INTRODUCTION TO ORAL MEDICINE

Dr. Marwah Waleed Sh.

- **Oral medicine** is defined as “the dental specialty placed at the interface between medicine and dentistry and is concerned with the diagnosis and

management of (non-dental) pathology affecting the oral and maxillofacial region.

- “Oral medicine specialists provide clinical care to patients with a wide variety of orofacial conditions, including oral mucosal diseases, orofacial pain

syndromes, salivary gland disorders, and oral manifestations of systemic diseases.

There is a growing need to implement this specialty globally، due to the rapid progress in both medicine and dentistry.

- Oral medicine is concerned with clinical diagnosis and non-surgical management of non-dental pathologies affecting the orofacial region (the mouth and the face).
  Many systemic diseases have signs or symptoms that manifest in the orofacial region. Pathologically, the mouth may be afflicted by many cutaneous and gastrointestinal ,haematological and many other systemic diseases .
- There is also the unique situation of hard tissues penetrating the epithelial continuity (hair and nails are intra-epithelial tissues) ,Examples: lichen planus, Behçet's disease and pemphigus vulgaris.
- Moreover, it involves the diagnosis and follow-up of pre-malignant lesions of the oral cavity, such as leukoplakias or erythroplakias and of chronic and acute pain conditions such as paroxysmal neuralgias, continuous neuralgias, myofascial pain, atypical facial pain, and

- Another aspect of the field is managing the dental and oral condition of medically compromised patients such as cancer patients suffering from related oral mucositis, bisphosphonate-related osteonecrosis of the jaws or oral pathology related to radiation therapy.
- Additionally, it is involved in the diagnosis and management of dry mouth conditions (such as Sjögren’s syndrome) and non-dental chronic orofacial pain, such as burning mouth syndrome, trigeminal neuralgia and temporomandibular joint disorder ,So in order to get an accurate diagnosis of the patient we have to take adequate history from the patient.

THE FIRST STEP IN DEALING WITH THE PATIENT IS THE HISTORY TAKING

- The basis of a true history is good communication between dentist and patient.
  The patient's problem, whether it has a medical diagnosis attached or not, needs to be identified.
  A good history is one which reveals the patient's ideas, concerns and expectations as well as any accompanying diagnosis.

- Often the history alone reveals a diagnosis. A good example is with the complaint of headache where the diagnosis can be made from the description of the headache and perhaps some further questions.
- For example, in cluster headache the history is very characteristic and reveals the diagnosis without the need for examination or investigations.
  To obtain a true, representative account of what is troubling a patient and how it has evolved over time, is not an easy task. It takes practice, patience, understanding and concentration.

CONSULTATION SKILLS

- The skills required to obtain the patient's true story can be learned and go beyond knowing what questions to ask. Indeed 'questions' may need to be avoided, as they limit the patient to 'answers'..
- Complete the history by reviewing what the patient has told you. Repeat back the important points so that the patient can correct you if there are any misunderstandings or errors.

NOTE

During or after taking their history, the patient may have questions that they want to ask you. It is very important that don't give them any false information.

WHAT TYPES OF QUESTIONS THE DENTIST SHOULD ASK THE PATIENT

1. Open questions

These are seen as the gold standard of historical inquiry. They do not suggest a ‘right’ answer to the patient and give them a chance to express what is on their mind. Examples include questions such as ‘How are you?’. There are other similar open questions but it may be effective just to let the patient start speaking sometimes.

Open questions can be used to obtain specific information about a particular symptom as well. For example: ‘Tell me about your pain’ .

2. Questions with options

- Sometimes it is necessary to ‘pin down’ exactly what a patient means by a particular statement. In this case, if the information you are after cannot be obtained through open questioning then give the patient some options to indicate what information you need.
- Technique must be used with care as there is a danger of getting the answer you wanted rather than what the patient meant.
- Try to avoid using specific medical terms such as :Burning type of pain If you can use an open question such as: what was the pain is similar to?’, rather than suggesting options. Therefore never describe the type of the pain to the patient who is complain from neurological type of pain by describe the electrical stimulation on the trigger area.

3.Leading questions

- These are best avoided if at all possible. They tend to lead the patient down an avenue that is framed by your own assumptions.
- For instance, a male patient presents with episodic ulceration pain. The dentist must know if he is a smoker so you start asking questions that would help you to decide if it’s aphthous . It is much better to ask an open question such as: ‘Have you noticed anything that makes your pain worse?’.
- The first thing to be start with the history is the age! ... etc. **The age** of the patient is important in the following major problem including chronic and recurrent **condition from the earlier stages.**

I have any skin lesion , pain at the joint, dry mouth ,

1. • Degenerative bone and joint disease that affected the TMJ.
2. • Chronic brain syndrome.
3. • Malnutrition, mental disorder.
4. • Drugs. This because the old patients have a related changes in the pharmadynamic and pharmakinetic of the drugs also the drug to drug reaction ,drug –food reaction all of these will alter the absorption, distribution, metabolism, exertion,
5. • Bone and cortical trabecular bone decreased as a result it will be more potential for osteoporotic fractures.
6. • Muscle. The number of the muscle fibers decreased atrophy as a result the flexion of the joint decreased which lead to slowly muscle regeneration ,increased auto immune diseases.

- **Changes in the Joints include:**

1.Cartilage erosion 2.Calcium deposit increased

3.Water in cartilage decreased 4.Osteoarthritis

- Iincreased Other changes:

• Dentin decreased • Gingival retraction

• Bone density lost • The papilla of the tongue decreased which lead to taste change • Taste threshold for salt and sugar increased • Salivary secretion decrease

• Potential loss of the teeth.

While other changes on the mucosal surface

- Increase in the potential infection on the mucosal surface
- Malignancy incidence
- Response to acute infection reduced
- Potential recurrence of latent herpes zoster also the immune system changes
- Secretary immunoglobulin IgA decline• Thymus gland involved thymopoietin decreased • Lymphoid tissue decreased
- Antibody production impaired • T. Lymphocyte decreased
- Autoantibody increased

- 2.**SEX**.
- Malignant melanoma the incidence is increasing in male
- Mucous membrane pemphigoid ,cicatrical pemphigoid more in female
- Epulis and pregnancy epulies occur in female because of the circulating
estrogen are highest
- S.C.C more in males
- Mucocele more in female
- 3.**Presenting complaint (PC)**

- 4.**History of presenting complaint** (HPC).The dentist should gain as much information about the specific complaint.
- A.Site: Where exactly is the pain?
- B.Onset: When did it start, was it constant/intermittent, gradual/ sudden?
- C. Character:What is the pain like e.g. Sharp, burning, tight?
- D• Radiation: Does it radiate/move anywhere?
  E. Associations: Is there anything else associated with the pain e.g. Sweating, vomiting.
- F• Time course: Does it follow any time pattern, how long did it last?
- •G Exacerbating/relieving factors: Does anything make it better or worse?
  H• Severity: How severe is the pain, consider using the 1-10 scale?

- 5. **Past medical history (**PMH): Gather information about a patients with other medical problems
- 6.**Drug history** (DH): Find out what medications the patient is taking, including dosage and how often they are taking them e.g. Once-a-day, twice-a-day,… etc
- At this point it is important idea to find out if the patient has any allergies.

- **Immune suppression medication mainly used in oral medicine**

1. Cyclosporine 2. Azathioprine 3. Steroids, Examples: Prednisone, methylprednisolone, dexamethasone. **Steroids** stop the body from making cytokines that cause inflammation, deplete certain immune cells called T and B cells and eosinophils, and make it more difficult for immune cells to travel to spots of infection or injury though the body.

- 4.Colchicine:**Side effects** : diarrhea, nausea and vomiting. ❑ may also cause liver, kidney or muscle damage ❑ can lead to low blood cell counts. ❑ This medication may cause dangerous interactions with other medications, so a full medication check is necessary.
  5.Azathioprine (Imuran):Used in many other autoimmune diseases that have an oral manifestation❑ **cause** a rare type of lymphoma (cancer) of the liver, spleen, and bone marrow that can be fatal
  6.Dapsone may cause serious side effects including:• yellowing of the skin or eyes (jaundice) • numbness or tinging in hands or feet• unusual thoughts or behavior• new or worsening cough • fever • trouble breathing, swelling.

- 7 .**Family history** (FH): A family health history (also referred to as a family medical history, a family history, or medical family tree) is a compilation relevant information about medical conditions affecting a patient and his/her close family members.
- Two features that distinguishes a family health history from a patient’s medical history are that a family history extends beyond enumeration of the patient’s major health problems to identify those experienced by each member of that patient’s immediate family and its indication of about the patients family history, e.g diabetes or cardiac history.

- Genetic conditions within the family e.g. Polycystic kidney disease, hematological diseases like heamophilia , a family history should go back at least 3 generation the nature of the relationships among family members autosomal recessive like
- Sickle cell anemia
- Alpha thalassaemia
  Autosomal dominant .neurofibromatosis ,myotonic dystrophy
  Huntingtons disease
  Cardiovascular disorders include hypertrophic cardiomyopathy (HCM), Marfan’s syndrome (MFS),
  Familial hypercholesterolemia.

- 8 .**Social history (SH):** This is the opportunity to find out a bit more about the patient’s background. Remember to ask about smoking and alcohol. Also find out who lives with the patient. Smoking:There are lesions related to the smoking like leukoplakia , nicotinic stomatitis
- Alcohol history:the elevated of MCV mean corpuscular volume in the absence of vitamin B 12 or folate deficiency or unexplained abnormal liver function test.

- 9.**Review of systems (ROS)**:Gather a short amount of information regarding the other systems in the body that are not covered in your HPC.

  These are the main systems you should cover:

- CVS
- Respiratory
- GI
- Neurology
- Genitourinary/renal system
- Musculoskeletal
- Psychiatry

- **Summarising**

After taking the history, it’s useful to give the patient a run-down of what they’ve told you as the dentist understand it. For example: ‘So, from what I understand you’ve been losing weight, feeling sick, had trouble swallowing –with ulceration of the tongue and the whole thing’s been getting you down. Is that right?’

EXAMINATION OF THE PATIENT

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A complete examination covers the following three areas:

- 1.The General Examination: briefly assesses the patient’s general appearance
- 2.The Extra oral Head and neck Soft Tissue examination: focuses on the head and neck.
- 3.The Intraoral soft tissue examination: determines if the soft tissue is within normal limits (WNL).

A. General examination

- A thorough examination includes observing the patient’s general appearance. It may give clues to medical conditions.
- As the patient enters the room, and during history taking, observe the patient’s general appearance, symmetry, gait, and mobility. During the history taking, note any facial asymmetries, lesions or scars. For example, if the patient is in a wheelchair, the dentist need to find out the reason for this in your medical history. This could affect dental treatment in several ways.

- If the patient had suffered a stroke, they may need assistance transferring to the dental chair. As well, the medications the patient is taking following a stroke could affect your treatment.
- Additionally, the patient could have trouble maintaining adequate oral hygiene due to physical limitations. If the patient has decreased mobility of the head and neck, this should be noted, as it may affect the patient’s ability to tolerate dental procedures.

B. EXTRA ORAL. HEAD AND NECK EXAMINATION

1.Asymmetries

2. Abnormal colour of the face

3.Facial features

1. ASYMMETRIES

Asymmetries of the head and neck are assessed by standing directly in front of the patient. So the patient may have to sit on the side of the chair. Compare one side of the head and neck to the other.

Most people are not completely symmetrical, but significant asymmetries should be noted.

Examples of asymmetries are: previous surgeries, nerve paralysis from CVA/stroke, tumors, and infections. Details of the asymmetries should be noted in the chart – such as “3 cm scar in left submandibular area from submandibular gland stone.

2. Abnormal color of the face

The patient’s exposed skin should also be examined. Clues to the patient’s medical status may be obtained. If petechiae, ecchymosis, or hematoma are seen, then further information should be obtained from the patient about bleeding problems, or medications such as blood thinners.

If the patient’s skin appears yellowish, more information is needed about possible jaundice or liver problems. Clubbing of the fingers may be a sign of heart or respiratory problems. Other causes should be noticed by the dentist

1.Vitiligo is a condition in which the skin loses its pigment cells (melanocytes). This can result in discoloured patches in different areas of the body, including the skin, hair and mucous membranes 2.Melasma. Melasma (also known as chloasma) is noticed by tan or brown patches that may appear on the forehead, cheeks, upper lip, nose, and chin. Although this condition is often called the “pregnancy mask,” men can also develop it. It may also occur in women who are taking birth control pills or postmenopausal estrogen. Melasma may go away after pregnancy, but if it remains, it can be treated with certain prescription.

- 3.**Pigmentation alteration:** as a result of skin damage (post inflammatory hyper- or hyperpigmentation). Skin infection, blisters, burns, or other trauma to the patient here there will be decrease or increase of pigmentation in the affected area. This type of alteration is usually not permanent.
  4. **other factors, including lifestyle modifications, hormonal changes, excessive exposure to the su**n, repeated friction/exfoliation, and just growing older
  5.**Yellowing of the skin and the whites of the eyes** — the main sign of infant jaundice usually appears between the second and fourth day after birth. (To check for infant jaundice, press gently on baby's forehead or nose. If the skin looks yellow where pressed, it's likely that baby has mild jaundice). The skin, whites of the eyes and mucous membranes turn yellow because of a high level of bilirubin, a yellow-orange bile pigment. Jaundice has many causes, including hepatitis, gallstones and tumors. In adults, jaundice usually more serious

6.**Pale skin** can be a sign that patient have a shortage of normal red blood cells (anemia), which means that less oxygen is delivered to the body.

- **This can be from a nutritional deficiency, blood loss, or a blood cancer like leukemia. Other causes of pale skin include low blood pressure or infection.**

7. **Brown spots** are caused by the overproduction of melanin in the skin. Melanin is the pigment that gives the skin, hair and eyes their color. Produced by cells called melanocytes. Melanocytes as sponges that soak up sunlight.

8. **When the kidneys stop working,** toxins build up in skin.This build-up can cause color changes to the skin. other causes of skin discoloration is related to pigments called urochromes being retained in the skin. Normally these are excreted by healthy kidneys. Patients with this condition tend to have a grayish, almost metallic color skin. Another discoloration is called uremic frost.

9. **The presence of the basal cell carcinoma**

10. **Blue nevi** are localized benign proliferations of melanocytes. They may be congenital or acquired. There are two types. **Common blue nevi** range in size from 2–10 mm. They present as small round to oval, smooth-surfaced, well-defined papules with a bluish-black pigmentation. **Cellular blue nevi** are less common and tend to be >1 cm. They are also bluish-black and may be mistaken for nodular melanoma. Rarely, cellular blue nevi can undergo malignant transformation.

3.Facial features

Face has gradually swollen into a rounded shape, this is moon faces. It is often related to **obesity** but can be from **Cushing's syndrome.** That's why people sometimes refer to it as **a Cushingoid appearance. Cushing's syndrome occurs when the body is exposed for long periods to high levels of a hormone called cortisol.**

A. Symptoms and Causes of Moon Faces

Round, full, or puffy face. The sides of face may become so round from the build-up of fat that the ears can't be seen from the front of face. Fat deposits in the sides of the skull can also make the face look rounder.

- A high release of hormones, especially cortisol, is a cause of moon face. This is called **hyperadrenocorticalism or hypercortisolism**.(The adrenal glands, triangular-shaped glands that sit on top of the kidneys, release the cortisol). The conditions that most commonly lead to hypercortisolism and the symptom of moon faces include: **Increased release of a hormone (ACTH) from the pituitary gland; ACTH prompts the adrenal gland to produce cortisol. Nonpituitary tumors – such as tumors of the lung, pancreas, or thymus – which may also cause big releases of ACTH, Benign tumors or cancers in the adrenal gland.**

Note// Moon Faces and Cushing Syndrome: It can be difficult to diagnose ,because signs and symptoms such as facial swelling can be caused by other conditions. But it is more likely to be Cushing's syndrome if moon faces gets worse gradually along with other characteristic symptoms

Long-term use of steroids such as prednisone can cause many of the same signs and symptoms of Cushing’s syndrome. In fact, weight gain with fat redistribution such as moon faces is one of the most common signs of steroid use. The risk of developing these signs depends on the dose of medication and how long take it.

Long-term use of steroid medications like prednisone for conditions such as rheumatoid arthritis or other autoimmune conditions. To confirm that moon faces is the result of **abnormal cortisol levels, blood and urine** tests should be done to confirm the cause of high cortisol levels, other tests, such as an MRI or CT scan.

- B. **Hypotonic faces**
- Along with the rest of the muscles in the body the muscles in the face can also be slightly weaker which sometimes means that the children may lack a puzzled expression or generally not be very expressive at all.
- **Noses**: They may have a prominent bridge/root, a bulbous or dimpled/creased tip and the nostrils are narrow and it looks as though the part just below where glasses would sit bulges out slightly.
  Eyes :They can be small, almond shaped and either upward or downward sloping with hooded upper and lower eyelids. They can also be wide set.
- **Mouth**:This is generally noted as being small, sometimes with a thin upper lip and long featureless philtrum (the channel that runs between the nose and the mouth) so that sometimes the top lip is straight i.e. It doesn't have a 'bow shape'.
  Face :The cheekbones may be flat, this is called malar flatness. As the children get older ,it is sometimes the case that their faces become longer and the flatness then becomes more apparent. The forehead can also seem broad and flat.

- C. **Down syndrome** often have a characteristic facial appearance that includes a **flattened appearance to the face, outside corners of the eyes that point upward (upslanting palpebral fissures), small ears, a short neck , and a tongue that tends to stick out of the mouth.** Three features that are found in nearly every person with Down syndrome are:
  Epicanthic folds (extra skin of the inner eyelid, which gives the eyes an almond shape)
  Upslanting palpebral fissures (slanting eyes)
  Brachycephaly (a smaller head that is somewhat flattened in the back)The nose is pinched, the eyes are sunken, the temples hollow, the ears cold and retracted, the skin of the forehead tense and dry, the complexion livid, the lips pendent, relaxed, and cold. The Hippocratic face is so called because it was first described by Hippocrates.

4.**Malar rash :**is a red or purplish facial rash with a “**butterfly**” pattern. It covers your cheeks and the bridge of the nose, but usually not the rest of the face. The rash can be flat or raised. A malar rash can occur with many different diseases and conditions, from sunburn to lupus.

5 .**Face of mal nutritional :**Acute malnutrition pertains to a group of linked disorders that includes kwashiorkor, marasmus, and intermediate states of marasmic kwashiorkor. They are distinguished based on clinical findings, with the primary distinction between kwashiorkor and marasmus being the presence of edema in kwashiorkor.

SCALY SKIN

- Repeated skin irritation due to environmental factors, such as the sun, the wind, dryness or excessive humidity, may cause skin desquamation, that is the detachment of big scales from the epidermis, which sometimes look like fine dust. However, desquamation may also be the result of some condition, such as an allergic reaction, a fungal or staphylococcus infection, an immune system disorder or cancer, and of oncological treatments. In these cases, desquamation is usually accompanied by itching.
- **RED SPOTS**
- There is a large number of dermatological causes and diseases for the appearance of red spots or rash, including infections, heat, allergens, immune system disorders and medications.

SKIN MOLES

Moles are dark dots or spots on the skin that usually appear during childhood and adolescence. They are caused by groups of pigmented cells. In general they are harmless, but it is best to check them with a dermatologist if they change size, shape or color, or if itching or bleeding occurs, since some may become cancerous.

In general, it is important to pay attention to skin appearance because, regardless of the type of skin you have, there are certain characteristics that could be a sign of a skin problem.

Examination of the patient
EXTRA ORAL examination

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Out lines:

The followings is important before we get into the subject:

A. The terminology in this subject including the lymphoma ,lymphadenitis ,lymphatic vessels ,lymphatic system ,lymphatic fluid..

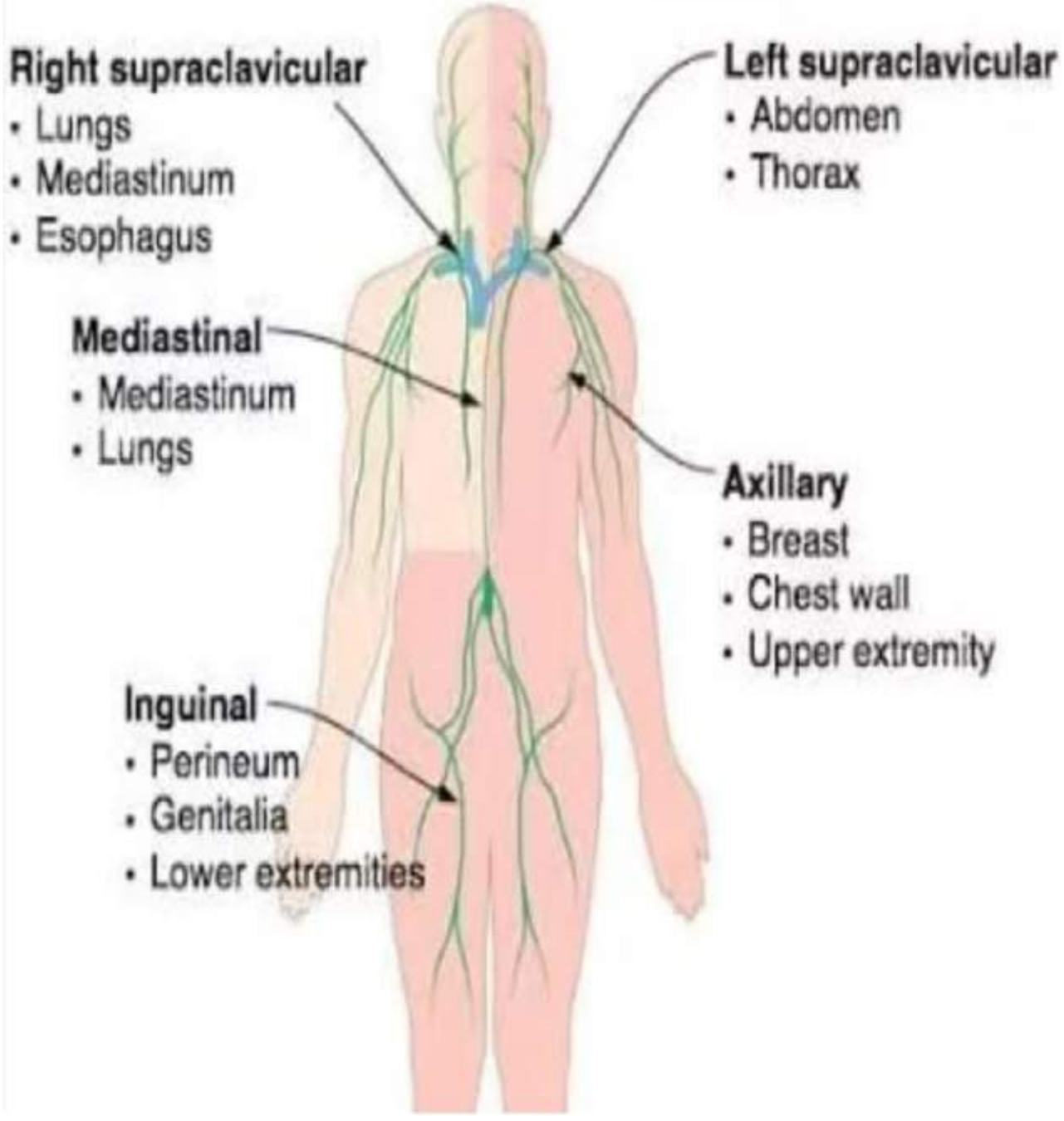
B. The function of the lymph node , anatomy ,and drainage

The lymph node examination

- **Consistency: Soft (insignificant), rubbery (classically lymphoma), hard (classically malignancy & granulomatous infection**). **Tender (classically infection) vs. Non-tender (classically malignancy).**
- **Lymph nodes are part of the immune system.** As such, they are most readily palpable when fighting infections. Infections can either originate from the organs that they drain or primarily within the lymph node itself, referred to as lymphadenitis.

