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# PHARMACOLOGICAL MANAGEMENT OF ORAL LESION

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**Abstract:** Oral ulcerations caused by aphtous lesions, leukoplakia, scarlet fever, syphilis, NOMA, mucormycosis herpetic lesions, candidiasis, discoid lupus erythematous, ulcerative lichen planus, mucous membrane pemphigoid, spongy nevus, oral submoucs fibrosis and pemphigus vulgaris are treated in a step-up fashion that may include topical, intralesional, and systemic pharmaceutical treatment. This page discusses the most often used therapy agents, methods, and dosages. Although the emphasis is on local pharmacologic therapy, systemic illnesses that frequently occur with such oral lesions are briefly discussed, as is the appropriate care.

**Keywords:** Pharmacology, Leukoplakia, Scarlet Fiever, Syphilis, Noma, Mucormycosis, Herpetic lesion, Candidiasis, Discoid lupus, Eruthematous, Ulcerative Lichen Planus, Mucous membrane Pemphigoid, Spongy Nevus, Oral Submoucs Fibrosis, Pemphigus Vulgaris, Treatment.

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The authors declare no conflicts of interest.

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# *GESTION PHARMACOLOGIQUE DES LÉSIONS BUCCALES*

**Résumé:** Les ulcérations buccales causées par des lésions aphteuses, la leucoplasie, la scarlatine, la syphilis, le NOMA, les lésions herpétiques de mucormycose, la candidose, le lupus érythémateux discoïde, le lichen plan ulcéreux, la pemphigoïde des muqueuses, le naevus spongieux, la fibrose sous-moucs buccale et le pemphigus vulgaire sont traitées de manière à inclure un traitement pharmaceutique topique, intralésionnel et systémique. Cette page traite des agents thérapeutiques, des méthodes et des dosages les plus souvent utilisés. Bien que l'accent soit mis sur le traitement pharmacologique local, les maladies systémiques qui surviennent fréquemment avec de telles lésions buccales sont brièvement discutées, ainsi que leurs soins appropriés.

**Mots clés** : Pharmacologie, Leucoplasie, Fièvre écarlate, Syphilis, Noma, Mucormycose, Lésion herpétique, Candidose, Lupus discoïde, Éruthémateux, Lichen plan ulcéreux, Pemphigoïde des muqueuses, Naevus spongieux, Fibrose sous-moucs buccale, Pemphigus vulgaire, Traitement.

## Introduction

Oral cavity lesions can be caused by a variety of etiology, including inflammatory, infectious,

traumatic, immunologic, or neoplastic conditions. The most common problem faced by the budding dentist is to identify the lesions and to advice the correct treatment plan or to prescribe the correct pharmacological therapy for these white or red lesions. As the surgical therapy may cast the permanent scar not only on the physical body of the patient but also in the minds of the patients. Hence, the need of less invasive option such as the pharmacological alternative to invasive therapies. With the upcoming boom and advancement in bioengineering and biomedicine, the efficiency as well as the potency of the drugs has been increased in recent times. This article discusses some of the most frequent oral lesions that clinicians may face, as well as the suggested pharmacologic to such oral lesions [1].

Soft tissue lesions in the oral cavity should be detectable by the general dentist. Some of these lesions may be symptomatic, while others may be coincidental findings during the routine check up or secondary findings observed by the dentist. Their origin could be either local or systemic [2].

When oral manifestations are present, they primarily affect the palatal and alveolar mucosa, are usually asymptomatic, and are discovered in routine dental examination [3].

This article provides an overview of the current pharmacological treatment of the oral lesions which we have tried to summarise into-Developmental (Spongy Nevus, Dariers's Disease, Dyskeratosis congenita), Preneoplastic conditions (Lichen Planus, Oral Submucous Fibrosis, Discoid Lupus Erythematosus) and Preneoplastic lesions (Leukoplakia, Carcinoma in Situ, etc), bacterial oral lesions (Scarlet Fever, Syphilis, Cancrum Oris), Viral oral lesions (Infectious Mononucleosis, Mumps, Vericella Zoster) and Fungal lesions (Candidiasis, Cocxydiomycosis, Mucormycosis).

## 1. Develeopmental Lesions

### A. Spongy nevus

Hyde originally characterised white sponge nevus (WSN), a rare hereditary leucokeratosis, in 1909. WSN lesions are readily identifiable and clinically significant; they often manifest as bilateral white spongy plaques over the buccal mucosa and the patients do not experience any discomfort. Other typical locations for the lesion include the tongue, mouth's floor, and alveolar mucosa. White, swollen, folded, along with spongy lesions found in the oral mucosa are the disease's hallmark [4]. Since the clinical presentation is so recognisable, a biopsy is typically not required. The microscopic characteristics of WSN are distinctive but not always pathognomonic. Common hallmarks of the spinous layer cells include prominent hyperparakeratosis and significant acanthosis with clearing of the cytoplasm; however, comparable microscopic findings may be linked to leukoedema as well as hereditary benign intraepithelial dyskeratosis [5].

Although WSN sufferers don't have any noticeable physical pain, they frequently express displeasure with the way the lesions look or a change in the texture of their mucosa. Nystatin, antihistamines, and vitamins are among the common therapeutic therapies used for WSN patients. Tetracycline, penicillin, and azithromycin have shown some clinical effects. Long-term low-dose systemic antibiotic treatment kept the WSN in remission. Systemic antibiotics or topical retinoic acid applications have only recently yielded a small number of advantages, but both are ineffective [4].

### B. Dariers disease

An autosomal dominant cutaneous disorder known as Darier disease (DD) is brought on by a genetic mutation that affects the ATP2A2 gene of chromosome 12. Darier and White initially described DD in 1889. Multiple hard, greasy, and hyperkeratotic papules which merge into plaques, particularly affecting seborrheic regions, are its clinical hallmark [6]. Oral lesions could be present in Darier's disease, an unusual autosomal dominant genodermatosis. White papules that are part of oral lesions that range in intensity. The palate, gingiva, buccal mucosa, and tongue are the most often impacted areas. The extent of the mouth lesions generally matched the degree of severity of the skin illness. There has been sporadic parotid edoema and oral mucosal involvement. Two patients' parotid sialograms showed strictures in the major ducts, pointing to an obstructive aetiology [7] (Table 1).

