

## Medscape Reference Reference

- News
- Reference
- Education
- MEDLINE



# Aphthous Stomatitis

---

- Author: Jeffrey M Casiglia, DMD, DMSc; Chief Editor: Dirk M Elston, MD [more...](#)

Updated: Jun 7, 2012

## Background

Aphthous stomatitis, or recurrent aphthous ulcers (RAUs) or canker sores, are among the most common oral mucosal lesions physicians and dentists observe. Recurrent aphthous ulcer is a disorder of unknown etiology that can cause clinically significant morbidity. One or several discrete, shallow, painful ulcers are visible on the unattached mucous membranes. Individual ulcers typically last 7-10 days. Larger ulcers may last several weeks to months and can scar when healing.

Although the process in idiopathic recurrent aphthous ulcers is usually self-limiting, in some individuals, the ulcer activity can be almost continuous. Similar ulcers can be noted in the genital region. [Behçet syndrome](#), [systemic lupus erythematosus](#), and [inflammatory bowel disease](#) are systemic diseases associated with oral recurrent aphthous ulcers.

## Pathophysiology

The classic categorization of recurrent aphthous ulcer is division into 3 clinical forms: recurrent aphthous ulcer minor, recurrent aphthous ulcer major, and herpetiform recurrent aphthous ulcer. Recurrent aphthous ulcer affects the following nonkeratinized or poorly keratinized surfaces of the oral mucosa:

- Labial and buccal mucosa
- Maxillary and mandibular sulci
- Unattached gingiva
- Soft palate
- Tonsillar fauces
- Floor of the mouth
- Ventral surface of the tongue

## Recurrent aphthous ulcer minor

Recurrent aphthous ulcer minor is the most common form, accounting for 80% of all cases. Discrete, painful, shallow, recurrent ulcers smaller than 1 cm in diameter characterize this form. At any time, one or more ulcers can be present. Lesions heal without scarring within 7-10 days. The periodicity varies between individuals, with some having longer ulcer-free episodes and some never being free from ulcers.

## Recurrent aphthous ulcer major

Recurrent aphthous ulcer is formerly known as periadenitis mucosa necrotica recurrens. This form is less common than the others and is characterized by oval ulcers greater than 1 cm in diameter. In this relatively severe form, many major aphthae may be present simultaneously. Ulcers are large and deep, may have irregular borders, and may coalesce. Upon healing, which may take as long as 6 weeks, ulcers can leave scarring, and severe distortion of oral and pharyngeal mucosa may occur.

### Herpetiform recurrent aphthous ulcer

This least common form (5-10% of cases) has the smallest of the aphthae, commonly no larger than 1 mm in diameter. The aphthae tend to occur in clusters that may consist of tens or hundreds of minute ulcers. Clusters may be small and localized, or they may be distributed throughout the soft mucosa of the oral cavity.

## Epidemiology

### Frequency

#### United States

- Recurrent aphthous ulcers are the most common oral mucosal disease in North America. They affect 20% of the population, with the incidence rising to more than 50% in certain groups of students in professional schools. Children from high socioeconomic groups may be affected more than those from low socioeconomic groups.<sup>[1]</sup>

#### International

- Recurrent aphthous ulcers occur worldwide and are reported on every populated continent. Recurrent aphthous ulcers affect 2-66% of the international population.<sup>[2]</sup>

### Mortality/Morbidity

- Unless recurrent aphthous ulcer is associated with a systemic disease, such as Behçet syndrome or inflammatory bowel disease, it rarely leads to clinically significant morbidity or mortality.

### Sex

- In children and in some adult communities who are affected, the incidence of recurrent aphthous ulcer is higher in female individuals than in male individuals.

### Age

- Recurrent aphthous ulcer minor is the most common form of childhood recurrent aphthous ulcer. Approximately 1% of American children may have recurrent aphthous ulcers, with onset before age 5 years. The percentage of patients who are affected decreases after the third decade.
- Recurrent aphthous ulcer major has a typical onset after puberty and can persist for the remainder of an individual's life, although after late adulthood episodes become much less common.
- Herpetiform recurrent aphthous ulcer first occurs in the second decade of life; the majority of persons have onset when younger than 30 years. The frequency and the severity of episodes may increase during the third and fourth decades and then decrease with advancing age.

## Contributor Information and Disclosures

Author

**Jeffrey M Casiglia, DMD, DMSc** Lecturer, Harvard School of Dental Medicine; Private Practice, Salem, Massachusetts

Jeffrey M Casiglia, DMD, DMSc is a member of the following medical societies: [American Academy of Oral Medicine](#) and [American Dental Association](#)

Disclosure: Nothing to disclose.

