

pigment is found as well as moderate fibrosis located deeper in the dermis compared with untreated tattoos. The tannic acid and oxalic acid combination has a better cosmetic outcome than tannic acid alone.

Many wavelengths are needed to treat multicoloured tattoos, and not one laser system alone can be used to remove all the available inks and combinations of inks. The composition of tattoo ink varies greatly among like-coloured pigments. This may explain differences in response of seemingly similar tattoo ink to laser treatment in different patients.<sup>4</sup> The popular black 'gothic' style tattoo anecdotally appears more difficult to remove by QS nanosecond lasers. The newer QS picosecond lasers, which appear to be generally more effective, may be the answer to laser-resistant tattoos.<sup>5</sup> Side-effects include hypo- and hyperpigmentation, textural change, and scarring. The latter two effects are more commonly seen with the QS ruby than the QS Nd:YAG laser. When seen, scarring or textural changes are subtle and discrete.<sup>6</sup>

The 'Rejuvi Tattoo Remover' technique is being marketed as a safe, simple, cheap, quick and noncolour-selective method of tattoo removal. Only small areas are treated at a time, so the overall cost may not differ greatly from that of a series of standard QS laser treatments. There are no laws regulating this kind of practice and our anecdotal evidence suggests that such a method is not only less effective than laser treatment, but can also result in unacceptable scarring. Tighter regulation and accountability by legislation are needed to protect patients from nonmedical personnel practising cosmetic or medical procedures.

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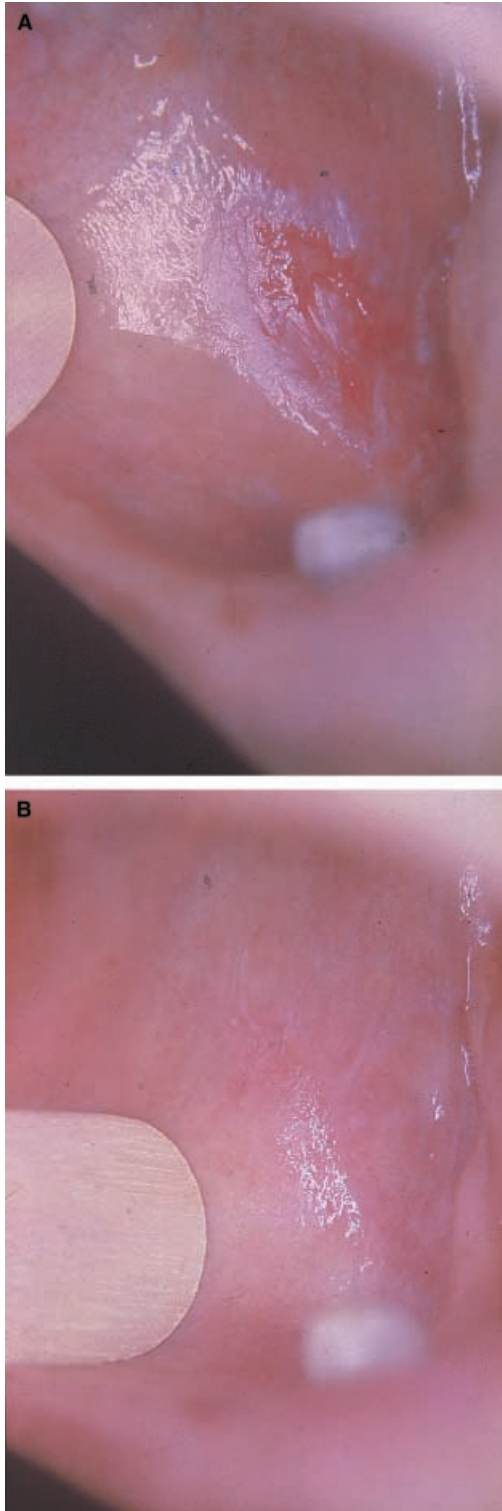
## Treatment of oral lichen planus with topical pimecrolimus 1% cream

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SIR, Oral lichen planus (OLP) is a chronic inflammatory disease that occurs in about 1.9% of the population.<sup>1</sup> No cure for OLP exists. Treatment is focused primarily on reducing symptoms through immune response modulation, mainly using corticosteroids with widely known side-effects.<sup>2</sup> We describe the first three patients with OLP who were managed using topical pimecrolimus 1% cream.

