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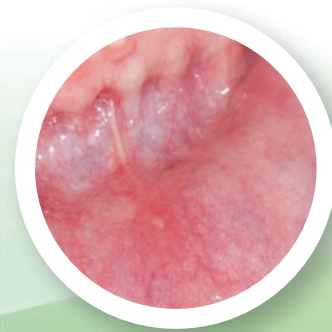
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Knowledge for Clinical Practice



Recurrent Aphthous Stomatitis

Howard E. Strassler, DMD, FAGD, FAGD



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ABSTRACT

Recurrent aphthous ulcers are commonly found in the general population. They consist of minor, major, and herpetiform types. A number of factors are considered to be possible etiological factors for recurrent aphthous ulcers; however, their exact etiology remains unclear. Several systemic diseases and conditions associated with oral ulcerations and other causes of oral ulcerations must be considered during the differential diagnosis. Once a definitive diagnosis for recurrent aphthous ulceration has been made, the patient can be given palliative care for the lesions as well as advice and recommendations on nutrition, oral hygiene practices, and other factors that may be associated with his or her recurrent aphthous ulcers.

EDUCATIONAL OBJECTIVES

The overall goal of this article is to provide the reader with information and scientific data on recurrent aphthous stomatitis. On completion of this course, the participant will be able to do the following:

1. List and describe the different types of recurrent aphthous ulcers;
2. Differentiate between recurrent aphthous ulcers and herpes simplex ulcers;
3. List and consider the different types of ulcers and associated conditions that must be part of the differential diagnosis for recurrent aphthous ulcers; and
4. Provide an overview of the types of treatments available for the different categories of recurrent aphthous ulcer patients.



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Recurrent Aphthous Stomatitis

Oral lesions are quite common and practitioners frequently see both painless and painful varieties. The presence of painful oral ulcers that do not seem to be healing can make a patient worry that these ulcers may be forms of oral cancer. These patients will schedule a dental visit to get a diagnosis. The most common oral mucosal ulcerations include the recurrent aphthous ulceration (RAU) and recurrent aphthous stomatitis (RAS), also known as canker sores. RAS is typically painful and has a reddened appearance. It is classified by three distinct clinical forms: minor, major, and herpetiform.^{1,2,3,4}

Clinical appearance and location

Minor RAS are typically found on the buccal or labial mucosal tissues, the soft palate, and the floor of the mouth. (Figure 1) Minor RAS have been reported to cause 70 to 87 percent of all forms of RAS,⁵ with more than 17 percent of the population being reported to have minor RAS.⁶ The clinical appearance of minor RAS is characteristically one of shallow, isolated, and yet painful recurrent ulcers approximately 5-10 millimeters in size covered by a whitish, yellow-gray pseudomembrane and surrounded by a raised reddened halo.¹⁻⁴ During an outbreak a patient may have one to five of these lesions measuring less than 10 millimeters each.^{7,8} Usually the adjacent soft tissues appear healthy.

In contrast, major RAS come together to form much larger lesions that are greater than 10 millimeters in size. (Figure 2) These lesions can be extremely painful and cause patients to change their eating and drinking habits to avoid discomfort. These lesions can persist for weeks or even months at a time.⁷ Seven to fifteen percent of RAS are major. These lesions are typically seen on a patient's

lips, tongue, soft palate, and palatal fauces. The size and duration of these lesions can sometimes lead to soft tissue scarring. Herpetiform RAS is the least common form of aphthous ulcer and has been reported to represent 5 to 10 percent of lesions seen in patients.^{5,7,9} (Figure 3) These lesions usually cluster together in groups of 10 to 100, often



Figure 1a. Minor recurrent aphthous stomatitis ulcerative lesion on lower labial mucosa



Figure 1b. Minor recurrent aphthous stomatitis ulcerative lesion on lower buccal mucosa