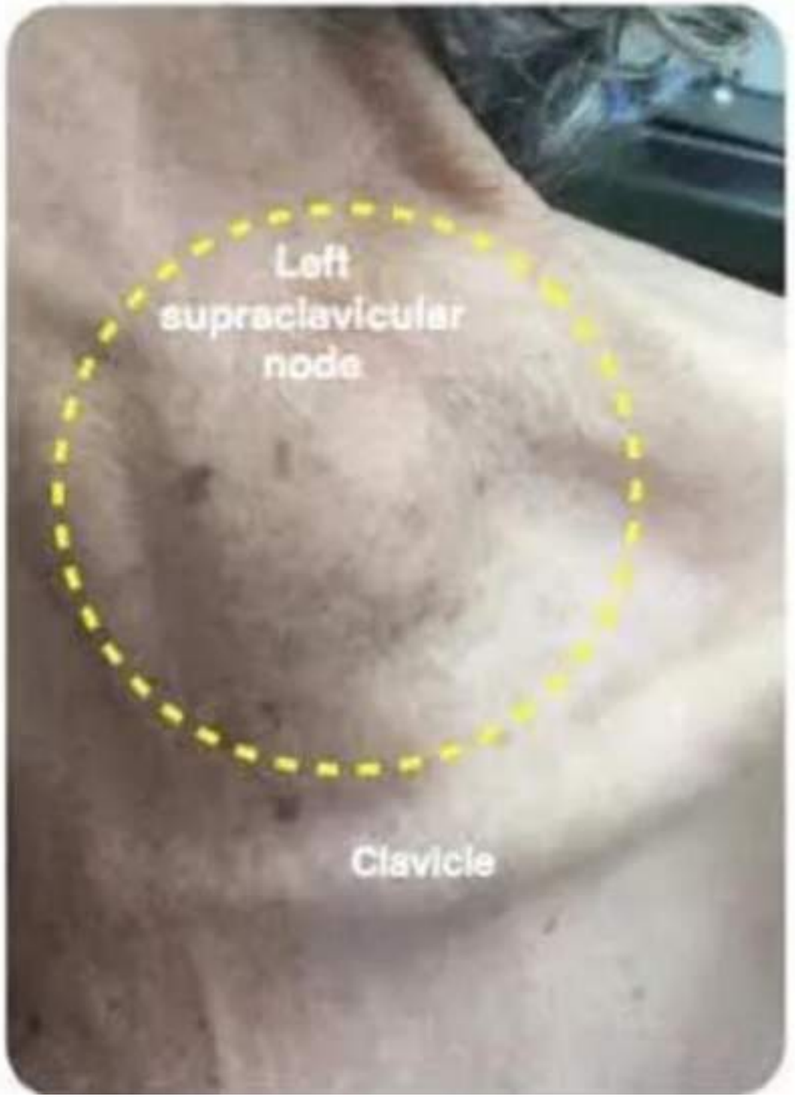
Lymph Node Exam Technique

- Always evaluate for symmetry: clinically significant nodes classically asymmetric.
- Identify salivary glands by location as non-lymph nodes.
  Identify carotid artery/bulb by pulsation as non-lymph nodes.
- Supraclavicular fossa most significant area: often indicates a **process deep in body.**
  Left supraclavicular node (Virchow's node) classical sign of **abdominal process.**
  Right superclavicular node classic sign of **intrathoracic process**.

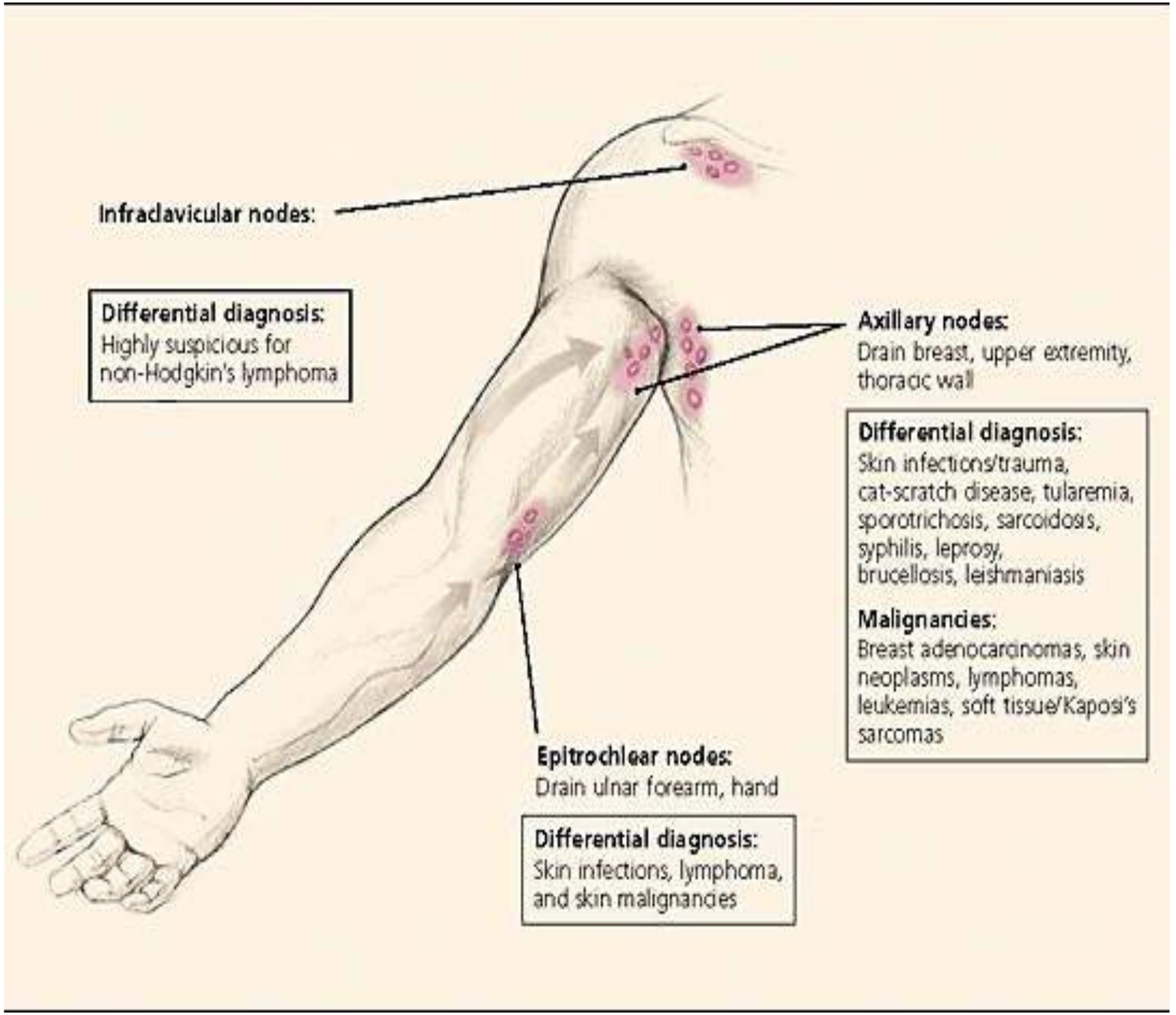


Virchow's Node

Suggests abdominal malignancy
(stomach, gallbladder, pancreas, kidneys, testicles, ovaries, lymphoma, prostate)



- Infraclavicular fossa nodes: classically **breast cancer or malignant lymphoma.**
  Epitrochlear lymph nodes: best felt when moving fingers up and down.
  The major lymph node groups are located along the **anterior and posterior aspects of the neck** and on the underside of the jaw.
- If the nodes are quite big, the dentist may be able to see them bulging under the skin, particularly if the enlargement is asymmetric (i.e. It will be more obvious if one side is larger than the other).
  To palpate, use the pads of **all four fingertips as these are the most sensitive parts of hands**. Examine both sides of the head simultaneously, walking the fingers down the area in question while applying steady, gentle pressure. The major groups of lymph nodes as well as the structures that they drain.


Infraclavicular nodes:
Differential diagnosis:
Highly suspicious for non-Hodgkin's lymphoma
Axillary nodes:
Drain breast, upper extremity, thoracic wall
Differential diagnosis:
Skin infections/trauma, cat-scratch disease, tularemia, sporotrichosis, sarcoidosis, syphilis, leprosy, brucellosis, leishmaniasis
Malignancies:
Breast adenocarcinomas, skin neoplasms, lymphomas, leukemias, soft tissue/Kaposi's sarcomas
Epitrochlear nodes:
Drain ulnar forearm, hand
Differential diagnosis:
Skin infections, lymphoma, and skin malignancies

- **Nodes are generally examined in the following order:**

-Anterior Cervical (both superficial and deep): Nodes that lie both on top of and beneath the sternocleidomastoid muscles (SCM) on either side of the neck, from the angle of the jaw to the top of the clavicle. This muscle allows the head to turn to the right and left. The right SCM turns the head to the left and vice versa. They can be easily identified by asking the patient to turn their head into your hand while you provide resistance.

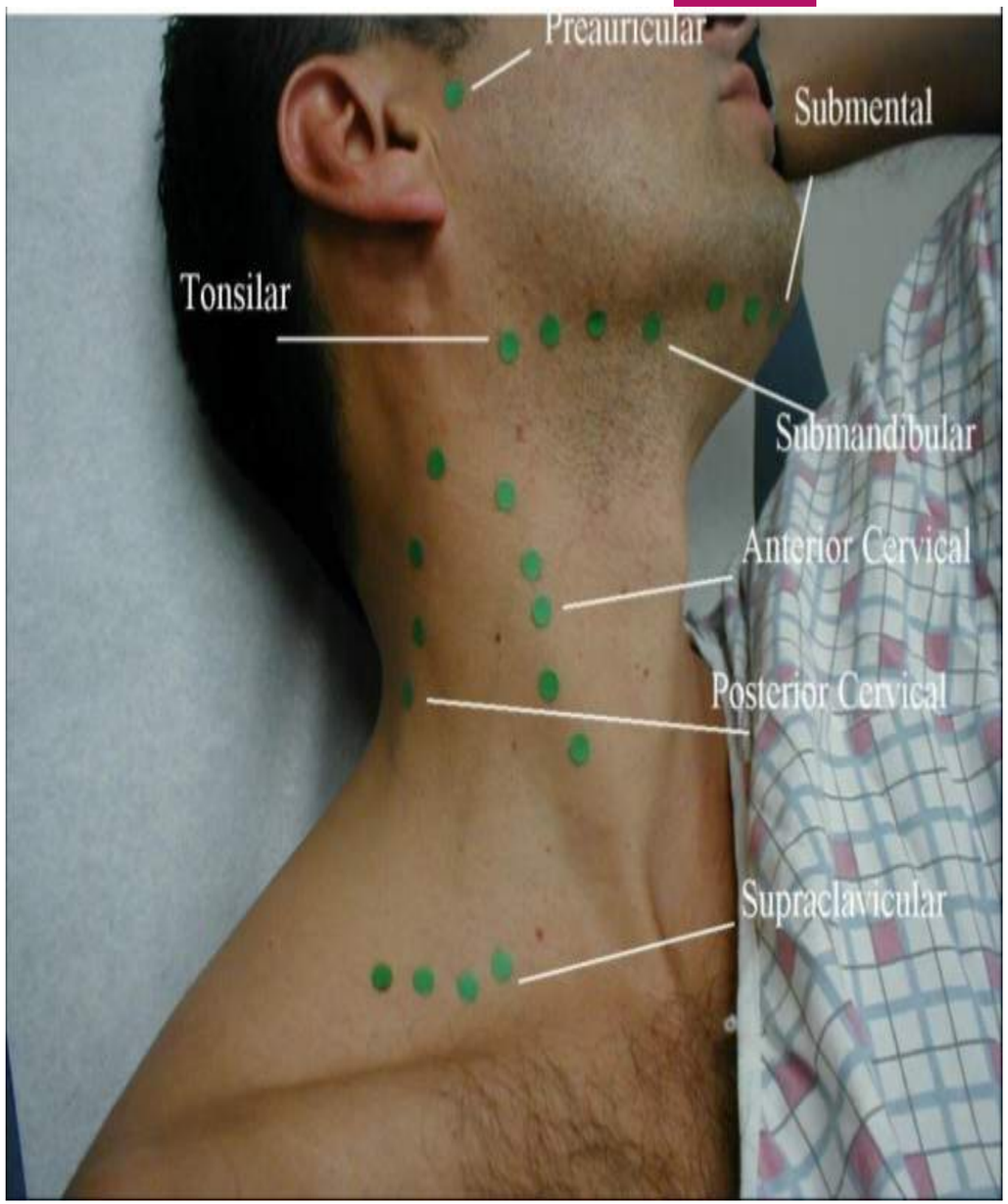
Drainage: the internal structures of the throat as well as part of the posterior pharynx, tonsils, and thyroid gland.

-**Posterior Cervica**l: Extend in a line posterior to the SCMs but in front of the trapezius, from the level of the mastoid bone to the clavicle.

Drainage: The skin on the back of the head. Also frequently enlarged during upper respiratory infections (e.g. Mononucleosis).

-**Tonsillar**: Located just **below** the angle of the mandible.

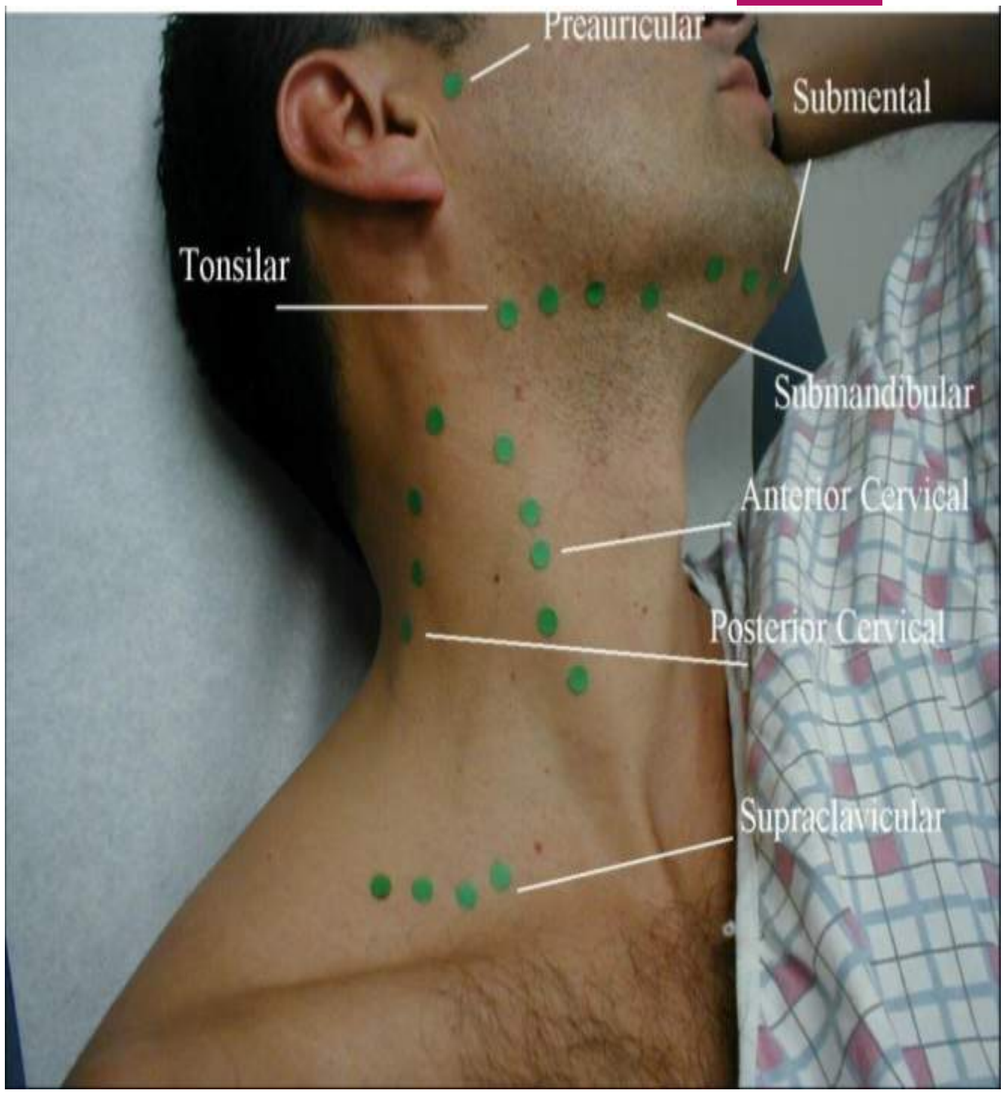
Drainage: The **tonsilar and posterior pharyngeal regions.**



-Sub-Mandibular: Along the underside of the jaw on either side. **Drainage**: The structures in the floor of the mouth.

–**Sub-Mental**: Just below the chin. **Drainage**: The teeth and intra-oral cavity.

-**Supra-clavicular**: In the hollow above the clavicle, just lateral to where it joins the sternum. **Drainage**: Part of the throacic cavity, abdomen.



- A number of other lymph node groups exist. However, palpation of these areas is limited to those situations when a problem is identified in that specific region (e.g. The **pre-auricular** nodes, located in front of the ears, may become inflamed during infections of the external canal of the ear).
  Firm, tender, enlarged and warm. Inflammation can spread to the overlying skin, causing it to appear reddened.
  If an inflammation remains untreated, the center of the node may become necrotic, resulting in the accumulation of fluid and debris within the structure.

- This is known as an abscess and feels a bit like a tensely filled balloon or grape (Fluctuance).
  Following infection, lymph nodes occasionally remain permanently enlarged, though they should be non-tender, small (less the 1 cm), have a rubbery consistency and none of the characteristics described above or below. It is common, for example, to find small, palpable nodes in the submandibular/tonsillar region of otherwise healthy individuals. This likely represents sequelae of **past pharyngitis or dental infections.**
- Malignancies may also involve the lymph nodes, either primarily (e.g. lymphoma) or as a site of metastasis.

- In either case, these nodes are generally: **Firm, non-tender, matted (i.e. Stuck to each other), fixed (i.e. Not freely mobile but rather stuck down to underlying tissue), and increase in size over time.**
- The location of the lymph node may help to determine the site of malignancy. **Diffuse, bilateral** involvement suggests a **systemic** malignancy (e.g. lymphoma) while those limited to a specific anatomic region are more likely associated with a local problem. Enlargement of nodes located **only on the right** side of the neck in the anterior cervical chain, for example, would be consistent with a **squamous cell carcinoma,** frequently associated with an intra-oral primary cancer.

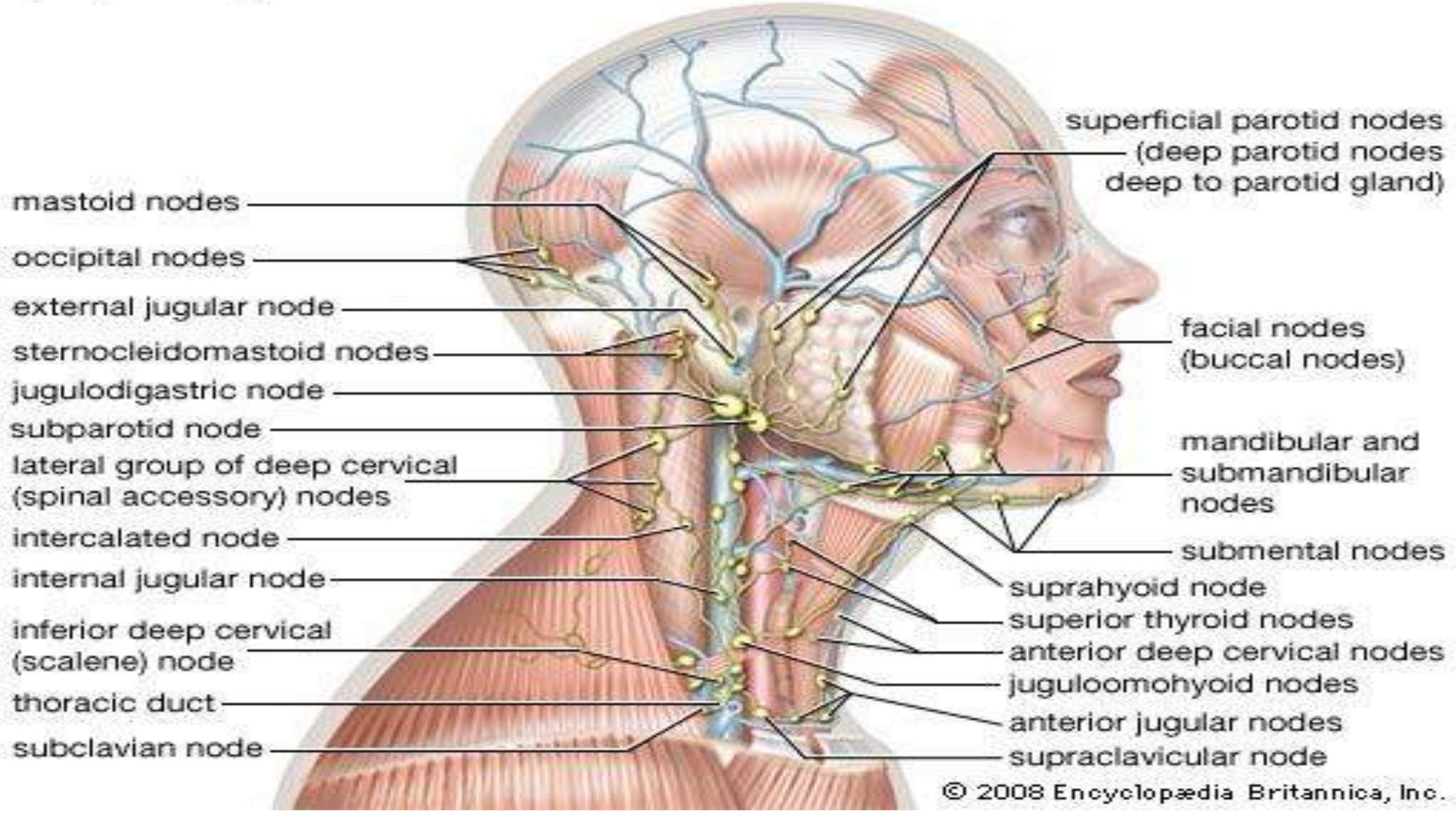
- **Diffuse upper airway infections** (e.g. Mononucleosis), systemic infections (e.g. Tuberculosis) and inflammatory processes (e.g. Sarcoidosis) can all cause **lymphadenopathy** (i.e. Lymph node enlargement). HIV infection can also cause adenopathy in any region of the body, **including head/neck, axilla, epitrochlear, inguinal** and other areas where there are lymph nodes. In these settings, the findings can be symmetric or asymmetric. Historical information as well findings elsewhere in the body are critical to making these diagnoses.

  Furthermore, it may take **serial examinations over** the course of weeks to determine whether a node is truly enlarging, suggestive of malignancy, or responding to therapy/the passage of time and regressing in size, as might occur with other inflammatory processes.”

- So in order to make clinical examination of the L.N. , the dentist need inspection and palpation technique: use the pads of the index and middle finger(The “flat” of the fingers not the tip) to move the skin in circular motions over the underlying tissues in each area; palpate both sides of the neck simultaneously small nodes (< size of distal phalanx of pinky finger) are normal unless in unusual location (preauricular).
  In abnormal nodes, describe in terms of location, size delimitation (discrete or matted together)mobile or fixed, consistency (soft, hard, firm),tenderness.
- **THE DENTIST SHOULD BE WELL KNOWN ABOUT THE location and drainage OF THE:**

- **Preauricular** – in front of tragus of ear (eye),
- **Postauricular** – behind ear, over mastoid process (ear).
- **Parotid-** very difficult to make a diagnosis.
- **Occipital** – posterior to mastoid process, at base of skull.
- **Submental** –inside mentus of the mandible (floor of mouth).
- **Submandibular** – near submandibular salivary glands (oral cavity).
- Angular,submental,Suboccipital,Retrosternocleidomastoid,retroauricular , ,supraclavicular,infraclavicular,pre-sternocleidomastoidret.
- **Cervical chains,anterior chain** runs along the SCM (pharynx, tonsils),**posterior chain** runs along the trapezius clavicular (abdomen, thorax, breast).
- **Supraclavicular** – Virchow's node (ominous finding in cancer patient) axillary.