### C. Dyskeratosis congenita

A genetic bone marrow failure disease called dyskeratosis congenita (DC) is characterised by aberrant pigmentation of the skin, dystrophy of nails, oral premalignant leukoplakia and a propensity to cancer, with a higher risk of squamous cell carcinoma and hematolymphoid neoplasms. Depending on the damaged gene, DC is diverse at the genetic level. X-linked, autosomal dominant, or autosomal recessive inheritance patterns are all possible for DC [8].

## 2. Precancancerous lesions

### A. Lichen planus

An inflammatory mucocutaneous disorder called lichen planus is distinguished by its distinctive violet-colored, polygonal flat-topped papules as well as plaques. Serious pruritus is common. Skin lesions can be disfiguring, and when they affect the vaginal or oral mucosa, they can be crippling. Squamous cell cancer may form within lesions as a result of oral lichen planus. Additionally, the scalp and nails may be affected. On the basis of the usual clinical appearance as well as the biopsy specimen of the lesion,

Table 1: Pharmacological treatments of dariers disease [7]

| | |
|---|---|
| Topical retinoids | Isotretinoin was used topically. It was utilised in a dosage of 0.05% administered twice daily for three months. |
| Fluorouracil | a medication with a solid safety record that has been demonstrated to be beneficial in treating Darier illness |
| Diclofenac sodium, | Diclofenac sodium 3% was administered for 3 to 8 months, and all lesions showed a noticeable improvement and were almost completely gone. |
| Steroids | Although topical steroids are frequently used to treat Darier disease, no studies have been discovered to yet to support their use or efficacy. To lessen irritability, they have typically been taken in conjunction with retinoids.The danger of bacterial superinfections in some individuals, as demonstrated in clinical practise, may also support the use of a combination of steroids and antibiotics. |
| Oral retinoids | The negative effects were dose-related and included nosebleeds, skin thinning, dryness of the mucous membranes, pain, and a rise in pruritus. Since a very long time ago, isotretinoin has been utilised as well to treat this illness. |
| Cyclosporine | Treatment with cyclosporine 3 mg/kg/day has been shown to be beneficial. |
| Doxycycline | Doxycycline 100 mg/day, which is frequently used to treat acne, was recently used to treat Darier illness and was successful. |
| Microgynon | Over the course of two years, a female patient was treated with Microgynon, a combination oral contraceptive pill, which helped to reduce itching and improve skin fragility. |

Table 2:The pharmacological treatment of Lichen Planus [10]

| | |
|---|---|
| *Antifungals* | In 37% of the OLP lesions (superimposed candidal infections), Candida albicans is found, which aggravates the condition and causes symptoms. This might be the case because maintaining good oral hygiene becomes challenging in erosive lesions of the gingiva along with oral mucosa, which can result in fungus infections. Clobetasol, Miconazol, Amphoterecin B, Tab Griseofulvin |
| *Corticosteroids* | The primary component of the treatment for oral lichen planus is regarded to be corticosteroids, which can be administered orally, intralesionally, or both. Flucinoloneacetonide Disodium, betamethasone phosphate, Clobetasol propionate, Fluticasone spray, Triamcenolone acetonide, Methyl Prednisolone, Betamethasone |
| *Immunosuppressans and Other Systemic Drugs* | Agents known as immunosuppressants are used to block the immune system's ability to attack and harm the host. Cyclosporine, Tacrolimus, Primacrolimus |

lichen planus is diagnosed. Despite the fact that numerous research have looked into and suggest an immunologic pathophysiology, the exact cause of lichen planus remains uncertain. T-cells in particular, which are lymphocytes, are crucial. Antigen-presenting cells, adhesion molecules, and inflammatory cytokines are other variables [9] (Table 2).

**B. Oral submucous fibrosis**

Chewing betel results in a precancerous disease called oral submucous fibrosis (OSMF).Based on clinical signs and histopathological confirmation, OSMF is a diagnosis. The oral mucosa blanching, teeth and gingiva discoloration, and trismus are the main symptoms of hypovascularity. Arecoline in betel nuts and copper, which cause fibroblast dysfunction and fibrosis, are two of betel quid's main ingredients. Numerous intracellular and extracellular signalling pathways may be active. A fibrous bands that limits the opening of the mouth (trismus) is typical of the further advanced stage of OSF. It worsens issues with speech, mastication, oral hygiene, and possibly swallowing. The growth of fibrous bands causes the lip to thicken and take on a rubbery appearance. The lips change into an oval shape and are hard to retract or evert [11] (Table 3).

**C. Discoid lupus erythematous**

If discoid lesions are present and SLE is ruled out, the patient has chronic DLE (WHO 695.40). DLE is a long-lasting condition that mostly affects the skin and/or mucous membranes. There are, however, questionable cases when patients with DLE exhibit some systemic symptoms but not enough to be diagnosed with SLE. Also possible in SLE are discoid lesions. One of the borderline LE types connected to minimal systemic involvement is the subacute cutaneous LE.Discoid oral lesions, also known as oral DLE or discoid lesions, are chronic

Table 3: The pharmacological treament of OSMF includes [12]

| | |
|---|---|
| Steroids | are presently the most often used medications. There are several types of glucocorticoids that are employed, including short-acting hydrocortisone, intermediate-acting triamcinolone, and long-acting betamethasone and dexamethasone. They work by decreasing inflammation and raising inflammatory cell death. |
| Buflomedial hydrochloride | is a vasoactive substance that improves microcirculation. By alleviating ischemia effects, it has an impact on the tissues in diffuse fibrosis. |
| Nylidrin | is a sympathomimetic drug that causes vasodilation of the skeletal muscles' arterioles and is chemically related to the epinephrine-ephidrine series. |
| Antioxidants | They are used because excessive reactive oxygen species, such as oxygen ions as well, as well as peroxides, are present in areca nuts, which is one of the pathogenic mechanisms. Carcinogenesis results from their damage to vital cellular macromolecules as DNA, proteins, and membrane lipids. |
| Nutritional supplements | These are utilised since certain research show that vitamin and micronutrient deficits encourage the onset and development of OSMF. Additionally, to battle the nutritional deficiency brought on by the gradual loss of the capacity to open the mouth and the ensuing trouble with eating, both of which may expedite the disease's progression. |
| Vitamin supplements | They are utilised as common supplements and are known to hasten ulcer healing and ease symptoms. Long-term, however, vitamin usage alone has not produced any results that have been deemed satisfactory. |
| Minerals like zinc and magnesium | Zinc is a component of numerous enzymes and is crucial for DNA synthesis as well as cell division. In addition, zinc acts as an antagonist of copper and may mitigate the consequences of the overexpression of lysyl oxidase brought on by copper. Magnesium ions have stabilising impacts on excitable membranes and are crucial for numerous enzyme activities. |

