

BIOLOGIC THERAPIES IN PSORIASIS: THE KEY ROLE OF THE DERMATOLOGY NURSE SPECIALIST

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Biologic drugs are an important new advance in the treatment of psoriasis and the dermatology nurse specialist has a key part to play in managing the treatment of psoriasis patients with these new therapies. Guidelines drawn up by the British Association of Dermatologists (BAD) prioritise the role of the specialist nurse by stressing that, with the appropriate training and support, dermatology nurses can play a pivotal part in all stages of psoriasis management with biologics, from initial patient screening through to treatment administration and monitoring (Smith et al, 2005): 'Safe prescribing of biologic therapies requires good infrastructure and specialist nursing personnel. With additional training, a nurse may take responsibility for a number of the tasks outlined in the patient pathway including screening, treatment administration, patient education, prescription coordination for home drug delivery, patient support and monitoring and data collection.'

This supplement aims to outline how, by taking steps to enhance their existing knowledge of new biologic therapies, and gain further experience and confidence in the practical skills needed to administer them, more specialist nurses can fulfil this key role envisaged by the BAD.

Immunology, psoriasis and biologics Immune inflammatory responses – what goes wrong in psoriasis?

The immune system performs two key roles which are crucial to our survival. While it is designed to recognise and ignore body tissues as 'self', foreign substances, also known as antigens, are flagged up as 'non-self' and targeted for destruction. The immune system also

functions as an internal surveillance system, seeking out foreign cells (such as cancer cells), recognising them as 'non-self' and rejecting them. All these tasks are achieved through a complex network of specialised organs, cells and molecules. One group of cells which play a particularly vital role in psoriasis are the cytokines. These are protein messengers which stimulate fellow immune cells, including T-cells, helping to recruit them into the skin and causing increased immune activity and inflammation.

Inflammation is a key event in the immune response. It acts as an alarm, launching a chain of coordinated immune reactions that ultimately result in elimination of the offending agent and repair of the damaged tissue. Inflammation can be set off by various biological, chemical or physical trigger factors that cause tissue irritation or harm. Overall, the inflammatory response can be thought of as a five-step cascade of processes:

- ▶▶ Step 1: the blood vessels swell and start to leak (*Figure 1*). This results in increased blood flow to the skin, causing the redness seen in psoriasis and giving immune cells and chemical messengers easy transport to the area of inflammation
- ▶▶ Step 2: once the blood vessels have become more permeable, immune cells can leave the vessel and travel to the inflammatory site
- ▶▶ Step 3: upon arrival at the affected area, the immune cells release cytokines and other chemical mediators that amplify the response by enlisting other cells to join with them. It is this recruitment drive which accelerates the overall inflammatory process
- ▶▶ Step 4: at this stage, T-cells take over

and initiate a cascade in cytokine production. This then starts a cycle that causes more T-cell activation and further cytokine production. At this point, in psoriasis, the whole inflammatory process is growing and enlarging in the skin (*Figures 2,3*)

▶▶ Step 5: in healthy individuals, the inflammation eventually resolves once the threat or injury passes. However, in psoriasis patients the inflammatory processes remain ongoing and progresses with redness and thickening of the skin (Marieb, 2004).

What goes wrong in psoriasis is a failure to 'switch off' the inflammatory processes occurring in the skin. The balance of inflammatory cytokines is skewed (*Figure 4*), meaning that the response is not dampened down as normal and the inflammation instead carries on chronically. Failure to deactivate cytokines perpetuates inflammation, and their enduring presence in the skin leads to the tissue destruction which characterises chronic inflammation.

But what causes this process to start in the first place? It is now widely accepted that psoriasis arises from an 'autoimmune' reaction where the immune system mistakenly recognises the body's own cells as foreign. In effect, a false alarm is then sent to the skin cells to communicate that they have been 'damaged', setting in motion an ongoing process of accelerated and active repair that causes psoriasis (*Figure 5*) (Lebwohl, 2003; Bonish and Nickoloff, 2005).

TNF-alpha – the key disease driver

One particular cytokine, known as tumour necrosis factor alpha (TNF-alpha), has been pinpointed as a key problem in psoriasis. Patients possess

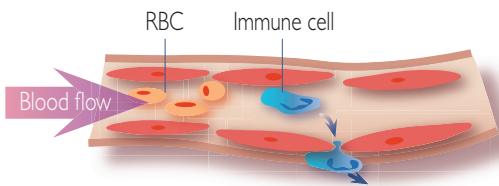


Figure 1. Blood vessels leak immune cells.

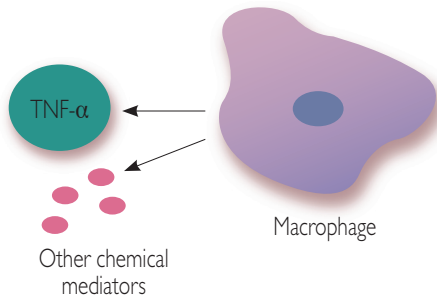


Figure 2. Immune cells release cytokines to attract T-cells.

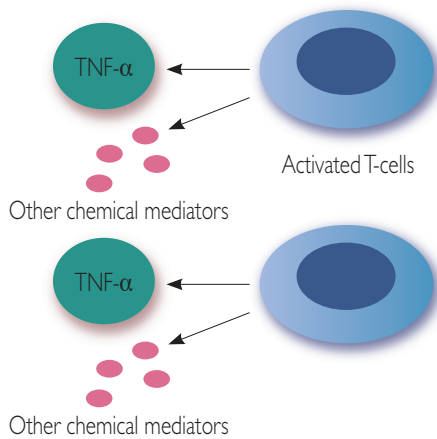


Figure 3. T-cells initiates cytokine production.

