugs used in Homeopathy are safe and offer betterment by enhancing the energy to expel psoriasis without any side effects.Homeopathic medicines commonly used in cases of psoriasis are Ars alb, Arg Nit, Baryta Mur, Corralium, Crab apple, Hudrocytole, Kali ars, Kali Brom, Lycopodium, Nat sulp, Phosphorus, Psoralea, Psorinum, Pulsatilla, Radium Brom, Sulphur, Sulphur Iod, Syphilinum, Silicea, Thuje. Thyroidinum, Urtica urens, etc. these medicines should be taken under the advice and diagnosis of a qualified Homeopath[72]. The main idea of Homeopathic treatment is that "Discover health and happiness with peace of mind and proper treatment."

Types of psoriasis and their treatment regimens

Plaque psoriasis (psoriasis vulgaris):

The plaque psoriasis is the most common form, although several other distinctive clinical variants of psoriasis are recognized. It affects 80 to 90% of people with psoriasis. Plaque psoriasis typically appears as raised areas of inflamed skin covered with silvery white scaly skin. These areas are called plaques[31].

Clinical features

Plaque psoriasis is most typically characterized by circular-to-oval red plaques distributed over extensor body surfaces and the scalp. The plaques usually exhibit scaling as a result of epidermal hyperproliferation and dermal inflammation. Multiple lesions show a tendency towards bilateral symmetry. The extent and duration of the disease is highly variable from patient to patient, and up to 10-20% of the patients with plaque psoriasis also experience psoriatic arthritis. Acute flares or relapses of plaque psoriasis may also evolve into more severe disease, such as pustular or erythrodermic psoriasis. Plaque psoriasis is universal in its occurrence and varies with race, geography, and environmental factors (eg. Sun exposure). Pustular flares of disease may be provoked by systemic corticosteroid therapy. Such flares can be fatal. Other than this, disease-related mortality is exceedingly rare in psoriasis, and even then, the primary cause of mortality is related to its therapy. Adverse effects of systemic treatments (eg. Hepatic fibrosis from methotrexate) and phototherapy (eg

psoralen plus UVA [PUVA] - induced skin cancers with metastases) are the primary disease-related causes of death[73].

Morbidity is much greater problem in patients with psoriasis and is often related to pruritis, dry and peeling skin, fissuring, and the adverse effects of therapy. By far, the patient's quality of life is most affected in plaque psoriasis, and studies have demonstrated patients with psoriasis have deficiencies in quality of life similar to those for persons with congestive heart failure. Self-consciousness and embarrassment about appearance, inconvenience, and the high cost of antipsoriatic treatment regimens all add to the morbidity of this chronic and relapsing disease. Patients report prominent itchy, red areas with increased skin scaling, mild to severe itching, pitting and separation of the plate from the nail beds of nails, lesions and peeling on the scalp and extensor surfaces and new lesions appear at sites of injury or trauma to the skin. (Bulletin)

This isomorphic phenomenon (Koebner reaction) typically occurs 7-14 days after the skin has been injured and has been found in 38-76% of patients with plaque psoriasis. In some patients, so called reverse-Koebner reactions have also been noted in which pre-existing psoriatic plaques actually clear after injury or trauma to the skin. This disease usually worsens in the winter and improves in the summer. Significant joint pain, stiffness, and deformity are reported in the 10-20% of patients with psoriasis who develop psoriatic arthritis[74].

Prevalence

Plaque psoriasis can affect persons of any race; however, epidemologic studies have shown a higher prevalence in western European and Scandinavian populations. In these groups, 1.5-3% of the population is affected by the disease. The highest documented disease prevalence is in Artic Kasach'ye with 12% of the population affected, followed by Norway, where 4.8% of the population has psoriasis. Lower prevalence rates for psoriasis have been reported among Japanese and Inuit populations. Psoriasis is thought to be rare in West Africans and African Americans and is nearly absent in North American Indians. Psoriasis was undetected in the Samoan population and in the study that examined 26,000 South American Indians. Psoriasis affects adult males and females equally. Among children and adolescents, plaque psoriasis has been found to affect females more than males, but this observation may be due to earlier age of onset in females. Plaque psoriasis first appears during 2 peak age ranges. The first peak occurs in persons aged 16-22 years, and the second occurs in persons aged 57-60 years. Females develop plaque psoriasis earlier than males, and patients with positive family history for psoriasis also tend to have an earlier age of onset. For siblings of patients whose psoriasis appeared before age 15 years, a 3-fold higher risk exists of developing disease compared with siblings of patients who presented after age 30 years[74,75].