Lymphatic system of the head and neck



- Differentiation from **lymphomas** requires the use of clinical features, histology, immunophenotyping, and gene rearrangement studies for monoclonal population detection. Common differential diagnoses to be considered are listed below.
- Neoplasms)Squamous cell carcinoma,Nasopharyngeal carcinoma,Thyroid carcinoma(
  Generalized lymphadenopathy from infectious etiologies,These include the following: Bacteria ,Viruses (eg, Epstein-Barr virus [infectious mononucleosis], cytomegalovirus, HIV) ,Parasites (eg, toxoplasmosis).
- Nasal granulomatous disease: Wegener granulomatosis, Lymphomatoid granulomatosis,Infections (eg, leishmaniasis, syphilis)

Generalized lymphadenopathy

- is defined as enlargement of more than **2 noncontiguous** lymph node groups. A thorough history and physical examination are critical in establishing a diagnosis. Causes of generalized lymphadenopathy include infections, autoimmune diseases, malignancies, histiocytoses, storage diseases, benign hyperplasia, and drug reactions.

  1. Infections: Generalized lymphadenopathy is most often associated with **systemic viral infections**.

  Infectious mononucleosis results in widespread adenopathy. **Roseola infantum** (caused by human herpes virus 6), cytomegalovirus (CMV), varicella, and adenovirus all cause generalized lymphadenopathy.

- Human immunodeficiency virus (HIV) is often associated with generalized adenopathy, which may be the presenting sign. Children with HIV are at increased risk for tuberculosis, as well.
  Some bacterial infections present with generalized adenopathy. Examples include typhoid fever caused by **Salmonella typhi, syphilis, plague, and tuberculosis.**
  Less common **bacteremias,** including those caused by endocarditis, result in generalized lymphadenopathies.

- **2.Malignancy** is often associated with constitutional signs, such as **fever, anorexia, nonspecific aches and pains, weight loss, and night sweat**s. The acute leukemias and lymphomas often present with these nonspecific findings.
- Generalized lymphadenopathy is present at diagnosis in two thirds of **children** with acute lymphoblastic leukemia (**ALL**) and in one third of children with acute myeloblastic leukemia (**AML**). Abnormalities of peripheral blood Counts usually lead to the correct diagnosis. The lymphomas more often present with **regional** lymphadenopathy, but generalized lymphadenopathy occurs.

- Constitutional signs and symptoms observed in the leukemias are **less** reliable findings in the lymphomas. Only one third of children with Hodgkin disease and 10% with non-Hodgkin lymphoma display them. Malignancies usually present with nodes that tend to be firmer and less mobile or matted; however, this finding can be misleading. While **Benign reactive lymph nodes may be associated with fibrotic reactions that make them firm.**

- **3. Storage diseases:** Generalized lymphadenopathy is an important manifestation of the lipid storage diseases. In Niemann-Pick disease, sphingomyelin and other lipids accumulate in the spleen, liver, lymph nodes, and CNS. In Gaucher disease, the accumulation of the glucosylceramide leads to the engorgement of the spleen, lymph nodes, and the bone marrow.

- **4.Drug reactions: Adverse drug reactions can cause generalized lymphadenopathy.** Within a couple of weeks of initiating **phenytoin**, some patients experience a syndrome of regional or generalized lymph node enlargement, followed by a severe maculopapular rash, fever, hepatosplenomegaly, jaundice, and anemia. These symptoms abate 2-3 months after discontinuation of the drug. Several other drugs are implicated in similar symptomatology, including mephenytoin, pyrimethamine, phenylbutazone, allopurinol, and isoniazid.

  5. Autoimmune etiologies include juvenile rheumatoid arthritis, which often presents with adenopathy, especially during the acute phases of the disease. Sarcoidosis and graft versus host disease also merit consideration.

Cervical lymphadenopathy

- Cervical lymphadenopathy is a common problem in **children**
  Cervical nodes drain the tongue, external ear, parotid gland, and deeper structures of the neck, including the larynx, thyroid, and trachea.
  Inflammation or direct infection of these areas causes subsequent engorgement and hyperplasia of their respective node groups.
  Adenopathy is most common in Cervical nodes in children and is usually related to infectious etiologies.
- Lymphadenopathy **posterior to the sternocleidomastoid** is typically a more **ominous** finding, with a higher risk of serious underlying disease.

- **1. Infectious aetiologies** :Cervical adenopathy is a common feature of many **viral** infections. Infectious mononucleosis often manifests with posterior and anterior cervical adenopathy. Firm tender nodes that are not warm or erythematous characterize this lymph node enlargement. Other viral causes of cervical lymphadenopathy include adenovirus, herpesvirus, coxsackie virus, and CMV. In **herpes gingivostomatitis, impressive submandibular and submental adenopathy** reflects the amount of oral involvement.

- Bacterial infections:Cervical adenopathy by causing the draining nodes to respond to local infection or infection localizing within the node itself as a **lymphadenitis.**
  Bacterial infection often results in enlarged lymph nodes that are warm, erythematous, and tender. Localized cervical lymphadenitis typically begins as enlarged, tender, and then fluctuant nodes.
  In patients with cervical adenopathy, determine whether the patient has had recent or ongoing sore throat or ear pain. The dentist should examine the oropharynx, paying special attention to the posterior pharynx and the dentition.
  The classic manifestation of group A streptococcal pharyngitis is sore throat, fever, and anterior cervical lymphadenopathy. Other streptococcal infections causing cervical adenopathy include otitis media, impetigo, and cellulitis.
  Atypical mycobacteria cause subacute cervical lymphadenitis, with nodes that are large and indurated but not tender. The only definitive cure is removal of the infected node.

- Mycobacterium tuberculosis may manifest with a suppurative lymph node identical to that of atypical mycobacterium. Intradermal skin testing may be equivocal. A biopsy may be necessary to establish the diagnosis.
  Cat scratch disease, , presents with subacute lymphadenopathy often in the cervical region. The disease develops after the infected pet (usually a kitten) inoculates the host, usually through a scratch. Approximately 30 days later, fever, headache, and malaise develop, along with adenopathy that is often tender

- **2.Non infectious etiologies** :Kawasaki disease is an important cause of cervical adenopathy. These children have fever for at least 5 days, and cervical lymphadenopathy is one of the 5 diagnostic criteria (of which 4 are necessary to establish the diagnosis).

Submaxillary and submental lymphadenopathy

- These nodes drain the teeth, tongue, gums, and buccal mucosa. Their enlargement is usually the result of localized infection, such as pharyngitis, herpetic gingivostomatitis, and dental.

- Other Neck Masses:Cystic Hygroma,Sialadenitis (Submandibular Gland), Vascular malformations,Squamous Cell Carcinoma of the head and nec ,Lymphoma,Leukemia
  Other midline Neck Masses (into hyoid region):Thyroglossal Duct Cyst,Dermoid cyst,Cystic Hygroma,Thyroid tumor

Posterior Cervical Nodes (behind sternocleidomastoid)

- **Drainage** Pattern from ,Scalp,Neck,Arm and pectoral skin,Thorax,Cervical and axillary node drainage Lymphadenopathy Causes,Tuberculosis,Lymphoma (especially Hodgkin’s Lymphoma),Head and neck cancer.

Preauricular nodes (anterior to ear tragus)

Drainage Pattern from Lateral Eyelids,Palpebral Conjunctiva,Temporal skin,Anterior Ear Pinna,External auditory canal,Lymphadenopathy Causes: Non-ocular,Squamous Cell Carcinoma or Basal Cell Carcinoma (Rodent ulcer,Epithelioma,Chancre on face,Erysipelas,Ophthalmic Herpes Zoster,Rubella,Trachoma,Atypical Mycobacterial Infection,Cat Scratch Disease.Type I Branchial Cleft Cyst Pilomatrixoma,Parotid Gland tumor ,Parotid Gland inflammation (Parotitis)

Supraclavicular Nodes:

Drainage pattern:Right supraclavicular node,Mid-chest,Esophagus,Lungs,Left supraclavicular node,Virchow’s Node,Thoracic duct drainage (Chest, Abdomen)
Lymphadenopathy Causes:Malignancy (represents 90% of cases age>40 years old),Lymphoma,Mediastinal disease,Tuberculosis,Histoplasmosis and other Fungal Lung Infections,Sarcoidosis

Generalized Acute Cervical Lymphadenopathy

Causes:Common Causes: Tinea Capiti, Infectious Mononucleosis (Epstein Barr Virus),Cytomegalovirus,Adenovirus

Less common causes: Secondary Syphilis,Lice infestation,Serum Sickness,Severe drug allergy (e.g. Penicillin),Cat Scratch Disease ,Rubella,Generalized Furunculosis,Cystic Hygroma.

Tonsillar Nodes (below angle of jaw)

Tinea Capitis,Pharyngitis (Mononucleosis, Upper Respiratory Infection),Atypical Mycobacterial Infection,Cat-Scratch Disease,Rubella,Dental Infections.

Drainage Pattern:Tongue.

Submaxillary gland,Submental node

Drainage:Lip and Mouth mucosa,Medial Conjunctiva

Submental Nodes (below chin)

Drainage Pattern from :Lower lip,Floor of Mouth,Tip of Tongue,Skin of Cheek

Lymphadenopathy Causes:Mononucleosis (Epstein-Barr Virus),Cytomegalovirus,Toxoplasmosis,Thyroglossal Duct Cyst,Dermoid cyst.

Anterior Cervical Nodes or Jugular Nodes

(anterior border of sternocleidomastoid).

Drainage Pattern from :Tongue (except apex),Tonsil,Ear Pinna,Parotid Gland.

Occipital or Suboccipital nodes

(base of skull, below occiput).Suboccipital Lymphadenopathy may causes Headache.**Drainage** Pattern:Back of Scalp and Head .Lymphadenopathy Causes :Local infection,Tinea Capitis,Lice,Seborrheic,Dermatitis, SecondarySyphilis,Neoplasm including metastases,Lymphoma.


Thank
You

The Examination of the Eye

Dr. Marwah Waleed Sh.

Outlines:-

- The Examination of the Eye.
- The examination of the skin
- The examination of the thyroid gland
- The examination of the salivary gland

- The eye is composed of different types of tissues, this unique feature makes the eye susceptible to a wide variety of diseases and provides insights into many systemic problems. Almost any part of the eye can give important clues to the diagnosis of systemic diseases which may be evident on a routine eye examination.

1.Diabetes

The underlying cause of diabetic retinopathy is microvascular leakage leading to exudation which occurs in the layers of retina affecting vision. **Excess** glucose interferes with normal metabolism of the lens and result in premature cataracts.

2.Hypertension :may produce no abnormalities if detected early ,but assessment of fundus is essential to detect such changes.

Hypertensive retinopathy ranges from grade 1 to grade 4, grade 4 being severe form called malignant hypertensive retinopathy. The retinal changes and swelling of the optic nerve resulting in vision loss is associated with a systolic pressure of > 220 mm Hg and a diastolic pressure of >110mm Hg.

- Treatment for hypertension may result in resolution of retinal signs. If left unattended for too long ,permanent damage to vision may occur because of optic nerve and retinal circulation being affected by hypertension.
- Both diabetes and hypertension may also affect nerves of the eye leading to muscle paralysis causing squint, double

3.Thyrotoxicosis

Excessive thyroid levels may cause protruding eyes, limitation of eye movements, double vision and corneal disease due to exposure and dryness.

- In severe form, the optic nerve may get damaged resulting in permanent loss of vision. Symptoms in the eye may appear before any other systemic features. also the dentist should notice the exophthalmus ,which is bulging of the eye anteriorly out of the orbit it could be bilateral as in Graves disease or unilateral often seen in orbital tumor, complete or partial dislocation from the orbit is possible from trauma or swelling from the surrounding tissue.

4.Cancer: can start in the eye or spread from anywhere in the body. Cancer can occur in any part of the eye and depending upon its location it may or may not affect vision. It especially holds true in children who can have cancer called retinoblastoma. The cancer may be evident as a white reflex, squint, recurrent redness, vision loss and in advanced cases may threaten life. So, early detection and timely treatment may be both vision saving and lifesaving.

- **The tissue surrounding** the eye is a common area to find lesions associated with sun damage such as basal cell carcinoma. Metal frames increase sun damage around the eye area which could lead to skin cancer. Other ocular signs should be evaluated such as indications of pemphigoid affecting the eye.

- Pay close attention to the **color of the sclera**, Yellow sclera is associated with jaundice and may indicate an undiagnosed case of hepatitis (A or B), other **liver dysfunction or a blood disorder.**

- Blue sclera is associated with osteogenesis imperfecta which may include alteration of the structure of dentin. Pupil size may help identify patients who are at risk for medical emergencies due to illegal drug use. Lichen planus, may associated with eye involvment.

- **A simple way to exam the eye:**

Naffzigers methods. Stand behind the seated patient. Tilt the head backwards and observe the eye ball, our plane of vision should be on the superciliary ridges, by the examination the globes in this maner it will be possible to confirm or eliminate the presence the protruism. Exophthalmos mean the recession of the eye usually occur in serious wasting disease. Also the followings may affected the eye like Sjogrens syndrome ,Reiters disease ,Stevens johnson syndrome,Behcets disease.

Clinical Examination of The Orbit

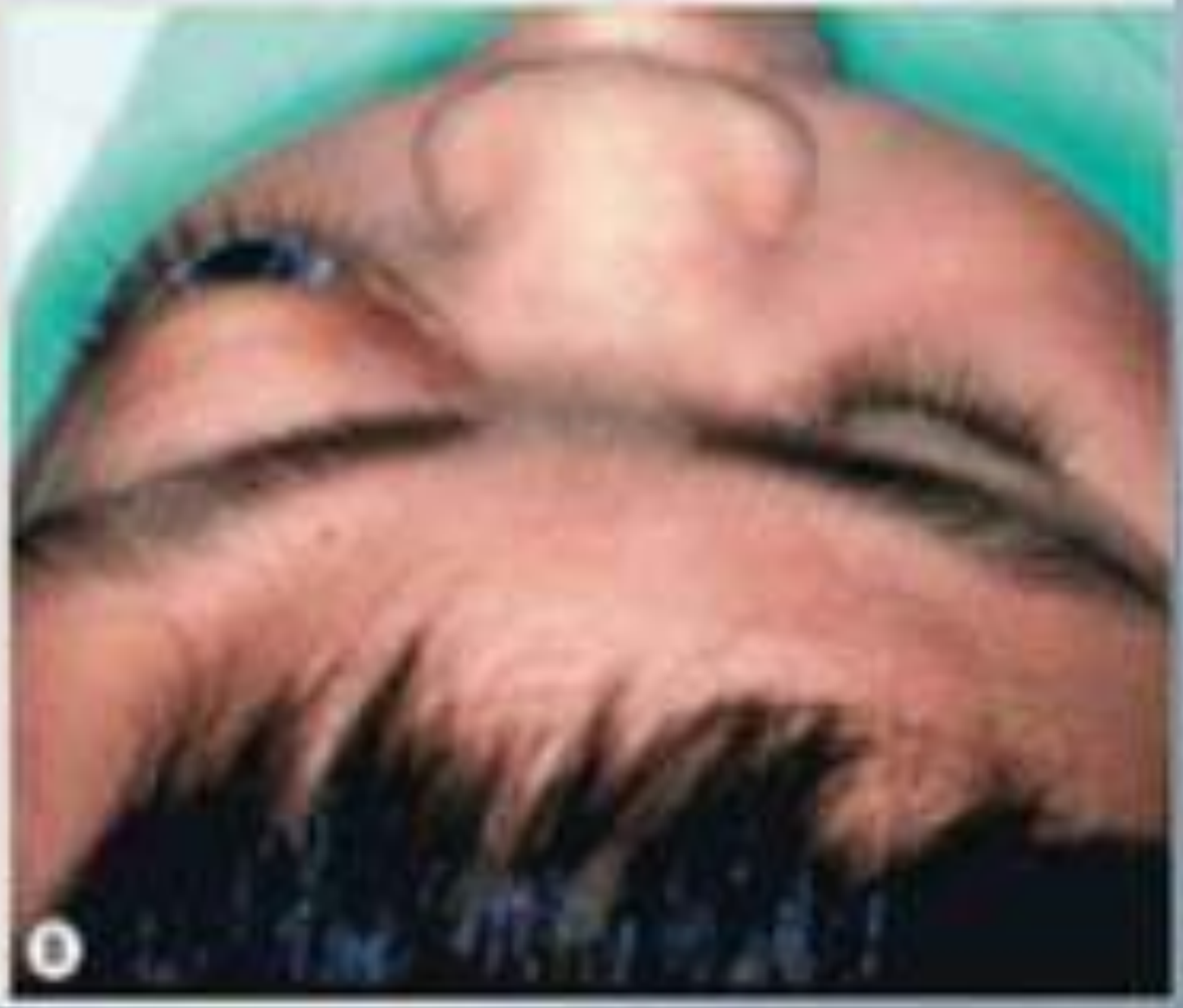
A Inspection

2 Globe Position

- Proptosis (Axial forward Protrusion of the globe)

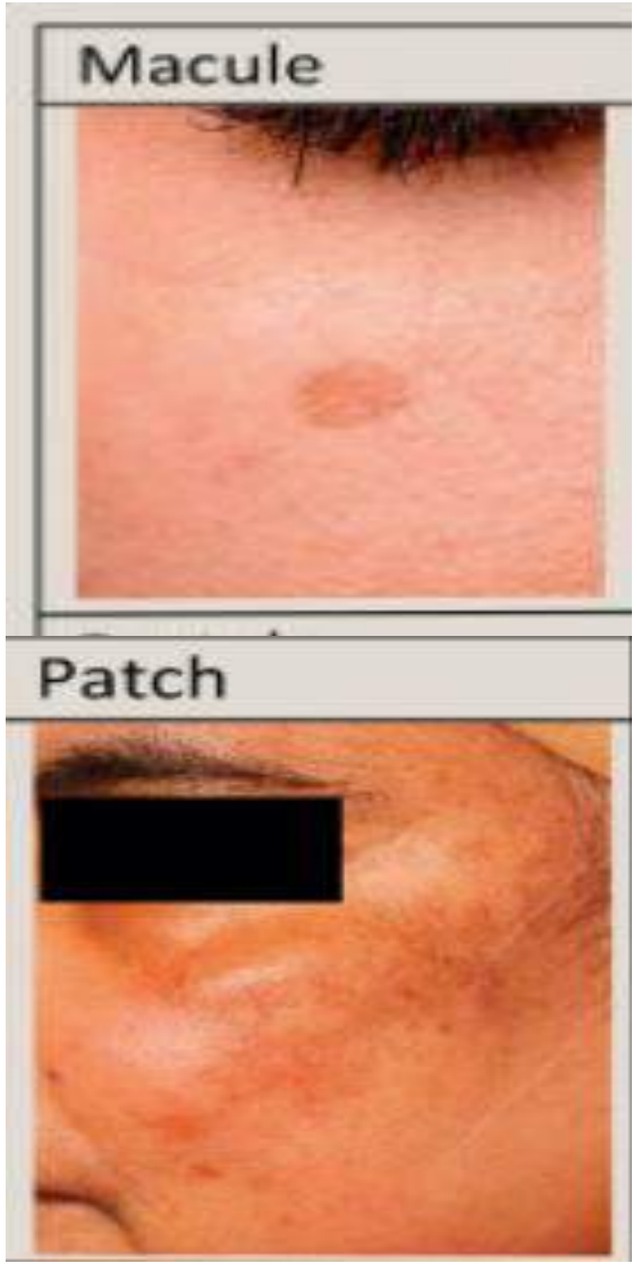
"Nafziger Test"

- *Looking from above*
- *Bring Upper & Lower orbital margins in the same plane*
- *Look whether the cornea is coming out of this plane*



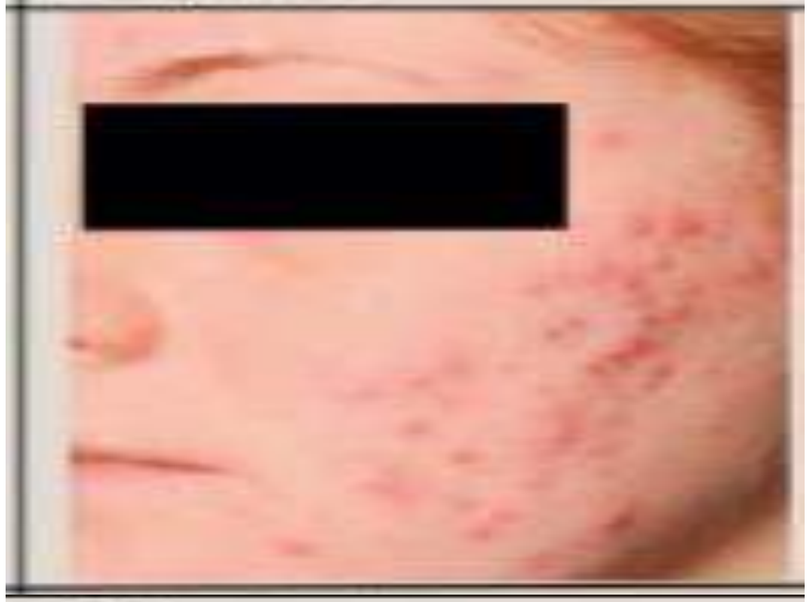
Skin examination

- **Macule**: A macule is a change in surface color, without elevation or depression and, therefore, nonpalpable, well or ill-defined, variously sized, but generally considered less than either 5 or 10 mm in diameter at the widest point.
- **Patch**: A patch is a large macule equal to or greater than either 5 or 10 mm across, depending on one's definition of a macule Patches may have some subtle surface change, such as a fine scale or wrinkling, but although the consistency of the surface is changed, the lesion itself is not palpable.



- **Papule**: A papule is a circumscribed, solid elevation of skin with no visible fluid, varying in size from a pinhead to less than either 5 or 10 mm in diameter at the widest point.
- **Plaque**: A plaque has been described as a broad papule, or confluence of papules equal to or greater than 1 cm, or alternatively as an elevated **plateau-like** lesion that is greater in its diameter than in its depth.
- **Nodule**: A nodule is morphologically similar to a papule in that it is also a palpable spherical lesion less than 1 cm in diameter. However, it is differentiated by being centered deeper in the dermis.
- **Tumour**: Similar to a nodule but larger than 1 cm in diameter.
- **Vesicle**: A vesicle is small blister, a circumscribed, fluid-containing, epidermal elevation less than either 5 or 10 mm in diameter at the widest point ,the fluid is clear serous fluid.

