Dr. Rehab Faisal

CLASSIFICATION OF RED AND WHITE TISSUE REACTIONS -:

- **INFECTIOUS DISEASES**

  Oral Candidiasis

  Hairy Leukoplakia

- **PREMALIGNANT LESIONS**

  Oral Leukoplakia and Erythroplakia

  Oral Submucous Fibrosis

- **IMMUNOPATHOLOGIC DISEASES**

  Oral Lichen Planus

  Drug-Induced Lichenoid Reactions

  Lichenoid reactions of Graft-versus-Host Disease

  Lupus Erythematosus

- **ALLERGIC REACTIONS**

  Lichenoid Contact Reactions

  Reactions to Dentifrice and Chlorhexidine

- **TOXIC REACTIONS**

  Reactions to Smokeless Tobacco Smoker's Palate

- **REACTIONS TO TRAUMA**

  Mechanical, chemical and thermal.

- **OTHER RED AND WHITE LESIONS Benign Migratory Glossitis (Geographic Tongue) Leukoedema**

  White Sponge Nevus

  Hairy Tongue

White Lesions

White lesions of the oral mucosa are a multifactorial group of disorders the color of which is produced by the scattering of the light through an altered epithelial surface. The diagnosis and differential diagnosis of oral white lesions should be made on the basis of the medical history, clinical features, and laboratory tests.

O Leukoplakia

O Hairy leukoplakia

O Lichen planus

O Lichenoid reactions

O Linea alba

O Nicotinic stomatitis

O Uremic stomatitis

O Chemical burn

O Candidiasis

O Chronic biting

O Geographic tongue

O Hairy tongue

O Furred tongue

O Materia Alba of the gingiva

O Fordyce's granules

O Leukoedema

O White sponge nevus

O Papilloma

O Verrucous carcinoma

O Squamous-cell carcinoma

O Skin and mucosal grafts

Red Lesions

Red lesions are a large, heterogeneous group of disorders of the oral mucosa. Traumatic lesions, infections, developmental anomalies, allergic reactions, immunologically mediated diseases, premalignant lesions, malignant neoplasms, and systemic diseases are included in this group.

O Traumatic erythema (ecchymosis or as hematoma)

O Thermal burn (due to contact with very hot foods, liquids, or hot metal objects)

O Radiation mucositis

O Geographic tongue

O Median rhomboid glossitis

O Denture stomatitis

O Erythematous candidiasis

O Squamous-cell carcinoma

O Erythroplakia

O Plasma-cell gingivitis

O Granulomatous gingivitis

O Desquamative gingivitis

O Linear gingival erythema (HIV)

O Hemangioma

O Lupus erythematosus

O Hereditary hemorrhagic telangiectasia

O Anemia

O Thrombocytopenic purpura

O Infectious mononucleosis

White & Red lesions of oral mucosa-:

A white appearance of the oral mucosa may be caused by a variety of factors .

- Hyperkeratosis: an increased production of keratin .

- Keratosis: keratinization of epithelium that is not normally keratinized.

-Acanthosis: is a benign thickening of stratum spinosum .

-Intra and extracellular: accumulation of fluid in the epithelium may also result in clinical whitening.

-Necrosis: of the oral epithelium may occur when the oral mucosa is exposed to toxic chemicals, microbes (particularly fungi can produce whitish pseudomembranes consisting of sloughed epithelial cells) and neutrophils, which are loosely attached to the oral mucosa.

• **The term white patch**: is often used clinically to describe the appearance of lesion presenting as white areas on the oral mucosa without evidence of significant enlargement, erythema or ulceration.

E.g. Leukoplakia: is defined as a predominately white lesion that cannot be characterized as any other definable lesion. Two types:

-Homogenous leukoplakia.

-Non homogenous leukoplakia

The White lesions appear white due to the following:

-Hyperkeratosis (the ability of abnormal keratin to evenly reflect the visible light spectrum) because of hydration or water imbibtion in a manner similar to the reaction seen in the stratum corneum of epidermis following prolonged soaking in water.

-Superficial materials: necrosis of epithelium, food remnants, plaque & inflammatory exudates.

-Sub-mucosal changes which are diminished vascularity & covered by normal epith.

• **Erythroplakia (red lesion):** is defined as a red lesion of the oral mucosa that cannot be characterized as any other definable lesion. The lesion comprises an eroded red lesion that is frequently observed with a distinct demarcation against the normal-appearing mucosa.

Red lesions appear so due to-:

-Thin epithelium (atrophy), so underlying vessels become closer to the surface.

-Loss of keratin layer.

-Increased no. or dilated blood vessels (inflamed).

-Change in the intrinsic nature of the epithelium Such as epithelium dysplasia.

Note: atypia refers to cells while the dysplasia refers to tissue.

Cellular a typia: cellular changes with cytologically characterized malignant and premalignant lesion.

Epithelial dysplasia is defined in general terms as a precancerous lesion of stratified squamous epithelium characterized by cellular atypia and loss of normal maturation short of carcinoma in situ.

Carcinoma in situ is defined as a lesion in which the full thickness of squamous epithelium shows the cellular features of carcinoma without stromal invasion.

Criteria Used for Diagnosing Epithelial Dysplasia

- Cellular and nuclear pleomorphism (different size and shape).

- Increased nuclear-cytoplasmic ratio.

- Loss of polarity of basal cells .

- Nuclear hyperchromatism and prominent nucleoli .

- Enlarged nuclei

- Basal cell hyperplasia .

- Drop-shaped rete ridges .

- Irregular epithelial stratification

- Increased and abnormal mitosis.

- Loss of intercellular adherence.

-Abnormal keratinization.

• **Oral candidiasis:**

C. albicans, C. tropicalis, and yeast like fungus are comprised together over 80% of the species isolated from human Candida infections. It is opportunistic infection. The C. albicans is usually a weak pathogen, and candidiasis is said to affect the very young, the very old, and the very sick.

Predisposing factors-:

• **Local predisposing factors:**

-Denture wearing.

-Smoking.

-Topical and inhalation steroid.

-Xerostomia.

-Poor oral hygiene.

*** General predisposing factors:**

-Immunosuppressive diseases.

-Immunosuppressive drugs.

-Chemotherapy.

-Endocrine disorder.

-Debilitated patients (diabetes mellitus, anemia, malnutrition, leukemia and bone marrow transplantation).

Diagnosis:

• On clinical appearance.

• Smear from the infected area, which comprises epithelial cells.

• Culture on Sabouraud agar medium.(More sensitive)

Classification of oral candidiasis:

□**Acute**:

* Acute pseudo-membranous candidiasis (thrush).

* Acute atrophic candidiasis (antibiotic sore-mouth).

Chronic:

Chronic Plaque-Type and Nodular Candidiasis (Candidal leukoplakia)(Chronic hyperplastic candidiasis).

Candida –associated lesions:

* Denture stomatitis

* Angular cheilitis

* Median rhomboid glossitis.

Thrush: It is a superficial infection of the upper layers of the mucosal epithelium and presents with loosely attached membranes comprising fungal organisms and cellular debris, which leaves an inflamed, sometimes bleeding area if the pseudomembrance is removed.

Diagnosis: by clinical appearance & confirmation by smear or culture.

Acute atrophic candidiasis (antibiotic sore-mouth):

An erythematous surface may not just reflect atrophy but can also be explained by increased vascularization. The lesion has a diffuse border. It is affect the dorsum of tongue and palate in patient who are using inhalation steroid, smoking and treatment with broad-spectrum antibiotics.

Diagnosis: by history and smear.

Chronic plaque type (candidal leukoplakia):

The typical clinical presentation is characterized by a white plaque, which may be indistinguishable from an oral leukoplakia. The chronic plaque type and nodular candidasis have been associated with malignant transformation.

Candida –associated lesions:

***Denture stomatitis:-** diffuse inflammation of the maxillary denture- bearing area, sometime with angular chelilitis .

The denture serves as a vehicle that protects the microorganisms from physical influences such as salivary flow.

Clinically appear as patchy red, thin surface with pain and burning.

Angular cheilitis-:

Its infected fissures of the commissures of the mouth often surrounded by erythema. The lesions are frequently coinfected with both Candida and Staphylococcus aureus.

Causes:

-Decreased vertical dimension.

-Nutritional deficiency (iron, vit. B, folic acid)

-Diabetes.

-Co-existent denture stomatitis.

- Dry skin

Clinically: deep cracks, sometimes covered with a white membrane, develop at the corners of the mouth (commisures).

Diagnosis: history, clinical examine, blood investigation, smear and culture.

Median Rhomboid Glossitis:- clinically characterized by an erythematous lesion in the center of the posterior part of the dorsum of the tongue (immediately anterior to the circumvallate papillae). The lesion has an oval configuration, a symptomatic; erythema resulting from atrophy of the filiform papillae and the surface may be lobulated.

The lesion shows a mixed bacterial/fungal microflora. Smokers and denture-wearers have an increased risk of developing median rhomboid glossitis.

Treatment of oral candidiasis-:

Topical and systemic administration of antifungal like:

• Nystatin Cream, rinse or tablets (100.000 IU applies to affected area (3–4 times/ day).

- Pastille (100,000 IU) dissolves 1 pastille slowly after meals (4times/day), usually for 7 days.

- Oral suspension, apply after meals (4times/day) usually for 7 days and (100,000U) continue use for several days after post clinical healing.

• Amphotericin B (tab. 200mg orally four times daily) or :

- Amphotericin B Lozenge (10 mg slowly dissolved in mouth (3–4times/days) after meals (1✖4). or

-Oral suspension 100mg/ml) Placed in the mouth after food and retained near lesions (4times/day for 2weeks).

The lesion will rapidly respond and will not recurrent provided the predisposing factors have also been eliminated

 Cleaning of mucosal surfaces of the denture by brushing and soak it in a solution of ½ teaspoon of sodium hypochloride in 1 cup of water or in topical antimycotic agent for duration of the treatment.

•Miconazole (Oral gel) apply to the affected area (3–4 times daily).

•Miconazole Cream applies twice per day and continues for (10–14 days).

It is the best antifungal to treat angular cheilitis.

•Hairy leukoplakia (HL):

One of etiological factors of Leukoplakia is viruses; it is associated with HIV infection. The lesion is not pathognomonic for HIV since other immune deficiencies, such as immunosuppressive drugs and cancer chemotherapy, are also associated with HL.

HL is strongly associated with Epstein-Barr virus (EBV).

Clinically:

The typical clinical appearance is vertical white folds along the borders of the tongue. The lesions may also be displayed as white and somewhat elevated plaque, which cannot be scraped off. It also presents on (dorsum of tongue and in the buccal mucosa).

The diagnosis of HL is based on clinical characteristics and histopathologic examination.

▼Premalignant lesions :

Oral leukoplakia (LP): It is a clinical term implaying no particular histological changes or behavior, but there is no doubt that a small percentage are premalignant .Leukoplakia is more common in men (over the age of 50 and infrequently encountered below the age of 30), but recent studies show that now almost as many women are affected.

Clinically:

White, well- demarcated plaque. The surface texture can vary from a smooth thin surface to a leathery appearance with surface fissures sometimes referred to as “cracked mud”.

Oral leukoplakia may be found at all sites of the oral mucosa. The floor of the mouth and the lateral borders of the tongue are high-risk sites for malignant transformation.

Etiological factors:

•Tobacco usage, either smoking or chewing.

•Alcohol.

•Viruses: Leukoplakia increase in AIDS (hairy leuk.), EBV, HPV16.

•Candida (candidal leukoplakia).

•Oral epithelium atrophy, there is a tendency for leukoplakia to develop in atrophic epith. Like Iron deficiency anemia.

Oral erythroplakia (LP): Oral erythroplakia is not as common as oral leukoplakia, and the prevalence has been estimated to be in the range of (0.02 to 0.1%).

Clinically:

The lesion comprises an eroded red lesion that is frequently observed with a distinct demarcation against the normal-appearing mucosa. It is a symptomatic; some patients may experience a burning sensation in conjunction with food intake.

Note: Another type of oral leukoplakias are referred to as verrucous or verruciform leukoplakia where the white component is dominated by papillary projections, similar to oral papillomas. It is usually encountered in older women, and the lower gingiva is a predilection site. The malignant potential is very high.

Management of leukoplakia:

-Local irritants if present must be removed.

-If dysplasia present, treated by surgical excision, laser excision and topical application of vit. A may achieve remission.

-Follow up.

Oral submucous Fibrosis:

Is a chronic disease that affects the oral mucosa as well as the pharynx and the upper two-thirds of the esophagus. The etiology of submucous fibrosis is areca nuts.

Clinically: fibrotic bands located beneath an atrophic epithelium, loss of resilience, which interferes with speech, tongue mobility, and a decreased ability to open the mouth.

Oral Medicine

References :

- Burket’s Oral Medicine 12th edition 2015.

- Burket’s Oral Medicine 11th edition 2008.

- CAWSON'S ESSENTIALS OF ORAL PATHOLOGY AND ORAL MEDICINE seven edition 2002.

Immuno-Pathologic diseases: Dr. Rehab Faisal

Oral lichen planus: (OLP)

The etiology of OLP is not known, but in the recent studies evident the immune system has a primary role in the development of this disease .OLP is a chronic inflammatory disease of skin and mucous membrane; it mainly affects patients of middle age or over especially women, it is common and if untreated can persist for many years.

Clinically:

OLP may contain both red and white elements and provide together with the different textures, types of OLP

$ Reticulum

$ Papules

$ Plaque-like

$ Bullous

$ Erythematous (atrophic)

$ Ulcerative.

The distribution of lesion is mostly the buccal mucosa particularly posteriorly; the next most common site is the tongue, lip, palate and gingiva. The lesions are very often symmetrical, but in some cases are more prominent on one side than another.

-Reticular: - is characterized by fine white lines or striae that may form a network but can also show annular (circular) patterns. The striae often display a peripheral erythematous zone, which reflects the subepithelial inflammation, most frequently this form is observed bilaterally in the buccal mucosa and rarely on the mucosal side of the lips .

-Papular type:- It is clinically characterized by small white dots, sometimes the papular elements merge with striae as part of the natural course.

-Plaque-type:- shows a homogeneous well-demarcated white plaque often, but not always, surrounded by striae. Plaque-type lesions may clinically be very similar to homogeneous oral leukoplakia.

Note: Typically, the reticular, papular, and plaque-like forms of OLP are asymptomatic, although the patient may experience a feeling of roughness.

-Erythematous (atrophic) OLP:- is characterized by a homogeneous red area. It is present in the buccal mucosa or in the palate and striae are frequently seen in the periphery. Some patients may display erythematous OLP affecting attached gingiva.

-Ulcerative type:- Clinically, the fibrin-coated ulcers are surrounded by an erythematous zone frequently displaying radiating white striae. As for the erythematous form of OLP, the affected patient complains of a smarting sensation in conjunction with food intake.

Histopathology:

-Hyperkeratosis.

- A subepithelial band–formed infiltrate dominated by T lymphocytes and macrophages

-Degeneration of basal cells known as liquefaction degeneration. These features refer to the immune system being involved in the pathogenesis of OLP.

Diagnosis: - A biopsy for histopathology examination.

Treatment -:

-Topical corticosteroid.

-Kenalog in ora-base ointment (1% Triamicnolone in oral past) 2-4 times daily.

-In severe cases, the treatment become with systemic corticosteroid.

How can differentiate clinically between LP and OLP?

- In LP the demarcation is usually very distinct, while in OLP the white components have a more diffuse transition to the normal oral mucosa.
- The lack of a peripheral erythematous zone in LP.

Drug-Induced Lichenoid Reactions :-(DILRs)

Drugs or their metabolites act as haptens trigger a lichenoid reaction, like Penicillin, gold, and sulfonamides. The other drugs like antihypertensive agents (methyldopa), thiazide (diuretic) & anti-malaria.

Clinically: Lichenoid drug eruptions appear similar to lichen planus and may be severely pruritic .

Management: Discontinuance or change the drug and symptomatic treatment with topical steroids are often sufficient.

Lichenoid reaction of graft-versus-host disease: (GVHD)

The oral lesion of GVHD has the same clinical appearance of OLP but the lesion is usually more generalized, also skin involvement (pruritic maculopapular primarily affecting the palms and soles), however the oral cavity may be the primary or even the only site of chronic GVHD.

Lupus Erythematosus: (SLE, DLE)

There are two types which are chronic discoid L.E. (localized type) and systemic L.E. (disseminated type). Etiology not known but genetic factors appears to be important. Autoimmune disease involves immune complexes. Environmental factors as sun exposure, drugs, chemical substances, and hormones which all have been reported to aggravate the disease. Females are affected much more frequently than males.

Clinically:

The oral lesions observed in SLE and DLE are similar in their characteristics. The typical clinical lesion comprises white striae with a radiating orientation, and these may sharply terminate toward the center of the lesions, which has a more erythematous appearance. The most affected sites are the gingiva, buccal mucosa, tongue, and palate.

DLE is restricted to the skin and usually occur on the face. These lesions may form butterfly-like rashes over the cheeks and nose known as malar rash. While the SLE characterized by skin rash (maculopapular), lymphadenopathy, kidney, liver, lung & nervous system are also frequently involved.

Diagnosis: SLE diagnosis with 4 or more of 11 criteria present at any time.

-Malar rash.

-Discoid lesion.

-Photosensitivity.

-Presence of oral ulcers.

-Non erosive arthritis of two joints or more.

-Serositis.

-Renal disorder.

-Neurological disorder.

-Hematological disorder (leukopenia, lymphopenia, thrompocytopenia and hemolytic anemia)

-Immunologic disorder (anti-DNA, anti-SM, or antiphospholipid antibodies).

-Direct immunohistochemistry is conducted to reveal granular deposition of IgM, IgG, IgA, and C3 (lupus band test) anti-nRNA (antinuclear ribonucleo-protein)

Laboratory Findings :

-Antinuclear antibodies are frequently found in patients with SLE and can be used to indicate a systemic involvement, but patients with other rheumatologic diseases, such as Sjögren's syndrome and rheumatoid arthritis, may be positive .

-Moderate to high titers of anti-DNA and anti-Smith antibodies are almost pathognomonic of SLE.

-Antibodies associated with Sjögren's syndrome, SLE [anti-SS-A(RO) and anti-SS-B(La.)

Management:

-Topical steroids to relief of oral symptoms such as clobetasol propionate gel 0.05%, betamethasone dipropionate 0.05%

-Immunosuppressive drugs used to treat LE.