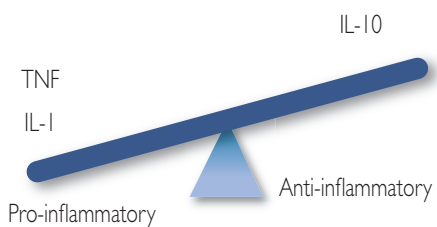


Figure 4. Imbalance of inflammatory molecules remains in psoriasis.

an excess of this potent chemical messenger, which triggers cells to cause inflammation and activate other immune cells, including T-cells, leading to an overall ramping up of immune activity in the body. In psoriasis sufferers, TNF-alpha is not switched off and its production is

not properly controlled so it continues to drive inflammatory processes, causing a cycle of ongoing chronic inflammation and tissue damage (Lebwohl, 2003; Bonish and Nickoloff, 2005).

There is now ample evidence to support the central role of TNF-alpha in psoriasis. Skin biopsies taken from psoriasis sufferers have actually shown increased levels of TNF-alpha in their psoriatic plaques. Anti-TNF acts by influencing other immune and inflammatory cells. Neutrophils and mast cells are two additional types of inflammatory cells which appear during an inflammatory response such as that seen in psoriatic lesions. Their primary function is to ingest and destroy antigens but mast cells also release histamine which contributes to the redness and swelling seen in psoriasis. T-cells also play a key role in psoriasis by propagating the destructive cycle which occurs at the climax of the inflammatory cascade (see step 4 above).

Immune mediated inflammatory disorders

Psoriasis belongs to a family of diseases known as IMIDs (immune mediated inflammatory disorders). This group of conditions affect different parts of the body but is linked by shared inflammatory pathways. Although their specific causes are unknown, each is believed to result from a 'mix-up' by the immune system which triggers an aberrant immune reaction leading to inflammation. Psoriasis is an IMID and this blanket term also covers rheumatoid arthritis which affects the joints, ankylosing spondylitis which targets the spine and Crohn's disease and ulcerative colitis (UC) which involve inflammation in the gut. As with psoriasis, TNF-alpha is also implicated in the other IMIDs where it imposes an ongoing inflammatory burden at the site of disease. As such, all these IMIDs, including psoriasis, can be effectively treated by therapeutic agents which reduce the levels of this inflammatory protein. Due to their shared underlying pathology, there is an association with greater comorbidity between psoriasis and the other IMIDs. Indeed, one study showed that over 11% of Crohn's disease patients and more than 5% of UC patients also suffer from

psoriasis, compared to only around 1% of healthy individuals (Yates et al, 1982). Psoriasis is also associated with arthritis and 15% of patients with psoriasis also suffer from psoriatic arthritis (Griffiths et al, 2006).

Causes of psoriasis

The causes of psoriasis are not yet fully understood but the disease is thought to stem from a combination of factors – both genetic and environmental. The evidence for a genetic link in psoriasis is strong and a number of studies being carried out worldwide are beginning to identify candidate genes for the disease. It is likely that no single gene is responsible but rather that a person carries a genetic 'tendency' to develop psoriasis which may be triggered into action by outside influences. Some of the key exacerbating factors for psoriasis are (Stevenson and Zaki, 2002):

- ▶▶ Alcohol: excessive alcohol consumption in men is associated with worsening psoriasis

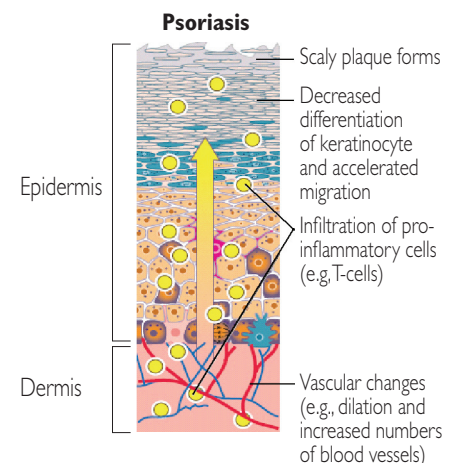
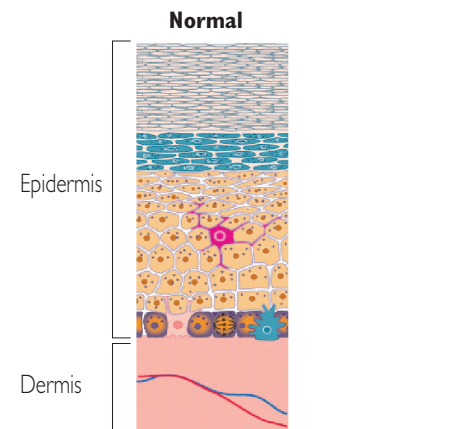


Figure 5. Psoriasis is activated by accelerated repair mechanisms in skin cells.

- ▶ Tobacco: associated with certain forms of psoriasis such as palmar-plantar psoriasis
- ▶ Physical injury: psoriasis tends to appear on the body at sites of physical injury
- ▶ Infection: streptococcal infections have been associated with outbreaks of guttate psoriasis and linked to treatment-resistant forms
- ▶ Weather: although sunlight is beneficial for most sufferers, it can make symptoms worse for patients with sun-sensitive skin
- ▶ Hormonal factors: fluctuating hormone levels, for example around the time of a woman's period or during pregnancy, may have a bearing on female patients' psoriasis
- ▶ Drugs: there are more than 200 drugs which can exacerbate psoriasis. Nurses should be aware, in particular, of those commonly prescribed medications such as beta-blockers, some anti-malarials and bupropion which can make the condition worse
- ▶ Stress: experiencing stress also exacerbates the symptoms of psoriasis.

