Psoriasis is a chronic relapsing skin condition affecting 1.5-3% of the population in Europe and North America. It is characterised by well-demarcated red patches (plaques) with variable degrees of thickening and surface scaling. Psoriasis can occur at any age, but onset shows a bimodal distribution - the largest peak occurs in the second decade with another peak around the age of 50 years. Males and females are equally affected. Many cases are mild and even the chronic form is not considered a life-threatening disease. However, its effects can be devastating for many patients. Studies have shown that psoriasis produces a reduction in quality of life at least equal to, if not greater than, chronic conditions such as chronic obstructive pulmonary disease or diabetes mellitus. In recent years, there has been an increased understanding of the pathogenesis of psoriasis, and new therapeutic options have become available. This bulletin will focus on the contemporary management of psoriasis in primary care.

**INTRODUCTION**

Psoriasis has 3 principal histological features: epidermal hyperplasia; dilated prominent blood vessels in the dermis and an inflammatory infiltrate of leucocytes, predominantly into the dermis. Previously it was thought to be a disease primarily of epidermal keratinocyte proliferation resulting in a secondary cutaneous inflammatory infiltrate; however, it is now recognised that psoriasis is an immune-mediated disease. Some studies have suggested a cell-mediated adaptive immune response mechanism whereby the epidermal and capillary proliferation results from activity of pro-inflammatory cytokines and activated T cells, stimulated by some external trigger. However, there is also evidence of a wider disturbance of innate immune responses in psoriasis patients. These findings have aided the development of new therapeutic options (e.g. targeting T cells and cytokines). Although the initial trigger of psoriasis remains unclear, both environmental and genetic factors are thought to be involved. Depending on the region, 35-50% of people with psoriasis have a first degree relative with the disease and monozygotic twins have at least equal to, if not greater than, chronic conditions such as chronic obstructive pulmonary disease or diabetes mellitus. Some studies have suggested a cell-mediated adaptive immune response mechanism whereby the epidermal and capillary proliferation results from activity of pro-inflammatory cytokines and activated T cells, stimulated by some external trigger. However, there is also evidence of a wider disturbance of innate immune responses in psoriasis patients. These findings have aided the development of new therapeutic options (e.g. targeting T cells and cytokines).

**CLINICAL PRESENTATION**

A diagnosis of psoriasis is usually based on history and clinical examination. Laboratory investigations are rarely helpful. Table 1 outlines the main types of psoriasis. The commonest form is chronic plaque psoriasis (psoriasis vulgaris) which accounts for up to 90% of all cases. This presents as papulosquamous plaques (salmon pink or red) of varying size and thickness and covered by white scales. The plaques are usually well delineated from the surrounding skin. They are usually symmetrically distributed and are most commonly found on the extensor aspects of elbows and knees, in the scalp (rarely beyond the hairline), the lumbosacral region and the umbilicus. A helpful diagnostic aid, not always present, is the Koebner phenomenon where psoriatic lesions develop at sites of trauma (e.g. surgical wounds, abrasions). When psoriasis affects the hands and feet (non pustular) may result in severe pain and disability disproportionate to the affected areas. When psoriasis affects the scalp, the affected sites are often shiny red and devoid of scales. Affected nails display pitting and nail-plate detachment; in the absence of psoriasis elsewhere, this may be mistaken for a fungal infection. Psoriasis affecting the inverse psoriasis and genital areas resembles exfoliative dermatitis and is most often seen in patients with pre-existing, difficult to control (or neglected) psoriasis. It requires urgent attention and hospitalisation because of risk of septicaemia, hypothermia and dehydration. According to the American Psoriasis Association, St. James’s Hospital, and the National Psoriasis Foundation, the following types of psoriasis are most common:

<table>
<thead>
<tr>
<th>Description</th>
<th>Clinical Features</th>
<th>Affected Population</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic plaque psoriasis</td>
<td>Salmon pink / red papulosquamous plaques</td>
<td>All ages but bimodal distribution: peaks in 2nd and 5th decades</td>
<td>See text for full details</td>
</tr>
<tr>
<td>Guttate psoriasis</td>
<td>Acute inflammatory disease; Papules &lt; 1cm in diameter appear on trunk 2 weeks after β-haemolytic Strep. infection</td>
<td>Children / adolescents</td>
<td>Often clears spontaneously; May develop de novo but up to 18% may have existing psoriasis</td>
</tr>
<tr>
<td>Palmoplantar pustular psoriasis</td>
<td>Crops of white pustules appear on palms and soles, change to brown and disappear</td>
<td>Females: Males = 9:1 (4th and 5th decades); more common in smokers</td>
<td>Relapsing remitting course; up to 25% have chronic plaque psoriasis</td>
</tr>
<tr>
<td>Generalised pustular psoriasis</td>
<td>Acute skin inflammation due to waves of pustules; systemically unwell (fever)</td>
<td>Patients discontinuing oral or potent topical corticosteroids; previously unaffected individuals</td>
<td>Frequently requires hospitalisation; risk of dehydration; septicemia hypoalbuminaemia</td>
</tr>
</tbody>
</table>