keratinizing lesions containing the oral mucosa as well as vermilion border, characterised by a border zone comprising irradiating white striae alongside telangiectasia with a central atrophic red region with minute white spots.If discoid cutaneous lesions are present and other oral disorders can be ruled out, unusual oral discoid lesion are included. Despite the word "discoid," the appearance of the lesions varies and cannot be used as a conclusive criterion [13, 14] (Table 4).

## 3. Neoplastic precancerous lesions

### A- Leukoplakia

Oral squamous cell carcinoma has been linked to the presence of potentially malignant diseases in 15-48% of cases. The most common potentially malignant condition of the oral mucosa is oral leukoplakia (OL) [15] Oral leukoplakia (OL) is a premalignant lesion described as "a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion" [16]. The aim of this paper was to assess the nonsurgical treatment of oral leukoplakia (OL). A medline search from 1983 to 2009 was conducted. The topical or systemic nonsurgical treatments or combination of both was reviewed. The primary outcomes of interest were clinical resolution, malignant transformation, follow-up, and recurrence of OL. Studies showed a rate higher than 50% of clinical resolution with photodynamic therapy, beta-carotene, lycopene, or vitamin A. Few studies reported rates of recurrence from 5 to 67% and of malignant transformation from 8 to 23%. There is a lack of randomized clinical trials that assess the effectiveness of nonsurgical treatment of OL. At this time, randomized controlled trials for nonsurgical treatment of OL demonstrate no evidence of effective treatment in preventing malignant transformation and recurrence. It reinforces that even after clinical resolution, OL should be regularly followed [13]. Oral leukoplakia is a white patch or plaque that develops in the oral cavity and is closely linked to smoking [17].

### Etiology

Risk factors include all forms of tobacco use, including cigars, cigarettes, beedis, and pipes. Other synergistic risk factors include alcohol consumption, chronic irritation, fungal infections such as candidiasis,

Table 4: Pharmacological management of Oral Lesions

| | |
|---|---|
| Topical and intralesional steroids | Start with a powerful topical treatment that contains 3–5 mg/mL of intradermal triamcinolone. |
| Antimalarials | Start using 200 mg per day; provide not more than 6.5 mg/kg per day. |
| Topical tacrolimu | topical ointment with 0.1% |
| Thalidomide | 100 to 200 mg/day for the initial dose and 50 to 100 mg/day on average for maintenance |
| Azathioprine | 50 to 100 mg/day is the typical initial dose, while 25 to 50 mg/day is the typical maintenance dose. |
| Cyclosporin | 4 to 5 mg/kg/day as a starting dose, which can be lowered if conditions become better |
| Mycophenolate mofetil | Regular dosage is 1 g twice daily. |
| Methotrexate | 5 to 15 mg once a week, after which a 2.5 mg test dosage is administered. |
| Acitretin | 0.5 to 1 mg/kg/day |

| HISTOLOGICAL CHANGES |
|---|
| 1. Loss of polarity of basal cells |
| 2. More than one layer of cell with basaloid appearance |
| 3. Drop-shaped rete-ridges |
| 4. Increased nuclear-cytoplasmic ratio |
| 5. Nuclear hyperchromatism |
| 6. Enlarged nucleoli |
| 7. Keratinization of single cells or cell groups in the prickle cell layer |
| 8. Abnormal form of mitosis |
| 9. The presence of mitotic cells in the superficial epithelium |
| 10. Cellular and nuclear pleomorphism |
| 11. Irregular epithelial stratification |
| 12. Loss of intercellular adherence |

Figure 1. Showing the histological changes, which occurs during leukoplakia [15].

oral galvanism due to restorations, bacterial infections, sexually transmitted lesions such as syphilis, combined micronutrient deficiency, viral infections, hormonal disturbances, and ultraviolet exposure [15].

**Clinical apperence**

The two main varieties of OL are homogeneous (which appears as a flat white lesion, is a uniform, thin white region altering or not with normal mucosa) and non-homogeneous (which includes speckled (the speckled variety is a white and red lesion with a primarily white surface), nodular and verrucous1.

**Histological changes** (Figure 1)

**Pharmacological treatment of leukoplakia** (Figure 2)

**B- Oral-Intra Epithelial Carcinoma**

Slaughter and his colleagues pioneered the notion of "field cancerization" for oral malignancies over 60 years ago.Based on their analysis of a large number of squamous cell carcinoma (SCC) cases, they determined that oral SCC had a tendency to expand laterally rather than in-depth, and they proposed that growth occurred "by a process of lateral cancerization" from precancerous lesions. Furthermore, they hypothesized a "multicentric origin" for oral SCC, particularly in "early lesions" (precancerous lesions), by displaying multiple histological evidence of multicentric foci of borderline lesions. Although their idea has recently garnered a lot of attention in the field of cell competition research there have been no active trials for developing

| THERAPY | Systemic Alfa tocoferol | Systemic Beta-carotene | Systemic Isotretinoin | Systemic Vitamin A | Systemic Lycopene | Topical Bleomycin | Topical Tretinoin | Topical Isotretinoin |
|---|---|---|---|---|---|---|---|---|
| DOSES | 400 IU | 30 mg/day<br>90 mg/day<br>360 mg<br>20 mg/day<br>60 mg/day | 300.000 IU | 200.000–<br>300.000<br>IU<br>1–5 mg | 4–8 mg | 0,5%<br>1% | 0,05%<br>gel | 1% |

Figure 2. Showing the pharmacological treatments of leukoplakia [16].

diagnostic standards for these borderline cancers of the oral mucosa in the previous sixty years. This is due to the difficulty in diagnosing oral borderline cancers ranging from epithelial dysplasia to early stages of SCC. One method of dealing with oral borderline cancers would be to subjectively classify them into three stages of epithelial dysplasia and carcinoma in situ (CIS) [18].

