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A review on apthous ulcers with homoeopathic treatment

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Abstract
Aphthous Ulcer is ulcer in the oral cavity affecting the daily lives of individuals suffering from it. The pain when having food or drinks make it one of the most sought out disease in the clinics. Though it is self-limiting, it may also cause long term complications as in cases of major aphthae.

Keywords: Aphthae, recurrent aphthous stomatitis, dental, homoeopathy, homoeopathic medicine

Introduction
The word aphthai initially was use in relation to disorders of mouth [1]. Hippocrates (460-370 BC) first used the Greek word apthae which means burning i.e., feature of the disease RAS (recurrent aphthous stomatitis) [2]. Von Mikulicz and Kummel (1888), however was the first to give the valid clinical description of RAS [3]. Apthae may be cause by mechanical trauma, systemic diseases, drug side-effects and infections. Recurrent Aphthous Stomatitis (RAS) is ulcers of the oral mucosa and presents first in childhood or adolescence [4]. It maybe acute or chronic and self-limiting [5]. It is painful, cause irritation and affects the patient's Quality of Life (QoL) especially during talking, eating [6]. The size of the ulcer may vary from less than 1 mm to greater than 1 cm in size [7].

Epidemiology
The prevalence of RAS is 5-25% of the population [8]. 70-87% population are affected by minor recurrent aphthous ulcer and these ulcers are usually less than 1 cm in diameter and regress within 7 to 10 days. Major aphthous ulcer however is bigger in size and is more painful in nature [9].
RAU is defined as having a aphthous ulcer at least 2 times per year and is more prevalent in children, females, higher social classes and non-smokers [10]. Prevalence decreases in elders [11]. Stress during a student life may predispose to apthae [9]. There is relation with family as well and the disorder is mainly noticed at around the time of puberty [12].

Predisposing factors/causes of apthous ulcer
The etiology is unknown with many factors interplaying the cause, these include the genetic factors which have shown to be in family relations, local trauma causing irritation to the oral mucosa [6], cessation of smoking which show increase of ulcer as compare to nicotine use as this helps increased the mucosal keratinization preventing formation of ulcer [6, 13], endocrine relations and hormones especially predisposing in females during menstruation time and puerperium [4, 14], drugs due their adverse side effects and disappear after discontinuation of drug [14], hematinic deficiency in which when supplements are provided improvement sets in [6, 14], inflammatory bowel disease in Crohn where ulcers occurs from mouth to anus [4, 6], food allergens various food hypersensitivity such as cows' milk, gluten, chocolate, nuts, cheese, azo dyes, flavouring agents and preservatives may have relation of food with ulcers [8, 15, 16, 17].
Sodium Lauryl Sulfate (SLS) containing toothpaste has been reported to increase RAU [6], and microbial agents implicated in causing ulcers however H. Pylori shows no relation with RAU [4, 14, 18] stress and anxiety leading to habits such as lip biting [19]. RAS is seen in immunological disorders and the Human Immunodeficiency Virus (HIV) infection as well [10].

Pathogenesis [5, 6, 20, 21]

In individuals predisposed to RAU, the enzyme superoxide Dismutase (SOD) initiates the cascade of Proinflammatory cytokines causing an inflammatory response against the oral mucosa. There are sign of inflammation with massive leukocytic infiltration and oedema. In the pre-ulcerative phase, monocytes and lymphocytes (mainly of the T type) with single mast and plasmatic cells accumulate under the basal cell layer [5, 20] followed by the development of a localized painful papular swelling surrounded by erythemathous halo with mononuclear cell infiltration. There is rupture of the papule and formation of a fibrous membrane covering which gets infiltrated by polynuclear leukocytes and mononuclear cells. Finally, there is healing with epithelial regeneration and coverage of the ulcer [6].

