How can I help a patient with severe recurrent aphthous ulceration?

Commentary by
NORMAN A. FIRTH
BDS, MDSc, FRACDS, FFOP(RCPA)

Recurrent oral ulcers can be a difficult clinical problem. What treatments options are currently available?

Case scenario

Recently, a young man presented with a history of severe recurrent aphthous ulceration occurring over the last two or three years. When I saw him, large typical aphthous ulcers were visible on all surfaces of the buccal mucosa. He was unable to eat and had some difficulty with fluids. He had tried all of the usual over-the-counter preparations, and I was at a bit of a loss about what to advise. Should he be investigated further and what treatments can help in this situation?

Dr Firth is Senior Lecturer in Oral Diagnosis and Radiology, School of Dentistry, University of Otago, Dunedin, New Zealand.

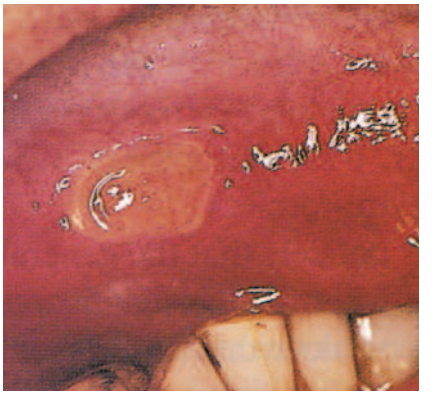

Figure 1. A minor aphthous ulcer.

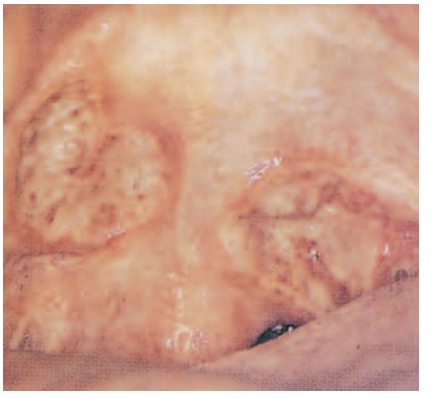

Figure 2. Major aphthous ulceration.

Commentary

There are three categories of aphthous ulceration: minor, major and herpetiform.

Minor aphthous ulcers are by far the most common, accounting for more than 80% of cases. Episodes of recurrent ulceration often begin in childhood or adolescence. The ulcers are typically small (2 to 4 mm in diameter) but may be larger (up to 1 cm). They are usually round or ovoid, clearly defined (often with an erythematous margin), and produce noticeable pain. One or more ulcers may occur on nonkeratinised mucosa, such as the lips, floor of the mouth, buccal mucosa or ventral aspects of the tongue; occasionally, the tip of the tongue is affected. The ulcers heal in five to 10 days.

Major aphthous ulceration occurs in approximately 10% of cases, and patients who develop it often have a history of recurrent minor aphthous ulceration. Major aphthous ulcers often appear first during childhood or adolescence and are accepted to be greater than 1 cm in diameter; rarely, they may be multiple. The ulcers are generally round or ovoid, with clearly defined margins and a yellowish slough, and the periphery is often erythematous. The ulcers may last for over a month, causing severe discomfort, and may heal with scarring. Both keratinised and nonkeratinised oral mucosal sites can be affected.

Herpetiform aphthous ulcers are very rare and consist of many small ulcers (up to 100) that coalesce to produce larger ulcers. This form of aphthous ulceration is more common in females than in males.