Early onset psoriasis, which usually strikes in the 20s and causes more severe disease, is associated with a positive family history. In contrast, the other main type of psoriasis, type-II or late-onset, usually appears in a person's fifth decade of life and does not have the familial link. Just as the cause of psoriasis is not clear, no one is conclusively certain of the different mechanisms which occur in the development of psoriasis.

Quality of life

For the several million patients with psoriasis, the condition can have devastating emotional and social consequences. All members of the dermatology team will be used to seeing psoriasis sufferers who report that the disease dramatically affects their quality of life, impacting on morale, relationships and employment. Patients may worry about the negative perception of their disease by others, which can lead to anxiety, stress and low self-esteem. Although patients may be reluctant to discuss it, psoriasis can also impact on sexual activity, especially if a person has

psoriatic joint pain, itching or lesions in the groin. When surveyed, over a quarter of patients aged under 55 reported difficulties with sexual activities. In terms of employment, psoriasis can have a huge effect: the majority of psoriasis sufferers (60% in total), will miss an average of 26 days work per year due to the disease. The financial burden of caring for psoriasis should especially be borne in mind when discussing quality of life concerns with patients with severe disease, those on low income or self-employed patients (Savin, 2003).

To put this important issue into context, the reduced quality of life experienced by psoriasis sufferers is comparable to that of other major chronic conditions, including heart disease and diabetes. Strikingly, patients with psoriasis may even have a lower quality of life than some cancer sufferers (Figure 6) (Rapp et al, 1999).

Taken together, the distressing physical, emotional and social consequences of psoriasis highlight the need for effective pharmacological therapies for this disease. Dermatology teams can use compelling quality of life data, such as that shown above, to emphasise to others the importance of getting severe psoriasis treated. The Dermatology Life Quality Index (DLQI) is a patient-reported outcome measure which nurses regularly utilise to assess the impact of psoriasis on patients' quality of life.

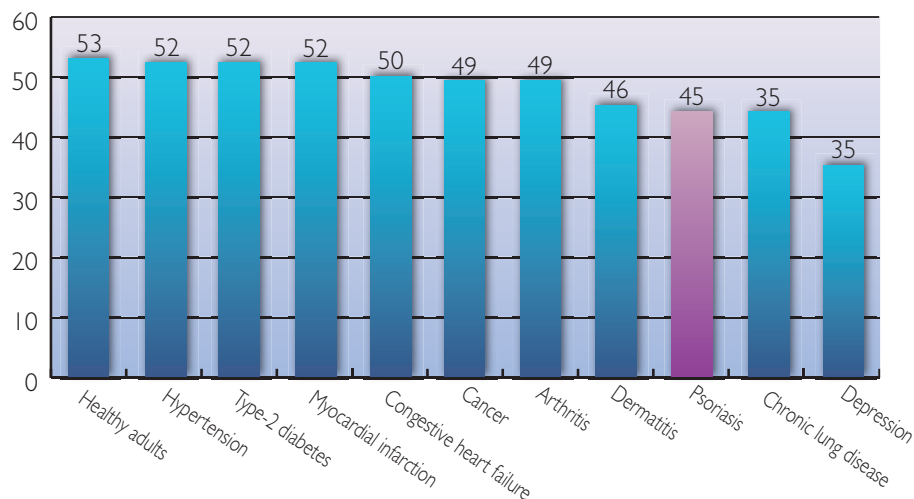


Figure 6. Evidence shows that patients with psoriasis may even have a lower quality of life than some cancer sufferers (Rapp et al, 1999).

While the DLQI measures the psychological impact of the psoriasis on quality of life, there is another measure called the PASI. This is an objective technique used to assess the physical severity of the disease.

PASI (Psoriasis Area Severity Index) scoring Why should healthcare professionals use PASI?

PASI is a more objective measure which is particularly important when using biologics, as patients must reach a certain PASI score before qualifying for treatment. The PASI measure paints a simple picture of psoriasis which nurses can easily understand and use to gauge the effectiveness of new treatments.

Strengths and weaknesses

Thanks to its objectivity, PASI is now regarded as the gold standard tool for assessing disease severity in psoriasis. Before deciding whether to grant a new drug a licence in psoriasis, regulatory watchdogs will look for certain levels of improvement in PASI scores seen in clinical trials. In clinical trials the effectiveness of a drug will be measured upon its ability to reach PASI 75 which is a 75% improvement of the psoriasis. The US Food and Drug Administration demands that new psoriasis drugs achieve a 75% improvement in PASI score (PASI 75) before it will acknowledge the treatment as being sufficiently effective. As well as being a globally recognised tool for describing how bad a patient's psoriasis is, PASI benefits from being systematic,

reproducible and sensitive to change. It is also a relatively simple procedure to perform with sufficient practice.

Despite its strengths, PASI does have some shortcomings. First and foremost, it is only suitable for assessing chronic plaque psoriasis. This means that PASI cannot be used to measure and monitor patients with other forms of psoriasis such as pustular psoriasis. PASI is also focused specifically on the skin symptoms of psoriasis. It does not cover the nail disease which is often associated with psoriasis, nor does it take into account arthritic joint symptoms.