▼Allergic Reactions:

Lichenoid Contact Reactions (LCRs): are considered as a delayed hypersensitivity reaction to constituents derived from dental materials. Hg is usually considered the primary etiologic factor; other amalgam constituents may initiate LCR.

Clinically :

LCRs display the same reaction patterns as seen in OLP. The most clinical difference between OLP and LCR is the extension of the lesions. LCRs are confined to sites that are in contact with dental materials, such as the buccal mucosa and the border of the tongue, non-symptomatic, but when erythematous or ulcerative the patient may has discomfort from spicy and warm food constituents. Lichenoid reactions in contact with composites have been observed on the mucosal side of both the upper and lower lips.

Management :

Replacement of dental materials in direct contact with LCR

Reactions to Dentifrice and Chlorhexidine:

Delayed hypersensitivity reactions to toothpastes and mouth washes have been reported, but these reactions are rare.

Clinically: fiery red edematous gingiva, which may include both ulcerations and white lesions.

▼Toxic Reactions:

Reactions to smokeless tobacco: Smokeless tobacco can be divided into three different groups: chewing tobacco, moist snuff, and dry snuff. The lesion may be noted as wrinkles at the site of application or may display a white and leathery lesion which sometimes contains ulceration.

Smoker's palate: The most common effects of smoking are presented clinically as dark brown pigmentations of the oral mucosa (smoker's melanosis) and as white leathered lesions of the palate, usually referred to as nicotine stomatitis or smoker's palate. As part of this lesion, red dots can be observed representing orifices of accessory salivary glands, which can be enlarged.

▼Reactions to trauma-:

Mechanical: like

-linea alba due to chronic chewing & sucking of the cheek produce a thin band on buccal mucosa bilaterally at the level of the occlusal plane.

-Frictional hyperkeratosis clinically characterized by a white lesion without any red elements and observed in areas of the oral mucosa subjected to increased friction caused by food intake (edentulous alveolar ridge or any part of oral mucosa exposed to trauma), non-symptomatic.

Chemical :

-Aspirin burn: in the buccal sulcus adjacent to painful tooth lead to white sloughy epithelium.

-Uremic stomatitis: extensive pseudomembranous white lesion in patients with renal failure due to increase blood urea nitrogen level (above 50 mg/dl(

Thermal: Smokers of cigarettes, cigars and pipes.

▼Other Red and White lesions :

Benign migratory glossitis (geographic tongue) :

It is an annular lesion affecting the dorsum and margin of the tongue. The typical clinical presentation comprises a white, yellow, or gray slightly elevated peripheral zone, reflecting atrophy of the filiform papillae. Non symptomatic

Etiology = genetic factors.

Management: no treatment but topical anesthesia when symptom is reported.

Leukodema: etiology unknown.

Clinically: is a white alteration of the oral mucosa. The condition is found bilaterally in the buccal mucosa and sometimes at the borders of the tongue .

Diagnosis: gentle stretching results in a temporary disappearance, by this way can differentiate from other oral keratosis like LP.

Management: There is no demand for treatment as the condition is no symptomatic.

White sponge nevus: is an autosomal dominant disorder.

Clinically: It is a white lesion with an elevated and irregular surface. The most affected sites are the buccal mucosa, but the lesion may also be in other areas of the oral cavity covered by keratinized epithelium.

Management: no treatment.

Hairy tongue:

The etiology of hairy tongue is unknown in most cases.

Number of predisposing factors that have been related to this disorder:

-Neglected oral hygiene ،

-a shift in the microflora ،

-antibiotics and immunosuppressive drugs ،

-Oral candidiasis.

-Excessive alcohol consumption.

-Therapeutic radiation.

-Smoking habits.

Clinically :

Hairy tongue is characterized by an impaired desquamation of the filiform papilla, which leads to the hairy-like clinical appearance.The elongated papillae have to reach lengths in excess of 3 mm.The lesion is commonly found in the posterior one-third of the tongue but may involve the entire dorsum. Hairy tongue may adopt colors from white to black depending on food constituents and the composition of the oral micro-flora.

Diagnosis: The diagnosis is based on the clinical appearance.

Management :

The treatment of hairy tongue is reduction or elimination of predisposing factors and removal of the elongated filiform papillae. The patients should be instructed on how to use devices developed to scrape the tongue.

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References :

- Burket’s Oral Medicine 12th edition 2015.

- Burket’s Oral Medicine 11th edition 2008.

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Thank you

Oral Cancer

Dr. Rehab Faisal

The incidence of oral cancer is age related, which may reflect time for the accumulation of genetic changes and duration of exposure to initiators and promoters (these include chemical and physical irritants, viruses, and hormonal effects), cellular aging, and decreased immunologic surveillance with aging.

The oral cavity includes the lips, the labial and buccal mucosa, and the anterior two-thirds of the tongue, the retromolar pad, the floor of the mouth, the gingiva, and the hard palate. The oropharynx includes the palatine and lingual tonsils, the posterior one-third (base) of the tongue, the soft palate, and the posterior pharyngeal wall. Approximately 95% of oral cancer occurs in people older than 40 years, with an average age at diagnosis of approximately 60 years.

The majority of oral cancers involve the lateral borders and base of the tongue. The lips, gingiva, dorsal tongue, palate, and salivary glands are less common sites. Individuals who have had a previous cancer are at high risk of developing a second primary oral cancer. The WHO has listed several oral conditions as having the potential to transform into oral cancer, including lichen planus, leukoplakia, erythroplakia, actinic cheilitis, and submucous fibrosis.

Etiology and risk Factors:

***Tobacco and alcohol:** Tobacco and alcohol are risk factors for oral and oropharyngeal cancer. Tobacco contains potent carcinogens, including nitrosamine, nicotine, and metabolites of these constituents.

***Nutritional Factors:**

Vitamin A may play a role in oral cancer. This hypo thesis is based on population studies in which deficiency was associated with the risk of SCC. The consumption of fruits and vegetables which is associated with a reduced risk for oral cancer, this may be due to the antioxidant vitamins C and E and flavonoids.

***Human Papilloma Virus:**

HPVs are DNA viruses that infect various epithelial surfaces. There are more than 120 types of HPVs. HPV-16 and -18 are considered high-risk subtypes due to their association with malignant tumors. The virus penetrates the host cell and integrates into the host cell genome where it can replicate. HPV is transmitted by direct contact, primarily by means of vaginal, anal, and oral sex.

***Other Risk Factors:**

There is no evidence that denture use, denture irritation, irregular teeth or restorations, and chronic cheek-biting habits are related to oral cancer risk. It is possible that chronic trauma, in the presence of other risk factors and carcinogens, may promote the transformation of epithelial cells. In lip cancer, sun exposure, fair skin and a tendency to burn, pipe smoking, and alcohol are identified risk factors.

Patient undergoing allogeneic hematologic stem cell transplantation (HSCT) are at an increased risk of developing secondary neoplasms, particularly leukemia and lymphomas, which may manifest in the oral tissues.

Pathogenesis:

(SQUAMOUS CELL CARCINOMA)

Carcinogenesis is a genetic process that leads to a change in molecular function, cell morphology, and ultimately in cellular behavior. This process is not limited to the epithelium but involves a complex epithelial, connective tissue, and immune function interaction. Major genes involved in OSCC include oncogenes and tumor suppressor genes (TSGs).

The extracellular enzymes, cell surface molecules, and immune function play a role in the development and spread of oral cancer; viruses and carcinogens are involved as well.

Oncogenes:

Although proto-oncogenes increase cell growth and effect differentiation and are likely involved in carcinogenesis, few have been consistently reported in head and neck squamous cell carcinoma.

Tumor Suppressor Genes:

TSGs negatively regulate cell growth and differentiation. Functional loss of TSGs is common in carcinogenesis and in OSCC. Both copies of a TSG must be inactivated or lost for loss of function. TSGs involved in head and neck squamous cell carcinoma are P53, Rb (retinoblastoma).

The development of malignant epithelial neoplasms is associated with disruption of cell-to-cell and cell-to- matrix adhesion.

Cell Surface Changes

Changes in cell surface receptors and major histocompatibility class I and class II antigens have been reported and may indicate that immune surveillance and immune function may be affected in patients with oral cancer.

Presenting Signs and Symptoms:

- Discomfort is the most common symptom that leads a patient to seek care and may be present at the time of diagnosis in up to 85% of patients.
- Individuals present with a mass in the mouth or neck.
- Dysphagia, odynophagia, otalgia, limited movement, oral bleeding, neck masses, and weight loss may occur with advanced disease.
- Loss of sensory function especially when it is unilateral.
- Loss of function involving the tongue can affect speech, swallowing, and diet. Possible tissue changes may include a red, white, or mixed red and white lesion; a change in the surface texture producing a smooth, granular, rough, or crusted lesion; or the presence of a mass or ulceration.

- Lymphatic spread of oral carcinoma most commonly involves the submandibular and digastric nodes, and the upper cervical nodes, but can also involve the remaining nodes of the cervical chain.

Lymph nodes associated with cancer become enlarged and firm to hard in texture, and with progression may become fixed and not mobile.

Staging of Oral Cancer—TNM System:

The American Joint Committee on Cancer (AJCC) has developed Tumor-Nodes-Metastasis (TNM) staging system of cancer, which reflects the prognosis, and is therefore determinants for the treatment strategy. T is the size of the primary tumor, N indicates the presence of regional lymph nodes, and M indicates distant metastasis.

The staging system for OSSC combines the T, N, and M to classify lesions as stages 1 through 4. The AJCC classification is principally a clinical description of the disease.

Stage grouping

Stage 0	Tis N0 M0
Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III.	T3 N0 M0
	T1 N1 M0
	T2 N1 M0
	T3 N1 M0

Treatment of OSSC depends on:

- Cell type
- Degree of differentiation.
- The site and size of the primary lesion.
- Lymph node status.
- The presence of local bone involvement.
- The ability to achieve adequate surgical margins
- The presence or absence of metastases.

Surgery and radiation are used in the treatment of oral cancer; chemotherapy and targeted therapy are used together with principle therapeutic modalities of radiation and surgery; however, combined radiation and chemotherapy with or without surgery is usually employed for more advanced disease.

Diagnostic Aids:

The definitive test for diagnosis remains tissue biopsy. Several aids to the oral examination have been suggested in the past, including light technologies, vital tissue staining using toluidine blue (TB), and computer-assisted cytology of oral brush biopsy specimens. Additional markers based on blood of saliva samples are also under investigation.

Adjunctive clinical techniques such as:

1. **Toluidine blue (vital tissue staining).**
2. **Exfoliative cytology (computer-assisted cytology).**
3. **Brush biopsy.**
4. **Chemiluminescence.**
5. **Tissue auto fluorescence.**
6. **For bone involvement** can be used the Routine radiology, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (also can indicate the extent of some soft tissue lesions).

All these have been suggested to increase our ability to identify areas of dysplasia/early OSSC that are not visible to naked eye.

1. **Toluidine blue staining** (vital tissue staining): is a vital dye (tolonium chloride) that is believed to stain nucleic acids. It has been used to identify mucosal abnormalities and as a useful way for demarcating the extent of a potentially malignant lesion prior to excision.

- Positive retention of toluidine blue (particularly in areas of leukoplakia, erythroplakia, and uptake in a peripheral pattern of an ulcer) may indicate the need for biopsy. False-positive dye retention may occur in inflammatory and ulcerative lesions, but false- negative retention is uncommon. A return appointment in 14 days, providing time for inflammatory lesions to improve, may lead to a decrease in false-positive results.
- If the lesion is stained, the test is positive, biopsy immediately.

2. **Exfoliative cytology:** microscopic examination of cells desquamated from a tissue surface or lesion as a means of detecting malignancy and microbiological changes.

   Indications for oral cytology:
   - Diffused lesions
   - Premalignant or malignant lesions.
   - Patient not indicated for biopsy.

3. **Brush biopsy:** the use of a specially designed circular brush (Oral CDx Brush), which is used to sample cells of the suspected epithelial lesion.

   Clinically:
   - The brush may be moistened with water or the patient's saliva and applied to the surface of the lesion.
   - Contact between the brush and the mucosal surface with moderate pressure applied.
   - The brush is then rotated until pinpoint bleeding is noted, signaling entry into the lamina propria and obtaining epithelial cells.
   - Removed cells are transferred to a glass slide.
   - A fixation step follows immediately by flooding the slide with fixative solution (alcohol/propylene glycol).

- Allowing it to air dry the stained with pap stain (modified Papanicolaou test).
- Analyzed microscopically via a computer-based imaging system.

4. **Chemiluminescence:** clinical inspection of oral mucosa with the aid of chemiluminescent blue/white light (Vizilite system) was recently suggested to improve the identification of mucosal abnormalities.
5. **Tissue auto fluorescence:** the use of optical spectroscopy systems to provide tissue diagnosis (is a non-invasive technique used in detection of the soft tissue lesions). Oral cavity fluorescence using blue light excitation was reported due to interaction with collagen and modified by epithelial cellular and related to collagen breakdown and increased hemoglobin absorption of light.

- **Normal cell emit green light.**
- **Dysplastic cells emit red light.**

  This phenomenon is utilized in the detection of cancer using fluorescence spectroscopy.

Surgical biopsy: classified as

1. Exisional biopsy: involve total removal of the lesion with slight peripheral and in depth safety margins, such biopsies have a diagnostic and therapeutic.

2. Incisional biopsy: involves the removal of a representative portion of the target lesion and the part of healthy tissue.
3. Aspiration biopsy is only useful for deep lesions.

Malignant tumors of the salivary glands:

Most salivary gland tumors spread by local infiltration, by perineural or hematogenous spread and, less commonly, via lymphatics.

Non-Hodgkin's lymphoma:

Non-Hodgkin's lymphoma (NHL) may primarily be localized in the oral soft tissues (e.g. the gingiva, palate, and tongue). Oral NHL may be one of the manifestations of human immunodeficiency virus (HIV) infection. Hodgkin's lymphoma rarely occurs in the mouth, in contrast to NHL. The clinical presentation of oral NHL is a sub-mucosal swelling, sometimes bilaterally, especially at the junction of the hard and soft palate and the gingiva. NHL may also be located within the jaw bones, particularly in the mandible and symptoms may consist of unilateral anesthesia of the lower lip and sometimes swelling of the involved part of the bone.

Diagnosis:

-FNA (fine needle aspiration) biopsy.

-Incisional biopsy in conjunction with immunocytochemistry is a useful aid in diagnosing malignant lymphoma.

-In most cases, a biopsy is required.

Complications of Cancer treatment:

- Acute complication include ulcerative mucositis occur during the course of radiotherapy and combined radio-chemotherapy because of direct tissue toxicity and possibly secondary bacterial irritation, these reactions resolve over weeks to months following the completion of therapy.
- Chronic complications or late radiation reactions occur due to change in the vascular supply, epithelial atrophy, fibrosis in connective tissue and muscle, and change in the cellularity of tissues. These complications develop slowly over months to years. The connective tissue and musculature may demonstrate increased fibrosis, which may result in limited movement and altered function like in bone.

1. Mucositis:

Ulcerative oral mucositis is a painful and debilitating condition that is a dose- and rate-limiting toxicity of cancer therapy. It's characterized by severe pain, increased risk of local and systemic infection, compromised oral and pharyngeal function and oral bleeding that affect quality of life; may lead to hospitalization. . Increased risk of mucositis has been associated with poor oral hygiene, tobacco use, hypo salivation at baseline, and older age.

Clinical manifestation:

The first signs of mucositis may be a white appearance to the mucosa, caused by epithelial hyperplasia/hypertrophy and intraepithelial edema, or a red appearance due to hyperemia and epithelial thinning. Pseudomembrance formation represents ulceration with a fibrous exudate with oral debris and microbial components.

2. Tissue Necrosis:

Soft tissue and osteonecrosis:

Soft tissue necrosis may involve any oral site, including the cheeks, tongue and involvement of tissue overlying bone that has received high-dose radiation may predispose patients to necrosis of bone. The Post radiation osteonecrosis (PRON) may be chronic or progressive. Radiation therapy causes endarteritis that affects vascularity, resulting in hypo vascular, hypo cellular, and hypoxic tissue that is unable to repair or remodel itself effectively when a challenge occurs, the challenge may take the form of trauma (such as from surgical procedures), active periodontal disease or denture trauma.

Symptoms and signs are discomfort or tenderness at the site, bad taste, paraesthesia and anesthesia, extra oral and oroantral fistulae, secondary infection causing secondary osteomyelitis, and pathologic fracture.

3. Speech and mastication:

Abnormal speech may follow surgery or radiation due to removal of structure and because of hypo salivation and fibrosis that affects tongue mobility, mandibular movement, and soft palate function.

4. Nutrition: taste and smell impairment:

Radiation therapy produces changes in the patient's taste, the taste may be affected directly, due to an effect on the taste buds, or indirectly, due to hypo salivation and secondary infection. Taste often will recover slowly over several months, but permanent alteration may result.

Zinc supplementation (zinc sulfate, 220 mg twice daily) may be useful for some patients who experience taste disturbances.

5. Mandibular dysfunction

Musculoskeletal syndromes may arise due to fibrosis of muscles, which may follow radiation and surgery. Limited opening has been related to radiation exposure of the upper head of the lateral pterygoid muscle.

6. Chronic and post-therapy pain.

Pain Management in Head and Neck Cancer:

- Topical anesthetic (give topical anesthesia)
- Analgesic (Elevate pain threshold)
- Anti-inflammatory (Reduce inflammation; mild to moderate)
- Antimicrobial (Modify pathologic process)
- Anticonvulsant (Modify pathologic process)
- Anxiolytic (Antianxiety)
- Antidepressant (Reduce depression; analgesic effect; promote sound sleep)
- Muscle relaxant (Reduce muscle tension or spasm).

Oral Medicine

References:

- Burket's Oral Medicine 12th edition 2015.
- Burket's Oral Medicine 11th edition 2008.
- CAWSON'S ESSENTIALS OF ORAL PATHOLOGY AND ORAL MEDICINE seven edition 2002.

Oral diagnosis (case sheet): Dr. Rehab Faisal

Oral diagnosis is the branch of dentistry dealing with identification of oral diseases whether of local or systemic origin. The purpose of obtaining information and recording it in an orderly manner is to establish a diagnosis and distinguish one disease from another; the data base may be compatible with a variety of disease process which constitutes the differential diagnosis.

Objective:

- Define oral diagnosis and diagnostic process.
- Identify steps of diagnostic process.
- Define the case history, its items and objectives of each.
- Identify types of clinical evaluation.
- Define the signs and symptoms, giving example s for each.

