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Review Article

# Risks and Complications in Fungal Infections

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## Abstract

Diseases caused by fungi have increased in frequency and clinical importance, due to the increased use of potent immunosuppressive drugs in transplants, in anticancer therapy, and by the appearance of viral infections that cause immunodeficiency. The facial skin and the oral mucosa are regions where fungal infections can be found on many occasions. They can be classified in various ways, depending on their evolutionary behavior and form of presentation. Each species tends to produce its own clinical features, although often several of them cause almost identical conditions, other times they are so pathognomonic that it is easy to identify the species, just by examining the affect. Therefore, an exhaustive bibliographical review was carried out on the main orofacial manifestations and risks produced by fungi.

**Keywords:** Fungal Infections; Immunodeficiency; Pathognomonic

## Introduction

Mycoses are diseases caused by fungi that constitute a very frequent cause of consultation and will be influenced by systemic aspects and environmental factors. Etiopathogenesis is varied, as are the risks and complications to which these patients are exposed. In this chapter we will address fundamental aspects such as concept, etiopathogenesis, clinical characteristics, main risks and treatment recommendations [1,2].

## Objective

To describe some of the main complications and risks of fungal conditions in the buccomaxillofacial complex.

## Reference Search Methods

The scientific information was compiled through a search using the following descriptors in English: The Medical Subject Headings (MeSH): "dermatology, oral cavity, Risks, Complication, Head and Neck.

### Analysis strategy

The search was based solely on fungal conditions of the buccomaxillofacial complex.

### Developing.

### Candida albicans

It is a fungal disease caused by any of the species of the genus Candida. Due to its way of establishing itself, it is recognized as an opportunistic disease with mucocutaneous affection. Due to its high frequency at present, the presence of factors favoring the growth and pathogenic transformation of the germ must be taken into account and investigated.

It is the most frequently reported species in the literature that produces a cosmopolitan infection, which presents suddenly, followed by prolonged periods of evolution and in some cases it can spread to the bloodstream, worsening the patient's prognosis and survival [1-3].

There are multiple causes that can influence the appearance of this pathological entity, as well as its form of presentation, treatment and prognosis.

| Risk factor's | Examples |
|---|---|
| Related to the oral cavity | Improper use of oral prosthesis, xerostomia, poor oral hygiene, decreased salivary pH. |
| local factor | Contact with contaminated water |
| Toxic habits | smoking |
| Drug therapy and alteration of the oral flora. | Use of antibiotics or steroids. Radiation and chemotherapy. |
| Related to systemic diseases and debilitating conditions | HIV/AIDS, Immunopathies, endocrinopathies (Diabetes Mellitus, hypothyroidism), hematological disorders (lymphomas, leukemias, aplastic anemia, agranulocytosis, neutropenia), and epithelial dysplasia. Neoplasms, starvation, burns [1, 2] |
| Related to nutritional status | Serious and extensive, drug addiction, |
| factors | Tuberculosis and other diseases |

**Table a**

This disease has been extensively studied and has been classified taking into account multiple factors. Below are some of the different classifications that have been used.

| Classifications |
|---|
| Superficial |
| deep |
| Erythematous. |
| Hyperplastic. |
| Pseudomembranous. |
| Angular cheilitis (commissural stomatitis). |
| Monilias chronic granuloma |
| Chronic localized mucocutaneous candidiasis. |
| Diffuse chronic candidiasis. |
| Chronic atrophic oral candidiasis. |
| Denture stomatitis or subplaque palatitis. |
| Chronic localized mucocutaneous candidiasis. |
| Syndrome of candidiasis in endocrinopathies. |
| Leukoplakia-candidiasis (Plake-like). |
| Nodular shape. |

**Table b**

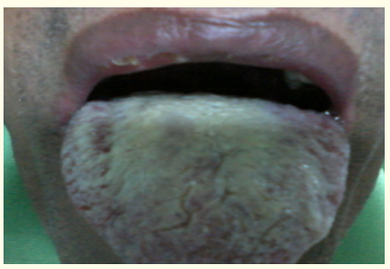

**Figure 1:** Patient with collagen disease with candidiasis lesion on the palate and tongue. Courtesy of Dr. Otto Alemán Miranda.

