



## RECURRENT APHTHOUS STOMATITIS (RAS): GUIDELINE FOR DIFFERENTIAL DIAGNOSIS AND MANAGEMENT

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**ABSTRACT.** *Aim Recurrent aphthous stomatitis (RAS) is a painful and common ulcerative form that can pose a diagnostic challenge. In fact, similar oral ulcers can appear secondary to a variety of welldefined pathological conditions. Thus, the purpose of this work was to update the current knowledge about RAS Methods A narrative review is presented aiming to clarify the extensive differential diagnosis of RAS and its management. Results Clinically, RAS ulcers need to be differentiated from Behçet's disease, nutritional deficiencies, Crohn's disease and ulcerative colitis, PFAPA, MAGIC, HIV and xerostomia-related oral ulcers. A thorough medical history and review of symptoms, in addition to a careful evaluation of any oral feature, will help the clinician understand whether the ulcers are related to a systemic disorder or can be defined as idiopathic. The management of RAS is also challenging and currently there is not a defined treatment for controlling the symptoms. Conclusion As a first aid in relieving the pain, topical applications of corticosteroids, antibiotics, and analgesics are highly recommended, while systemic therapy of RAS should be used in the case of multiple painful ulcerations compromising the quality of life of the patient. Also, natural anti-inflammatory substances from medicinal herbs, in the form of essential oils and extracts are promising agents in the management of RAS.*

**Introduction.** Idiopathic recurrent aphthous stomatitis, also referred to as recurrent aphthous stomatitis (RAS), is a common ulcerative disease of the oral mucosa with a prevalence of 2–10% [Altengurg et al., 2014]. The cause of aphthous ulcers is still unknown, even if many factors are thought to be involved in the disease

[Riera Matute and Alonso, 2011]. Ulcers occur in healthy individuals in childhood, adolescence, or in subjects under 30 years of age, and have the tendency to decrease in severity and frequency over time [Riera Matute and Alonso, 2011]. RAS starts with a typical burning sensation lasting from 2 to 48 hours until an ulcer is formed [Akintoye and Greenberg, 2014]. Typically, RAS is localised on the buccal and labial oral mucosa (Fig. 1, 2), and on the surface of the tongue. It is characterised by the development of painful round shallow ulcers [Edgard et al., 2017]. The necrotic centre of the ulceration is covered by a yellowish-grey pseudo-membrane and surrounded by a reddish edge (Fig. 3). Ulcers have a centrifugal growth and healing is achieved usually within 7–14 days by re-epithelialisation, which starts from the margins [Tarakji et al., 2015; Cui et al., 2016].

**Conclusion.** New pharmacological molecules differently acting from chemicals, able to reduce the inflammation process without side effects to the host, while promoting the wound healing processes are strongly needed. Natural anti-inflammatory substances from medicinal herbs, as in the form of essential oils as well as extracts, can be worthwhile in the management of RAS [Li et al., 2016]. The biological activity of essential oils and polyphenols from plants and herbs is related to the presence of different chemical classes. In this regard, terpenes and terpenoids in essential oils are promising agents in the prevention and treatment of inflammatory and autoimmunity disorders suggesting them as potential chemopreventive and therapeutic agents. Further interesting capabilities have been ascribed to polyphenols from extracts, which molecules include tannins, flavonoids and lignin-carbohydrate complexes strongly associated to anti-inflammatory, antioxidant and antimicrobial properties [Milia et al., 2020; Milia et al., 2021]. The hopeful use of nanotechnology should be a strategy to increase the activity of bioactive natural molecules in the releasing of beneficial and safe substances to treat RAS [Manconi et al., 2018; Pinna et al., 2019]. Although the large evidence of biocompatibility in oral cell lines, adequate clinical trials are still necessary to validate the use of medicinal herbs in humans [Porter and Scully, 2002].

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