The immunopathogenesis involves a cell-mediated immune response mechanism, and generation of T-cells and Tumour Necrosis Factor alpha (TNF-α) by macrophages and mast cells. The TNF- α cytokine, a major inflammatory mediator, induces initiation of the inflammatory process by its effect on endothelial cells adhesion and a chemotactic effect on neutrophils. IL-10 usually stimulates epithelial proliferation and thus helps in epithelization. Increased levels of interleukin-2 (IL-2), TNF- α which both promotes inflammation and low levels of IL-10 which is an anti-inflammatory cytokine have been reported in the oral lesion of RAS patient. TNF- α stimulates Major Histocompatibility (MHC) expression which promotes the local tissue damage by causing the cytotoxic T-cells (CD8+ cells) action in the ulcerative process. Natural killer (NK) cells activated by IL-2 also plays a role [20, 21].

Cytology: Cytologic smears from the RAU lesions shows "Anitschkow's cells" which are the presence of elongated nuclei (seen as a caterpillar pattern in longitudinal section), with few radiating processes towards the nuclear membrane [22]. However, these cells are not pathognomic of RAU [23].

Clinical presentation [4, 5, 12, 24]

There are three clinical subtypes of RAS [4, 5, 12, 24]

- **Minor RAS (Miculiz's aphthae):** These represents 70-85% of all cases. These occur in the buccal mucosa, labial mucosa, and floor of the mouth. The ulcers have a yellow–grey base and halo of redness, tend to grow in crops with variable patterns from single ulcers up to over 20 at one time and are 10 mm in diameter. They are self-limiting and resolve within 4-14 days without leaving scars [4, 5, 12, 24].
- **Major RAS (Sutton's disease/ periadenitis mucosa necrotica recurrens):** As the name suggests they are of severe nature affecting around 15% of RAU patients. The ulcers are over 1 cm in size persists for about 4 weeks with one to three ulcers being present at a time. Any mucosal site can be involved; appearing on the lips, soft palate and pharynx, this causes severe symptoms, including pain on swallowing and gagging. The ulcers often heal with scarring [4, 5, 12, 24].
- **Herpetiform RAS:** These accounts for 1-10% of RAU cases. It is characterized by recurrent outbreaks of small, pinhead sized, deep and painful ulcers of more than 20-100 at a time common in women and older age group patient of 2-3 mm in size. These merge to form larger ulcerations with an irregular contour and healing occurs within 14 days and resolve without scarring [4, 5, 12, 24].

Diagnosis

The diagnosis of RAS is based on the patient history and clinical features. There is no specific diagnostic test, but systemic causes have to be ruled out. A biopsy of the lesions can be done in the case of diagnostic uncertainty [4, 5, 12].

Laboratory investigations such as complete blood counts, red cell folate, serum ferritin levels, and vitamin B12 and where vitamin B12 deficiency is detected, antibodies to intrinsic factor have to be done [12].

Natah *et al*. in 2004 proposed the diagnostic criteria for minor RAU [14]. The diagnosis of primary RAU minor (idiopathic) or secondary RAU minor (that occurs in association with systemic diseases) can be made if the condition fulfils the four major criteria plus at least one of the minors (supportive) criteria [14]. The major and minor criteria for diagnosis of minor RAU are illustrated in Tables 1 and 2 as proposed by Natah *et al*. in 2004.

Table 1: Major criteria for recognizing and diagnosing the condition as RAU minor [14]

Major criteria	Description
1.External appearance	Single or multiple round/oval shaped ulcers which are less than 1 cm in diameter, are shallow with regular margins and a yellow–grey base surrounded by thin erythematous halos.
2.Recurrence	At least three attacks of RAU within the past 3 years and the recurrences are not on the same site.
3.Mechanical hyperalges	The lesion is painful and exacerbated by movement of the area.
4.Self-limitation of the c	The ulcer heals spontaneously without sequelae.