Image courtesy of HIVDent



Figure 2. Major recurrent aphthous stomatitis ulcerative lesion

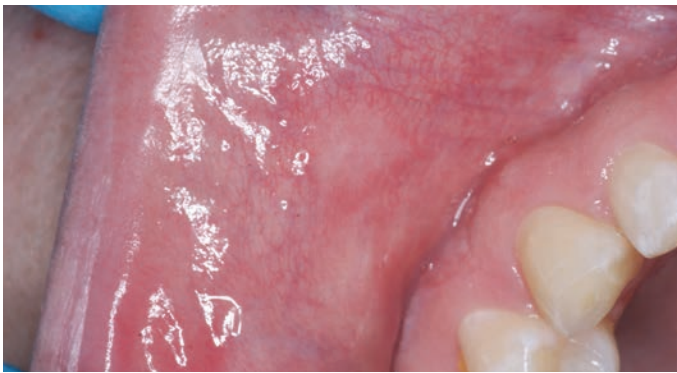


Figure 3. Herpetiform recurrent aphthous stomatitis lesion

Image courtesy of Klaus Peter

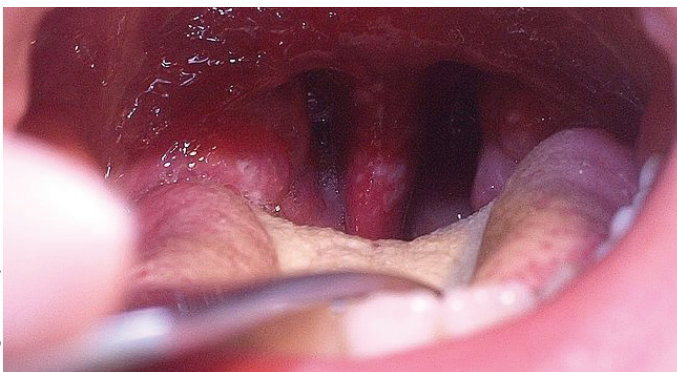


Figure 4. Herpangina

in the posterior areas of the mouth. They can last 7 to 30 days and can develop into larger coalesced lesions with the potential for scarring. Even though these lesions appear to be herpetiform in appearance, herpes simplex virus cannot be recovered from these lesions.¹⁰

No matter what type of RAS a patient has, they are located on nonkeratinized mucosal tissues of the mouth.^{2,4,11} Some patients will report feeling localized pain or a burning sensation 24 to 48 hours before the ulcer actually appears.⁴ Most patients will report that they have recurrences two to four times a year; however, some patients may have an almost continuous series of ulcers wherein some will appear as earlier ones are still healing.⁴ (Table 1)

Differential diagnosis

Usually the differential diagnosis for RAS is made based on the patient's history and the clinical appearance of the lesion(s). Many other mucosal lesions have an ulcerated appearance, and it is important to differentiate RAS from other ulcerated lesions (including, and especially, oral cancer). This can be done based on the location of the ulceration and the presence or absence of other symptoms. In some cases biopsy and histologic examination may be necessary to provide a definitive diagnosis. Herpes simplex virus (HSV) infections can have a similar appearance to RAS. HSV infections are differentiated from RAS by their diffuse gingival erythema and a fever that precedes the oral vesicles and ulcers.³ HSV is located in keratinized tissues (i.e., the attached gingivae, hard palate).¹² In contrast, RAS is present on movable (nonkeratinized) mucosal tissues with no vesicle formation or presence of fever. (Table 2)

Viral infections that are less frequent, including the varicella zoster virus, can also be associated with oral ulcers or present with other symptoms. In the case of herpangina (Figure 4), there is fever and malaise. Erythema multiforme is an autoimmune disease and can present with oral ulcers; however, the patient's history (for example, an autoimmune response to taking antibiotics) and the appearance of extraoral skin macules on the face and body differentiate these from RAS. (Figure 5) Similarly, pemphigus vulgaris presents with systemic signs of lesions on the skin as well as intraorally and, in the case of hand-foot-and-mouth disease, as the name suggests, there are also skin lesions with vesicles preceding the ulcers. (Figure 6) Oral lichen