## Coauthor(s)

**Ginat W Mirowski, MD, DMD** Adjunct Associate Professor, Departments of Oral Pathology, Medicine, and Radiology, Indiana University School Medicine

Ginat W Mirowski, MD, DMD is a member of the following medical societies: [American Academy of Dermatology](#) and [American Medical Women's Association](#)

Disclosure: Nothing to disclose.

**Christy L Nebesio, MD** Dermatologist

Christy L Nebesio, MD is a member of the following medical societies: [Alpha Omega Alpha](#)

Disclosure: Nothing to disclose.

## Specialty Editor Board

**David P Fivenson, MD** Associate Director, St Joseph Mercy Hospital Dermatology Program, Ann Arbor, Michigan

David P Fivenson, MD is a member of the following medical societies: [American Academy of Dermatology](#), [Medical Dermatology Society](#), [Michigan Dermatological Society](#), [Michigan State Medical Society](#), [Photomedicine Society](#), [Society for Investigative Dermatology](#), and [Wound Healing Society](#)

Disclosure: Nothing to disclose.

**Richard P Vinson, MD** Assistant Clinical Professor, Department of Dermatology, Texas Tech University Health Sciences Center, Paul L Foster School of Medicine; Consulting Staff, Mountain View Dermatology, PA

Richard P Vinson, MD is a member of the following medical societies: [American Academy of Dermatology](#), [Association of Military Dermatologists](#), [Texas Dermatological Society](#), and [Texas Medical Association](#)

Disclosure: Nothing to disclose.

**Warren R Heymann, MD** Head, Division of Dermatology, Professor, Department of Internal Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School

Warren R Heymann, MD is a member of the following medical societies: [American Academy of Dermatology](#), [American Society of Dermatopathology](#), and [Society for Investigative Dermatology](#)

Disclosure: Nothing to disclose.

**Catherine M Quirk, MD** Clinical Assistant Professor, Department of Dermatology, University of Pennsylvania

Catherine M Quirk, MD is a member of the following medical societies: [Alpha Omega Alpha](#) and [American Academy of Dermatology](#)

Disclosure: Nothing to disclose.

## Chief Editor

**Dirk M Elston, MD** Director, Ackerman Academy of Dermatopathology, New York

Dirk M Elston, MD is a member of the following medical societies: [American Academy of Dermatology](#)

Disclosure: Nothing to disclose.

## References

1. Crivelli MR, Aguas S, Adler I, Quarracino C, Bazerque P. Influence of socioeconomic status on oral mucosa lesion prevalence in schoolchildren. *Community Dent Oral Epidemiol*. Feb 1988;16(1):58-60. [[Medline](#)].