Types of clinical examination:

A-complete examination:

1. History taking.

2. Clinical examination.

3. Supplementary diagnostic aids.

B- Screen types of examination:

1. Brief clinical examination of the teeth, supporting structures and mouth.

2. Limited radiographic examination.

C-Emergency type of examination:

- For diagnosis and management of acute and emergency conditions.
- Limited to the procedure related to the complaint of the patient.

Diagnosis: it includes the following…..

1. Case history (personal data, chief complain, present illness, past medical history, past dental history and family history).
2. Clinical examination (intra oral and extra oral examination).
3. Diagnostic aids (radiographic examination, biopsy and biochemical investigations).

Person data:

- Patient name.
- Age (include the diseases affect certain age group e.g. certain diseases affect children as acute herpetic gingiva stomatitis, measles and rickets. While in older age group, patients are subjected to atrophic and degenerative age changes, in addition to some malignancy or carcinoma or leukoplakia).
- Sex: some patients carry mixed names, certain diseases or condition, related to either sex e.g. hemophilia usually certain in male, while females are usually carrier the diseases (sex linked diseases).
- Marital status:
  1. (Psychological stress of some married people, may predispose certain oral diseases)
  2. Gingivitis and gingival enlargement related to pregnancy.
  3. Could be a source of infection in some contiguous diseases.
- Occupation: it causes oral lesions due to systemic absorption of metallic or non-metallic compound as workers in bismuth, lead and mercury factories.

- **Chief complain:**
  1. It is written in patient's own words.
  2. There may be more than one single complaint.
  3. Symptoms: pain, burning, dry mouth, parasthesia and loose teeth.
- Sign: any change or changes observed by examiner as in color, shape, form or size of tissues, in addition to pulse rate, blood pressure, mass, ulcer, erosions and pigmentation.

- Symptoms: are subjective information reported by patient, these are usually the first aspects of history to be recorded. The symptoms may be described by parent or guardian, as in children and mentally compromised patients.

  e.g.

  1. Pain, burning sensation.
  2. Altered taste.
  3. Foul odor.
  4. Dryness of the mouth.
  5. Bleeding.
  6. Swelling.

  - Present illness.

  1. Onset of complain.
  2. Character of onset.
  3. Severity of complaint.
  4. Course of complaint.
  5. Duration
  6. Location of complaint.
  7. Distribution.
  8. Prior occurrence.
  9. Exacerbating factors.
  10. Relieving factors.
  11. Associated phenomenon like fever, spontaneous bleeding and bad odor.

- **Past medical history:**

1. Serious illness (heart attack, bleeding disorders).
2. Fits or faints.
3. Hospitalization.
4. Allergic.
5. Medications take in the last six months.
6. Childhood diseases (as rheumatic fever).

- Past dental history:
- Frequency of visiting dentist and purpose of visit.
- Administration of local anesthesia.

- Past and surgical procedures, bleeding and healing process.
- Previous orthodontic treatment.
- Periodontal diseases and previous periodontal treatment.
- History of denture wearing, causes of teeth loss

Oral Medicine

References :

- Burket’s Oral Medicine 12th edition 2015.
- Burket’s Oral Medicine 11th edition 2008.
- CAWSON'S ESSENTIALS OF ORAL PATHOLOGY AND ORAL MEDICINE seven edition 2002.

Thank you

SALIVARY GLAND DISEASES

Dr. Rehab Faisal

Normal function and health of the mouth depend on normal secretion of saliva by the major and minor glands. Failure of salivary secretion causes a dry mouth (xerostomia) which is promotes oral infection.

Salivary gland anatomy and physiology:

Saliva is the product of the major and minor salivary glands and is highly complex mixture of water and organic and nonorganic components, the saliva is highly modified and it is carried via a branching duct system into the oral cavity.

Acinar cells of Salivary Glands: Classified as either:

-Serous cells: produce a thin watery secretion

-Mucous cells: produce a more viscous secretion.

Salivary gland secretary unit:

- Composed of terminal acini
- Intercalated, striated and excretory ducts
- Myoepithelial cells

The major Salivary gland is paired structures and includes the parotid, submandibular and sublingual .

Parotid: serous

Submandibular: mucous & serous

Sublingual: mucous

Salivary function:

- Aid is mastication, deglutination
- Salivary lysozyme, IgA and other antibacterial substances protect against caries and oral cavity infections
- Saliva also aids in speech

Anatomy of the parotid gland:

CN VII branches roughly divide the PG into superficial and deep lobes while coursing anteriorly from the stylomastoid foramen to the muscles of facial expression. While the submandibular gland is located in the submandibular triangle of the neck, inferior & lateral to mylohyoid muscle. The posterior-superior portion of the gland curves up around the posterior border of the mylohyoid and gives rise to Wharton's duct .The sublingual gland lies on the superior surface of the mylohyoid muscle and are separated from the oral cavity by a thin layer of mucosa .

Investigative methods:

-Sialometry: measure the amount of saliva produced in a certain time.

-Sialochemistry: measure the composition of the saliva.

-Sialography:by introduce the iodine-containing contrast medium through the opening of their duct.

-Sonography: using ultrasonic pattern.

-Cytology & Biopsy: (Sjogren's syndrome & lymphoma)

-Scintigrahy: using radioactive isotopes to demonstrate the function of the SG. (i.v injection of Technetium Tc-99)

-Computed Tomography and MRI.

-Curry's test :(given the patient 5mg pilocarpine i.v and saliva is collected and calculated).

-Serologic evaluation: as in sjogren's syndrome, IgG, ESR.

Specific Diseases and Disorders of the Salivary Glands:

- Developmental Abnormalities
- Sialolithiasis (Salivary Stones) (Obstructive Disorders).
- Extravasation and Retention Mucoceles and Ranulas (Obstructive Disorders)
- Inflammatory and Reactive Lesions
- Allergic Sialadenitis
- Viral Diseases
- Bacterial Sialadenitis
- Systemic Conditions with salivary gland involvement.

1. Developmental Abnormalities

-Complete absence (aplasia or agenesis) of salivary glands (rare)
-Accessory Salivary Ducts (are common and do not require treatment)
-Darier's Disease (Salivary duct abnormalities). Sialography of parotid glands in this condition revealed duct dilation, with periodic stricture affecting the main ducts.

2. Sialolithiasis or salivary stone:

Sialoliths are calcified organic materials, results in a mechanical obstruction of the salivary duct is the major cause of unilateral diffuse parotid or submandibular gland swelling .
The etiology of sialolith formation is still unknown, yet several factors that cause pooling of saliva within the duct are known to contribute to stone formation:
Inflammation.
Irregularities in the duct system .
Local irritants .
Anticholinergic medications.
Increase serum calcium.

Thought an initial organic nidus that progressively grows by deposition of layers of inorganic and organic substances. May eventually obstruct flow of saliva from the gland to the oral cavity.

Salivary stone occurs at sub-mandibular gland (80-90%) due to:
- the torturous course of Wharton's duct
- higher calcium and phosphate level
- Position of the submandibular glands, which leaves them prone to stasis.

Clinical features:

- Acute, painful and intermittent swelling of the affected salivary gland.
- The ductal obstruction may occur at meal time when saliva producing is at its maximum, the resultant swelling is sudden and can be painful .
- Gradually reduction of the swelling can result but it recurs repeatedly when flow is stimulated.

- Tender.
- Fistulae, a sinus tract, or ulceration may occur over the stone in chronic cases.

Diagnostic approaches:

- Plain occlusal film: Effective for intraductal stones.
-CT Scan and Ultrasound.
- Sialoendoscopy for visualizing and removing sialoiths (less than 1mm diameter)

Sialolithiasis Treatment:

- During the acute phase, therapy is primarily supportive. Standard care includes analgesics, hydration, antibiotics, and antipyretics, as necessary.
- Stone excision.
- Gland excision.

3. Extravasation and Retention Mucoceles and Ranulas :

The most type of salivary and soft tissue cyst is the extravasation mucocele, mainly affect the minor salivary glands. It is a swelling caused by pooling of saliva at the site of a traumatized or obstructed minor salivary gland duct. Lower lip is the common site.

It is divided into two types:

Mucous extravasation type: due to laceration of minor salivary glands duct by trauma.

Mucous retention type: due to obstruction of minor S.G. ducts which cause back up of saliva.

Extravasation: is the leakage of fluid from the ducts or acini into the surrounding tissue.

Retention: narrowed ductal opening that cannot adequately accommodate the exit of saliva produced, leading to ductal dilation and surface swelling.

Mucoceles:

Clinical features: Superficial, painless, smooth-surfaced swellings that can range from a few millimeters to a few centimeters in diameter, rounded swelling, fluctuant and bluish due to the thin wall.

Treatment: mucocele should be excised with the underlining gland.

Ranulas: (larger form of mucocele) : Is a term used for mucoceles that occur in the floor of the mouth (sub-lingual or submandibular salivary glands).

Clinical features : Ranulas are unilateral (2-3cm); slow-growing, soft, and movable mass located in the floor of the mouth, painless but may interfere with speech or mastication .They tend to be larger than mucocele & can fill the floor of mouth & elevate tongue and located lateral to the midline. If the lesion extends deep into the soft tissue, it can cross the midline. Superficial ranula can have a bluish in color, but when the lesion is deeply seated, the mucosa may have a normal appearance.

Treatment:

Marsupialization due to the excessive recurrence rate of 60-70% and sublingual gland removal via intraoral approach. Postsurgical complications include lesion recurrence, sensory deficits of the tongue, and damage to Wharton's duct.

4. Salivary Gland Infections:

- Acute bacterial sialadenitis.

-Chronic bacterial sialadenitis.

-Viral infections.

Bacterial Sialadenitis: - represents inflammation mainly involving the acinoparenchyma of the gland . Acute infection more often affects the parotid gland than the submandibular gland (due to the presence of bacteria in dental plaque of upper 1nd molar which lies near parotid gland orifice). **It occurs in patient with:**

- Decreased salivary flow or following surgery.

- Dehydration.

- Restricted flowed which will lead to bacterial colonization and invasion of the ducts.

Pathogenesis :

Retrograde contamination of the salivary ducts and parenchyma tissue by bacteria inhabiting the oral cavity.Stasis of salivary flow through the ducts and parenchyma promotes acute suppurate infection.

Acute Suppurative Parotitis:

Sudden onset of unilateral or bilateral enlargement of the pre/post auricular areas extends into the angle of the mandible .

Typical clinical features are:

Painful indurated swelling in one or both parotids, tenderness and erythematous skin of the involved gland .Fever, regional lymph nodes are enlarged and tender, purulent discharge exudes from parotid duct.

Treatment : Increase hydration and improve oral hygiene, Culture of the discharge and specific antibiotic and drainage.

Chronic Sialadenitis :

Is complication of duct obstruction, it's usually unilateral and asymptomatic or with painful swelling of the gland. The predisposing factors are a calculus or a stricture.

Treatment:

-Initial management should be conservative and includes the massage and antibiotics for acute exacerbations .

-Should conservative measures fail, consider removing the gland.

5. Viral diseases:

1. Mumps :Classically designates a viral parotitis caused by the RNA paramyxovirus and causes painful swelling of the parotid and sometime other glands.and is highly infectious and transmitted by direct contact with salivary droplets….

It is acute sialadenitis, sometimes with purulent discharge, endemic in the community, enters through upper respiratory tract. It affects school children from age 4-6 years and can affect older up to 40 years.

Clinical presentation :

Salivary gland inflammation and enlargement, unilateral then bilateral (within 1-5 days), peri-auricular pain, headache, fever, anorexia, malaise and myolgia .

- 90% the parotid is affected،

- 10% the sub-mandibular is affected.

DIAGNOSIS: Is made by the demonstration of antibodies to the mumps S and V antigens and to the hemagglutination antigen.Serum amylase level may be elevated.

Treatment: is symptomatic, vaccination is important for prevention . Rare fatalities have occurred from viral encephalitis, myocarditis, and neuritis.

Complications : Mild meningitis، Encephalitis ،Deafness ،Pancreatitis ، thyroiditis ،Infertility، Oophoritis ،Epididymitis and Orchitis ،Testicular atrophy and sterility.

2. HIV-SGD is salivary gland swelling, primarily in the parotid glands and frequently bilateral.

6. Allergic Sialadenitis: Enlargement of the salivary glands associated with exposure to various pharmaceutical agents and allergens. It is acute salivary gland enlargement, often accompanied by itching over the gland.

Treatment: Allergic sialadenitis is self-limiting. Avoiding the allergen and maintaining hydration.

7. Functional Disorders: may be either:

1. Sialorrhea (Ptylism): (Increase in saliva flow)

-Physiological stimuli such as the smell or taste of food.

-Acute infection (herpetic gingivitis, pemphigus)

- Metal poisoning (mercury stomatitis).

- After surgery of oral.

-Drug such as pilocarpin, oral contraceptive pills.

-Psychological and neurological (mental retardation, epilipsy and facial paralysis.)

Treatment: Firstly find the underlying cause. In most condition give propanthen (15mg/day): anticholinergic drug.

2 .Xerostomia (Decrease in saliva flow)

Mumps, Sjogrens syndrome, post-irradiation.

Sjögren's Syndrome:

-Most common immunologic disorder (chronic autoimmune disease) associated with dryness of mouth (xerostomia) and dryness of the eyes (keratoconjunctivitis sicca), exocrine dysfunction and lymphocytic infiltration.

- 90% cases occur in women and average age of onset is 50 years. It is classified as primary or secondary.

- **Secondary** Sjögren's syndrome has salivary and/or lacrimal gland dysfunction in the setting of another connective tissue disease (eg, systemic lupus erythematosus, rheumatoid arthritis, scleroderma.)

- **Primary** Sjögren's syndrome is a systemic disorder that includes both lacrimal and salivary gland dysfunctions without another autoimmune condition.

The clinical feature :

-Is unilateral or bilateral salivary gland swelling occurs, may be permanent or intermittent .

-In early stages the mucosa appear moist but salivary flow rate is diminished then it appear dry, red shiny and the tongue is typically red ، papillae atrophy and the dorsum becomes lobulated.

- Mucosa may be painful and sensitive to spices and heat.

-Patients often have dry, cracked lips and angular cheilitis.

- Coronal ulceration and conjunctivitis.

- Patient complains of dirt or foreign body in the eye.

- Increased incidence of dental caries and candidal infection.

- Increased incidence of bacterial sialadenitis.

Investigation and diagnosis:

-Salivary flow rate (stimulated parotid flow rate) is normally more than 1.5ml/min.

-Schirmer test: assess lacrimal flow if it is more than 0.5 ml/min.

-Immunological investigation, Rh factor, anti-Ro and anti-La.

-Sialography: variable degree of sialectasis found in patients with SS.

-Labial gland biopsy: focal lymphocytic sialadenitis, ductal dilation and periductal fibrosis. (Best sole diagnostic criterion).

-MRI or CT can be helpful also. In sialography a snowstorm appearances of contrast medium due to leakage of contrast material through the ductal wall.

-Lip biopsy is important to avoid the risks of damage to the facial nerve or parotid fistula.

Treatment:

- Artificial saliva, oral rinses and gels, mouthwashes and water sipping due to Xerostomia .
- Salivary stimulants: chewing sugar-free gum or lemon.
- Pilocarpine (5mg) and Cevimeline (30mg). Both medications are muscarinic agonists and give 3 times /day.
- Preventive dental care: flouride rinse, dental hygiene measures (candidal infection)
- Peroidic ophthalomological exam. (Dry eyes are best managed by periodic use of artificial tears.
- Antibiotic in case of episodes of bacterial sialadenitis.

Sialadenosis: Non-specific term used to describe a non-inflammatory non-neoplastic enlargement of a salivary gland, usually the parotid.

Condition associated with Sialadenosis:

-Endocrine disorders (DM, Diabetes insipidus, hypothyroidism).

-Nutritional conditions (general malnutrition, alcoholism.)

-Neurogenic medications (antihypertensive drugs and sympathomimetic drugs used for treating asthma) .

Radiation Injury : Salivary glands are often within the field of radiation therapy for head and neck cancers, the low dose radiation to a salivary gland causes an acute tender and painful swelling within 24 hrs.

-Serous cells are especially sensitive and exhibit marked degranulation and disruption.

- Continued irradiation leads to complete destruction of the serous acini and subsequent atrophy of the gland.

Oral Medicine

References :

- Burket's Oral Medicine 12th edition 2015.

- Burket's Oral Medicine 11th edition 2008.

- CAWSON'S ESSENTIALS OF ORAL PATHOLOGY AND ORAL MEDICINE seven edition 2002.

THANK YOU

Salivary Gland Tumors:

Benign Tumors: - Pleomorphic Adenoma

-Monomorphic Adenoma

-Papillary Cystadenoma Lymphomatosum

-Oncocytoma

-Others

Malignant Tumors: Include the following ……..

- Mucoepidermoid Carcinoma.

- Adenoid cystic carcinoma.

- Acinic cell carcinoma.

- Adenocarcinoma.

- Lymphoma.

The majority of salivary gland tumors (about80%) arise in the parotidglands, the submandibular glands (10 to 15% of tumors), and the remaining tumors develop in the sublingual or minor salivary glands.

-Any tumors arising from salivary duct epithelium are adenocarcinomas. For minor salivary glands, pleomorphic adenoma is the most common benign tumor.

-The mucoepidermoid carcinoma is the most common malignant tumor and the risk of malignancy for all salivary tumors increases as the size of the tumor decreases.

PLEOMORPHIC ADENOMA:

Is the most common tumor of the salivary glands (about 60% of all salivary gland tumors.(. It is often called a mixed tumor because it consists of both epithelial and mesenchymal elements. Pleomorphic adenomas may occur at any age, but the highest incidence is in the fourth to sixth decades of life. It also affects the children .

Clinical Presentation.:

-slow growing painless, firm, and mobile masses.

-usually occur in the posterior inferior aspect of the superficial lob, while in the submandibular gland present as well-defined palpable masses.

-It is difficult to distinguish these tumors from malignant neoplasms and indurated lymph nodes. Pleomorphic adenomas can vary in size, depending on the gland in which they are located .

-In the parotid gland, the tumors are usually several centimeters in diameter but can reach much larger sizes if left untreated. Intraoral, mostly occur on the palate, followed by the upper lip and buccal mucosa.

Treatment:

-Surgical removal with adequate margins is the principal treatment. Because of its microscopic projections, this tumor requires a wide resection to avoid recurrence .

-A superficial parotidectomy is sufficient for the majority of this lesion.

MONOMORPHIC ADENOMA:

A monomorphic adenoma is a tumor that is composed predominantly of one cell type, as opposed to a mixed tumor (pleomorphic adenoma), in which different elements are present .