Carcinoma in situ is a kind of superficial cancer that spreads laterally through the epithelial layer of the skin and occasionally into the mucosa, including the oral cavity.It is the most severe epithelial stage.Although this lesion encompasses the full thickness of the epithelium, the basement membrane remains intact .In every way, these mucosal lesions are similar to leukoplakia, except that the dysplastic characteristics are more severe and include practically all layers of the epithelium. The most notable aspect of carcinoma in situ is that the dysplastic epithelial cells do not infiltrate the underlying connective tissue stroma [18].

**Clinical presentation**

The lesions may present clinically as white plaques or as ulcerated, eroded, or reddish patches throughout the oral mucosa.

The most common sites of occurrence of these lesions are the floor of the mouth, tongue, or lips, among others.

The lesion may manifest clinically as either leukoplakia or erythroplakia at times, and in some cases, both leukoplakia and erythroplakia are present [19].

**Histopathology**

Histologically, hyperkeratosis may or may not be present on the lesion's surface, and if it is, it is usually hyperparakeratosis.

The epithelium is normally hyperplastic, but it can sometimes be atrophic.

Characteristics such as individual cell keratinization

Keratin pearl development, for example, is extremely rare; in fact, if keratin pearls are discovered, invasive carcinoma should be suspected rather than carcinoma in situ.

One of the most frequent hallmarks of carcinoma in situ is the dysplastic epithelial cells' loss of orientation and polarity.

There is usually a distinct line of separation between normal and dysplastic epithelium that runs from the surface to the connective tissue.

The basement membrane of the epithelium is always intact [19].

**Pharmacological treatment**

Systemic bleomycin and topical 5-fluorouracil4 have been characterised as chemotherapeutic methods. Candidates for systemic chemotherapy must have strong renal function and be able to endure the medication therapy's related side effects. Fever, chills, emesis, anorexia, and weight loss are common adverse effects of systemic chemotherapy, as is local response at the tumour site. When poor healing precludes surgical procedures, topical 5-fluorouracil has been reported to be an effective treatment for vaginal cancer in situ following pelvic irradiation.Historically, surgical excision and/or radiation therapy were used to treat oral cancer. The morbidity associated with radiation therapy for oral cavity cancer is considerable for both edentulous and natural dentition patients. Radiation caries and poor denture retention may be subsequent sequelae to the discomfort associated with postradiation xerostomia [15].

When tumours are multicentric or widely disseminated, surgical removal of oral cancer in situ may result in considerable functional impairments. Cryosurgery has also been shown to be effective for carefully chosen oral lesions. These include lesions of the front area of the floor of the mouth and the buccal mucosa that are superficially infiltrative or exophytic, lesions close to bone, multicentric esions, and lesions that recur after surgery and/or radiation therapy [20].

## 4. Bacterial oral lesions

**A. Scarlet fever**

Scarlet fever is a rash in school-age and adolescent children that is most usually associated with bacterial pharyngitis. It is a blanching, papular rash known colloquially as a "sandpaper" rash. Streptococcus pyogenes is the causative bacteria, and it produces an endotoxin that is primarily responsible for the infection's skin manifestation. This is categorised as group A and is known as Group A Strep (GAS). The rash is not hazardous on its own, but it is a sign of GAS infection, which has both suppurative and non-suppurative implications.Scarlet fever is frequently linked with acute pharyngitis. As a result, there is fever, sore throat, swallowing pain, and cervical adenopathy. If there is no pharyngitis, the source of infection could be a GAS-infected lesion or burn. Scarlet fever is caused by both vectors of infection, which are indistinguishable from one another. The rash is a blanched, papular rash. It differs from an allergic reaction macular rash in its stealthy onset and lack of confluence of the lesions.The fundamental reason it feels like sandpaper is a lack of convergence. It is also important to note that there are no vesicles or pustules present. Vesicles are more associated with chickenpox's "dew on a rose petal" appearance in its early stages. Pustules are more likely to be caused by a local infection, such as impetigo or erysipelas. The rash appears 2 to 3 days after infection, but it can appear up to 7 days later. The trunk, underarms, and groin are the first to be afflicted, and it eventually spreads to the extremities. Palms and soles are usually spared [21].

**Oral manifestations**

The circumoral area is likewise spared, giving it a pallor-like appearance. The "strawberry tongue" begins with a white coating of hyperplastic papillae on the tongue.

The skin rash is most evident on the face and is sometimes referred to as "sunburn with goose pimples."

The oral cavity has generalised edoema, uvula elongation, and diffuse petechiae, particularly across the soft palate; the palate seems congested and inflammatory, and the hard palate has punctiform redness.

There is halitosis and generalised congestion of the oral mucosa.

By the fourth or fifth day of the sickness, the white coating over the dorsum of the tongue has been gone due to desquamation; the tongue has turned meaty red with many hyperplastic fungiform papillae, and the condition is known as "raspberry tongue" [19].

**Oral complications of scarlet fever**

Scarlet fever causes a number of oral problems, including cancrum oris, ulceration with perforation of the palate, osteomyelitis, peritonsillar abscess, mastoiditis, and temporomandibular joint abnormalities, among others [19].

**Pharmacological treatment** (Figure 3)

**B. Syphilis**

Syphilis is an infectious disease caused by the filamentous, anaerobic bacterial spirochete Treponema pallidum. Although instances can be passed from mother to child or through hematogenous dissemination, the illness is primarily transmitted through direct contact with a syphilitic lesion. This contact occurs most frequently during vaginal, anal, or oral intercourse [23]. The disease is generally classified into two types: Acquired syphilis and Congenital syphilis.

**Acquired syphilis**: It is most commonly obtained through venereal means, such as sexual contact with an infected partner, but in many situations, the disease is acquired inadvertently by professionals such as dental surgeons, nurses, or other personnel while negligently handling infected patients.

Acquired syphilis presents itself in three stages:

a. Primary syphilis
b. Secondary syphilis
c. Tertiary (late) syphilis.