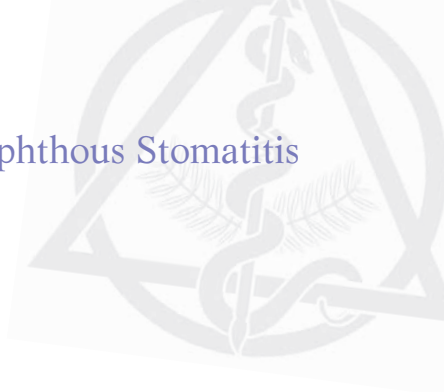


Table 1. Characteristics of recurrent aphthous ulcer (stomatitis) (RAU or RAS)

Type of RAS	Characteristics			
	Size (mm)	Duration (days)	Scarring	Percent of RAU
Minor RAS	5-10	10-14	no	70-87%
Major RAS	>10	>14	yes	7-15%
Herpetiform RAS	<5	10-14	yes	5-10%
Both major RAS and herpetiform RAS can persist for several weeks or months.				

Adapted from Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis. *J Am Dent Assoc.* 2003;134:200-207.

Table 2. Differential diagnosis of RAS

Differential Diagnosis	Oral Appearance	Other Symptoms
Recurrent aphthous ulcers	Single or multiple ulcers on unattached mucosal tissues	May be linked with oropharyngeal or gastrointestinal ulcers
Herpes simplex virus	Single or multiple ulcers on attached gingivae	Preceded by fever and vesicles
Varicella zoster virus (shingles)	Intraoral and extraoral ulcers with unilateral distribution	Prodromal pain and burning; may cause scarring and neuralgia
Herpangina	Multiple ulcers on the hard palate, soft palate, and/or oropharynx	Fever and malaise
Erythema multiforme	Lesions on both attached and unattached mucosa; lip crusting; may be preceded by HSV infection	Sudden onset of skin macules and papules; target lesions on the skin
Pemphigus vulgaris	Vesiculobullous lesions on attached and unattached mucosa; Positive Nikolsky's sign	Lesions can occur on the skin
Hand-foot-and-mouth disease	Ulcers preceded by vesicles	Skin lesions, low-grade fever, malaise
Oral lichen planus	Erosive and reticular lesions on buccal mucosa, gingival, palate, tongue; Wickham's (white) striae	May be symptomatic; lesions may occur on the skin

Adapted from Ship JA, Chavez EM, Doerr PA, Henson BS, et al. Recurrent aphthous stomatitis. *Quintessence Int.* 2000;95-112.



Figure 5. The appearance of erythema multiforme

planus may or may not have extraoral signs; however, its appearance differs from RAU and the history also helps differentiate it. (Table 2)

Possible contributory factors for RAS

The possible causes of RAS have drawn significant research focus, but there are still no definitive answers. Causation of RAS can include local and systemic conditions, immunologic, genetic, and infectious microbial factors. Five major categories of predisposing conditions have been described as contributing to RAS.^{1,2}

Local factors

A causative factor that has been associated with RAS has been trauma in the area where the ulcer forms. The trauma can include anesthetic injections, sharp foods causing oral trauma, traumatic toothbrushing, and trauma during dental treatment.¹ Interestingly, many patients identified with RAS do not get lesions after dental trauma,¹³ and even patients with ill-fitting dentures do not demonstrate RAS.¹⁴

Microbial etiology

While it has been suggested that some oral bacteria and viruses may be causative agents for RAS, the results have



Figure 6. Extraoral lesions of hand-foot-and-mouth disease

not been positive.^{10,15} Investigations into a microbial etiology for RAS are continuing to expand researchers' understanding of the role that viruses play in RAS outbreaks and recurrences.¹

Systemic Factors

Patients with systemic disorders including Behçet's disease,^{7,16,17} Crohn's disease and ulcerative colitis,¹⁸ Reiter's syndrome,¹⁹ oral and genital ulcers with inflamed cartilage syndrome,²⁰ cyclic neutropenia,²¹ gastrointestinal disorders,²² and immune-compromised conditions such as HIV/AIDS²³ have demonstrated RAS more often than the normal population. (Figure 7) Other conditions that can result in oral ulcers include MAGIC disease and Sweet syndrome. These however are associated with systemic signs and symptoms that in the case of MAGIC disease and Behçet's disease can include genital ulceration, and in the case of Behçet's disease also ocular ulcers.

