

An evaluation of a chemical cautery agent and an anti-inflammatory ointment for the treatment of recurrent aphthous stomatitis: a pilot study.

Rhodus NL.

Quintessence Int 1998; 29(12): 769-73

OBJECTIVE: Recurrent aphthous stomatitis is a very common condition, currently treated with anti-inflammatory agents, which palliate the symptoms. The purpose of this clinical trial was to compare a medication commonly used to treat recurrent aphthous stomatitis, Kenalog-in-Orabase, and a newer agent, Debacterol. **METHOD AND MATERIALS:** Sixty patients diagnosed with recurrent aphthous stomatitis were enrolled in the study. Twenty patients were assigned to each of the two treatment groups, and 20 age- and sex-matched patients were assigned to the control group, which received no treatment. After the diagnosis was made, clinical examinations and ulcer measurements were performed, and a subjective evaluation of symptoms (100-mm visual analog scale) was completed by each subject. The subjects did not use any other medications. Both agents were applied topically (the frequency varied depending on the group of subjects) at specified intervals. Ulcer measurements and subjective evaluations were made at days 0, 3, 6, and 10 for all subjects. **RESULTS:** In both treatment groups, by day 10, 100% of the ulcers had clinically healed and were no longer causing pain. Patients in the Debacterol group reported a significantly greater decrease in pain at 3 days (> 70%) than did subjects in the other groups (< 20%), although the size of the ulcer did not differ significantly in any of the groups. After day 6, 80% of the ulcers in the Debacterol group had clinically disappeared and no longer caused symptoms, as compared to about 30% in the other groups. **CONCLUSION:** Patients subjectively reported significantly greater relief from symptoms with Debacterol than with Kenalog-in-Orabase or no treatment. The relief of symptoms associated with recurrent aphthous stomatitis may or may not correspond to clinical improvement, and these two topical medications may affect signs and symptoms of the lesions differently.

Aphthous ulcers.

Messadi DV, Younai F.

Dermatol Ther. 2010 May-Jun;23(3):281-90.

Aphthous ulcers are one of the most common oral diseases worldwide. Their clinical presentation is characterized by multiple, recurrent, small, round, or ovoid ulcers with circumscribed margins and erythematous haloes present in different sizes. Oral lesions similar to aphthous ulcers may be present in several systemic diseases. This article will summarize the differential diagnosis of aphthous ulceration, with emphasis on a practical guide for the management of recurrent aphthous ulceration, including topical and systemic therapy.

Auto-inflammatory syndromes and oral health.**Scully C, Hodgson T, Lachmann H.****Oral Dis. 2008 Nov;14(8):690-9.**

Auto-inflammatory diseases (periodic syndromes) are rare childhood-onset disorders which are characterized by fluctuating or recurrent episodes of fever and inflammation affecting serosal surfaces, joints, eyes and/or skin without significant autoantibody production or an identifiable underlying infection. They are disorders of innate immunity and the underlying genetic defect has been identified in most of the syndromes. Diagnosis relies on clinical symptoms and evidence of an elevated acute phase response during attacks, supported by finding mutations in the relevant genes. Several syndromes can lead to systemic AA amyloidosis. Aphthous-like oral ulceration has been reported as one manifestation in several of the syndromes, including periodic fever, aphthous-stomatitis, pharyngitis, adenitis (PFAPA) familial Mediterranean fever (FMF), hyperimmunoglobulinaemia D and periodic fever syndrome, tumour necrosis factor receptor associated periodic syndrome and pyogenic sterile arthritis, pyoderma gangrenosum, acne (PAPA). Chronic jaw recurrent osteomyelitis has been recorded in chronic recurrent multifocal osteomyelitis. Advances in the molecular pathogenesis of these syndromes and the regulation of innate immunity have enhanced diagnosis, and rationalized therapies. This article reviews the periodic fever syndromes relevant to oral health and the suggested association of FMF with Behçet's disease.