Management is the same as pleomorphic adenoma.

Papillary cystadenoma lymphomatosum:

-It is known as Warthin's tumor, is the second most common benign tumor of the parotid gland .

-It represents ≈6 to 10% of all parotid tumors and is most commonly located in the inferior pole of the gland, posterior to the angle of the mandible.

Clinical features: well-defined, slow-growing mass in the tail of the parotid gland. It is usually painless unless it becomes superinfected.

-Surgical removal, recurrences is rare

Malignant Tumors-:

MUCOEPIDERMOID CARCINOMA:

-It is the most common malignant tumor of the salivary glands mainly in the parotid gland and the second tumor in the submandibular gland, after adenoid cystic. The palate is the second most common site .Men and women are affected equally by this tumor, and the highest incidence occurs in the third to fifth decades of life.

-Mucoepidermoid carcinoma consists of both epidermal and mucous cells .

-The tumor is classified as of either a high grade or a low grade, depending on the ratio of epidermal cells to mucous cells. The low-grade tumor has a higher ratio and is a less aggressive lesion whereas the high-grade form is considered to be a more malignant tumor and has a poor prognosis.

Clinical Presentation:

-The clinical course of this lesion depends on its grade. The high-grade mucoepidermoid carcinomas often demonstrate rapid growth and a higher likelihood for metastasis،

-Pain and ulceration of overlying tissue are associated with this tumor .

-If the facial nerve is involved, the patient may exhibit a facial palsy.

Treatment :

-A low-grade mucoepidermoid carcinoma can be treated with a superficial parotidectomy if it involves only the superficial lobe .

-High grade lesions should be treated by wide excision but the tumor may recur .

-Neck dissections may be necessary for lymph node removal and staging in high-grade lesions.

-Postoperative radiation therapy has been shown to be a useful adjunct in treating the high-grade tumor.

ACINIC CELL CARCINOMA:

Acinic cell carcinoma represents about 1% of all salivary gland tumors. This tumor occurs with a higher frequency in women.

Clinical presentation:

- These lesions often present as slow growing masses .

- Pain may be associated with the lesion but is not indicative of the prognosis .

- The superficial lobe and the inferior pole of the parotid gland are common sites of occurrence .

- Bilateral involvement of the parotid gland has been reported in approximately 3% of cases.

Treatment:

-Acinic cell carcinomas initially undergo a relatively benign course,the treatment consists of superficial parotidectomy, with facial nerve preservation if possible .

-When these tumors are found in the submandibular gland, total gland removal is the treatment of choice .

ADENOID CYSTIC CARCINOMA:

Adenoid cystic carcinomas make up about 6% of all salivary gland tumors and are the most common malignant tumors of the submandibular and minor salivary glands. The tumor affects men and women equally and usually occurs in the fifth decade of life.

Clinical presentation:

Adenoid cystic carcinoma usually presents as a firm unilobular mass in the gland. The tumor is painful, and parotid tumors may cause facial nerve paralysis in a small number of patients. Unfortunately, the tumor's slow growth may delay diagnosis for several years.

Treatment:

Because of the ability of this lesion to spread along the nerve sheaths, radical surgical excision of the lesion is the appropriate treatment.

Radical surgery refers to the removal of blood supply, lymph nodes and sometimes adjacent structures of a diseased organ or tumor during surgery.

CARCINOMA EX PLEOMORPHIC ADENOMA:

Carcinoma ex pleomorphic adenoma is a malignant tumor that arises within a pre-existing pleomorphic adenoma. The malignant cells in this tumor are epithelial in origin and this tumor represents 2 to 5% of all salivary gland tumors.

Clinical presentation:

These tumors are slow growing and present for 15 to 20 years before they suddenly increase in size and become clinically apparent. It occurs more often in pleomorphic adenomas that have been left untreated for long periods of time (It is for this reason that early removal of pleomorphic adenomas is recommended).

Treatment:

-This is a malignant salivary gland tumor that has an aggressive course and that carries a very poor prognosis. Surgical removal with postoperative radiation therapy is the recommended treatment.

- Early removal of benign parotid gland tumors is recommended to avoid the development of this lesion.

Lymphoma :

A salivary gland is the first clinical manifestation of the disease. Primary lymphoma of the salivary glands probably arises from lymph tissue within the glands It is a rare. The major forms of lymphoma are non-Hodgkin's lymphoma (NHL) and Hodgkin's disease .

Clinical feature:

A rapidly growing tumor with extensive local growth, invasion of surrounding tissues, cervical node metastasis but high rates of distant metastasis

Treatment :

Early and aggressive surgery with close follow up is required.

Oral Medicine

References :

- Burket's Oral Medicine 12th edition 2015.

- Burket's Oral Medicine 11th edition 2008.

- CAWSON'S ESSENTIALS OF ORAL PATHOLOGY AND ORAL MEDICINE seven edition 2002.

THANK YOU

AUTOIMMUNE DISEASES

The term autoimmune disease refers to a disorder in which there is evidence of an immune response against self, caused by the body producing an immune response against its own tissues (self-antigen), which mean the loss of tolerance to selfantigen. It may be primarily due to either antibodies (autoantibodies) or immune cells, but a common characteristic is the presence of a lymphocytic infiltration in the target organ. Normally, the immune system recognizes the tissues in the body are not "foreign" also called self-antigen and does not attack them; this is what's called tolerance (the normal status of immunologic non responsiveness to self-antigen).

Autoantibodies

In some autoimmune diseases, B cells mistakenly make antibodies against tissues of the body (self-antigens) instead of foreign antigens.These autoantibodies either interfere with the normal function of the tissues or initiate destruction of the tissues. (e.g.) People with myasthenia gravis experience muscle weakness because autoantibodies attack a part of the nerve that stimulates muscle movement.

Typical features of autoimmune disease:-

• Significantly more common in women.
• Onset often in middle age.
• Family history frequently positive.
• Levels of immunoglobins (autoantibodies) usually raised.
• Circulating autoantibodies frequently also detectable in un affected family members.
• Often an increased risk of developing other autoimmune diseases.
• Immunoglobuline and/or complement often detectable at sites of tissue damage (e.g. pemphigus vulgaris).
• Immunosuppressive treatment frequently limits tissue damage.

Autoimmune disorders fall into two general types:

1-Those that damage many organs (systemic autoimmune diseases)
2- Those where only a single organ or tissue is directly damaged by the autoimmune process (localized). However, the distinctions become blurred as the effect of localized autoimmune disorders frequently extends beyond the targeted tissues, indirectly affecting other body organs and systems.

Some of the most common types of autoimmune disorders include:

Systemic Autoimmune Diseases

• Rheumatoid arthritis (RA) and Juvenile RA (JRA) (joints; less commonly lung, skin)
• Lupus [Systemic Lupus Erythematosus] (skin, joints, kidneys, heart, brain, red blood cells, other)

• Scleroderma (skin, intestine, less commonly lung)
• Sjogren's syndrome (salivary glands, tear glands, joints)
• Goodpasture's syndrome (lungs, kidneys)
• Wegener's granulomatosis (blood vessels, sinuses, lungs, kidneys)
• Polymyalgia Rheumatica (large muscle groups)
• Guillain-Barre syndrome (nervous system)

Localized Autoimmune Diseases
• Type 1 Diabetes Mellitus (pancreas islets)
• Hashimoto's thyroiditis, Graves' disease (thyroid)
• Celiac disease, Crohn's disease, Ulcerative colitis (GI tract)
• Multiple sclerosis , Addison's disease (adrenal)
• Primary biliary cirrhosis, Autoimmune hepatitis (liver)
• Temporal Arteritis / Giant Cell Arteritis (arteries of the head and neck)

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Systemic Lupus Erythematosus
Systemic lupus erythematosus (SLE) is the prototypical autoimmune disease characterized by the production of numerous autoantibodies. Organ injury is secondary to either the direct binding of autoantibodies to self-antigens or the deposition of immunocomplexes in vessels or tissues. In addition to systemic and isolated cutaneous lupus (chronic discoid lupus), a distinct syndrome of drug-induced lupus is recognized. Unlike SLE, drug-induced lupus rarely affects the kidney and is reversible on discontinuation of the offending agent.

Clinical Manifestations
Skin is affected in up to 85% of SLE patients. In addition, cutaneous lupus can occur without multisystem involvement. Skin lesions of lupus can be classified into l**upus-specific** (having diagnostic clinical or histopathological features) and **nonspecific lesions**.
Three subtypes of **lupus-specific skin lesions** have been described: **acute, subacute, and chronic.**
Acute cutaneous lupus : represented by the butterfly rash—mask-shaped erythematous eruptions involving the malar areas and bridge of the nose. Bullous lupus and localized erythematous papules also belong to the acute lupus category.
Chronic cutaneous lupus affects the skin of the face or scalp in about 80% of cases . The least common subtype, **subacute cutaneous lupus**, includes papulosquamous (psoriasiform) and annular-polycyclic eruptions usually on the trunk and arms.
Nonspecific but suggestive skin manifestations of lupus are common and include alopecia , photosensitivity, Raynaud’s phenomenon, livedo reticularis, urticaria, erythema, telangiectases, and cutaneous vasculitis.

ETIOLOGY

The specific etiology of SLE is not known with certainty, but immunocomplexes, autoantibodies, and genetic, infectious, environmental, and endocrine factors play significant roles.

Renal Manifestations. Kidney involvement occurs in up to 50%–60% of patients with SLE and is a primary cause of morbidity and mortality in this population Clinically, renal disease in SLE can range anywhere from asymptomatic proteinuria to rapidly progressive glomerulonephritis with renal failure.

Musculoskeletal : Musculoskeletal manifestations occur in about 95% of patients with SLE, and arthralgia is the first presenting symptom in about 50% of cases. Nonersive symmetric arthritis most commonly affecting hands, wrists, and knees is typical of SLE.

Central Nervous System :occurs in about 20% of patients with SLE and is usually due to cerebral vasculitis or direct neuronal damage. CNS manifestations include psychosis, stroke, seizures and transverse myelitis and are associated with poor overall prognosis.

Cardiovascular Cardiovascular involvement in SLE is classically manifested by vasculitis and pericarditis.

Other Manifestations

Fatigue, depression, and fibromyalgia-like symptoms are commonly present and can be debilitating.

Oral Manifestations

The oral mucosa is affected in a significant percentage of lupus patients, with the predominant types of oral lesions being **ulcerations, erythematous lesions, and discoid lesions**. These ulcerations cannot be easily distinguished from other common oral conditions, such as aphthous ulcers, although they occur with increased frequency on the palate and in the oropharynx and are characteristically painless.

Discoid oral lesions are similar to those occurring on the skin and appear as whitish striae frequently radiating from the central erythematous area, giving a so-called *brush border*. Atrophy and telangiectases are also frequently present. Buccal mucosa, gingiva, and labial mucosa are the most commonly affected intraoral sites. **Isolated erythematous** areas are also common, especially on the palate.

Laboratory Findings

Anemia, leukopenia, and thrombocytopenia are among the most common manifestations of SLE. Elevation of erythrocyte sedimentation rate with normal C-reactive protein levels is characteristic of SLE.

Diagnosis

Diagnosis of SLE is based on the compatible symptoms and signs in the presence of suggestive laboratory abnormalities. Diagnostic criteria include:

1. Acute cutaneous lupus (e.g., malar rash or photosensitivity and other)

2. Chronic cutaneous lupus (e.g., classic discoid lupus and other)
3. Oral ulcers or nasal ulcers
4. Nonscarring alopecia
5. Synovitis involving 2 or more joints, characterized by swelling or effusion
OR tenderness in 2 or more joints and at least 30 minutes of morning stiffness
6. Serositis
7. Renal :Urine protein greater than or equal to 500 mg protein/24 hours
OR red blood cell casts
8. Neurologic disease (Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy, acute confused state).
9. Hemolytic anemia
10. Leukopenia (<4000/mm3 at least once)
OR Lymphopenia (<1000/mm3 at least once)
11. Thrombocytopenia (<100,000/mm3) at least once
Immunologic criteria
1. ANA level above laboratory reference range
2. Anti-dsDNA antibody level above laboratory reference range
3. Anti-Sm: presence of antibody to Sm nuclear antigen
4. Antiphospholipid antibody positivity
5. Low complement
Low C3
Low C4
Low CH50
6. Direct Coombs' test in the absence of hemolytic anemia

The proposed classification rule is as follows: classify a patient as having SLE if 4 of the clinical and immunologic criteria are satisfied, including at least one clinical and one immunologic criterions, OR if he or she has biopsy-proven nephritis compatible with SLE in the presence of antinuclear antibodies (ANAs) or anti-double-stranded DNA (dsDNA) antibodies.

Discoid lupus erythematosus

- DLE is essentially a skin disease with mucocutaneous lesions indistinguishable clinically from those of systemic lupus.
- Significant autoantibody production is present.
- It occurs predominantly in females in the third or fourth decade of life.
- Typical cutaneous lesion appear as red patches in sun-exposed area, such as face, extremities, these lesions expand by peripheral extension and are usually disk-shaped.

Signs
Discoid lupus erythematosus well-defined red plaques with an adherent scale and follicular plugging which may result in scarring and post-inflammatory hyperpigmentation

TREATMENT
The oral ulcerations of SLE are transient, occurring with acute lupus flares. Symptomatic lesions can be treated with high-potency topical corticosteroids or intralesional steroid injections.

Dental Management
The dental management of the lupus patient should take into account the complex pathologic manifestations of the disease, including oral aspects and complications of immunosuppressive treatment.

Risk of Infection
Daily treatment with higher doses of prednisone (over 7.5– 10 mg/day) or other glucocorticoids, treatment with high doses of cyclophosphamide, and high disease activity are risk factors for infection in SLE patients. Impaired immune function that is part of this disease is also felt to contribute to their increased susceptibility to infection.
A baseline complete blood count should be obtained before dental treatment of SLE patients, as leukopenia, neutropenia, and/ or thrombocytopenia can occur. If possible, elective oral surgical procedures with the potential for bacteremia should be delayed until the absolute neutrophil count is over 1000 cells/mm3, as neutropenia may be transient and respond to treatment with glucocorticoids.

Risk of Bleeding
Traditionally, platelet transfusions have been recommended in surgical patients with platelet counts below 50,000 per mm3.

Adrenal Suppression/Secondary Adrenal Insufficiency
The surgical duration of an oral surgery procedure, the use of general anesthesia, the presence of infection, whether or not additional glucocorticoids are administered to reduce postoperative swelling, and the underlying health of the patient should be considered when deciding if it is necessary to prescribe supplemental glucocorticoids.

Oral Complications
SLE can be found in conjunction with Sjögren's syndrome, which is usually termed secondary Sjögren's syndrome. Sjögren's syndrome increases the risk of caries and other oral complications, which should be managed accordingly.

Scleroderma

Describes a group of clinical disorders characterized by thickening and fibrosis of the skin. The generalized form, systemic sclerosis, is a multisystem connective tissue disease in which the fibrosis extends to the internal organs, including the heart, lungs, kidney, and gastrointestinal tract. There are two main forms, **systemic sclerosis (SSc) and localized sclerodema**.

SSc is further divided into **limited cutaneous scleroderma** (previously called CREST syndrome for calcinosis cutis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) and **diffuse cutaneous scleroderma**.

Patients with limited scleroderma often have a long history of Raynaud's phenomenon before the appearance of other symptoms. They have skin thickening limited to hands and frequently have problems with digital ulcers and esophageal dysmotility.

Diffuse scleroderma patients have a more acute onset, with constitutional symptoms, arthritis, carpal tunnel syndrome, and marked swelling of the hands and legs. They also characteristically develop widespread skin thickening (progressing from the fingers to the trunk), internal organ involvement (including gastrointestinal and pulmonary fibrosis), and potentially life-threatening cardiac and renal failure. Other possible variants are overlap syndromes with SLE, Sjögren's syndrome, RA, and dermatomyositis.

Localized scleroderma refers to scleroderma primarily involving the skin, with minimal systemic features. There are two major types of localized scleroderma: linear scleroderma and morphea.

Linear scleroderma is characterized by a band of sclerotic induration and hyperpigmentation occurring on one limb or side of the face.

Morphea is characterized by small violaceous skin patches or larger skin patches that indurate and lose hair and sweat gland function.

ETIOLOGY AND PATHOGENESIS

The etiology of SSc is unclear, but the pathogenesis is characterized by vascular damage and an accumulation of collagen and other extracellular matrix components at involved sites.

CLINICAL MANIFESTATIONS

PSS sclerosis is a chronic multisystem disorder characterized by intense fibrosis involving the skin, vasculature, synovium, skeletal muscles, and internal organs. The following is an overview of frequently encountered clinical manifestations.

Raynaud's Phenomenon. Raynaud's phenomenon, a paroxysmal vasospasm of the fingers that results in a change in the

colorof the fingertips as a response to cold or emotion, is the most common finding of PSS.

Cutaneous Manifestations. The thickening of the skin of PSS patients always begins in the fingers. Early skin changes, starting with pitting edema, often involve the whole

hand and the extremities. In several months, the edema is replaced by a tightening and hardening of the skin, which results in difficulty in moving the affected parts.

Musculoskeletal Manifestations. Polyarthralgias and morning stiffness affecting both small and large joints are frequent in patients with scleroderma. Inflammatory joint pain with markedly swollen fingers often appears to be true synovitis and can lead to the premature diagnosis of rheumatoid arthritis.

Gastrointestinal Manifestations. Distal esophageal motor dysfunction is the most frequent gastrointestinal finding; it results from weakness and in coordination of esophageal smooth muscle and leads to distal dysphagia. Intestinal fibrosis leading to severe intestinal malabsorption can also occur.

Cardiac Manifestations. *Patchy fibrosis* is a term used to describe the myocardial lesions associated with SSc. Hypertension, dysrhythmias, conduction disturbances, and left ventricular hypertrophy can develop.

Pulmonary Manifestations. Pulmonary interstitial fibrosis is now the most frequent cause of death in patients with scleroderma since renal disease has become a treatable complication.

Renal Manifestations. Until recently, renal involvement was the most dreaded and deadly complication of scleroderma. The use of high-dose corticosteroids for the treatment of scleroderma has been implicated in precipitating renal crisis in some patients.

Laboratory Evaluation and Diagnosis

The 2013 criteria include and apply various weights to the skin thickening, pulmonary manifestations, Raynaud's syndrome, telangiectases, and laboratory abnormalities (anticentromere, antitopoisomerase I and anti-RNA polymerase III).
Circulating antinuclear autoantibodies are present in >90% of scleroderma patients.
anticentromere, antitopoisomerase I and anti-RNA polymerase III are highly specific for the disease.

