

## ANGULAR CHEILITIS: A MULTIDISCIPLINARY APPROACH TO DIAGNOSIS AND MANAGEMENT

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### ABSTRACT

Angular Cheilitis (AC) represents a multifaceted oral pathology characterized by erythematous lesions at the labial commissures. Despite its prevalence, AC is often inadequately addressed due to its polymorphic etiology, which can encompass infectious agents, nutritional deficits, and systemic conditions. This article provides a systematic review of the pathophysiology, clinical presentation, and etiological factors of AC, including nutritional deficiencies, infectious agents, and systemic diseases. Emphasizing a multidisciplinary strategy, we discuss the collaborative roles of dental, medical, and dermatological expertise in the accurate diagnosis and effective management of AC. We outline diagnostic criteria, appropriate laboratory tests, and imaging techniques tailored to address the multifaceted nature of the condition. Management strategies encompass a range of options from topical treatments and medications to dietary modifications and preventative measures, with an emphasis on evidence-based practices. This review advocates for integrated care models to optimize treatment efficacy, patient compliance, and to mitigate the recurrence of AC. Our analysis aims to enhance the understanding of AC and to provide a framework for its management, contributing to better patient care and opening avenues for future research.

**Key words:** Angular Cheilitis, Multidisciplinary Management, Diagnostic Criteria, Evidence-Based Treatment

### INTRODUCTION

Angular Cheilitis (AC), characterized by inflammation and fissuring at the labial commissures, presents a diagnostic and therapeutic challenge in clinical practice. The prevalence of AC is notable across various populations, at all ages, rendering its importance in both dental and general medical fields. Often manifesting as a

symptom complex rather than an isolated condition, AC is an indicator of systemic health issues ranging from micronutrient deficiencies to immunological disorders.[1] The complexity of AC's etiology requires a multidisciplinary approach to care, involving dental, medical, and dermatological expertise. Such collaborative efforts are crucial for comprehensive patient

management, ensuring that underlying systemic conditions are addressed alongside the local oral pathology. Despite the availability of treatment modalities, recurrence and persistent morbidity associated with AC indicate a need for more refined diagnostic and management protocols.[2]

This article aims to elucidate the pathophysiological mechanisms of AC, delineate the clinical presentation, and explore the various etiological factors that contribute to its development. We emphasize the significance of an accurate diagnostic process, informed by a synthesis of clinical examination findings and appropriate laboratory investigations. Furthermore, we review the current management strategies, highlighting the role of evidence-based treatment options, and discuss the importance of preventative measures. Through this integrative review, we aim to enhance understanding and provide a structured framework for the effective management of AC, ultimately contributing to improved patient outcomes and quality of care.

## **MATERIALS AND METHODS**

This review utilized a systematic search of electronic databases including PubMed, MEDLINE, and EMBASE for studies related to Angular Cheilitis (AC). Keywords used in the search strategy encompassed "Angular Cheilitis," "Cheilosis," "Perleche," combined with "diagnosis," "treatment," "pathophysiology," "etiology," and "management." Studies were selected based on relevance to AC's clinical aspects, pathogenesis, multidisciplinary management approaches, and treatment outcomes. Inclusion criteria comprised peer-reviewed articles, clinical trials, and review articles in

English. Exclusion criteria eliminated non-English articles, animal studies, and articles not focusing on AC's clinical management. Data extraction prioritized information on diagnostic methods, treatment strategies, and outcomes, with a secondary focus on epidemiological data. Statistical analysis was not applicable due to the narrative nature of this review.

## **RESULTS**

The etiology of AC is diverse and multifactorial, involving a combination of local and systemic factors that compromise the integrity of the oral commissures. Nutritional deficiencies are among the main causes of AC; inadequate intake or malabsorption of essential vitamins and minerals, such as iron, vitamin B2 (riboflavin), vitamin B3 (niacin), and vitamin B12, can contribute to the development of AC by impairing epithelial repair and immune function.[3,4]

Infectious agents are also pivotal in the pathogenesis of AC, with *Candida albicans* being the most common fungal pathogen implicated. *Staphylococcus aureus* and beta-hemolytic streptococci are notable bacterial pathogens that may colonize the lesions. The overgrowth of these organisms can be attributed to factors such as a moist environment, lip licking, and local skin trauma.[5,6]

