several other promising candidate genes, including neuregulin-1 and dysbindin.[12] Interestingly, neuregulin-1 and dysbindin proteins are known to have important roles in neurodevelopment and synaptic functions, like DISC-1.

In addition to deficits in neural development, several aspects of the pathogenesis of schizophrenia have been studied, including dysfunctions of glutamatergic and dopaminergic neurotransmission. Possible environmental factors superimposed on genetic vulnerability include virus infection as well as gestational and birth complications. By studying genetically engineered mice with susceptibility factors such as DISC-1 in combination with environmental stresses, it may be possible to provide a more definitive, integrated model for the pathogenesis of schizophrenia in the future.

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Partner notification for the control of sexually transmitted infections

Effectiveness in resource poor countries is unproved

Partner notification (also termed partner management or contact tracing in some settings) is a well established public health activity in programmes to control sexually transmitted infection.[1] The approach is based on the premise that the sexual partners of people with sexually transmitted infections are likely to be infected but may be asymptomatic and may not otherwise seek care. Partners can be reached through several different strategies including those led by infected "index" patients (patient led), by health providers (provider led), or by a combination of approaches (conditional referral—index patients are encouraged to ensure that partners attend by an agreed date, after which the provider will notify the partner). The public health objectives of each of these strategies are the same: to increase the coverage of care of sexually transmitted infections—by identifying and when necessary treating those people known to be at high risk for sexually transmitted infections [2]; to interrupt the cycle transmission of infection; and to reduce the incidence of new infections and the overall burden of disease. This is the theory. In practice, do partner notification strategies work?

The evidence for the effectiveness of strategies for partner notification has recently been reviewed.[3] This systematic Cochrane review is the first to include studies of partner notification in low income countries—an economic definition, but one that includes many countries where sexually transmitted infections contribute substantially to the overall burden of adult disease.[4] The authors of the review found 11 randomised controlled trials, which compared two or more strategies for partner notification, and only two of these studies had been undertaken in poor countries, both of them in southern Africa. This imbalance raises questions about transferring study findings (and by implication conclusions and recommendations for policies and programmes) to settings far different from those where the original research was undertaken—a concern raised by the authors of the review.

The systematic review concluded that provider led referral (or a choice between patient led and provider led referral) is more likely to result in partners presenting for medical care than patient led referral, and that conditional referral for patients with gonorrhoea is more effective than patient led referral. In addition a slight increase in partners treated was seen in one study, which used nurse led health education and lay counselling as the intervention.

What are the resource and programmatic implications of these findings for public sector health systems in settings that are poor in resources—those, for example, struggling to provide adequate care and attention in an average of well under five minutes per patient? Will providers in such settings really have time to undertake the steps needed to ensure that partner referral programmes are successful? Given the myriad competing concerns on health budgets, are partner notification interventions for sexually transmitted infections likely to be cost effective? Moreover, what are the implications of implementing either provider led or patient led referral programmes in settings of widely different cultural, social, and economic environments from the ones where most studies are undertaken—settings where, for example, there will be highly differential rates of power in sexual relationships[5] or a risk of

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gender based violence?[6] 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.[7] Although these approaches may sometimes be justified in public health terms, should they 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.

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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.[1]

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),[2,3] teratogenicity (oral retinoids),[4] and cancer (PUVA, which is psoralen and long wave ultraviolet radiation; cyclosporine),[5,6] 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.[7] 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 proinflammatory cytokine tumour necrosis factor-α (TNF-α) and exhibit profound effects on psoriasis.[8,9] 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

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