Foods and nutritional status have also been associated with RAS.³ Among those reported in the literature are chocolate, gluten, toothpaste ingredient allergies, folic acid, iron, selenium and zinc, as well as vitamins B1, B2, B6 and B12 deficiencies.¹ Some studies have associated stress with RAS,^{24,25} however more recent clinical evaluations and surveys have raised questions about the correlation between stress and RAS recurrences.²⁶ Toothpastes containing sodium lauryl sulfate (SLS) have been implicated in increasing the rate of RAS.^{27,28} SLS



Figure 7. Herpes simplex virus lesion in HIV/AIDS patient

is a detergent that provides the foaming action in oral health care products. It is believed that this action may cause destabilization of the cell membranes and eventually epithelial desquamation of the oral soft tissue in sensitive patients.²⁹ Oral care products that are SLS-free include Tom's of Maine Fluoride-Free Clean and Natural Toothpaste. Rowpar Pharmaceuticals also manufactures oral care products that are SLS-free. Additionally, one in vitro study also found that a low-level SLS dentifrice was beneficial and protective, reducing the incidence of RAS.³⁰

Genetic factors

Ship and others have found a definite link among families wherein RAS are present.³¹ In fact, it is statistically more likely for identical twins to both have RAS than for both twins who are non-identical to have them.³²

Immunologic conditions

Patients can be at risk for RAS due to immunological abnormalities that result in immune imbalances. Localized T-cell dysfunction and antibody-dependent cellular cytotoxicity have been implicated.^{1,4} Patients with HIV/AIDS are at a higher risk for RAS, as well as for other oral ulcers and lesions.^{23,33}

Treatment recommendations

Even with the signs and symptoms of RAS, it still may be necessary to perform a biopsy to confirm the

diagnosis. Once a diagnosis has been established, the patient who seeks help due to RAS wants to minimize the discomfort and hopefully treat the ulcers to lessen the course of the disease. Symptomatic treatment of the condition's acute phase is important. Even though the etiology of RAS is not clear, it might be helpful for the patient to keep a diary in the hope of discovering any associated conditions that might have caused the recurrence. From this record, a practitioner can provide the patient with some recommendations to assess if the factor/condition may be contributory.

The goals of treatment of RAS are to decrease symptoms, reduce the number and size of ulcers, and increase the periods of time between recurrences.⁴ When recommending treatment, the goal should be to control the RAS for the longest duration with the minimum number of adverse side effects. There are few controlled trials that have evaluated treatments for RAS.⁴ While the use of chlorhexidine gluconate mouthwashes and topical steroids can reduce the severity and duration of the RAS, neither has influenced the frequency of recurrences.³⁴

A consensus report in the *Journal of the American Dental Association* describes taking a systematic approach to the treatment of RAS through a classification system based on ulceration severity and patient symptoms. Type A RAS patients have the least severe form of the disease and Type C the most severe.⁴ Type A refers to RAS episodes lasting only a few days with mild discomfort; lesions recur only a few times a year. Type B patients experience painful ulcers occurring each month and lasting 3 to 10 days. Type C RAS patients have painful, chronic courses of the disease—as one ulcer heals, another is developing.

