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Review Article

Diagnosis and Management of Mouth Ulcer

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ABSTRACT

Oral ulceration is a common clinical problem with a broad differential diagnosis ranging from minor mechanical trauma and recurrent aphthous stomatitis (RAS) to infections, immune-mediated disorders, nutritional deficiencies, medication-related lesions and oral malignancy. Although many uncomplicated ulcers are self-limiting, persistent, recurrent, atypical or indurated lesions require systematic assessment so that significant local or systemic disease is not missed. This review summarizes the current approach to the diagnosis and management of mouth ulcers, with emphasis on clinical history, oral examination, classification according to duration and recurrence, identification of local and systemic causes, appropriate laboratory investigation, indications for biopsy and referral, and evidence-informed symptomatic treatment. RAS is discussed in detail because it is the most common recurrent ulcerative disorder. Management is individualized according to severity and underlying cause; general measures, pain control, topical corticosteroids and protective agents are commonly used for uncomplicated aphthous disease, while systemic therapies and specialist interventions are reserved for selected severe or refractory cases. Recent evidence also supports selected non-pharmacological approaches such as photobiomodulation/laser therapy for short-term pain and healing outcomes, although treatment parameters and long-term recurrence effects require further standardization. The review emphasizes that a non-healing oral ulcer should not automatically be labeled as aphthous and that biopsy or specialist assessment may be required when the clinical course is persistent or suspicious.

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INTRODUCTION

An oral ulcer is a localized loss of the oral epithelial surface with exposure of underlying connective tissue. Oral ulceration may occur as an isolated local event or as a manifestation of a broader inflammatory, infectious, hematologic, gastrointestinal, dermatologic or neoplastic disorder. The clinical appearance of different diseases can overlap considerably; therefore, diagnosis should not rely on ulcer appearance alone. History, duration, number, recurrence pattern, location, morphology, associated symptoms, medication exposure and systemic features all contribute to a structured diagnosis.

Recurrent aphthous stomatitis (RAS), commonly called canker sores, is the most frequent recurrent ulcerative disorder of the oral mucosa. Typical lesions are painful, shallow, round or oval ulcers with an erythematous halo and a yellow-grey fibrinous base. RAS is usually diagnosed clinically after other causes of recurrent ulceration have been considered. The disease is multifactorial and may be associated with local trauma, stress, nutritional deficiencies, immune factors, gastrointestinal disease and other systemic conditions. Contemporary management focuses on reducing pain, shortening the active episode, improving oral function and, where possible, reducing recurrence.

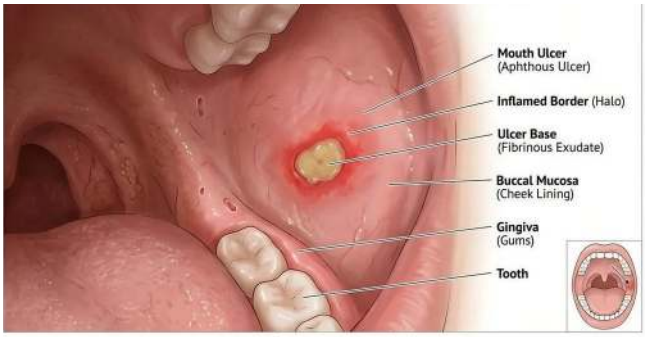


Figure 1: ***Mouth ulcer***

A clinically important distinction is between an uncomplicated ulcer that is expected to heal and a lesion that is persistent, atypical, indurated, enlarging, recurrent in an unusual pattern or associated with systemic findings. Expert guidance recommends further investigation and consideration of biopsy when an oral ulcer remains unexplained, particularly when it persists beyond approximately two weeks or fails to respond to an appropriate initial approach.

Mouth ulcers, also referred to as oral ulcers, are common lesions of the oral mucosa characterized by localized loss or disruption of the epithelial lining, resulting in exposure of the underlying connective tissue. They may occur on the lips, buccal mucosa, tongue, gingiva, hard or soft palate, and floor of the mouth. Although many oral ulcers are self-limiting and heal within a few days to weeks, recurrent, persistent, unusually large, or painful ulcers may significantly affect eating, drinking, speaking, swallowing, and overall quality of life.

