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## THE ROLE OF MICROBIAL FACTORS IN THE DEVELOPMENT OF ANGULAR CHEILITIS

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### Abstract

Angular cheilitis is a condition characterized by inflammation in the corners of the mouth, a chronic course, and frequent relapses, which in turn leads to a significant deterioration in patients' quality of life. Numerous factors leading to the development of this disease have been studied, with microorganisms playing a key role, specifically the fungus *Candida albicans* and the bacterium *Staphylococcus aureus*. It has been established that the combined effects of these microorganisms, along with associated factors, lead to the development of angular cheilitis. This article will review studies on the onset of this pathology and the causes of frequent relapses despite treatment. Biofilms, structures that facilitate the establishment of microorganisms and the avoidance of treatment, play a key role in this process, thereby maintaining the inflammatory process. Therefore, when treating angular cheilitis, microbial factors must be considered, appropriate diagnostics must be performed, and appropriate comprehensive treatment methods must be selected, not just symptomatic relief.

**Keywords:** Angular cheilitis, *Candida albicans*, *Staphylococcus aureus*, biofilm, mixed microflora.



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## **Introduction**

Angular cheilitis is a disease characterized by inflammatory lesions of the skin and mucous membranes of the corners of the mouth. The main symptoms include hyperemia, maceration of the skin in the corners of the mouth, cracks, crusts, and painful discomfort. This disease is protracted and characterized by frequent relapses, necessitating not only symptomatic treatment but also a comprehensive approach, including etiotropic treatment [1,7].

Factors contributing to the development of angular cheilitis include mechanical irritation, malocclusion, wearing dentures, increased salivation, vitamin deficiency, and impaired immune function in patients [1,7]. All these factors contribute to a protracted course of inflammation, making the tissues more sensitive. Despite this, microorganisms play a key role in the development of this pathology, determining the symptoms of the disease, triggering frequent relapses, and being found in affected areas with a high frequency of occurrence [2–4]. The microorganisms most frequently found in preparations from the corners of the mouth include yeast-like fungi of the genus *Candida* (mainly *C. albicans*) and the bacterium *Staphylococcus aureus*, which provoke the development of the disease not only in combination, but also separately [2–4].

## **Materials and Methods**

In our study, we examined scientific research on angular cheilitis, focusing specifically on the role of microorganisms in the development of this pathology. We reviewed clinical data on the microbial composition and frequency of pathogen detection in angular cheilitis, examined publications analyzing the causes of symptom recurrence after antimicrobial therapy, taking into account predisposing factors, and examined experimental studies and reviews on *Candida-Staphylococcus* dual biofilms and their resistance mechanisms.

We examined publications in clinical dentistry, dermatology, and microbiology, including articles, reviews, and clinical guidelines published over the past 10 years, from 2015 to 2025 [1–12].



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## **Results**

According to bacteriological studies, most patients with angular cheilitis have combined pathogenic microorganisms in the affected area. According to a study by Öhman S.C., Jontell M., and Dahlen G., *Staphylococcus aureus* and *Candida albicans* are found in the corners of the mouth in a significant proportion of patients with angular cheilitis, and microbial contamination was detected in all patients with this diagnosis [3]. Further studies also came to the same conclusion: *S. aureus*, *Candida* spp., and streptococci were found in more than 80% of cases, but *S. aureus* and representatives of the genus *Candida* fungi remained the most frequently encountered microorganisms [4]. Studies by Federico J.R., Basehore B.M., and Zito P.M. present similar data, according to which the frequency of detection of *Candida* spp. exceeds 50%, and the combination of bacteria and fungi leads to prolonged inflammation [1,7].

If patients are found to have *Candida* spp. and/or *S. aureus* in the corners of the mouth, especially in cases of frequent relapses and the ineffectiveness of standard treatment, this is a serious diagnostic signal [1,7].

One of the main reasons for the chronic course of the disease is the ability of microorganisms to form biofilms. It has been shown that *Candida albicans* not only actively attaches to tissues but also helps *S. aureus* colonize these same areas, forming stable communities in which staphylococci firmly bind to fungal hyphae, increasing resistance to therapy and infection [8,11].

Of particular interest is the phenomenon of so-called "commensal protection," in which the *Candida* biofilm matrix protects *S. aureus* from the effects of antibiotics [10]. The fungal colonies themselves also exhibit resistance, with the polysaccharide matrix (especially  $\beta$ -1,3-glucan) reducing sensitivity to antifungal agents [9]. As a result, treatment provides only external improvement, as the underlying inflammatory focus persists. As soon as additional irritation (maceration, excess salivation, minor trauma) occurs, symptoms return [5–7]. Therefore, if a biofilm infection is suspected, it is advisable to use a combined treatment approach, including antifungal agents and antibiotics (as indicated), as well as eliminating all local risk factors. Otherwise, there is a high risk of relapse [5–7].