TREATMENT

The treatment of PSS depends on the extent and severity of skin and organ involvement. D-penicillamin has shown promise in the management of PSS by decreasing both skin thickening and organ involvement.

Oral Manifestations

The clinical signs of scleroderma of the mouth and jaws are consistent with findings elsewhere in the body. The lips become rigid, and the oral aperture narrows considerably. Skin folds are lost around the mouth, giving a masklike appearance to the face. The tongue can also become hard and rigid, making speaking and swallowing difficult.

Involvement of the esophagus causes dysphagia. Oral telangiectasia is equally prevalent in both limited and diffuse forms of PSS and is most commonly observed on the hard palate and the lips. When the soft tissues around the temporomandibular joint are affected, they restrict movement of the mandible, causing pseudoankylosis.

The linear form of localized scleroderma may involve the face as well as underlying bone and teeth. Dental radiographic findings have been reported and widely described; these classic findings (which include uniform thickening of the periodontal membrane, especially around the posterior teeth) are found in less than 10% of patients.

Other characteristic radiographic findings include calcinosis of the soft tissues around the jaws.The areas of calcinosis will be detected by dental radiography and may be misinterpreted as radiographic intrabony lesions. A thorough clinical examination will demonstrate that the calcifications are present in the soft tissue.

Patients may also have oral disease secondary to drug therapy or xerostomia. Gingival hyperplasia can result from the use of calcium channel blockers; pemphigus, blood dyscrasias, or lichenoid reactions may result from penicillamine use.

Xerostomia results in an increased susceptibility to dental caries, *Candida* infections, and periodontal disease.

DENTAL MANAGEMENT

The most common problem in the dental treatment of scleroderma patients is the physical limitation caused by the narrowing of the oral aperture and rigidity of the tongue. Procedures such as molar endodontics, prosthetics, and restorative procedures in the posterior portions of the mouth become difficult, and the dental treatment plan may sometimes need to be altered because of the physical problem of access. The oral opening may be increased an average of 5 mm by stretching exercises. One particularly effective technique is the use of an increasing number of tongue blades between the posterior teeth to stretch the facial tissues. In addition, mechanical devices that assist the patient in performing the stretching exercises are available. If these approaches are insufficient, a bilateral commissurotomy may be necessary. When treating a patient with diffuse scleroderma, the extent of the heart, lung, or kidney involvement should be considered, and appropriate alterations should be made before, during, and after treatment. Patients with extensive resorption of the angle of the mandible are at risk for developing pathologic fractures from minor trauma, including dental extractions. Patients with Sjögren's syndrome should have daily fluoride treatments and make frequent visits to the oral hygienist.

Rheumatoid Arthritis

RA is a disease characterized by symmetrical, inflammatory arthritis of small and large joints affect up to 2% of the population in the United States over the age of 60 years, with a higher prevalence in women.

SUBTYPES

Juvenile arthritis (JA) is a term to describe any arthritis in children. A subset, juvenile idiopathic arthritis (JIA) includes those children with chronic arthritis. Some clinicians refer to this subset as juvenile RA.

In general, symptoms of JIA include joint pain, swelling, tenderness, warmth, and stiffness for at least 6 weeks without another cause. Similar to RA in adults, these children may have severe joint and organ damage.

There are seven classifications of JIA: systemic arthritis, oligoarthritis, polyarthritis—rheumatoid factor (RF) negative, polyarthritis—RF positive, psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis. Felty's syndrome is characterized by neutropenia and splenomegaly in conjunction with RA. These patients have additional susceptibilities to bacterial infection if neutropenia is severe.

ETIOLOGY

The pathogenesis of RA is unknown, but it appears to be multifactorial, involving genetic,immune, and infectious etiologies.

CLINICAL MANIFESTATIONS

RA is a symmetric polyarthritis often involving the proximal interphalangeal joints of the fingers and metacarpophalangeal joints of the hands. ; the wrists, elbows, knees, and ankles also can be affected. In some patients, all joints may be involved, including the TMJ and the cricoarytenoid joint of the larynx. Affected joints develop redness, swelling, and warmth, with eventual atrophy of the muscle around the involved area. Cervical spine disease may cause C1–C2 subluxation and spinal cord compression. One long-term complication of RA is a marked increase in cardiovascular disease.

Oral Manifestations

The treatment of RA can cause oral manifestations. The long-term use of methotrexate and other antirheumatic agents such as D-penicillamine and NSAIDs can cause stomatitis. Cyclosporine may cause gingival overgrowth. Direct effects of the disease are also seen. Patients with long-standing active RA have an increased incidence of periodontal disease, including loss of alveolar bone and teeth. Although the increased dental and periodontal disease may be chiefly related to a decreased ability to maintain proper oral hygiene. Sjögren's syndrome is a common complication of RA.

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DIAGNOSIS AND LABORATORY EVALUATION

The initial diagnosis of RA is made primarily by observing clinical features. As with many autoimmune diseases, a list of diagnostic criteria is used to evaluate patients.

Rheumatoid arthritis: add score A through D; a score of ≥6 of 10 is needed for classification of a patient as having definite rheumatoid arthritis

Classification	Score
A. Joint involvement	
• 1 large joint (shoulders, elbows, hips, knees, ankles)	0
• 2–10 large joints	1
• 1–3 small joints (with or without large joints)	2
• 4–10 small joints (with or without large joints)	3
• >10 joints (at least one small joint)	5
B. Serology (at least 1 test result is needed for classification)	
• Negative rheumatoid factor (RF) and negative anticitrullinated protein antibody (ACPA)	0
• Low-positive RF or low-positive ACPA	2
• High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)	
• Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
• Abnormal CRP or abnormal ESR	1
D. Duration of symptoms	
• <6 weeks	0
• ≥6 weeks	1

DENTAL MANAGEMENT

The most common complication that affects dental treatment relates to the toxicity of the drugs used to treat RA. It is imperative that the dentist knows the drugs the patient is currently taking and their possible side effects and interactions with other drugs. The most common adverse effects of NSAIDs involve the gastrointestinal (GI) tract and the kidneys. In addition, many patients take aspirin at dosages approaching 5 g per day or take an equivalent dosage of NSAIDs. These drugs affect platelet function, causing a prolongation of the bleeding time and possible hemorrhage after surgery. Patients with severe RA who have had joints surgically replaced with prosthetic joints may require prophylactic antibiotic therapy before invasive dental procedures.

Patients with cervical spine disease may have C1–C2 subluxation and spinal cord compression. Hyperextension of the neck must be avoided. Prolonged morning stiffness is common in RA, so later morning appointments may be best for patients. Patients with severe RA who have prosthetic joints may require prophylactic antibiotic therapy beforeinvasive dental procedures, though the evidence for the practice is very limited. Patients with Sjögren's syndrome may require additional instruction in personal oral care and instruction on diet and dietary modifications.

The dentist should determine if the RA patient has a form of the disease that affects the bone marrow (such as Felty's syndrome) since such patients have an increased risk of developing infection due to neutropenia and hemorrhage secondary to thrombocytopenia.

T.M.J involvement

R.A. is the important inflammatory disease of T.M.J (T.M.J involvement ranges from 40 to 80%).

The clinical features of T.M.J involvements are:

• Limitation in movement of mandible.
• T.M.Js bilaterally involved, tenderness, swelling over the joint area
• Morning stiffness
• Deviation of mandible on opening
• Ankylosis of the joint with facial asymmetry

Management :

• On diagnosis the clinical radiograph shows flatting of the condyle, loss of contour and irregularity of the articular surface.
• Joint space may be widened (acute phases) but later narrowed.
• Underlying bone may be osteoporotic.

Treatment of TMJ disorders:

• By giving of non-steroidal anti-inflammatory drugs.
• Any abnormalities in occlusion should be corrected.
• In severe symptoms (intra-articular steroids should be considered).
• Surgical treatment (placement of prosthetic joints) is indicated in sever functional impairment or pain).
• Use of a flat plane occlusal appliance may be helpful (if Para functional habits are increasing the symptoms).

Reference: Burket's Oral Medicine **,** 12th edition ,2015

Neuromuscular Diseases

Definition

Are diseases that affect both nerve and muscle tissue .Neuromuscular disorders represent a spectrum of nerve related diseases and conditions that affect the body's voluntary muscles cause weakening of muscles in the body because of interrupted communication between the nervous system and the muscles it controls. Typically, these diseases can be managed to improve quality and length of life, but are incurable.

Classification of neuromuscular disorders:

- CEREBROVASCULAR DISEASE
- MULTIPLE SCLEROSIS
- ALZHEIMER'S DISEASE
- SEIZURE DISORDERS
- PARKINSON DISEASE
- MYASTHENIA GRAVIS

Cerebrovascular Disease

Cerebrovascular disease refers to disorders that result in damage to the cerebral blood vessels leading to impaired cerebral circulation**.**

A cerebrovascular accident (CVA), or complete stroke, is a sudden impairment in cerebral circulation resulting in death or a focal neurologic deficit lasting more than 24 hours.

Transient ischemic attack (TIA), defined as a reversible, acute, short-duration, focal neurologic deficit ("mini stroke") resulting from transient (reversible within 24 hours) and localized cerebral ischemia;

Reversible ischemic neurologic defect (RIND), defined as a reversible, acute, focal neurologic deficit due to transient and localized cerebral ischemia but resulting in neurologic deficits that last more than 24 hours; and

Stroke in evolution, defined as progressive worsening of stroke symptoms.

Clinical Manifestations

The clinical manifestations of stroke vary depending on the size and location of the affected brain region. The most common signs and symptoms include sensory and motor deficits, changes (paresis) in extra ocular muscles and eye movements, visual defects, sudden headache, altered mental status, dizziness, nausea, seizures, impaired speech or hearing, and neurocognitive deficits such as impaired memory, reasoning, and concentration.

General symptoms following stroke:-

- variable motor paralysis
- sensory loss
- visual difficulties
- speech impairment

Types of cerebrovascular diseases

Cerebrovascular Accident (CVA) or Stroke either due to:-

1- Atherosclerosis(85%) leading to cerebral ischemia and infarction result from ischemia due to atherosclerotic disease, thromboembolic events, and occlusion of cerebral blood vessels, with neurologic deficits related to the loss of neural function in tissues distal to the event.

2- Cerebral hemorrhage (15%) result from hemorrhagic events leading to infarction, most often related to hypertension, trauma, substance abuse, or aneurysmal rupture.

Three major types of ischemic stroke syndromes have been described:

1- small vessel (lacunar),

2- large vessel (cerebral infarction)

3- Brainstem stroke

Lacunar strokes:- result from obstruction of the small (<5 mm diameter) penetrating arterioles.

Age and uncontrolled hypertension are the greatest predisposing factors. Symptoms usually include unilateral motor or sensory deficit without visual field changes or disturbances of consciousness or language. The prognosis for recovery from lacunar infarction is fair to good, with partial or complete resolution usually occurring over four to six weeks.

Cerebral infarction (large vessel):- is characterized by extensive downstream ischemia, usually due to a thromboembolic event along the distribution of the internal carotid artery and cerebral arteries. Emboli often originate from the heart after acute myocardial infarction or in hyperdynamic conditions such as chronic atrial fibrillation.

Hypertension is an important risk factor in the development of thrombosis, particularly at the carotid bifurcation, and treatment of severe hypertension is essential for the prevention of stroke. High level brain functions are affected, and the prognosis is poor.

Brainstem infarction: - results from occlusion of small or large vessels supplying the brainstem, resulting in variable deficits ranging from motor and sensory deficits to death when respiratory centers are affected.

D.D. of CVA

Seizures, hypoglycemia, intracranial tumors, trauma, infection, encephalitis, multiple sclerosis (MS), and prolonged migrainous Aura.

Diagnosis

Stroke should be considered whenever a patient experiences the clinical manifestations. Laboratory evaluation of the stroke patient includes compete blood count, comprehensive metabolic panel, urinalysis, coagulation profile, and, when indicated, blood culture, echocardiography, and lumbar puncture.

Treatment

The outcome of stroke and related TIAs and RIND is significantly affected by the timeliness of treatment. Early intervention is critical to prevention, treatment, and recovery.

TIAs and RIND are treated by reduction in hypertension (lifestyle changes such as diet, exercise, smoking cessation, and stress reduction; medical therapy for hypertension; and anticoagulant or antiplatelet medications).

Once intracranial hemorrhage has been excluded as the source of acute cerebral ischemia, thrombolysis with intravenous tissue plasminogen activator (t-PA) can improve reperfusion, minimize infarction, and reduce disability.

After a completed stroke, treatment focuses on:

1. The prevention of further neurological damage, through the reduction of underlying risk factors.

2. Rehabilitation procedures, including speech and physical therapy.

3. An intracranial hemorrhage should also be treated as a medical emergency of airway maintenance and requires the transfer of the patient to an intensive care unit with close monitoring.

4. The surgical treatment of a hemorrhaging aneurysm consists of closing off the blood vessels that supply the area and removing the abnormality.

Oral Health Considerations

Following stroke, patients may experience several oral problems, including masticatory and facial muscle paralysis, impaired or lost touch and taste sensation, diminished protective gag reflex, and dysphagia. These problems can lead to impairment of food intake, poor nutrition, and weight loss due to diminished taste satisfaction, chewing capacity, and swallowing; choking; and gagging. Diminished motor function of masticatory and facial muscles may also reduce food clearance from the mouth and teeth and alone or combined with the presence of diminished dexterity of the arms or hands may adversely affect oral hygiene and increase the risk for caries and periodontal disease. Creative and effective use of adjuvant oral hygiene techniques

and devices (oral antimicrobial rinse, oral irrigation, floss holders) represents an important approach to oral health promotion and disease prevention, supported by frequent recall examination and prophylaxis. Replacement of missing teeth and adequacy of removable and fixed prostheses are essential to effective chewing and diet.

Important points of Oral Health Considerations:-

1- As the first line of medical management of stroke patients is often on anticoagulant therapy, the patient may have a predisposition to excessive bleeding. It may be necessary to confer with the patient's physician to obtain current coagulation values (PT, INR) so as to ensure that the patient is stable for more invasive dental treatment.

2-Xerostomia is a common side effect of the medications used in the management of cerebrovascular disease. Patients can then be susceptible to a higher caries rate.

3- Stroke patients have physical disabilities, which can affect the orofacial area.

4- Patients with weakness in the muscles of the orofacial area may have poor control of oral secretions, a reduced gag reflex, and changes in their ability to masticate, leading to poor nutrition.

5- Patients with apraxia affecting the orofacial region may have impaired voluntary movements, such as protruding the tongue, expectorating.

6- Careful history taking, checking of blood pressure prior to treatment, avoidance of lengthy appointments.

Multiple Sclerosis

MS is characterized by multiple areas of central nervous system (CNS) white matter inflammation, demyelination, and gliosis (scarring). Myelin is critical for propagation of nerve impulses, and when it is destroyed in MS, slowing and/or complete block of impulse propagation are manifested by abnormal muscular and neurologic signs and symptoms, associated with the myelination of axons within the central nervous system.

The disease occurs more frequently among women. The average age of onset is during the fourth decade of life, but MS may occur at any age. The disease presents in the form of recurrent attacks

Etiology

1- An immunologic (autoimmune disease) basis is strongly suggested by the presence of activated T lymphocytes and autoantibodies to glycoproteins detected in MS lesions.

2- Environmental exposure in MS , and two common infectious agents to be implicated in the pathogenesis of this disease are Epstein–Barr virus and human herpesvirus 6. Other viruses that have been implicated in the pathogenesis of MS include measles, mumps, rubella, parainfluenza, vaccin, and human T-lymphotropic virus

3- increased antibody titers against measles virus, rubella virus, mumps virus, Epstein-Barr virus, herpes simplex viruses 1 and 2, and human herpes virus 6 (HHV-6) have been found in the cerebrospinal fluid and serum.

4- Genetic influences also appear to play a significant role in the development of MS.

Clinical Manifestations

The most common symptoms following an acute exacerbation include impairment of vision, muscular incoordination, and bladder dysfunction.

1. The clinical signs and symptoms of MS depend on the site of the demyelinating lesion of the CNS involved, and frequently affected areas include the optic chiasm, brainstem, cerebellum, and spinal cord.

2. More than 60% of individuals with MS have visual disturbances caused by demyelinating lesions of the second cranial nerve. The loss of vision usually occurs over a period of several days, with partial recovery within 1 month.

3. Other ophthalmic symptoms include ―color blindness‖ and diplopia caused by involvement of the third, fourth, and sixth cranial nerves.

4. Uhthoff's sign, found in MS, is characterized by rapid vision loss following a body temperature increase that is associated with strenuous exercise.

5. MS patients frequently complain of electric shock–like sensations that are evoked by neck flexion and radiate down the back and into the legs. This is referred to as **Lhermitte's symptom** and is generally self-limiting but may persist for Years

6. Weakness or paresthesia of the extremities, with an increase in the deep tendon reflexes, is another common early finding in cases of MS.

7. Bladder dysfunction, euphoria, ataxia, vertigo, and generalized incoordination

8. The majorities of cases of MS are chronic and are characterized by exacerbations and remissions over a period of many years.

9. During acute episodes, severe neurologic involvement is evident. This slowly resolves, but some permanent neurologic involvement remains after each episode.

Diagnosis

1. Clinical and is based on the age of the patient, the presence of neurologic signs that cannot be explained by a single lesion, the progressive nature of the disease, and a history of exacerbations and remissions.
2. There are no definitive laboratory tests for MS, but demyelinating changes can be seen on (MRI) in more than 90% of cases. MRI demonstrates characteristic abnormalities of MS in >95% of patients. MS plaques are visible as hyperintense focal areas.
3. Evoked potentials measure CNS electrical potentials, and abnormalities are detected in up to 90% of patients with MS.
4. CSF is often analyzed in patients suspected of having MS, and positive findings include an increase in total protein and mononuclear white blood cells.

Treatment

1- High doses of **intravenous corticosteroids** may arrest the progress of MS; about 85% of patients with relapsing-remitting MS show objective signs of neurologic improvement during treatment with intravenous corticosteroids. Glucocorticoids are used to manage both initial attacks and acute exacerbations of MS. Intravenous methylprednisolone is typically administered at a dose between 500 and 1000 mg/d for three to five days to reduce the severity and length of an attacks

2- Long-term treatment with immunosuppressants may reduce the frequency of relapse in patients with MS. Azathioprine is probably the safest drug in this category and has reduced relapse to 70% of study patients in 3 years. Administration of methotrexate appears to be the best therapy for slowing deterioration in patients with chronic progressive MS.
3- The use of interferon-γ-1b and -1a has shown promise; both have been shown to reduce clinical attacks and lesions

Oral Health Considerations

Individuals may present with signs and symptoms of MS.