Oral ulceration can develop due to a wide range of local and systemic factors. Common local causes include accidental biting, sharp teeth, poorly fitting dentures, orthodontic appliances, thermal injury, chemical irritation, and excessive mechanical trauma. Recurrent aphthous stomatitis is another important cause and is characterized by recurrent episodes of painful ulcers, particularly on non-keratinized oral mucosa. Nutritional deficiencies involving iron, folate, vitamin B12, and other micronutrients may also contribute to recurrent ulceration.

In addition to local factors, oral ulcers can sometimes represent a manifestation of systemic diseases. Gastrointestinal disorders such as celiac disease and inflammatory bowel disease, hematological abnormalities, immune-mediated disorders, and certain infections may present with oral ulceration. Viral, bacterial, and fungal infections can also produce ulcerative lesions. Therefore, a detailed clinical history and appropriate examination are important for determining the probable cause.

Drug-associated oral ulceration should also be considered during diagnosis. Certain medicines may produce direct mucosal irritation, immune-mediated reactions, xerostomia, or other changes that predispose patients to ulcer formation. A complete medication history can

therefore provide important information when evaluating recurrent or unexplained oral ulcers.

The clinical appearance of an ulcer provides valuable diagnostic information. Important features include the number of lesions, site, size, shape, border, depth, surrounding erythema, presence of induration, duration, recurrence pattern, and associated symptoms. A single acute ulcer following trauma may require only local supportive care, whereas multiple recurrent ulcers or ulcers associated with systemic symptoms may require laboratory investigations and specialist evaluation.

The management of mouth ulcers depends primarily on the underlying cause and severity of the lesion. Treatment may include removal of local irritants, maintenance of good oral hygiene, topical analgesics, antiseptic preparations, topical corticosteroids, protective oral gels or pastes, nutritional supplementation when a deficiency is confirmed, and treatment of an underlying systemic or infectious condition. In selected patients with severe or recurrent disease, systemic therapy or specialist-directed treatment may be required.

Early recognition of potentially serious lesions is particularly important. An ulcer that persists beyond the expected healing period, repeatedly occurs at the same site, becomes progressively larger, develops an indurated or irregular border, bleeds without an obvious cause, or is associated with a neck swelling, unexplained weight loss, or difficulty in swallowing requires further clinical assessment. Persistent oral ulceration may occasionally be associated with oral potentially malignant disorders or oral malignancy, making appropriate referral and, when indicated, biopsy essential.

Recent advances in oral healthcare have also encouraged the development of improved topical drug-delivery systems, including mucoadhesive gels, oral films, patches, lozenges, sprays, and in-situ gels. These systems are designed to prolong contact between the active ingredient and the ulcerated mucosa, provide local pain relief, and potentially improve therapeutic effectiveness. Natural products and herbal ingredients are also being investigated for their anti-inflammatory, antimicrobial, antioxidant, analgesic, and wound-healing properties.

Thus, diagnosis and management of mouth ulcers require an integrated approach involving clinical assessment, identification of causative factors, differential diagnosis, appropriate investigations, symptomatic treatment, and management of the underlying condition. A systematic understanding of oral ulceration can help healthcare professionals distinguish uncomplicated self-limiting lesions from ulcers requiring further investigation and specialized management.

Objectives

- To describe the definition and clinical classification of oral ulcers.
- To summarize common local, infectious, immune-mediated, systemic, drug-related and neoplastic causes.
- To explain a structured history and oral examination for patients presenting with ulceration.
- To discuss appropriate laboratory and special investigations.
- To outline the differential diagnosis of acute, chronic and recurrent oral ulcers.
- To review non-pharmacological and pharmacological management strategies.

Clinical Significance of Mouth Ulcer

Most simple oral ulcers are benign and heal spontaneously, but oral ulceration has a wide differential diagnosis. A useful clinical framework is to classify the lesion by duration (acute versus chronic), number (solitary versus multiple), and pattern (first episode versus recurrent). An ulcer lasting less than two weeks is commonly considered acute; persistence for two weeks or more warrants increased diagnostic attention, particularly if there is no clear local cause.