Table 2: Minor criteria for recognizing and diagnosing RAU minor [14]

Minor criteria	Description
1. Family history of RAU	A positive family history of RAU is present
2. Age at onset	The first RAU attack started before the age of 40 years.
3. Location of ulcers	Occur on non-keratinized oral mucosa.
4. Duration of the lesion	Each bout of ulceration lasts from a few days to two weeks.
5. Pattern of recurrence	Irregular
6. Histological examination	Shows non-specific inflammation.
7. Presence of a precipitating factor	The attacks are triggered by hormonal changes, exposure to certain foods or drugs, intercurrent infections, stress and local trauma.
8. Presence of haematinic deficiencies	Laboratory investigations reveal an accompanying haematinic deficiency. In particular, ferritin, folate, iron, vitamin B and zinc
9. Negative association with smoking	RAU patient is a non-smoker or develops the ulcer after stopping
10. Therapeutic trial with gluco-corticosteroids	Positive response to treatment with local or systemic steroids.

Differential diagnoses

1. **Herpetic ulcers (caused by HSV1 and HSV2):** HSV-1 at any age but typically in children and mainly affects above waistline, the HSV-2 mainly genital herpes can also lead to gingivostomatitis. Intra-oral and gingival vesicles rupture within several hours to 1 or 2 days along fever and pain with difficultly in eating and drinking [25].
2. **Pemphigus vulgaris:** Oral erosions on the buccal and palatine mucosae which are painful, tender and heal very slowly. Nikolsky sign is positive [26].
3. **Oral squamous cell carcinoma:** A biopsy is to be done for non-healing ulcer persisting for more than 21days to stage and grade the neoplasia [26].
4. Herpangina is an enteroviral infection characterised by a small number of vesicles (to 2 mm to 3 to 4 mm) at the soft/hard palate junction with high fever, an extremely sore throat and headache which may enlarge, rupture, and produce small, punched-out ulcers [25].
5. **Crohn's disease:** It is an inflammatory bowel disease with ulcer presenting from mouth to anus has to be ruled out.
6. **Reiter syndrome:** The syndrome is a tetrad of symptoms- conjunctivitis, non-gonococcal urethritis, mucocutaneous lesion and arthritis with oral manifestation of painless aphthous like ulcer, pruritic spots and geographic tongue [26].
7. **Contact stomatitis:** Ulcer at localized site after repeated contact with causative agent which clinically presents as erythema followed by vesicle then erosion that can become extensive [26].
8. **Traumatic ulcer:** The traumatic ulcer results from mechanical trauma, chemical, electrical, or thermal stimulus, malposed, or malformed teeth [26]. The ulcer have a yellowish floor, fibrinous centre, red and inflammatory margin without induration [27].
9. **Oral Lichen planus [26, 28]:** Oral Lichen Planus (OLP) is a chronic inflammatory mucocutaneous disorder of stratified squamous epithelium that affects oral and genital mucous membranes, skin, nails, and scalp. They have reticular lesions like lace appearance in oral cavity.
10. **Behcet's syndrome:** It is a multisystem disease with painful "aphthous-like ulcers" in the oral cavity affecting young males [22].

Management [4, 5, 12, 14]

RAS has no curative treatment [4], however, it may be self-limited and limiting trauma to the oral mucosa by eliminating sharp food, hard foods, triggering foods like nuts, chocolate, acid beverages or foods, salty foods, spicy food (pepper, curry), alcoholic and carbonated drinks have been shown to be helful [5, 12].

The goals of treatments are: to ensure adequate food intake by palliation of pain symptoms, reducing the time duration of ulcer and its recurrence, Glucocorticoids and antimicrobial therapy are the traditional treatments for RAU which are given as topical pastes, mouthrinses, intralesional injections. Maintenance of good oral hygiene, sodium lauryl sulfate (SLS) free toothpaste and occasional topical anesthetics are useful to palliate the pain [14].

Kathy Abascal and Eric Yarnell [29] have given alternative treatment and Herbs which helps in acute outbreaks of RAS which includes

Berberine-containing herbs [29] like Coptis spp. (goldthread) and its rootlets are used for ulcers of mouth [29].

