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Oral fungal infections

•Fungi are eukaryotic and possess a defined nucleus and other cellular inclusions.

•Fungi have a rigid cell wall consisting of polysaccharide (mannan, glucan and chitin) complexed with protein.

•Fungi are aerobic and most require an organic carbon and a simple nitrogen source for growth.

•Fungi that reproduce by asexual means form conidia.

•Fungi grow as yeasts or moulds; yeasts produce oval yeast cells by budding; moulds produce hyphae and reproductive conidia or spores.

•Dimorphic fungi (e.g. Candida albicans) grow as either yeasts or moulds.

•Fungal infections are classified as superficial, opportunistic or systemic.

•Most fungal infections arise from the environment or the host's endogenous flora.

•Laboratory diagnosis is based on microscopy, culture, biochemical tests .

•Phagocytosis and cell-mediated immunity are essential for recovery from fungal infections.

•Chronic progressive fungal disease mainly occurs in patients with compromised tissues and/or immune systems.

Candida culture(Yeast)

Classification

There are three groups of interest to dentists:

1-Dermatophytes cause superficial skin infections e.g. ring worm and athletes foot.
2- Opportunistic fungi, which are present in the environment or in the human normal microflora, cause disease especially in the compromised host, e.g. Candia spp. and Aspergillus spp.
3- Systemic pathogens, which are the most virulent, can cause systemic disease in previously healthy individuals e.g. Blastomyces spp. and Cryptococcus spp.

Pathogenesis and immunity

Individuals with a normal immune system have a high natural resistance to most fungal infections. In addition to a range of innate defence mechanisms, the two main immunological mechanisms involved appear to be phagocytosis by neutrophils, with or without the assistance of opsonizing antibodies, and the development of cell-mediated immunity. These mechanisms ensure that the fungi in the human microflora remain in a non-pathogenic state and that any fungi that enter the body from exogenous sources are eliminated sooner or later. However, som e fungi have developed strategies to evade parts of the host defence mechanisms, and in addition there are a number of non-fungal factors that predispose host to infection, including diseases and drugs that can affect elements of the innate, humoral or cell-mediated immune responses . Fungal infections in the oral and perioral regions occur either as primary localized lesions or as manifestations of systemic mycoses. By far the most common group of fungal infections that dental practitioners diagnose and treat are caused by Candida spp. Some of the rarer mycoses with oral manifestations, such as histoplasmosis, are found almost exclusively in the USA, while others such as mucormycosis are found particularly in immuno-compromised individuals.

The host defenses against opportunistic infection of candida species are:

1. The oral epithelium, which acts both as a physical barrier preventing microorganisms from entering the tissues, and is the site of cell mediated immune reactions.
2. Competition and inhibition interactions between Candida spp and other microorganisms in the mouth.
3. Saliva, which possesses both mechanical cleansing action and immunologic action, including salivary IgAs antibodies, which aggregate candida organisms and prevent them adhering to the epithelial surface; and enzymatic components such as lysozyme, lactoperoxidase and antileukoprotease.

PATHOGENESIS. Candida's pathogenic factors

Pathogenesis 1

Adhesion is an important determinant of *Candida's* virulence

– *Candida* produces a large number of adhesins that mediate adherence to host epithelial and endothelial cells.

– Strains with faulty adhesins are a virulent

Pathogenesis 2

• *Candida* produces many enzymes that contribute to its pathogenicity

– Produces 9 proteinases involved in invasion of tissues by degradation of extracellular matrix proteins.

– Produces adenosine which blocks neutrophil degranulation, thus impairing phagocytosis.

Pathogenesis 3

• *Candida* adapts rapidly to changes in host environment

– Shifts between phenotypes in a reversible and random fashion

– Produces genetically altered variants at a high rate

– This adaptation makes it difficult for host defenses to attack and eliminate infection

Candidal carriage in the oral cavity

The carriage rate of Candida spp. in the oral cavity is relatively high but only a few individuals develop oral candidosis. The transition from carrier state to infection appears to depend on environmental factors and changes in the host defences that allow some yeast cells to express virulence factors which are normally repressed. Wide variations have been reported in the oral carriage rate of Candida spp. The dorsum of the tongue is the primary oral reservoir of the organism in carriers, although Candida spp. can also be found in dental plaque and on intra-oral appliances. Eight Candida species are of medical importance, of which C. albicans, C. glabrata, C. dubliniensis, C. tropicalis, and C. krusei are the most frequently isolated.