Important associated symptoms include fever, malaise, weight loss, dysphagia, odynophagia, skin lesions, genital ulcers, ocular symptoms, gastrointestinal complaints, joint symptoms and recurrent infections. These findings may suggest an underlying systemic disorder rather than isolated idiopathic aphthosis.

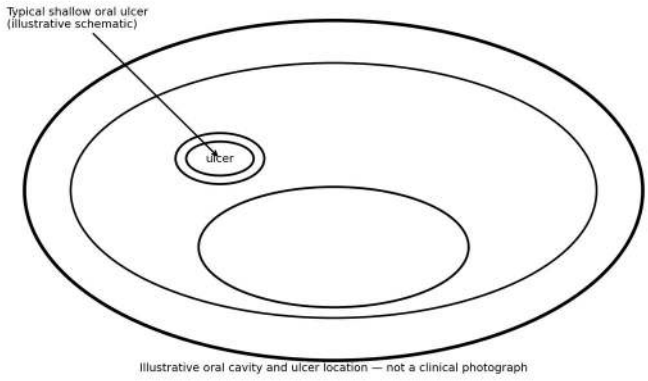


Figure 2: ***Illustrative schematic of an oral ulcer and its relationship to the oral cavity.***

Illustrative Anatomy and Appearance

Classification of Mouth Ulcers

Clinical category	Typical pattern	Examples	Diagnostic emphasis
Acute ulcer	Short duration; often resolves within days to <2 weeks	Trauma, burns, viral infection, acute mucositis	Trigger, infection, number and systemic symptoms
Chronic ulcer	Persistent, often ≥2 weeks	Chronic traumatic ulcer, immune-mediated disease, neoplasia	Induration, edge, base, growth and biopsy need
Recurrent ulcer	Repeated episodes with healing between attacks	RAS, systemic disease-associated aphthosis	Recurrence pattern and associated systemic features
Solitary ulcer	One dominant lesion	Traumatic ulcer, neoplasia, localized infection	Site, persistence and local irritant
Multiple ulcers	Several simultaneous lesions	RAS, viral disease, immune-mediated disease, drug reactions	Distribution, prodrome and systemic manifestations

Recurrent Aphthous Stomatitis (RAS)

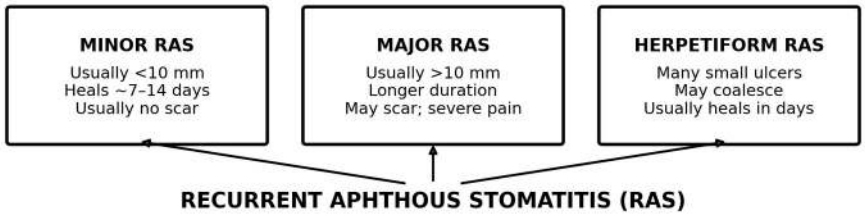


Figure 3: ***Original schematic classification of recurrent aphthous stomatitis (RAS).***

RAS is a chronic, recurrent inflammatory condition characterized by episodic painful oral ulceration in the absence of a specific identifiable systemic cause. The disease is often diagnosed clinically. Three classical clinical patterns are recognized: minor, major and herpetiform aphthous ulcers. The distinction is based on lesion size, number, duration and tendency to scar.

1. **Minor RAS :** Minor aphthae are the commonest form. They are usually small, shallow and painful, commonly affecting non-keratinized mucosa such as the labial and buccal mucosa and ventral tongue. They generally heal without scarring. Symptoms can nevertheless interfere with eating, speaking and oral hygiene.

2. **Major RAS :** Major aphthae are larger and deeper, may persist for several weeks and may heal with scarring. Pain and functional impairment can be substantial. Severe or persistent major aphthae should prompt assessment for associated systemic disease and consideration of specialist management.
3. **Herpetiform RAS :** Herpetiform aphthae consist of numerous small ulcerations that can occur in clusters and occasionally coalesce into larger irregular lesions. Despite the name, they are not caused by herpes simplex virus. The clinical distinction from viral ulceration depends on history, distribution, associated vesicles and systemic findings.