*Patient 1.* A 44-year-old woman was seen in November 2002, with plaques in the mouth and a moderate burning sensation first noticed in January 2002. She had been a heavy smoker for 25 years until 1996, and had received nystatin treatment from April to October 2002. Examination showed white homogeneous and reticular plaques covering the dorsum of the tongue, erosions and scars on the right upper and lower gingiva, and a reticular plaque on the left buccal mucosa. Three biopsy specimens were taken. Two samples established the diagnosis of OLP. One sample revealed hyperorthokeratosis with a slight dispersed chronic inflammatory infiltrate, which corresponded to the white homogeneous lingual plaque. Tests for hepatitis B and C virus were negative. Laboratory analyses were normal. Pimecrolimus cream 1% (Elidel®; Novartis, Mexico) was administered topically twice daily after meals and following oral hygiene; by itself in the morning but with the addition of adhesive denture paste (dilution 1 : 10) at night. Substantial pain relief was reported after the first week of treatment. At 4 weeks, clearance of OLP lesions was observed and all symptoms had resolved, with the exception of three small plaques on the tongue. Based on the previous biopsy and considering the possibility of tobacco-related keratosis, the remaining three plaques on the tongue were removed surgically after 2 months of pimecrolimus treatment; these demonstrated hyperkeratosis microscopically. The patient continued pimecrolimus treatment at night, three times weekly, until April 2003. In May 2003, no recurrences were observed; also, oral candidosis was not detected by exfoliative cytology.

*Patient 2.* A 37-year-old woman with an 11-year history of rheumatoid arthritis was seen in the dermatology department in January 2003, due to recurrent symptomatic OLP. She had first been seen in November 1999 for erosions and ulcerations on the vermilion border of the lower lip, of more than 4 years' duration. Biopsy had confirmed the diagnosis of OLP. Since then, persistent lesions, alternating with short periods (< 3 months) of remission, were observed under different topical therapies (alclometasone dipropionate 0.05% cream, mometasone furoate cream, clobetasol propionate ointment) and sun block protection. During follow-up, she developed chronic anaemia associated with arthritis therapy (azathiopr-



**Figure 1.** (A) Painful erosion and ulceration on right buccal mucosa in patient 3, before topical administration of pimecrolimus. (B) Clinical appearance after 2 weeks of treatment.

ine) and erythematous candidosis on the tongue and lip. Oral candidosis was inconsistently managed by topical antifungals for 6 months. No other significant data were obtained from her medical records. After a brief period without OLP lesions, an erosion on the vermillion border of the lower lip developed in January 2003. Pimecrolimus 1% cream was administered topically twice daily, alternating with sun block protection, for 3 months. Clearance of the erosion was seen after 2 weeks of treatment. After 8 months of follow-up, no recurrences had appeared.

*Patient 3.* A 68-year-old man was first seen at the dental school clinic in May 2003, because of painful bilateral reticular, erosive and ulcerative lesions on the buccal mucosa, which had developed in October 2001 (Fig. 1A). The patient had an 11-year history of partial nephrectomy due to renal lithiasis, controlled hyperthyroid disease (levothyroxine), a strong alcohol habit until 1985 and a slight tobacco habit. In December 2001, oral lesions were managed as candidosis (ketoconazole) and as a complication of anaemia (dietary supplementation). Biopsy from the left buccal lesion established the diagnosis of OLP. Laboratory tests were normal. Hepatitis B and C serological tests were negative. Pimecrolimus was administered topically five times daily from June 2003, using adhesive denture paste occasionally. After 2 weeks of treatment, a marked decrease of symptoms, clearance of the right lesion (Fig. 1B) and reduction of the left lesion were observed. Fifteen days later, after a period of anxiety, minor erosions reappeared on the buccal mucosa. Manifestations of OLP disappeared from the right and left sides after 3 and 5 weeks of pimecrolimus treatment, respectively. No candidosis had developed by September 2003, and he is still under management, without reactivation of OLP.

Tacrolimus and pimecrolimus are among the most promising topical immunomodulating agents.<sup>3</sup> Tacrolimus has been shown to be effective in management of OLP.<sup>4</sup> Pimecrolimus (ASM 981), an ascomycin macrolactam derivative and newer calcineurin inhibitor,<sup>5</sup> is related to tacrolimus and shares the same cellular binding targets and mechanism of action.<sup>6</sup> Pimecrolimus is an inhibitor of T-cell and mast-cell activation, recently approved by the U.S. Food and Drug Administration for treatment of atopic dermatitis,<sup>7</sup> but proposed in other diseases. To our knowledge, pimecrolimus has not previously been shown to be effective in lichen planus. Our patients had lesions confined to the mouth, and experienced rapid remission of their symptomatic chronic diseases.