For the Type A RAS patient, identifying the cause is useful. The cause may be localized trauma in the area where the outbreak occurs. If it is suspected that the lesion was initiated by trauma, it is helpful to identify the cause and modify the behaviors that might have been responsible (e.g., changing to a softer toothbrush, modifying the brushing actions where toothbrush trauma is suspected or known to have been contributory). Usually medication is



not necessary. For symptomatic relief, the use of an over-the-counter topical anesthetic can be recommended.⁴

Treatment of Type B RAS patients needs to be more aggressive. Options include the use of topical ointments, gels and creams to control both the symptoms and duration of the RAS. Applying topical medications during the early onset of the ulcer provides the best results.³ It is important to discuss with the patient the possible etiologies that may have precipitated the episode, including trauma, stress, changes in diet, and changes in oral hygiene. If the patient has experienced prodromal symptoms such as burning, tingling, or swelling in the area, corticosteroid ointments at this stage can terminate progression of the recurrence. It is important to review the patient's medical history to ensure that there are no contraindications to the use of steroids. If the ulcers recur in the same area, alternative treatments can include symptomatic relief with topical anesthetics mixed with high-potency corticosteroids such as clobetasol

ointment 0.05% in Orabase 1:1. Flucinomide ointment 0.05% in Orabase 1:1.⁴ Zilactin can also be used—it has been shown to adhere better than Orabase and may provide better protection and pain relief from the ulcer.^{35,36}

Rinses can also be used to reduce the number and severity of ulcers. Use of a dexamethasone elixir (0.5mg/5ml) as a mouthwash or gargle has been reported to be useful in treating all three classes of RAS when the areas are difficult to access with topical gels and ointments.^{23,37}

Patients that fall into the Type C category — those who present with the greatest severity of RAU combined with continuous cycling of healing and ulceration — are in this author's view better managed by oral medicine specialists. If there is no oral medicine specialist in your area, a periodontist or oromaxillofacial surgeon should be consulted. Treatment for these patients can include intralesional injections of corticosteroids to boost local response.⁴ Also, more potent topical corticosteroids would be used and in

Table 3. Treatment of RAS		
Category	Symptoms and Recurrences	Care
Type A	RAS last a few days Mild discomfort Recur a few times a year	Symptomatic relief with over-the-counter topical anesthetic Oral hygiene advice
Type B	Painful ulcers Occur each month Last 3 to 10 days	Symptomatic relief with over-the-counter topical anesthetic mixed with a high-potency corticosteroid Use of corticosteroid ointment at prodromal stage to avert progression Uses of rinses: - Dexamethasone elixir - Barrier rinses for oral mucosal coating Advice on removing possible etiologies Advice on oral hygiene Ongoing assessment of nutrition and fluid intake
Type C	Painful, chronic ulcers As one ulcer heals, another develops	Refer to oral medicine specialist Treatment may include: - Intralesional injections of corticosteroids - More potent corticosteroids than Type A or Type B - Use of immunosuppressants in the most severe cases



some cases immunosuppressants might also be used. All of these medications have higher risks of potential adverse reactions than recommendations for Type A and Type B RAS patients.⁴ (Table 3)

An ongoing assessment of nutrition and fluid intakes such as vitamin and mineral supplements is critical in caring for patients who have persistent and painful RAS. To control the oral lesion pain, topical anesthetics should be recommended. The discomfort of these lesions can cause patients to avoid eating, and the use of liquid supplements such as Ensure (Abbott Laboratories) can provide much needed nutrition during this time. Patients should be advised to avoid citrus fruits and other acidic foods and beverages, foods that require significant mastication, and salty and spicy foods. Patients should also be told to limit alcoholic beverage intake.⁴

Conclusion

RAS can be a very frustrating condition for both patients and clinicians. There is no cure for RAS and, while there are indications of what may cause certain cases, the etiology is still unclear. RAS can also occur due to a number of systemic conditions. Before implementing treatment, a definitive diagnosis must be made and in some instances, a biopsy of the site may be necessary. A patient with RAS should be treated with palliative therapy along with topical anesthetics. In the more severe cases, the patient should be monitored for nutrition and adequate intake of fluids. The proper management of RAS can make a significant difference in maintaining a patient's quality of life.³³