**Oral manifestations**

**a. Primary syphilis**

The oral lesion of primary syphilis is known as "chancre," and it usually appears three weeks following contact with the pathogen.

The majority of oral lesions occur on the lip; additional sites include the tongue, palate, gingiva, uvula, and tonsils, among others.

Primary syphilis oral lesions begin as a painless lump around 1 centimetre in diameter, which eventually breaks down with the development of an ulcer.

The majority of male patients acquire lesions on the upper lip, whereas the majority of female patients get chancres on the lower lip.

Tongue lesions are most typically detected on the lateral surface of the anterior two-thirds area or on the dorsal surface, and they are frequently associated with pain.

The folate papilla is enlarged, and the uvula is red and inflamed. Furthermore, the tonsils have edoema, redness, and surface erosions or ulcerations.

| DRUG | DOSE/ FREQUENCY | DURATION |
|---|---|---|
| PENICILLIN | 250 MG (400,000 UNITS)BID-TID ORALLY (CHILDREN WEIGHING <27 KG) | 10 DAYS |
| PENICILLIN | 500 MG (800,000 UNITS) BID-TID ORALLY (ALL PATIENTS WEIGHING >27 KG) | 10 DAYS |
| PENICILLIN G BENZATHINE | 600,000 UNITS IM (CHILDREN WEIGHING <27KG) | SINGLE DOSE |
| PENICILLIN G BENZATHINE | 1.2 MILLION UNITS IM ( ALL PATIENTS WEIGHING >27 KG) | SINGLE DOSE |
| ERYTHROMYCIN ESTOLATE | 20-40 MG KG/DAY ORALLY IN 2-4 DIVIDED DOSES | 10 DAYS |
| ERYTHROMYCIN ETHYLSUCCINATE | 40 MG/KG/DAY ORALLY IN 2-4 DIVIDED DOSES | 10 DAYS |
| CLARITHROMYCIN | 7.5 MG/KG EVERY 12 HOURS(CHILDREN) 250 MG BID (ADULTS) | 10 DAYS |
| AZITHROMYCIN | 12 MG/KG/DAY ORALLY 5 DAYS (CHILDREN) 500 MG ORALLY ON DAY 1, FOLLOWED BY 250 MG ORALLY ON DAYS 2-5 ( ADULTS) | 5 DAYS |
| CLINDAMYCIN | 8-16 MG/KG/DAY ORALLY IN 3-4 DIVIDED DOSES (CHILDREN) 600 MG/DAY IN 2-4 DIVIDED DOSES (ADULTS) | 10 DAYS |

Figure 3. Showing the pharmacological treatment of scarlet fever [22].

Chancres are highly contagious and can be painful owing to secondary infection.

The lymph nodes are swollen on both sides. These are painless and rubbery in texture.

Scarring normally heals oral chancres after 3-6 weeks [19].

**b. Secondarysyphilis**

Secondary lesions are usually mucocutaneous in form and appear 6 to 8 weeks after the primary infection.

Mucous patches, which are commonly seen over the tongue, lips, buccal mucosa, gingiva, tonsils, larynx, pharynx, and palate, are characterised by multiple, flat, irregular or circular, slightly raised, painless, white round erosions.

Mucous patches are covered by a thin yellowishgray (glistening) slough and are surrounded by a painful erythematous halo.

Multiple "mucous patches" in the oral cavity can sometimes combine to form irregularly linear "snail track" ulcers. This stage is also contagious since both the ulcer drainage and the patient's saliva contain many Treponema pallidum organisms.

Moist papules with a "split pea" appearance are common at the angle of the mouth.

The mucous patches can sometimes develop superficial epithelial necrosis, resulting in sloughing and exposing of the underlying connective tissue. The tongue is frequently fissured in secondary syphilis [19].

**c. Tertiary syphilis**

Tertiary syphilis intraoral lesions are known as "gumma" and can be found on the hard and soft palate, tonsils, lips, and tongue, among other places.

They often ulcerate by core necrosis and generate painless, deep, spherical ulcers with punched-out edges and a wash-leathery floor.

In tertiary syphilis, increasing necrosis and sloughing frequently leads to palate perforation and the establishment of oro-nasal communication.This is a very common finding in tertiary syphilis, and it frequently causes breathing and swallowing issues.

In rare circumstances, destruction of the soft palate and uvula may result in nasopharyngeal airway blockage.

On the tongue, there is frequently superficial glossitis known as "syphilitic glossitis"; because these lesions appear as diffuse, big leukoplakic patches, the condition is also known as "syphilitic leukoplakia."

The sickness is not communicable at this stage. In tertiary syphilis, the loss of filliform and fungiform papilla results in a bare tongue. Furthermore, as the so-called 'gumma' lesions heal, they produce significant deformation of the tongue and soft palate [19].

**Phamacological treatment**

**Primary and secondary syphilis**

• Among adults: -Benzathine penicillin G 2.4 million units IM in a single dose

• Among childrens and Infants: Benzathine penicillin G 50,000 units/kg body weight IM, up to the adult dose of 2.4 million units in a single dose [24].

**Tertiary syphilis**

Tertiary Syphilis with normal CSF Examination: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals [24].

**Latent syphilis**

Among Adults: -Early Latent Syphilis: Benzathine penicillin G 2.4 million units IM in a single dose.

Late Latent Syphilis: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals [24].

**C. Noma (cancrum oris)**

Noma (cancrum oris) is a destructive, disfiguring, necrotizing disease that primarily affects young malnourished children in central Africa (Niger, Nigeria), where HIV infection has not been reported to play a role, in contrast to southern Africa (Zimbabwe, South Africa), where it appears to be an important co-factor, despite the fact that the age distribution of affected subjects is wider. Noma has a fulminating course and is usually fatal if left untreated. The pathogenesis of noma is influenced by complex dynamic interactions between dento-gingival polybacterial plaque and host immunological deficiency, malnutrition, general state of debilitation, and environmental and socioeconomic variables [25].

In immunocompromised patients, the condition is most likely caused by infection with fusospirochetal organisms. Fusobacterium necrophorum, Fusobacterium nucleatum, and Prevotella intermedia are among the microbes.The disease is more common in children aged 1 to 10 years; it was very common among starving prisoners (particularly children) in Nazi concentration camps during World War 2. The disease begins with the formation of a painful, red, indurated papule over the gingiva; at this stage, it looks like a typical ANUG with extreme edema [19] (Figure 4, 5).