**PATHOPHYSIOLOGY OF PSORIASIS**

Psoriasis has many aspects of chronic inflammatory disease and is a systemic disease. Many patients with psoriasis have symptoms outside the skin, such as joint pain and discomfort, fatigue and depression. Psoriasis appears on trunk 2 weeks after beta-haemolytic streptococcal infection, but up to 18% may have existing psoriasis. Erythrodermic psoriasis resembles exfoliative dermatitis and is most often seen in patients with pre-existing, difficult to control (or neglected) psoriasis. It requires urgent attention and hospitalisation because of risk of septicaemia, hypothermia and dehydration.
MANAGEMENT OF PSORIASIS

The impact of psoriasis on a patient’s well-being varies greatly and is irrespective of the extent of the disease. Therefore, management should be individualised to optimise response, and should involve both non-pharmacological and pharmacological treatment.

Initial evaluation will identify the extent and severity of disease. It is advisable to keep a record (graphic or otherwise) to serve as a baseline for monitoring the effects of therapy. Definition of psoriasis severity may encompass subjective and objective assessment. The psychosocial impact of disease (in terms of self-esteem and disease-related restrictions on work/social activities) should be assessed. These problems may not be directly linked with extent of objective disease; however, if they are present, they may result in resistance to, and/or lack of compliance with, the treatment plan. Formal measurement techniques (e.g. Psoriasis Severity and Area Index (PSAI)) or the Dermatology Life Quality Index (DLQI) may be used to quantify disease extent (generally used in specialist settings only).

The “Rule of Tens” has been proposed to identify severe psoriasis i.e: Body Surface Area (BSA) involved >10% (where the outstretched hand, including digits = 1% BSA), or PASI >10 or DLQI >10. It is important to look for co-morbidities that may require treatment. Psoriatic arthritis is reported in at least 5% of cases. Recent studies suggest there is an increased risk of cardiovascular disease in patients with moderate – severe psoriasis (thought to be due to the presence of circulating pro-inflammatory factors).

NON-PHARMACOLOGICAL MANAGEMENT

Patient education is vital. Patients should be informed that psoriasis is a lifelong disease requiring lifelong monitoring and/or intervention; otherwise they may discontinue treatment as soon as an acute attack settles down, leading to the risk of early relapse. Patients should be advised to avoid any aggravating factors such as excess alcohol, cigarette smoking or stress. As a general principle, patients should be advised to maintain adequate hydration of their skin (see below), even when their disease is stable. This will relieve dryness and diminish scaling which is often embarrassing for the patient.

PHARMACOLOGICAL MANAGEMENT: TOPICAL THERAPIES

Emollients hydrate and soften the skin and have an anti-pruritic effect. In mild psoriasis, twice daily application has been shown to reduce itchiness, soreness, redness and scaling in up to 35% of patients. Emollients with higher levels of white soft paraffin are more effective, but because they are greasy, they may not be acceptable to patients. In addition to their role in maintaining hydration in stable psoriasis, emollients may help to reduce inflammation when psoriasis is in an inflammatory, eruptive or unstable phase i.e. where a general irritancy to all other topical agents may be present.

Coal tar is recognised as an effective treatment in inducing remission in psoriasis, although its mode of action is unclear. Coal tar may be applied directly to skin, used on the scalp (shampoo) or added to the bath. Crude coal tar extracts are most effective, but are not acceptable to many patients because they have a foul odour, are messy to handle and stain clothes and bedding. Commercially available creams are cleaner but less effective. Coal tar is generally applied twice daily to the skin: in the morning it is left on for 10-15 minutes before being showered off, while at night it is allowed to dry on the skin before going to bed. Coal tar shampoos are effective in scalp psoriasis; they are generally applied once-twice weekly. In the inpatient setting coal tar may be used in conjunction with ultraviolet B (UVB) radiation or with topical corticosteroids (TCS) to improve remission.