Unlike a personal consultation with a member of the dermatology team, PASI does not reflect the patient's perspective and sheds no light on the impact of disease on patients' quality of life. For this reason, the DLQI is available as an adjunct to PASI to help nurses assess quality of life. It is important to bear in mind that despite being an objective measurement overall, each step in the PASI process relies on nurses' subjective observations. It is therefore important to make sure that colleagues within a team are all in line with each other when it comes to carrying out PASI evaluations and share similar opinions on what constitute severe disease. The PASI equation is (see Figure 8 for abbreviation codes):

$$\begin{aligned} \text{PASI} = & 0.1 \times (\text{Eh} + \text{Ih} + \text{Sh}) \times \text{Ah} + \\ & 0.2 \times (\text{Eu} + \text{Iu} + \text{Su}) \times \text{Au} + \\ & 0.3 \times (\text{Et} + \text{It} + \text{St}) \times \text{At} + \\ & 0.4 \times (\text{El} + \text{Il} + \text{Sl}) \times \text{Al} \end{aligned}$$

Four body areas

The PASI equation may seem daunting at first, but can be broken down into two simple steps. Firstly, calculate how much of a patient's total body area is affected by psoriasis. For the purposes of working out the area, the body is divided into four sections – the head, upper limbs (including the hands), trunk (including axillae and the groin) and the lower limbs (including the buttocks) (Figure 7). This quartet of body sections accounts for 10%, 20%, 30% and 40% of total body area, respectively. Scoring areas can be tricky so a sequential approach is recommended, focusing on each area

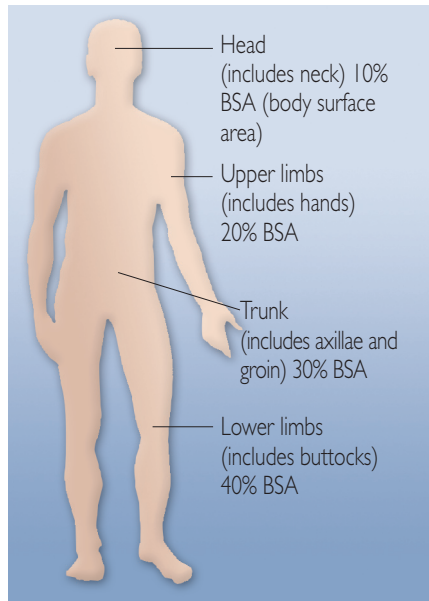


Figure 7. For the purposes of PASI, the body is divided into four sections.

of the body in turn starting with the head. Look at each area alone as 100% and then estimate the amount of area covered by psoriasis as a percentage of this whole. The percentage figure

obtained for each body area should be matched up to the corresponding score on the PASI scoring sheet (Figure 8) and then completed in the relevant box. For example, a patient with psoriasis covering a quarter of their head would have a percentage area of 25% and hence a head area score of 2. A figure 2 should hence be added to the fifth row down in column one of the PASI score sheet.

There are two useful tools at nurses' disposal to help them estimate area. The 'Gestalt' method involves imagining all of a patient's plaques in each area 'bunched up' and then judging how much skin (as a percentage of the total) is diseased versus normal. The Hand Method, as the name suggests, uses the patient's hand as a unit of measurement. Each hand is taken to equate to 1% of the total body surface area (BSA). As the head and neck represent 10% of total BSA they amount to 10 hands, the upper extremities are 20 hands, the trunk is 30 hands and the lower extremities account for the remaining 40 hands. You then

Psoriasis area and severity index (PASI) scoring sheet							
Date:		Patient name:					
Scoring key							
Score	0	1	2	3	4	5	6
Erythema Induration Scaling	None	Slight	Moderate	Severe	Very severe	N/A	N/A
Area %	0	<10	10–29	30–49	50–69	70–89	90–100
Scoring table							
	Head (H)	Upper limbs (U)	Trunk (T)	Lower limbs (L)			
Erythema (E)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
Induration (I)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
Scaling (S)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
Sum (E+I+S)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
Area score	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
Same x Area	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>			
	x0.1	x0.2	x0.3	x0.4			
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	=	<input type="text"/>	

Figure 8. The PASI scoring sheet.

need to work out what each number of hands represents in terms of area involvement for each area.

Once the area has been successfully tallied up, the second step in the PASI process is to assess the individual severity characteristics of the disease. These three signs are redness (also known as erythema), scaling (also called desquamation) and plaque thickness (referred to medically as induration). The severity of each of these signs is rated on a scale of 0–4 where 0 = no symptoms; 1 = mild/slight; 2 = moderate; 3 = severe; and 4 = very severe.

Practical pointers on PASI scoring

PASI is a hands-on skill, which must be practised and perfected over time. Nurses often find that scoring each area can be the hardest aspect to quantify, with a tendency to overestimate the psoriasis coverage. It is a matter of personal choice which area estimation method each member of the dermatology team opts to use when carrying out PASI evaluation. The Gestalt method is straightforward when a patient's percentage area falls in the middle of a PASI score bracket, but for more borderline cases the Hand Method may be required. When using the Hand Method it is important to bear in mind the size of the patient's hand in relation to their overall body area, as this method only gives an accurate result when the psoriasis sufferer is of average relative frame.

When PASI scoring an area of the body containing a clustering of both old and new plaques, it is those plaques seen in the majority which should be scored. Be wary of simply 'averaging out' the severity of the signs, as this will lead to the overall score being diluted.

Similarly, when a patient has a broad range of plaques with different characteristics, the key is to assess the overall psoriasis picture, pull out the common features and score those. Scoring erythema can prove a challenge once the healing process is underway. As such, it is important to learn how to distinguish residual hyperpigmentation from inflammatory psoriasis.

A fundamental part of the PASI process is to note down which systemic therapies a patient is receiving as well as their overall score. This is vital because leaving out this key information may affect a patient's ability to qualify for biologic therapy and lead to them being unjustly excluded. In the near future, PASI scoring is set to become a compulsory process for dermatology clinics using biologic therapy. It will be used both to feed back objective data on patients' improvements to primary care trusts and to allow upkeep of a 'biologics registry' and for entering data into the BAD Biologics Register.