Systemic diseases further complicate the picture; conditions that lead to immunosuppression, such as diabetes mellitus, HIV/AIDS, and other immunodeficiency disorders, are strongly associated with the occurrence of AC. Moreover, systemic inflammation, as seen in inflammatory bowel diseases like Crohn's disease, can manifest as AC and may even

serve as a diagnostic clue to the underlying systemic condition.[7,8]

Environmental factors, including poor oral hygiene and the use of certain medications, can predispose individuals to AC by creating an environment conducive to the proliferation of pathogenic organisms or by disrupting the normal oral flora. Habits such as lip licking, thumb sucking, or the use of orthodontic appliances can introduce or exacerbate these risk factors.[9]

The interaction between these local and systemic factors necessitates a thorough evaluation of patients presenting with AC. A holistic approach to patient history taking and clinical examination is paramount in elucidating the potential causes and formulating an effective management plan.

### **Pathophysiology**

The pathophysiology of AC is a complex interplay of biological processes influenced by both local and systemic factors. Locally, the anatomy of the labial commissures creates a naturally moist environment, predisposing these areas to irritation and maceration. When the oral commissures are repeatedly exposed to saliva, especially under conditions such as overclosure of the mouth in denture wearers or chronic lip licking, an ideal environment is formed for microbial colonization and infection. This local environmental change can be exacerbated by a reduction in saliva flow or alterations in saliva composition, often seen in xerostomia, further contributing to tissue breakdown and lesion formation.[10]

The transition of *Candida* from a commensal organism to a pathogenic one is facilitated by a disrupted local environment and is a common feature in the development of AC. The fungal hyphae penetrate the epithelial cracks, inciting an inflammatory response.

Bacterial superinfection can further exacerbate this inflammatory process, leading to the characteristic erythema and fissuring.[11]

Systemically, nutritional deficiencies play a critical role in the pathogenesis of AC. Deficiencies in B vitamins, iron, and zinc can compromise epithelial integrity and immune defense mechanisms, thereby diminishing the tissue's ability to resist and recover from microbial insults. Additionally, systemic conditions that impair immune function, such as diabetes mellitus, can diminish the local immune response, rendering the individual more susceptible to the development of AC.[12]

The immunological aspect of AC's pathophysiology involves both innate and adaptive immunity. A compromised barrier function leads to increased antigenic exposure, triggering an inflammatory cascade that involves various cytokines and immune cells. This immune response, while aimed at containing the infection, can contribute to the chronicity of lesions if the underlying causes are not addressed.[13]

Furthermore, AC can also be indicative of systemic inflammatory states, such as those found in Crohn's disease or other autoimmune disorders, where mucocutaneous manifestations are common. In such cases, the local pathology at the labial commissures may be a reflection of a systemic imbalance or pathology.

Understanding the pathophysiological mechanisms of AC is essential for the development of targeted interventions that not only address the local symptoms but also consider the systemic health of the patient. This comprehensive approach ensures that treatment strategies are holistic and patient-centric, thereby improving the prognosis and reducing the incidence of recurrence.[14]

### **Clinical Presentation**

Angular Cheilitis (AC) typically presents clinically with erythema, maceration, and fissuring at one or both of the labial commissures. Patients often report discomfort, which can range from a mild burning sensation to severe pain, especially when the lesions are stretched during activities such as eating, speaking, or yawning. The affected areas may also exhibit crusting and bleeding, and in chronic cases, there can be a secondary infection that exacerbates these symptoms.[15]

The clinical presentation of AC can be influenced by the underlying etiology. For example, in cases associated with candidal infection, there might be concomitant oral manifestations, such as a white pseudomembranous coating, which can be scraped off to reveal a reddened base. In bacterial infections, there may be a golden crust indicative of impetigo. Where AC is linked to nutritional deficiencies, signs of the specific deficiency, such as glossitis or koilonychia, may also be present.[16]

Differentiating AC from other oral pathologies is critical for effective management. Conditions such as herpetic stomatitis, impetigo, or perioral dermatitis can present with lesions around the mouth that may mimic AC. Herpetic lesions are typically vesicular and localized, impetigo is characterized by honey-colored crusting, and perioral dermatitis often presents as a rash of small papules or pustules. It is important to note that AC lesions are confined to the commissures and do not typically present with vesicles or pustules unless there is a secondary infection.[17]