### Pathological events in noma

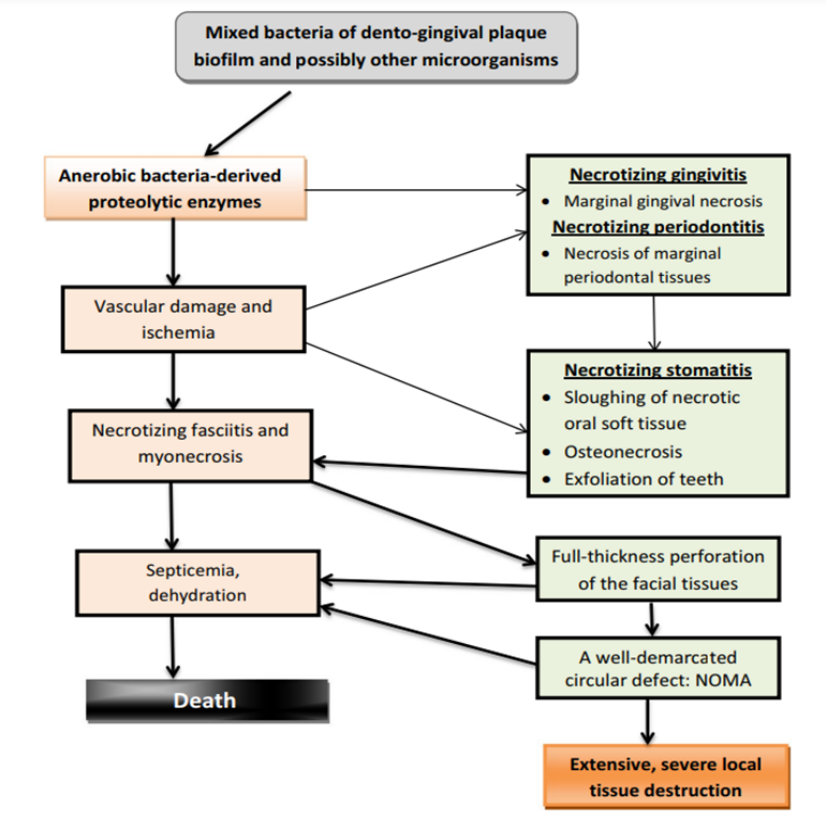


Figure 4. Showing the pathological events in NOMA

| ANTIBIOTICS | WOUND CARE | FLUID, ELECTROLYTES, AND NUTRITION | SURGICAL REPAIR |
|---|---|---|---|
| Penicillin in conjunction with metronidazole or streptomycin is a reasonable regimen. Others choose metronidazole monotherapy since Noma is primarily linked with anaerobic microbes. Some people prefer the combination of amoxicillin and metronidazole. Antibiotics can be administered to youngsters who can ingest oral medication in tablet or syrup form. Penicillin dosage. VK is dosed at 25 to 50 mg/kg/day in three separate doses; metronidazole is dosed at 30 mg/kg/day in three or four divided doses. Parenteral therapy with penicillin G Procaine may be delivered to children who cannot tolerate oral medication. The dose is 25,000 to 50,000 units/kg/day, divided one to two times each day, with a maximum of 4.8 million units/24 hours. | To limit the risk of subsequent infection, wound care must be meticulously attended to. The wound should be treated regularly with antiseptic-soaked gauze. If feasible, rinse the mouth daily with a solution of chlorhexidine Di gluconate (0.12 to 0.20%). This can be done for up to a week. | Acute Noma requires rehydration with electrolyte correction, followed by nutritional rehabilitation with a high protein diet rich in key micronutrients. | The purpose of surgery is to improve both cosmetic appearance and oral functionality such as eating, drinking, swallowing, and speaking. If trismus is present, the first surgical operation is to rectify it. This necessitates the severe removal of fibrous bands that impede jaw opening. Following that, numerous flap techniques may be used, ranging from simple flaps and autoplasty to complicated procedures including microsurgery. |

Figure 5. Pharmacological treatment

## 5. Viral infections

### A. Infectious mononucleosis

The acute sickness in humans known as either infectious mononucleosis (IM) or glandular fever has only one known cause: EBV or Epstein bar virus or HHV type 4 [26]. Sprunt and Evans (Sprunt 1920) first used the term "infectious mononucleosis" to refer to a state that resembled an acute infectious sickness and was accompanied by abnormally large peripheral blood lymphocytes [27]. EBV is a double-stranded DNA oncogene that is a member of the Herpesviridae virus family and is categorised under the order Herpesvirales [26]. The clinical condition known as infectious mononucleosis, which typically affects teens and young adults and lasts for several weeks, is characterized by a painful throat, enlargement of the cervical lymph nodes, exhaustion, and fever [27]. BV is mostly transmitted from an infectious person who is infected to a person or people by the distribution of saliva that includes the live virus. The typical method of transmission is oral contact [26]. Exudative pharyngitis with enlargement of the tonsils and uvula, periorbital and eyelid edoema, and symmetrical cervical and postauricular lymphadenopathy are among the clinical indicators that increase the likelihood of a diagnosis [27] The incubation period or the latency period of the disease is usually 6 weeks but it can extend to over 32-49 days according to studies.

Diagnosis and lab tests -A primary EBV infection cannot always be diagnosed with a single antibody test. At the beginning of clinical disease, 75% of patients will develop VCA IgM antibodies, and 95% will eventually produce them. The first month of illness is when VCA IgG antibodies are initially discovered, depending on the assay platform and antigen employed in the experiment [27] The median first day of discovery for antibodies against EBNA-1. As a result, primary EBV infection cannot be ruled out by the presence of EBNA-1 antibodies during an acute illness [27]. Because there aren't many recent references on IM It is not unexpected that there is currently no global diagnostic methodology for this disease's laboratory inquiry and testing [26].