Candida albicans is better adapted than other species for growth in the mouth, particularly through its ability to adhere to oral and acrylic surfaces, and is the most common species present in health and disease. Candida dubliniensis, usually in combination with other Candida spp., has been associated with AIDS patients, although its role in infections in other groups of patients is uncertain.

Candidal carriage state is not considered a disease, but when Candida spp become pathogenic and invade host tissues, oral candidiasis can occur.

The predisposing factors are:

• **LOCAL FACTORS**

– Dentures;
– Low pH of the saliva;
– Neglected hygiene etc.

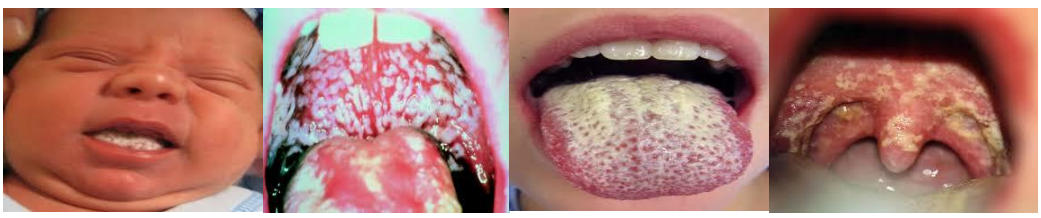
• **SYSTEMIC FACTORS**

– Systemic diseases;
– HIV/AIDS;
– Immunosuppression
– Oncological treatment;
– Drugs misuse and Antibiotic treatment etc.

Oral candidosis

1-Pseudomembranous candidosis (PMC)

Pseudomembranous candidosis is characterized by the presence of white plaque-like lesions on the oral mucosa and has traditionally been most frequently found in the mouths of neonates and in the elderly. Pseudomembranes occur on the surface of the labial and buccal mucosa, hard and soft palate, and tongue. The lesions can be removed by gentle scraping to reveal the underlying erythematous mucosa and this is a diagnostic clinical feature of the infection. When viewed by light microscopy, the removed pseudomembranes are seen to consist of desquamated epithelial cells and fungal elements. Pseudomembranous candidosis is often described as 'oral thrush' and is generally regarded as an acute infection resulting from an underlying host predisposition. Management and correction of any host related factor generally results in resolution of the condition. However, in recent years and with the advent of HIV infection and the increasing incidence of AIDS, a more chronic variant of pseudomembranous candidosis has been reported that can persist for several months if not years. Furthermore, in such immunocompromised individuals, progression of the oral infection to an oesophageal involvement is often evident and this can lead to added complications such as difficulties in swallowing and chest pain. The increasing prevalence of steroid inhaler use, particularly in young adults as part of the management of asthma, has been associated with frequent cases of pseudomembranous candidosis in the soft palate.



2-Erythematous candidiasis and denture-related candidiasis.

This form of candidiasis may arise as a consequence of a number of different factors and local conditions:

- following acute pseudomembranous candidosis after the white plaques are shed and infection persists;
- de now in patients with AIDS;
- in patients receiving prolonged drug therapy, for example topical steroids or broad-spectrum antibiotics;
- most commonly related to denture wearing.

The lesions of erythematous candidiasis consist of red areas of varying sizes and can appear on any part of the oral mucosa. The dorsum of the tongue is commonly affected in non-denture-related infections and lesions may be painful, fiery-red, and shiny **. While atrophic changes cha**racterize some of these erythematous lesions this is not a constant feature and therefore the use of the term 'atrophic' . The duration and severity of erythematous candidosis is very variable and there seems little value in diagnosing lesions as either acute or chronic when they can persist for many weeks or months, if untreated. Erythematous candidosis related to dentures is the most common form of oral candidosis and is present in about 50% of denture wearers. It is also associated with patients who wear orthodontic appliances. It is sometimes called 'denture sore mouth'. The affected area presents as a red, swollen, inflamed mucosa, commonly involving the palatal mucosa beneath the fitting surface of both complete and partial upper dentures . The lower ridge is seldom affected.