Etiology and Risk Factors

Cause/category	Examples / relevance
Local factors	Cheek or lip biting, sharp tooth/restoration, ill-fitting appliances, thermal injury, chemical irritation, aggressive brushing.
Nutritional factors	Iron deficiency, vitamin B12 deficiency, folate deficiency and other nutritional disturbances may be associated with recurrent ulceration.
Infectious causes	Herpes simplex virus, varicella-zoster virus, enteroviruses and selected bacterial/fungal infections can produce oral ulceration.
Immune/inflammatory disorders	Behçet disease, inflammatory bowel disease, celiac disease, lupus and other immune-mediated disorders may present with oral ulcers.
Hematologic disorders	Anemia, neutropenia, cyclic neutropenia and other blood disorders can be associated with recurrent or persistent ulcers.
Drug-related causes	Some medicines can induce mucositis, ulceration or lichenoid/immune-mediated reactions; a medication timeline is therefore important.
Psychological/physiological factors	Stress, sleep disturbance, hormonal variation and other patient-specific triggers may contribute in susceptible individuals.
Neoplastic causes	Persistent or indurated ulcers may represent oral squamous cell carcinoma or another neoplastic process and should not be assumed to be aphthous.

Pathogenesis of Recurrent Aphthous Stomatitis

The exact pathogenesis of RAS remains incompletely understood. Current models support a multifactorial process involving genetic susceptibility, altered local immune responses, epithelial injury and inflammatory mediators. T-cell-mediated inflammation is an important component of lesion development. Local trauma may initiate ulceration in susceptible mucosa, while systemic factors such as hematinic deficiency, gastrointestinal disease, stress and immune dysregulation may modify severity or recurrence.

Because the biological mechanisms are heterogeneous, treatment is mainly directed toward controlling inflammation and pain and supporting mucosal healing rather than providing a universally curative therapy. Identification and correction of an associated systemic cause may reduce recurrence in selected patients.

Clinical Features to Record

- Onset: first episode or recurrent problem.
- Duration of the current ulcer and usual healing time.
- Number of ulcers and whether they appear simultaneously.
- Size, shape, depth, border, base and surrounding erythema.
- Anatomic site and whether mucosa is keratinized or non-keratinized.
- Pain intensity and effect on eating, drinking, speaking and sleep.
- Local trauma, dental appliances, sharp teeth or recent dental procedures.
- Recent infections, fever or systemic illness.
- Skin, eye, genital, gastrointestinal and joint symptoms.
- Current and recently started medicines.

- Smoking, alcohol exposure, oral hygiene products and possible dietary triggers.
- Family history and previous investigations or treatments.

Diagnostic Approach

Diagnosis begins with a careful history and complete oral examination. The clinician should inspect all oral mucosal surfaces, palpate suspicious lesions and examine regional lymph nodes when appropriate. The lesion should be documented with site, size and duration, and serial photographs may be useful in clinical practice when consent and appropriate privacy procedures are followed.

