

# Systematic Review on Recurrent Aphthous Ulcer

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## Abstract

Recurrent aphthous ulcers are common painful mucosal conditions affecting the oral cavity. Despite their high prevalence, etiopathogenesis remain unclear. This review article summarizes the case report ,clinical presentation, diagnostic criteria and recent trends in the management of recurrent aphthous stomatitis

**Keywords:** diagnostic criteria, recurrent aphthous stomatitis, stress ulcers, ulcer activity index immunomodulation.

## INTRODUCTION

The term “aphthous” is derived from a greek word “aphtha” which means ulceration. Recurrent aphthous stomatitis is one of the most common painful oral mucosal conditions seen among patients. These present as recurrent, multiple, small, round or ovoid ulcers with circumscribed margins, having yellow or gray floor and are surrounded by erythematous halo, present first in childhood or adolescence.

## CASE REPORT

A 37-year old male patient was reported in the department of Oral Medicine And Radiology suffering from RAS for 3 years.

A single ulcer was noted on the lateral surface of tongue since 2 days. Treatment of symptoms improved his conditions for short period. Results of general physical examination was normal. Further hematological investigation showed normal folic acid and iron levels, but a vitamin B 12 level in the lower limits of normal range. Treatment with parenteral vitamin B12 lead to rapid improvement. 2 months follow up revealed complete recovery without recurrence of RAS.

## Predisposing Factors

- Genetics: A genetic predisposition for the development of aphthous ulcer is strongly suggested as about 40% of patients have a family history .Various associations with HLA antigens and RAS have been reported. These associations vary with specific racial and ethnic origins.
- Trauma : trauma to the oral mucosa due to local anesthetic injections , sharp tooth, dental treatments , and tooth brush injury may predispose to the development of recurrent aphthous ulceration. Wray et al in 1991 proposed that mechanical injury may aid in identifying and studying patients prone to aphthous stomatitis.
- Tobacco: several studies reveal negative association between cigarette smoking,

smokeless tobacco and RAS. Possible explanations given include increased mucosal keratinization; which serves as a mechanical and protective barrier against trauma and microbes. Nicotine is considered to be the protective factor as it stimulates the production of adrenal axis and reduces production of TNF alpha and IL 1,6.

- Drugs: angiotensin converting enzyme inhibitor captopril, goldsalts, nicorandil, phenindione, phenobarbital, sodium hypochloride.
- Hematinic deficiencies: deficiencies of iron, vit B12, folic acid predispose development of RAS.
- Hormonal changes: conflicting reports exist regarding association of hormonal changes in women and RAS.
- Stress: stress has been emphasized as a causative factor in RAS. It has been proposed that stress may induce trauma to oral soft tissue by parafunctional habits such as lip or cheek biting and this trauma may predispose to ulceration. Recent studies shows that psychological stress may act as triggering factor rather than a etiological factor in susceptible RAS patients.

## Etiopatho Genesis

Etiopatho genesis of RAS is unclear , and the authors suggest strong genetic background and involvement of cell mediated immunity.

It is currently thought that an unknown antigen stimulates keratinocytes, resulting in cytokine secretion and leukocyte chemotaxis. TNF alpha has been found to be significantly increased in the saliva of RAS patients. Cytokines are responsible for irritation of inflammatory process, by interfering adhesion of vascular membrane and causes defective chemotaxis, leading to painful papule which eventually get ulcerated and covered by fibrinous slough and again infiltrated by plasma cells, monocytes and lymphocytes.

**Clinical Presentation**

RAS is characterized by recurrent bouts of solitary or multiple shallow painful ulcers, at intervals of few months to few days. RAS has been described under 3 different clinical variants as classified by STANLEY in 1972.