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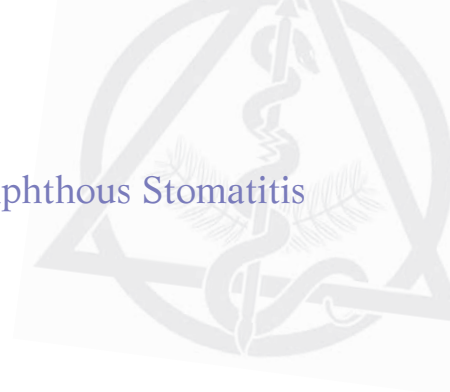
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1. A _____ is a form of ulcer that occurs with recurrent aphthous stomatitis.
 - a. minor recurrent aphthous ulcer
 - b. major recurrent aphthous ulcer
 - c. herpetiform recurrent aphthous ulcer
 - d. all of the above
2. Minor RAS are typically found on the _____.
 - a. buccal or labial mucosal tissues
 - b. soft palate
 - c. floor of the mouth
 - d. all of the above
3. The clinical appearance of minor RAS is characteristically one of shallow, isolated ulcers approximately _____ in size covered by a _____ and surrounded by a raised reddened halo.
 - a. 5-10 mm; whitish, yellow-grey membrane
 - b. 5-10 mm; whitish, yellow-grey pseudomembrane
 - c. 2-5 mm; reddish pseudomembrane
 - d. 5-10 mm; reddish membrane
4. Major RAS come together to form lesions that are _____ in size and can cause patients to change their eating and drinking habits to avoid _____.
 - a. greater than 10 millimeters; weight gain
 - b. less than 5 millimeters; discomfort
 - c. greater than 10 millimeters; discomfort
 - d. less than 10 millimeters; discomfort
5. _____ of recurrent aphthous ulcers is major.
 - a. Seven to ten percent
 - b. Seven to fifteen percent
 - c. Ten to fifteen percent
 - d. Fifteen to thirty percent
6. Major aphthous ulcers are typically found on the patient's _____.
 - a. palatal fauces
 - b. hard and soft palate
 - c. lips, tongue and soft palate
 - d. a and c
7. _____ is/are typically preceded by fever.
 - a. Herpangina
 - b. Herpes simplex ulcers
 - c. Hand-foot-and-mouth disease
 - d. all of the above
8. Recurrent aphthous ulcers are located on _____.
 - a. keratinized mucosal tissues of the mouth
 - b. nonkeratinized mucosal tissues of the mouth
 - c. mucosal tissues of the mouth and on the skin
 - d. all of the above
9. Some patients will report feeling localized pain or a burning sensation _____ before the ulcer actually appears and report that they have recurrences _____.
 - a. 12 to 24 hours; two to four times a month
 - b. 24 to 48 hours; two to four times a month
 - c. 12 to 24 hours; two to four times a year
 - d. 24 to 48 hours; two to four times a year
10. Usually the differential diagnosis for RAS is made based on the _____.
 - a. clinical appearance
 - b. patient's history and the clinical appearance
 - c. patient's history, clinical appearance and radiographs
 - d. none of the above
11. A biopsy and histologic examination may be necessary to provide a _____ diagnosis.
 - a. quick
 - b. differential
 - c. definitive
 - d. all of the above
12. Ulcers associated with herpes simplex virus infections are differentiated from recurrent aphthous ulcers by _____.
 - a. their diffuse gingival erythema
 - b. the fever that precedes them
 - c. their location on keratinized tissues
 - d. all of the above
13. _____ can involve oral ulcerations and is the result of a viral infection.
 - a. Varicella zoster virus
 - b. Lichen planus
 - c. Pemphigus
 - d. all of the above
14. The oral ulcers associated with erythema multiforme can be differentiated from RAS by _____.
 - a. the patient's history
 - b. the appearance of extraoral skin macules on the face and body
 - c. the size of the ulcers
 - d. a and b
15. Wickham's striae are seen with _____.
 - a. pemphigus vulgaris
 - b. herpangina
 - c. lichen planus
 - d. all of the above
16. A(n) _____ is possibly causative for RAS.
 - a. immunologic factor
 - b. genetic factor
 - c. local or systemic condition
 - d. all of the above