2. Axéll T, Henricsson V. The occurrence of recurrent aphthous ulcers in an adult Swedish population. *Acta Odontol Scand*. May 1985;43(2):121-5. [Medline].
3. Gallo Cde B, Mimura MA, Sugaya NN. Psychological stress and recurrent aphthous stomatitis. *Clinics (Sao Paulo)*. 2009;64(7):645-8. [Medline]. [Full Text].
4. Huling LB, Baccaglini L, Choquette L, Feinn RS, Lalla RV. Effect of stressful life events on the onset and duration of recurrent aphthous stomatitis. *J Oral Pathol Med*. Feb 2012;41(2):149-52. [Medline]. [Full Text].
5. MacPhail LA, Greenspan D, Feigal DW, Lennette ET, Greenspan JS. Recurrent aphthous ulcers in association with HIV infection. Description of ulcer types and analysis of T-lymphocyte subsets. *Oral Surg Oral Med Oral Pathol*. Jun 1991;71(6):678-83. [Medline].
6. Burton-Kee JE, Mowbray JF, Lehner T. Different cross-reacting circulating immune complexes in Behçet's syndrome and recurrent oral ulcers. *J Lab Clin Med*. Apr 1981;97(4):559-67. [Medline].
7. Eglin RP, Lehner T, Subak-Sharpe JH. Detection of RNA complementary to herpes-simplex virus in mononuclear cells from patients with Behçet's syndrome and recurrent oral ulcers. *Lancet*. Dec 18 1982;2(8312):1356-61. [Medline].
8. Jorizzo JL. Behçet's disease. In: Freedberg IM, Eisen AZ, Wolff K, et al, eds. *Dermatology in General Medicine*. Vol 2. New York: McGraw-Hill Professional; 1999:2161-5.
9. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. *N Engl J Med*. Oct 21 1999;341(17):1284-91. [Medline].
10. Studd M, McCance DJ, Lehner T. Detection of HSV-1 DNA in patients with Behçet's syndrome and in patients with recurrent oral ulcers by the polymerase chain reaction. *J Med Microbiol*. Jan 1991;34(1):39-43. [Medline].
11. Adisen E, Aral A, Aybay C, Güreç MA. Salivary epidermal growth factor levels in Behçet's disease and recurrent aphthous stomatitis. *Dermatology*. 2008;217(3):235-40. [Medline].
12. Ferguson MM, Wray D, Carmichael HA, Russell RI, Lee FD. Coeliac disease associated with recurrent aphthae. *Gut*. Mar 1980;21(3):223-6. [Medline].
13. Ferguson R, Basu MK, Asquith P, Cooke WT. Jejunal mucosal abnormalities in patients with recurrent aphthous ulceration. *Br Med J*. Jan 3 1976;1(6000):11-13. [Medline].
14. Wray D. Gluten-sensitive recurrent aphthous stomatitis. *Dig Dis Sci*. Aug 1981;26(8):737-40. [Medline].
15. Yasar S, Yasar B, Abut E, Asiran Serdar Z. Clinical importance of celiac disease in patients with recurrent aphthous stomatitis. *Turk J Gastroenterol*. Feb 2012;23(1):14-8. [Medline].
16. Miller MF, Garfunkel AA, Ram C, Ship II. Inheritance patterns in recurrent aphthous ulcers: twin and pedigree data. *Oral Surg Oral Med Oral Pathol*. Jun 1977;43(6):886-91. [Medline].
17. Wilhelmsen NS, Weber R, Monteiro F, Kalil J, Miziara ID. Correlation between histocompatibility antigens and recurrent aphthous stomatitis in the Brazilian population. *Braz J Otorhinolaryngol*. May-Jun 2009;75(3):426-31. [Medline].
18. Kozlak ST, Walsh SJ, Lalla RV. Reduced dietary intake of vitamin B12 and folate in patients with recurrent aphthous stomatitis. *J Oral Pathol Med*. Feb 7 2010;[Medline].
19. Carrozzo M. Vitamin B12 for the treatment of recurrent aphthous stomatitis. *Evid Based Dent*. 2009;10(4):114-5. [Medline].
20. Baccaglini L, Lalla RV, Bruce AJ, Sartori-Valinotti JC, Latortue MC, Carrozzo M, et al. Urban legends: recurrent aphthous stomatitis. *Oral Dis*. Nov 2011;17(8):755-70. [Medline]. [Full Text].
21. Yasui K, Kurata T, Yashiro M, Tsuge M, Ohtsuki S, Morishima T. The effect of ascorbate on minor recurrent aphthous stomatitis. *Acta Paediatr*. Dec 10 2009;[Medline].
22. Sun A, Chu CT, Wu YC, Yuan JH. Mechanisms of depressed natural killer cell activity in recurrent