Causes[73,75]

Exacerbating causes of plaque psoriases can be divided into local and systemic factors.

Local factors are as follows:

- **Trauma:** All types of trauma have been associated with the development of plaque psoriasis (eg. Physical, chemical, electrical, surgical, infective, and inflammatory types of injury). Even excessive scratching can aggravate or precipitate localized psoriasis. The development of psoriatic plaques at a site of injury is known as the Koebner reaction. See history for more details on the Koebner reaction.
- **Sunlight:** Most patients generally consider sunlight to be beneficial for their psoriasis. Most report a decrease in illness severity during the summer months or periods of increased sun exposure; however, a small minority find that their symptoms are aggravated by strong sunlight, and these individuals actually experience a worsening of their disease in the summer. Severe sunburn can lead to an exacerbation of plaque psoriasis via the Koebner reaction.

Systemic factors are as follows:

- **Infection:** pharyngeal streptococcal infections have been shown to produce a clinically distinctive disease flare known as guttate psoriasis. Some evidence suggests that subclinical streptococcal colonization or overgrowth could be responsible for refractory plaque psoriasis. Telfer NR, Chalmers
- **HIV:** An increase in psoriasis activity has been observed in patients who are or become infected with HIV. The extent and severity of skin disease initially appears to parallel the disease stage. Psoriasis often becomes less active in advanced HIV infection.
- **Drugs:** a number of medications have been shown to cause an exacerbation of psoriasis. Lithium and withdrawl from systemic corticosteroids are well-known to cause flares of disease. Beta blockers, antimalarials, and nonsteroidal anti-inflammatory drugs (NSAID's) have also been implicated.

- **Smoking:** An increased risk of chronic plaque psoriasis exists in persons who smoke cigarettes.
- **Alcohol:** Alcohol is considered a risk factor for psoriasis, particularly in young to middle-aged males.
- **Endocrine:** Psoriasis severity has been noted to fluctuate with harmonal changes. Disease incidence peaks at puberty and during menopause. Pregnant patient's symptoms are more likely to improve than worsen, if any changes occur at all. In contrast, the disease is more likely to flare in the postpartum period, again if any changes occur at all.

Diagnosis of Plaque psoriasis[73,54]

The diagnosis of psoriasis is usually made on the basis of clinical findings, and ancillary laboratory tests are very rarely required.

Several cardinal features of plaque psoriasis can be readily observed during the physical examination such as:

- **Plaques:** Psoriasis manifests as elevated lesions that vary in size from one to several centimeters. The thickened epidermis, expanded dermal vascular compartment, and infiltrate of neutrophils and lymphocytes account for the psoriatic lesions being raised and easily palpable. The number of lesions may range from few to many at any given time. The plaques are irregular to oval and are more often located on the scalp, trunk, and limbs, with a predilection for extensor surfaces such as the elbows and knees. Smaller plaques may coalesce into larger lesions, especially on the legs and sacral regions. Fissuring within plaques can occur when lesions are present over joint lines or on the palms and soles.
- **Well-circumscribed margins:** psoriatic plaques are well defined and have sharply demarcated boundaries. Psoriatic plaques occasionally appear to be immediately encircled by a paler peripheral zone referred to as the halo or ring of Woronoff.
- **Red color:** the color of psoriatic lesions is a very distinctive rich, full, red color. When present on the legs, lesions sometimes carry a blue or violaceous tint.
- **Scale:** Psoriatic plaques typically have a dry, thin, silvery-white or micaceous scale; however, the amount and thickness of this scale is quite variable. Removing the scale reveals a smooth, red, glossy membrane with tiny punctate bleeding points. These points represent bleeding from enlarged dermal capillaries after removal of the overlying suprapapillary epithelium. This phenomenon is known as Auspitz sign.
- **Symmetry:** Psoriatic plaques tend to be symmetrically distributed over the body. Lesions typically have a high degree of uniformity with few morphologic differences between the 2 sides.