The palatal lesions have been categorized into three types depending on severity:

Type 1 as localized pinpoint hyperaemia;

Type 2 as diffuse erythema and oedema of the denture-bearing area of palatal mucosa;

Type 3 as inflamed hyperplastic epithelium.

The factors that predispose to denture-related candidosis are largely local, for example trauma, poor denture hygiene and carbohydrate-rich diets. Occasionally other factors such as xerostomia, iron and folate deficiency and diabetes mellitus may be involved. Patients should be encouraged to clean the fitting surface thoroughly with a toothbrush each evening and soak the denture overnight in an antiseptic solution such as dilute hypochlorite for acrylic dentures or 2% chlorhexidine for metal dentures. Patients should also be discouraged from wearing dentures during sleep. In addition, anti-fungal therapy should be instituted and topical therapy sustained for at least 3–4 weeks.

3-Angular cheilitis

This disease can be associated with any type of oral candidosis but is most frequently seen as a complication of denture-related candidosis in edentulous patients. However, dentate young adults can also present with this condition. As with all forms of oral candidosis, angular cheilitis has a multifactorial aetiology , though the relative importance of the different factors remains uncertain.

Maceration of the epithelium at the angles of the mouth by saliva trapped in mucosal folds appears to be an important factor, especially in denture-related forms of the disease. The clinical signs vary from areas of inflammation at the angles of the mouth to ulcerated and crusted fissures . The presence of distinctive yellow crusts, not unlike the typical lesions of impetigo, may suggest involvement of Staphylococcus aureus. Since the lesions are usually only mildly irritating, most patients do not seek medical or dental treatment. The importance of Candida species, S. aureus and (β-haemolytic streptococci in the aetiology of the lesions is not clear but in many cases the use of specific antimicrobial agents leads to considerable improvement in the condition. The source of these micro-organisms is mainly from the mouth or also the nose in the case of S. aureus.

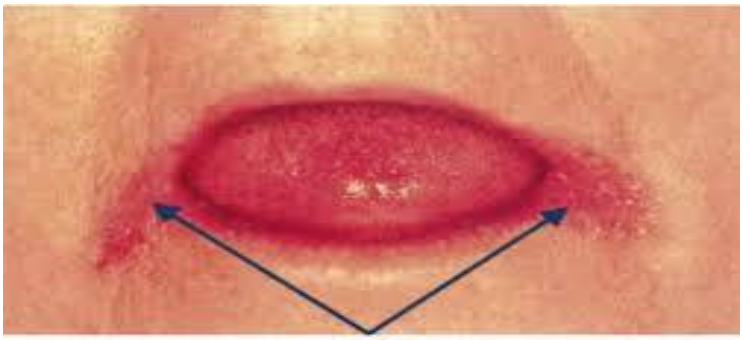
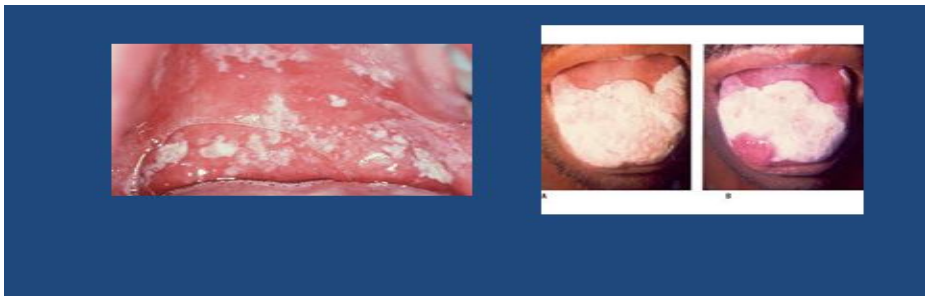


Photo showing bilateral
Angular Cheilitis

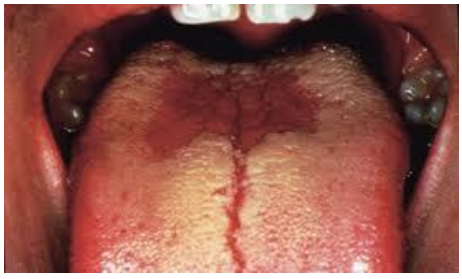
4-Chronic hyperplastic candidosis (candidal leukoplakia)

