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Current concepts in diagnosis and management of oral aphthous ulcers

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Abstract
Recurrent aphthous stomatitis represents one of the most prevalent oral mucosal conditions encountered in dental practice, affecting between two and ten percent of the general population. The condition manifests as painful, recurrent ulcerations that significantly impair patients' quality of life. While the precise etiology remains incompletely understood, current evidence implicates multifactorial pathogenesis involving immune dysregulation, genetic predisposition, nutritional deficiencies, and environmental triggers. Management strategies range from topical corticosteroids to emerging biological therapies. This review synthesizes current evidence on clinical presentation, diagnostic approaches, and evidence-based management protocols for dental practitioners.

Keywords: Recurrent aphthous stomatitis, oral ulceration, oral lesion, immune dysregulation, clinical management, dental practice

Introduction
Recurrent aphthous stomatitis constitutes the most common inflammatory condition affecting the oral mucosa [1]. The condition typically manifests during childhood or adolescence and presents as recurrent, painful ulcerations on non-keratinized oral mucosa [2]. Despite its high prevalence and significant impact on patients' daily functioning, the underlying pathophysiological mechanisms remain poorly defined [1]. Current understanding suggests a predominantly T-cell mediated inflammatory process with contributions from genetic, immunological, nutritional, and microbial factors [2]. Accurate diagnosis requires careful clinical assessment and appropriate exclusion of systemic conditions that may present with similar oral ulcerations [3]. This review provides dental clinicians with an updated, evidence-based framework for diagnosis and management.

Clinical Presentation and Classification
Clinical Subtypes
Recurrent aphthous stomatitis manifests in three distinct clinical forms based on ulcer morphology and distribution [4]. Minor aphthous ulcers represent the most common variant, accounting for approximately eighty-five percent of cases, and present as round or ovoid lesions measuring less than one centimeter in diameter [2]. These lesions typically heal within ten to fourteen days without scarring [4]. Major aphthous ulcers exceed five millimeters in diameter, persist for six weeks or longer, and frequently result in scarring upon resolution [5]. Herpetiform aphthous ulcers present as multiple small pinpoint lesions that may coalesce into larger irregular ulcerations [4].

Anatomical Distribution
Aphthous ulcerations characteristically affect non-keratinized oral mucosa, predominantly involving the labial and buccal mucosa, tongue, and soft palate [2]. This distribution pattern serves as an important diagnostic criterion, distinguishing aphthous ulcers from recurrent herpes simplex virus infections, which primarily affect keratinized mucosa [3]. The ulcers typically present with a characteristic yellow-gray pseudomembrane surrounded by an erythematous halo [1].

Quality of Life Impact
The condition significantly impairs patients' quality of life across multiple domains [6]. Affected individuals report substantial difficulties with eating, drinking, and speaking during active episodes [7]. Studies demonstrate that recurrent aphthous stomatitis negatively affects oral health-related quality of life, with severity correlating with ulcer number and size [6].

Pathophysiology and Etiology
Immunological Mechanisms
Current evidence suggests that recurrent aphthous stomatitis represents a multifactorial T-cell mediated immune disorder [2]. The pathogenesis involves dysregulated cellular immunity with altered T-cell homeostasis and predominantly Th1 and Th17 responses [1]. Genetic predisposition plays a significant role, with family history reported in up to forty-six percent of affected patients [2].

Microbiome Alterations
Recent investigations have identified significant alterations in oral microbiota composition among patients with

recurrent aphthous stomatitis. Affected individuals demonstrate decreased microbial diversity and increased prevalence of specific bacterial genera, including Actinobacillus and Prevotella. These microbial shifts may contribute to disease pathogenesis through modulation of local immune responses [8].

Nutritional Deficiencies

Hematinic deficiencies represent important contributing factors in a subset of patients [2]. Studies demonstrate significantly higher frequencies of iron, vitamin B12, and folate deficiencies in affected individuals compared to healthy controls [9]. Vitamin D deficiency may play a role in aggravating ulcerative episodes, particularly in patients presenting with multiple concurrent lesions [10]. Gender and age influence the pattern of nutritional deficiencies, with ferritin deficiency more common in young females and vitamin B12 deficiency more prevalent in young adult males [9].