The following are psoriatic variations and associations that can be observed in persons with plaque psoriasis:

- **Nail psoriasis**: Cindy Li, DO, Richard K Scher, MD Nail changes are commonly observed in patients with plaque psoriasis. Nails may exhibit pitting, onycholysis, subungual hyperkeratosis, or oil-drop sign. A proper assesment of any patient suspected of having psoriasis should include careful examination of the nails.
- **Psoriasis in children**: plaque psoriasis manifests slightly differently in children. Plaques are not as thick, and the lesions are less scaly. Psoriasis may often appear in the diaper region in infancy and in flexural areas in children. The disease more commonly affects the face in children compared with adults.
- **Inverse psoriasis:** This is a variant of psoriasis that spares the typical extensor surfaces and affects intertriginous (i.e. axillae, inguinal folds, inframammary creases) areas with minimal scale.

Complications

Complications of the disease are relatively uncommon. Approximately 10-20% of all cases of plaque psoriasis are associated with psoriatic arthritis. Pruritis, one of the main symptoms of plaque psoriasis, is quite variable in intensity but should not be ignored. Emotional instability (eg. high levels of anxiety, depression) that might be induced by the disease often manifests as an increased tendency to scratch. Many of the complications of plaque psoriasis are related to the treatments for the disease. Overly aggressive use of topical steroids could produce progression from plaque psoriasis to pustular and erythrodermic forms. Topical steroids used with occlusion increase the risk of developing cutaneous atrophy. Potential adverse effects of systemic agents and phototherapy should be monitered on a regular basis and treated as soon as possible. Alcoholism can also be considered a complication of psoriasis. Male patients with severe disease are particularly at risk for this type of substance

abuse. Plaque psoriasis may evolve into erythrodermic or generalized pustular psoriasis in rare instances[76].

Treatment[77-81]

Plaque psoriasis is chronic skin condition. Any approach to the treatment of this disease must be considered for the long term. Treatment regimens must be individualized according to age, sex, occupation, personal motivation, other health conditions, and available resources. Disease severity is defined by the number and extent of plaques present, as well as by the patient's perception and acceptance of the disease. Treatment, therefore, must be designed with the patient's specific expectations in mind rather than the extent of the body surface area involved. Many treatments exist for psoriasis; however, the construction of an effective therapeutic regimen is not necessarily complicated. Three basic treatment modalities are available for the overall management of psoriasis (i.e. topical agents, phototherapy, and systemic agents, including biologic therapies). All of these treatments may be used alone or in combination.

- **Topical therapy:** Outpatient topical therapy is the first-line approach in the treatment of plaque psoriasis. A number of topical treatments are available (eg. corticosteroids, coal tar, anthralin, calcipotriene, tazarotene). No single topical agent is ideal for plaque psoriasis, and many are often used concurrently in a combined approach. With the different adverse effect profiles for the various agents, using a rotational therapeutic approach in which different topical agents are used sequentially over time in the same patient is common. In general, the effects of topical therapy should become evident within the first 2-3 weeks of use. Clearing of scale is usually observed first, followed by flattening of the treated plaques. Resolution of erythema may take 6-8 weeks. Auxillary agents such as keratolytics can often be added to these preparations. However some auxillary agents are incompatible with the active ingredients of these preparations. For example, salicylic acid inactivates calcipotriene.
- **Phototherapy**: Initiate phototherapy only in the presence of extensive and widespread disease (generally practically defined as more lesions than can be easily counted). Resistance to topical treatment is another indication for phototherapy. Proper facilities are required for the 2 main forms of phototherapy. UVB irradiation uses light with wavelengths of 290-320 nm (visible light range, 400-700 nm). Narrow-band UVB therapy offers superior efficacy with less risk of burning. UVB therapy is usually combined with one or more topical treatments. The Goeckerman regimen uses coal tar followed by UVB exposure and has been shown to induce disease remission in more than 80% of patients. The Ingram method is based on anthralin application following a tar bath and UVB treatment. Now, UVB is more commonly combined with topical corticosteroids, calcipotriene, tazarotene, or simply bland emollients. UVB phototherapy is extremely effective for trating moderate-to-severe plaque psoriasis. The major drawback of this therapy is the time commitment required for treatments and the accessibility of the UVB equipment. Patients may dislike the unfavourable odor when coal tar is added. Home ultraviolet therapy can overcome some of the logistical problems associated with phototherapy. Because of the expense of the home units, it is most suitable for patients who require long term maintainence therapy. Narrow-band UVB phototherapy uses a fluorescent bulb with a narrow emission spectrum that peaks at 311 nm (UVB spectrum, 290-320 nm). This selective and relatively longer wavelength is more effective than broadband UVB for the treatment of plque-type psoriasis. PUVA photochemotherapy, also known as PUVA, uses the photosensitizing drug methoxsalen (8-methoxypsoralens) in combination with UVA irradiation to treat patients with more extensive disease. UVA irradiation uses light with wavelengths of 320-400 nm. PUVA interferes with DNA synthesis, decreases cellular proliferation, and induces apoptosis of cutaneous lymphocytes, leading to a localized immunosuppression. More than 85% of patients report relief of disease symptoms with 20-30 treatments. Therapy is usually administered 2-3 times per week in an outpatient setting, with maintainence treatments every 2-4 weeks until remission. Adverse effects of PUVA therapy include nausea, pruritis and a burning sensation. Long-term complications include increased risk of photo damage to the skin and (more importantly) skin cancer. PUVA has been combined with oral retinoid derivatives to decrease the cumulative dose of UVA radiation to the skin. Excimer laser UVB