This form of candidosis usually presents as individual lesions on the oral mucosa of the cheek near the commissure, at the angles of the mouth, or on the surface of the tongue. The white patches cannot be rubbed off, in contrast to the lesions of pseudomembra-nous candidosis, and are indistinguishable from leukoplakias due to other causes. The presence of speckled, red-white areas in the lesion has clinical importance, since areas with this appearance have a higher chance of malignant transformation. Histologically the surface epithelium is parakeratinized and markedly hyperplastic, with candidal hyphae invading the parakeratinized layer at right angles to the surface but remaining relatively superficial . The role of C. albicans in the aetiology of these epithelial changes remains unresolved. Candida spp. may be a co-factor in epithelial hyperplasia, play a part in the malignant transformation of cells, or simply super-infect an already thickened area of abnormal epithelium. The fact that prolonged antifungal therapy leads to resolution of some of these lesions suggests that Candida may play a causative role in at least some cases. An accurate diagnosis of candidal leukoplakia is important, since 5–11% of the lesions can become malignant.



Median rhomboid glossitis

Median rhomboid glossitis is seen as a symmetrical shaped area in the midline of the dorsum of the tongue. The condition is chronic and represents atrophy of the filiform papillae. Recovery of *Candida* from this area is high, and the condition would appear to be strongly associated with both smoking and the use of inhaled steroids.



Chronic mucocutaneous candidosis

This is a rare group of disorders characterized by persistent superficial candidal infection of the mouth, other mucosal surfaces, the skin and nails. The oral lesions resemble those of chronic hyper-plastic candidosis and can involve any part of the mucosa. The clinical patterns of presentation can be classified in a number of ways but four main subgroups are identified, based on clinical features and age of onset . Chronic mucocutaneous candidosis (CMC) must be confirmed by taking swabs and smears from the lesions and by histological examination of biopsies. In addition, appropriate clinical and laboratory investigations should be performed to define the extent of immunological or endocrine dysfunction.

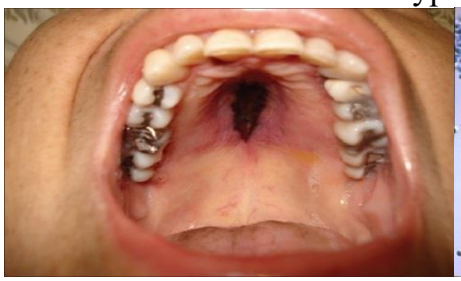
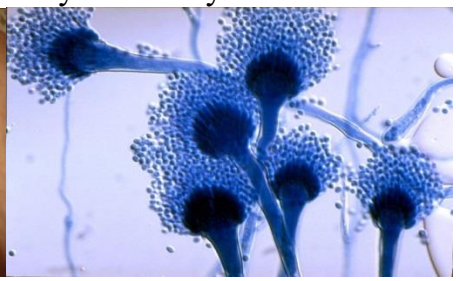
Oral manifestations of systemic mycoses

In most instances the oral lesions are secondary to the primary infections, typically granulomatous lesions found in the lungs and on the skin. The oral lesions may, however, be the initial presenting sign of the disease, as is the case for histoplas-mosis. In general, the main habitat for these organisms is the soil and infection is usually acquired by inhalation, with the primary lesions occurring in the lungs. In the majority of cases these heal without causing illness, but in progressive disease, sometimes related to lung cavitation, infection disseminates to the skin, mucous membranes and internal organs. The lesions tend to be chronic granulomas, and diagnosis is by direct demonstration of the yeast-like form of the fungus in smears of sputum or in biopsy specimens. Culture and identification of pathogens from clinical samples is useful in diagnosis, as is serology in certain infections. Many of the dimorphic fungi are sensitive to amphotericin B but azole drugs, for example fluconazole, are replacing amphotericin for some infections.

