Immunomodulatory drugs for psoriasis

BOEHNCKE, Wolf-Henning


DOI: 10.1136/bmj.327.7416.634
PMID: 14500410

Available at: http://archive-ouverte.unige.ch/unige:29674

Disclaimer: layout of this document may differ from the published version.
gender based violence? Should strategies found to be (just) effective in one type of setting be so easily recommended in an entirely different milieu? Concerns over the feasibility and effectiveness of partner notification for sexually transmitted infections in resource poor settings are compounded by the relative lack of specificity of many diagnoses of sexually transmitted infections in these settings. In the absence of highly sensitive and specific diagnostic tools at low cost, providers rely on approaches that may result in relatively high levels of overdiagnosis of sexually transmitted infections, especially in women. Although these approaches may sometimes be justified in public health terms, they should be the basis for recommending management of partners if we are not sure that the individual known as the index patient is truly infected? Partner notification has come a long way since its inception in the 19th century but has much further to go in terms of knowing what is effective in resource poor settings. While many studies concentrate on the issue of effectiveness before considering allocation of resources, it is time to build on the findings of this review and carry out methodologically sound trials to determine what is appropriate and acceptable to individuals in a variety of resource poor communities. This should be the first step in deciding whether partner notification is justified for programmes to control sexually transmitted infections globally.

Sarah Hawkes lecturer
(sarah.hawkes@lshtm.ac.uk)

David Mabey professor
Phillippe Mayaud senior lecturer
London School of Hygiene and Tropical Medicine, London WC1E 7HT

Competing interests: None declared.


Immunomodulatory drugs for psoriasis
New “biologics” offer much promise

With a prevalence of 2-3%, psoriasis is among the most common skin diseases. Clinical hallmarks comprise erythematous plaques covered by silvery scaling and a chronic recurrent course. Psoriasis is now considered an autoimmune disease in which antigen presentation to cutaneous T helper cells triggers secretion of cytokines, causing proliferation of keratinocytes and expression of adhesion molecules on endothelial cells. These attract additional effector T cells from the circulation, which are then activated in an antigen specific manner, leading to secretion of more cytokines and perpetuation of the process.

Although topical treatments are sufficient for many patients, about 20% need additional systemic drugs. All of these bear a considerable potential for serious side effects, such as hepatotoxicity and nephrotoxicity (methotrexate, cyclosporine), teratogenicity (oral retinoids), and cancer (PUVA, which is psoralen and long wave ultraviolet radiation; cyclosporine), which limits their long term use. The limitations of treatments on the one hand and a growing understanding of the pathogenesis of psoriasis on the other have stimulated much interest in the field of immunomodulation for the management of this chronic disease.

Earlier this year the US Food and Drug Administration approved alefacept for use in psoriasis. Alefacept interferes with the activation of T lymphocytes by blocking the co-stimulator CD2 molecule. It also mediates T cell elimination by inducing programmed cell death. Both mechanisms are believed to contribute to the drug’s clinical effectiveness. The availability of alefacept is a major breakthrough in medical and immunological terms. Not only does it prove clinical effectiveness of a strategy rationally deduced from insights in lymphocyte biology at the molecular level, but many contraindications for established systemic treatments do not apply to alefacept, which facilitates its clinical use.

Alefacept can be regarded as the pioneer of a novel class of selective immunomodulatory drugs for the treatment of psoriasis. Since these are either naturally occurring molecules, such as antibodies and cytokines, or modifications thereof, such as soluble receptors or fusion proteins (as in the case of alefacept), they are referred to as biologics. Well over 40 such compounds are being developed for psoriasis, some of which have already been approved by the Food and Drug Administration for other chronic inflammatory diseases mediated by T lymphocytes—for example, rheumatoid arthritis. Given the very similar pathogenesis of these conditions at the molecular level, several of these drugs may prove effective in the management of psoriasis. Evidence supporting this notion is available for infliximab and etanercept, which are both approved for rheumatoid arthritis. These biologics block the effect of the pro-inflammatory cytokine tumour necrosis factor-α (TNF-α) and exhibit profound effects on psoriasis. Infliximab is a humanised monoclonal antibody, whereas etanercept represents the soluble tumour necrosis factor-α receptor. All three drugs allow moderate to severe psoriasis to be managed on an outpatient basis, since they are administered once (alefacept) or twice weekly (etanercept), or just three times overall with intervals of several weeks (infliximab). This convenient dosing...
Comparing cannabis with tobacco—again

Link between cannabis and mortality is still not established

A recent editorial in this journal implied that as many as 30 000 deaths in Britain every year might be caused by smoking cannabis.1 The authors reasoned that since the prevalence of smoking cannabis is about one quarter of the number attributable to smoking tobacco might be about one quarter of the number attributed to tobacco cigarettes (about 120 000). The idea that the use of cannabis increases mortality is worthy of closer examination. How do we assess this issue?

Use of cannabis increases mortality is worthy of closer examination. How do we assess this issue?

The idea that the number of deaths attributable to smoking cannabis might be about one quarter of the number attributed to tobacco cigarettes (about 120 000) is valid because the prevalence of smoking cannabis is about one quarter that of smoking tobacco. The authors reasoned that since the prevalent of smoking cannabis is about one quarter of the number attributable to smoking cannabis might be about one quarter of the number attributed to tobacco cigarettes (about 120 000). The idea that the use of cannabis increases mortality is worthy of closer examination. How do we assess this issue?

Firstly, we need to examine published data regarding use of cannabis and mortality. These data come from two large studies. The first study done in a cohort of 45 450 male Swedish conscripts, age 18-29 when interviewed about the use of cannabis, reported no increase in the 15 year mortality associated with the use of cannabis after social factors were taken into account.2 The second study was performed in a cohort of 65 171 men and women age 15-49, who were members of a large health maintenance organisation in California, United States. They completed a questionnaire assessing their use of cannabis, and reported no increase in mortality associated with use of cannabis over an average of 10 years of follow up, except for AIDS related mortality in men.3 A detailed examination showed that the mortality link between cannabis and AIDS was not a causal one. Thus published data do not support the characterisation of cannabis as a risk factor for mortality.

Secondly, we need to consider the time course of exposure to cannabis and its potential relation to mortality. No acute lethal overdoses of cannabis are

References

1 Asadullah K, Volk HD, Sterry W. Novel immunotherapeutics for psoriasis. 