Behçet's disease (Adamantiades-Behçet's disease).**Kaneko F, Togashi A, Saito S, Sakuma H, Oyama N, Nakamura K, Yokota K, Oguma K.****Clin Dev Immunol. 2011;2011:681956. Epub 2010 Nov 1.**

Adamantiades-Behçet's disease (ABD) is characterized by starting with oral aphthous ulceration and developing of the systemic involvements. The pathogenesis of ABD is closely correlated with the genetic factors and the triggering factors which acquire delayed-type hypersensitivity reaction against oral streptococci mediated by IL-12 cytokine family. HLA-B51 is associated in more than 60% of the patients and its restricted CD8+ T cell response is clearly correlated with the target tissues. Bes-1 gene encoded partial *S. sanguinis* genome which is highly homologous with retinal protein, and 65 kD heat shock protein (Hsp-65) released from streptococci is playing an important role with human Hsp-60 in the pathogenesis of ABD. Although Hsp-65/60 has homologies with the respective T cell epitope, it stimulates peripheral blood mononuclear cells (PBMCs) from ABD patients. On the other hand, some peptides of Hsp-65 were found to reduce IL-8 and IL-12 production from PBMCs of ABD patients in active stage.

Common oral lesions: Part I. Superficial mucosal lesions.**Gonsalves WC, Chi AC, Neville BW.****Am Fam Physician. 2007 Feb 15;75(4):501-7.**

Common superficial oral lesions include candidiasis, recurrent herpes labialis, recurrent aphthous stomatitis, erythema migrans, hairy tongue, and lichen planus.

Recognition and diagnosis require taking a thorough history and performing a complete oral examination. Knowledge of clinical characteristics such as size, location, surface morphology, color, pain, and duration is helpful in establishing a diagnosis. Oral candidiasis may present as pseudomembranous candidiasis, glossitis, or perlèche (angular cheilitis). Oral candidiasis is common in infants, but in adults it may signify immune deficiency or other illness. Herpes labialis typically is a mild, self-limited condition. Recurrent aphthous stomatitis most often is a mild condition; however, severe cases may be caused by nutritional deficiencies, autoimmune disorders, or human immunodeficiency virus infection. Erythema migrans is a waxing and waning disorder of unknown etiology. Hairy tongue represents elongation and hypertrophy of the filiform papillae and most often occurs in persons who smoke heavily. Oral lichen planus is a chronic inflammatory condition that may be reticular or erosive. Certain risk factors have been associated with each of these lesions, such as poor oral hygiene, age, tobacco use, and alcohol consumption, and some systemic conditions may have oral manifestations. Many recommended therapies for oral lesions are unsupported by randomized controlled trials.

Effect of stressful life events on the onset and duration of recurrent aphthous stomatitis.

Huling LB, Baccaglioni L, Choquette L, Feinn RS, Lalla RV.

J Oral Pathol Med. 2011 Nov 12. doi: 10.1111/j.1600-0714.2011.01102.x.

Background: Recurrent aphthous stomatitis (RAS) is a common and painful oral mucosal disease. Possible etiologies include genetics, vitamin deficiencies, trauma, immune dysfunction, and stress. The goal of this study was to examine the relationship between the occurrence, type, and magnitude of stressful events and the onset and duration of RAS episodes. Methods: One hundred and sixty subjects with a history of RAS completed a weekly phone survey for up to 1 year, providing data on the occurrence of RAS episodes and details of any stressful events they experienced during the previous week. During RAS episodes, subjects also completed daily paper diaries that recorded incidence and duration of the RAS episode. Stressful events were quantified using the validated Recent Life Changes Questionnaire (RLCQ) and were classified as mental or physical stressors. Results: Stressful life events were significantly associated with the onset of RAS episodes ($P < 0.001$), however, not with the duration of the RAS episodes. Experiencing a stressful life event increased the odds of an RAS episode by almost three times (OR = 2.72; 95% CI = 2.04-3.62). When controlled for each other, mental stressors had a larger effect (OR = 3.46, 95% CI = 2.54-4.72) than physical stressors (OR = 1.44; 95% CI = 1.04-1.99) on the occurrence of RAS episodes. RAS episodes did not occur more frequently or last longer with increasing stress severity. Conclusions: In patients with a history of RAS, stressful events may mediate changes involved in the initiation of new RAS episodes. Mental stressors are more strongly associated with RAS episodes than physical stressors.

