

## Oral candidiasis

*Oral candidiasis* (or candidal stomatitis, oropharyngeal candidiasis and moniliasis) is the specific oral mycosis caused by yeast-like fungi of *Candida* genus.

More than 50% of disease cases is related with commonly spread fungi *Candida albicans*; other causative species for candidiasis in descending rate are *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, or *C. krusei*. *C. albicans* pertain to the normal representatives of oral microflora, where they can be found in modest amounts. However, in some specified conditions these fungal members exert serious *opportunistic infections* rendering local or severe systemic disease..

*C. albicans* are *dimorphic fungi*. In mouth they are often present as *yeast forms* or blastospores with questionable virulence whereas mouldlike fungal *hyphal forms* are capable of invading host tissues. Transition between these two phases largely depends on changes of environmental conditions.

In addition candidae create *pseudohyphae* - long filaments composed of oval fungal cells that are closely attached on their poles. It occurs due to incomplete separation of cells after division. A and B serotypes are identified by serological testing of *C. albicans*. Representatives of A group are characteristic for normal oral microbiota; by contrast, the members of B group arise actively in immunocompromised hosts.

Overall, all the details of transformation of oral saprophytic *Candida* into aggressive fungal pathogens are not yet clear completely. It is considered that candidal strains with enhanced capacity to adhesion and colonization are generally more pathogenic. In particular, the strains with high expression of certain adhesins (e.g., hyphal wall protein 1 or extracellular mannoprotein) are referred to as more active pathogens. Similarly, pathogenic fungi produce large amounts of hydrolytic enzymes such as proteases, phospholipases and hyaluronidase.

*Oral candidiasis* is regarded as the *most frequent opportunistic infection of oral cavity* that affects humans. Likewise, it is the most typical form of candidal infection and the most common form of oral mycosis at all.



Figure 2. Oral candidiasis

Candidiasis affects newborns and infants, but most of all - immunocompromised persons, namely patients with HIV infection and acquired immunodeficiency syndrome (AIDS); patients with cancer under cytostatic chemotherapy; patients, treated with antibiotics of broad spectrum of action with deep oral or intestinal dysbiosis.

Primary carriage of *C. albicans* predisposes to its further opportunistic infection. By far, elevated candidal carriage is typical for persons, wearing dentures; patients, aggressively treated with broad spectrum antibiotics or immunosuppressive drugs; HIV patients; diabetes and cancer patients; patients with “dry mouth” (or xerostomia); individuals with abundant consumption of sugar-containing nutrients, heavy smokers and some others. Thus candidiasis is often named as “a disease of the diseased”.

Candidal infection is divided into acute and chronic, primary and secondary.

**Primary oral candidiasis** originates from resident fungi and affects oral cavity and perioral area. By contrast, **secondary** disease emerges after spread of disseminated candidal infection that occupies the mouth and other body compartments.

Nevertheless, dissemination of oral candidiasis to other body sites (or invasive infection) is generally seldom situation. It happens predominantly in immunocompromised patients.

There are 3 main forms of oral candidiasis:

- (1) pseudomembranous;
- (2) erythematous;
- (3) hyperplastic.

**1. Pseudomembranous candidiasis**, or *thrush*, demonstrates white pseudomembranous spots upon oral mucosa that contain epithelial and fungal cells mixed with fibrin and cellular decay. They resemble “cottage cheese” or “curdled milk”. The covering film is easily removed showing red mucosal bottom. These lesions usually affect tongue, palate and buccal epithelium. Acute pseudomembranous oral candidiasis is registered in 5% of newborns and early infants. They become infected in delivery by contact with maternal vaginal canal harboring candidae. Chronic pseudomembranous candidiasis arises mainly in immunocompromised persons, e.g., HIV patients.

**2. Erythematous** form of the disease exposes typical smooth and reddened lesions, which are located mainly upon the tongue dorsum or palate. The lesions are usually painful. Substantial loss of lingual papillae (or depapillation) is common here. In most of cases this fungal infection is the result of long-term antibiotic treatment or corticosteroid therapy. That’s why it is often named as “antibiotic induced stomatitis” or “antibiotic sore mouth”.

Erythematous illness covers up to 60% of total oral candidiasis if taken with related clinical forms such as angular stomatitis and denture- related stomatitis. The latter is associated with chronic erythematous candidiasis.

**3. Hyperplastic candidiasis** is a seldom form of disease with the incidence of about 5%. It is named as nodular or plaque-like candidiasis. This variant produces white firm nodular lesions predominantly found upon both sides of buccal mucosa.

***Candida-associated lesions*** are the oral injuries caused by *Candida* fungi in association with other pathogenic microorganisms. Two basic forms are known - **angular cheilitis and denture related stomatitis**.

***Angular cheilitis*** is the infection-based inflammation at mouth angles. About 20% of disease is caused solely by candidal species, whereas 60% originate from association of *C. albicans* and *S. aureus*. This pathology renders angular soreness and erythematous inflammation that may result in angular Assuring. The syndrome affects elderly adults and often accompanies denture related stomatitis

***Denture related stomatitis*** is a low or moderate inflammatory complication that affects edentulous elderly adults wearing oral appliances (*dentures*). It is generally ascertained that more than 50-60% of denture-wearing individuals exhibit denture related stomatitis.

Dominating causative agents in this pathology are *Candida* fungi (above 90% of total number of cases). Thus the disease is commonly termed as “*Candida-associated denture induced stomatitis*” or CADIS.

Mucosal surface under dentures demonstrates highest grades of fungal colonization in comparison with normal unaffected mucosa. It creates acidic, moist and relatively anaerobic surrounding that promotes further candidal growth. In addition, poor adjustment of oral prostheses causes micro-injuries of gingival mucosa. *Candidae* easily attach to the surface of damaged tissues and polymeric surface of dentures with their multiple pits and fissures. Microbial adherence and colonization stimulates local inflammation. This leads to continuous irritation of oral mucosa resulting in erythematous lesions.

Chronic denture related stomatitis creates the stable reservoir for candidal infection that in worsen conditions may expand to other areas of oral cavity.

***Diagnosis of oral candidiasis*** grounds on clinical findings but requires laboratory confirmation of fungal infection. Sampling is made from lesion sites by oral smears, swabs or rinsing. Microbial smears are examined by Gram stain demonstrating grampositive candidal cells with pseudohyphae. Fungal culture is made on *Sabouraud medium*.

Oral rinse examinations help to discriminate between “normal” candidal carriage and oral candidiasis. About 7,000-7,500 colony-forming units of *candidae* per 1 ml of oral rinse can be found in disease condition.

Treatment of oral candidiasis presumes administration of topical antifungal dnigs, such as miconazole, nystatin, levorin, or amphotericin B. Severely immunocompromised patients, e.g., with candidiasis in AIDS, need systemic anti-fungal therapy with oral or intravenous drugs (amphotericin B, azoles or others).

Proper oral hygiene strongly reduces candidal propagation in oral cavity. It presumes adequate toothbrushing, smoking cessation, oral rinsing after inhalation steroid use, and regular denture disinfection with denture cleaner preparations (e.g., chlorhexidine or sodium hypochlorite).