Coal tar has been used for many years in psoriasis. It is thought to act by inhibiting DNA synthesis. It is particularly useful for localised plaques in primary care. It may be administered as low dose therapy (0.1%, gradually increasing concentration) which is left on the affected site for up to 20 hours before washing off. Alternatively, higher concentrations (>1%) may be used and left for 30 minutes before washing off. It has been reported to induce prolonged remission. In the inpatient setting dithranol may be applied to more extensive psoriasis areas, using a special non-smudging zinc oxide (Lassar’s) paste which is covered with special dressing left on for up to 20 hours. It may also be combined with UVB radiation to prolong remission.

Adverse effects include severe skin irritation to non-psoriatic skin; patients need to be educated on the importance of avoiding non-affected skin. Dithranol causes temporary staining of the skin and permanent staining to clothes, baths etc, therefore acceptability may be a problem.

Vitamin D Analogue treatments act by inhibiting epidermal cell proliferation and enhancing cell differentiation. They are regarded as a mainstay of treatment for plaque psoriasis. They are available as ointments, creams or solution for once/twice daily application. Improvement becomes apparent within 2 weeks. Treatment should continue for at least 6-8 weeks; some patients may be continued on maintenance treatment. Calcipotriol (available as 50mcg/g cream and 50mcg/ml solution) is reported to be more efficacious than calcitriol (available as 3mcg/g ointment) but calcitriol is less irritant. These agents may be combined with TCS to improve response and reduce the dosage and duration of each treatment, especially TCS. They may also be combined with oral psoriasis therapies and phototherapy.

Adverse effects. These agents are irritant to perilesional skin, causing redness, soreness, peeling and pruritus in up to 35% of patients during the first weeks of treatment; the face and flexural areas are particularly vulnerable. Although this is usually self-limiting, it may require a break in treatment. As calcitriol is less irritant than calcipotriol, it may be possible to use calcitriol in the more sensitive areas. Vitamin D analogues do not appear to interfere with calcium metabolism; there is a risk of hypercalcaemia only if the maximum dose is exceeded (>100g cream/week or >60ml solution/week for calcipotriol; >30g/day for calcitriol).

Topical corticosteroids (TCS) have anti-inflammatory, immunosuppressive and antiproliferative activities. Short-term studies have confirmed the efficacy of TCS in psoriasis. They have a rapid onset of effect and the availability of different strengths (from the very mild 1% hydrocortisone to the super potent 0.05% clobetasol propionate) allows titration of the potency commensurate with the individual patient’s disease. [See NMIC bulletin on Eczema 2007; Vol 12: 5, for information on potency of TCS]. There is no evidence that twice daily application is more effective than once daily use. TCS are useful for limited areas of psoriasis especially if non-affected skin (BSA) involved >10% (where the outstretched hand, including digits = 1% BSA), or PASI >10 or DLQI >10.15
on the face and in flexural areas where mild strengths are sufficient. Potent TCS are useful in the initial treatment of psoriatic lesions on hands, feet and scalp (which are often difficult to treat); such use should be reviewed every few days, with the aim of reducing potency as soon as possible. TCS can be used in combination with any of the other topical agents; these combinations should be tried before deciding to abandon topical therapy altogether. Adverse effects. Tachyphylaxis (tolerance of effects with ongoing treatment) has been reported after 4 weeks’ use of the more potent TCS and rapid relapse / rebound flares-up have been seen on discontinuation of such treatment. Guidelines recommend that potent TCS should not be used regularly for >7 days and should be kept under constant review. Chronic usage also results in thinning and telangiectasia of the skin. Systemic effects (such as Cushing’s Syndrome; suppression of the hypothalamic-pituitary axis) may occur if there is chronic usage on large areas of the body.

Topical retinoids. Tazarotene acts by reducing the high rate of epidermal keratinocyte proliferation in psoriasis. Studies have shown a dose-related effect in 60-70% patients with plaque psoriasis treated for up to 12 weeks. Tazarotene may also be combined with other topical therapies, such as TCS or vitamin D analogues to improve response and reduce the dosage of each treatment. Adverse effects. Tazarotene causes dose-related erythema, pruritus and burning of the skin in 10-25% of patients. All retinoids are teratogenic; its use is contraindicated during pregnancy or in women of child-bearing potential without adequate contraceptive measures because of the risk of systemic absorption.