therapy can deliver high-dose light to limited plaques.

- **Systemic agents:** initiate systemic treatment only after both topical treatments and phototherapy have been unsuccessful. Consider systemic therapy for patients with very active psoriatic arthritis. Patients who have disease that is physically, psychologically, socially, or economically disabling are also considered candidates for systemic treatment. All patients must be informed of the risks and adverse effects of systemic therapy before treatment is initiated.
- **Biologic therapies:** These relatively new systemic therapies provide selective, immunologically directed intervention at key steps in the pathogenesis of the disease. These steps include:
    - Inhibiting the initial cytokine release and Langerhans cell migration;
    - Targetting activated T cells, preventing further T-cell activation, and eliminating pathologic Tcells;
    - Blocking the interactions that lead to T-cell activation or migration into tissue;
    - Altering the balance of T-cell types; and
    - Inhibition of proinflammatory cytokines, such as tumor necrosis factor.

Similar to the systemic agents, these therapies are typically reserved for more severe and recalcitrant cases. Patients with active psoriatic arthritis in addition to their skin disease should also be considered.

Prognosis[80]

The course of plaque psoriasis is unpredictable. Predicting the duration of active disease, the time or the fequency of relapses, or the duration of remission is impossible. The disease rarely is life threatening but often is intractable to treatment, with relapses occurring in most patients. Both early onset and a family history of disease are considered poor prognostic indicators. Some suggest that stress is also associated with an unfavourable prognosis. Environmental factors (particularly sunlight and warm weather) help alleviate the disease and are considered advantageous.

Flexural psoriasis (inverse psoriasis)

It appears as smooth inflamed patches of skin. It occurs in skin folds, particularly around the genitals (between the thigh and groin), the armpits, under an overweight stomach (pannus), and under the breasts (inframammary fold). It is aggravated by friction and sweat, and is vulnerable to fungal infections. In some patients, psoriasis localises to the skin folds and genitals. Armpits Groin Under the breasts Umbilicus (navel) Penis Vulva Natal cleft (between the buttocks) around the anus[18].

Clinical features

Due to the moist nature of the skin folds the appearance of the psoriasis is slightly different. It tends not to have silvery scale, but is shiny and smooth. There may be a crack (fissure) in the depth of the skin crease. The deep red colour and well-defined borders characteristic of psoriasis may still be obvious. Over these sites, the lesions tend to be flatter with a glazed reddish surface without the typical scales. These are smooth inflamed psoriasis in folds of skin without scaling. Scaly plaques may sometimes occur however, particularly on the circumcised penis[18,19].

Complications

Complications of flexural psoriasis include chaffing and irritation from heat and sweat, Secondary fungal infections particularly candid (thrush), lichenification (a type of eczema) from rubbing and scratching, sexual difficulties because of embarrassment and discomfort, thinned skin due to long term overuse of strong topical steroid creams. Lesions may preferentially occur on flexural surfaces like groin, axilla, umbilicus, or inframammary regions[20].

