

## Drugs that may exacerbate psoriasis

**D**uring the last 30 years, much has been written about the factors which will precipitate a recurrence of psoriasis. These include infection, HIV, trauma, pregnancy and drugs.<sup>1,2</sup> *This review concentrates on those drugs which have been clearly shown, or are widely reputed, to make psoriasis worse. There is insufficient clinical evidence to justify the inclusion of many drugs which have been included in published lists of drugs said to exacerbate psoriasis.*

### Defining flare

It is important that clinicians understand what they mean when they say that something exacerbates psoriasis. Technically, this situation would occur if the drug makes the patient worse than they were initially. *The idea of a terrible case of psoriasis relapsing back to the terrible state that it was in, is not within the definition of flare and the term should not be used. It is unrealistic to think that any drug, once it wears off, will do anything other than allow the psoriasis to revert back to its original state.*<sup>3</sup>

### Lithium<sup>2,4-8</sup>

It has been recognized for at least twenty years that lithium can exacerbate psoriasis.<sup>9,10</sup> When polled, a substantial number of the Editorial Advisory Board polled were in agreement that lithium is the one drug which causes the most problems,<sup>3,11</sup> and its use often makes it difficult to control the patient's psoriasis.<sup>3,12</sup> It may even cause pustular or erythrodermic psoriasis in a significant proportion of affected patients. *Lithium does not aggravate a pre-existing psoriasis in all cases,<sup>6,7</sup> and therefore is not contraindicated in all patients with psoriasis.*

- *When there is a clear relationship between lithium treatment and the patient's psoriasis, it is advisable to confer with the psychiatrist<sup>6</sup> and discuss the possibility of lowering the dose.<sup>6,12</sup>*
- *When this is not possible, switch to another drug and then the psoriasis can be managed more successfully.<sup>3,6</sup>*
- *If the lithium carbonate cannot be replaced successfully, we end up having to use more potent treatments on the psoriasis.<sup>6</sup>*

### Corticosteroids

Even though oral corticosteroids are impressively effective, their use should be avoided in the treatment of psoriasis because of the *rebound* that invariably follows their use.<sup>2,3,5,7,8,13</sup> In some cases, the flare-up may be even worse than the original attack.<sup>6</sup>

### Beta blockers

Reports suggesting that beta blockers can make psoriasis worse first appeared more than twenty years ago.<sup>14</sup> However, dermatologist's experience with beta blockers varies and their role in exacerbating psoriasis is not nearly as clear cut as it is for lithium. One dermatologist consulted felt that beta blockers almost never worsen psoriasis<sup>11</sup>, others felt that beta blocker treatment may result in a psoriaform rash<sup>6</sup> or the aggravation of an existing psoriasis.<sup>4-8,13</sup>

Beta blockers are not contraindicated in psoriasis. However, when there is a clear relationship between the exacerbation of the psoriasis and the intake of a beta blocker, it could sometimes help to switch from a non-cardioselective beta 2 blocker to a cardioselective beta 1 blocker. If the patient

already takes a beta 1 blocker, it may be advisable to switch to another drug in that class, because they do not cross react.<sup>6</sup>

### **Antimalarials**

Our Editorial Advisory panel were not unanimous as to whether this group of drugs can induce psoriasis *de novo*. One advisor<sup>7</sup> felt that antimalarials can cause pustular or erythrodermic psoriasis in a significant proportion of treated patients, even though not every patient experiences worsening of their psoriasis. Although further study is needed, he pointed out that antimalarials are often used to treat Crohn's disease and that there has been a several fold increase in the prevalence of psoriasis in patients with Crohn's disease. Other Editorial Advisors noted that although antimalarials were reported to exacerbate psoriasis, they were not contraindicated. One Advisor pointed out that rheumatologists have shown that antimalarial drugs rarely if ever precipitate psoriasis, and he personally has never seen antimalarials precipitate or exacerbate psoriasis.<sup>3</sup>

### **Non-steroidal Anti-inflammatory Drugs (NSAIDs)**

There are anecdotal reports suggesting that NSAIDs adversely affect psoriasis, but such a relationship is unproven. One would only consider discontinuing a NSAID if the patient's psoriasis worsened on starting, and improving after stopping that drug.<sup>6</sup> One should not forget that NSAIDs are still useful in treating psoriatic arthritis.<sup>7</sup>

### **Alcohol**

Baughmann *et al* followed up 1200 patients with psoriasis and felt that alcohol exacerbated some patient's disease<sup>15</sup>, as did three of our experts polled.<sup>2,5,8</sup> Poikolainen *et al* found that alcohol intake was a risk factor for psoriasis in young and middle aged men.<sup>16</sup> Consumption of alcohol was found to be less common in females regardless of their psoriasis.<sup>17</sup> Alcohol might be a problem only with higher doses. If we take an iconoclastic approach, perhaps we might say that some patients are too drunk to follow instructions and treat their disease.<sup>3</sup>

### **Topical anthralin and coal tar**

These are simply local irritants<sup>3</sup> and are a problem only when too high a concentration has been used, or when used on irritated, or extensive thick, plaques. Consider this a Köbner phenomenon.<sup>6,13</sup>

### **Other drugs**

ACE inhibitors<sup>2,4</sup> gold salts<sup>5,6</sup> and interferon<sup>3-5</sup> were reported by members of our Editorial Advisory panel as occasional triggers of a psoriatic flare.