1- Trigeminal neuralgia (TGN), which is characterized by electric shock–like pain, may be an initial manifestation of MS in up to 3% of cases. MS-related TGN is similar to idiopathic TGN. Features of MS-related TGN include possible absence of trigger zones and continuous pain with lower intensity.
2- Medications often used to manage TGN are similar to those used for treatment of idiopathic TGN.
3- Patients with MS may also demonstrate neuropathy of the maxillary (V2) and mandibular branches (V3) of the trigeminal nerve, which may include burning, tingling, and/ or reduced sensation.
4- Neuropathy of the mental nerve can cause numbness of the lower lip and chin.
5- **Myokymia** may be seen in patients with MS and consists of rapid, flickering contractions of the facial musculature secondary to MS lesions affecting the facial nerve.
6- Facial weakness and paralysis may also be evident in MS patients.
7- Dysarthria that results in a scanning speech pattern is often seen in patients with MS.
8- Temporomandibular disorder and headache.
Evaluate cranial nerve function, if cranial nerve abnormalities are detected, the individual should be referred to a neurologist for further evaluation.
It is recommended to avoid elective dental treatment in MS patients during acute exacerbations of the disease due to limited mobility and possible airway compromise.
Patients with significant dysfunction may require dental treatment in an operating room under general anesthesia due to the inability to tolerate treatment in an outpatient setting.
In addition, electric toothbrushes and oral hygiene products with larger handles may be necessary for completing oral hygiene in patients with significant motor impairment. be aware of possible interactions of these medications with those commonly used and prescribed in dentistry, as well as oral and systemic side effects of these agents.

ALZHEIMER'S DISEASE (AD)

Dementia is defined as an acquired deterioration in cognitive abilities that impairs the successful performance of activities of daily living. Memory is the most com-

mon cognitive ability lost with dementia; other mental faculties affected include problem-solving skills, judgment, visuospatial ability, and language.
The genetic basis of AD has been studied extensively, and specific genetic mutations have been implicated in both the familial and sporadic forms of the disease. Familial AD is an autosomal dominant disorder with onset typically prior to age 65 year.

Clinical Manifestations

AD is a slowly progressive disorder represented by a continuum recognizes three stages of AD: (1) preclinical AD, (2) mild cognitive impairment due to AD, and (3) dementia due to AD.
Preclinical AD occurs before changes in cognition, and everyday activities are observed and primarily used for research purposes.
Cognitive impairment (CI) due to AD is characterized by mild changes in memory and other cognitive abilities that are noticeable to patients and families but are not sufficient to interfere with day to-day activities.
Dementia due to AD is characterized by changes in two or more aspects of cognition and behavior that interfere with the ability to function in everyday life. The initial signs of AD involve retrograde amnesia from progressive declines in episodic memory. This may initially go unrecognized or be viewed; however, as the disease progresses, memory loss begins to affect performance of daily activities, including following instructions, driving, and normal decision making.
As AD progresses, the individual is often unable to work, gets confused and lost easily, and may require daily supervision. Also language impairment, loss of abstract reasoning and skills. Advanced AD is characterized by loss of cognitive abilities, agitation, delusions, and psychotic behavior.
Patients may develop muscle rigidity associated with gait disturbances and often wander aimlessly.
In end-stage AD, patients often become rigid, mute, incontinent, and bedridden. Help is needed for basic functions, such as eating and dressing, and patients may experience generalized seizure activity. Death often results from malnutrition, heart disease, pulmonary emboli, or secondary infections.

Diagnosis

Diagnosis of preclinical AD primarily utilizes biomarker assessment, including markers of Aβ protein deposition in the brain, and markers of downstream neurodegeneration (elevated CSF tau protein and brain atrophy on MRI.
Clinical diagnosis of AD is based on an individual's medical history together with the clinical and neurologic examination findings.

Criteria include a history of progressive deterioration in cognitive ability in the absence of other known neurologic or medical problems.
Possible AD refers to those who meet the criteria for dementia but have another illness that may contribute to the neurologic status, such as:- hypothyroidism or cerebrovascular disease, vitamin deficiency, depression, delerium, side effects of drugs and toxicity and excessive use of alcohol .
Diagnostic analysis of CSF may show a slight increase in tau protein and a lower concentration of Aβ peptide compared with healthy individuals or those with other dementias.
Electroencephalographic (EEG) studies typically demonstrate generalized slowing without focal features. Neuroimaging is important in evaluating suspected AD to exclude alternative causes of dementia, such as cerebrovascular disease, subdural hematoma, or brain tumor.
MRI and CT typically reveal dilatation of the lateral ventricles and widening of the cortical sulci, particularly in the temporal regions.
Volumetric MRI uniformly demonstrates shrinkage in vulnerable brain regions (brain atrophy).

Treatment

There is no cure for AD, and therapy is aimed at slowing the progression of the disease. **Cholinesterase inhibitors** are approved to treat mild to moderate cases of AD and are considered the standard of care.
Memantine, a noncompetitive *N*-methyl-d-aspartate receptor antagonist believed to protect neurons from glutamate-mediated excitotoxicity, is used for treatment of moderate to severe AD.
Studies have demonstrated greater cognitive and functional improvement when memantine is used in conjunction with cholinesterase inhibitors compared to monotherapy.
Antidepressants, such as selective serotonin reuptake inhibitors, are commonly used to treat depression, which is often seen in the mild to moderate stages of AD.
Antipsychotic agents are used for those patients who display aggressive behavior and psychosis, especially in the later stages of the disease.
Other agents that have been reported to be of clinical value in the treatment of AD include antioxidants, such as α-tocopherol (vitamin E), cholesterol-lowering drugs, anti-inflammatories, and herbal

Oral Health Considerations

Oral and dental health is a major issue in patients with AD because significant deterioration in oral health status is commonly observed with advancing disease.

Patients with AD appear to be at higher risk for developing coronal and root caries, periodontal infections, temporomandibularn joint abnormalities, and orofacial pain compared to healthy subjects.

Patients with AD should be placed on an aggressive preventive dentistry program, including an oral examination, oral hygiene education, prosthesis adjustment, and a three-month recall.

It is recommended to complete restoration of oral health-care function in the earliest stages of AD because the patient's ability to cooperate diminishes as cognitive function declines. Time-consuming and complex dental treatment should be avoided in persons with severe AD.

Medications used to treat AD can cause a variety of orofacial reactions and potentially interact with drugs commonly used in dentistry. Cholinesterase inhibitors may cause sialorrhea, whereas antidepressants and antipsychotics are often associated with xerostomia. In addition, dysgeusia and stomatitis have been reported with use of antipsychotic agents. Antimicrobials, such as clarithromycin, erythromycin, and ketoconazole, may significantly impair the metabolism of galantamine, resulting in central or peripheral cholinergic effects.

Anticholinesterases may increase the possibility of gastrointestinal irritation and bleeding when used concomitantly with NSAIDs.

Local anesthetics with adrenergic vasoconstrictors should be used with caution in AD patients taking tricyclic antidepressants due to potential risk of cardiovascular effects, such as hypertensive events or dysrhythmias.

Parkinsonism

Is a neurodegenerative disorder characterized by:

1- Rigidity 2- tremors, 3- bradykinesis, and 4-impaired postural reflexes (postural instability).

The most common form of parkinsonism is Parksinson's disease (paralysis agitans), but parkinsonism is seen in a variety of disorders such as postencephalitic parkinsonism, and post-traumatic parkinsonism following closed head injury.

Many of the signs of Parkinson's disease are found in the head and neck. The typical ―masklike‖ facial appearance with infrequent blinking and lack of expression is caused by bradykinesis.

The muscle rigidity also causes difficulty in swallowing, resulting in saliva drooling.

Speech affected because of the lack of muscle control, and mandibular tremor results in masticatory difficulties, especially in those with removable dental appliances.

Abnormalities in oral behavior, such as purposeless chewing, grinding, and sucking movements, are also well recognized in patients with Parkinson's disease and make dental treatment especially difficult.

Treatment

Drug treatment is often not required early in the course of Parkinsonism.

1- Patients with mild symptoms but no disability may be helped by amantadine. This drug improves all of the clinical features of Parkinsonism.

2- Anticholinergics are more helpful in alleviating tremor and rigidity than in alleviating bradykinesia, but these drugs have many side effects.

3- Levodopa, a dopamine precursor that can cross the blood-brain barrier, improves all the major features of Parkinsonism.

Bell's palsy

Bell's palsy is recognized as a unilateral paresis of the facial nerve. The dysfunction has been attributed to an inflammatory reaction involving the facial nerve.

A relationship has been demonstrated between Bell's palsy and the isolation of herpes simplex virus 1 from nerve tissues.

Bell's palsy begins with slight pain around one ear, followed by an abrupt paralysis of the muscles on that side of the face. The eye on the affected side stays open, the corner of the mouth drops, and there is drooling.

As a result of masseter weakness, food is retained in both the upper and lower buccal and labial folds. The facial expression changes remarkably, and the creases of the forehead are flattened.

Due to impaired blinking, corneal ulcerations from foreign bodies can occur.

Causes

Although the exact reason Bell's palsy occurs isn't clear, it's often linked to e xposure to a viral infection. Viruses that have been linked to Bell's palsy include the virus that causes:

- Cold sores and genital herpes (herpes simplex)
- Chickenpox and shingles (herpes zoster)
- Mononucleosis (Epstein Barr)
- Cytomegalovirus infections
- Respir atory illnesses (adenovirus)
- German measles (rubella)
- Mumps (mumps virus)
- Flu (influenza B)

Symptoms

Signs and symptoms of Bell's palsy come on suddenly and may include:
1. Rapid onset of mild weakness to total paralysis on one side of face occurring within hours to days
2. Facial droop and difficulty making facial expressions, such as closing eye or smiling
3. Drooling
4. Pain around the jaw or in or behind ear on the affected side
5. Increased sensitivity to sound on the affected side
6. Headache
7. A decrease in ability to taste
8. Changes in the amount of tears and saliva
9. In rare cases, Bell's palsy can affect the nerves on both sides of face

Diagnosis

There's no specific test for Bell's palsy. Look at face and ask to move facial muscles by closing eyes, lifting brow, showing teeth and frowning, among other movements.

Other conditions such as a stroke, infections, Lyme disease and tumors can also cause facial muscle weakness, mimicking Bell's palsy, may recommend other tests, including:

Electromyography (EMG). This test This test can confirm the presence of nerve damage and determine its can confirm the presence of nerve damage and determine its severity. An EMG measures the electrical activity of a muscle in response to stimulation and the nature severity. An EMG measures the electrical activity of a muscle in response to stimulation and the nature and speed of the conduction of electrical impulses along a nerve.and speed of the conduction of electrical impulses along a nerve.

Imaging scans.

Imaging scans. Magnetic resMagnetic resonance imaging (MRI) or computerized tomography (CT) may be needed onance imaging (MRI) or computerized tomography (CT) may be needed on occasion to rule out other possible sources of pressure on the facial nerve, such as a tumor or skull on occasion to rule out other possible sources of pressure on the facial nerve, such as a tumor or skull fracture

Treatment

Commonly used medications to treat Bell's palsy include:

Corticosteroids, such as prednisone, are powerful anti-inflammatory agents. If they can reduce the swelling of the facial nerve, it will fit more comfortably within the

bony corridor that surrounds it. Corticosteroids may work best if they're started within several days of when symptoms started.

Antiviral drugs. The role of antivirals remains unsettled. Antivirals alone have shown no benefit compared with placebo. Antivirals added to steroids .However, despite this, valacyclovir (Valtrex) is sometimes given in combination with prednisone in people with severe facial palsy.

Physical therapy

Paralyzed muscles can shrink and shorten, causing permanent contractures. A physical therapy by massage and exercise of facial muscles to help prevent this from occurring.

Surgery

In the past, decompression surgery was used to relieve the pressure on the facial nerve by opening the bony passage that the nerve passes through. Today, decompression surgery isn't recommended. Facial nerve injury and permanent hearing loss are possible risks associated with this surgery.

Myasthenia gravis

Is a disease characterized by progressive muscular weakness on exertion, secondary to a disorder at the neuromuscular junction.

It is autoimmune disease ,autoantibodies combine with and may destroy the acetylcholine receptor sites at the neuromuscular junction, preventing the transmission of nerve impulses to the muscle .The initial signs of this disease commonly occur in areas innervated by the cranial nerves (frequently, the eye muscles).

Patients present with

1. ptosis, diplopia
2. difficulty in chewing or swallowing
3. respiratory difficulties
4. limb weakness
5. or some combination of these problems.

Oral and facial signs

1. The facial muscles of expression are involved
2. Tongue edema making eating difficult for patients
3. difficulty in chewing; these patients will be unable to finish chewing a bolus of food because of the easy fatigability of the muscles

Treatment

1. Anticholinesterase drugs such as neostigmine and pyridostigmine bromide
2. thymectomy

3. Long-term cortico-steroids and immunosuppressive drugs are necessary.

Dental management

1-A respiratory crisis may develop from the disease itself or from over medication.

2- Dental treatment should be performed in a hospital where endotracheal intubation

3-The airway must be kept clear because aspiration may occur in patients whose swallowing muscles are involved.

4-Adequate suction and the use of a rubber dam are aids in these cases.

5-The dentist should avoid prescribing drugs that may affect the neuromuscular junction, such as: Narcotics, tranquilizers, and barbiturates.

Certain antibiotics, including tetracycline, streptomycin, sulfonamides, and clindamycin, may reduce neuromuscular activity and should be avoided.

SEIZURE DISORDERS & Epilepsy

A seizure is a paroxysmal event due to abnormal, excessive, hypersynchronous discharges from neuronal aggregates in the CNS. The term *epilepsy* describes a group of neurologic disorders characterized by recurrent seizure activity.

1- Focal, 2- generalized and 3- unknown seizures are currently the three major categories of seizure activity used in clinical practice.

1-The focal seizure category (Partial Seizures)

Includes partial seizures; this type of seizure activity originates within networks limited to one hemisphere and clinical manifestations of these seizures depend on the site of origin. Simple partial seizures reflect neuronal discharge from a discrete cortical locus, such as the motor cortex of the frontal lobe, or in subcortical structures, and generally not associated with impaired consciousness.

Simple partial seizures consist of clonic activity, which are rapid jerks that also can be accompanied by somato-sensory phenomena, visual changes/distortions, and auditory, olfactory, and gustatory

2- Generalized seizures arise from both cerebral hemispheres simultaneously and have distinctive clinical features that facilitate diagnosis. The underlying pathophysiology of generalized seizures is attributed to abnormal neuronal excitability.

a- Absence seizures (petit mal) are a type of generalized seizure that is characterized by sudden, brief lapses of consciousness without loss of body tone and may be attributed to abnormal oscillatory rhythms generated during sleep by circuits connecting the thalamus and cortex.

b- **Tonic-clonic (grand mal)** seizures are generalized seizures that present with dramatic clinical features, most notably, tonic contracture and uncoordinated clonic muscular movements.

Other types of generalized seizures include atypical absence, atonic, and myoclonic seizures. 3- Those seizures that cannot be classified as either focal or generalized are termed **unknown seizures**.

Etiology usually varies according to patient,s age.

The most common seizures arising in late infancy and early childhood are febrile seizures without evidence of associated CNS infection; these usually occur between 3 months and 5 years of age and have a peak incidence between 18 and 24 months.

Isolated, non recurrent, generalized seizures among adults are caused by multiple etiologies, including metabolic disturbances, toxins, drug effects, hypotension, hypoglycemia, hyponatremia, uremia, hepatic encephalopathy, drug overdoses, and drug withdrawal.

Cerebrovascular disease may account for approximately 50% of new cases of epilepsy in patients older than 65 years. Other etiologies for epilepsy include degenerative CNS disease, developmental disabilities, and familial/genetic factors. Epilepsy occurs more frequently in individuals who have neurologic-based disabilities, such as cerebral palsy and autism.

Epilepsy

Epilepsy is a condition characterized by abnormal, recurrent, and excessive neuronal discharges precipitated by many different disturbances within the central nervous system.

These aberrant discharges may cause episodes of sensory and motor abnormalities as well as loss of consciousness.

Common causes of epilepsy:

1-Infants are much more likely to suffer from epilepsy after complications at birth, such as anoxia lack of oxygen traumatic brain injury during delivery, intracranial injury, metabolic disorders, abnormal brain development and congenital malformations.

2- Predominant causes in children and adolescents include head trauma and acute or febrile infections, fever, brain tumors, genetic disorders and brain scarring.

3- Young adults with alcohol or drug abuse commonly suffer from generalized seizures after periods of severe abuse.

4- Epilepsy in older adults occurs as a complication of any of the previously mentioned causes but is more often associated with cerebrovascular diseases such as stroke, brain scarring, abnormal brain development, head trauma and brain tumors.

International Classification of Epileptic Seizures

1- Partial (focal) seizures
Simple partial seizures
Complex partial seizures
Partial seizures leading to secondarily generalized seizures
2- Generalized Seizures
Absence seizures (petit mal)
Typical

Atypical

Tonic-clonic seizures (grand mal)

Myoclonic seizures
Clonic seizures
Tonic seizures
Atonic seizures (astatic seizur

Generalized seizures

The majority of generalized seizures are called either:-
1 -tonic-clonic seizures (grand mal).(MOST COMMON TYPE 90% of epileptics experience it alone or in combination with another type of seizure)
2 -absence (petit mal) seizures

Tonic-clonic seizures (A grand mal seizure) :characteristically begins with an aura. The aura may be experienced as epigastric discomfort, as an emotion, or as a hallucination of hearing, vision, or smell.
The aura is followed seconds to minutes later by unconsciousness, or a cry,
then tonic muscle spasms; this rigid phase lasts about 30 seconds. Because of the spasm of the respiratory muscles, the patient does not breathe and becomes cyanotic during this period.
The tonic phase is followed by a clonic phase composed of convulsive jerky movements, incontinence, and tongue biting.

Absence seizures (petit mal):

Is the second most common type of seizure and it occurs without an aura and with few or no clonic or tonic movements.

Absence seizures present almost exclusively in children and frequently disappear during the second decade of life.