CE QUIZ

17. Investigations into a microbial etiology for RAS are continuing to expand researchers' understanding of the role that _____ play in RAS outbreaks and recurrences.
 - a. bacteria
 - b. viruses
 - c. prions
 - d. all of the above
18. Patients with _____ have demonstrated RAS more often than the normal population.
 - a. Crohn's disease
 - b. Immune-compromised conditions
 - c. MAGIC disease
 - d. all of the above
19. Patients that fall into the Type C category, those who present with the greatest severity of RAU combined with continuous cycling of healing and ulceration, are in this author's view better managed by _____.
 - a. pediatricians
 - b. oral medicine specialists
 - c. general physicians
 - d. a and c
20. There is an association of deficiency of vitamin _____ and recurrent aphthous ulcers.
 - a. B1 and B2
 - b. B6
 - c. B12
 - d. all of the above
21. The goal of treatment of recurrent aphthous ulcers is to _____.
 - a. reduce the number and size of ulcers
 - b. increase the periods of time between recurrences
 - c. decrease symptoms
 - d. all of the above
22. According to the classification system for recurrent aphthous ulcers in the consensus report of the Journal of the American Dental Association, a Type B patient has painful ulcers occurring each month and lasting for _____.
 - a. 1 to 3 days
 - b. 2 to 5 days
 - c. 3 to 10 days
 - d. 5 to 7 days
23. For a Type A patients with recurrent aphthous ulcers, _____ can be recommended for symptomatic relief.
 - a. an over-the-counter topical anesthetic
 - b. an oral corticosteroid
 - c. an anti-viral agent
 - d. b or c
24. _____ is a prodromal symptom that the patient may experience prior to the existence of visible recurrent aphthous ulcer lesions.
 - a. Swelling
 - b. A tingling sensation
 - c. A burning sensation
 - d. all of the above
25. For a Type B patient with recurrent aphthous ulcers, _____ can be used to treat the condition.
 - a. topical anesthetics
 - b. high potency topical corticosteroids
 - c. rinses
 - d. all of the above
26. Use of a dexamethasone elixir (0.5mg/5ml) as a mouthwash or gargle has been reported to be useful in treating _____ when the areas are difficult to access with topical gels and ointments.
 - a. minor and major recurrent aphthous ulcers
 - b. herpetiform aphthous ulcers
 - c. only major aphthous ulcers
 - d. a and b
27. Intralesional injections of corticosteroids have been used to boost local response in patients with severe recurrent aphthous ulcerations.
 - a. antibiotics
 - b. corticosteroids
 - c. antiviral agents
 - d. a and b
28. An ongoing assessment of _____ is critical to caring for patients who have persistent and painful RAS.
 - a. nutrition and fluid intakes
 - b. body temperature
 - c. brain function
 - d. all of the above
29. The management of RAS can make a significant difference in a patient's _____.
 - a. morbidity
 - b. mortality
 - c. quality of life
 - d. none of the above
30. Herpetiform recurrent aphthous ulcers are the _____ common form of aphthous ulcer and usually cluster together in groups of _____.
 - a. least; 20 to 50
 - b. most; 20 to 50
 - c. least; 10 to 100
 - d. most; 10 to 100

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EDUCATIONAL OBJECTIVES

1. List and describe the different types of recurrent aphthous ulcers;
2. Differentiate between recurrent aphthous ulcers and herpes simplex ulcers;
3. List and consider the different types of ulcers and associated conditions that must be part of the differential diagnosis for recurrent aphthous ulcers; and
4. Provide an overview of the types of treatments available for the different categories of recurrent aphthous ulcer patients.

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Please evaluate this course using a scale of 3 to 1, where 3 is excellent and 1 is poor.

1. Clarity of objectives ③ ② ①
2. Usefulness of content ③ ② ①
3. Benefit to your clinical practice ③ ② ①
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5. Quality of written presentation ③ ② ①
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7. Clarity of quiz questions ③ ② ①
8. Relevance of quiz questions ③ ② ①
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