Complications

Patients can experience a number of complications as a result of their psoriasis and dermatology nurses in particular need to be adept at recognising and responding to these potential co morbidities:

- ▶▶ An increased risk of skin cancer is associated with photo chemotherapy (>200 treatments) and as some patients will already have received their full life quota of light therapy an awareness of this risk is important. This danger is compounded by immunosuppressive drug therapy because, as previously discussed, part of the immune system's function is to patrol the body and purge cancerous cells
- ▶▶ Lichen simplex chronicus is a thickened area of skin which results from rubbing and scratching, and frequently coexists with psoriasis. This complication tends to develop mostly in patients who scratch itchy lesions
- ▶▶ Fungal nail infections can also develop in the nails of psoriasis sufferers so nurses should consider clipping patients' nails as a way of diagnosing this problem
- ▶▶ Gout and psoriasis have a well-established relationship and yet gout is often overlooked in the day-to-day dermatology clinic. It is therefore important to check uric acid levels
- ▶▶ Liver impairment is a potential problem with psoriasis drugs such as methotrexate and renal impairment with ciclosporin, hence the need for regular blood monitoring
- ▶▶ Disturbances in lipid regulation are also associated with psoriasis

and it is important to monitor the patients' cholesterol levels. Different lifestyle factors such as reduced physical exercise and excess alcohol consumption can contribute to an increased risk of vascular disease in psoriasis patients.

Biological therapies for psoriasis

Biological therapies or 'biologics' are a new development in the treatment of psoriasis. These specially designed proteins intervene in the immune process to dampen down wayward responses which occur in psoriasis. Two of the biologics currently available, infliximab and etanercept, interfere with the action of TNF-alpha and, by blocking this key offender, remove both the ignition and accelerator which drive the inflammatory reactions responsible for causing and maintaining psoriasis. The third licensed biological therapy, efalizumab, is a recombinant humanized monoclonal antibody that binds specifically to a leukocyte cell surface protein. By this mechanism, efalizumab inhibits the binding of LFA-1 to ICAM-1, which interferes with the adhesion of T lymphocytes to other cell types. By preventing LFA-1 and ICAM binding, efalizumab alleviates signs and symptoms of psoriasis by inhibiting several stages in the immunologic cascade. Most importantly, from the perspective of patients who have failed on a number of other drugs or still have significant psoriasis despite ongoing conventional therapy, biologics offer a new hope for effective treatment. All are delivered by injection, either subcutaneously or intravenously.

Three biological therapies currently hold a licence in psoriasis, where they are all specifically indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients who fail to respond to other systemic therapies including methotrexate, ciclosporin or PUVA (psoralen and long wave ultraviolet radiation), or have a contraindication or are intolerant to these standard treatments. Efalizumab (Raptiva [Serono, Feltham]) is indicated for psoriasis alone, whereas etanercept (Enbrel [Wyeth, Maidenhead]) and infliximab (Remicade [Schering Plough, Welwyn Garden City]) can be used to treat both the skin symptoms of the disease and psoriatic arthritis

(Electronic Medicines Compendium, 2006a,b,c).

Efalizumab

Efalizumab is a monoclonal antibody (specific for only one type of antigen) that binds to a key communication and transport molecule on T-cells known as LFA-1. In this way, efalizumab interferes with T-cells' ability to travel to their site of attack in the skin and also stubs out their communication channels with other immune cells. This prevents T-cells from becoming activated in the first place and stops them from being regenerated once spent (Jullien et al, 2004).

Etanercept

Etanercept is a genetically engineered (recombinant) protein that mimics the natural soluble receptor for TNF-alpha in the body. It therefore binds reversibly to TNF-alpha molecules and prevents them from docking with, and activating, their target receptors on the surface of skin cells. In this way, the TNF-alpha is prevented from sending its usual inflammatory messages into the cells (Electronic Medicines Compendium, 2006a). It is important to note that etanercept can and is intended to be used as intermittent treatment.

Infliximab

Infliximab is a chimeric monoclonal antibody that binds to TNF-alpha with high affinity and good specificity so it does not interfere with the working of other non-psoriasis-related cytokines. Importantly, infliximab also clasps onto its target TNF-alpha molecules with high avidity, meaning that it does not later release these agents and allow delayed activation of the target cells. Due to its structure, infliximab is also able to capture multiple TNF-alpha molecules, joining forces with other infliximab antibodies to form a complex. The fact that infliximab is able to bind to all three possible forms of TNF-alpha – the transmembrane, soluble and receptor-bound types – may explain its rapid onset and effectiveness (Electronic Medicines Compendium, 2006b).

Evidence of effectiveness

As biologics have only been introduced into use in dermatology clinics relatively recently, most of the evidence of their

effectiveness derives from clinical studies conducted during their development process. For all of these agents, profound improvements in psoriasis have been seen, far surpassing the benefits usually seen with conventional systemic therapies.

Efalizumab

In clinical studies, around 27% of psoriasis patients experienced a 75% improvement in their psoriasis (PASI 75) after 12 weeks of treatment with efalizumab. Overall, all patients treated with efalizumab achieved significantly better responses than those given placebo. In a longer-term trial of efalizumab carried out for up to two years, the PASI 75 responder rate was 42% (Electronic Medicines Compendium, 2006c; Menter et al, 2006).