Diagnosis and Differential Diagnosis

Clinical Diagnosis

Diagnosis of recurrent aphthous stomatitis relies primarily on careful history taking and clinical examination [2]. Characteristic features include recurrent oral ulcerations appearing at least four times annually, absence of preceding vesicles, and typical distribution on non-keratinized mucosa [4]. No definitive laboratory test exists for confirmation [3].

Laboratory Investigations

Laboratory screening should be performed in patients with frequent recurrences or severe presentations [2]. Recommended investigations include complete blood count and assessment of serum iron, ferritin, vitamin B12, and folate levels [11]. Screening for autoantibodies, including gastric parietal cell, thyroglobulin, and thyroid microsomal antibodies, may be indicated in select cases [2]. Patients demonstrating anemia or hematinic deficiencies may benefit from replacement therapy [12].

Differential Diagnosis

The differential diagnosis encompasses numerous conditions presenting with oral ulcerations [3]. Behçet disease represents a critical systemic condition characterized by recurrent oral and genital ulcerations [13]. Oral ulcers constitute the most common manifestation of Behçet disease, occurring in over ninety-eight percent of affected patients [14]. Clinical features that may distinguish Behçet disease from simple recurrent aphthous stomatitis include increased number of concurrent ulcers, involvement of the soft palate and oropharynx, and presence of concurrent genital ulcerations [15].

Other important differential diagnoses include inflammatory bowel disease, celiac disease, periodic fever aphthous stomatitis pharyngitis and adenitis syndrome, and reactive arthritis [3, 16]. Viral infections, particularly herpes simplex virus, can be differentiated by their predilection for keratinized mucosa and presence of vesicular prodrome [3].

Management and Treatment

Topical Therapies

Topical corticosteroids represent the first-line treatment approach for recurrent aphthous stomatitis [2, 3]. These agents reduce inflammatory response and accelerate healing time [4]. Commonly employed formulations include clobetasol propionate and triamcinolone acetonide [5]. Topical antiseptics and anesthetics provide symptomatic relief and may reduce secondary infection risk [3].

Laser Therapy

Low-level laser therapy has emerged as a promising treatment modality for recurrent aphthous stomatitis [17]. Multiple systematic reviews demonstrate significant pain reduction and accelerated healing with laser treatment [18-19]. Both carbon dioxide and diode lasers have shown efficacy in reducing ulcer duration and pain intensity [20]. The treatment modality demonstrates favorable safety profiles with minimal adverse effects [21].

Systemic Therapies

Severe or refractory cases may require systemic therapeutic interventions [4]. Systemic corticosteroids provide effective short-term management for major aphthous ulcers but carry risks of significant adverse effects with prolonged use [5]. Immunomodulatory agents, including colchicine, may benefit patients with Behçet disease or complex aphthosis [22].

Emerging Therapies

Phosphodiesterase-4 inhibitors represent novel therapeutic options for refractory cases. Roflumilast demonstrates efficacy in reducing flare frequency, ulcer number, duration, and pain intensity in patients with severe recurrent aphthous stomatitis. The agent exhibits a favorable safety profile and may provide alternative treatment for patients unresponsive to conventional therapies [23].

Nutritional Supplementation

Correction of identified hematinic deficiencies represents an important management component [24]. Supplementation with iron, vitamin B12, or folate may reduce ulcer frequency and severity in deficient patients [25]. Omega-3 fatty acid supplementation shows promise in reducing disease severity and improving quality of life [26].

Conclusion

Recurrent aphthous stomatitis represents a common yet complex oral mucosal condition requiring systematic diagnostic evaluation and individualized management approaches. Clinical diagnosis relies on characteristic presentation patterns and appropriate exclusion of systemic disease. Initial management employs topical corticosteroids with consideration for laser therapy based on available resources and patient preferences. Laboratory screening for nutritional deficiencies should be performed in appropriate clinical contexts. Severe or refractory cases warrant referral for systemic therapy consideration. Emerging biological therapies offer promise for managing treatment-resistant disease. Ongoing research continues to elucidate pathophysiological mechanisms and refine therapeutic strategies for this challenging condition.

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