Guidelines for diagnosis and management of aphthous stomatitis.**Femiano F, Lanza A, Buonaiuto C, Gombos F, Nunziata M, Piccolo S, Cirillo N. *Pediatr Infect Dis J.* 2007; 26(8):728-32.**

Aphthous ulcers are the most common oral mucosal lesions in the general population. These often are recurrent and periodic lesions that cause clinically significant morbidity. Many suggestions have been proposed but the etiology of recurrent aphthous stomatitis (RAS) is unknown. Several precipitating factors for aphthous ulcers appear to operate in subjects with genetic predisposition. An autoimmune or hypersensitivity mechanism is widely considered possible. Sometimes aphthous ulcers can be the sign of systemic diseases, so it is essential to establish a correct diagnosis to determine suitable therapy. Before initiating medications for aphthous lesions, clinicians should determine whether well-recognized causes are contributing to the disease and these factors should be corrected. Various treatment modalities are used, but no therapy is definitive. Topical medications, such as antimicrobial mouth-washes and topical corticosteroids (dexamethasone, triamcinolone, fluocinonide, or clobetasol), can achieve the primary goal to reduce pain and to improve healing time but do not improve recurrence or remission rates. Systemic medications can be tried if topical therapy is ineffective.

Oral ulcers: clinical aspects. A tool for dermatologists. Part I. Acute ulcers.**Muñoz-Corcuera M, Esparza-Gómez G, González-Moles MA, Bascones-Martínez A. *Clin Exp Dermatol.* 2009 Apr;34(3):289-94.**

Oral ulcers are generally painful lesions that are related to various conditions developing within the oral cavity. They can be classified as acute or chronic according to their presentation and progression. Acute oral ulcers are associated with conditions such as trauma, recurrent aphthous stomatitis, Behçet's disease, bacterial and viral infections, allergic reactions or adverse drug reactions. Chronic oral ulcers are associated with conditions such as oral lichen planus, pemphigus vulgaris, mucosal pemphigoid, lupus erythematosus, mycosis and some bacterial and parasitic diseases. The correct differential diagnosis is necessary to establish the appropriate treatment, taking into account all the possible causes of ulcers in the oral cavity. In the first part of this two-part review, acute oral ulcers are reviewed.

***Oral ulcers: clinical aspects. A tool for dermatologists. Part II. Chronic ulcers.* Muñoz-Corcuera M, Esparza-Gómez G, González-Moles MA, Bascones-Martínez A. *Clin Exp Dermatol.* 2009 Jun;34(4):456-61.**

Oral ulcers are generally painful lesions that are related to various conditions developing within the oral cavity. They can be classified as acute or chronic according to their presentation and progression. Acute oral ulcers are associated with conditions such as trauma, recurrent aphthous stomatitis, Behçet's disease, bacterial and viral infections, allergic reactions or adverse drug reactions. Chronic oral ulcers are associated with conditions such as oral lichen planus, pemphigus vulgaris, mucosal pemphigoid, lupus erythematosus, mycosis and some bacterial

and parasitic diseases. The correct differential diagnosis is necessary to establish the appropriate treatment, taking into account all the possible causes of ulcers in the oral cavity. In this second part of this two-part review, chronic oral ulcers are reviewed.

Periodic fever, aphthous stomatitis, pharyngitis and adenitis syndrome.

Kusuhara K.

Nihon Rinsho Meneki Gakkai Kaishi. 2011;34(5):401-7.

Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome is a non-hereditary autoinflammatory disease, characterized by relatively regular recurrence of febrile episodes of 3-6 days duration, accompanied by aphthous stomatitis, pharyngitis/tonsillitis, and/or cervical adenitis. It is considered to be the most common periodic fever syndrome in Japan. Although no responsible gene is identified, some genetic factors may confer the predisposition toward this disorder. Important differential diagnosis includes hereditary periodic syndromes and cyclic neutropenia. Although its etiology is still to be elucidated, a recent study suggested an environmentally triggered activation of complement and IL-1 β /IL-18 during PFAPA syndrome flares, with induction of Th1-chemokines and subsequent retention of activated T cells in peripheral tissues. This study also demonstrated the possibility that IP-10/CXCL10 might serve as a potential biomarker to differentiate PFAPA syndrome from other periodic fever syndromes. Therapeutic strategy for PFAPA syndrome has not been well established. Recent advances in the understating of etiology and pathophysiology might lead to re-evaluation of recent therapeutic options and/or development of new treatment.

Practical aspects of management of recurrent aphthous stomatitis.

Altenburg A, Abdel-Naser MB, Seeber H, Abdallah M, Zouboulis CC.

J Eur Acad Dermatol Venereol. 2007 Sep;21(8):1019-26.