The most common presentations include pseudomembranous and erythematous candidiasis and cheilitis, which are predictive of the development of AIDS. In the first there are white plaques that are removed leaving erythematous mucosa. In erythematous candidiasis, red patches of varying size commonly appear on the palate or on the dorsal surface of the tongue [4,5].

Angular cheilitis appears as a redness, ulceration or fissure, in one or both corners of the mouth. It can appear alone or along with other forms of yeast infection. Hyperplastic candidiasis is unusual in patients with HIV. The white areas are due to hyperkeratosis and, unlike the pseudomembranous form, cannot be removed, so they can be confused with hairy leukoplakia.

These lesions can affect the oral cavity and pharynx, may present asymptomatic, or more commonly with discomfort in the oral tissues and oropharynx, with burning sensation and dysgeusia. It is almost pathognomonic to have a creamy, whitish or yellowish coating or patches (thrush) in both the mouth and pharynx.

In addition, bluish-red lesions, flat or raised and with an irregular shape, may also be evidenced. Bleeding from gastrointestinal lesions, difficulty breathing from pulmonary lesions, and bloody sputum from pulmonary lesions may affect the prognosis of patients.

When candidiasis settles specifically in the pharynx and respiratory tract, considered an esophageal infection, it is an indication of severity. Symptoms include pain in the thoracic region, nausea, and sore throat. The esophagus can become partially obstructed by coatings and patches that build up. In some rare cases, certain ulcers can perforate the esophagus. Esophageal candidiasis can spread, or spread, to the stomach and intestines. Since esophageal candidiasis can cause pain on swallowing, if not treated promptly, sufferers may not get enough nutrition and lose weight [5,6].

Here are some recommendations for the treatment of pseudomembranous and erythematous candidiasis

- Nystatin Suspension (500,000 Units (U) for every 5 ml (240ml) In adults, 200,000 to 400,000 U are applied orally every 4 or 6 hours for up to 14 days. In premature children and low-weight infants: 100,000 U every 6 hours Older infants: 200,000 U orally every 6 hours Children over 5 years old the same as adults.
- Fluconazole (150 mg capsule) single dose of 50 milligram (mg) per day or 100 mg per day in severe infections. For 7 to 14 days. In immunocompromised patients it can be extended up to 30 days.
- Fluconazole (200 mg suspension) in children is calculated from 3 to 6 milligrams per kilogram (KG) of weight.
- Itraconazole (100 mg capsule) 100 mg daily for 15 days, orally. In patients with AIDS or neutropenia 200mg.
- If there are no improvements, switch to systemic treatment (amphotericin B (50 mg bulb) 0.3, 0.7 to 1 mg/KG of weight per day by intravenous infusion) The maximum dose is 50 mg per day. In children the usual dose is calculated at 0.25 mg per kg of weight up to a maximum dose of 1 mg/kg/day [5,7].

## These recommendations were taken from the Cuban national drug formulary

## Histoplasma capsulatum

Histoplasmosis is a generalized fungal infection, caused by Histoplasma Capsulatum (HC), where the professional must keep in mind two possibilities:

- Some series 30% of the lesions begin in the oral cavity.
- That it is almost always involved in the general picture of the mouth.

HC microconidia penetrate the respiratory tract by inhalation and, thanks to their small size, manage to reach the alveoli of the host, where at 37 °C, they become yeasts. In this form, they manage to survive inside macrophages, which transport them to all organs through the blood and lymphatic pathways. After several weeks, specific T cell-mediated immunity develops, and macrophages are activated, thus killing the organism. The intensity of the condition and, consequently, the clinical form that will develop depend on the number of conidia inhaled, as well as on the integrity of the host's immune response.

The disease has a special predilection for the reticuloendothelial system that mainly affects the spleen, liver, lymph nodes, and bone marrow. Oral lesions appear nodular, ulcerative, or vegetative on the vestibular mucosa, gums, tongue (see figure), palate, and lips. Ulcerated areas are usually covered with a gray membrane and are indurated [8-10].

