

Review of the current evidence on the diagnosis and management of recurrent aphthous stomatitis

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Recurrent aphthous stomatitis (RAS) is the most common oral mucosal lesions. Aphthous ulcers affect up to 25% of the general population, and a 3-month recurrence rates are as high as 50%. The objective of this study was to highlight the main points that general practitioners (GPs) should take into consideration. There are 3 clinical presentations of RAS: minor, major, and herpetiform ulceration.¹ Minor ulcers are less than one centimeter (slightly less than 0.5 inch) in diameter, and do not leave scars. The sores usually heal within 2 weeks. Major ulcers are almost 0.5 inch or more in diameter, take longer than minor ulcers to heal, and may leave scars. Herpetiform ulcers are clusters of dozens of smaller ulcers. This form is rare. Most patients have only 1-3 ulcers, and some have recurrences only 2-4 times each year (simple aphthosis). Others may have almost continuous disease activity with new lesions developing as older lesions heal, or may have ulcers associated with systemic diseases (complex aphthosis). The RAS is located ulcers in the mouth, usually inside the lips, on the cheeks, or on the tongue. Ulcers are covered with a yellow layer and have a red base, no fever present (in most cases), lesions usually heal in 7-14 days, and lesions tend to recur. The clinical features of RAS that might be noted when the practitioner is examining the patient is shown in **Table 1**.

Most patients feel a tingling sensation in an area of inflammation before an ulcer appears. An ulcer takes 2-3 days to form completely. The exact cause of this disease is not known. There are many predisposing and environmental factors that are thought to be involved with the development of RAS including: hormonal changes, blood problems, such as anemia or deficiencies in iron, folate or vitamin B12, weakened immune system, allergies to food, such as coffee, chocolate, cheese, nuts, and citrus fruits, stress, viruses and bacteria, trauma to the mouth, poor nutrition, and certain medications.¹ Other environmental factors, such as the systemic disease associated with RAS (celiac disease, Behçet's disease, and human immunodeficiency virus associated with RAS) should refer to the appropriate specialists as it is very difficult for GPs to diagnose and manage such diseases.

The diagnosis of RAS is typically established from the history and clinical presentation. However, it is important to differentiate aphthous ulcers from other stomatology mucocutaneous diseases that have

ulcerative manifestations.¹ Usually these conditions can be differentiated from RAS by the location of the lesion, or the presence of an additional symptom. Herpes simplex virus (HSV) infections may have similar appearing lesions, however, primary HSV infections present with a diffuse gingival erythema and fever, preceding oral mucosal vesicles and ulcers.¹ In addition, recurrent HSV lesions are found primarily on attached keratinized mucosa, such as the hard palate or gingiva. Ulcers of RAS are not preceded by fever or vesicles, and they occur almost exclusively on movable oral mucosa, such as the buccal and labial mucosa, tongue, and soft palate. Recurrent aphthous lesions can be differentiated from varicella zoster virus (VZV) infections (shingles) based on clinical presentation (VZV lesions have a unilateral extraoral and intraoral distribution pattern following the trigeminal nerve), and symptoms (VZV infections have a prodrome of pain and burning prior to lesion eruption). Less common oral viral infections, such as herpangina and hand-foot-and-mouth disease should also be included in the differential diagnosis of RAS when initial symptoms occur. However, Coxsackie virus-related oral ulcers present with other symptoms, such as a low-grade fever or malaise, and will resolve within 1-2 weeks.¹ Erythema multiforme presents with painful oral ulcers, however unlike RAS, erythema multiforme lesions occur on both attached and movable mucosa, and usually involve crusting of the lips with skin macules and papules. Approximately two-thirds of the patients with planus show ulcerative lesions, which primarily occur on the buccal mucosa. However, secondary sites on the gingiva and hard palate will distinguish planus from RAS. In addition, planus is not always painful, whereas pain is usually the chief complaint in RAS. Vesiculobullous oral lesions that tend to rupture within hours of occurrence, resulting in painful erosions or ulcerations are characteristic of cicatricial pemphigoid and pemphigus vulgaris. These lesions may occur on both attached and unattached oral mucosa, and a biopsy will reveal a characteristic histomorphometric pattern.

There is no specific management in the treatment of RAS, therefore, many therapies have been tried, and few have been subjected to double-blind randomized controlled study. The aim of the treatment of RAS is to decrease symptoms, reduce ulcer number and size, and increase disease-free periods. The treatment approach should be determined by the disease' severity (pain), the patient's medical history, the frequency of flare-ups, and the patient's ability to tolerate the medication. Some patients that have RAS episodes lasting for only a few days, occurring only a few times a year, are those that need palliative therapy for pain. Chlorhexidine mouthwashes¹ are widely used for the symptomatic

Table 1 - Clinical features of recurrent aphthous stomatitis (RAS).

Type of RAS	Site	Peak age of onset (decade)	Number of ulcers	Size of ulcers (mm)	Duration	Heal with scarring
Minor	Non keratinized mucosa especially labial/buccal mucosa. Dorsum and lateral borders of tongue	Second	1-5	<10	7-14 days	No
Major	Keratinized and non keratinized mucosa, particularly soft palate	First and second	1-3	>10	2 weeks-3 months	Yes
Herpetiform	Non-keratinized mucosa but particularly floor of the mouth and ventral surface of the tongue	Third	5-20 (up to 100)	1-2	7-14 days	No

treatment of RAS and considered helpful by many patients, particularly if oral hygiene is difficult to maintain due to oral ulceration

Drug therapy is considered for patients who experience multiple episodes of RAS each month and/or present with symptoms of severe pain and difficulty in eating. The GPs should determine the possible nutritional deficiencies or allergies causing the onset of the disease before initiating the application of medications for RAS. Kozlak et al² suggested that consuming sufficient amounts of vitamin B12 and folate may be a useful strategy to reduce the number and/or duration of RAS episodes. The traditional treatment of RAS includes glucocorticoids and antimicrobial therapy. These medications have been applied as topical pastes, mouth rinses, intra-lesional injections, and systemically by oral route. Topical anesthetics such as 2% viscous lidocaine hydrochloride is used to palliate the pain. Topical medications are washed away from the target area, therefore it is better to use different kinds of adhesive vehicles in combination with the drug. Topical corticosteroids may limit the inflammatory process associated with the formation of aphthae. Those medications can act on the lymphocytes and alter the response of effector cells to precipitants of immunopathogenesis (such as, trauma, and food allergies). Al-Na'mah et al³ concluded that the novel dexamucobase was found to be equally effective in treating oral aphthous ulceration with some advantages, as the widely used preparation Oralone (Kenalog in Orabase). Babaee et al⁴ evaluated the efficacy of a paste containing myrtus communis (Myrtle) in the management of RAS (randomized controlled trial). Myrtle is a particular herb used in some cultures as treatment for mouth ulcers. This study has shown myrtle to be effective in decreasing the size of ulcers, pain severity, and the level of erythema and exudation, and improving the quality of life in patients who suffer from RAS.

Systemic medication is indicated for severe and constantly recurring ulcerations, and topical

management is not effective in this cases. Pakfetrat et al⁵ conducted a double-blind randomized clinical trial to compare colchicine versus prednisolone (immunomodulant agents) in RAS and reported that low dose prednisolone and colchicine were both effective in treating RAS. Given that the 2 therapies had similar efficacy, yet colchicine was associated with more side effects.

It is recommended that continuous education training of the GPs will increase their knowledge to diagnose and manage RAS because that disease is very common seen in dental clinics and the GPs should be familiar to deal with simple types of RAS such as minor, major, and Herpetiform.

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