In the presence of unfavorable conditions and residual microbial colonization, even an effective course of treatment does not prevent the recurrence of angular cheilitis symptoms [5]. A number of scientific studies have noted the need not only for therapy but also for a comprehensive diagnosis, including microbiological testing and identification of factors that reduce the effectiveness of treatment: dentures, maceration, excess saliva, and bad habits [6]. Current clinical guidelines also note that sustained remission can only be achieved with a comprehensive approach that considers both the microbial and mechanical causes of the disease [1,7].

**Table 1. Frequency of microorganism detection in angular cheilitis (based on literature data)**

Microorganism/microbial association	Frequency of detection among patients with AC, %	Sources
Candida albicans	50–85	[1–4,7]
Candida spp. (no-albicans)	5–20	[1,4,7]
Staphylococcus aureus	30–60	[3,4,6]
Streptococci (Streptococcus spp.)	15–35	[3,4]
Mixed infection (Candida + S. aureus)	25–50	[3–6]
Absence of clinically significant microflora	<10	[1,7]

Note: The range of results is due to differences in study design, microbiological diagnostic methods, and clinical sample composition.

Microbiological testing is advisable in cases of long-standing angular cheilitis and regular relapses. Furthermore, the presence of suspected combined fungal-bacterial infection (factors that increase the risk of developing fungal and staphylococcal infections, if standard treatment has failed) is also an indication for culture and microscopy [1,6,7]. In routine clinical practice, it is necessary to take a swab from the lesion and examine it for at least the presence of Candida spp. and bacterial flora. In recurrent cases, antimicrobial susceptibility testing is



also advisable, especially given the increasing resistance of microorganisms and the role of biofilms [6,9].

**Table 2. Pathogenetic role of microbial factor in angular cheilitis**

Pathogenetic mechanism	Microbial involvement	Clinical significance	Sources
Presence of microorganisms in the corners of the mouth	Candida albicans, S. aureus	Inflammation begins, cracks appear	[1,3,7]
Formation of a stable biofilm	Candida spp., S. aureus	The disease prolongs, medications are less effective	[8–11]
Joint action of microorganisms	Candida + S. aureus	Infection persists longer, causes more tissue inflammation	[8,10,11]
Increased resistance to therapy	Biofilm forms of Candida	Relapses after treatment	[9–11]
Reactivation in the presence of local factors	Opportunistic microflora	Frequent exacerbations with salivation, prosthetics	[5–7]

## Discussion

Clinical and laboratory data from the reviewed scientific studies confirm the primary role of microbial factors in the development of angular cheilitis. Mechanical damage to the skin and mucous membranes at the corners of the mouth, in the form of maceration, friction, and microcracks, facilitates the entry of pathogens into these areas, which is subsequently accompanied by inflammation caused not by single microbes, but by combinations of Candida fungi and Staphylococcus bacteria [1,3,5,8,10,11]. This mechanism explains why treatment is sometimes ineffective. The main errors in choosing therapy for angular cheilitis include the use of only one drug, without considering the possible fungal and bacterial nature of the infection, excessively short courses of therapy, without eliminating persistent irritants, and the failure to perform microbiological testing in patients with chronic or recurrent cheilitis [1,6,7].



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For the prescribed therapy to be effective, it is first necessary to confirm or exclude the involvement of *Candida* spp. and *S. aureus*, and eliminate local predisposing factors such as salivation, malocclusion, and problems with dentures or their care. The key role is played by the correct choice of medications, focusing on the composition of the microbial association, using combination treatment regimens when necessary. All this will lead to a reduced risk of relapse [1, 6, 7].

### **Conclusions**

1. In most patients with angular cheilitis, the primary pathogens are most often *Candida* spp. and *Staphylococcus aureus*, which are often found in mixed microbial associations [3,4].
2. The presence of mixed biofilm leads to a pronounced interaction, with *C. albicans* promoting the attachment and colonization of *S. aureus*, which increases resistance to therapy and provokes relapses [8,10,11].
3. Therapy is effective only if microbiological testing is performed (especially in protracted cases), therapy is selected taking into account the possible mixed nature of the infection, and local factors that contribute to inflammation are excluded [1,5–7].

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