The symptoms of this disease are non-specific and can be difficult to distinguish from the manifestations of other infectious diseases, especially disseminated tuberculosis, which complicates its diagnosis and treatment.

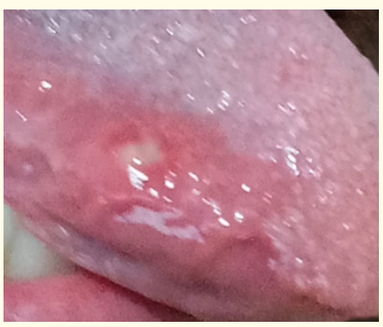

**Figure 2:** Patient with histoplasmosis lesion on the tongue. Courtesy of Dr. Otto Aleman Miranda.

Ulcerative or granulomatous, irregular, red, painful and pointed lesions.

They can initially present in the oral cavity and can affect any part of the mucosa. The diagnosis requires biopsy, they are located in the gums, tongue, palate and lips.

Currently, this condition has been achieving social repercussions due to

- That it is an endemic disease in large areas of the American continent.
- It is recognized as an opportunistic infection marker of AIDS, so its clinical and epidemiological importance has spread as this viral pandemic has advanced.
- It is closely related to certain jobs, which is why it is also considered in some regions as an occupational disease [10,11].
- Its incidence and prevalence has risen internationally, which is why various experts on the subject link its increase to tourism and migration.

The forms of presentation are

- Acute pulmonary histoplasmosis
- Chronic pulmonary histoplasmosis
- Progressive disseminated histoplasmosis

The diagnosis can be supported by direct examination, cultures, detection of fungal antigens, detection of antibodies in serum and cerebrospinal fluid, and imaging.

The treatment of histoplasmosis depends on the severity of the clinical picture. The benign forms generally do not require antifungal treatment, but rather symptomatic measures. For moderate forms, the recommended treatment is itraconazole, while for severe forms, the drug of choice is amphotericin B.

## Coccidioides Immitis

Coccidioidomycosis is a fungal infection, which is almost always acquired from the environment. Most infections are relatively mild or Asymptomatic, however, severe or lethal disease also develops, especially in the elderly and immunosuppressed people [11,12].

Coccidioidomycosis is caused by dimorphic fungi, transmitted by the soil, ascomycetes Coccidioides immitis and C. posadasii. It is normally limited to the respiratory tract.

Its form of presentation is variable (Table C)

| Form of presentation | Main complications |
|---|---|
| Primary pulmonary coccidioidomycosis | |
| Progressive pulmonary coccidioidomycosis | |
| disseminated coccidioidomycosis | Myalgia. |
| Coccidioidomycosis in immunosuppressed people | Pain in the oropharynx. |

**Table c**

For the diagnosis of this mycosis, direct examination is used, which is carried out from clinical samples such as: scrapings of skin lesions, ulcers, purulent discharge from abscesses and sputum. Serological methods such as tube precipitation, immunodiffusion, and complement fixation allow the detection of circulating antibodies against this fungus [12-14].

Treatment options range from observation to antifungal drugs, depending on the severity of the disease and risk factors for spread. Azoles such as fluconazole, itraconazole, and ketoconazole, as well as amphotericin B, can be used. The treatment of choice in critically

ill patients with disseminated coccidioidomycosis or CNS attack is amphotericin B at a dose of 1 mg/kg/day. In moderate infections, fluconazole 200 to 400 mg daily is used.

## Cryptococcus neoformans

Cryptococcosis is a systemic, chronic disease produced by yeasts classified as basidiomycetes that belong to the genus Cryptococcus. It is worldwide in distribution and affects people with or without immunosuppression.