### **Drug histories**

We have an aging population and changing treatment patterns. Many of our Editorial Advisors felt that a patient's drug history should be taken.<sup>2,4-8,11,13</sup> This might ascertain not only which drugs, topical and systemic, are being taken, but also exactly how they are being used.<sup>2</sup>

Once psoriasis is triggered, it takes a couple of weeks before the patient becomes aware of the flare-up. Comprehensive drug histories are time consuming BUT we MUST carefully ascertain whether or not the patient has been exposed to lithium. After seeing thousands of psoriatic patients over a period of 30 years, with the exception of lithium, drug-induced exacerbation of psoriasis is not nearly the problem that one would believe.

Dr. John Voorhees

### **Exacerbations of psoriasis in perspective**

*It is very difficult to give general guidelines and the best advice is that the relationship between the intake of any particular drug and exacerbation of psoriasis, is only important when the relationship is clear in your particular patient.<sup>6</sup> For practical purposes, the only major concern involves lithium, and rarely beta blockers and questionably, non-steroidals.<sup>3</sup>*

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# Drug Treatments Introduced in 1998

Of 39 new drugs that gained regulatory approval in 1998, only three (**Miglitol**, Diastabol<sup>®</sup>, Bayer-Sanofi; **Mizolastine**, Mizolen<sup>®</sup>, Synthélabo - Galderma; **thalidomide**, Thalidomid<sup>®</sup>, Celgene) were granted dermatological indications.<sup>1</sup> Late in 1998, as a therapeutic group, when ranked by the number of active research and development projects, dermatologicals ranked 13 out of 17<sup>2</sup>, and when ranked by global sales, dermatological drugs were well down the list in 8th position out of 16.<sup>3</sup> Although there has been no noticeable reduction in the incidence of skin

disease, there have been signs that a number of major pharmaceutical companies have a diminished interest in pursuing new drugs to treat skin disease. Perhaps reallocation of resources may be part of the reason why so few new drugs for skin diseases were introduced in 1998.

*Dr. Stuart Maddin, Editor*

## References

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2. *Phamaprojects*, 1998
3. *IMS Health*, 1998

Indication	Generic / Trade <sup>®</sup> / Company Names	Approval Date
<b>Anti-acne</b>	<b>Adapalene</b> solution 0.1% Differin <sup>®</sup> Galderma	Canada 1995 USA 1998
	<b>Tretinoin</b> gel 0.25% Avita <sup>®</sup> Penederm	Canada 1997 USA 1998
for moderate acne plus contraceptive use	<b>Norgestimate / ethinyl estradiol</b> Ortho Tri-cyclen <sup>®</sup> Johnson & Johnson	USA 1996 Canada 1998
for moderate to severe acne non- responsive to other treatments	<b>Cyproterone acetate/ ethinyl estradiol</b> Diane 35 <sup>®</sup> , Berlex	Canada 1998
<b>Antibacterial</b> for secondarily infected skin lesions.	<b>Mupirocin calcium</b> cream 2% Bactroban Cream <sup>®</sup> SmithKline Beecham	USA 1997 Canada 1998
	Uses include some complicated skin and skin structure infections.	<b>Trovaflaxacin (oral), Alatroflaxacin (IV)</b> Trovan <sup>®</sup> Pfizer
<b>Antifungal</b> for the treatment of T. versicolor	<b>Oxiconazole</b> nitrate Oxizole <sup>®</sup> Stiefel	Canada 1998
		Oxistat <sup>®</sup> Glaxo Wellcome USA 1997

Indication	Generic / Trade® / Company Names	Approval Date
<b>Antiherpes</b> recurrent herpes simplex in HIV patients*; suppression of genital herpes in immunocompromised patients; herpes zoster.	<b>Famciclovir</b> Famvir® SmithKline Beecham	USA 1997, 1998*
supplemental indication for neonatal patients	<b>Acyclovir sodium</b> Zovirax® Glaxo Wellcome	USA 1998
<b>Anti-HPV</b> for genital and peri-anal warts	<b>Imiquimod</b> Aldara® 3M Pharmaceuticals	Europe 1998 USA 1997
	<b>Miglitol</b> Diastabol® Bayer - distributed by Sanofi	USA 1998
<b>Cutaneous T-cell Lymphoma</b> orphan drug status	<b>Denileukin diftitox</b> Ontak® Seragen / Ligand Pharmaceuticals	USA APPROVAL RECOMMENDED
<b>Diabetic ulcer</b>	<b>Becaplermin gel 0.01%</b> Regranex® Ortho McNeil	Canada 1998
<b>Erythema nodosum leprosum</b>	<b>Thalidomide</b> Thalidomid® Celgene	USA 1998
<b>HIV</b>	<b>Abacavir</b> Ziagen® Glaxo Wellcome	USA 1998
	<b>Efavirenz</b> Sustiva® DuPont Pharmaceuticals	USA 1998
	<b>Nevirapine</b> Viramune® Boehringer Ingelheim	USA 1998
(combination formulation reduces the number of tablets required daily)	<b>Zidovudine 300 mg / lamivudine 150 mg</b> Combivir® Glaxo Wellcome	Europe 1998 USA 1997
<b>Kaposi's sarcoma</b> newly encapsulated formulation	<b>Doxorubicin</b> Caelyx® Schering Canada	Canada 1998
<b>Lyme disease</b>	<b>Lyme disease vaccine</b> LYMErix® SmithKline Beecham	USA 1998