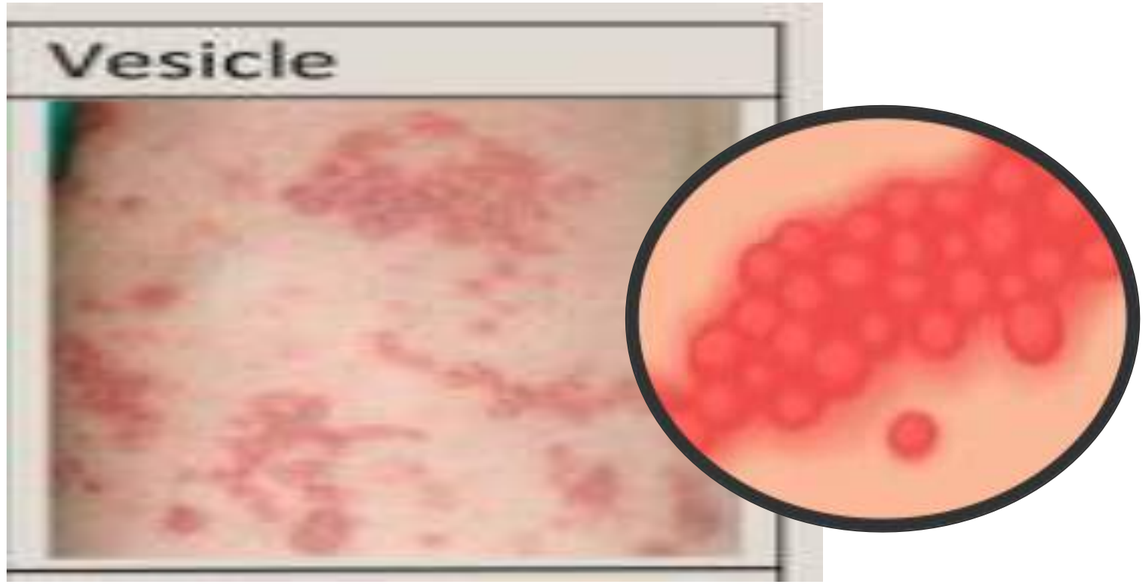
Papule



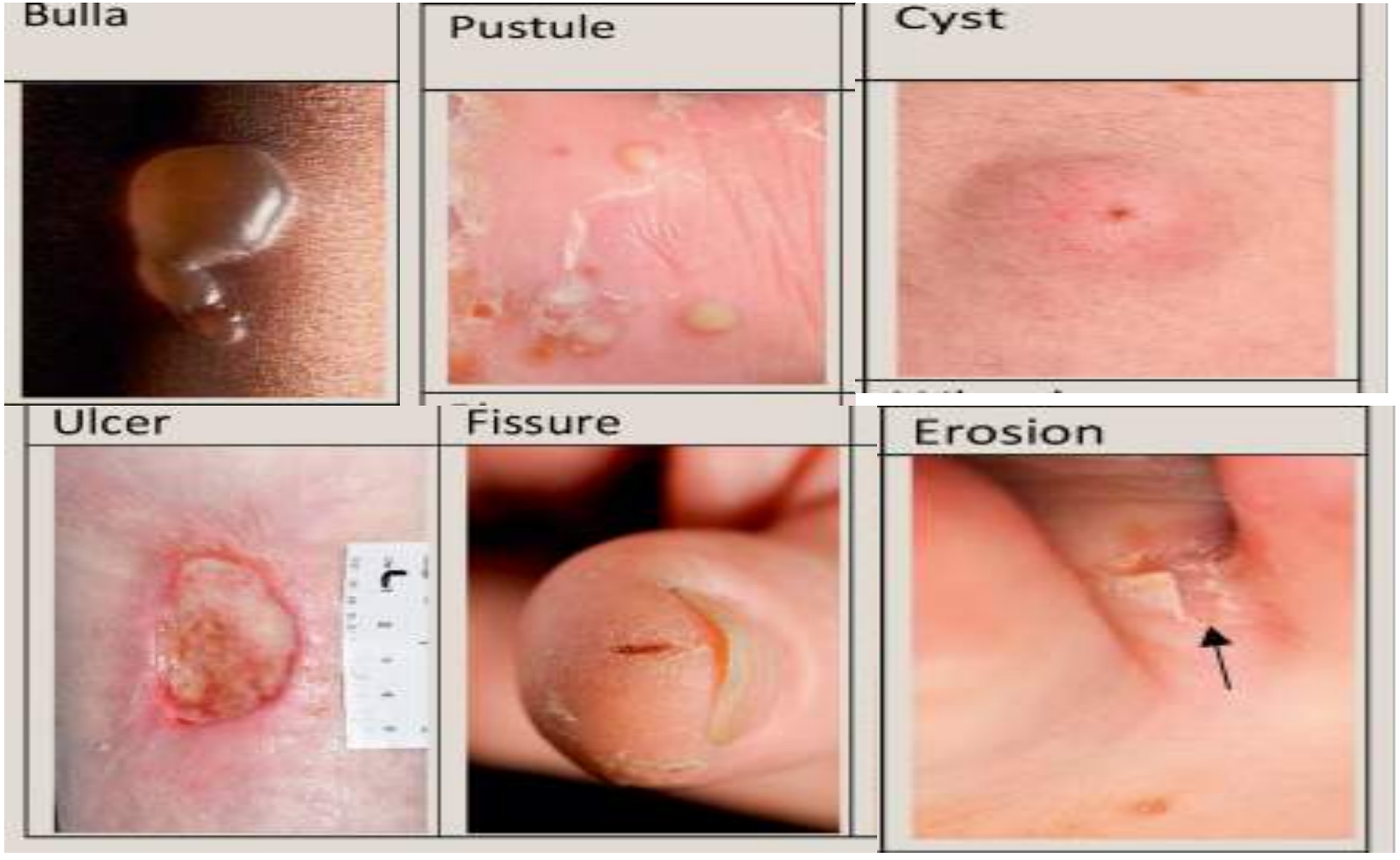
Plaque

Nodule

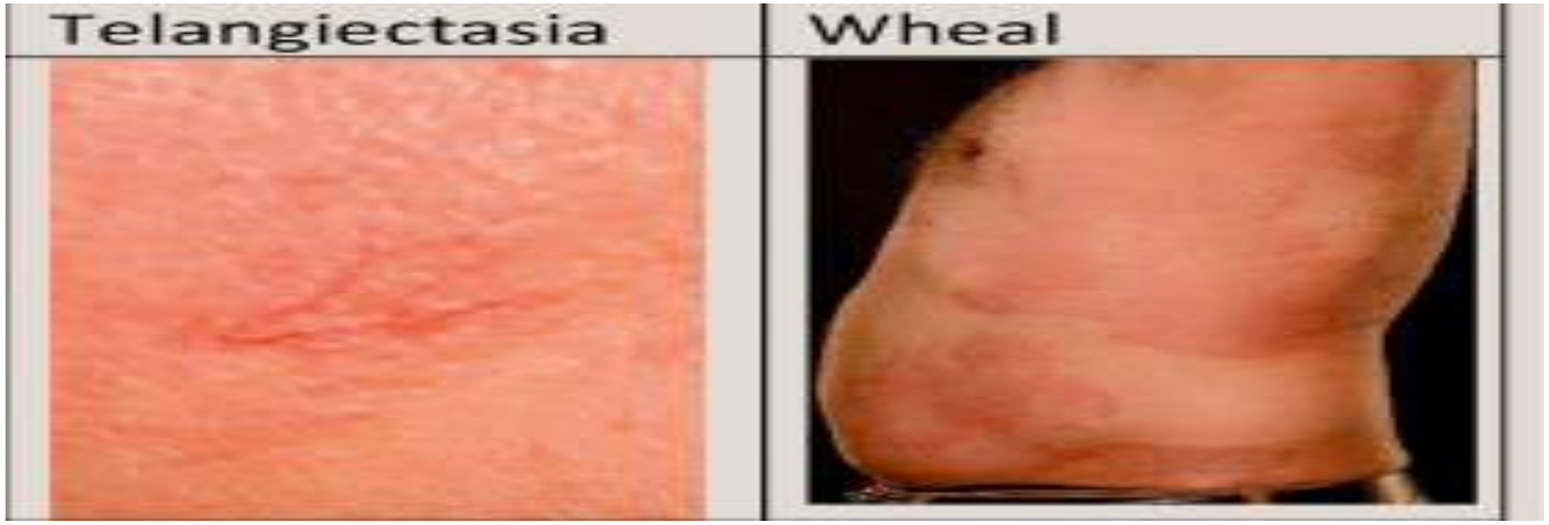
Vesicle

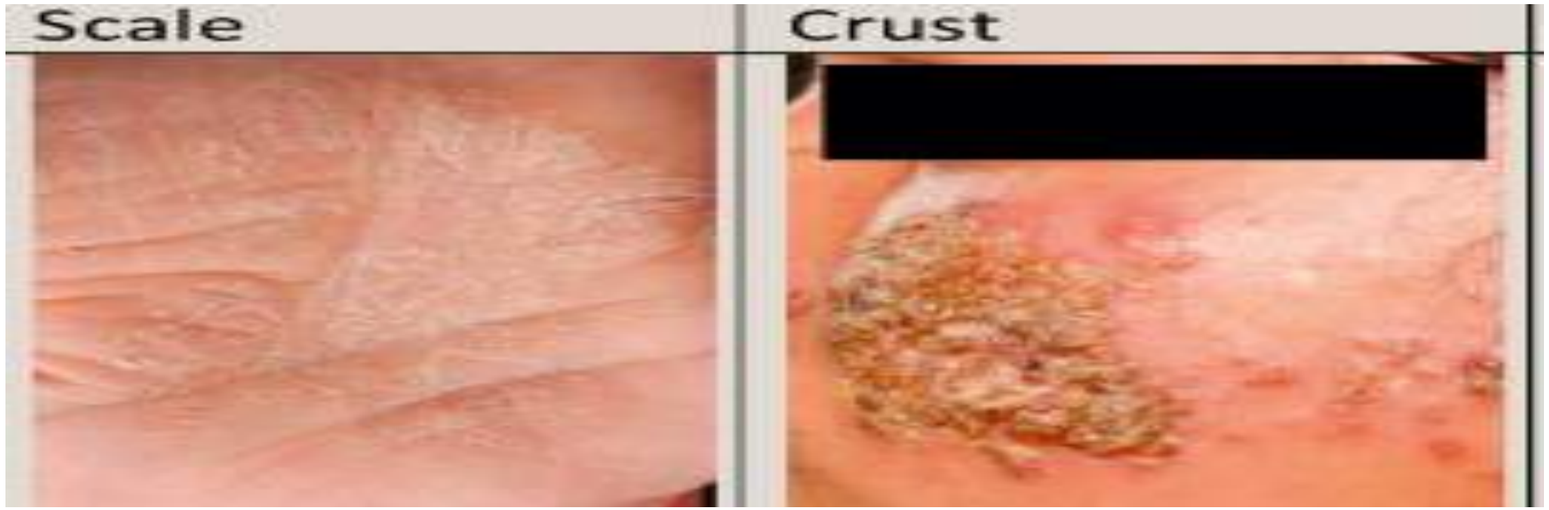


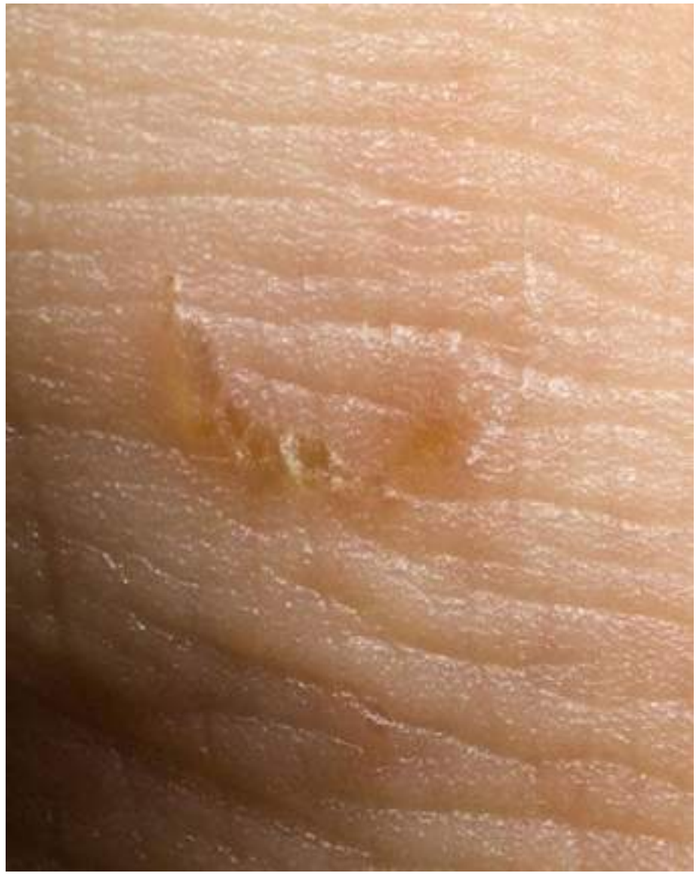
- **Bulla**: is a large blister, a rounded or irregularly shaped blister containing serous or seropurulent fluid, equal to or greater than either 5 or 10 mm.
- **Pustule**: is a small elevation of the skin containing cloudy or purulent material (pus) usually consisting of necrotic inflammatory cells. These can be either white or red.
- **Cyst**: A cyst is an epithelial-lined cavity containing liquid, semi-solid, or solid material.
- **Erosion**: is a discontinuity of the skin exhibiting incomplete loss of the epidermis, a lesion that is moist, circumscribed, and usually depressed.
- **Ulcer**: is a discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
- **Fissure**: is a crack in the skin that is usually narrow but deep.


Bulla
Pustule
Cyst
Ulcer
Fissure
Erosion

- **Wheal**: is a rounded or flat-topped, pale red papule or plaque that is characteristically evanescent, disappearing within 24 to 48 hours. The temporary raised bubble of taut skin on the site of a properly-delivered intradermal injection is also called a welt, itself frequently referred to as simply "raising a wheal" in medical texts.
- **Telangiectasia**: represents an enlargement of superficial blood vessels to the point of being visible.
- **Burrrow**: appears as a slightly elevated, grayish, tortuous line in the skin, and is caused by burrowing organisms or secondary lesions
- **Scale**: dry or greasy laminated masses of keratin that represent thickened stratum corneum.
- **Crust**: dried serum, pus, or blood usually mixed with epithelial and sometimes bacterial debris.

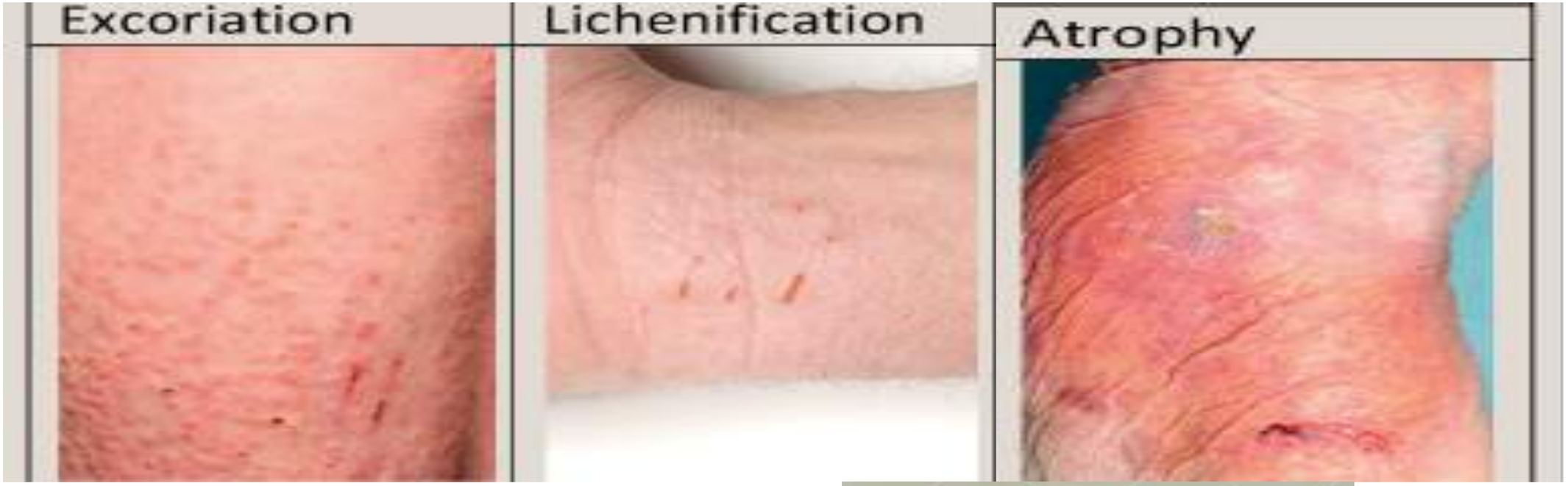


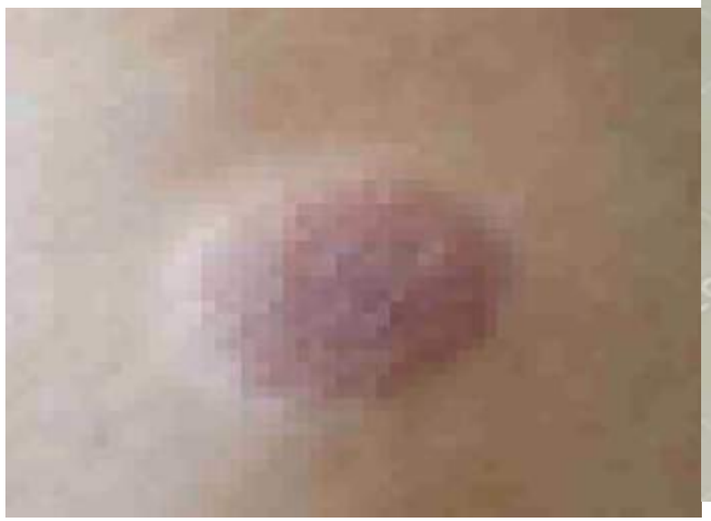




Burrow

- **Lichenification**: **epidermal** thickening characterized by visible and palpable thickening of the skin with accentuated skin markings.
- **Excoriation**: a punctate or linear abrasion produced by mechanical means (often scratching), usually involving only the epidermis, but commonly reaching the papillary dermis.
- **Induration**: **dermal** thickening causing the cutaneous surface to feel thicker and firmer.
- **Atrophy**: refers to a loss of tissue, and can be epidermal, dermal, or subcutaneous. With epidermal atrophy, the skin appears **thin**, translucent, and wrinkled. Dermal or subcutaneous atrophy is represented by **depression** of the skin.
- **Maceration**: softening and turning white of the skin due to being **consistently wet.**

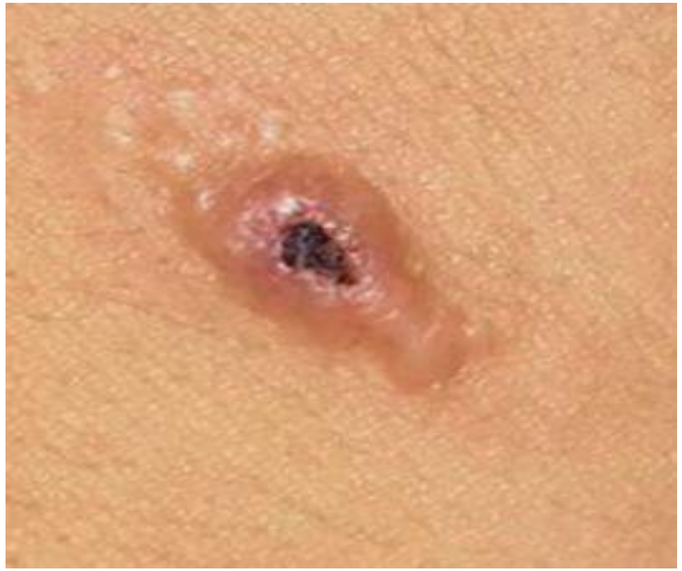




Induration

Maceration

- **Umbilication**: formation of a depression at the top of a papule, vesicle, or pustule"Configuration" refers to how lesions are locally grouped ("organized"), which contrasts with how they are distributed.



Other terminals:-

- **Agminate**: in clusters
- **Annular or circinate:** ring-shaped
- **Arciform** or arcuate: arc-shaped
- **Digitate**: with finger-like projections
- **Discoid** or nummular: round or disc-shaped
- **Figurate**: with a particular shape

Abnormal Color of the Skin

- **Brown (melanin):** the major component of skin color ; it is the presence or absence of melanin in the melanosomes in melanocytes and melanin in keratinocytes that is responsible for epidermal pigmentation.
- Two groups of pigmentary disorders are commonly distinguished: the disorders of the quantitative and qualitative distribution of normal pigment and the abnormal presence of exogenous or endogenous pigments in the skin. The first group includes hyperpigmentations, which clinically manifest by darkening of the skin color, and leukodermia, which is characterized by lightening of the skin.
- Y**ellowish** of the skin, **brownish** of skin .

Other points to be noticed in the skin

- **Sweating** usually in hyperthyroidism,psychonearoces cold clammy skin
- **Dry skin** mostly in fever ,hypothyroidism,dehydration.
- **Pigmentation** of the skin in the Addison disease .adrenal insufficiency .Also may occur in the followings:
- Arsenic poising
- Chronic liver disease
- Therapeutic irradiation
- Intestinal irradiation
- Intestinal malabsorption
- Malignant cochexia
- Gangrene may lead to blackness
- Flashings of the skin may be occur due to emotional causes hormone imbalance ,fever hyperthyroidism

Physical Examination of the Thyroid Gland

Accurate physical examination of the thyroid gland and the neck, together with a palpation of the radial pulse and a look at the patient, can easily make a correct pathological diagnosis in the majority of cases. .

- Determining the **size** of the thyroid gland, whether it is enlarged or not.
- Detecting **nodules** in the thyroid gland whether solitary or multiple.
- The **consistency** of an enlarged thyroid gland as well as the consistency of the nodules, whether cystic, soft, firm, or hard.
- Determining the presence of enlarged **cervical** lymph nodes, their size, and their consistency.

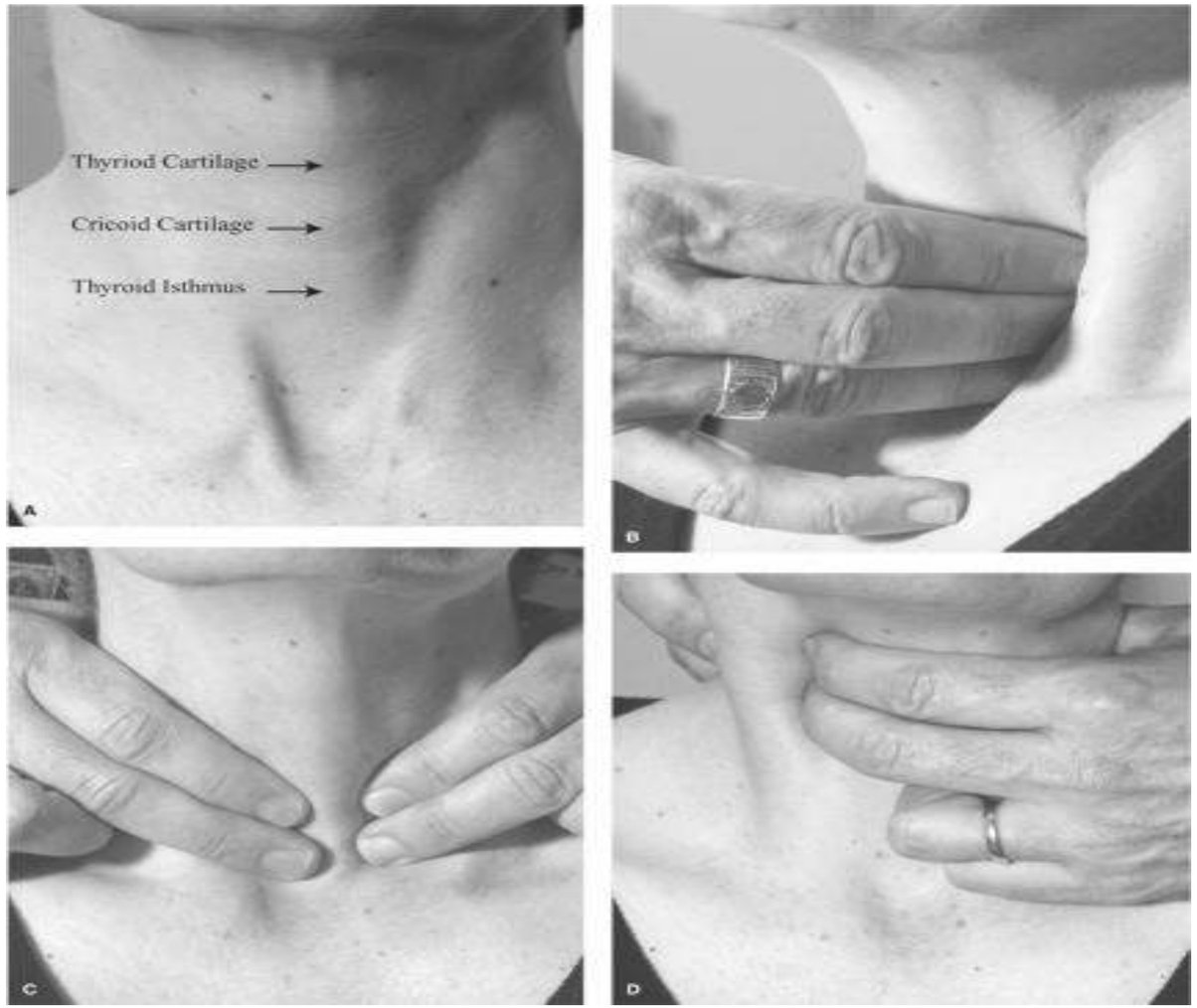
- **Tachycardia** and **exophthalmos**, and together with the history, one can readily make an accurate assessment of the patient's apparent thyroid complaint as to:

1) whether the patient has no enlarged thyroid gland,
2) whether the patient is hyperthyroid,
3) whether the patient has a benign or malignant thyroid condition.