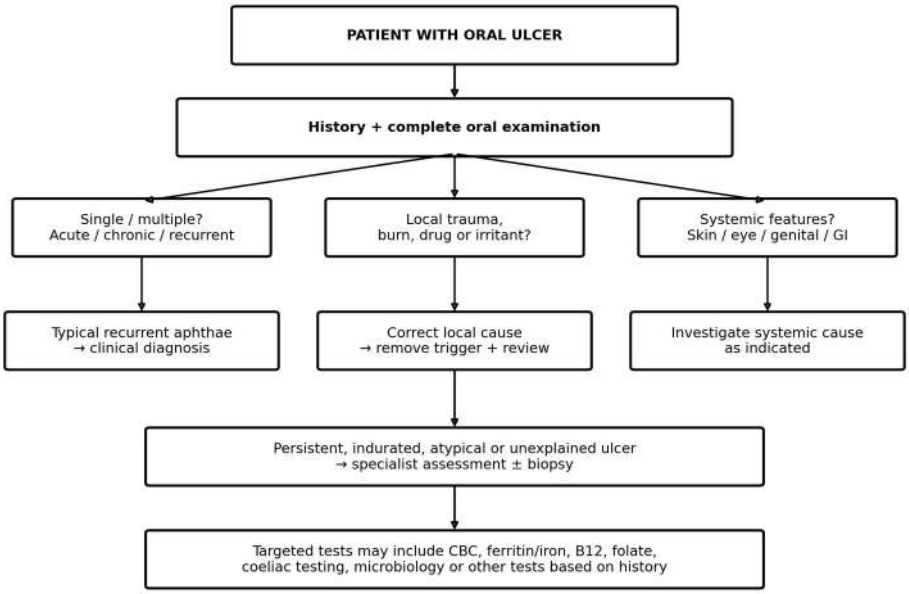


Figure 3: ***Structured diagnostic pathway for an oral ulcer. This is an original educational flowchart based on published diagnostic frameworks.***

1. **History :** History should establish whether the lesion is acute, chronic or recurrent. Recurrent episodes with complete healing between attacks support aphthous disease, but recurrent ulcers can also accompany systemic disorders. The clinician should ask about trauma, dental appliances, new medicines, infections, nutritional status and systemic symptoms.
2. **Oral Examination :** Important examination findings include the ulcer's size, shape, depth, border, floor, surrounding mucosa and exact location. An ulcer with firm induration, rolled or irregular margins, unexplained bleeding, progressive enlargement, fixation or associated cervical lymphadenopathy deserves particular attention.
3. **Laboratory Investigations :** Laboratory testing should be targeted rather than automatic for every single self-limited ulcer. In patients with frequent, prolonged, large or otherwise atypical ulcers, reasonable investigations may include complete blood count, iron studies/ferritin, vitamin B12 and folate. Additional testing such as coeliac serology, inflammatory markers, microbiological testing or evaluation for gastrointestinal disease should be guided by the clinical history.
4. **Biopsy :** Biopsy is considered when the diagnosis remains uncertain, the ulcer persists despite appropriate management, the lesion is atypical or suspicious, or malignancy is part of the differential diagnosis. Expert consensus documents particularly emphasize biopsy consideration for unexplained ulcers lasting more than approximately two weeks or ulcers that do not respond to an initial treatment period. The biopsy site and technique depend on the clinical differential and should be selected by an appropriately trained clinician.

Differential Diagnosis

Condition	Typical clues	Useful investigations	Management direction
Traumatic ulcer	Clear local mechanical/thermal/ chemical trigger	Usually clinical; reassess after removing cause	Remove irritant; symptomatic care; reassess
RAS	Recurrent, painful, shallow ulcers; usually non-keratinized mucosa	Clinical; CBC/iron/B12/folate when indicated	Topical therapy; treat associated cause
HSV-related disease	Vesicles/ulcers, often clustered; systemic symptoms may occur	Viral testing in selected cases	Antiviral therapy when clinically indicated
Behçet disease	Oral ulcers plus genital, ocular, skin or vascular features	Clinical + specialist evaluation	Multidisciplinary management
Inflammatory bowel disease	Oral lesions with GI symptoms or other systemic findings	GI assessment, inflammatory tests, endoscopy as indicated	Treat underlying disease
Celiac disease	Recurrent aphthous-like ulcers with nutritional/GI features	Coeliac serology ± further evaluation	Dietary/systemic management
Drug-related ulceration	Temporal relationship to medicine; may have widespread mucosal involvement	Medication review; selected tests/biopsy	Prescriber review and supportive care
Oral lichen planus/immune mucositis	Erosions/ulcers with characteristic surrounding changes	Clinical ± biopsy/direct immunofluorescence depending on differential	Specialist-directed anti-inflammatory therapy
Oral squamous cell carcinoma	Persistent solitary ulcer, induration, irregularity, growth or nodes	Biopsy and histopathology	Urgent specialist/oncologic pathway

Red-Flag Features

- Ulcer persists for about two weeks or longer without a clear benign cause.
- Induration, fixation, irregular or rolled margins.
- Progressive enlargement or unexplained bleeding.
- Persistent unilateral lesion or unexplained neck lymphadenopathy.
- Significant weight loss, dysphagia or systemic deterioration.
- Recurrent major ulcers or very frequent episodes.
- Multiple mucosal sites or associated genital, ocular, skin or gastrointestinal symptoms.
- Failure to improve after an appropriate initial treatment period.
- Immunocompromised state or significant hematologic abnormalities.