Diagnosis:

1. History & physical examination are critical because the diagnosis may based on clinical findings.
2. A complete neurological examination (testing of cranial nerves)
3. Blood studies: complete blood count, mg, calcium , glucose to identify metabolic cause
4. Toxins screen: to identify seizure due to drugs, lumber puncture to exclude any infectious cause
5. Brain imaging: underlying CNS structural abnormalities or pathology
MRI and CT
6. EEG (to classify the seizure & to determine the type of anticonvulsant)

Treatment

Antiepileptic drugs (AEDs)

*phenytoine: long half life,dosed less frequently cause gingival over growth, hirsutism, coarsening of facial featuers

*carbamazepine: hepatotoxicity, leukopenia,aplastic anemia
*Lamotrigine: skin rash
*Valproic acid: treatment of G.tonic clonic,can cause bone marrow suppressison & hepatotoxicity
*Additional drugs as topiramate, gabapentin & oxcarbazepine
*surgical procedures: limited removal of hippocompus & amygdala, temporal lobectomy or hemispherectomy
*Vagus nerve stimulation: placement of an electrode on the left vagal nerve leading to wide spread activation of cortical & sub cortical pathways

Discontinuation of pharmacologic therapy is considered when seizure control has been achieved. The following patient characteristics yield the greatest chance of remaining seizure free after discontinuation of drug therapy:
(1) Complete medical control of seizures for one to five years;
(2) Single seizure type; (3) normal neurologic examination, including intelligence; and (4) a normal EEG.
Many patients are often withdrawn successfully from medication after an interval of two to four years without seizures who meet the above criteria and who clearly understand the risks and benefits.

Patients may use three or more drugs to successfully treat refractory epilepsy; however, up to 30% of patients are resistant to all medical therapies. Surgical procedures may be indicated for these patients.
Deep brain stimulation (DBS) and responsive neurostimulation systems are also currently used for treatment of refractory epilepsy.
Gene therapy is currently being investigated as an alternative treatment modality for epilepsy refractory to standard therapies.

Oral health consideration

* Uncontrolled Patients should be referred to a hospital
*Patient with implanted vagus nerve stimulator do not require antibiotic prophylaxis
*we must avoid any triggers of the patient seizures activity
*Placement of fixed prosthesis is recommended rather than removable prosthesis.
*Patient taking the medication mentioned requires laboratory evaluation prior to dental treatment
*Aspirin& NSAD should be avoided in patient taking valproic acid
*Gingival over growth intraoral lesion & lips enlargement
*Xerostomia:
Reduced salivary flow may result from the use of AEDs, may observe increased dental caries and oral candidiasis in patients using these agents.
Topical fluoride should be considered for patients with seizure disorders who are at increased risk of developing dental caries, and antifungal agents should be prescribed if oral candidiasis develops. Additional oral findings in patients taking AEDs may include stomatitis, glossitis, and ulcerations.

Reference: Burket's Oral Medicine,12th edition ,2015

Pigmented Lesions of the Oral Mucosa

Oral and perioral pigmentation may be physiologic or pathologic in origin. Physiologic pigmentation is typically brown in appearance. However, in the course of disease, the oral mucosa and perioral tissues can assume a variety of discolorations, including brown, blue, gray, and black. Such color changes are often a tributed to the deposition, production, or increased accumulation of various endogenous or exogenous pigmented substances. However, although an area may appear pigmented, the discoloration may not be related to actual pigment but rather to the deposition or accumulation of organic or inorganic substances, including various metals and drug metabolites.

Endogenous Pigmentation

Melanin is found universally in nature. Melanin is the pigment derivative of tyrosine and is synthesized by melanocytes, which typically reside in the basal cell layer of the epithelium. Investigations into normal melanocyte homeostasis have yielded the discovery that keratinocytes actually control melanocytic growth. Yet the mechanisms by which melanocytes are stimulated to undergo cell division remain poorly understood. Their presence in the skin is thought to protect against the damaging effects of actinic irradiation, as well as to act as scavengers in protecting against various cytotoxic intermediates. The role of melanocytes in oral epithelium is not clear.

Overproduction of melanin may be caused by a variety of mechanisms, the most common of which is related to increased sun exposure. However, intraorally, hyperpigmentation is more commonly a consequence of physiologic or idiopathic sources, neoplasia, medication or oral contraceptive use, high serum concentrations of pituitary adrenocorticotropic hormone (ACTH), postinflammatory changes, and genetic or autoimmune disease. Thus, the presence or absence of other systemic signs and symptoms, including cutaneous hyperpigmentation, is of great importance from the standpoint of diagnosing the cause of oral pigmentation. However, if the etiology of the pigment cannot be ascertained, a tissue biopsy is warranted for definitive diagnosis and is especially critical for the diagnosis of focal pigmentation since malignant melanoma can present in a variety of different configurations.

In addition to biopsy and histologic study, various laboratory and clinical tests, including diascopy, radiography, and blood tests, may be necessary for definitive diagnosis of oral pigmentation. Dermascopy, also known as epiluminescence microscopy, is another increasingly employed clinical test that can be useful in the diagnosis of melanocytic lesions.

Focal Melanocytic Pigmentation:

Freckle/Ephelis

The cutaneous freckle, or ephelis, is a commonly occurring, asymptomatic, small (1–3 mm), well-circumscribed, tan- or brown-colored macule that is often seen on the sun-exposed regions of the facial and perioral skin. Ephelides are most commonly observed in light-skinned individuals and are quite prevalent in red- or light blond–haired individuals. Although the pigmentation itself is focal in nature, most patients have multiple freckles. Freckles are thought to be developmental in origin. Ephelides are usually more abundant in number and darker in intensity during childhood and adolescence. Freckles tend to become darker during periods of prolonged sun exposure (spring, summer) and less intense during the autumn and winter months. Yet the increase in pigmentation is solely related to an increase in melanin production without a concomitant increase in the number of melanocytes. With increasing age, the number of ephelides and color intensity tends to diminish. In general, no therapeutic intervention is required.

Oral/Labial Melanotic Macule

The melanotic macule is a unique, benign, pigmented lesion that has no known dermal counterpart. Melanotic macules are the most common oral lesions of melanocytic origin. Although the etiology remains elusive, trauma has been postulated to play a role. Sun exposure is not a precipitating factor. Melanotic macules develop more frequently in females, usually in the lower lip (labial melanotic macule) and gingiva. However, any mucosal site may be affected. Although the lesion may develop at any age, it generally tends to present in adulthood.

Congenital melanotic macules have also been described occurring primarily in the tongue. Overall, melanotic macules tend to be small (<1 cm), well circumscribed, oval or irregular in outline and often uniformly pigmented. Once the lesion reaches a certain size, it does not tend to enlarge further. Unlike an ephelis, a melanotic macule does not become darker with continued sun exposure. Overall, the oral melanotic macule is a relatively innocuous lesion, does not represent a melanocytic proliferation, and does not generally recur following surgical removal.

Oral Melanoacanthoma

Oral melanoacanthoma is another unusual, benign, melanocytic lesion that is unique to the mucosal tissues. Oral melanoacanthoma is an innocuous melanocytic lesion that may spontaneously resolve, with or without surgical intervention. Most patients report a rapid onset; and acute trauma or a history of chronic irritation usually precedes the development of the lesion. A biopsy is always warranted to confirm the diagnosis, but, once established, no further treatment is required.

Oral melanoacanthoma usually presents as a rapidly enlarging, ill-defined, darkly pigmented macular or plaque-like lesion, and most develop in black females.20,21 Although lesions may present over a wide age range, the majority occur between the third and fourth decades of life. In rare instances, multiple lesions may present simultaneously.

Oral melanoacanthomas are typically asymptomatic, although pain has been reported. Although any mucosal surface may be involved, the buccal mucosa is the most common site of occurrence. The size of the lesion is variable, ranging from small and localized to large, diffuse areas of involvement, measuring several centimeters in diameter. The borders are typically irregular in appearance, and the pigmentation may or may not be uniform.

Cutaneous melanoacanthoma represents a pigmented variant of seborrheic keratosis and typically occurs in older Caucasian patients. Dermatosis papulosa nigra is a relatively common facial condition that typically manifests in older black patients, often female, and represents multiple pigmented seborrheic keratosis. These small papules are often identified in the malar and preauricular regions of the face.

Diagnosis

The clinical presentation, in association with the history, may be disconcerting and should lead the clinician to consider malignant melanoma in the differential diagnosis.

Melanocytic Nevus

Melanocytic nevi include a diverse group of clinically and/or microscopically distinct lesions. Unlike ephelides and melanotic macules, which result from an increase in melanin pigment synthesis, nevi arise as a consequence of melanocytic growth and proliferation. In the oral cavity, the intramucosal nevus is most frequently observed, followed by the common blue nevus. In general, both genetic and environmental factors are thought to play a role in nevogenesis. The effect of sun exposure on the development of cutaneous nevi is well recognized. However, there are also age- and location-dependent differences in the presentation, number, and distribution of nevi. Although most melanocytic nevi are acquired, some may present as congenital lesions (including in the oral cavity).

Familial atypical multiple mole and melanoma syndrome is characterized by the formation of histologically atypical nevi, epithelioid blue nevus may be associated with the Carney complex, markedly increased numbers of common nevi are characteristic in patients with Turner's syndrome.

Cutaneous nevi are a common occurrence. The average Caucasian adult patient may have several nevi; some individuals may have dozens. The total number of nevi tends to be higher in males than females. In contrast, oral melanocytic nevi are rare, typically present as solitary lesions, and may be more common in females.

Oral melanocytic nevi have no distinguishing clinical characteristics. Lesions are usually asymptomatic and often present as a small (<1 cm), solitary, brown or blue, well circumscribed nodule or macule. Up to 15% of oral nevi may not exhibit any evidence of clinical pigmentation. Once the lesion reaches a given size, its growth tends to cease and may remain static indefinitely.

Oral nevi may develop at any age; however, most are identified in patients over the age of 30. The hard palate represents the most common site, followed by the buccal and labial mucosae and gingiva.

The nevus cells initially maintain their localization to the basal layer, residing at the junction of the epithelium and the basement membrane and underlying connective tissue .These junctional nevi are usually small (<5 mm), macular or nonpalp ble, and tan to brown in appearance. Over time, the clustered melanocytes are thought to proliferate down into the connective tissue, often in the form of variably sized nests of relatively small, rounded cells. Nonetheless, some nevus cells are still seen at the mucosalsubmucosal junction. Such nevi often assume a dome-shaped appearance and are referred to as compound nevi. As the lesion further matures, the nevus cells completely lose their association with the epithelial layer and become confined to the submucosal tissue, often with an associated decrease in the amount of pigmentation. At this point, the lesion is given the designation of intramucosal nevus and, clinically, may appear brown or tan or even resemble the color of the surrounding mucosa.

The 'common' blue nevus, which is the most frequent histologic variant seen in the oral cavity, is characterized by an intramucosal proliferation of pigment-laden, spindle-shaped melanocytes. The blue nevus is described as such because the melanocytes may reside deep in the connective tissue and the overlying blood vessels often dampen the brown coloration of melanin, which may yield a blue tint. Biopsy is necessary for diagnostic confirmation of an oral melanocytic nevus since the clinical diagnosis includes a variety of other focally pigmented lesions, including malignant melanoma.

Malignant Melanoma

Malignant melanoma is the least common but most deadly of all primary skin cancers. Similar to other malignancies, extrinsic and intrinsic factors play a role in the

pathogenesis of melanoma. A history of multiple episodes of acute sun exposure, especially at a young age; immunosuppression; the presence of multiple cutaneous nevi; and a family history of melanoma are all known risk factors for the development of cutaneous melanoma.

Cutaneous melanoma is most common among white populations that live in the sun belt regions of the world. However, mortality rates are higher in blacks and Hispanics. The incidence is increasing in patients, especially males, over the age of 45. The incidence is decreasing in patients under the age of 40. Overall, there is a male predilection, but melanoma is one of the most commonly occurring cancers in women of childbearing age.

The clinical characteristics of cutaneous melanoma are best described by the ABCDE criteria: asymmetry, irregular borders, and color variegation, diameter greater than 6 mm, and evolution or surface elevation. These criteria are very useful (although not absolute) in differentiating cutaneous melanoma from other focally, pigmented melanocytic lesions.

Primary mucosal melanomas comprise less than 1% of all melanomas. The majority develop in the head and neck, most in the sinonasal tract and oral cavity. The prevalence of oral melanoma appears to be higher among black-skinned and Japanese people than among other populations. The tumor presents more frequently in males than females.

Oral melanoma may develop at any age, but most present over the age of 50. Any mucosal site may be affected; however, the palate represents the single most common site of involvement. The maxillary gingiva is the second most frequent site. Oral melanomas have no distinctive clinical appearance. They may be macular, plaque-like or mass forming, well-circumscribed or irregular and exhibit focal or diffuse areas of brown, blue, or black pigmentation. Up to one-third of oral melanomas may exhibit little or no clinical evidence of pigmentation (amelanosis).In some cases, oral melanomas may present with what appear to be multifocal areas of pigmentation. This phenomenon is often explained by the fact that some tumors may exhibit both melanotic and amelanotic areas.

Additional signs and symptoms that may be associated with oral melanoma are nonspecific and similar to those observed with other malignancies. Ulceration, pain, tooth mobility or spontaneous exfoliation, root resorption, bone loss, and paresthesia/anesthesia may be evident. However, in some patients, the tumors may be completely asymptomatic. Thus, the clinical differential diagnosis may be quite extensive. It is for this reason that a biopsy of any persistent solitary pigmented lesion is always warranted. Oral mucosal malignant melanoma is associated with a very poor prognosis. Studies have demonstrated 5-year survival rates of 15 40%.Regional lymphatic metastases are frequently identified and contribute to the

poor survival rates. Less than 10% of patients with distant metastases survive after 5 years.

Multifocal/Diffuse Pigmentation

Physiologic Pigmentation

Physiologic pigmentation is the most common source of multifocal or diffuse oral mucosal pigmentation. Dark-complexioned individuals, including blacks, Asians, and South-Americans, frequently show patchy to generalized hyperpigmentation of the oral mucosal tissues. Although in many patients, the pigment is restricted to the gingiva, melanosis of other mucosal surfaces is not uncommon .The pigment is often observed in childhood and usually does not develop de novo in the adult. If there is a sudden or gradual onset of diffuse mucosal pigmentation in adulthood, even in darker-skinned patients, other sources for the melanosis should be given consideration.

Drug-Induced Melanosis

Medications may induce a variety of different forms of mucocutaneous pigmentation, including melanosis. The chief drugs implicated in drug-induced melanosis are the antimalarials, including chloroquine, hydroxychloroquine, quinacrine, and others. Other common classes of medications that induce melanosis include the phenothiazines, such as chlorpromazine , oral contraceptives, and cytotoxic medications such as cyclophosphamide and busulfan .

Intraorally, the pigment can be diffuse yet localized to one mucosal surface, often the hard palate, or it can be multifocal and involve multiple surfaces. Some drugs may even be associated with a specific pattern of pigmentation. Much like other forms of diffuse pigmentation, the lesions are flat and without any evidence of nodularity or swelling. Sun exposure may exacerbate cutaneous drug-induced pigmentation.

Smoker's Melanosis

Diffuse melanosis of the anterior facial maxillary and mandibular gingivae, buccal mucosa, lateral tongue, palate, and floor of the mouth is occasionally seen among cigarette smokers. Most smokers (including heavy smokers) usually fail to show such changes. However, it is probable that in certain individuals, melanin synthesis is stimulated by tobacco smoke products. Indeed, among dark-skinned individuals who normally exhibit physiologic pigmentation, smoking stimulates a further increase in oral pigmentation. The pigmented areas are brown, flat, and irregular; some are even geographic or map-like in configuration. Alcohol has also been associated with increased oral pigmentation. In alcoholics, the posterior regions of

the mouth, including the soft palate, tend to be more frequently pigmented than other areas. It has been suggested that alcoholic melanosis may be associated with a higher risk of cancers of the upper aerodigestive tract.
Diffuse or patchy melanotic pigmentation is also characteristically associated with oral submucous fibrosis. Unlike smoker's melanosis, oral submucous fibrosis is a preneoplastic condition caused by habitual chewing of areca (betel) nut.

Post inflammatory (Inflammatory) Hyperpigmentation

Postinflammatory hyperpigmentation is a well-recognized phenomenon that tends to develop more commonly in darkcomplexioned individuals. Most cases present as either focal or diffuse pigmentation in areas that were subjected to previous injury or inflammation. The acne-prone face is a relatively common site for this phenomenon. Although unusual, postinflammatory pigmentation may also develop in the oral cavity. In rare cases, the mucosa overlying a nonmelanocytic malignancy may become pigmented. Oral pigmentation has also been described in patients with lichen planus (lichen planus pigmentosus).

Melasma (Chloasma)

Melasma is a relatively common, acquired symmetric melanosis that typically develops on sun-exposed areas of the skin and frequently on the face. The forehead, cheeks, upper lips, and chin are the most commonly affected areas. There is a distinct female predilection, and most cases arise in darker-skinned individuals. Unlike other forms of diffuse melanosis, melasma tends to evolve rather rapidly over a period of a few weeks. Sun exposure tends to be an exacerbating, if not precipitating, event. The term melasma is most appropriately used to describe the pigmentary changes associated with pregnancy or ingestion of contraceptive hormones. Both pregnancy and use of oral contraceptives have also been associated with oral mucosal melanosis. Rare cases of idiopathic melasma have also been described in females and, much less commonly, males. Melasma may spontaneously resolve after parturition, cessation of the exogenous hormones, or regulation of endogenous sex-hormone levels.

Melanosis Associated with systemic or Genetic Disease:

Hypoadrenocorticism (Adrenal Insufficiency,Addison's Disease)

Hypoadrenocorticism is a potentially life-threatening disease, as much for its systemic complications as it's under diagnosis. A variety of etiologies may precipitate adrenal insufficiency. In adults, autoimmune disease represents one of the most

common causes. However, infectious agents, neoplasia, trauma, certain medications, and iatrogenic causes may lead to adrenal destruction or an impairment of endogenous steroid production. In rare cases, adrenal insufficiency may also be a consequence of genetic disease. Regardless of etiology, the end result is essentially the same, that is, a decrease in endogenous corticosteroid levels. As steroid levels decrease, there is a compensatory activation of ACTH secretion from the anterior pituitary gland. ACTH then acts on the adrenal cortex to stimulate steroid production and ACTH secretion stops. If low steroid levels persist, there is a loss of feedback inhibition, resulting in persistent secretion of ACTH into the serum. Concurrently, the serum levels of a-melanocyte-stimulating hormone (a-MSH) also increase.