What are the requirement from the dentist in order to have an accurate diagnosis?

- Gentleness in palpation.
- Care in detecting and describing all possible abnormalities in the thyroid gland and in the neck.
- A clinicopathological correlation to achieve accuracy.
- Inspection and palpation examination of the neck.

- Inspects and palpates the neck. From behind, palpates the neck. The dentist inspects the neck for gross diffuse enlargement,
- Asymmetry, skin changes, signs of inflammation, or gross nodularity.
- The patient is asked to swallow saliva or small quantities of fluid repeatedly during the examination.



- A normal thyroid gland is **rarely** palpable. An enlarged thyroid gland is readily palpable.
- Any nodule on the neck near the area where the thyroid gland is normally located and which moves with **deglutition** can be said to constitute part of a primary thyroid pathology.
- Consistency of a diffusely enlarged thyroid **gland** in terms of hard, firm, and soft, and the consistency of a thyroid **nodule** in terms of cystic and solid.

- A **solid** thyroid nodule may be one that has purely gross tissue content, no fluid content, or one that has both tissue and fluid content.

- Clinically, a **cystic** thyroid nodule is usually **soft** on palpation. However, it may be **firm** if it is tensely filled with fluid. A solid thyroid nodule, on the other hand, may be soft, firm, or hard on palpation. Notes down the mobility of the enlarged thyroid gland and the nodules.
- Mobility of a diffusely enlarged thyroid gland is best determined not so much by its movement with deglutition but by its degree of **fixation** to the underlying prevertebral fascia.

- **Normally**, the whole thyroid gland and the trachea to which it is attached can be easily moved sideways over the surface of the prevertebral fascia.
- The mobility of a **thyroid nodule**, is best determined by its degree of **fixation to the tracheal fascia.**
- A thyroid nodule that is **not** adherent to the tracheal fascia is usually movable.
- Mobility of a thyroid gland pathology is best determined by its degree of **fixation** to either the ttracheal fascia or the prevertebral fascia, or both.

The important data that should be derived from a physical examination of the thyroid gland and the neck.
Palpation of thyroid gland and the neck.

I. Thyroid gland not palpable or barely palpable

II. Thyroid gland palpable

A. Diffuse glandular enlargement

- Size
- Consistency
- Mobility

B. Nodular glandular enlargemen

- Location
- Number
- Size
- Consistency
- Mobility

III. Enlarged cervical lymph nodes

- Location
- Number
- Size
- Consistency

The examination of the salivary gland

- Which of the glands is affected? Most commonly, it is the **parotid**. Conditions differentially affect the different salivary glands.
- If there is **swelling**, is it unilateral or bilateral? Is it **constant** or does it comeand go? Is the swelling **painful**? Pain may be referred to the **ear or throat.**
- **How long** has the patient experienced symptoms? Has any **mass** increased in size since it was first noticed?
- Are symptoms affected by **eating**?
- Is there a feeling of **dry** mouth?
- Are there **systemic** symptoms suggestive of **infection, autoimmune disease, sarcoidosis or malignancy?**
- Is there anything of **relevance** in the current medical and dental history, or medication and immunization record?

Examine the major salivary glands

The parotid glands:

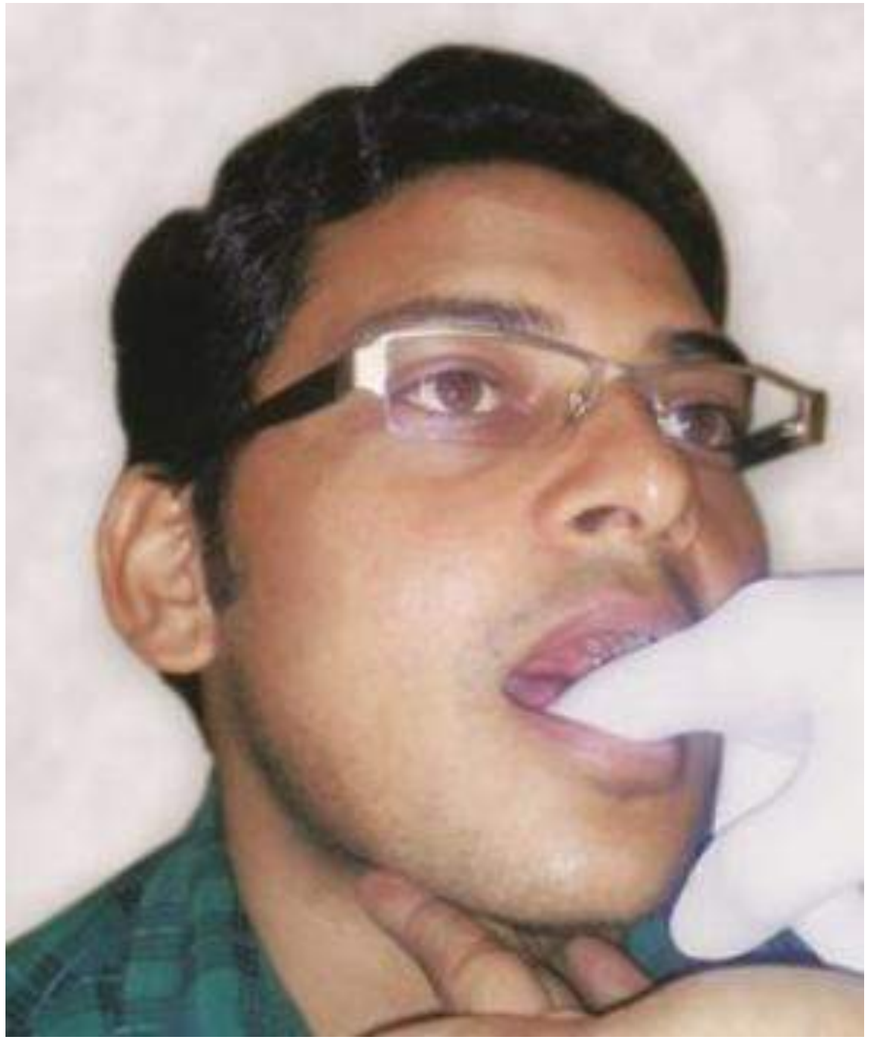
- Swellings of the parotid are apparent as a **loss** of the angle of the jaw. The **accessory** lobe may also cause a lump anterior to the ear. The **deep** lobe needs to be inspected and palpated through the mouth. Swelling can displace the ipsilateral tonsil.
- Try to differentiate between generalized swelling of the gland, which tends to be due to obstruction of the duct or inflammatory disease, or localized lumps, which are more likely to be tumors
- Ask the patient to **clench** their teeth to allow palpation of the masseter. The anterior part of the parotid duct can be felt as it crosses the anterior border of the masseter muscle and occasionally a stone can be palpated in this part of the duct.

- Inspect the **orifice** of the duct in the mouth opposite the second upper molar by retracting the cheek with a spatula. •**Pressure** on the body of the gland may lead to the extrusion of pus at the orifice in patients with **parotitis**.
- Examine the **facial nerve**. Any facial weakness or asymmetry is highly suggestive of **malignancy**.
- Differentiating a swollen parotid gland and cervical lymphadenopathy may be very difficult clinically. Usually it is possible to feel in front of lymph node.

The submandibular gland

- Submandibular gland pathology usually involves swelling beneath and **anterior to the angle** of the jaw.
- Inspect the orifices of the duct by asking the patient to **lift** their tongue to the roof of the mouth, noting the presence of inflammation or pus or indeed a visible impacted stone.
- Examine **bimanually** with the index finger of one hand inside the mouth and fingers of the other hand over the outer surface of the lump in the neck. Under normal circumstances, the gland is **not** palpable but, if enlarged, can be felt 2-3 cm anterior to sternomastoid, below the horizontal ramus of the mandible. The gland has a **rubbery** consistency. The gland should not be fixed to the floor of the mouth or tongue. Check the course of the duct for a stone.

- Attempt to differentiate between a **submandibular** swelling and superior cervical lymph nodes which are deep to sternomastoid.
- The **sublingual** glands lie just beneath the mucosa in the **floor** of the mouth and empty directly into the mouth or into the submandibular duct. The gland is **not** discretely palpable, and the duct openings usually visible.



Terminology

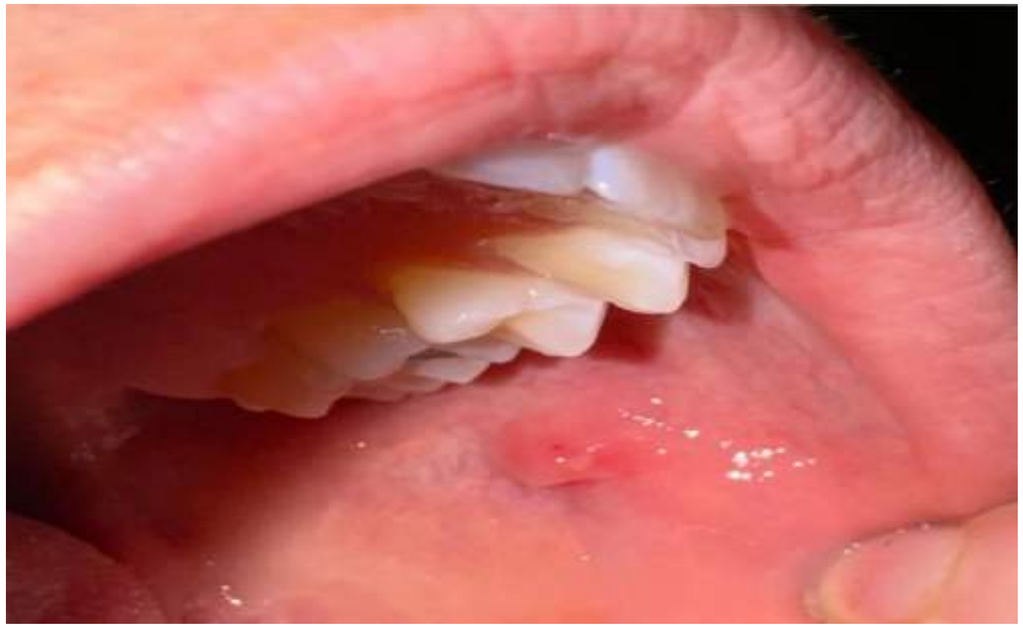
- **Sialadenitis** refers to inflammation of a salivary gland and may be acute or chronic, infective or autoimmune.
- **Sialolithiasis** refers to **stone-related** disease within the ductal systems of a gland.
- **Sialectasis** refers to the dilation of a duct due to stones or strictures.
- **Sialadenosis** refers to non-neoplastic, non-inflammatory swelling with acinar **hypertrophy and ductal atrophy.**

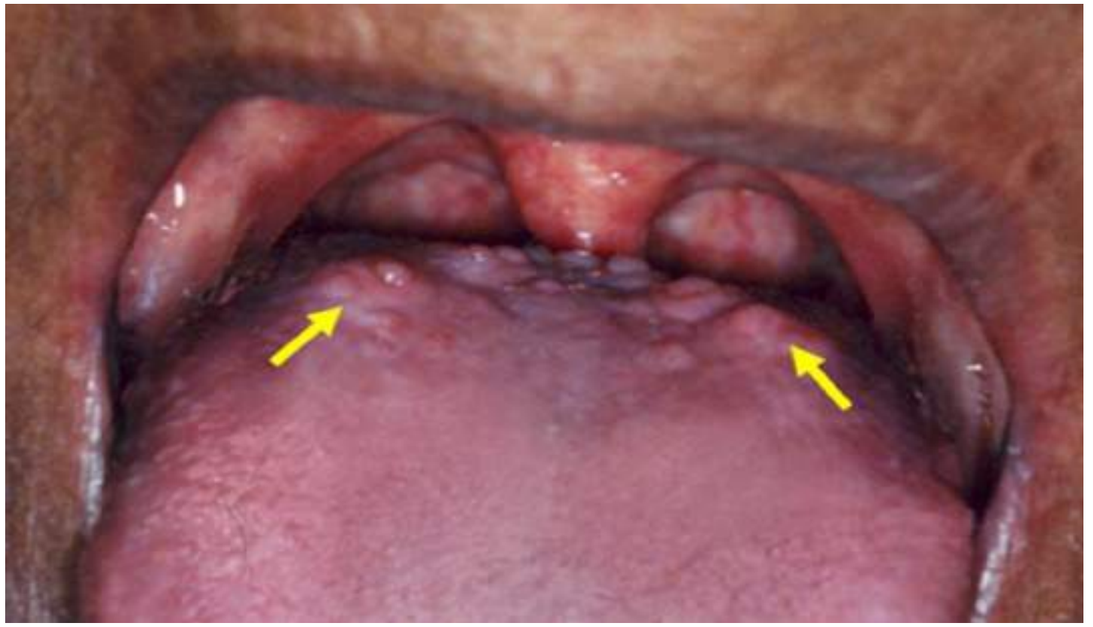
INTRA ORAL EXAMINATION

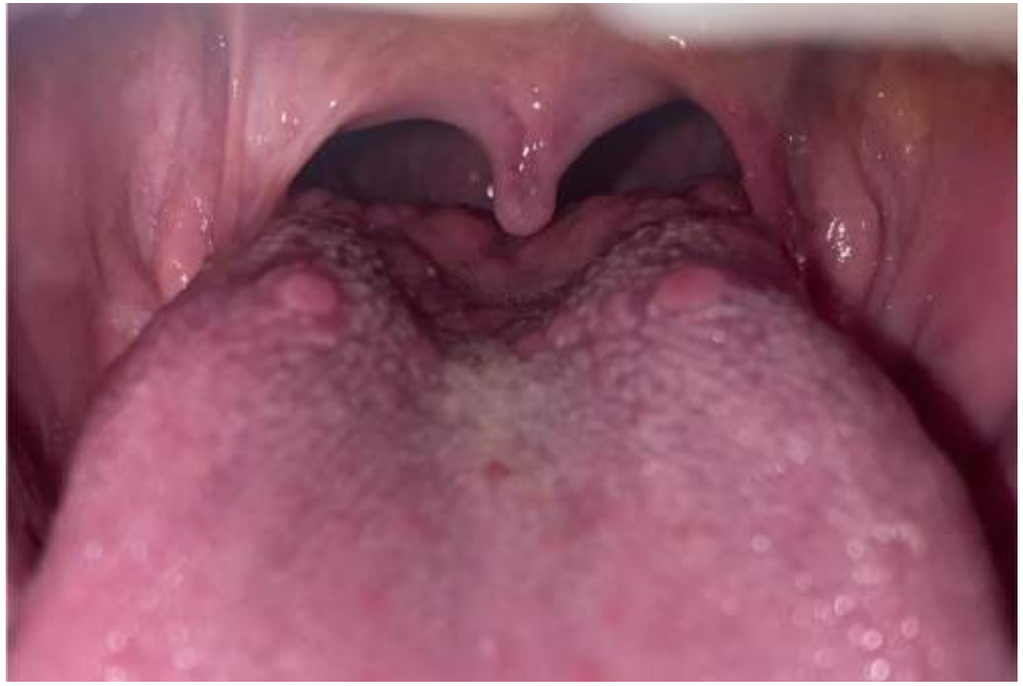
Dr. Marwah Waleed

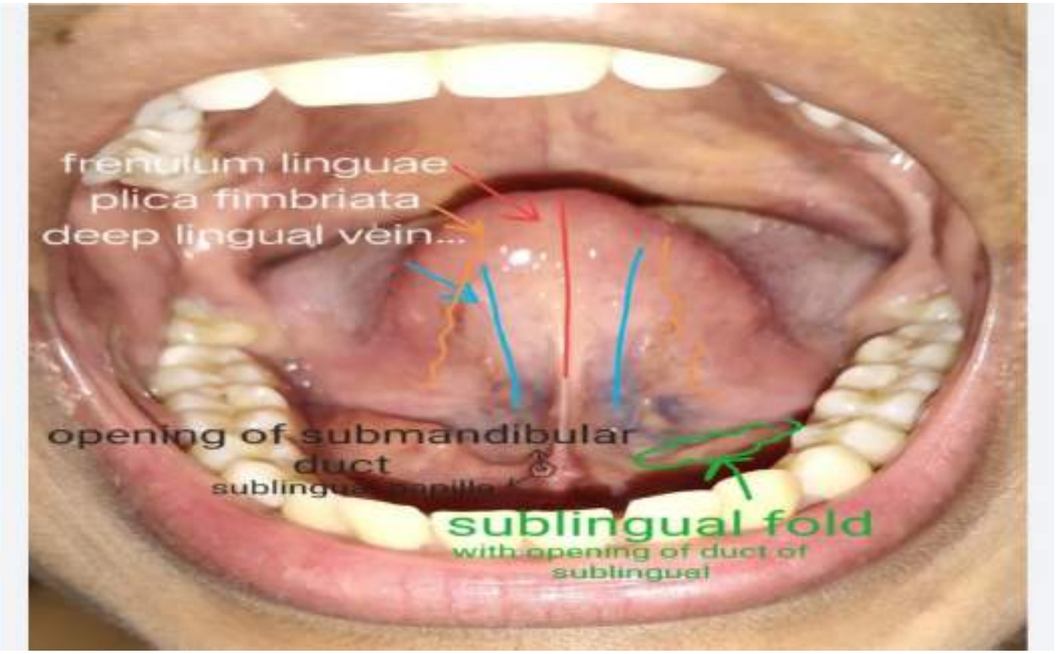
Normal structures that may be mistaken for lesions

- • **Stensen's duct is** the duct of the parotid gland. It opens into the mouth on the posterior buccal mucosa opposite the maxillary molars. The duct opening may be flat or slightly raised.
- • The **circumvallate papillae** form a V-shaped row of rounded papillae at the junction of the anterior 2/3s and the posterior 1/3 of the tongue.
- • The **lingual tonsils** are found on the posterior-lateral aspect of the oral tongue. They may become enlarged with viral infections.
- • **Plicafimbriata** are folds of mucosa on the ventral surface of the tongue on either side of the lingual frenum. The folds may looked fringed due to mucosal tags.








frenulum linguae
plica fimbriata
deep lingual vein...
opening of submandibular duct
sublingual fold
with opening of duct of sublingual

Variations of Normal

1. **Fissured tongue** is a common condition. Multiple grooves are seen on the dorsum or occasionally the lateral tongue. This is reported in 2% to 5% of the population.
2. **Fordyce granules** are ectopic sebaceous glands that occur on the oral mucosa. They are commonly seen on the buccal mucosa or the lateral vermillion of the upper lip. They appear as groups of yellowish-beige slightly raised areas (papules) measuring 1 to 3 mm diameter.
3. **Varicosities** are enlarged veins, commonly seen on the ventral tongue. These are usually seen in older patients. Varicosities blanch on pressure. A glass slide or glass test tube can be used to press on the varicosity. The pressure causes collapse of the vein with disappearance of the purple color. On releasing the pressure, the blood flows back into the vein, and the purple color returns.

Common oral pathology

1. **Geographic tongue** a common benign condition seen in 1% to 3% of the population. The eitiology is unknown. The classic features are multiple pink or red circular or semicircular well-demarcated areas on the dorsum or lateral aspect of the tongue. The erythema is partially surrounded by a slightly raised yellowish-white rim or border. It may be seen in association with fissured tongue.
2. **Linea Alba** (white line) appears as a white (hyperkeratotic) horizontal line along the buccal mucosa at the level of the occlusal plane. This is a common condition and is often bilateral. It is due to frictional irritation or sucking trauma.
3. **Benign vascular lesions** appear as red or purple areas on the oral mucosa. These are usually seen in older patients. They blanch on pressure. A glass slide or glass test tube can be used to press on the varicosity. The pressure causes collapse of the blood vessels with disappearance of the purple color. On releasing the pressure, the blood flows back into the blood vessels, and the purple color returns.
4. **Morsicatio buccarum** or cheek biting appears as a ragged slightly translucent area on the buccal mucosa. Most patients, when asked, will admit that they bite their cheek repeatedly.

The examination of the teeth

• Several environmental factors like virus infections, toxins and radio- or chemotherapy may cause missing of permanent teeth. However, most of the cases are caused by **genetic** factors. The genetic factors may be dominant or recessive and it is obvious that in many cases multiple genetic (and environmental) factors are acting together.

• Dominant inheritance of congenitally missing teeth has been shown both in **hypodontia** and **oligodontia**. However in both cases the amount and identity of missing teeth may vary between relatives. In hypodontia, the variability may extend to no teeth actually missing ("reduced penetrance”).

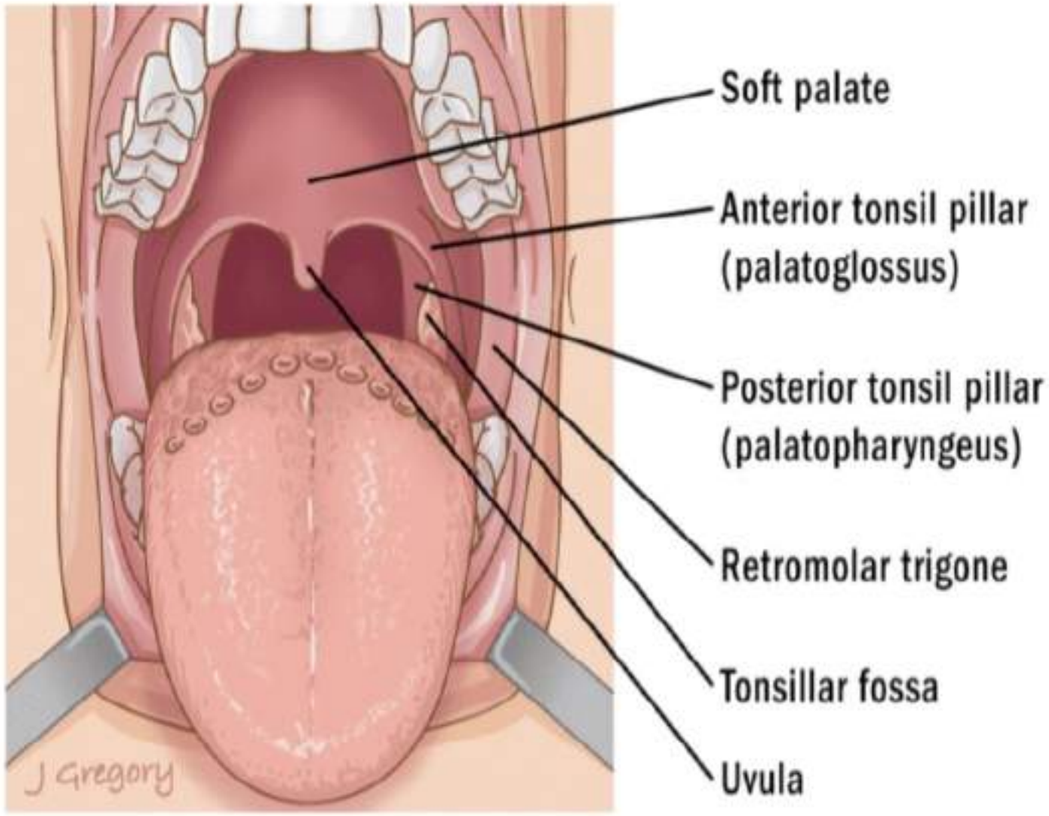
- An example of recessive inheritance is given by recessive incisor hypodontia (RIH).
- In this condition, a recessive gene causes congenital missing of several incisors, including lower permanent incisors and often deciduous
- Supernumerary teeth are classified according to morphology and location (In the primary dentition, morphology is usually **normal** or **conical**.) There is a greater variety of forms presenting in the permanent dentition. **Four** different morphological types of supernumerary teeth have been described:

• conical • tuberculate • supplemental • odontome.