Diagnosis

The description in the case scenario that is described above is consistent with a diagnosis of major aphthous ulceration. However, given that 'all surfaces of the buccal mucosa' were affected and that major aphthous ulceration is rare, other diagnoses should be excluded:

- Erythema multiforme is uncommon but does occur in young men – it is

How to make a nystatin–tetracycline mouthwash

- Combine tetracycline hydrochloride (2.5 g), nystatin (2.5 MU) and tragacanth compound, a suspending agent (powder, 2 g), in distilled water (50 mL) and glycerine (100 mL).
- Dispense freshly prepared solution in amber glass. Note that it expires in 7 days.
- Instruct the patient to use 10 mL of the mixture, held in the mouth for 2 to 4 minutes, 4 times daily for 5 days.

episodic in nature and produces extensive shallow ulceration that may include entire buccal mucosal surfaces. The lips are commonly affected and blood crusting on the lips is a characteristic feature. The clinical appearance and a biopsy would confirm the diagnosis.

- Lichen planus is a relatively common disorder of the oral mucosa. Generally, the buccal mucosa is involved – extensive ulceration (although uncommon) may involve the entire surfaces.
- Lichenoid drug reactions are more frequently associated with oral mucosal ulceration than idiopathic lichen planus. The presence of white striae on the buccal mucosa in nonulcerated areas and a biopsy of such an area would confirm the diagnosis.
- Pemphigus vulgaris is a rare condition that typically affects the oral mucosa prior to the onset of skin lesions. Patients generally note the development of new lesions and failure of old lesions to heal rather than recurrent episodic ulceration. Skin lesions generally develop after about six months, so the longer history described in this case would tend to exclude pemphigus vulgaris.
- Mucous membrane pemphigoid generally occurs in elderly women and is therefore unlikely.
- Other causes of oral mucosal ulceration should also be considered, including factitious injury.

Approximately 10 to 20% of patients with aphthous ulceration have an underlying deficiency. Investigations for anaemia as well as folate, vitamin B_{12} and iron deficiencies are warranted for a patient with a significant ongoing problem of recurrent aphthous ulceration.

Patients with Behçet's syndrome may present initially with oral ulceration only, and subsequently develop other manifestations. Patients who are HIV positive may develop aphthous ulceration either for the first time or have more frequent episodes and larger ulcers than they had in previous years.

Treatment

Assuming that the oral ulcers are typical of major aphthae from the history and clinical examination, treatment may include topical corticosteroids, such as 0.05% betamethasone dipropionate ointment or cream (Diprosone, Diprosone OV, Eleuphrat) or 0.1% betamethasone valerate cream or ointment (Betnovate, Celestone). Injection of triamcinolone acetonide (10 mg/mL, Kenacort-A 10) directly into the lesions may be helpful. Nicotine in the form of chewing gum (Nicorette Chewing Gum) or patches (Nicabate, Nicabate CQ Clear, Nicorette Patch) may prove beneficial in reducing the frequency and improving healing time in some cases of major aphthous ulceration.

A combination of nystatin and tetracycline in a mouthwash may reduce secondary infection and is often helpful in resolving persistent ulceration (see the box on page 67). For preventing ulceration or reducing the frequency with which ulcers occur, some patients find a chlorhexidine gluconate mouthwash useful (Chlorhexidine Mouthwash, Plaquacide Mouthrinse, Savacol Freshmint Antiseptic Mouth & Throat Rinse, Savacol Mouth & Throat Rinse); alcohol free preparations are preferable but may not be as widely available as others. In some cases, a benzydamine hydrochloride mouthwash (Difflam Anti-inflammatory Solution) is also effective. Combined preparations of chlorhexidine gluconate and benzydamine are also available (Difflam-C Anti-inflammatory Antiseptic Solution, Difflam-C Alcohol Free Solution).

More recently, systemic administration of thalidomide or azathioprine (Azahexal, Azamun, Imuran, Thioprine) has been shown to be effective in some cases. Thalidomide has been shown to be effective in some HIV-positive patients, and a nystatin–tetracycline mouthwash often brings about rapid resolution of ulceration.

Summary

Recurrent major aphthous ulceration presents the clinician with a difficult problem in terms of ongoing management. Investigation of underlying disease states may be necessary, and a number of treatment strategies may be required. MT