1. Minor RAS is also known as Miculiz’s aphthae or mild aphthous ulcer. It is the most common variant (80%) ulcers vary from 8-10 mm in size. It is most commonly seen in the non - keratinized mucosal surfaces like labial mucosa, buccal mucosa , and floor of mouth. Ulcers heal within 10-14 days without scarring.
2. Major RAS is also known as Periapadenitis Mucosa Necrotica Reccurrens or Suttons disease. It affects about 10-15% of patients. Ulcers exceed 1 cm in diameter. Most common sites of involvement are lips, soft palate, and fauces. Masticatory mucosa like dorsum of tongue or gingiva may be occasionally involved. The ulcers persist for upto 6 weeks and heal with scarring.
3. Herpetiform ulceration is characterized by recurrent crops of multiple ulcers, may be upto 100 in number. These are small in size measure 2-3 mm in diameter. Lesions may coalesce to form large irregular ulcers. These ulcers last for about 10-14 days. Unlike herpetic ulcers, these are not pre-

ceded by vesicles and do not contain viral infected cells. These are most common in women and have a later age of onset than other clinical variants of RAS.

**Ulcer Activity Index**

Mumucu et al. in 2009 proposed a composite index to monitor the clinical manifestations associated with oral ulcers in patients of RAS and Behcets disease. The index evaluated the oral ulcer activity, ulcer related pain, and functional disability. Oral ulcer activity was recorded as number of ulcers in the past 1 month. This was scored 0 if there were no ulcers, and as 1, if the number of ulcers was greater or equal to one. The pain status was evaluated on a visual analogue scale. This is a 100 mm line with extreme values at either end. The patients have to mark the intensity of pain on the line.

**DIAGNOSIS**

Diagnosis of RAS is based on history, clinical manifestations and histopathology. Other causes of recurrent oral ulcerations must be ruled out. Diagnostic Criteria for minor RAU were proposed by Natah et al in 2004. They proposed that diagnosis of idiopathic RAU and secondary RAU is established when 4 four major and one minor criteria are fulfilled .

| Major Criteria   | Description   |
|--|---|
| • Clinical appearance single or multiple round or ovoid ulcers - | shallow, regular margins, Yellow grey base, surrounded by erythematous margin, never preceded by vesicles. less than 1 cm in diameter |
| • Recurrence -   | atleast three attacks of RAU within past 3 years., ulcers do not appear in same focal site  |
| • Mechanical hyperalgesia -                                      | painful lesion, exacerbated by movement of ulcer affected area  |
| • Self limitation of condition -                                 | ulcer heals spontaneously without sequelae with or without treatment.   |

| Minor Criteria                       | Description   |
|--------------------------------------|---|
| • Family history -                   | Positive family history of RAU present.                                     |
| • Age of onset -                     | First attack of RAU below 40 years.   |
| • Location -                         | Non keratinized oral mucosa.  |
| • Duration -                         | Ulcers last from few days to few weeks.                                     |
| • Pattern of recurrence -            | Irregular   |
| • Histopathology -                   | Non specific inflammation   |
| • Presence of precipitating factor - | Attacks triggered by hormonal changes, exposure to certain foods and drugs. |

### Treatment

- Treatment of RAS has major goals - Ulcer management, Pain management, Nutritional Management, disease control. The relative importance and priority of each goal depends on the severity of the condition.
- Primary line of treatment  
Topical gels, creams and ointments. The primary treatment of RAS lesion utilizes topical anti-inflammatory agents. Strong topical corticosteroids when compounded with mucosal adherents (eg: orabase, isobutyl cyanoacrylate) are effective despite limited contact time
- Secondary line of treatment  
For the patient whose symptoms are not relieved by the primary line of treatment or whose signs and symptoms warrant a more aggressive treatment modality, prednisone should be considered for both HIV-negative and HIV-positive. Prednisone, an anti-inflammatory and an immuno suppressive agent, can be used in combination with topical gels and rinses.
- Tertiary line of treatment  
Thalidomide, an inhibitor of tumour necrosis, can be used. Factor K, has been shown to be an effective treatment for severe RAS, despite the potential for significant side effects. Use of thalidomide in children has been documented with some success, but long term effect have not been established.

### CONCLUSION

Recurrent Aphthous Stomatitis is a very common, recurrent painful ulceration occurring in the oral cavity. The etiopathogenesis of this disease is unclear. Treatment strategies must be directed toward providing symptomatic relief by reducing pain, increasing the duration of ulcer free periods, and accelerating the ulcer healing.