Oropharynx

Examine the oropharynx by placing a mirror or tongue depressor on the dorsal surface of the tongue applying gentle pressure without having the patient stick their tongue out. The dentist should be able to visualize the posterior pharyngeal wall, anterior and posterior pillars and the tonsillar crypt and tonsils, if present. These areas are normally not palpated unless there is a need.

Normal anatomy of the oropharyngeal area



Posterior Pharyngeal Wall

The tissue in this area should appear **very vascular** but otherwise homogenous in color tending towards reddish pink. The surface may be **smooth** or appear to have small coral pink to translucent, gelatin-like, homogenous surface prominences which are consistent with normal areas of scattered lymph tissues (**lymphoid aggregates).** Pathologic findings include:

- **Homogenous and non-tender erythema** associated with post nasal drip and/or smoking.
- **Erythema and purulent exudate** associated with pharyngitis (infection of the pharynx) may cover portions of the pharyngeal wall.
- **Ulcers**, **erosions** or noticeable enlargements or growths.

Anterior and Posterior Pharyngeal Pillars

- The anterior and posterior pillars should appear **vascular**, **smooth** and **symmetrical**. **Atypical** findings one may encounter include lymphoid aggregates(as found on the posterior pharyngeal wall), areas of **pale scarring** in a radial or stellate pattern from **tonsillectomy**, or torn or absent pillars also a result of this surgery.

Pathologic findings include:

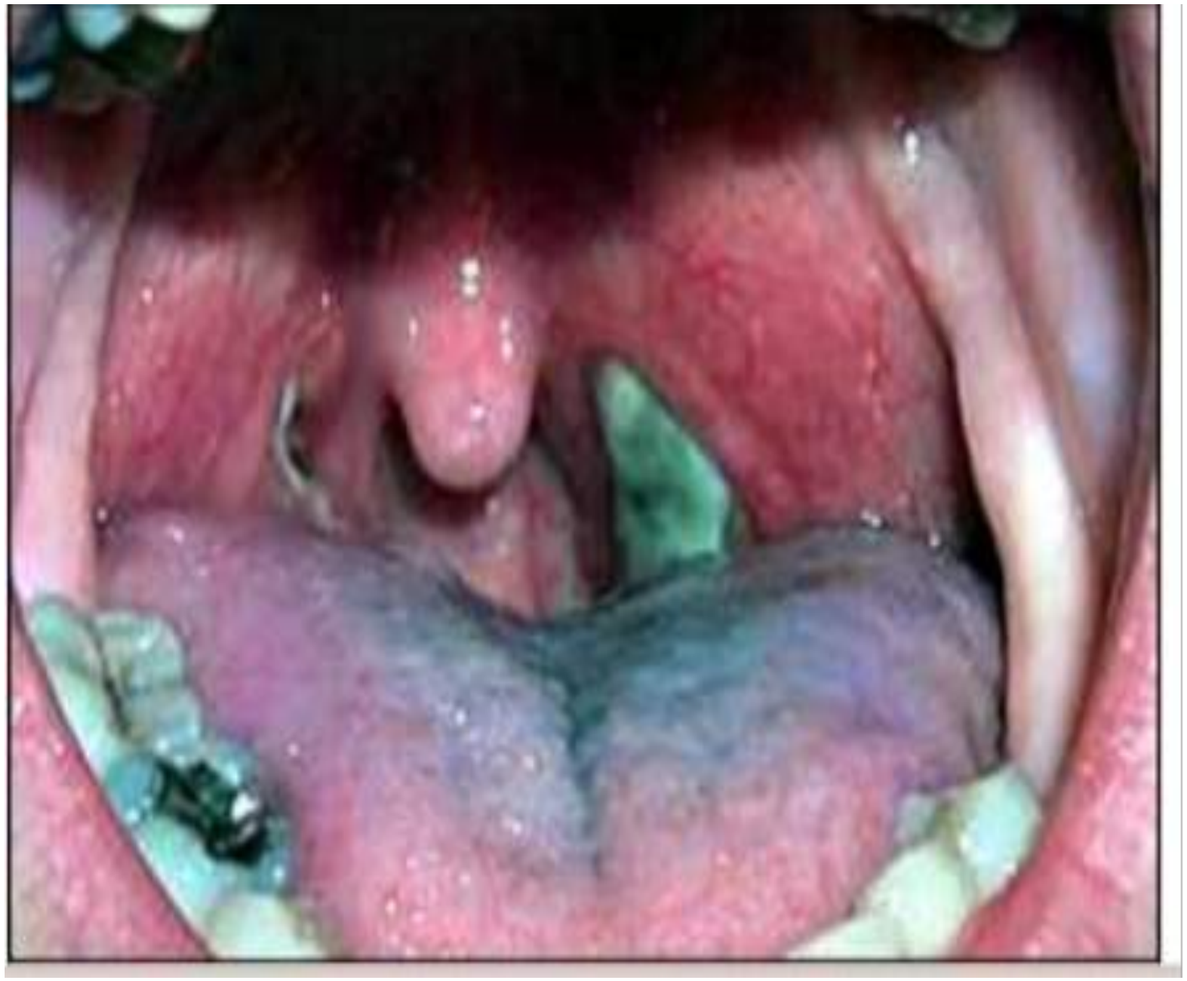
- **Asymmetry**, unless due to tonsillectomy
- **Lesions** of any kind
- **Erythema** associated with tenderness or exudates

Tonsillar Crypt

- The tonsils are examined using **direct** visualization. Dentist will observe **rough, lobular, and coral to light pink** tissue of varying amounts between the anterior and posterior pharyngeal pillars.
- **Atypical** presentations include excessively large or asymmetrical tonsils, cratered surfaces without evidence of erythema or exudates.
- Occasionally, individuals have large crypts in the tonsils that collect food debris, bacteria and hardened material. Patients with this type of cryptic tonsil often complain of **halitosis**(those patients attend to the dentist complaining from bad odor in the mouth). After a tonsillectomy one may observe residual tonsil tissue or a regrowth of lymph tissue in the area.

Pathologic findings include:

- **Swelling**, asymmetry, erythema and/or surface exudates
- **Erythema** and/or dysphagia may also be associated with mouth breathing and may indicate a nasal obstruction. (Dysphagia mean painful or difficult swallowing)



Streptococcal infection of the tonsils.

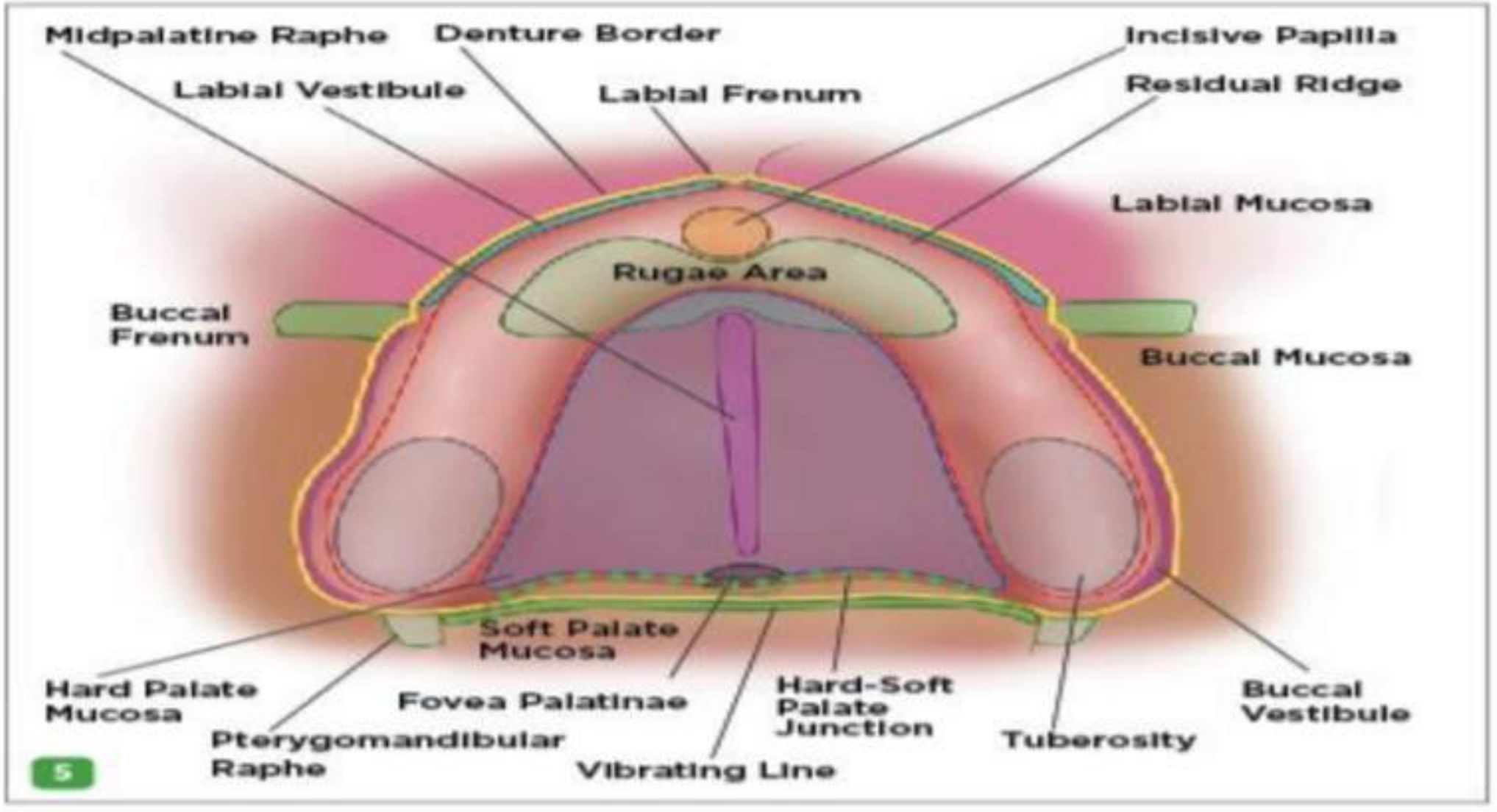
Soft Palate and Uvula

- This area is examined using **direct vision** and is normally **not** palpated unless necessary. If palpation is necessary a topical anesthetic should be used by the dentist and the tissues should be palpated from the mid line out towards the lateral surfaces.
- Normally, this area is slightly **less vascular** than the oropharynx and is usually reddish pink in color .Observe the area as the patient **says "ah."** The tissue should **appear loose, mobile and symmetrical during function**.
- The tissue will have a homogenous, **spongy** consistency on palpation. Atypical observations include yellowish coloring due to increased adipose tissue (especially in **older** patients), excessively long or short uvulas and uvulas that appear slightly asymmetrical at rest. Occasionally one will discover a **bifid** (cleft) uvula. Pathologic findings include:
- **Lesions** of any kind
- **Loss of function** or lack of symmetry during function.

Examination of the hard palate

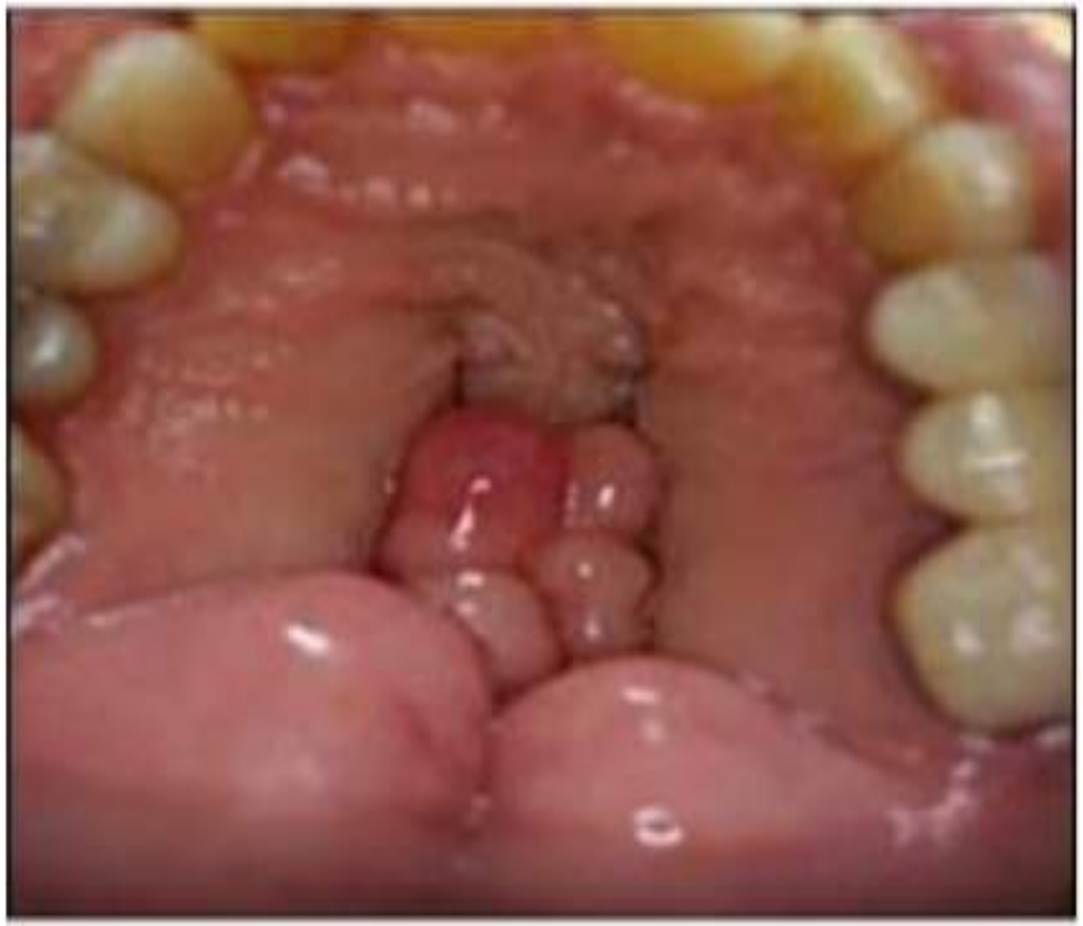
- The dentist should use **firm** pressure and try not to slide the fingers along the tissue of the hard palate .
- In general, the tissue is a homogenous **pale pink color, firm** to palpation towards the anterior and lateral to the midline while more **compressible** towards the posterior and medial to the apices of the teeth. The normal structures of the hard palate should be identified:
- **Incisive papilla –** protuberance of soft tissue lingual to the maxillary central incisors which covers the incisive foramen and normally appears **redder** than the surrounding tissues
- **Raphe** – slightly elevated line extending from the incisive papilla to the soft palate).
- **Rugae** – corrugated ridges radiating laterally from the raphe.

Normal structures of the anterior hard palate



Normal structures of the posterior hard palate.

- **Maxillary tuberosities –** area distal to the last molars the tissue should be a homogenous pink color and firm to palpation.
- The torus palatinus is the most common atypical finding in the hard palate. These tori may range have a smooth surface texture. Often the larger tori will have traumatic ulcers or other traumatic lesions on their surfaces.



Extreme example of a multilobulated torus palatinus.

- Tori are not usually considered a problem unless prosthetic appliances are being considered. Tori also make it difficult to expose intraoral radiographic films.
- **The Pathologic findings include:**

1. **Pigmented macules** – pigmented lesions of any type should be identified to rule out **melanoma**. The palate is also a common area for unintentional **tattoos** resulting from pencil leads being jabbed into the tissues while playing with a pencil or holding it in the mouth.
2. **Thermal burns –** the anterior palate is the most common area for this type of traumatic injury

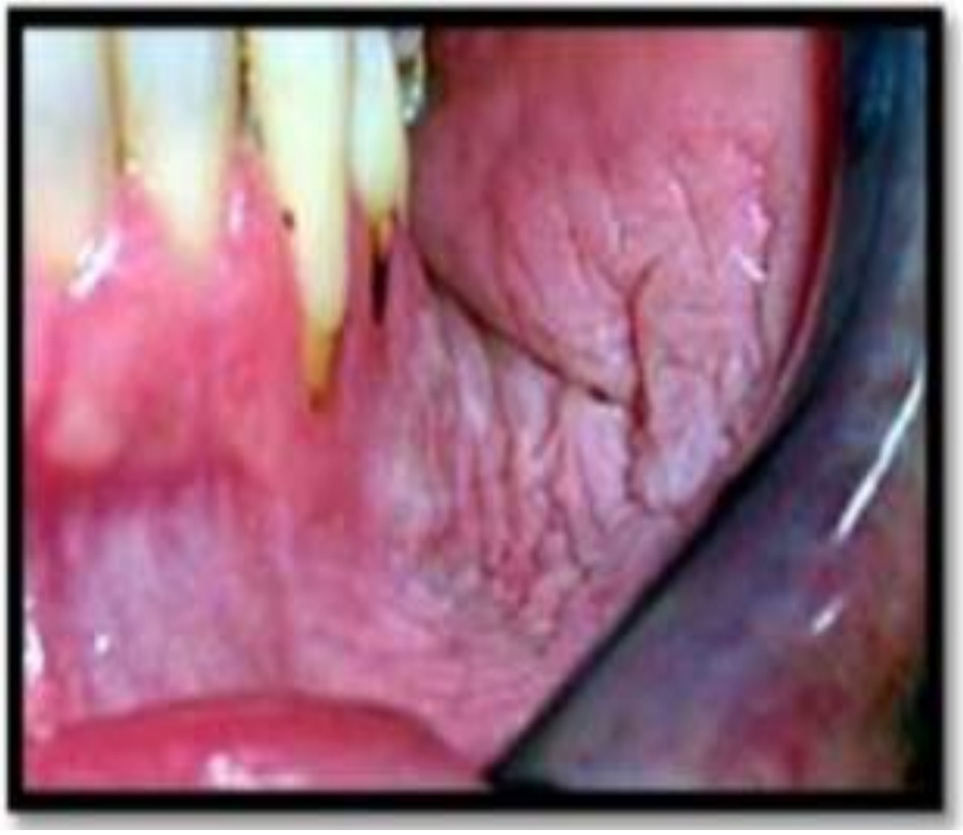
Nicotine stomatitis – whitening and fissuring of the attached gingiva of the hard palate and inflammation of the minor salivary gland ducts.
Papillary hyperplasia – development of finger-like projections usually under a poorly fitting full or partial denture
Other traumatic lesions – abrasions and lacerations resulting from eating injuries.
Systemic related lesions – lesions related to lupus are commonly found in the palate and the palate is a prime location for the **blue nevus.**

Buccal Mucosa

- The buccal mucosa is examined using **direct and indirect vision** followed by **bi-digital** palpation of the entire area. Be sure to pull the tissues away from the retromolar area and stretch the mucosa away from the mucogingival junction.
- The buccal mucosa should be bidigitally palpated pressing the tissue between the index finger and thumb of one hand. Normal tissues of the buccal mucosa appear moist and pink/dark pink.
- They are soft and pliable on palpation with no discernible indurations. Stensen's duct should be identified with or without the presence of a parotid papilla.
- Linea alba, Fordyce's granules and leukoedema are common **atypical** findings on the buccal mucosa. feeling small papules within the tissues usually indicative of **sclerotic or fibrotic minor salivary glands.**

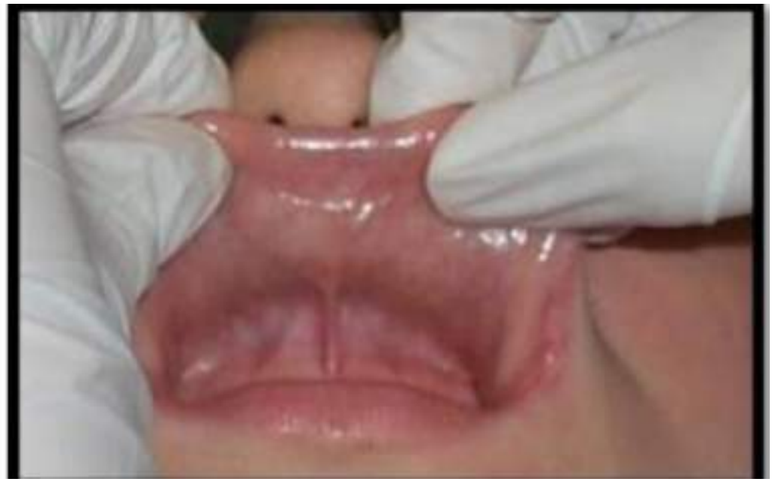
- Varicosities may often present on the buccal mucosa of older patients. The buccal mucosa is also a prime area for stress related habits such as cheek chewing (morsicatio buccarum).
- Assisting the patient in stress reduction techniques and providing awareness of the habit is helpful.
- Pathologic findings associated with the buccal mucosa include:
- **Traumatic injuries** – thermal burns, cheek bites, ulcers, traumatic fibroma
- **Leukoplakia** associated with spit tobacco
- **Neoplastic changes** – erythroplakia, speckled leukoplakia and pigmented lesions
- **Systemic disease** – oral lichen planus, lupus, lipomas, aphthous ulcers, erythema multiforme, and Crohn’s disease.

Leukoplakia associated with spit tobacco.

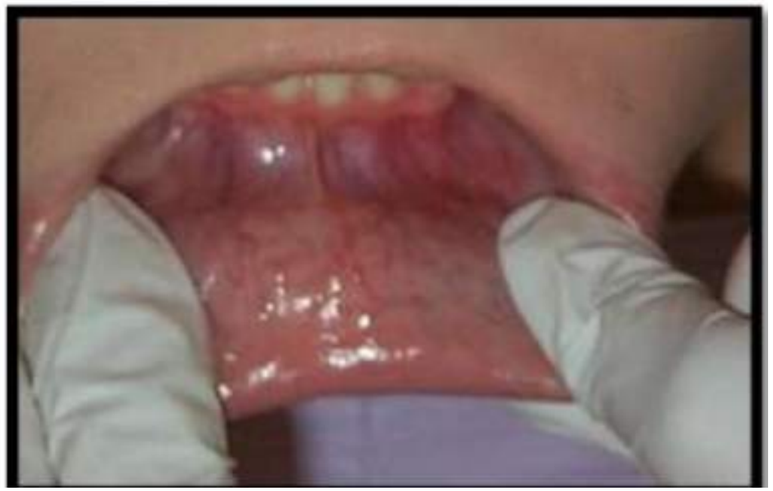


Labial Mucosa

- The labial mucosa is examined using **direct** vision by averting the tissues over the fingers or thumbs followed by **bidigital** palpation of the tissues of the lips.
- Move the tissues from side to side and visualize the frena. Normal lip tissues are a homogenous deep pink color which changes gradually to a deep red color with more prominent vascularity near the mucolabial vestibule. The tissues should be moist and have uniform consistency and thickness when palpated.



Visual examination of the upper labial mucosa.



Visual examination of the lower labial mucosa.