Management of Mouth Ulcer

Management should be individualized according to the cause, severity, duration, recurrence pattern and patient-specific risks. The main objectives are pain control, protection of the ulcer, promotion of healing, maintenance of nutrition and hydration, correction of precipitating factors, and treatment of an underlying systemic disorder when present.

1. General and Supportive Measures

- Avoid hard, sharp, very spicy, salty or strongly acidic foods when they aggravate pain.
- Maintain gentle oral hygiene to reduce secondary irritation and infection risk.
- Use adequate fluids and soft foods when chewing is painful.
- Identify and remove obvious local trauma, such as a sharp tooth edge or poorly fitting appliance.
- Consider avoidance of oral-care products that the patient repeatedly identifies as a trigger.
- Use simple analgesic measures when appropriate and safe for the individual patient.

2. Topical Pharmacological Therapy

For uncomplicated RAS, topical therapy is generally the initial pharmacological approach. Published reviews and consensus recommendations commonly discuss topical corticosteroids as an important first-line

anti-inflammatory treatment. Examples used in clinical practice include triamcinolone acetonide dental paste and other topical corticosteroid preparations selected according to lesion site and patient factors. Topical anesthetics may provide short-term pain relief, while protective/barrier preparations can reduce mechanical irritation.

Therapeutic group	Potential role	Important considerations
Topical corticosteroids	Reduce local inflammatory activity; commonly used for RAS	Use appropriate formulation and duration; assess for secondary candidiasis or other complications
Topical anesthetics/analgesics	Short-term reduction of pain	Avoid excessive use; consider swallowing/ numbness risks
Antiseptic mouth rinses	May reduce microbial burden and support symptom control in selected patients	Not a substitute for diagnosis; avoid irritating preparations
Barrier/protective agents	Physically shield ulcerated mucosa and reduce mechanical pain	Useful as adjunctive therapy
Hyaluronic-acid based products	Support mucosal protection and may improve short-term symptoms/healing	Evidence varies by formulation

3. **Systemic Therapy :** Systemic therapy is generally reserved for severe, frequent, major or refractory aphthous disease, or for ulceration associated with an underlying systemic condition. Published reviews describe systemic corticosteroids and selected immunomodulatory agents in specialist-managed cases. Thalidomide has demonstrated efficacy in severe RAS in systematic reviews, but its adverse-effect profile and strict safety considerations mean that it is not a routine treatment for ordinary mouth ulcers. Systemic therapy should therefore be individualized and supervised by an appropriate clinician.
4. **Laser and Photobiomodulation** : Photobiomodulation/low-level laser therapy has received increasing attention as an adjunctive approach for RAS. Recent systematic reviews and meta-analyses report reductions in pain and, in several trials, shorter healing time compared with control interventions. However, treatment devices, wavelengths, energy parameters and protocols vary between studies. Therefore, laser therapy should be regarded as a clinician-directed adjunct rather than a universal replacement for diagnosis and conventional treatment.
5. **Management of Underlying Causes :** When an underlying cause is identified, management should address that condition. Examples include correction of iron, folate or vitamin B12 deficiency when confirmed; removal of a traumatic dental source; review of a suspected medication reaction with the prescribing clinician; and specialist management of Behçet disease, inflammatory bowel disease, celiac disease, hematologic disorders or immune-mediated mucosal disease. Treating the underlying disorder may be more important than repeatedly treating the ulcer itself.

Management According to Severity

Severity	Typical situation	General approach	Escalation
Mild / isolated	Single small ulcer with no red flags	Reassurance, trigger avoidance, oral hygiene, analgesia ± topical protective/corticosteroid therapy	Review if persistent
Moderate / recurrent	Several episodes, multiple lesions or significant pain	Topical anti-inflammatory therapy + pain control + assess triggers and nutritional/ systemic factors	Investigate if frequent/prolonged
Severe / major	Large/deep ulcers, prolonged healing, major functional impairment	Specialist evaluation; topical plus selected systemic therapy	Oral medicine/dental/medical referral