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Indication	Generic / Trade® / Company Names	Approval Date
<b>Male pattern hair loss</b>	<b>Finasteride</b> 1 mg tab Propecia® Merck	Canada 1998 USA 1997
<b>Pain relief – topical</b>	<b>Lidocaine / prilocaine</b> cream patch Emla® Astra	Canada 1998 USA 1998
<b>Psoriasis</b> first generic cyclosporin	<b>Cyclosporine liquid</b> Sang Cya® SangStat	USA 1998
in children aged two years and older with mild to moderate psoriasis	<b>Calcipotriol</b> Dovonex® Leo	Canada 1998
<b>Rosacea</b> new dosage formulation.	<b>Metronidazole 0.75%</b> Metro-lotion® Galderma	USA 1998
<b>Skin augmentation</b>	<b>Polymethylmethacrylate</b> Artecoll® Canderm	Canada 1998
<b>Skin substitute</b>	<b>Graftskin</b> Apligraf® Novartis	Canada 1997 USA 1998
<b>Urticaria</b> chronic idiopathic in children 2–5 years New dosage formulation.	<b>Cetirizine</b> Zyrtec® Pfizer	USA 1998
	<b>Mizolastine</b> Mizolen®	<i>Synthélabo co-marketed with Galderma</i>
Germany 1998	<b>UV induced skin discoloration</b> New dosage combination.	<b>Hydroquinone 4% / glycolic acid / antioxidant complex</b>
Lustra® (Viquin Forte® in Canada) Medicis Pharmaceutical	Canada 1998 USA 1998	<b>Vulvar &amp; vaginal atrophy</b>
combined hormone replacement	<b>Estradiol / norethindrone</b> Activelle® (Estracomb® patch in Canada) Novo Nordisk	Canada 1998 USA 1998

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## Update on Drugs

Class	Name/Company	Approval Dates and Comments
<i>Antiviral</i>	<b>Imiquimod</b> Aldara <sup>®</sup> Cream 3M Pharmaceuticals	Approved by the Canadian HPB January, 1999. Imiquimod was approved by the US FDA in 1997 for the treatment of external genital and perianal warts / condyloma acuminata in adults.
<i>Anti-AIDS</i>	<b>Abacavir</b> Ziagen <sup>®</sup> Glaxo Wellcome	Approved by the US FDA December, 1998. Ziagen is a reverse transcriptase inhibitor, taken twice daily without food or drink restrictions. In clinical trials, about 3% of patients experienced a potentially fatal hypersensitivity reaction.
<i>Male-pattern hair loss</i>	<b>Finasteride 1 mg tablets</b> Propecia <sup>®</sup> Merck	Propecia <sup>®</sup> has now been approved by eight EU countries (Denmark, Finland, France, Germany, Italy, Portugal and Sweden), as well as Canada, the US and other countries worldwide.
<i>Lyme disease</i>	<b>Lyme disease vaccine</b> LYMERix <sup>®</sup> SmithKline Beecham	Approved by the US FDA for active immunization against Lyme disease in people aged 15-70. LYMERix <sup>®</sup> contains antigen from the only species of Borrelia burgdorferi found in the US. SmithKline Beecham are also developing a multivalent vaccine for use in Europe to combat several of the most common strains (B. burgdorferi, B. afzeli and B. garinii) found there.
<i>Metastatic Melanoma</i>	<b>Aldesleukin</b> Proleukin <sup>®</sup> Chiron	Approved by the Canadian HPB for the new indication, treatment of metastatic melanoma. This recombinant form of IL-2 is approved in the US for treating malignant metastatic melanoma, and in Canada, Europe and the US for treating metastatic renal cell carcinoma. This drug has been granted Orphan Drug status by the FDA for treating non-Hodgkin's lymphoma and acute myelogenous leukemia.
<i>Varicella Vaccine</i>	<b>Varicella Vaccine</b> Varivax <sup>®</sup> Merck Frosst	Approved in Canada for use in children aged one year and older. This vaccine is already available in the US, Taiwan, Phillipines, Malaysia, Hong Kong and Brazil.
<b>Drug news</b>		
<i>Male-pattern hair loss</i>	<b>Minoxidil</b> Taisho	More than five years after being submitted for approval, minoxidil has been recommended for OTC sale by The Japanese Central Pharmaceutical Affairs Council.

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