PHOTOTHERAPY / PHOTOCHEMOTHERAPY

UVB phototherapy is used to treat patients who are refractory to topical therapies or who have widespread disease. Narrowband UVB radiation is more efficacious and safer than broadband UVB phototherapy. Dosage is individually titrated and used under specialist supervision (usually used 2-3 times weekly). It may be combined with any of the above topical therapies to improve response and prolong remission. Adverse effects include burning of the skin and photoageing. There is a potential risk of skin cancer with increasing cumulative dosage, although a recent review of 25 years’ of use of UVB phototherapy did not show a significant increase in skin cancers within the review period.

PUVA photochemotherapy combines the use of a topical or oral photosensitiser (psoralen) with UVA radiation therapy. Results have shown that this is an extremely effective treatment with a significant duration of remission. Adverse effects include severe nausea and headache during treatment (mainly due to oral psoralen). Skin burning, photosensitivity and photoageing are also reported with use. There is a concern that treatment carries an increased risk of skin cancers, especially in fair-skinned individuals who have received >250 treatments.

PHARMACOLOGICAL MANAGEMENT: SYSTEMIC THERAPIES

Systemic agents are generally reserved for patients who have not responded to an adequate trial of topical therapy / phototherapy or who cannot tolerate these therapies. They are usually prescribed under specialist supervision. Before they are prescribed, it is important to check the patient’s immune status and to look for the presence of hepatitis or other liver disease or other co-morbidity that might restrict the use of these second-line agents. Each treatment has a clearly identified toxicity profile, therefore the patient must be educated on the need to take as directed and to report any toxicity. Oral corticosteroids should not be used in the management of psoriasis; they can result in a rebound effect leading to generalised pustular psoriasis.

Oral systemic therapies

The oral systemic therapies currently used for psoriasis are outlined in Table 2.

Table 2 Oral Systemic Therapies for Psoriasis

<table>
<thead>
<tr>
<th>Drug*</th>
<th>Clinical Uses</th>
<th>Dosage Regimen</th>
<th>Adverse Effects</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (immuno-suppressant)</td>
<td>Refractory psoriasis erythrodermic / general pustular psoriasis</td>
<td>2.5 – 22.5 mg once weekly **</td>
<td>Nausea very common Bone marrow suppression Hepatotoxicity Liver fibrosis (when cumulative dose &gt; 1.5g) Drug interactions Teratogenicffects spermatogenesis</td>
<td>Regular FBC, LFTs and U&amp;E (weekly initially) Ensure adequate contraception (males and females) Measure type III procollagen quarterly after dose &gt; 1.5g</td>
</tr>
<tr>
<td>Ciclosporin (immuno-suppressant)</td>
<td>Severe cases of chronic plaque psoriasis [and other types] Rapid onset of effect</td>
<td>2.5-5mg/kg/day [titrate dose] Blood level affected by many interacting drugs (Duration 6-9 months)</td>
<td>Renal dysfunction and hypertension [dose and/or duration – dependent] Raised bilirubin Multiple drug interactions</td>
<td>Regular U&amp;E, LFTs and BP monitoring; Avoid other nephrotoxic drugs</td>
</tr>
<tr>
<td>Acitretin (Vitamin A analogue i.e. not immuno-suppressant)</td>
<td>Particularly useful for erythrodermic / pustular psoriasis. Can be used with UVB and in patients with HIV/cancer</td>
<td>25-50mg/day [titrate dose] (Duration 6-9 months)</td>
<td>Teratogenic++ (contraception needed for 2 years post treatment) Skin dryness common Raised lipids Skeletal abnormalities</td>
<td>Ensure adequate contraception Regular testing of lipids and LFTs Skeletal evaluation as appropriate</td>
</tr>
</tbody>
</table>

**Please check the Summary of Product Characteristics (SPC) for complete information on each medicine **

Methotrexate is regarded as a mainstay of treatment for suitable patients. It is important to undertake weekly blood tests (see table 2) in the initial phase of treatment. As most serious / fatal problems are due to an absolute or relative overdosage, patients should be given clear instructions on how to take the weekly dosage regimen (strength and number of tablets, day of week to be taken).
Long-term treatment (>1 year) is possible, but there is a risk of liver fibrosis when the cumulative dose reaches 1.5g. It is recommended to monitor type III procollagen levels (marker for liver fibrosis) regularly with prolonged usage.

**Ciclosporin** exerts its effects within 2 weeks. However, it potentially interacts with many drugs and substances that are metabolised by the cytochrome P450 system. Moreover, its long-term usage is restricted to 6-9 months due to the development of renal dysfunction and hypertension.

**Acitretin** is non-immunosuppressive, therefore it can be combined with other modalities such as phototherapy. However, because it is teratogenic adequate contraceptive measures must be maintained in users for up to 2 years post discontinuation of treatment. Usage is usually restricted to 6-9 months’ treatment.