**Treatment modalities**

Infectious mononucleosis presently has no recognised particular treatment. Ass the proverb goes prevention is better thant cure, hence , researchers in the field have long prioritised the creation of an EBV vaccine. A vaccination to prevent infectious mononucleosis and EBV-related malignancies should undergo additional clinical trials, according to the National Cancer Institute [27]. A group of drugs from the antiviral family most commonly effective to treatment of viral infections are used such as acyclovir and valcyclovir , but these show no compelling evidence of a clinical benefit. There are no controlled studies demonstrating the therapeutic efficacy of gancclovir and valganciclovir in the treatment of EBV infections but is effectively used to treat immunocompromised hosts with EBV infection [27].

### B. Oral herpes infection

The main signs of oral herpes are the development of vesicles and ulcers, which go away on their own in 5 to 10 days. Herpes simplex virus type 1 is frequently the main culprit, although epidemiology has changed, and herpes simplex virus-2, which was linked to herpes genitalis, but it's also present in cases of herpes labialis [28]. Because productive infection (i.e., viral replication) and lytic activity are modest, primary HSV-1 infections are typically moderate or asymptomatic. Labialis [29]. Meningoencephalitis, dermatitis above the waist, and the majority of oral and pharyngeal infections are all caused by HSV-1; the majority of genital and anal infections are caused by HSV2.1,2 Both kinds can result in primary or recurrent infections in the oral, perioral, or vaginal regions, depending on sexual practises.When contaminated saliva or bronchial secretions are in touch with the finger, 1,2HSV infections (herpetic whitlow) result [30]. The primary herpes simplex virus-1 infection might be asymptomatic or result in gingivostomatitis; after that, the virus ascends the trigeminal nerve's sensory axons and establishes latency in the sensory ganglia. Stress, fever, ultraviolet radiation, trauma, or menstruation are just a few of the factors that might make it reactivate [30]. The susceptible host becomes infected by the herpes simplex virus type 1 through epithelial breaches brought on by mechanical, physical, or chemical trauma. However, preexisting infections caused by pathogens or commensals overgrowth that cause the oral mucosa to become inflamed and cause disruption of epithelial integrity and loss of barrier function could potentially encourage infection [29].

The typical primary oral HSV-1 infection is characterised by a productive infection, lytic activity that is localised to the site of entry, focused against the epithelial cells.Exudate with uncommonly visible pinhead vesicles forms on the oral mucosa. Vesicles degrade quickly, agglomerate, and form tiny, uncomfortable red sores. The tongue, vermillion, gingival, buccal, hard, and soft palatal mucosae, as well as the pharyngeal (with pharyngotonsillitis) and nasal (with rhinitis) mucosae, less frequently develop primary herpetic gingivostomatitis lesions [29]. The recurrent herpes labialis occurs typically at the junction of the vermillion and the cutaneous lip. Intraorally, it usually occurs on the keratinized mucosa, which distinguishes it from the recurrent aphthous lesions [28]. HSV-1 has known for its reoccurrence and this reoccurrence has major complications associated with it including Herpetic pneumonia, Herpetic esophagitis, Erythema multiform, Periodontal disease and apical periodontitis. Antiviral therapy aims

to stop the spread of viruses. When the majority of lesions reach the vesicular stage, which happens during the first 24 hours of lesion development, peak viral titers happen. As a result, the best time to begin treatment is at the earliest signs, ideally in the prodromal stage [28].

Lab tests- Viral isolation in tissue culture is the traditional method for diagnosing and identifying viruses. Observing the cytopathic effects (CPE) of the virus-inoculated cells is the aim of virus isolation. CPE refers to the deteriorating alterations that virus-infected cells go through. The type of host cell, the viral type, and the virus concentration all affect how quickly CPE develops [30].

Treatment- Topical anaesthetics like viscous lidocaine or benzocaine can be applied to treat pain. Zilactin is a topical drug that binds to the mucosa and contains hydroxypronyl cellulose. It can be used to shield lesions from irritants [28] (Table 5).

**C- Mumps**

The parotid gland swelling that characterises mumps, a common viral disease in children. The mumps vaccine, which can prevent the disease, is now virtually commonly used in affluent nations [31]. The parotid gland enlargement is the telltale sign of infection. Orchitis and oophoritis, which can develop in adult men and women, respectively, as well as encephalitis, aseptic meningitis, and pancreatitis are further complications of the mumps. The causative agent for mumps is the paramyxovirus , which is a RNV virus . Only people can contract the moderately to extremely contagious disease known as the mumps. The virus can be transferred through direct touch, droplet dispersion, or contaminated meats. 15 to 24 days, on average, are needed for incubation (median: 19 days) [10]. Prior to the onset of clinical symptoms and for several days later, infected persons are most contagious. However, the mumps virus can be isolated from saliva as early as 7 days before to the development of clinical symptoms and up until 9 days afterwards.

Lab Tests: Because mumps-virus replication is sporadic, there is a little window of opportunity for effective virus isolation or detection. Within the first week of symptoms, virus can be easily isolated from saliva, CSF, urine, or seminal fluid. On day 3 following incubation with a mumps-virus clinical isolate, HeLa cell culture immunohistochemically stained with a monoclonal antibody to the virus (MAB846, Chemicon International) revealing fluorescent signal indicating virus antigen expression.Successful viral isolation rates drastically decline after the first week [3].

Treatment- Mumps cannot be treated with a specific antiviral medication. Treatment is primarily symptomatic and supportive because the condition is typically benign and self-resolving, such as using analgesics to treat parotitis or orchitis-related discomfort or doing a lumbar puncture to treat headaches caused by meningitis. Mumps vaccines (panel) are available as monovalent vaccines or in combination with other vaccines (which is almost universal), such as the measles-mumps-rubella (MMR) combination.

Type of vaccine • Live attenuated mumps virus • Primarily administered in the measles–mumps–rubella combination. Studies have revealed that, with some variation, initial seroconversion rates for mumps virus-neutralizing antibodies following immunisation are generally satisfactory high for all strains [31].