Severity	Typical situation	General approach	Escalation
Refractory / atypical	Persistent, indurated, unexplained or treatment-resistant lesion	Re-evaluate diagnosis; targeted tests and biopsy when indicated	Urgent specialist assessment

Prevention of Recurrence in RAS

1. Identify personal triggers such as trauma, specific foods, stress or oral-care products.
2. Maintain good oral hygiene while minimizing mechanical trauma.
3. Address confirmed nutritional deficiencies rather than using indiscriminate supplementation.
4. Consider a sodium-lauryl-sulfate-free toothpaste in patients who report recurrent aphthae associated with conventional toothpaste.
5. Manage systemic disorders that may contribute to recurrent ulceration.
6. Use a symptom/ulcer diary when recurrence is frequent to identify patterns.
7. Seek specialist evaluation when ulcers become unusually frequent, large, prolonged or associated with systemic symptoms.

Role of the Pharmacist and Dental/Medical Team

Pharmacists can contribute by identifying potentially ulcerogenic medicines, checking for inappropriate self-medication, counselling on topical product use and recognizing red flags that warrant dental or medical referral. Dentists and oral medicine specialists play a central role in lesion examination, differential diagnosis, biopsy decisions and management of local causes. Physicians may be required when oral ulceration is a manifestation of hematologic, gastrointestinal, autoimmune, infectious or systemic disease. Multidisciplinary care is particularly valuable in severe or recurrent cases.

Recent Evidence and Emerging Approaches

Recent literature has expanded the therapeutic landscape beyond conventional topical corticosteroids. Systematic reviews have evaluated topical agents, hyaluronic acid, barrier preparations, laser/photobiomodulation, herbal and complementary interventions and selected systemic immunomodulators. The most consistent short-term evidence remains focused on pain reduction and acceleration of healing, while evidence for durable prevention of recurrence is less consistent. A 2025 umbrella review synthesized 41 reviews and concluded that topical corticosteroids and low-level laser therapy consistently improve short-term pain/healing outcomes, while systemic agents such as colchicine and thalidomide are more appropriate for selected refractory disease because of adverse-effect and evidence-quality considerations.

An important research gap is the lack of standardized treatment parameters for physical therapies and the heterogeneity of outcome measures used across clinical trials. Future studies should use standardized diagnostic criteria, validated pain scales, objective healing measures, longer follow-up and clear recurrence endpoints.

Patient Education

Patients should be advised that many simple mouth ulcers heal spontaneously, but persistent or unusual lesions should not be repeatedly self-treated without assessment. They should seek professional evaluation if an ulcer lasts around two weeks or longer, repeatedly returns with increasing severity, becomes hard or enlarges, is associated with unexplained bleeding or neck swelling, or occurs with systemic symptoms. Patients should also avoid deliberately applying caustic chemicals or unapproved substances to the ulcer because chemical injury can worsen mucosal damage.

Future Perspectives

1. Development of standardized diagnostic criteria for recurrent oral ulceration.
2. Large multicenter trials comparing topical corticosteroids, barrier agents, hyaluronic acid and photobiomodulation using common outcome measures.
3. Better biomarkers for distinguishing idiopathic RAS from systemic-disease-associated aphthosis.
4. Personalized treatment based on recurrence pattern, immune phenotype and nutritional status.

5. Long-term studies evaluating recurrence prevention rather than only short-term pain relief.

CONCLUSION

Mouth ulceration is a clinical sign rather than a single disease. The diagnostic process should begin with careful characterization of duration, number, recurrence, site, morphology and associated systemic features. Recurrent aphthous stomatitis is common and is usually managed with supportive care, pain control and topical anti-inflammatory treatment, while severe or refractory disease may require specialist-directed systemic therapy. The presence of a persistent, indurated, atypical or unexplained ulcer changes the diagnostic priority: malignancy and other significant causes must be excluded rather than assuming aphthous disease. Targeted laboratory testing can identify nutritional or systemic contributors in selected patients, and biopsy is an important diagnostic tool when the clinical course is suspicious or unexplained. Current evidence supports several adjunctive approaches, including photobiomodulation, but treatment should remain individualized and diagnosis should always precede repeated symptomatic therapy.

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