Treatment

Flexural psoriasis responds quite well to topical treatment but often recurs. Weak topical steroids (often in combination with an antifungal agent to combat thrush) may clear flexural psoriasis but it will usually recur sometime after discontinuing treatment. Stronger topical steroids need to be used with care, only for a few days, thinly and very accurately applied to the psoriasis. If the psoriasis has cleared, stop the steroid cream. The steroid cream may be used again when the condition recurs. Overuse of topical steroids in the thin-skinned body folds may cause strech marks, marked thinning of the skin and can result in long term aggravation of psoriasis (tachyphylaxis). Vitamin D-like compounds Calcipotriol cream is an effective and safe treatment for psoriasis in the flexures and should be applied twice daily. If it irritates, it can be applied once daily and hydrocortisone cream 12 hours later. Systemic agents are rarely required for limited flexural psoriasis and phototherapy is relatively ineffective because the folds are hidden from light exposure[19].

Guttate psoriasis

Clinical features

'Gutta' is Latin for tear drop; guttate psoriasis looks like shower of red, scaly tear drops that have fallen

down on the body. Guttate psoriasis is characterized by numerous small round spots (differential diagnosis- pityriasis rosea- oval shape lesion that tend to affect most of the body. Lesions are usually concentrated around the trunk and upper arms and thighs. Face, ears and scalp are also commonly affected but the lesions may be very faint and quickly disappear in these areas. Occasionally there may be only few scattered lesions in total[15].

Diagnosis

The diagnosis of guttate psoriasis is made by the combination of history, clinical appearance of the rash, and evidence for preceding infection. The rash comes on very quickly, usually within a couple of days, and may follow a streptococcal infection of the throat. It tends to affect children and young adults and has a good chance of spontaneously clearing completely. Guttate psoriasis is associated with streptococcal throat infection. In some patients, particularly in children and young adults and after acute streptococcal infections, an acute or sub-acute eruption of small raindrop shaped lesions may develop. The eruption mainly affects the trunk and proximal extremities and the scaling may be less prominent. These are multiple dotted occurrence of psoriasis. In short they are small, red spots on the skin. Blood test reports generally show a low level of calcium in the blood (hypocalcaemia). Other changes on blood testing include low plasma albumin and zinc, high ESR (eroyhrocyte sedimentation rate), raised neutrophil count, reduced lymphocyte count and raised lactate levels[82].

Treatment

Management may include the treatment of an underlying streptococcal infection with antibiotics, phototherapy, topical agents including mild topical steroids, coal tar and calcipotriol. Guttate psoriasis rarely requires treatment with oral medication[83].

Pustular psoriasis

Generalized pustular psoriasis is a rare form of psoriasis, which presents as widespread pustules on a background of red and tender skin. Widespread patches may occur randomly on any part of the body. It is also known as acute generalised pustular psoriasis of von Zumbusch. Another form of pustular psoriasis is localised pustular psoriasis, which appears on the hands or feet (palmoplantar pustulosis). This needs to be distinguished from a localised form of generalised pustular psoriasis. It appears as raised bumps that are filled with non-infectious pus (pustules). The skin under and surrounding pustules is red and tender. Pustular psoriasis can be localised, commonly to the hands and feet (palmoplantar pustulosis), or generalised with widespread patches occuring randomly on any part of the body[83].

Clinical features

Initially the skin becomes dry, fiery red and tender. The patient may also have a fever, chills, headache, rapid pulse rate, and loss of appetite, nausea and muscle weakness. Within hours 2-3 mm pustules filled with non-infected pus appear on parts of the body especially the flexures and genital areas. After a day they coalesce to form lakes of pus, which then dry and peel to leave behind a glazed, smooth surface on which new crops of pustules may appear. Successive crops of pustules may appear and erupt every few days or weeks. The sudden onset of this condition can be quite alarming. If the patient survives the acute phase and its complications, remission occurs within days or weeks and the psoriasis reverts to its previous state or erythroderma may develop. Relapses are common. Inflammatory mediators attract neutrophils to the site of lesions in all psoriasitic lesions producing 'micro abscesses' visible on microscopy. Intense neutrophil accumulation may produce visible sterile pustules on psoriatic lesions or there may be a recalcitrant palmoplantar pustular eruption[84].

Complications

Rarely, acute and generalized pustule formation may occur associated with severe constitutional symptoms. This generalized pustular form of psoriasis may cause significant morbidity and sometimes mortality. These are mainly with pustulars blisters (white pustules surrounded by red skin). Death can result from cardio respiratory failure during the acute eruptive phase so it is very important to treat as early as possible Rocha-Pereira P, Santos-Silva A, Ludwig RJ, Herzog C, Rostock A, et al. Elderly patients are at greatest risk. Other complications include secondary bacterial infections, disturbed protein and electrolyte balance, especially low albumin and calcium, renal and liver impairment, malabsorption of nutrients and therapeutic drugs[85].