- aphthous ulcers. *Clin Immunol Immunopathol*. Jul 1991;60(1):83-92. [Medline].
23. Lewkowicz N, Kur B, Kurnatowska A, Tchorzewski H, Lewkowicz P. Expression of Th1/Th2/Th3/Th17-related genes in recurrent aphthous ulcers. *Arch Immunol Ther Exp (Warsz)*. Oct 2011;59(5):399-406. [Medline].
  24. Taylor LJ, Bagg J, Walker DM, Peters TJ. Increased production of tumour necrosis factor by peripheral blood leukocytes in patients with recurrent oral aphthous ulceration. *J Oral Pathol Med*. Jan 1992;21(1):21-5. [Medline].
  25. Hasan A, Childerstone A, Pervin K, et al. Recognition of a unique peptide epitope of the mycobacterial and human heat shock protein 65-60 antigen by T cells of patients with recurrent oral ulcers. *Clin Exp Immunol*. Mar 1995;99(3):392-7. [Medline].
  26. Miyamoto NT Jr, Borra RC, Abreu M, Weckx LL, Franco M. Immune-expression of HSP27 and IL-10 in recurrent aphthous ulceration. *J Oral Pathol Med*. Sep 2008;37(8):462-7. [Medline].
  27. Albanidou-Farmaki E, Pouloupoulos AK, Epivatianos A, Farmakis K, Karamouzis M, Antoniadis D. Increased anxiety level and high salivary and serum cortisol concentrations in patients with recurrent aphthous stomatitis. *Tohoku J Exp Med*. Apr 2008;214(4):291-6. [Medline].
  28. Borra RC, de Mesquita Barros F, de Andrade Lotufo M, Villanova FE, Andrade PM. Toll-like receptor activity in recurrent aphthous ulceration. *J Oral Pathol Med*. Mar 2009;38(3):289-98. [Medline].
  29. Arikan S, Durusoy C, Akalin N, Haberal A, Seckin D. Oxidant/antioxidant status in recurrent aphthous stomatitis. *Oral Dis*. Oct 2009;15(7):512-5. [Medline].
  30. Ozdemir IY, Calka O, Karadag AS, Akdeniz N, Ozturk M. Thyroid autoimmunity associated with recurrent aphthous stomatitis. *J Eur Acad Dermatol Venereol*. Feb 2012;26(2):226-30. [Medline].
  31. Ghodrathnama F, Wray D, Bagg J. Detection of serum antibodies against cytomegalovirus, varicella zoster virus and human herpesvirus 6 in patients with recurrent aphthous stomatitis. *J Oral Pathol Med*. Jan 1999;28(1):12-5. [Medline].
  32. Pedersen A, Hornsleth A. Recurrent aphthous ulceration: a possible clinical manifestation of reactivation of varicella zoster or cytomegalovirus infection. *J Oral Pathol Med*. Feb 1993;22(2):64-8. [Medline].
  33. Albanidou-Farmaki E, Giannoulis L, Markopoulos A, et al. Outcome following treatment for *Helicobacter pylori* in patients with recurrent aphthous stomatitis. *Oral Dis*. Jan 2005;11(1):22-6. [Medline].
  34. Birek C, Grandhi R, McNeill K, Singer D, Ficarra G, Bowden G. Detection of *Helicobacter pylori* in oral aphthous ulcers. *J Oral Pathol Med*. May 1999;28(5):197-203. [Medline].
  35. Elsheikh MN, Mahfouz ME. Prevalence of *Helicobacter pylori* DNA in recurrent aphthous ulcerations in mucosa-associated lymphoid tissues of the pharynx. *Arch Otolaryngol Head Neck Surg*. Sep 2005;131(9):804-8. [Medline].
  36. Mansour-Ghanaei F, Asmar M, Bagherzadeh AH, Ekbataninezhad S. *Helicobacter pylori* infection in oral lesions of patients with recurrent aphthous stomatitis. *Med Sci Monit*. Dec 2005;11(12):CR576-9. [Medline].
  37. Porter SR, Barker GR, Scully C, Macfarlane G, Bain L. Serum IgG antibodies to *Helicobacter pylori* in patients with recurrent aphthous stomatitis and other oral disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Mar 1997;83(3):325-8. [Medline].
  38. Hasan AA, Ciancio S. Association between ingestion of nonsteroidal anti-inflammatory drugs and the emergence of aphthous-like ulcers. *J Int Acad Periodontol*. Jan 2009;11(1):155-9. [Medline].
  39. Padeh S, Stoffman N, Berkun Y. Periodic fever accompanied by aphthous stomatitis, pharyngitis and cervical adenitis syndrome (PFAPA syndrome) in adults. *Isr Med Assoc J*. May 2008;10(5):358-60. [Medline].
  40. Rogers RS 3rd, Hutton KP. Screening for haematinic deficiencies in patients with recurrent aphthous stomatitis. *Australas J Dermatol*. Dec 1986;27(3):98-103. [Medline].