- **Phytolacca americana (poke root†):** for treating subacute ulcers along with a chronic problem [29].
- **Tannin-containing herbs:** prevent breakdown of mucosa and promote wound-healing [29].
- **Myrtus communis (myrtle) leaf:** used in European traditional medicine for management of pain and decreasing ulcer size [30].
- **Licorice:** Glycyrrhiza spp. (licorice) an adaptogen, an immune-modulator, and an inflammation-modulator and thus helps in treating aphthous ulcer [31].
- **Spilanthes:** Spilanthes acmella (*Acmella oleracea*) shows significant anti-inflammatory action against inflammation, and acts as analgesic in reducing pain [29].

Homoeopathic remedies for apthous ulcers [32, 33]

- ***Arsenicum album*:** There is swollen bleeding gums which are painful to touch, the ulcers have burning heat, livid and bluish, with stitching and burning blisters in mouth. The tongue is dry clean and red. Mouth tastes, sour, foul, salty, sweet in morning [32, 33].
- ***Baptisia tinctoria*:** Gums are ulcerated, loose dark or purple. Tongue yellow along the centre, putrid ulcers of buccal cavity with salivation, offensive faecal breath [32 ,33].
- **Borax veneta:** It is commonly use in aphthae of mouth and inner surface of cheek which bleed easily, there is white fungus like growth in the mucosa with pain especially when chewing of children and of old people [32, 33].
- **Hydrastis canadensis:** Stomatitis of nursing mothers or weakly children. Excessive secretion of thick, tenacious mucus, mouth is Bitter, peppery taste in mouth [32, 33].
- **Kalium chloricum:** Stomatitis, aphthous with oral mucous red, tumid with gray-based ulcers. Scurvy. Salivation, profuse secretion of acid saliva. Tongue, swollen, cold. Mercurial stomatitis, (as a mouth wash) [32, 33].
- **Mercurius solubilis:** There is induration with ulceration in the throat, nose, mouth, and on the lower limbs which sting and burn and have a lardaceous base, an ashy-white appearance. Burning pain, aggravated at night [32, 33].
- **Mercurius corrosivus:** Pale about mouth. Cracks in angles of the mouth. Edematous swelling of the face. Gums swollen, purple and spongy with tongue swollen and inflamed, red with black coat, covered with greyish white crust, moist edges. Exudation and ulcers on mucous membranes of mouth and throat [32, 33].
- **Muriatic acid:** Gums and glands swollen. Fetid breath. Gums are swollen, bleeding, ulcerating. Deep ulcers on tongue. Everything tastes sweet. Beer tastes like honey [32, 33].
- **Nux-vomica:** Breath foul, sour. Small aphthous ulcers with bloody saliva. Taste, bitter, sour, bad in morning. Gums, swollen, white and bleeding. Anterior half of tongue is clean, posterior is covered with deep coating which is white, yellow and with cracked edges. Needle-like sensation at edges of tongue [32, 33].
- **Sulphur:** Mouth tastes sour, sweetish, foul, bitter in

morning. Nursing sore mouth, gingivitis with throbbing pain and bleeding. Tongue is white with red tip and borders. Grinding of the teeth. Saliva, profuse with nauseous taste [32, 33].

- **Sulphuric acidum:** Aphthous mouth and gums which is yellowish and painful, difficulty in talking, as from want of elasticity of the parts; great weakness; ecchymoses [32, 33].
- **Nitricum acidum:** There is putrid breath increase salivation with bleeding of gums. Painful pimples on the sides of the tongue. Moist fissured or mapped tongue which is clean, red with centre furrow. Ulcers in soft palate with pain as of sharp splinter-like. Bites the tongue and cheek. Ulceration of tongue with tough ropy mucus [32, 33].

Conclusion

Recurrent aphthous stomatitis is an ulcer of the oral cavity which may be painful and troublesome. Treatment strategies are aimed towards improving the overall quality of life, by providing symptomatic relief by decreasing the pain, promoting healing of the ulcer and decreasing the duration of suffering. Proper counselling regarding severity and general management of mouth ulcer are to be done for the patients as minor and herpetiform apthous ulcer will heal within 14 days however, major apthous ulcer needs proper management and treatment.

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