Treatment

Generalised pustular psoriasis can be life threatening so hospitalisation is usually required. The aim is to prevent further fluid loss, stabilise body temperature and restore elctrolyte imbalance. Affected areas are treated with bland topical compresses. Antibiotics may be prescribed if infection has occurred. In severe cases or cases where recurrent outbreaks have exhausted the patient, systemic medications are used such as such as acitretin, an oral retinoid derived from vitamin A. Sometimes it is necessary to restart corticosteroids, usually temporarily. Other medications such as methotrexate, colchicine, cyclosporin, tioguanine and

hydroxyurea have been used with some success. Phototherapy (ultraviolet radiation), especially in combination with oral psoralens (PUVA) can be more useful. This is usually started once the patient has been stabilised on acitretin[84,86].

Nail psoriasis

It produces a variety of changes in the appearance of finger and toe nails. These changes include discolouring under the nail plate, pitting of the nails, lines going across the nails, thickening of the skin under the nail, and the loosening (onychlysis) and crumbling of the nail. Psoriatic nail disease has many clinical signs. Most psoriatic nail disease occurs in patients with clinically evident psoriasis; it only occurs in less than 5% of patients with no other cutaneous findings of psoriasis. An estimated 10-55% of all patients with psoriasis have psoriatic nail disease. How psoriasis of the nails develops is not completely known. It appears to result from a combination of genetic (inherited), immunologic, and environmental factors.

Arthropathic psoriasis (psoriatic arthritis)

It involves joint and connective tissue inflammation. Psoriatic arthritis can affect any joint but is most common in the joints of fingers and toes. This can result in a sausage-shaped swelling of the fingers and oes known as dactylitis. Psoriatic arthritis can also affect the hips, knees and spine (spondylitis). About 10-15% of people who have psoriasis also have psoriatic arthritis. Around 10% - 30% of people who develop psoriasis get a related form of arthritis called 'psoriatic arthritis' which cause inflammation of the joints. Patients may develop joint symptoms due to seronegative arthritis. The same immune and inflammatory factors that cause the skin lesions are thought to be responsible for the joint inflammation. A majority of patients with joint will have involvement of one or few peripheral joints asymmetrically. Some may develop a symmetrical peripheral arthropathy resembly rheumatoid arthritis[10,87].

Erythrodermic psoriasis

It is a particularly inflammatory form of psoriasis that involves widespread inflammation and exfoliation of the skin over most of the body surface. It may be accompanied by severe itching swelling and pain. It is often the result of an exacerbation of unstable plaque psoriasis, particularly following the abrupt withdrawal of systemic treatment[88].

Clinical features

This form of psoriasis can be fatal, as the extreme inflammation and exfoliation disrupt the body's ability to regulate temperature and for the skin to perform barrier functions. Chronic psoriasis may gradually evolve to spread over the whole skin surface to produce a generalized, diffuse redness with profuse scaling. This may rarely be the initial presentation of disease. This syndrome of 'erythroderma' also called exfoliative dermatitis is often associated with the disordered temperature regulation, hypoalbuminemia, anemia, and hyperuricemia. This is severe form of psoriasis with terrible itching and redness i.e. widespread redness, severe itching and pain. It may occur in association with von Zumbusch pustular psoriasis. It is the least common type of psoriasis and may occur once or more during a lifetime in 1 to 2 percent of people who develop psoriasis. It generally appears on people who have unstable plaque psoriasis. This means the lesions are not clearly defined. Widespread, fiery redness and exfoliation of the skin characterize this form. Severe itching and pain often accompanies it. The symptoms include severe redness and shedding of skin over a large area of the body. Exfoliation often occurs in large "sheets" instead of smaller scales with severe itching and pain and skin looks as if it has been burned. Heart rate increases and body temperature varies especially on very hot or cold days. Erythrodermic psoriasis is related to unstable plaque psoriasis, a type characterized by lesions which are not clearly defined. In most cases, it will occur in people with unstable plaque psoriasis. In rare cases, erythrodermic psoriasis can be the first instance of psoriasis for a patient[88,89].