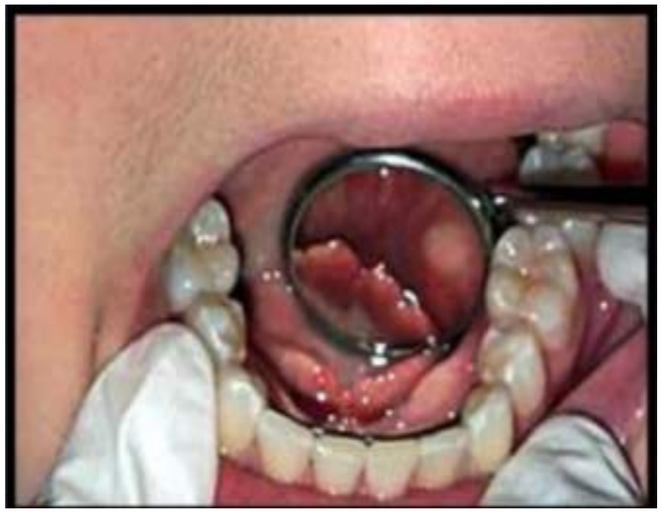
- **Sclerotic minor** salivary glands are common atypical findings as **Fordyce's granules.**
- Pathologic findings include the following:

- **Traumatic injuries** – abrasions, lacerations
- **Dry, cracked lips**
- **Angular cheilitis –** human herpes virus, Candida Albicans
- **Aphthous ulcers**
- **Neoplastic** changes

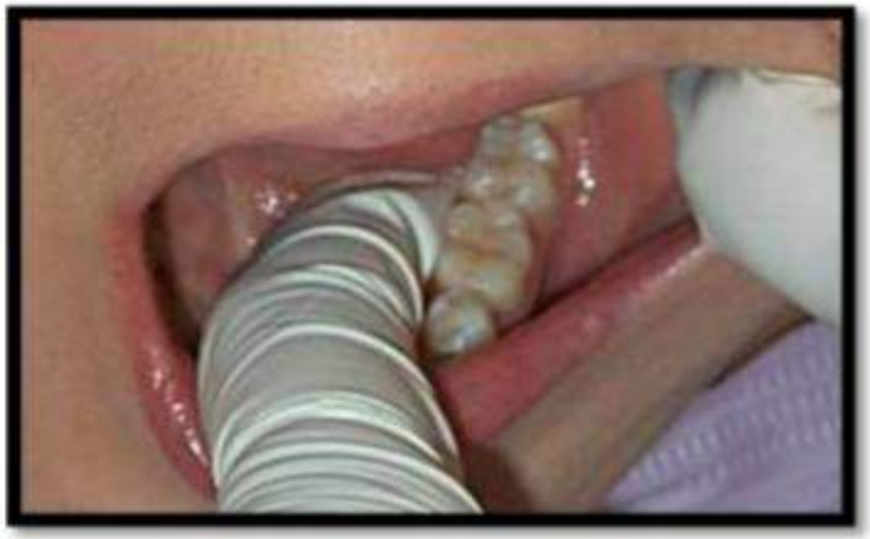
Bidigital palpation of the upper labial mucosa

Mandible

The body of the mandible will be examined using **direct and indirect** vision followed by **digital** palpation of the entire structure. The tissues of the floor of the mouth should be stretched away from the inferior border of the mandible with a mouth mirror.

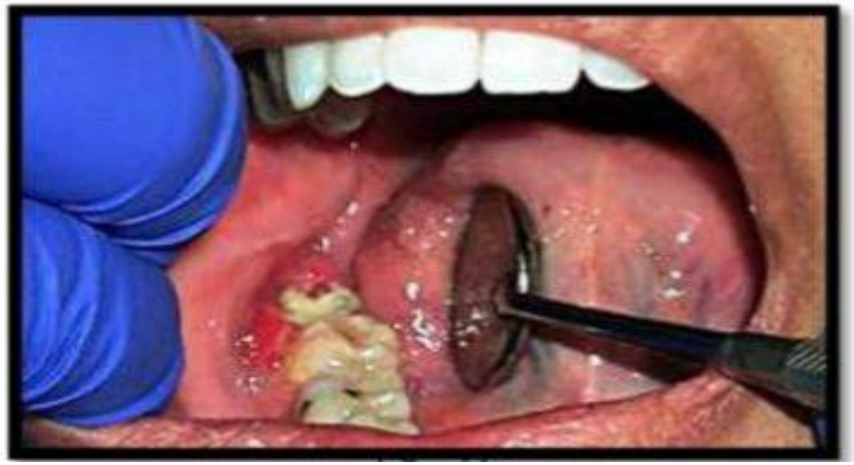


The mirror is used to visualize the anterior lingual portion of the mandible



Use digital palpation pressing the tissues against the body of the mandible for both the lingual and the facial aspects.

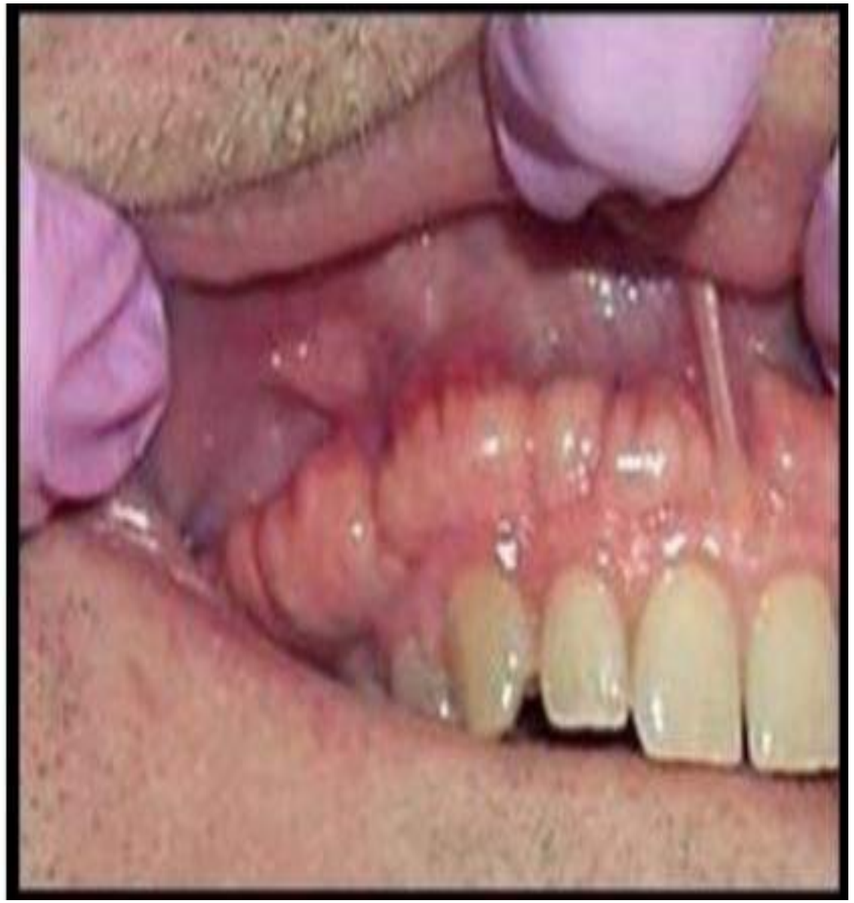
- Normal tissues will be a homogenous coral pink and have a firm consistency with no visible or palpable lesions. **Mandibular tori** and exostoses are the most common atypical findings in this area. The retromolar area may present with partially erupted third molars or scarring from third molar extraction. This area is also prone to **hyperkeratosis** from constant friction from masticatory function.
- Pathologic findings include:
- **Traumatic** lesions – ulcers, abrasions
- **Infections** – pericoronitis
- **Neoplastic** growths
- **Leukoplakia** associated with spit tobacco



Painful pericoronitis surrounding partially erupted tooth

Attached Gingiva

- The attached gingiva of the maxillary and mandibular arches is visually examined using both **direct and indirect** vision. The tissues should appear **pale** pink and homogenous in color and texture Following the visual examination, the attached gingiva is palpated using a **digital** technique.
- The tissue should feel firm to touch and tightly attached to the bone. The most common atypical finding in the area of the attached gingiva is **exostoses**.



Extensive exostoses on the maxillary facial surfaces.

Pathologic findings include:

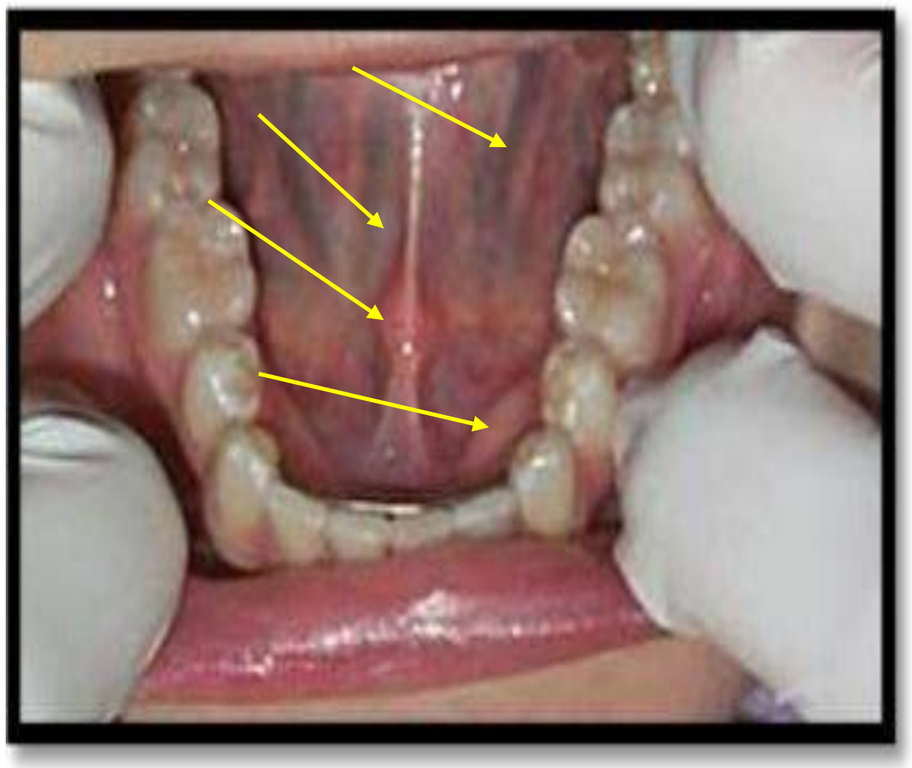
- **Inadequate zones** of attached gingiva – Less than 1 mm of attached gingiva is considered to be inadequate in most cases and the patient should be referred to a **periodontist** for evaluation of the affected area.
- **Mucogingival** involvement – areas with no attached gingiva or areas of extreme recession.
- **Frena problems** – tight frenum attachments or pulls.
- **Traumatic lesions** – ulcers, abrasions, burns.
- **Mucosal disease** such as lichen planus, pemphigus vulgaris,mucous membrane pemphigoid, lupus, and allergic type responses.

Salivary Flow and Consistency

- Salivary flow and consistency will vary with each patient. Some abnormal findings must be noted such as **frothy saliva** or **thick ropy** saliva. the actual flow of saliva appears normal. The mixture of serous and mucous saliva affects the perception of dryness as well.
- When problems arise with the parotid gland, the flow from Stensen's duct will be diminished. **Milking** the salivary glands from the tail toward the mid line assists the clinician in visually assessing the Stensen's duct orifice found next to the maxillary first molar.
- **Gauze** should be used to **dry the floor** of the mouth and visually asses the flow from the Wharton's duct orifice and other ducts of both the sublingual and submandibular glands.

Floor of the Mouth

- The floor of the mouth is examined using direct and indirect vision followed by **bimanual** palpation of the entire area. The patient should be asked to **raise the tongue** making direct visual examination of the tissues toward the midline of the floor of the mouth.
- The **mirror** should be used to examine the areas near the inferior border of the mandible. The tissues should appear moist and very vascular.

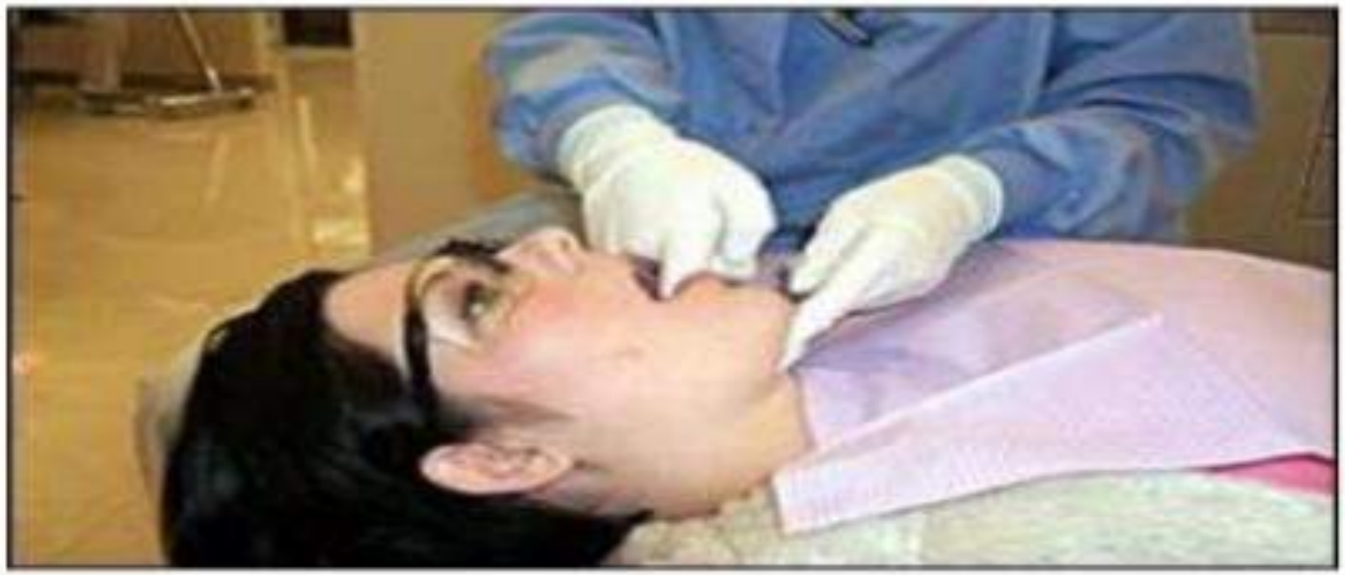


Visual examination of the floor of the mouth. Note the normal structures of the area.

The **normal anatomy** of the area should be identified including:

- **Sublingual caruncle** – small rounded projection at the base of the lingual frenum which houses Wharton's duct from the submandibular salivary gland.
- **Sublingual folds** – two oblique elevations found radiating laterally away from the lingual frenum on either side of the caruncle which house the ducts from the sublingual salivary gland, feel ridge-like and mobile.
- **Lingual frenum** – muscle attachment from the ventral surface of the tongue to the floor of the mouth. This attachment varies in length from person to person.
- **Varicosities** are the most common **atypical** observation in this area. Other atypical findings are **enlarged** lingual folds and caruncle and a short lingual frenum (ankyloglossia). (Ankyloglossia is only considered a problem if it begins to affect the speech

- **Bimanual** intraoral palpation with the index finger of the nondominant hand supported extraorally by the fingers of the dominant hand will allow the clinician to feel the structures of the area between the fingers as they are compressed together gently. The tissue will be soft on palpation with **firmer** areas noted in the area of the **suprahyoid muscles (**digastric, geniohyoid, mylohyoid)



Extra oral view of proper palpation technique.

• Assessment of **macroglossia** should include palpation of the sublingual glands; these will be **displaced** in true macroglossia. Macroglossia may be congenitally present in individuals with **acromegaly**. New-onset macroglossia in an adult is pathognomonic for amyloidosis and should be treated as such until proven otherwise.

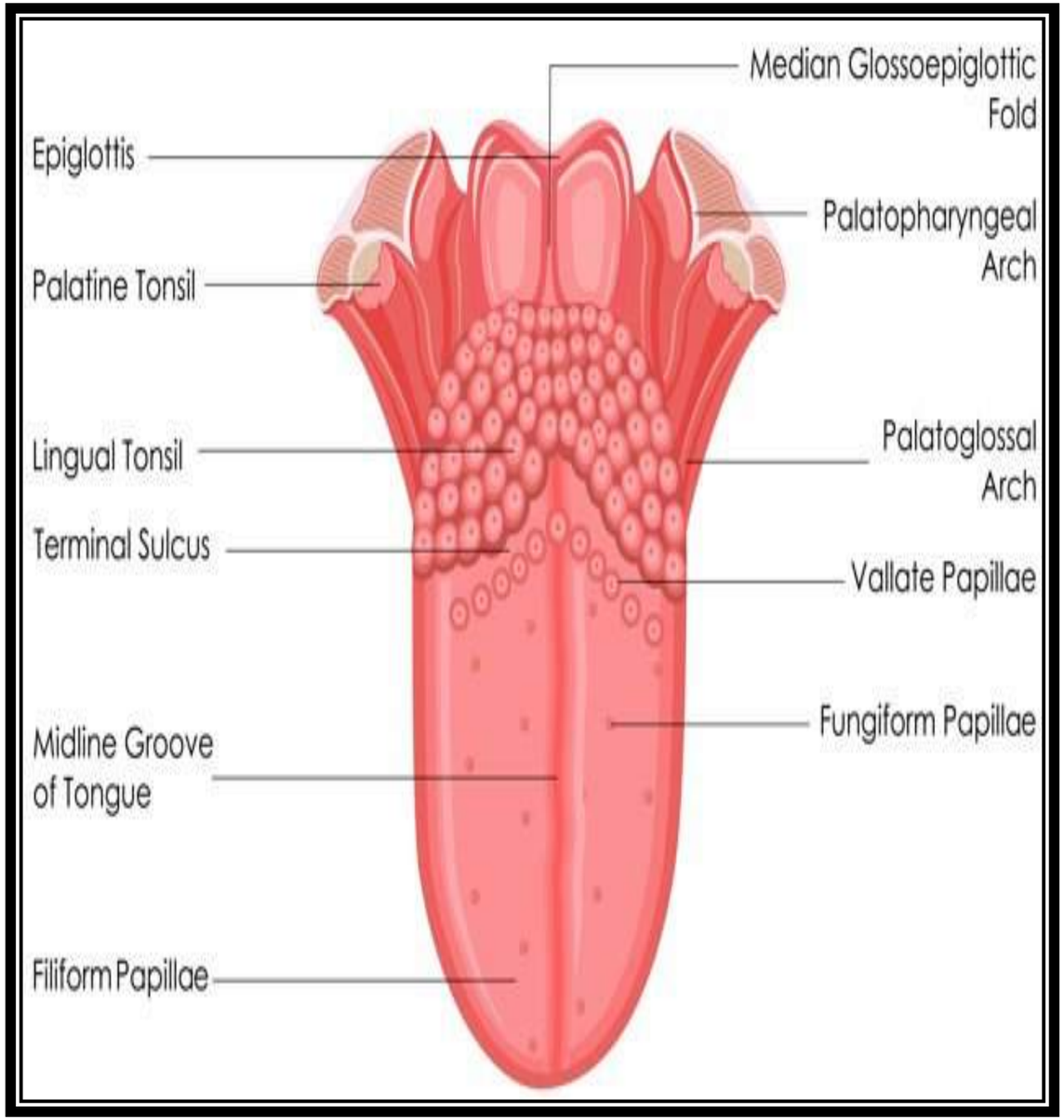
•"**Microglossia** may result from pseudobulbar palsy, damage to the **upper** motor neurons of the corticobulbar tracts that innervate the tongue. This presents with a small, stiff tongue. In **newborns** there may be an apparent **microglossia** resulting from a congenitally short lingual frenulum (**ankyloglossia**) commonly called **tie**".

Pathologic findings include:

- **Traumatic injuries ,** ulcers and mucoceles.
- **Salivary gland pathology** include ranula, sialoliths, ….
- **Neoplastic** changes.

Tongue. (The developmental)

- A small **nodule**, is the first evidence of the developing tongue in the floor of the **pharynx**. The fusion of the first pharyngeal arch creates a protuberance in the midline known as the tuberculum impar located at the base of the first arch .
- Later, two swellings develop on either side of the tuberculum impar. These swellings are known as the lateral lingual swellings or prominences. Swellings extend to form the anterior 2/3 of the tongue



Sensory supply

- **Anterior two-thirds: Lingual** nerve (a branch of the **mandibular** division of the trigeminal nerve – V3)
- **Posterior one-third**: **Glossopharyngeal** nerve (cranial nerve IX), plus a small branch of the internal laryngeal nerve (branch of the **vagus** nerve, cranial nerve X).
- **Taste sensation** is carried by special sensory nerve fibres of the **chorda tympani (**branch of the **facial** nerve). This nerve also carries secretomotor fibres to the submandibular and sublingual glands.

Motor supply

All the intrinsic and extrinsic tongue muscles are supplied by the hypoglossal nerve (cranial nerve XII) **EXCEPT** the **palatoglossus**, which is supplied by the pharyngeal branch of the vagus nerve. The tongue is examined using both direct and indirect vision. The most common place for cancer to occur on the tongue is the **lateral** border.

- **Latral borders:** White hairs along the sides of the tongue are the classic appearance of **oral hairy leukoplakia** which is a condition triggered by the Epstein-Barr virus (EBV). Sometimes the patches happen in other parts of the mouth. The patches may look hairy. Oral hairy leukoplakia happens most often in people with weak immune systems. **HIV** (human immunodeficiency virus) often causes this condition.• It is necessary for the dentist to have information regarding the **histopathological** features of this lesion: 1. Hyperkeratosis oral mucosa due to piling of keratotic squamous epithelium. 2. Cowdry type A intranuclear inclusions. 3. Balloon cells with margination of chromatin (nuclear beading); EBV present in clear cells of spinous layer 4. Variable koilocytosis, superimposed Candida infection, without inflammatory response

- **Ventral surface:** In general, the examination of the tongue should occur in the following steps:
- Have the patient touch the tip of the tongue to the roof of their mouth and inspect the ventral surface.
- Have the patient protrude the tongue straight out and inspect for deviation, color, texture, and masses. The ventral surface may have some visible vasculature. **Lingual varicosities a**re a common finding on the ventral surface of the tongue, especially in older patients.
- The **Glands of Blandin-Nuhn** (minor salivary glands found on the ventral surface of the tongue) may become enlarged prompting the need for a referral or diagnostic procedure to confirm the origin.

Dorsal surface

- Texture usually rough dorsal surface owing to papillae, which have three types. There should be **no hairs, furrows, or ulceration.**

Size. Should fit comfortably in mouth, tip against lower incisors.

Sublingual glands should **not** be displaced.

Atypical findings include: **fissuring scalloping, benign migratory glossitis ,and enlarged papilla**e. A **lingual thyroid** may rarely be found on the posterior dorsal surface at the foramen cecum.

- The tissues of the tongue should feel soft and resilient with no palpable indurations or masses. The normal anatomy of the tongue including:

- **Dorsal** surface – papillae (filiform, fungiform, circumvallate), median sulcus, sulcus terminals.
- **Lateral borders** – foliate papillae
- **Ventral** surface – lingual veins, plicafimbriata, lingual frenum

- The tongue is the **most** common intraoral site for oral cancer. Therefore, any sign of pathology should be investigated thoroughly.
- The **pathological** findings that are found on the tongue include:

- **Hairy tongue** – filiform papilla become elongated due to a variety of reasons from overuse of mouth rinses to not cleaning the tongue adequately.
- **Candidiasis** – fungal infection of the tongue often associated with deeply fissured tongues.
- **Glossitis** – inflammation of the tongue due to anemia, nutritional deficiencies … It is also important to note if the **tongue is coated** with dental biofilm. The tongue is home to the highest number of bacteria found anywhere in the oral cavity. Bacteria located on the tongue have been associated with **halitosis, increased pH of the saliva, and periodontal disease.**

Usually appear as

• An area of redness and loss of lingual papillae on the central dorsum of the tongue,

• Sometimes including lesions of the tongue and palate. It is seen in patients using **inhaled steroids and smokers,** and is usually a kind of **chronic atrophic oral candidiasis,**

• Hematinic deficiency and diabetes should be excluded

• Oral candidiasis, or thrush, is the result of infection of the oropharynx

by Candida albicans. Immunocompromised patients as:

• HIV

• Diabetic

•Odynophagia concurrent with this suggests that the **esophagus** is also involved.

Other causes

• Nutritional deficiencies iron

• Vitamin B12 deficiency. B12 deficiency will also beefy-red in color. Glossitis, by causing swelling of the tongue, may also cause the tongue to appear smooth. • Low-estrogen states may cause a “menopausal glossitis.

Geographic tongue may cause a burning sensation on the tongue.