** Biological systemic therapies**

These are immunosuppressive agents, designed to selectively interfere with the immune mechanisms that induce psoriasis. Their use is restricted to the treatment of moderate – severe psoriasis which has failed to respond to systemic therapies (and/or phototherapy) or where such treatments are contra-indicated or not tolerated. Clinical studies have shown significant improvement (as measured by PASI and Quality of Life scales) compared with placebo at 10-16 weeks. There are no studies comparing the relative efficacy of these agents and limited comparative data with oral systemic therapies. They are currently authorised for use under specialist supervision only. There are 2 main types:

**Anti-TNF-α agents** bind to tumour necrosis factor (TNFα), a cytokine involved in inflammatory processes. **Etanercept** is administered by S/C injection twice weekly; **infliximab** is administered by I/V infusion at weeks 0, 2, 6 and then every 8 weeks; **adalimumab** is administered by S/C injection every other week, starting one week after an initial loading dose. Adverse effects include administration site reactions (and acute infusion reactions for infliximab). Serious infections, including tuberculosis (extra-pulmonary or miliary), sepsis and other opportunistic infections have been reported with use of these agents; all patients must be evaluated for latent tuberculosis prior to treatment and use should be discontinued if the patient develops a serious infection. There have also been reports of worsening of congestive heart failure, rare reports of demyelinating disorders (optic neuritis and multiple sclerosis) and the development of autoantibodies and anti-treatment antibodies. The significance of these is unknown; it is recommended that patients be monitored for signs of autoimmune disorders when using these agents. There have been rare reports of the development of lymphoma with use of these agents.

**Efalizumab**, a monoclonal antibody, binds specifically to a leukocyte cell surface protein; this alters the activity of T lymphocytes and inhibits the immunologic cascade. It is administered as a weekly S/C injection.

Adverse effects include a flu-like syndrome occurring in the first 2 weeks of treatment and uncommonly thrombocytopenia; **platelet counts should be monitored.** Patients may experience a flare up of psoriasis that can be managed by topical therapy. However, in 5% of patients this may be severe, requiring discontinuation of therapy and use of another form of systemic therapy; this reaction is more likely to occur in non-responders. Because of its mode of action, efalizumab may also increase the risk or severity of infections and reactivate latent chronic infections such as tuberculosis; it is not yet known whether or not efalizumab can increase the risk of lymphoproliferative disorders or other malignancies in psoriasis patients.

**SUMMARY**

Figure 1 outlines the treatment plan for management of psoriasis in primary care. **Referral for expert dermatological opinion** is recommended when psoriasis (1) is severe, (2) is troubling to the patient, (3) has failed to respond to / is intolerant of adequate topical therapy or (4) presents as erythroderma or generalised pustular psoriasis (may need emergency intervention).

**Figure 1. Treatment Plan for Psoriasis in Primary Care**

Evaluate extent and degree of disease in the patient

If mild to moderate

**Topical Therapies**

<table>
<thead>
<tr>
<th>Trunk and Limbs</th>
<th>Face, Flexural / Genital Areas</th>
<th>Scalp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollients plus • Topical monotherapies (coal tar; dithranol; vitamin D analogues; TCS) • Topical combination therapy if refractory disease or to reduce dosage</td>
<td>Emollients plus • Mild potency corticosteroids • Calcitriol (used with caution)</td>
<td>• Coal tar shampoo 1-2 times weekly • Calcipotriol lotion / corticosteroid cream if not cleared by tar shampoo</td>
</tr>
</tbody>
</table>

If no response to treatments or if psoriasis is severe

Refer for dermatological opinion:(Patients with erythroderma or generalised pustular psoriasis require urgent referral)

Despite the development of newer agents such as the biological therapies, psoriasis remains an incurable disease that affects each patient differently. Maintenance of long-term control with satisfactory quality of life is the goal of treatment for each patient. The vast majority of patients will be managed by topical therapies in primary care. In order to ensure compliance, the patient must be included as a partner when drawing up the treatment plan.

**List of references available on request. Date of preparation: January 2008**

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. Prescribers are recommended to refer to the individual Summary of Product Characteristics for specific information on a drug.
References for bulletin on Management of Psoriasis in Primary Care (Volume 13: 6: 2007)

27. Retinoid drugs have a place in the treatment of psoriasis but pregnancy is an absolute contraindication to their use. Drugs & Ther Persp 2002; 18: 11-15
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