Causes

Specific medications including lithium, antimalarials and interleukin II are shown to be triggers of erythrodermic psoriasis. More causes include infections, calcium deficiency, sudden withdrawal of oral corticosteroids (prednisone), withdrawal of excessive use of strong topical corticosteroids, and strong coal tar preparations[89].

Treatment

Initial treatment usually includes medium-potency topical steroids and moisturizers combined with wet dressings, oatmeal baths and bed rest. Antibiotics may also be used. It is important to restore and maintain fluids in the body. Systemic psoriasis medications are most effective and are usually required to bring severe cases under control. These include methotrexate, acitretin (brand name Soriatane) or cyclosporine[90].

Scalp psoriasis (Pityriasis amiantacea)

Pityriasis amiantacea is a condition of the scalp characterised by thick, yellow-white scales densely coating the scalp skin and adhering to the scalp hairs as they exit the scalp. They are arranged in an overlapping manner like tiles on a roof or flakes of asbestos, hence the name. The underlying scalp skin may appear

normal, aside from the scale, or may be reddened or scaly.

Clinical features

Pityriasis amiantacea is often present without any obvious underlying cause, but may be associated with psoriasis, lichen simplex or seborrhoeic dermatitis.

Pityriasis amiantacea usually affects only part of the scalp but may occasionally involve the whole scalp. Young girls may have localised pityriasis amiantacea extending into the scalp from areas of chronic fissures in the skin behind the ears. It may extend from an area of lichen simplex of the scalp. Some hair loss is common is areas of pityriasis amiantacea but hair regrows normally if the condition is effectively treated. This hair loss is sometimes aggravated by the difficulty in combing the hair due to the very adherent, thick scale at the base of the hair shafts. If additional complications such as infection occur then hair loss may be associated with scarring and be permanent. The term tinea amiantacea is incorrect, because fungal infection, tinea capitis, is a very rare reason for this type of scaling. Scalp psoriasis may occur in isolation or with any other form of psoriasis. The back of the head is a common site but multiple discrete areas of the scalp or the whole scalp may be affected. Scalp psoriasis is characterised by thick silvery white patches of very red skin. Scalp psoriasis can be very mild, with slight, fine scaling. It can also be very severe with thick, crusted plaques covering the entire scalp, which commonly can cause hair loss.

Signs and symptoms of scalp psoriasis

Scalp psoriasis can appear anywhere on the scalp. Sometimes one small patch develops, which can be easy to hide with hair. Scalp psoriasis also can cover the entire scalp. It can even creep beyond the scalp, appearing on the forehead, back of the neck, or behind the ears. The reddish plaques can creep beyond the hairline and appear behind the ears. The silvery-white scale can cover the entire scalp. When scalp psoriasis develops, people have one or more of these signs and symptoms:

- **Reddish plaque on the scalp:** Plaques range from barely noticeable to thick and inflamed.
- **Silvery-white scale:** This often develops on the scalp and can be mistaken for dandruff.
- **Dandruff-like flaking:** This is common due to the continual shedding of the new skin cells. Unlike dandruff, scalp psoriasis causes a silvery sheen and dry scale on the scalp.
- **Dry scalp:** The scalp may be so dry that the skin cracks and bleeds.
- **Itching:** This is one of the most common symptoms. For some the itch is mild; others have intense itching that can interfere with everyday life and cause them to lose sleep.
- **Bleeding:** Because scalp psoriasis can be very itchy, almost everyone scratches. This can cause the scalp to bleed. Scratching also injures the skin, which tends to worsen the psoriasis. This is why dermatologists tell their patients "Try not to scratch your scalp."
- **Burning sensation or soreness:** The scalp can burn. It can feel extremely sore.
- **Temporary hair loss:** Scratching the scalp a lot or forcefully removing scale can cause hair loss. Once the scalp psoriasis clears, hair usually re-grows.

These signs and symptoms can come and go. Some people have only one mild flare. Others experience flare-ups that range in intensity, with some flare-ups being milder than other flare-ups. Many things can trigger a flare-up, including stress, cold, and a dry environment.

Treatment

For people with scalp psoriasis, the key is to loosen and remove scales, while providing as much moisture as possible. Scalp psoriasis requires slightly different regimes from psoriasis affecting the skin elsewhere. This is due to hair, which makes application of many topical products difficult and protects the scalp from the effects of ultraviolet light. Unfortunately, many scalp treatments for scalp psoriasis are messy and smelly. Most treatments will need to be used regularly for several weeks before a benefit is seen.