Uncommon oral fungal infections

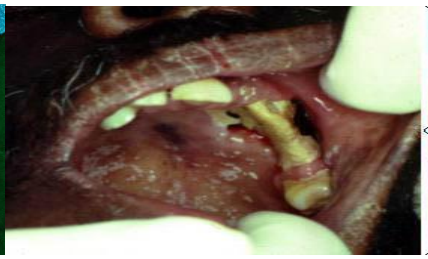
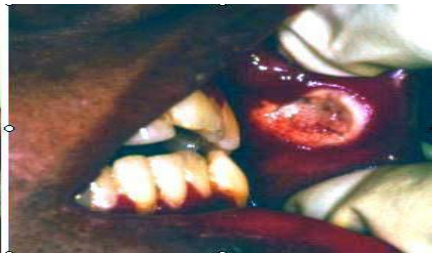
Aspergillosis

- Second commonest fungal infection in human
- Commonly seen with high dose of corticosteroid use, organ and marrow transplantation, increase use of immunosuppression against autoimmune diseases
- Lungs are commonly affected
- Also invade blood vessels causing thrombosis and infarctions
- Less commonly affect maxillary sinuses
- Oral lesions are typically black or yellow necrotic soft tissues

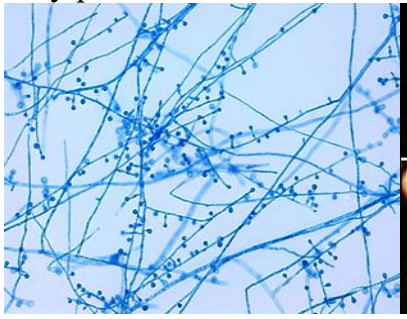
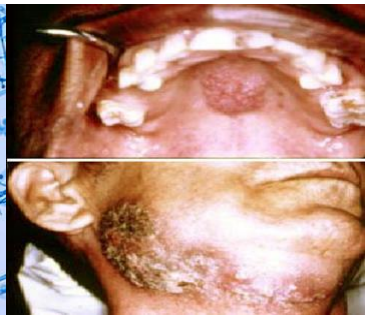
Cryptococcosis

- Primarily affects lungs and can lead to meningitis
- Caused by *Cryptococcus neoformans*, usually isolated in pigeon's and other birds' droppings
- Cutaneous lesions : Face, neck and scalp
- Oral lesions are rare; resembles superficial ulcerations, granulomas, nodules or indurated ulceration similar to carcinoma

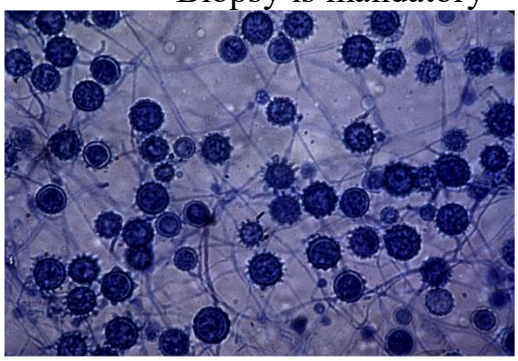
Blastomycosis

- Caused by *Blastomyces dermatitidis*
- When inhaled, spores produce disseminated or local respiratory infections
- Oral lesions are rare
- May produce ulcerated mucosal lesions in the oral cavity

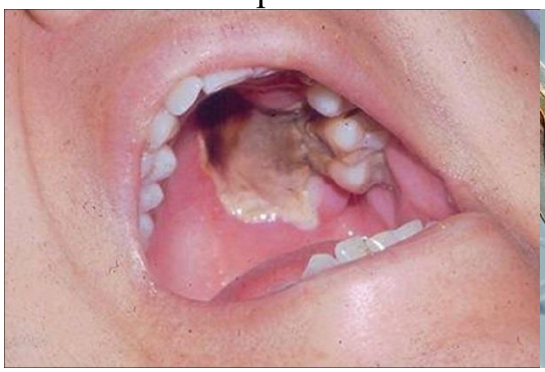
Histoplasmosis

- Caused by *Histoplasma capsulatum*; a dimorphic fungi
- Two forms; pulmonary and mucocutaneous
- Mucocutaneous form cause ulcerative/erosive lesions on tongue, plate and buccal mucosa
- Oral lesions: single ulcers, long term and may or may not be painful
- Always misinterpreted as malignant ulcers
- Biopsy is mandatory



Mucormycosis

- Caused by a saprophytic fungi found in soil, bread mold, decaying vegetation etc.
- Involvement of the oral cavity is secondary to paranasal sinuses or nasal cavity
- Usually present as a palatal necrosis or ulcerations
- Extends to adjacent structures causing extensive tissue necrosis and invasion of brain
- Organ transplant and poorly controlled diabetic patients are susceptible



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