Table 5: Systemic antiviral medications for the treatment of primary HSV infection [30].

| | ACYCLOVIR | VALACYCLOVIR | FAMCICLOVIR |
|---|---|---|---|
| DOSE | 400 | 1000 | 250 |
| FREQUENCY | 3 | 2 | 3 |
| DURATION | 7-10 | 7-10 | 7-10 |

## 6. Fungal infections

**A. Oral candidiasis**

A fairly prevalent disease in the head and neck area is candidiasis. This review will focus on the symptoms and treatments of intraoral, pharyngeal, and perioral conditions [32]. Roman candidates (candidatus) for public office wore the customary white robes that bear the genus name Candida. The terms candidiasis and candidosis are synonyms for the disease process commonly associated with Candida albicans [32]. At least seven more species of the Candida genus have been linked to the oral illness thrush, despite Candida albicans being by far the most prevalent species.

The majority of oral mycoses, also known as fungal infections, are brought on by opportunistic diseases. When host resistance is compromised, pathogenic conditions might start to develop and spread locally in the oral cavity [33]. Different type of candidias infections are- Actue psudomembranous Candiadiasis, Actue Atrophuc Candidiasis, Chronic Atrophic Candidiasis, Chronic Hyperplastic Candidiasis, Angular Cheilitis, Median Rhomboid Glossitis [32].

Lab Test- The clinical and cytological/histopathological evaluation of the oral tissues was the main focus of the diagnostic strategy for treating oral mycotic disorders. Most often, biopsy-based diagnosis assisted in confirming diseases with fungi that had been clinically detected [33]. A specific staining technique such periodic acid-Schiff is useful in making a conclusive diagnosis . To distinguish chronic hyperplastic candidiasis from leukoplakia and to assess the level of dysplasia, oral mucosal biopsy is advised [33].

Treatment – The primary plan of treatment of any kind of fungal infection including Candidiasis is 'anti-fungal' drug like –Nystatins,fluconazole, flucystine etc (Table 6).

Table 6. Showing treatment options for Oral Candidasis Infections.

| DRUG | DOSE | DURATION |
|---|---|---|
| ORAL SUSPENTION OF NYSTATIN | 100,000IU/ml 400,000-600,000IU/ml | Till 48hr |
| NYSTATIN | 10mg | 10 days |
| FLUCONAZOLE | 100-200 mg | 7-10 days |
| FLUCYSTINE | 10mg/ml | 7 days |

**B. Coxydiomycosis-**

Coccidioidomycosis is a fungal infection of the Western hemisphere that is endemic to the soil in areas with limited rainfall [34]. An endemic diathermal dimorphic fungal illness of humans and animals, coccidioidomycosis (CM) is only found in the Western Hemisphere. The illness was initially identified in Argentina, then later in California. Sixty per cent of infections are asymptomatic and 40% have a flu- like or pneumonic illness. Various manifestation of Coxydiomycosis is usually systemic affecting mainly respiratory system like plumonary , pulmonary complications such as- pleural effusion,-nodular, others include – cavitatry fibrocavitary, synovitis, osteomyletis, soft tissur infections, Cutaneous infectionsd, meningitis etc [34].

Lab Test- A mix of epidemiological, clinical, general laboratory, particular microbiological, serological, histopathological, and radiographic modalities are used to make a diagnosis of CM. Immunodiffusion (ID) assays have a low incidence of substantial false positives and can be quite sensitive. The University of California, Davis and Kern County Public Health laboratories, which employ almost identical practises, offer the most sensitive ID testing currently available. In essence, a positive ID IgM or ID IgG test is diagnostic [34].

Treatment- Primarily the , the drugs of choice for this disease belongs to two major group of drugs such aa- Polyenes &Azoles. The most commonly drugs used in Polyenes is the AmB deoxycholate where as Azoles is more pronound these days and include drugs such as-flucnazole, itraconazole, voriconazle. These are used in dosage of 400mg,100mg,200mg respectively [34]

**C. Mucormycosis-**

Blackfungus, also known as mucormycosis, is a non-septate filamentous fungal infection that can result in potentially fatal diseases. The majority of the time,immunocompromised and diabetic people are affected by this common illness, and while the symptoms of this dangerous infectious condition vary depending on the site of origin, the nose, sinuses, eye, and brain are typically most affected. Few of manifestations are the loosening of teeth, destruction of periodontal tissue and appearance of black necrotic eschar or dead bone in the palate, buccal vestibule or the maxillary alveolus along with formation of oro-nasal/oro-antral communication [35].

The mucormycetes fungus group of moulds, which spread in our environment's air but are more prevalent in soil linked with decomposing wood, rotting leaves, compost piles, and animal dung, are the cause of mucormycosis . Inhalation is the main method of infection transmission, which then affects the lungs and paranasal sinuses [35]. A uncommon but fatal fungal disease called mucormycosis frequently affects persons who have weakened immune systems. Mould fungi of the genera Rhizopus, Mucor, Rhizomucor, Cunninghamella, and Absidia of the Mucorales Order, Class Zygomycetes, are the source of the angioinvasive disease known as mucormycosis [35].

Lab Tests- Diagnosis necessitates detecting the mold in the afflicted tissue through biopsy and a confirmatory fungal culture. Additional possible tests include culture, Enzyme-linked immunosorbent assays, immunoblots, immunodiffusion tests and direct pathogen detection in bodily fluids such blood, serum, plasma, lung fluid, and urine. The blood tests to check for neutropenia include complete blood counts. Levels of blood glucose, iron, bicarbonates, andelectrolytes are among theother blood tests [35].

Treatment- Early identification by a doctor with a high index of suspicion, treatment of the underlying condition, complete debridement, and supportive antifungal therapy are all essential components of managing mucormycosis.Systemic anti-microbials and broad range antifungal medications are used in medical care to avoid secondary bacterial infections.Below are descriptions of the medical and surgical procedures [35] (Table 7).

Table 7: The table shows the drugs used to treat mucormycosis [35].

| Drug Name | Class of Drug | Administration | Dosage |
|---|---|---|---|
| AmphotericinB | Polyene | IV | Amphotericin B is 5–15 mg/kg/day |
| Itraconazole | Azole | Capsules, oral solution and IV | 100–200 mg/day |
| posaconazole | Azole | Oral suspension, delayed release tablet and IV | 200–300 mg/day |
| Isavuconazole | Azole | Oral and IV | 200 mg/day |
| Echinocandins | Cell wall inhibitor | IV | 50–70 mg/day |
| Deferasirox | Chelators | IV | 40–60 mg/day |

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