In summary, this is a primary approach to pimecrolimus as a potential treatment for OLP. More research is needed to evaluate the efficacy of pimecrolimus fully and to study potential inconveniences, as well as to establish its true role in comparison with other treatments for OLP.

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## Cutaneous alternariosis in an immunocompetent patient: analysis of the internal transcribed spacer region of rDNA and *Brm2* of isolated *Alternaria alternata*

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SIR, Although *Alternaria* has recently become recognized as an opportunistic pathogen,<sup>1</sup> alternariosis is rare in otherwise healthy patients.<sup>2</sup> It is still not known whether *A. alternata* isolated as a human pathogen is different from strains in the environment or whether such 'immunocompetent' patients have some as yet undetermined immunological abnormality.

We report a case of cutaneous alternariosis in an otherwise healthy patient. The isolate from the patient was identified morphologically as *A. alternata*. We analysed the internal transcribed spacer (ITS) region and the trihydroxynaphthalene reductase gene (*Brm2*) of the isolate in order to examine if there is some genetic difference between our isolate and strains of *A. alternata* isolated as saprophytes or plant pathogens. The DNA sequence of the ITS region of rDNA is

highly conserved in species and is often used for phylogenetic classification.<sup>3</sup> The analysis of the ITS region is also a useful method for diagnosing species of *Alternaria*.<sup>4</sup> *Brm2* is involved in the melanin synthesis pathway and is known to be useful for identifying species of dematiaceous fungi.<sup>5</sup> Analysis of these two DNA sequences will provide the most reliable answer to this question to date.

A 48-year-old woman was referred because of a reddish plaque on her right knee. Thirteen years previously, she had noticed a small pustule on her right forearm, which had developed into a palm-sized lesion and regressed spontaneously, leaving a scar. She had found a similar pustule on her right knee 2 years before presentation, and the lesion had slowly enlarged. She was tentatively diagnosed as having Reiter's disease and was prescribed ciclosporin and topical steroid by her physician, but the lesion failed to improve. Physical examination revealed a dark-reddish, irregularly shaped indurated plaque with pustules on her right knee (Fig. 1A) and a vermiculate scar on her right forearm (Fig. 1B). She reported mild pruritus and tenderness on the lesion.

Results of laboratory tests revealed normal full blood count and chemistry except for an elevated erythrocyte sedimentation rate (46 mm in the first hour). The results of a tuberculin test were positive, with 10 mm of erythema. No underlying disease was found despite careful examination. Histological examination revealed epidermal hyperplasia and marked granuloma in the dermis (Fig. 1C,D). Grocott and periodic acid–Schiff stains showed round fungal elements in the upper dermis (Fig. 1E). Cottony black colonies were isolated on potato dextrose agar. Microscopic examination of the isolated fungus revealed obpyriform conidia in chains with transverse and longitudinal septa, which is characteristic of *A. alternata* (Fig. 1F). Itraconazole was given, which resulted in almost complete cure in 3 months, leaving a vermiculate scar.

We analysed DNA sequences of the ITS region of rDNA and *Brm2* using previously described methods. Briefly, polymerase chain reaction (PCR) primers for the ITS region were selected so as to encompass the entire ITS region and 5-8S rDNA, and primers for the *Brm2* region were designed to be specific for *A. alternata* and to encompass the entire sequences of the *Brm2* (Fig. 2).<sup>5</sup> The sequences of the ITS region and *Brm2* of the isolate from our patient and other strains of *A. alternata* isolated as saprophytes or plant pathogens were almost identical (the GenBank accession number of the ITS region, which is significantly homologous to those in 64 previously identified strains, mostly with 98% identity, is AB094666, and the accession number of *Brm2*, which has 100% homology to AB015743, is AB094667). PCR of the ITS region of rDNA from cryopreserved biopsy specimens produced a band with the same size as that of the isolate (Fig. 2). The DNA sequence of this PCR product was identical to that of the ITS region of the isolate.

The original reports described alternariosis in 'immunocompetent hosts',<sup>2</sup> although little attention is paid to this