### **Diagnostic Approach**

Diagnosis is often clinical but can be supported by laboratory tests, such as microbial cultures or biopsy, particularly in atypical or treatment-resistant cases. The presence of underlying systemic conditions should be investigated based on the patient's history and presenting signs and symptoms. Angular Cheilitis (AC) is typically diagnosed through clinical examination, with the presence of characteristic lesions at the mouth's corners. Laboratory investigations are generally reserved for cases where initial treatments do not result in resolution. Infection being a prevalent underlying cause, cultures for *Candida* or bacteria may be undertaken at the outset.[18] The clinician's judgment guides the exploration of potential contributing systemic factors, such as nutritional deficits or immunosuppression. Should there be no improvement following primary treatment with antifungal or antibiotic agents within two to three weeks, further investigations are warranted. These may include a complete blood count with mean corpuscular volume (MCV), an iron panel including ferritin, assessments of folate, and vitamin B2, B6, and B12 levels, along with glucose metabolism tests.[19]

When Candidal infection is suspected in AC, a suite of tests can be employed:

- **Microscopic Examination:** Scrapings from the lesion, treated with periodic acid-Schiff (PAS) staining, can help visualize red or purple fungal elements. Gram staining can also aid in identifying these organisms, which appear dark blue.
- **Fungal Identification Tests:** These include the germ tube test in serum, chlamydospore formation on specific agars, and sugar assimilation tests for identifying specific *Candida* metabolic activities.

- **Fungal Culture:** Growth mediums such as Sabouraud dextrose agar with antibiotics, cornmeal agar, or chromogenic media are used for culturing and identifying the fungal species.

- **Immunological Assays:** Various assays like ELISA or radioimmunoassays can help diagnose fungal infections.

For bacterial involvement in AC, cultures are taken to determine the specific bacteria and their antibiotic sensitivities.[20,21]

In cases where oral candidiasis is established, additional testing for conditions such as HIV or diabetes may be recommended.

If AC is thought to stem from nutritional deficiencies:

- **Folic Acid and Vitamins B12 and B2:** Serum levels are measured, with homocysteine and methylmalonic acid serving as additional markers for B12 deficiency.

- **Iron and Zinc:** Serum concentrations provide insights into the sufficiency of these minerals.

When contact dermatitis is part of the differential diagnosis, patch testing can help identify specific allergens or irritants.[22]

In rare cases where malignancy is a concern, a biopsy of the lesion can provide definitive pathological diagnosis. Each of these diagnostic tools plays a vital role in the comprehensive assessment and management of AC, ensuring tailored and effective patient care.

The role of multidisciplinary teams is pivotal in the diagnostic process:

- **Dentists** assess for local factors such as malocclusion, saliva pooling, or denture-associated issues that may predispose to AC.

- **Physicians**, including general practitioners and internists, evaluate for

systemic diseases and nutritional deficiencies that could manifest as AC.

- **Dermatologists** assist in distinguishing AC from other cutaneous conditions and may conduct specialized tests like patch testing when contact allergies are suspected.

This collaborative approach ensures a holistic assessment, facilitating a tailored management strategy that addresses the multifactorial nature of AC. The ensuing segment of this article will expound upon the various management strategies, emphasizing the need for a personalized and evidence-based treatment plan.

### **Management Strategies**

The management of Angular Cheilitis (AC) is multifaceted, aimed at alleviating symptoms, eradicating infections, correcting underlying deficiencies or conditions, and preventing recurrence. Treatment modalities are often employed concomitantly to address the various contributing factors of AC.[23]

The therapeutic strategy for Angular Cheilitis (AC) hinges on determining whether the origin is infectious or non-infectious. Empirical treatment typically prioritizes managing infection, the more prevalent cause. Considering that excessive saliva and the ensuing eczematous breakdown is a common risk factor, protecting the labial commissures with topical barriers (such as petrolatum jelly, emollients, or lip balm) is crucial and often adequate for idiopathic AC cases.[24]

**Antifungal Therapies:**

For fungal etiologies, antifungal medications are administered topically to the affected areas, generally three times a day for a duration of two weeks. Agents include nystatin ointment, gentian violet solution (notably in pediatric cases where

discoloration is not a concern), ketoconazole cream, clotrimazole cream, and miconazole cream, the latter often used when a mixed bacterial and candidal infection is suspected due to its additional gram-positive bacteriostatic action.[25,26]

#### Topical Antiseptics and Antibiotics:

Topical antiseptics or antibiotics are employed for bacterial infections, with a regimen typically lasting one to two weeks. Mupirocin ointment and fusidic acid cream are common choices, with the latter used for its anti-staphylococcal properties.