41. Alidaee MR, Taheri A, Mansoori P, Ghodsi SZ. Silver nitrate cautery in aphthous stomatitis: a randomized controlled trial. *Br J Dermatol*. Sep 2005;153(3):521-5. [Medline].
42. Brice SL. Clinical evaluation of the use of low-intensity ultrasound in the treatment of recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Jan 1997;83(1):14-20. [Medline].
43. Femiano F, Buonaiuto C, Gombos F, Lanza A, Cirillo N. Pilot study on recurrent aphthous stomatitis (RAS): a randomized placebo-controlled trial for the comparative therapeutic effects of systemic prednisone and systemic montelukast in subjects unresponsive to topical therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Mar 2010;109(3):402-7. [Medline].
44. de Abreu MA, Hirata CH, Pimentel DR, Weckx LL. Treatment of recurrent aphthous stomatitis with clofazimine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Nov 2009;108(5):714-21. [Medline].
45. Shim Y, Choi JH, Ahn HJ, Kwon JS. Effect of sodium lauryl sulfate on recurrent aphthous stomatitis: a randomized controlled clinical trial. *Oral Dis*. Feb 22 2012;[Medline].
46. Demetriades N, Hanford H, Laskarides C. General manifestations of Behçet's syndrome and the success of CO<sub>2</sub>-laser as treatment for oral lesions: a review of the literature and case presentation. *J Mass Dent Soc*. Fall 2009;58(3):24-7. [Medline].
47. Hill SC, Stavrakoglou A, Coutts IR. Nicotine replacement therapy as a treatment for complex aphthosis. *J Dermatolog Treat*. Oct 13 2009;[Medline].
48. Hamdy AA, Ibrahim MA. Management of aphthous ulceration with topical quercetin: a randomized clinical trial. *J Contemp Dent Pract*. Jul 1 2010;11(4):E009-16. [Medline].
49. Arikan OK, Birol A, Tuncez F, Erkek E, Koc C. A prospective randomized controlled trial to determine if cryotherapy can reduce the pain of patients with minor form of recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. Jan 2006;101(1):e1-5. [Medline].
50. Eversole LR, Shopper TP, Chambers DW. Effects of suspected foodstuff challenging agents in the etiology of recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol*. Jul 1982;54(1):33-8. [Medline].
51. Hay KD, Reade PC. The use of an elimination diet in the treatment of recurrent aphthous ulceration of the oral cavity. *Oral Surg Oral Med Oral Pathol*. May 1984;57(5):504-7. [Medline].
52. Wright A, Ryan FP, Willingham SE, et al. Food allergy or intolerance in severe recurrent aphthous ulceration of the mouth. *Br Med J (Clin Res Ed)*. May 10 1986;292(6530):1237-8. [Medline].
53. Lalla RV, Choquette LE, Feinn RS, Zawistowski H, Latortue MC, Kelly ET, et al. Multivitamin therapy for recurrent aphthous stomatitis: a randomized, double-masked, placebo-controlled trial. *J Am Dent Assoc*. Apr 2012;143(4):370-6. [Medline].
54. Thornhill MH, Baccaglini L, Theaker E, Pemberton MN. A randomized, double-blind, placebo-controlled trial of pentoxifylline for the treatment of recurrent aphthous stomatitis. *Arch Dermatol*. Apr 2007;143(4):463-70. [Medline].
55. Axell T, Henricsson V. Association between recurrent aphthous ulcers and tobacco habits. *Scand J Dent Res*. Jun 1985;93(3):239-42. [Medline].
56. Bittoun R. Recurrent aphthous ulcers and nicotine. *Med J Aust*. Apr 1 1991;154(7):471-2. [Medline].
57. Sawair FA. Does smoking really protect from recurrent aphthous stomatitis?. *Ther Clin Risk Manag*. Nov 22 2010;6:573-7. [Medline]. [Full Text].
58. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. *Dent Clin North Am*. Jan 2005;49(1):31-47, vii-viii. [Medline].
59. Brice SL, Jester JD, Huff JC. Recurrent aphthous stomatitis. *Curr Prob Dermatol*. 1991;4(3):113-27.
60. Cantarini L, Vitale A, Bartolomei B, Galeazzi M, Rigante D. Diagnosis of PFAPA syndrome applied to a cohort of 17 adults with unexplained recurrent fevers. *Clin Exp Rheumatol*. Mar-Apr 2012;30(2):269-71. [Medline].