Etanercept

One of the key studies which evaluated etanercept in psoriasis looked at the effectiveness of the drug in 672 psoriasis patients. Half of the psoriasis sufferers receiving high-dose etanercept (50mg twice a week) had a 75% improvement in their psoriasis after 12 weeks (PASI 75). In the group of patients receiving the medium doses of etanercept (25mg twice a week), PASI 75 was achieved in 34% of sufferers after 12 weeks and 44% after 24 weeks. Overall, the improvements in skin symptoms seen with etanercept were paralleled by improvements in doctors' overall assessments of their patients' progress and quality of life (Leonardi et al, 2003).

Infliximab

The main trial to assess the efficacy of infliximab was the EXPRESS study which enrolled over 350 patients with moderate-to-severe plaque psoriasis. After 10 weeks of infliximab treatment more than 80% of patients attained at least a 75% improvement in their psoriasis (PASI 75), in addition, up to 60% of patients were almost completely (90%) cleared of their psoriasis. Importantly, this early improvement in psoriasis was maintained for six months, and in some cases up to a year later with what equates to only six infusions per year. The EXPRESS study confirmed that infliximab is generally well-tolerated and has a good risk-benefit balance (Reich et al, 2005, 2006).

Nail psoriasis (as measured by the Nail Psoriasis Severity Index (NAPSI)) also improved considerably with infliximab treatment. Overall, nail disease improved 25% by week 10 on infliximab and 67% after 24 weeks of treatment. This is important as current therapies do little to tackle the nail symptoms of psoriasis.

Guidelines

The BAD has recently drawn up guidelines covering the use of biologic therapy in psoriasis (Smith et al, 2005). The BAD has decided that on the balance of the available evidence, infliximab is likely to be the most effective biologic at 12 weeks, however there are no studies that have directly compared each of the biological drugs against one another. It also states however that we do not have enough evidence yet to know which drug is better in terms of efficacy and safety in the longer term. The National Institute for Health and Clinical Excellence (NICE) recently recommended etanercept and efalizumab for the treatment of psoriasis. A NICE single technology appraisal on infliximab is expected to be carried out in 2007 (NICE, 2006; Smith et al, 2005).

Practical considerations

For nurses, the practical points of biologic use will prove equally as important as the expected benefits. Specialist nurses have a key role to play in controlling the safety and effectiveness of these new drugs by being aware of contraindications, maintaining vigilance for side effects and monitoring psoriasis patients' progress. *Table 1* summarises some of the information on the three psoriasis biologics that dermatology nurses need to be familiar with – including dosage, potential side-effects and contraindications to use (Pearce et al, 2005; Electronic Medicines Compendium, 2006a,b,c).

Administering and monitoring biologics

Dermatology specialist nurses play a central role in the safe prescribing of biological therapies. With additional training, it is possible for them to take responsibility for a number of tasks in the patient pathway including screening, treatment administration, patient

education, prescription coordination for home drug delivery, patient support and data collection, e.g. PASI.

Eligibility

The first step in the successful use of biologics is to ensure that the patients who receive them are eligible. In addition to the licensed indications, the BAD has produced detailed guidelines on the criteria which psoriasis sufferers must fulfil in order to be considered for biologic treatment.

In summary, patients must have (Smith et al, 2005):

- ▶▶ Severe disease defined as a PASI score of 10 or more (or a BSA of 10% or greater if PASI is not applicable) and a DLQI score above 10
- ▶▶ Experienced at least 6 months of

severe psoriasis which is resistant to treatment, plus be a candidate for systemic therapy.

They must also fulfil at least one of the following clinical categories:

- ▶▶ Developed, or be at high risk of developing, clinically important drug-related toxicity where standard therapy cannot be used
- ▶▶ Proved intolerant to or unresponsive to standard systemic treatment
- ▶▶ Have become unresponsive to standard therapy
- ▶▶ Have disease that is only controlled by repeated inpatient management
- ▶▶ Significant unrelated comorbidity which precludes use of systemic agents such as ciclosporin or methotrexate
- ▶▶ Severe, unstable, life-threatening

disease (e.g. erythrodermic or pustular psoriasis)

- ▶▶ Psoriatic arthritis which fulfils rheumatologists' own guidelines (devised by the British Society of Rheumatology) for biologic treatment.

In exceptional circumstances, (for example, disabling acral disease, i.e. disease of the extremities or limbs), patients with severe disease may fall outside this definition but may be considered for treatment.

NICE guidance

NICE has reviewed etanercept and efalizumab for plaque psoriasis (NICE, 2006). Infliximab is being reviewed by NICE as a single technology appraisal in 2007. Etanercept is recommended for the treatment of psoriasis, within its

Table 1

The practical considerations of biologic treatment (Electronic Medicines Compendium, 2006a,b,c)

Practical points	Efalizumab	Etanercept	Infliximab
Administration route	Subcutaneous injection	Subcutaneous injection	Intravenous infusion
Dosing	0.7mg/kg for the first week and 1mg/kg every week thereafter	25mg/kg twice a week for six months Or 50mg/kg twice a week for three months, followed by maintenance doses of 25mg twice per week for a further three months	5mg/kg at weeks one, two and six, then maintenance doses every eight weeks
Contraindications	<ul style="list-style-type: none"> • Hypersensitivity to efalizumab or any of its ingredients • Active tuberculosis or other severe infection • History of malignancy • Any immunodeficiency • Guttate, erythrodermic or pustular psoriasis 	<ul style="list-style-type: none"> • Hypersensitivity to etanercept or any of its ingredients • Sepsis or risk of sepsis • Active infection including TB, chronic or localised infection 	<ul style="list-style-type: none"> • Hypersensitivity to infliximab or any of its ingredients – including mouse proteins • Active tuberculosis or other severe infection such as sepsis, abscesses or opportunistic infections • Moderate or severe heart failure
Most frequently reported side-effects	<ul style="list-style-type: none"> • Headache • Chills • Fever • Nausea • Muscle aches 	<ul style="list-style-type: none"> • Injection site reactions (such as bleeding, bruising, redness, itching, pain and swelling) • Infection – including upper respiratory tract infections, bronchitis, cystitis and skin infections) • Allergic reactions • Pruritis 	<ul style="list-style-type: none"> • Infusion reaction • Headache • Dizziness • Nausea • Abdominal symptoms • Allergic reactions • Rash • Urticaria • Viral infections • Respiratory infections (cold, sinus infections, bronchitis, pneumonia)

licensed indications, administered at a dose not exceeding 25mg twice weekly, only when the following criteria are met:

- ▶▶ The disease is severe as defined by total PASI of 10 or more and a DLQI of more than 10
- ▶▶ The psoriasis has failed to respond to standard systemic therapies including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation); or the person is intolerant to, or has a contraindication to, these treatments.

It is recommended that etanercept treatment should be discontinued in those patients whose psoriasis has not responded adequately at 12 weeks. Efalizumab is provided with a second-line recommendation only if psoriasis has failed to respond to etanercept or they are shown to be intolerant of, or have contraindications to, treatment with etanercept (NICE, 2006).

Patient assessment

Both before, during and after biologic treatment, ongoing and thorough patient assessment is vital. Specialist nurses will be required to step in at various points in the patient care pathway to carry out these key screening and monitoring tasks. At initiation, a full raft of blood tests will be taken to screen for any underlying problems at baseline. The patient should also be screened for TB.

The TB algorithm

Ruling out active or latent tuberculosis (TB) is vital before commencing treatment as biologic therapy can reawaken dormant disease and increase infection risk.

A TB testing algorithm has been devised for this purpose and must be closely followed for all patients. If in doubt, patients should be referred to a chest physician for a complete work-up. As part of the TB testing process, psoriasis patients will need a pre-treatment chest X-ray and Mantoux test. For those patients who are on immunosuppressive therapy, a Mantoux test will not be helpful. An individual risk assessment should also be performed. If the annual risk of TB is greater than the risk of drug-induced

hepatitis, then chemoprophylaxis should be given. If the risk of hepatitis is greater the patient should be monitored regularly with any suggestive symptoms promptly investigated to permit early diagnosis of active disease (Ormerod et al, 2005).

Dermatology nurses will be required to carry out PASI and DLQI scoring at initiation, not only to check that patients fulfil the eligibility criteria for biologic treatment but also to obtain a benchmark score against which treatment improvements can be measured and monitored. Before beginning treatment, it is essential that any patients with contraindications to biologic therapy are identified and ruled out for safety purposes. Nurses will need to take a full history for all patients and should be suspicious of signs of infection such as fever and alert to any potential indicators of cardiac dysfunction such as oedema and shortness of breath.

Key questions to ask patients before commencing biologic treatment include:

- ▶▶ Do you currently have any symptoms of an active infection?
- ▶▶ In the past two weeks, have you experienced any of the following:
 - Fever
 - Night sweats
 - Sore throat
 - Runny nose
 - Face pain
 - Earache
 - Tooth pain
 - Cough
 - Breathing problems
 - Painful urination
 - Blood in the urine
 - Antibiotic use
 - Headache
 - Wound complications.
- ▶▶ Are you experiencing any right-sided abdominal pain, fever or severe fatigue?
- ▶▶ Have you had any recent surgery (recent surgery poses an infection risk and usually requires biologic therapy to be postponed):
 - If so, were there any complications?
 - Did you experience any drainage from your incision?
- ▶▶ Have you had a recent flu vaccine

or other vaccination (live vaccines are contraindicated in people receiving biologic therapy due to the risk of infection)?

- ▶▶ Are you taking any other medications (potential drug interactions must always be borne in mind)?
- ▶▶ Have you had any recent changes in your medical history such as heart failure, haematological or neurological events or malignancies (new medical conditions could constitute a contraindication to treatment)?
- ▶▶ Could you be pregnant (biologics should be avoided in pregnant or breastfeeding women)?
- ▶▶ Have you gained or lost weight since your last treatment (weight affects dosing so adjustment to the previously used dose may be necessary)?
- ▶▶ Did you have any hypersensitivity the last time you received a biologic?
- ▶▶ What was your response to your previous treatment?

Practicalities of infusion administration

Infliximab is given in a hospital environment via intravenous (IV) infusion and is therefore an area of biologic treatment where dermatology nurses have a very important role to play (Table 2). Efficacy and safety optimisation relies on patient treatment and support by healthcare professionals, particularly specialist nursing staff. IV infusion ensures that patients are fully concordant with their treatment and that nurses are present to monitor patients and quickly respond to any problems which may arise, as well as to offer patients reassurance and support during their therapy (Electronic Medicines Compendium, 2006b).