Weakness, poorly defined fatigue, and depression are some of the typical presenting signs of the illness. However, in some patients, the first sign of disease may be mucocutaneous hyperpigmentation. Generalized bronzing of the skin and diffuse but patchy melanosis of the oral mucosa are hallmarks of hypoadrenocorticism. Any oral surface may be affected. In some patients, oral melanosis may be the first manifestation of their adrenal disease. Diffuse hyperpigmentation is more commonly associated with chronic rather than acute-onset disease.

The diagnosis of oral addisonian pigmentation requires a clinicopathologic correlation. Endocrinopathic disease should be suspected whenever oral melanosis is accompanied by cutaneous bronzing. Treatment consists of exogenous steroid replacement therapy. With appropriate therapy, the pigmentation will eventually resolve.

Cushing's Syndrome/Cushing's Disease

Cushing's syndrome develops as a consequence of prolonged exposure to relatively high concentrations of endogenous or exogenous corticosteroids. Most cases are iatrogenic in origin and associated with poorly controlled or unmonitored use of topical or systemic steroids. Cushing's syndrome may also arise as a result of various endogenous etiologies, including an activating pituitary tumor (Cushing's disease) and a primary, activating, adrenal pathology (hyperadrenocorticism), as well as ectopic secretion of corticosteroids, ACTH, or corticotropin-releasing hormone by various neoplasms.

Overall, Cushing's syndrome is more prevalent in female patients. However, prepubertal onset is more commonly seen in boys. Apart from the wide array of systemic complications, including weight gain and the characteristic "moon facies," diffuse mucocutaneous pigmentation may be seen in a subset of patients, specifically those whose pathology is associated with increased ACTH secretion. Thus, in most cases, the affected patients have a primary pituitary neoplasm. The

pattern of oral pigmentation is essentially identical to that seen in patients with adrenal insufficiency.
Serum steroid and ACTH determinations will aid in the diagnosis, and the pigment often resolves following appropriate surgical, radiation, or medicinal therapy for the specific source of the endocrinopathy.

Hyperthyroidism (Graves'Disease)

Melanosis is a common consequence of hyperthyroidism (Graves' disease), especially in dark-skinned individuals. The pigmentation tends to resolve following treatment of the thyroid abnormality. The mechanism by which excessive thyroid activity stimulates melanin synthesis remains unclear.

Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome is an autosomal dominant disease. Clinical manifestations include intestinal polyposis, cancer susceptibility, and multiple, small, pigmented macules of the lips, perioral skin, hands, and feet. The macules may resemble ephelides, usually measuring <0.5 cm in diameter. However, the intensity of the macular pigment is not influenced by sun exposure. Although uncommon, similar-appearing lesions may also develop on the anterior tongue and buccal and labial mucosae. The lip and perioral pigmentation is highly distinctive, although not pathognomonic for this disease.

Café au Lait Pigmentation

Solitary, idiopathic café au lait ("coffee with milk") spots are occasionally observed in the general population, but multiple café au lait spots are often indicative of an underlying genetic disorder. Café au lait pigmentation may be identified in a number of different genetic diseases, including neurofibromatosis type I, McCune-Albright syndrome, and Noonan's syndrome. café au lait spots typically present as tan- or brown-colored, irregularly shaped macules of variable size. They may occur anywhere on the skin. Although unusual, examples of similar-appearing oral macular pigmentation have been described in some patients.

DEPIGMENTATION

Vitiligo

Common, acquired, autoimmune disease that is associated with hypomelanosis. Although the etiology and mechanisms remain unknown, the end result is a destruction of the melanocytes. In most cases, vitiligo is characterized by bilateral, symmetric areas of relatively generalized hypomelanosis. The vitiligenous lesions often present as well-circumscribed, round, oval or elongated, pale or white-colored macules that may coalesce into larger areas of diffuse depigmentation. As

the disease progresses, additional areas of involvement may become apparent. Topical corticosteroids and topical or, more commonly, systemic photochemotherapies (psoralen and ultraviolet A exposure) have proven to be effective nonsurgical therapies.

Hemoglobin and Iron- Associated Pigmentation

Ecchymosis

Traumatic ecchymosis is common on the lips and face yet is uncommon in the oral mucosa, except in cases related to blunt-force trauma and oral intubation. Immediately following the traumatic event, erythrocyte extravasation into the submucosa will appear as a bright red macule or as a swelling if a hematoma forms. The lesion will assume a brown coloration within a few days, after the hemoglobin is degraded to hemosiderin. patients taking anticoagulant drugs may present with oral ecchymosis, particularly on the buccal mucosa or tongue, either of which can be traumatized while chewing. Ecchymoses of the oral mucosa may also be encountered in patients with liver cirrhosis, leukemia, and end-stage renal disease undergoing dialysis treatment.

Purpura/Petechiae

Capillary hemorrhages will appear red initially and turn brown in a few days once the extravasated red cells have lysed and have been degraded to hemosiderin. The distinction between purpura and petechiae is essentially semantic and based solely on the size of the focal hemorrhages. Petechiae are typically characterized as being pinpoint or slightly larger than pinpoint and purpura as multiple, small 2 to 4 mm collections of extravasated blood. The same precipitating events can elicit either clinical presentation. Oral purpura/petechiae may develop as a consequence of trauma or viral or systemic disease . Petechiae secondary to platelet deficiencies or aggregation disorders are usually not limited to the oral mucosa but may occur concomitantly on the skin. Viral disease is more commonly associated with oral rather than cutaneous petechiae. In most cases, the petechiae are identified on the soft palate, although any mucosal site may be affected. When trauma is suspected, the patient should be instructed to cease whatever activity may be contributing to the presence of the lesions.

Hemochromatosis

Hemochromatosis is a chronic, progressive disease that is characterized by excessive iron deposition (usually in the form of hemosiderin) in the liver and other organs and tissues. Idiopathic, neonatal, blood transfusion, and heritable forms of this disease are recognized. Complications of hemochromatosis may include liver cirrhosis, diabetes, anemia, heart failure, hypertension, and bronzing of the skin.

Exogenous Pigmentation

Amalgam Tattoo

The single most common source of solitary or focal pigmentation in the oral mucosa is the amalgam tattoo. By definition, these are iatrogenic in origin and typically a consequence of the inadvertent deposition of amalgam restorative material into the submucosal tissue. The lesions are typically small, asymptomatic, macular, and bluish gray or even black in appearance. They may be found on any mucosal surface. However, the gingiva, alveolar mucosa, buccal mucosa, and floor of the mouth represent the most common sites. The lesions are often found in the vicinity of teeth with large amalgam restorations or crowned teeth that probably had amalgams, around the apical region of endodontically treated teeth with retrograde restorations or obturated with silver points, and in areas in and around healed extraction sites. If there is no radiographic evidence of amalgam, the lesion is not in proximity to any restored tooth, or the lesion suddenly appears, a biopsy is necessary. A typical differential diagnosis often includes melanotic macule, nevus, and melanoma.

Graphite Tattoos

Graphite tattoos are an unusual source of focal exogenous pigmentation. They are most commonly seen on the palate and represent traumatic implantation of graphite particles from a pencil. The lesions may be indistinguishable from amalgam tattoos, often presenting as a solitary gray or black macule. Since the traumatic event often occurs in childhood, many patients may not report a history of injury. Thus, a biopsy is often warranted.

Medicinal Metal-Induced Pigmentation

A variety of metallic compounds have been used medicinally for the treatment of various systemic diseases. With the exception of gold therapy (for rheumatoid arthritis), such medicaments are rarely or no longer in use. Gold and colloidal silver have both been associated with diffuse cutaneous pigmentation. Silver may cause a generalized blue-gray discoloration (argyria), whereas gold-induced pigment may appear blue-gray or purple (chrysiasis). In contrast to the systemic therapies, metal salts remain a component of some topical medications and other substances that are used in clinical practice. Examples include silver nitrate and zinc oxide .

Generalized black pigmentation of the tongue has been attributed to the chewing of bismuth subsalicylate tablets, a commonly used antacid. This phenomenon is unlike black hairy tongue , which is associated with elongation of the filiform papillae, hyperkeratosis, and superficial colonization of the tongue by bacteria.

Heavy-Metal Pigmentation

Diffuse oral pigmentation may be associated with ingestion of heavy metals. It remains an occupational and health hazard for some individuals who work in certain industrial plants and for those who live in the environment in and around these types of facilities. Other relatively common environmental sources include paints, old plumbing, and seafood. Lead, mercury, bismuth, and arsenic have all been shown to be deposited in oral tissue if ingested in sufficient quantities or over an extended period of time. These ingested metal salts tend to extravasate from vessels in areas of chronic inflammation. Thus, in the oral cavity, the pigmentation is usually found along the free marginal gingiva, where it often dramatically outlines the gingival cuff. This metallic line usually has a gray to black appearance. In some patients, the oral pigmentation may be the first sign of heavy-metal toxicity.

Additional systemic signs and symptoms of heavy metal poisoning may include behavioral changes, neurologic disorders, intestinal pain, and sialorrhea. Diffuse mucocutaneous melanosis may also be observed in some affected individuals.

Drug-Induced Pigmentation

Minocycline, which is a tetracycline derivative and frequently used in the treatment of acne, is a relatively common cause of drug-induced non–melanin-associated oral pigmentation.

Similar to tetracycline, minocycline can cause pigmentation of developing teeth. However, most patients are prescribed minocycline in early adulthood. When taken chronically, minocycline metabolites may become incorporated into the normal bone. Thus, whereas the teeth may be normal in appearance, the surrounding bone may appear green, blue, or even black. As a result, the palatal and alveolar mucosae may appear similarly and diffusely discolored. There is no treatment necessary for minocycline-induced pigmentation. The discoloration often subsides within months after discontinuation of the medication. However, the bone pigment may persist for longer periods of time, if not indefinitely.

Reference: Burket's Oral Medicine, 12th edition ,2015

Dr. Rehab Faisal

THE ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

HIV: There exist two recognized types of HIV: HIV-1 and HIV-2. Both have the same modes of transmission, and both may cause immunosuppression and AIDs.

The prime modes of transmission for HIV are :

-unprotected penetrative sex between men

-unprotected hetero- sexual intercourse،

-injection drug use ،

-unsanitary injections and blood transfusions

-Mother to child spread during pregnancy, delivery, or breast-feeding.

*In 5-15% of cases, HIV infection shows no clinical progress for periods up to 10 years, possibly because of variations in pathogenicity of HIV strains, or stronger host immune responses.

Diagnosis

-The diagnosis of HIV infection is obtained by appropriate laboratory testing. The standard HIV-antibody test (by taking plasma or serum which give positive test), however, cases of recent HIV infection may be missed as it takes several weeks (even months) for a measurable antibody response to develop.

-Detection of viral antigens, such as p24 protein, in the blood provides a more direct and reliable indicator of infection.

Pathogenesis:

For untreated HIV infection, a common pattern of disease progression has been established consisting of three phases: (1) primary infection, (2) prolonged (median=10 years) period of clinical latency, and (3) the appearance of clinically apparent disease.

HIV is a spherically shaped retrovirus whose outer coat, or envelope, consists of two layers of fatty molecules called lipids; these lipids are actually taken from the human cell membrane when newly formed virus particles bud from the cell. Within the envelope is the bullet-shaped core or capsid, which consists of about 2,000 copies of the HIV protein p24. The capsid encircles two single strands of HIV ribonucleic acid (RNA) and the enzymes (reverse transcriptase, integrase, and protease).

The human immunodeficiency virus directly infects lymphocytes and other cells, such as some macrophages, which carry the CD4 marker and causes lymphopenia so the virus kills T helper (CD4) cells and reverses the ratio of helper to suppressor lymphocytes.

The predominant portal of entry for HIV is through blood and/or mucosal exposure and dendritic cells at or near the mucosal surface of the involved sites play an important role in the initiation of HIV infection. Infection is enhanced where the mucosal tissues are ulcerated or inflamed, upon initial infection, a rapid sequence of virologic, immunologic, and clinical events occurs within the first 4 to 8 weeks of infection (i.e. primary infection). There is a rapid rise in plasma viremia and rapid dissemination of virus to lymphoid organs, particularly the gut-associated lymphoid tissue, are major factors in the establishment of the chronic and persistent infection that is a hallmark of HIV disease.

The clinical symptoms are characterized by varying degrees of fever, fatigue, maculopapular rash and headache, lymphadenopathy (generalized lymphadenopathy syndrome) with wide- spread persistent enlargement of lymph nodes which is a typical early sign, pharyngitis, myalgia, arthralgia, gastrointestinal distress, night sweats, and oral or genital ulcers.

The key feature of AIDS :

•Caused by a retrovirus — usually HIV-1

•Transmitted sexually or by intravenous drug abuse, and by blood or blood products

•Progressive deterioration mainly of cell-mediated immunity and deaths mainly due to opportunistic infections

•Immunodeficiency leads to opportunistic infections such as Pneumocystis carinii pneumonia

•Common oral lesions include candidiasis and hairy leukoplakia

•Greatly increased frequency of Kaposi's sarcoma and lymphomas, often in oral regions

•Neurological and psychological disorders may be associated.

ORAL LESIONS IN HIV DISEASE: Clinical indicators of a poor prognosis are oral thrush, herpes zoster or other persistent or recurrent infections, hairy leukoplakia, unexplained constitutional symptoms and lymphadenopathy. More than 90% of acquired immune deficiency syndrome (AIDS) patients have oral candidiasis and the infection is considered a portent of AIDS development.

Oral candidiasis:

The most common types of oral candidiasis in conjunction with HIV are pseudomembranous candidiasis, erythematous candidiasis, angular cheilitis, and chronic hyperplastic candidiasis. The main effect of the immunodeficiency and chief cause of death is infection by a great variety of microbes.

Viral mucosal infections

Herpetic stomatitis is less common than might be expected but can cause atypical or chronic ulceration. Severe orofacial zoster may indicate a poor prognosis. Cytomegalovirus can be found in some oral ulcers and the Epstein-Barr virus is the cause of hairy leukoplakia. Papillomaviruses have been isolated from proliferative lesions, such as verruca vulgaris, condyloma acuminatum and focal epithelial hyperplasia.

Bacterial infections

Infections by bacteria which rarely involve the oral tissues, such as Klebsiella pneumoniae, Enterobacter cloacae, and Escherichia coli, can develop.

Bacillary angiomatosis

Bacillary angiomatosis is a vascular proliferative disease caused by Bartonella henselae and should respond to antimicrobial therapy. However, it can mimic Kaposi's sarcoma clinically and, to some extent, histologically. It affects the skin more frequently than the oral cavity. Biopsy is essential to exclude Kaposi's sarcoma.

Systemic mycoses

Histoplasmosis or cryptococcosis can give rise to proliferative or ulcerative lesions.

Hairy leukoplakia

Hairy leukoplakia is highly characteristic of HIV infection.

Tumors

Nearly 50% of patients with AIDS have a malignant tumor at the time of presentation; the most frequent are Kaposi's sarcoma and non-Hodgkin lymphomas. Unlike non-AIDS patients, these tumors are particularly frequent in the head and neck region.

Kaposi's sarcoma (KS) in the mouth, particularly in a young male is pathognomonic of AIDS. It is usually associated with a CD4 lymphocyte count of less than 200/µL and frequently associated with other effects of HIV infection such as candidiasis, hairy leukoplakia or HIV-associated gingivitis. Though oral Kaposi's sarcoma may be the cause of early symptoms, the tumor is usually multifocal, with lesions affecting

Skin lymph nodes and viscera. KS is a multicentric neoplastic proliferation of endothelial cells and can involve any oral site, but most frequently involves the attached mucosa of the palate, gingiva, and dorsum of the tongue. The palate is the most frequent site and the lesions begin as blue purple or red purple flat discolorations that can progress to tissue masses that may ulcerate. The lesions do not blanch with pressure. Initial lesions are asymptomatic but can cause discomfort and interfere with speech, denture use, and eating when lesions progress. The differential diagnosis includes ecchymosis, vascular lesions, salivary gland tumor, and metastatic disease. Definitive diagnosis requires biopsy.

Lymphomas

AIDS-related lymphomas can develop in intraoral sites or salivary glands far more frequently than in HIV-negative persons. Typical sites within the mouth are the palate or gingiva, where the tumors form soft painless swellings which ulcerate when traumatized ex. Burkitt's lymphoma.

Autoimmune disease

The most common autoimmune phenomenon in AIDS is thrombocytopenic purpura. This can give rise to oral purple patches which may be mistaken for Kaposi's sarcoma, petechiae or blood blisters. Other autoimmune diseases reported in AIDS are lupus erythematosus and a Sjogren-like salivary gland disease.

Gingivitis and periodontitis

HIV-related periodontal disease includes necrotising gingivitis and accelerated periodontitis.

Salivary gland disease

“HIV salivary gland disease” (HIV- SGD), it encompasses a range of conditions, including xerostomia and benign (unilateral or bilateral) salivary gland enlargement in HIV-positive patients. The etiology of HIV-SGD is poorly understood, but the reactivation of a latent virus has been hypothesized. HIV-SGD is associated with a CD8+ cell lymphocytosis of the salivary glands and with the diffuse infiltrative lymphocytosis syndrome, also the chronic parotitis, possibly due to Epstein-Barr virus or cytomegalovirus, appears to affect children with AIDS particularly .

Clinical Manifestations: the primary sign of HIV-SGD is salivary gland swelling, primarily in the parotid glands and frequently bilateral. Xerostomia is a common symptom and salivary flow rates may be decreased, which may occur relatively early in HIV infection.

Diagnosis:

-HIV-SGD frequently resembles Sjögren's syndrome but can be distinguished it by lacking the anti-SS-a and anti-SS-B autoantibodies in the HIV-SGD population.

-Using immunohistochemical stains to differentiate the infiltrating cells, there is a preponderance of CD8+ cells in HIV-SGD compared with the CD4+ infiltrates that predominate in Sjögren's syndrome.

-Biopsy: the histopathology of an HIV–involved major gland demonstrates hyperplastic lymph nodes, lymphocytic infiltrates, and cystic cavities, with persistent enlargement of a major gland, a biopsy of the affected tissue may be necessary to exclude neoplasia particularly concern are lymphoma and Kaposi's sarcoma, both of which have been reported in the salivary glands of HIV-infected individuals.

Miscellaneous oral lesions

Mucosal ulcers and Major aphthae. They become more frequent and severe with declining immune function.

Oral hyperpigmentation, pigmentation may be secondary to Addison's disease due to fungal destruction of the adrenals .

Neurological disease

Orofacial effects include facial palsy and trigeminal neuropathy.

Oral Medicine

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Thank you