Special medicated shampoos and coal tar shampoos are suitable for most patients with scalp psoriasis. Ketoconazole, ciclopirox, zinc pyrithione and other antifungal shampoos are effective for dandruff and seborrhoeic dermatitis. They have varying effect in sebopsoriasis and psoriasis.

The shampoos work best if rubbed into the scalp well, and left in for 5 or 10 minutes and then reapplied. They are safe for daily use but may irritate if applied more than twice weekly. If you dislike the smell of coal tar, try shampooing again with a favourite brand, and use a conditioner.

More severe cases require leave-on scalp applications. Alcohol-based, foam or lotion forms of topical steroid and calcipotriol can reduce redness and itch but they don't lift scale very well. Use topical steroids intermittently; overuse results in more extensive and severe psoriasis. Salicylic acid and coal tar creams work much better, but are messy. Coconut oil compound ointment is a combination of coal tar, salicylic acid and sulphur and seems particularly effective. An advantage of the coconut-based

treatments is that they are wonderful conditioners for your hair. Leave on for at least an hour and shampoo off later. Most people rub the cream into the plaques at night and wash it off in the morning. Dithranol may be effective but is difficult to use and may be messy as it stains hair and fabrics. Use the scalp preparation daily at first then as the condition improves, reduce the frequency. Unfortunately in many cases the scale soon builds up again, so the creams may have to be applied regularly to keep the scalp clear. Cutting hair short helps control scalp psoriasis, probably by making the treatments easier to apply, but is not appealing to everyone.

Phototherapy is effective for chronic plaque psoriasis but difficult to deliver to the scalp. Special targeted devices and UVB combs have been devised, and appear very helpful. In some cases prolonged clearance has resulted from a course of treatment.

Systemic agents may be justified for a few patients with severe scalp psoriasis that has failed to respond to treatments described above. These include acitretin, methotrexate, cyclosporin and biological response mediators[18,54].

Psoriasis of the palms and soles

This type of psoriasis may predominantly affect the palms and soles in various ways such as typical scaly, red patches similar to psoriasis elsewhere, generalized thickening and scaling of the palms and soles (keratoderma) with sheets of tiny yellow- brown pustules (palmoplantar pustulosis)[91].

Clinical features

The palms and soles can become very dry and thickened, often with deep painful cracks (fissures), which can significantly interfere with activities. Psoriasis can be quite hard to differentiate from other forms of keratoderma, but signs of psoriasis elsewhere may help make a diagnosis. Palmoplantar psoriasis tends to be a chronic recurrent condition. The pustular form is reported to be much more common in tobacco smokers, but unfortunately giving up smoking doesn't always result in clearance of the psoriasis[91].

Treatment[90,92]

Mild psoriasis of the palms and soles may be treated with topical treatments such as:

- **Emolients:** Thick, greasy barrier creams applied thinly and frequently to moisturise the dry, scaly skin and help prevent painful cracking.
- **Coal tar**: Applied to improve the scale and inflammation. Because of the mess, often applied at night under cotton gloves.
- **Keratolytic agents**: Agents such as urea or salicylic acid to thin down thick scaling skin
- **Topical steroids:** Ultrapotent ointment applied initially daily for two to four weeks, if necessary under occlusion, to reduce inflammation, itch and scaling. Maintenance use only at weekends to avoid thinning the skin and causing the psoriasis to become more extensive.

Calcipotriol ointment is not very successful and may cause an irritant dermatitis on the face if a treated area inadvertently touches it. Dithranol is too messy for routine use on hands and feet. More severe disease usually requires phototherapy or systemic agents such as PUVA, acitretin and methotrexate

Conclusion

Psoriasis is a dreadful disease affecting physical, mental and social status of the victims. A new understanding of this complex disease has catalyzed the development of targeted biological treatments. These revolutionary therapies are not without potential risk, however. A review of alternative natural therapies provides some options for increasing safety and efficacy in the management of psoriasis. This review will surely prove to be an eye-opener for patients suffering from psoriasis as well as the medical practioners, pharmacists, nurses and other persons involved in the treatment of psoriasis and help them to understand the disease in a much batter way to carry out safe and effective treatment of the disease.

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