Treatment of recurrent aphthous stomatitis (RAS) remains, to date, empirical and non-specific. The main goals of therapy are to minimize pain and functional disabilities as well as decrease inflammatory reactions and frequency of recurrences. Locally, symptomatically acting modalities are the standard treatment in simple cases of RAS. Examples include topical anaesthetics and analgesics, antiseptic and anti-phlogistic preparations, topical steroids as cream, paste or lotions, antacids like sucralfate, chemically stable tetracycline suspension, medicated toothpaste containing the enzymes amyloglucosidase and glucoseoxidase in addition to the well-known silver nitrate application. Dietary management supports the treatment. In more severe cases, topical therapies are again very useful in decreasing the healing time but fail to decrease the interval between attacks. Systemic immunomodulatory agents, like colchicine, pentoxifylline, prednisolone, dapsone, levamisol, thalidomide, azathioprine, methotrexate, cyclosporin A, interferon alpha and tumour necrosis factor (TNF) antagonists, are helpful in resistant cases of major RAS or aphthosis with systemic involvement.

Prevalence of recurrent aphthous ulceration in Jordanian dental patients.**Safadi RA.****BMC Oral Health. 2009 Nov 22;9:31.**

BACKGROUND: Reviewing the literature, no studies were cited to report the prevalence of recurrent aphthous ulceration in Jordan. The aim of this study is to report the prevalence of recurrent aphthous ulceration in Jordanian subjects.

METHODS: A total of 684 dental patients who attended Jordan University of Science and Technology interviewed and administered to fill questionnaires related to history, size, shape, and duration of recurrent aphthous ulceration. Other related questions were also asked.

RESULTS: About 78% of subjects experienced recurrent aphthous ulceration. Approximately 85% of ulcers were less than one cm in diameter, 66% were circular in shape, 92% were painful, 82% interfered with eating, and 55% located in lips and buccal mucosa. Only 50% of participants related ulcers to stress. Sixty eight percent reported no association with tiredness and 85% no association with types of food ingested. Of the 39% who had blood tests carried out, 7% had vitamin B12 and 4% hemoglobin deficiency.

CONCLUSION: Recurrent aphthous ulceration is a common problem in Jordanian adults.

Recurrent aphthous stomatitis.**Zunt SL.****Dermatol Clin. 2003 Jan;21(1):33-9.**

Recurrent aphthous stomatitis remains a commonly occurring cause of oral pain and ulceration. Although the ulcerations of RAS are multifactorial and of unknown cause, recognition of the role of patient and environmental factors may be helpful in developing recommendations for treatment and prevention of future ulcers.

Recurrent aphthous stomatitis.**Chattopadhyay A, Shetty KV.****Otolaryngol Clin North Am. 2011 Feb;44(1):79-88**

Recurrent aphthous stomatitis is a common oral ulcerative disease, affecting 10% to 15% of the general US population. This article reviews the epidemiology and clinical presentations of recurrent aphthous stomatitis, including diagnosis and management.

Risk indicators for recurrent aphthous ulcers among adults in the US.**Chattopadhyay A, Chatterjee S.****Community Dent Oral Epidemiol. 2007 Apr;35(2):152-9.**

BACKGROUND AND AIMS: Recurrent aphthous ulcers (RAU) in the oral cavity are painful, causing substantial morbidity in the US and elsewhere in the world. Despite this, there is a lack of population-based studies representative of the US national adult population to describe the epidemiology, and estimate the true disease burden and association with independent risk factors. Although several studies have

investigated the role of various factors in RAU etiology, the epidemiology and etiology of RAU remain unclear. This study aims to establish the prevalence and describe the epidemiology of RAU in adults.

METHODS: Data from the Third National Health and Nutrition Examination Survey (NHANES III) were analyzed in SUDAAN using multivariable logistic regression, modeling RAU occurrences.

RESULTS: Overall, for all Americans regardless of age, prevalence of RAU was 1030 per 100,000 people (95% CI 830-1220). The prevalence of RAU among adults was 850 per 100,000 (95% CI 630-1070). The lower vestibule was the most commonly involved site. Multivariable analyses suggested that adjusted odds of RAU were greatest for those 17-29 years of age (adjusted OR 2.7; 95% CI 1.4-5.5), for men (adjusted OR 1.7; 95% CI 0.9-2.8), and for those with low serum insulin levels (OR 2.0; 95% CI 0.9-4.4). Never smokers had greater risk of RAU (OR 9.2, 95% CI 2.8-30.1) compared with those who smoked more than 10 cigarettes per day.

CONCLUSION: This study establishes the prevalence of RAU among adults in the US and demonstrates that whereas cigarette smoking is associated with lesser odds, low insulin levels might be independently associated with greater odds of RAU.