It can affect people with or without immunosuppression. It presents mainly as a chronic lung infection. The majority of cases in the oral mucosa have been reported in patients with AIDS who were presenting with the disseminated form of the infection. The infection is acquired by inhalation of the spores of the fungus, hence the organ that is primarily affected is the lung, from which it can spread to other parts of the body, especially the central nervous system and occasionally to the skin and mucosa. from the mouth In general, it is characterized by

- Sputum, cough, chest pain, dyspnea, fever, night sweats and malaise.
- Meningoencephalitis.
-

In the oral cavity it can cause the following conditions

- Gingival enlargements. (View Figure)
- Tumor-like lesions located on the tuberosity.
- Mucosa affected is erythematous, edematous, with a granular texture and with micro-ulcerations covered with serous secretion resembling reactive gingival hyperplasias [14-16].

**Figure 3:** Patient with gingival lesion due to cryptococcosis in the posterior-inferior region.

We currently have numerous diagnostic techniques, including specific culture, histopathology, and immunoassay techniques.

The treatment is directed and individualized according to the particular case.

## Blastomyces dermatitidis

Oral blastomycosis is a rare infection caused by inhaling a dimorphic fungus, called Blastomyces dermatitidis, found on wood and soil. This disease is also known as North American blastomycosis or Gilchrist's disease. It has 3 forms of presentation (Table d).

| Form of presentation | Key clinical features |
|---|---|
| Primary cutaneous blastomycosis | Traumatic inoculation. |
| pulmonary blastomycosis | Incubation period from 15 to 21 days. |
| disseminated blastomycosis | Chancre or primary complex |

**Table d**

The lesions produced by blastomycosis in the oral cavity are mainly located in the soft tissue area (gums, buccal mucosa, palate, tongue, floor of the mouth, and lips). The type of lesion that usually produces is a solitary type ulcer with a slightly warty surface.

Among its systemic complications are

- Hematogenous spread, which can cause involvement in multiple regions such as skin, prostate, epididymis, testicles, seminal vesicles, kidneys, vertebrae, ends of long bones, subcutaneous tissues, brain, oral mucosa or nasal, thyroid, lymph nodes, and bone marrow.
- Severe self-limited lung disease.
- Skin lesions with formation of papules or papulopustules, irregular wart-like papillae, and blisters.

Diagnosis is based on clinical evaluation or chest x-ray and is confirmed by identification of the fungus on laboratory tests. Treatment consists of itraconazole, fluconazole, or amphotericin B [16-18].

## Aspergillus

Aspergillosis is an opportunistic infectious disease, caused by a fungus that is normally found in the environment. Infections can be very aggressive if they are not detected and treated on time. When entering through the airway in most cases, it has a high tendency to spread to the lungs and even the brain.

Some authors classify it as non-destructive and invasive, depending on the clinical characteristics, there are also those who speak of invasive and separate two variants calling them allergic bronchopulmonary aspergillosis and bronchocentric granulomatosis (Figure 4).

## Among its complications are

- Disruption of tissue planes and vascular invasion.
- Bronchial affectation.

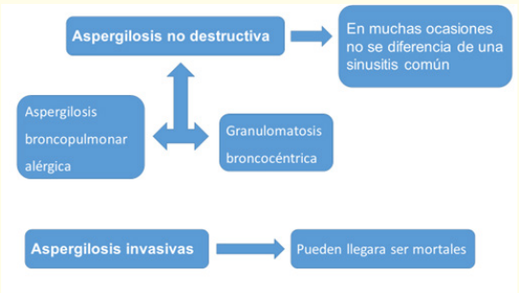


**Figure 4:** Representation of the classification of Aspergillosis according to its clinical forms of presentation. Courtesy of Dr. Otto Aleman Miranda.

- Infection and inflammation of the respiratory mucosa.
- Tissue necrosis.
- Formation of thrombi.
- Formation of infarct areas.
- Presence of hemorrhagic areas.
- Pleural effusion.
- Granulomas.
- Affection of the central nervous system.
- Meningitis.
- Encephalitis.
- Sinusitis.
- Nasal polyps.
- Disease of the lymph nodes.
- Aspergilloma.
- Fever and chills.
- Hemoptysis.
- Dyspnea.
- Pain in the thoracic region.
- Asthenia.
- Adynamy.
- Arthralgia.
- Headache or ophthalmopathies.
- Skin lesions.
- Systemic infection.
- ulcerated lesions with erythematous spots on the buccal mucosa (mulberry appearance).
- Granulomatous purpuric lesions.
- Lesions with a granulomatous, ocher appearance, with areas of central necrosis.
- Whitish lesions on tonsils.
- Hyperemic pustular lesions.