Practicalities of subcutaneous administration

Both efalizumab and etanercept are given by subcutaneous (SC) injection and so can be self-administered at home (Table 2). This may be more convenient for the patient but imposes a number of important practical considerations. Either the psoriasis patient themselves or a carer must be trained on how to

prepare and administer the injections, select the injection site, and be instructed on dosing (once-weekly administration for efalizumab versus twice-weekly for etanercept). Each injection requires approximately 15 minutes preparation and patients need to mix the efalizumab SC solution before administration whereas etanercept is supplied in a pre-mixed syringe. Specialist nurses have an important part to play in educating patients on the use of SC biologics and will be involved in training on injection techniques. Patient instruction DVDs and information leaflets are available from the respective drug manufacturers to support patient training. SC biologics must be stored in a fridge at 2–8°C and sharps disposal will be a necessary consideration, along with arrangements for the disposal of unused drugs. This can all be arranged through a third party healthcare service who has a contract with the drug company, e.g. Healthcare at Home or Clinovia. They will also have nursing support so the patient can be trained and supported at home on injection administration (Electronic Medicines Compendium, 2006a,c)

Injection site reactions

Injection site reactions are among the commonest adverse events encountered with SC biologics. These usually occur in the first month and last on average for 3–5 days. No treatment is usually necessary but topical corticosteroids or oral antihistamines can be used to help patients if required. Some psoriasis sufferers may develop recall injection site reactions where the skin reacts at the most recent injection site, with the simultaneous appearance of reactions at previous injection sites (Electronic Medicines Compendium, 2006a,c).

Dosage

Infliximab is dosed at 5mg/kg so the amount of drug will need to be calculated for each individual patient. Comprehensive dose charts are available which enable the required number of vials of infliximab to simply be read off on each row according to the individual patient's weight.

Monitoring

Monitoring is an essential part of IV infusion of biologic treatment. Infusion

reactions occur in around 8% of patients receiving infliximab and most are mild and easily managed. Nurses will need to monitor patients' vital signs every 30 minutes and watch for signs of infusion-related reactions such as (Electronic Medicines Compendium, 2006b):

- ▶▶ Flushing
- ▶▶ Chest pain
- ▶▶ Hypotension
- ▶▶ Urticaria
- ▶▶ Tachycardia
- ▶▶ Shortness of breath
- ▶▶ Rigor
- ▶▶ Back pain.

If an infusion reaction is observed, the infusion should be interrupted immediately and then restarted at a slower rate. Medical treatments such as paracetamol, chlorphenamine, corticosteroids, adrenaline and oxygen can also be utilised if needed. These drugs should be on standby before beginning the infusion, along with emergency equipment such as resuscitation aids and artificial airways in the unlikely event of a serious reaction. Adding a concomitant medication such

Table 2

The practicalities of intravenous (IV) administration versus subcutaneous (SC) injections (EMC, 2006a,b,c)

	IV administration	SC injection
Frequency of treatment	6–8 times/year (0,2,6, then every eight weeks)	Up to 104 times/year (etanercept) 52 times per year (efalizumab)
Setting	Daytime 'clinic-type' hospital visit	Self-administration by patient or carer at home
Administration	<ul style="list-style-type: none"> • Treatment prepared and administered by trained healthcare professional • Procedure involves IV cannulation • All aspects of treatment handled by hospital • Compliance and dosage guaranteed • Treatment takes up to four hours per visit 	<ul style="list-style-type: none"> • Patient or carer must be willing and able to self-administer • Procedure relatively painless • Patient or carer must be trained in preparation and administration procedures • Patient or carer must adhere to guidelines regarding storage, stock rotation and disposal of sharps/unused drugs • Patient or carer must place regular orders • Treatment takes about 15 minutes total time per injection
Support and back up	<ul style="list-style-type: none"> • Patient can be constantly monitored • Medical equipment/support on hand in case of problems • Regular visits provide opportunity to ask questions about treatment • Regular hospital visits for ongoing monitoring essential 	<ul style="list-style-type: none"> • Patients should have access to helpline • Regular hospital visits for on-going monitoring essential

as methotrexate may reduce potential antibodies to infliximab which may impact on infusion reactions (Electronic Medicines Compendium, 2006b).

Discontinuation of therapy

In certain cases, biologic therapy may have to be withdrawn, if severe drug-related toxicity develops. Therapy will also be withdrawn in cases where a patient fails to achieve a sufficient response within three months as indicated by PASI 75 scores or PASI 50 scores plus a five-point reduction in DLQI (NICE, 2006). Temporary withdrawal of biologic therapy is advisable during pregnancy, for severe intercurrent infection, for surgical procedures and for certain vaccinations.

Patient counselling

The BAD has highlighted that specialist nurses have a vital role to play in patient education and support. People with psoriasis may have a number of questions about the pre-treatment tests and criteria for biologic therapy and, with a sound knowledge of the medical reasons underlying these protocols, nurses can help explain these to patients.

All patients on biologics will also be provided with a package leaflet and an 'alert card' documenting drug dosage, with an emergency contact number. Nurses need to advise all their patients to be alert to the signs of potential infection, a possible side-effect of biologic therapy. Patients may express worry and fear over potential side-effects so part of the dermatology nurse's role is to offer reassurance, whilst emphasizing the importance of seeking medical help and reporting any symptoms suggestive of infection. In particular, patients should be encouraged to look out for possible indicators of TB – persistent cough, wasting/weight loss and low-grade fever. As the different routes of biologic administration each have their own features and considerations, patient choice should be a factor in deciding on the biologic treatment approach.

Conclusion

The BAD guidelines place considerable emphasis on ensuring that the

framework and infrastructure are in place to provide safe prescribing of biologics, and dermatology nurses are the keystone in this structure. From assessing eligibility, reassuring and monitoring patients during biologic administration and carrying out PASI scoring to help clinicians measure improvement, specialist nurses rank as one of the most important propriety groups within dermatology when it comes to the use of new biological therapies for psoriasis. **DN**

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Key Points

- » Biologic drugs are an important new advance in the treatment of psoriasis.
- » Psoriasis belongs to a family of diseases known as immune mediated inflammatory disorders.
- » The causes of psoriasis are not yet fully understood but the disease is thought to stem from a combination of factors – both genetic and environmental.
- » Specialist nurses have a vital role to play in patient education, treatment and support.