61. Chakrabarty AK, Mraz S, Geisse JK, Anderson NJ. Aphthous ulcers associated with imiquimod and the treatment of actinic cheilitis. *J Am Acad Dermatol*. Feb 2005;52(2 Suppl 1):35-7. [Medline].
62. Challacombe SJ, Barkhan P, Lehner T. Haematological features and differentiation of recurrent oral ulceration. *Br J Oral Surg*. Jul 1977;15(1):37-48. [Medline].
63. Embil JA, Stephens RG, Manuel FR. Prevalence of recurrent herpes labialis and aphthous ulcers among young adults on six continents. *Can Med Assoc J*. Oct 4 1975;113(7):627-30. [Medline].
64. Field EA, Brookes V, Tyldesley WR. Recurrent aphthous ulceration in children--a review. *Int J Paediatr Dent*. Apr 1992;2(1):1-10. [Medline].
65. Field EA, Rotter E, Speechley JA, Tyldesley WR. Clinical and haematological assessment of children with recurrent aphthous ulceration. *Br Dent J*. Jul 11 1987;163(1):19-22. [Medline].
66. G Oumlker E, Rodenhuis S. Early onset of oral aphthous ulcers with weekly docetaxel. *Neth J Med*. Oct 2005;63(9):364-6. [Medline].
67. Greenspan JS, Gadol N, Olson JA, et al. Lymphocyte function in recurrent aphthous ulceration. *J Oral Pathol*. Sep 1985;14(8):592-602. [Medline].
68. Hutton KP, Rogers RS 3rd. Recurrent aphthous stomatitis. *Dermatol Clin*. Oct 1987;5(4):761-8. [Medline].
69. Kleinman DV, Swango PA, Pindborg JJ. Epidemiology of oral mucosal lesions in United States schoolchildren: 1986-87. *Community Dent Oral Epidemiol*. Aug 1994;22(4):243-53. [Medline].
70. Letsinger JA, McCarty MA, Jorizzo JL. Complex aphthosis: a large case series with evaluation algorithm and therapeutic ladder from topicals to thalidomide. *J Am Acad Dermatol*. Mar 2005;52(3 Pt 1):500-8. [Medline].
71. Lewkowicz N, Lewkowicz P, Dzitko K, et al. Dysfunction of CD4+CD25high T regulatory cells in patients with recurrent aphthous stomatitis. *J Oral Pathol Med*. Sep 2008;37(8):454-61. [Medline].
72. Murray B, McGuinness N, Biagioni P, Hyland P, Lamey PJ. A comparative study of the efficacy of Aphtheal in the management of recurrent minor aphthous ulceration. *J Oral Pathol Med*. Aug 2005;34(7):413-9. [Medline].
73. Natah SS, Hayrinen-Immonen R, Hietanen J, Malmstrom M, Konttinen YT. Quantitative assessment of mast cells in recurrent aphthous ulcers (RAU). *J Oral Pathol Med*. Mar 1998;27(3):124-9. [Medline].
74. O'Sullivan EM. Nicorandil-induced severe oral ulceration. *J Ir Dent Assoc*. Winter 2004;50(4):157-9. [Medline].
75. Porter SR, Scully C, Flint S. Hematologic status in recurrent aphthous stomatitis compared with other oral disease. *Oral Surg Oral Med Oral Pathol*. Jul 1988;66(1):41-4. [Medline].
76. Porter SR, Scully C, Pedersen A. Recurrent aphthous stomatitis. *Crit Rev Oral Biol Med*. 1998;9(3):306-21. [Medline].
77. Savage NW, Seymour GJ, Kruger BJ. T-lymphocyte subset changes in recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol*. Aug 1985;60(2):175-81. [Medline].
78. Ship II, Morris AL, Durocher RT, et al. Recurrent aphthous ulcerations and recurrent herpes labialis in a professional school student population. *Oral Surg Oral Med Oral Pathol*. 1960;13:1191-202.
79. Spouge JD, Diamond HF. Hypersensitivity reactions in mucous membranes. I. The statistical relationship between hypersensitivity diseases and recurrent oral ulcerations. *Oral Surg Oral Med Oral Pathol*. Apr 1963;16:412-21. [Medline].
80. Ueta E, Umazume M, Yamamoto T, Osaki T. Leukocyte dysfunction in oral mucous membrane diseases. *J Oral Pathol Med*. Mar 1993;22(3):120-5. [Medline].
81. Veloso FT, Saleiro JV. Small-bowel changes in recurrent ulceration of the mouth. *Hepatogastroenterology*. Feb 1987;34(1):36-7. [Medline].

82. Vujevich J, Zirwas M. Treatment of severe, recalcitrant, major aphthous stomatitis with adalimumab. *Cutis*. Aug 2005;76(2):129-32. [[Medline](#)].
83. Wolverton SE. *Comprehensive Dermatologic Drug Therapy*. Philadelphia: WB Saunders; 2001:167-8.
84. Woo SB, Sonis ST. Recurrent aphthous ulcers: a review of diagnosis and treatment. *J Am Dent Assoc*. Aug 1996;127(8):1202-13. [[Medline](#)].
85. Wray D, Charon J. Polymorphonuclear neutrophil function in recurrent aphthous stomatitis. *J Oral Pathol Med*. Sep 1991;20(8):392-4. [[Medline](#)].

Medscape Reference © 2011 WebMD, LLC