Depending on the type of aspergillosis, treatment may include observation, antifungal medications, or, in some cases, open or minimally invasive surgery [19-21].

These conditions are not frequent in our consultations, but the professional must know them and be oriented to be able to diagnose them, or suspect that the condition exists. Allowing you to take the opportune and appropriate conduct, promptly inter-consulting with the specialists in charge of providing care to these conditions when the complications extend beyond the oral and maxillofacial complex.

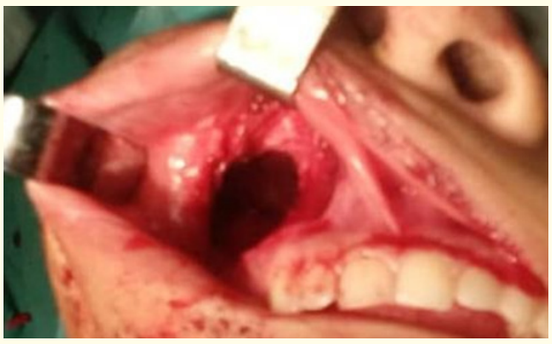

**Figure 5:** Patient who underwent a Cadwel Luck intervention. Courtesy of Dr. Otto Aleman Miranda.

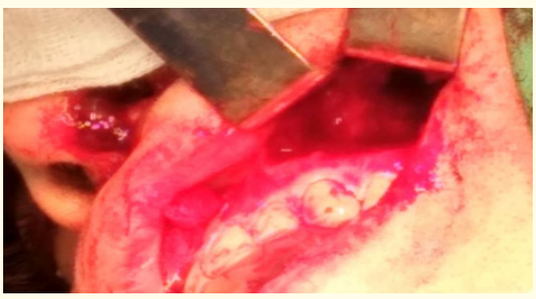

**Figure 6:** Patient who underwent a Cadwel Luck intervention to remove nasal polyps. Courtesy of Dr. Otto Aleman Miranda.

## Zigomycota/Mucor/Rhizopus

Zygomycoses are a group of infrequent fungal infections, which can be serious. Its etiology is given by ubiquitous fungi belonging to the class Zygomycetes. They are classified into Mucorales and Entomophtorales, each one with its particularities.

The spores of these fungi are transmitted by inhalation, through a series of percutaneous routes, or by ingestion. Patients with decompensated diabetes mellitus have a higher risk and worse prognosis. Other risk factors are hematological alterations, nutritional disorders, prolonged drug treatments (steroids and antibiotics) or chemotherapy. The fungus tends to cause thrombosis of major blood vessels in certain anatomical regions, leading to ischemia necrosis, gangrene, and extensive tissue damage.

These microorganisms normally live as saprophytes of plants or their remains, algae, some arachnids, as well as in the intestine and feces of amphibians, insectivorous mammals, and reptiles that feed on infected insects. Insects and reptiles can act as direct transmitters [21-24].

Its main complications are presented according to the evolutionary phase in which it is found (Table e).

| Evolutionary phase | Main complications |
|---|---|
| Phase I | Nasal obstruction. |
| Phase II | Affection of the nasal mucosa by a nodular lesion. |
| Phase III | Subcutaneous swelling that grows slowly and affects the mucosa and soft tissues of the midface region with their deformation. |

**Table e**

Diagnosis is made by mycological, laboratory, molecular biology, and histopathology studies.

Treatment is mainly based on antifungals and in some cases surgical procedures are performed [1,2,25].

## Conclusion

The main complications and risks of fungal conditions in the bucomaxillofacial complex, as well as their sequelae, were described. Based on a comprehensive review of the literature, as well as the author's previous experience. These injuries have a high international morbidity rate, and cause multiple physical, mental and social conditions.

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