#### Systemic Antifungal Agents:

Systemic antifungals are indicated in moderate to severe cases or when the infection extends beyond the oral cavity. These agents, such as fluconazole, itraconazole, and posaconazole, are typically reserved for cases not responsive to topical treatments. Their interactions with the hepatic cytochrome P450 system must be monitored due to potential drug interactions.[27]

#### Nutritional Interventions:

Nutritional supplementation is essential in cases where vitamin deficiencies are identified as contributing factors. While specifics are extensive, they generally include correcting avitaminosis and mineral deficiencies.[28,29,30]

#### Dental Interventions:

Dental adjustments are necessary for patients with ill-fitting dental devices, which can harbor fungi and contribute to AC. Dentures should be treated with antifungal agents and maintained with proper hygiene.

#### Adjunctive Measures:

In some instances, malocclusion or anatomical depressions at the commissures

might be addressed with dermal filler therapy, using substances like collagen or hyaluronic acid, to alter the mouth's contour and prevent saliva accumulation.[31,32]

#### Management of Contributory Chronic Conditions:

Tight glycemic control in diabetic patients and effective antiretroviral therapy in HIV/AIDS patients are critical for reducing the incidence of AC.[33,34]

#### Behavioral Modifications:

Eliminating habits such as tobacco use and lip-licking can significantly reduce the risk of AC development.

#### Considerations for Treatment Failure:

Failure to resolve AC may result from a variety of factors, including resistant *Candida* species, persistent risk factors, undiagnosed nutritional or systemic conditions, or unidentified immunosuppression. A follow-up within two weeks is advisable to assess treatment efficacy and address any ongoing issues.[35,36]

Management must be individualised, taking into account the specific etiologies and patient-related factors in each case of AC. In cases where AC persists despite these measures, reevaluation for undiagnosed systemic conditions or referral to a specialist may be warranted. The successful management of AC requires not only the resolution of the acute condition but also the identification and modification of predisposing factors to prevent recurrence.[37,38]



## DISCUSSIONS

Current research on Angular Cheilitis (AC) continues to underscore the complexity of its diagnosis and management. Recent studies have focused on refining the understanding of its etiopathogenesis, particularly the role of nutritional deficiencies and the microbiome in the oral cavity.[39,40,41] The literature increasingly supports a multifactorial approach to treatment, emphasizing the need to address both local and systemic factors. Advancements in diagnostic methods, such as more sensitive microbial cultures and molecular techniques, have improved the identification of pathogenic organisms involved in AC.[42]

## CONCLUSIONS

In conclusion, AC is a common condition that can be indicative of various underlying health issues. Effective management requires a thorough clinical evaluation, appropriate diagnostic tests, and a multidisciplinary approach to treatment that addresses both local and systemic factors. The importance of identifying and correcting underlying nutritional deficiencies or systemic conditions is evident for the successful resolution of AC. The use of topical antifungals and antibiotics remains a cornerstone of treatment, while lifestyle modifications play a critical role in preventing recurrence.

### Future Directions:

Future research should aim to delineate more clearly the pathophysiological mechanisms that contribute to AC, particularly the

The comparison of multidisciplinary approaches to traditional methods has been favourable towards the former. Traditional methods often focused solely on symptomatic treatment, primarily with topical agents, without a thorough investigation into underlying causes. In contrast, multidisciplinary strategies incorporate a broader clinical assessment and tailored interventions, engaging various healthcare professionals to address the patient's overall health.[43,44] This approach not only treats the present condition but also aims to prevent recurrence by modifying predisposing factors.[45]

genetic and immunological factors that may predispose individuals to this condition. Longitudinal studies could provide insights into the long-term efficacy of various treatment modalities and the role of patient compliance in the management of AC. Clinical trials are needed to evaluate the effectiveness of emerging treatments and to establish more comprehensive management protocols. Furthermore, as our understanding of the oral microbiome expands, there may be potential for new preventative and therapeutic approaches targeting microbial balance. In clinical practice, fostering interdisciplinary collaboration will be essential to optimize patient outcomes for those suffering from AC.

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