Recurrent aphthous ulceration or stomatitis (RAU/RAS) occurs in some systemic illnesses. These include Crohn's Disease and Ulcerative Colitis, Behcet's Syndrome, pemphigus, herpes simplex, histoplasmosis, and reactive arthritis (Reiter's Syndrome). Other causes of RAU include drug reactions, Marshall Syndrome, and MAGIC (Mouth and Genital ulcers with Inflamed Cartilage) syndrome. The ulcers themselves may become infected, **requiring treatment.**

Benign migratory glossitis, It is a common condition, characterized by areas of smooth, red depapillation (loss of lingual papillae) which migrate over time. The name comes from the map-like appearance of the tongue with the patches cause is unknown, but the condition is entirely benign (importantly, it does not represent oral cancer), and there is no curative treatment.

Black hairy tongue, possible causes or contributing factors include:

• Changes in the normal bacteria or yeast content of the mouth after antibiotic use• Poor oral hygiene• Dry mouth (xerostomia)• Regular use of mouthwashes containing irritating oxidizing agents, such as peroxide• Tobacco use• Drinking excessive amounts of coffee or black tea• Excessive alcohol use• Eating a soft diet that doesn't help to rub dead skin cells from your tongue

Neurological examination of the tongue

- The lower motor neurons of the hypoglossal nerve (CN XII), or the upper motor neurons originating in the motor cortex. Lesions of the motor cortex cause **contralateral tongue weakness.** Note any atrophy or fasciculation (spontaneous quivering movements caused by firing of muscle motor units) of the tongue while it is resting on the floor of the mouth.
- This could be demonstrating by ask the patient to stick their tongue straight out and note whether it curves to one side or the other. Ask the patient to move their tongue from side to side and push it forcefully against the inside of each cheek. Fasciculations and atrophy are signs of lower motor neuron lesions.

• **Bell's palsy** as well as **hypoglossal nerve injury** may be caused by a dental injection or a tumor. Both will have an effect on the patient's condition. Both may be temporary or longer lasting, depending on the etiology. With Bell’spalsy, which affects the **seventh** cranial (or facial) nerve, only **one** side of the patient's face is affected. There may be a rapid onset of mild weakness to a full-blown facial paralysis

• Unilateral atrophy of the tongue may be a sign after prolonged injury to this nerve. **Etiology**: Hypoglossal nerve injury may also be caused by

1. tumors2. stroke3. Degenerative diseases affecting muscles and nerves.

- Patients will have difficulty speaking, talking, and chewing with both of these conditions, Oral hygiene may be affected, Drooling, muscle aches, muscular atrophy, and difficulty swallowing are also signs. The tremors and inability to keep their mouths open may cause a

Parkinson's disease

- Medications will affect saliva(as well as blood pressure).
- A genetic condition
- Muscular dystrophy
- Loss of muscle tissue• Muscular weakness ,worsens over time
- Affected muscles may be localized (pelvis, shoulder, or face)
- May be more widespread throughout the body.

Huntington’s disease

1. Uncontrollable movements due to nerve cells in certain parts of the brain ,degrading and degenerating.
2. Genetic defect of chromosome four .
3. Ages of 30 and 40. rarely,(may occur in younger children or adolescents).
4. Patients may exhibit unusual movements including grimacing, head turning, abnormal gait,
5. wild movements of the extremities.
6. They also lack muscular control of the face and tongue.
7. Swallowing is also an issue.
8. Oral hygiene may be quite difficult due to the uncontrollable movements

Myasthenia gravis

1. An autoimmune neuromuscular disorder.
2. The etiology is unknown but it may be due to a tumor of the thymus.
3. Occur at any age though it is more common in young women and older men.
4. Patients experience partial or no facial expressions because of facial paralysis.
5. Muscle weakness in their tongues as well as palates, swallowing and chewing difficult.
6. Patients may also experience breathing difficulties due to weakened muscles of the chest wall.
7. A droopy head.

Some information regarding cyst that may be seen by the dentist

- They originated from epithelia rests in the line of union of facial or oral prominences, or from epithelial organs, such as:
- **Brachial cleft** (cervical cysts) may arises from the rest of epithelium in the visceral arch area, they are usually laterally disposed on the neck.
- **Thyroglossal duct** cyst may occur at any place along the course of the duct usually at or near the mid line.

• **Globulomaxillary** cysts: these cysts arise from epithelial rests after the fusion of medial, maxillary &lateral nasal prominences, they may have developed as primordial cysts from supernumerary tooth germ.
• **Anterior palatine** cyst: are situated in the midline of maxillary alveolar prominence & they believed to be from remnants of the fusion between two prominences, they may be primordial cyst of odontogenic origin.
• **Nasolabial cysts:** originated in the base of the wing of the nose & bulging in to the nasal & oral vestibule & the root of the upper lip. They may have developed at the line of cleft or due to excessive epithelial proliferation.


thank you

LABORATORY INVESTIGATIONS IN DENTISTRY

- **Dr. Marwah Waleed S.**

IRON DEFICIENCY ANEMIA

- Is a very common cause of anemia, because iron is major component of hemoglobin and essential for its proper function.
- Chronic blood loss due to any reason is the main cause of low iron level in the body as it depletes the body's iron stores to compensate for the ongoing loss of iron.
- Anemia that is due to low iron levels is called iron deficiency anemia.
- Young women are likely to have low grade iron deficiency anemia because of the loss of blood each month through normal menstruation ,wwithout any major symptoms as the blood loss is relatively small and temporary.

- Another common reason for iron deficiency anemia can be due to recurring or small ongoing bleeding, for instance from colon cancer or from stomach ulcers. Stomach ulcer bleeding may be induced by medications, even very common over-the-counter drugs such as aspirin and ibuprofen. Slow and chronic oozing from these ulcers can lead to loss of iron. Gradually, this could result in anemia.
- In infants and young children, iron deficiency anemia is most often due to a diet lacking iron.

The iron deficiency anemia shows the followings:

- 1- Red blood cell size and color (blood film): are smaller and paler in color than normal (**Microcytic ,hypochromic**)
- 2- Ferritin: a protein helps store iron in the body, and a **low** level of

ferritin usually indicates a low level of stored iron.

- 3-Total iron binding capacity (TIBC): is a blood test to see if there is too much or too little **iron** in blood. Iron moves through the blood attached to a protein called **transferrin** .TIBC: 240 to 450 mcg/dL
- 4- Serum iron test: Normal value range is: • Iron: 60 to 170 micrograms per deciliter (mcg/dL).

PERNICIOUS ANEMIA

- is a condition in which **the body can't make enough healthy red blood cells because it doesn't have enough vitamin B12.**
- People who have pernicious anemia can't **absorb** enough vitamin B12 due to a **lack of intrinsic factor (a protein made in the stomach).**
- This typically causes of **macrocytic** (large blood cell volume) anemia.
- Vitamin B12, along with foliate, is involved in making the heme molecule that is an integral part of hemoglobin.
- Folate deficiency can be the cause of anemia as well. It is caused by inadequate **absorption**, and also **long-term heavy alcohol** use.

- **Causes**:
- 1- A lack of intrinsic factor is a common cause of pernicious anemia as the body can't absorb enough vitamin B12.
- 2- Some pernicious anemia occurs because the body's small intestine can't properly absorb vitamin B12 which may be due to the bacteria in the small intestines
- 3- Certain diseases that interfere with vitamin B12 absorption ,4- certain
- medicines 5- Surgical removal of part of the small intestine ,6- Tapeworm infection .7-Strict vegetarians are at risk if they do not take adequate vitamin supplement.
- 8- Under-consumption of green, leafy vegetables , 9- Long-term alcoholics.

- **Signs and symptoms**
- Apart from the symptoms of anemia (fatigue, dizziness, etc.), the vitamin B12 deficiency may also have some serious symptoms like Nerve damage,
- **Neurological problems** such as confusion, dementia, depression, and memory loss. Symptoms in the **digestive tract** include nausea and vomiting, heartburn, abdominal bloating and gas, constipation or diarrhea, loss of appetite, and weight loss. Enlarged liver, a smooth, beefy red tongue.
- **Infants** who have vitamin B12 deficiency may have **poor reflexes** or unusual movements, such as face tremors. **Treatment:** by replacing the missing vitamin B12 in the body. People who have this disease may need Lifelong treatment.

APLASTIC ANEMIA

- Aplastic anemia is a blood disorder in which the body's **bone marrow doesn’t make enough new blood cells.** This may result in a number of health problems including arrhythmias, an enlarged heart, heart failure, infections and bleeding.
- Aplastic anemia is a rare but **serious** condition. It can develop suddenly or slowly and tends to worsen with time, unless the cause is found and treated.

- **Causes:**
- Damage to the bone marrow's stem cells causes aplastic anemia. In **more than half** of people who have aplastic anemia, the cause of the disorder is **unknown**.
- **1- A number of acquired diseases**, conditions, and factors can cause aplastic anemia including: Toxins, such as arsenic, and benzene, Radiation and chemotherapy, Medicines such as chloramphenicol, Infectious diseases such as hepatitis, Epstein-Barr virus, cytomegalovirus, parvovirus B19, and HIV. Autoimmune disorders such as lupus and rheumatoid arthritis.
- **2- Inherited conditions,** such as Fanconi anemia, Shwachman-Diamond syndrome, dyskeratosis congenital.

- **Signs and symptoms**
- The most common symptoms of aplastic anemia are **fatigue, shortness of breath, dizziness, headache, coldness in hands or feet, pale skin, gums and nail beds, Chest pain.**
- **Treatment:** includes blood transfusions, blood and marrow stem cell transplants, and medication.
- These treatments can prevent or limit complications, relieve symptoms, and improve quality of life.
- Blood and marrow stem cell transplants may **cure** the disorder. **Removing** a known cause of aplastic anemia, such as exposure to a toxin, may also cure the condition.

HEMOLYTIC ANEMIA

- Hemolytic anemia is a condition in which **red blood cells are destroyed** and removed from the blood stream **before** their normal lifespan is up.
- Hemolytic anemia can lead to various health problems such **as fatigue, pain, arrhythmias, an enlarged heart and heart failure.**
- There are many types of hemolytic anemias – some of which are inherited and others that are acquired.

- **1- Inherited hemolytic anemia's include:**
- Sickle cell anemia, Thalassemia, Hereditary spherocytosis,Glucose-6-phosphate dehydrogenase (G6PD) deficiency, Pyruvate kinase deficiency.
- **2- Acquired hemolytic anemia include:**
- Autoimmune hemolytic anemia, Drug-induced hemolytic anemia, Mechanical hemolytic anemia, certain infections and substances can also damage red blood cells and lead to hemolytic anemia.

- In **inherited** hemolytic anemia, this is due to affected genes .In each type of inherited hemolytic anemia the body makes **abnormal** red blood cells. The problem with the red blood cells may involve the hemoglobin, cell membrane, or enzymes that maintain healthy red blood cells.
- In **acquired** hemolytic anemia, the body makes **normal** red blood cells, however, some disease, condition, or factor **destroys** the cells too early. Examples include immune disorders, infections and reactions to medicines or blood transfusions.

THALASSEMIA

- Thalassemia’s are **inherited** blood disorders which cause the body to make fewer healthy red blood cells and less hemoglobin.
- The **two major** types of thalassemia are: Alpha- and beta thalassemia.
- The **most severe** form of alpha thalassaemia is known as **alpha thalassaemia major or hydrops fetalis.**
- The severe form of **beta thalassaemia** is known as **thalassaemia major or Cooley's anemia.** Thalassaemia affect both males and females. Severe forms are usually diagnosed in **early** childhood and are lifelong conditions.

- **Hemoglobin** in red blood cells has **two** kinds of protein chains:
- **Alpha globin and beta globin**. If the body doesn't make enough of these protein chains, red blood cells don't form properly and **can't carry** enough oxygen.
- Genes control how the body makes hemoglobin protein chains. When these genes are missing or altered, thalassemia’s occur.
- People who get abnormal hemoglobin genes from one parent but normal genes from the other are **carriers**. Carriers often have **no signs of illness** other than **mild** anemia. However, they can **pass** the abnormal genes on to their children.

Signs and symptoms:-

- Symptoms are caused by a **lack of oxygen** in the blood stream. The severity of symptoms depends on the severity of the disorder:
- People who are carriers can have mild anemia .
- People with **beta thalassemia intermedia** have **mild to moderate anemia.** They may also have other health problems including: slowed growth and delayed puberty; bone problems; and an enlarged spleen.
- People with **beta thalassemia major** have severe thalassemia. Symptoms occur within the first two years of life and include **severe** anemia and other serious health problems. Pale and listless appearance, Poor appetite, Dark urine, Slowed growth and delayed puberty, Jaundice, Enlarged spleen, liver and heart ,and bone problems.

- **Treatment**
- Treatment for thalassemia depends on the type and severity of the disorder. People who are carriers need little or no treatment.
- Three standard treatments are used to treat moderate and severe forms of thalassemia, these include **blood transfusions, iron chelation therapy, and folic acid supplements.**

SICKLE CELL ANEMIA

- Is a serious disease in which the body makes sickle shaped ("C"-shaped) red blood cells. It contain **abnormal** hemoglobin that causes the cells to have a sickle shape.
- Sickle cells **don’t** move easily through the blood vessels –they are **stiff and sticky and tend to form clumps and get stuck in the blood vessels and block blood flow**
- In limbs and organs, blocked blood vessels can cause **pain, serious infections, and organ damage.**
- Sickle cells usually die after about 10 to 20 days and the body can't reproduce red blood cells fast enough to replace the dying ones, which causes anemia.

Causes:-

People who have the disease inherit two copies of the sickle cell gene – one from each parent.

Signs and Symptoms:-The most common symptoms of sickle cell anemia are linked to **anemia and pain** .Sudden pain throughout the body is called a "**sickle cell crisis**", and often affects the bones, lungs, abdomen, and joints.

Treatment:-

- Sickle cell anemia has **no** widely-available cure. However, treatments can help relieve symptoms and treat complications. The goals of treating sickle cell anemia are to **relieve pain, prevent infections, eye damage and strokes, and control complications.**
- **Bone marrow transplants** may offer a cure in a small number of sickle cell anemia cases.

Other investigations that should be known by the dentist:-

Bleeding time:- used to assess the platelets function. By making a patient bleed then timing how long it takes for stop bleeding.

- Interpretation of bleeding time is affected by platelet function, Certain vascular disorders and Von Willebrand Disease—not by other coagulation factors such as haemophilia. Diseases that cause prolonged bleeding time include thrombocytopenia , disseminated intravascular coagulation (DIC),Glanzmanns thrombasthenia and Bernard-Soulier disease.
- Aspirin and other cyclooxygenase inhibitors can affect bleeding time. Other medication like Warfarin and heparin also increase bleeding time .
- It is also prolonged in hypofibrinogenemia.

Clotting time:- is the time required for a sample of blood to coagulate in vitro under standard conditions.

- There are various methods for determining the clotting time, the most common being the **capillary tube** method. It is affected by calcium ion levels and many diseases.
- Normal value of clotting time is **8 to 15 minutes**.
- It is used to **detect and diagnosis** a bleeding disorder or excessive clotting disorder ,used when the patient taking warfarin or when the patient have unexplained or prolonged bleeding or inappropriate blood clotting prolong in the patient may indicate **decrease** in the vitamin K or defective in **factor VII, or chronic low grade disseminated intravascular coagulation (DIC).**

Partial thromboplastin time (PTT) or Activated Partial thromboplastin time (aPTT or APTT):- is a medical test that characterizes blood coagulation .

- The typical reference range is betwen 30-50 sec. prolong APTT may indicate the use of **heparin** or the **antiphospholipid antibody** especially lupus anticoagulant also **the coagulation factor deficiency e.g hemophilia.**
- Also **sepsis-coagulation** factor consumption, the presence of antibodies against coagulation factor (**factor inhibitors**) and also deficiency of factors VIII, IX, XI and XII.

Erythrocytes sedimentation rate (ESR):- is a type of blood test that measures **how quickly erythrocytes (red blood cells) settle at the bottom of a test tube that contains a blood sample.** Other names: SED sedimentation rate; Westergren sedimentation rate Normally, red blood cells settle relatively **slowly**.

- A **faster-than-normal** rate may indicate **inflammation** in the body. Inflammation is part of the immune response system. It can be a **reaction** to an infection or injury. Inflammation may also be a **sign of a chronic** disease, an immune disorder, or other medical condition.
- These include arthritis, vasculitis, or inflammatory bowel disease. Also be used to monitor an existing condition as: •Headaches, Fever• Weight loss, Joint stiffness• Neck or shoulder pain, • Loss of appetite• Anemia

What do the results mean to the dentist?

- Infection,• Rheumatoid arthritis• Rheumatic fever,
- Vascular disease
- Inflammatory bowel disease,
- Heart disease
- Kidney disease
- Certain cancers

Sometimes the ESR can be slower than normal:- indicate a blood disorder, for the dentist such as:

- Polycythemia
- Sickle cell anemia
- Leukocytosis, an abnormal increase in white blood cells

- That dentist should know that if the results are not in the normal range, it doesn't necessarily mean that the patient have a medical condition that requires treatment.
- **A moderate ESR** may indicate pregnancy, menstruation, or anemia, rather than an inflammatory disease.
- Certain medicines and supplements can also affect the results. These include **oral contraceptives, aspirin, cortisone, and vitamin A.**
- **Note:-** An ESR **does not** specifically diagnose any diseases, but it can provide information about whether or not there is inflammation in the body.

INR:- stands for International Normalized Ratio, also referred to as **Prothrombin time (PT),** and is a standardized **measurement of the time it takes for blood to clot.** It is primarily used to diagnose unusual bleeding, blood clots, and monitoring people being treated with warfarin (an anti-clotting treatment).

- **The most common reasons for an INR test are**:

1. Monitoring as a part of warfarin therapy
2. In relation to liver function tests - liver dysfunction can lead to decreased production of certain clotting factors
3.Deep Vein Thrombosis (DVT) – a clot in a deep vein, commonly of the leg 4.Pulmonary Embolism (PE)
5.Atrial Fibrillation (AF) 6. Some cases of Heart failure (Left Ventricular, and Congestive Cardiac Failure).
7. Artificial heart valves of the mechanical type.

- The INR test result is given as a number, which is a **ratio** of:
- • The test sample's Prothrombin time* ***/*** The Prothrombin time of a normal sample of blood. = 1.0, up to 1.5, is therefore normal.
- A **low INR** result means the blood is 'not thin enough' or coagulates too easily and puts the patient at risk of developing a **blood clot.**
- A **high INR** result means that the blood coagulates too slowly and patient have a **risk of bleeding.**

***Prothrombin time** **(a protein made by the liver and the time it takes to clot the blood)**

- **Biopsy:-** is a way of diagnosing diseases. The dentist removes a sample of tissue or cells to be examined by a pathologist, usually under a microscope.
  - A pathologist is a specialist who is trained to examine a sample of tissue for signs and extent of disease.
  - Tissue for a biopsy is normally taken from a living subject. Examining tissue under a microscope can provide information about various conditions.

Types of biopsy:-

1-Excisional
2-Incisional
3-FNA
4- Thick (core) needle biopsy
5- Exfoliative cytology
6- Frozen section
7- Oral brush biopsy

Depending on the aim, a biopsy may be excisional or incisional:

1.An excisional biopsy is when a whole lump or targeted area is surgically removed. An incisional biopsy, or core biopsy, involves taking a sample of tissue.

2.Cytology means the study of the microscopic appearance of cells, esp. for the diagnosis of abnormalities and malignancies.

3.Fine needle aspiration (FNA) is sometimes considered a cytology test and is sometimes considered a biopsy. During fine-needle aspiration, a long, thin needle is inserted into the suspicious area.

4.Syringe biopsy: Is used to draw out fluid and cells for analysis & smeared on slide, it is **rapid & usually effective** to diagnose of malignant from benign neoplasm although it is not completely conclusive.

- **Advantages**: Small size of the needle **avoid** damage to vital structure & it is **valuable** in case when incisional biopsy contra indicated as in pleomorphic adenoma or other types of **malignant lesions in parotid gland.**
- **Disadvantage**: it requires experience, small specimen may be unrepresentative, definitive diagnosis is not always possible.

5.Core needle biopsy:

A larger needle with a cutting tip is used to draw a column of tissue out of a suspicious area. The sample are **larger** than FNA & **preserve** architecture of tissue ,give more definitive diagnosis than FNA , but there is **increase of the risk of seeding of neoplasm into the tissue & risk of damaging vital structures**. It is used when incisional biopsy is inaccessible e.g. laryngeal tumor.

6.Exfoliative cytology : which is the examination of cells scraped from the surface of a lesion , it is **quick & easy** ,**no local anesthesia i**s required ,also special techniques such as immune-staining can be applied. It is useful in detection of **virally** damaged cells, **acantholytic** cells of pemphigues & **candidal** hyphae. But it provides **no** information on deeper tissue & has no value in diagnosis of cancer.

7.Frozen sections:

- Frozen sections allows a stained slide to examined within 10 min of taking the specimen , the tissue is send fresh to lab. To be quickly frozen to about -70 c by liquid nitrogen or dry ice. Section is cut on refrigerated microtome and stained.
- **The main advantage**: is the time is **too little** so frozen section can be established at operation to **determine** whether tumor benign or malignant, but the section appear different from fixed material , also freezing artifacts can distort the cellular picture, and definitive diagnosis sometimes impossible.

8.Immunofluorecent staining: used to identify **pemphigus vulgaris** as autoantibody bound to epithelial prickle cells (to desmosomes) & in **mucous membrane pemphigoid** autoantibodies bond to the basement membrane.

- Other IMMUNOLOGIGICAL TESTS

Immunoglobulin's rheumatoid factor,HLA(human leukocyte antigens) ,type antinuclear antibody, anti-DNA-antibody, anti double strand DNA test , ant-Ro-ssa and anti-la-ssb.

9.Diagnostic ultrasound:- used in the **soft tissue lumps and salivary gland.**

10.Radioisotope imaging (nuclear scanning) very small quantities of radioactive arterials called radioisotopes to image parts of the body may be used in **salivary gland scanning l**ike in the **Sjogren syndrome** or in the **bone scanning.**

11 .Imaging:-

Conventional radiography example (bitewing ,periapical).
Computed tomography .in CT the dense bone is **white**, soft tissue is present **mid gray,** fat is **dark gray** and air is **black** and the dental filling may cause **artifact** ,Magnetic resonance imaging (MRI) : for the soft tissue salivary gland and TMJ.

12. Molecular –biological test:-

- Chromosome studies
- Comparative genomic hybridization
- DNA microarrays
- Fluorescence in situ hybridization (FISH)
- Polymerase chain reaction
- Gene map

13.Culture and Sensitivity Testing:-

- Used for **infection** of any kind--from an **upper respiratory infection ,to a jaw abscess to a urinary tract infection**--it's critical to know which antibiotics will be effective against the particular pathogen (i.e., disease-causing agent) causing the problem.
- This means that (1) The **species** and strain of bacteria (or other pathogen) must be identified and (2) The **drugs** most effective at inhibiting their growth must be determined by the antibiotic sensitivity test .ex .in pus salivary gland.
- Fungi by the direct smear from the area stained by the periodic acid shift or gram stain and the presence of the typical hyphae indicate the Candida proliferation.

- **Isolation and identification of candida albinos**
- **Specimen collection:**
- Samples were taken by a sterile swab, which rubbed and rotated vigorously over the mucosa, pressure put on the swabs in an attempt to pick up deeply seated microorganism. e.g. Swab was taken from the mucosa of palate beneath the upper complete denture.
- **Cultivation of candida albicans:**
- The sample that collected was cultured on sabouraud dextrose agar (SD) for the growth of candida albicans , and then the plates were incubated aerobically for 48-72 hrs at 37C.

- **Identification**
- Colony morphology: The Candida species was identified according to the following morphological appearance on sabouraud dextrose agar.
- The colonies appeared **medium size, moist, creamy, having a yeasty like odor, whitish cottony colonies.**
- Viruses: the use of the virology lab from the **fresh vesicle** or by the **titer** of the antibody in the patient **serum**.


Thank
You

Orofacial Pain

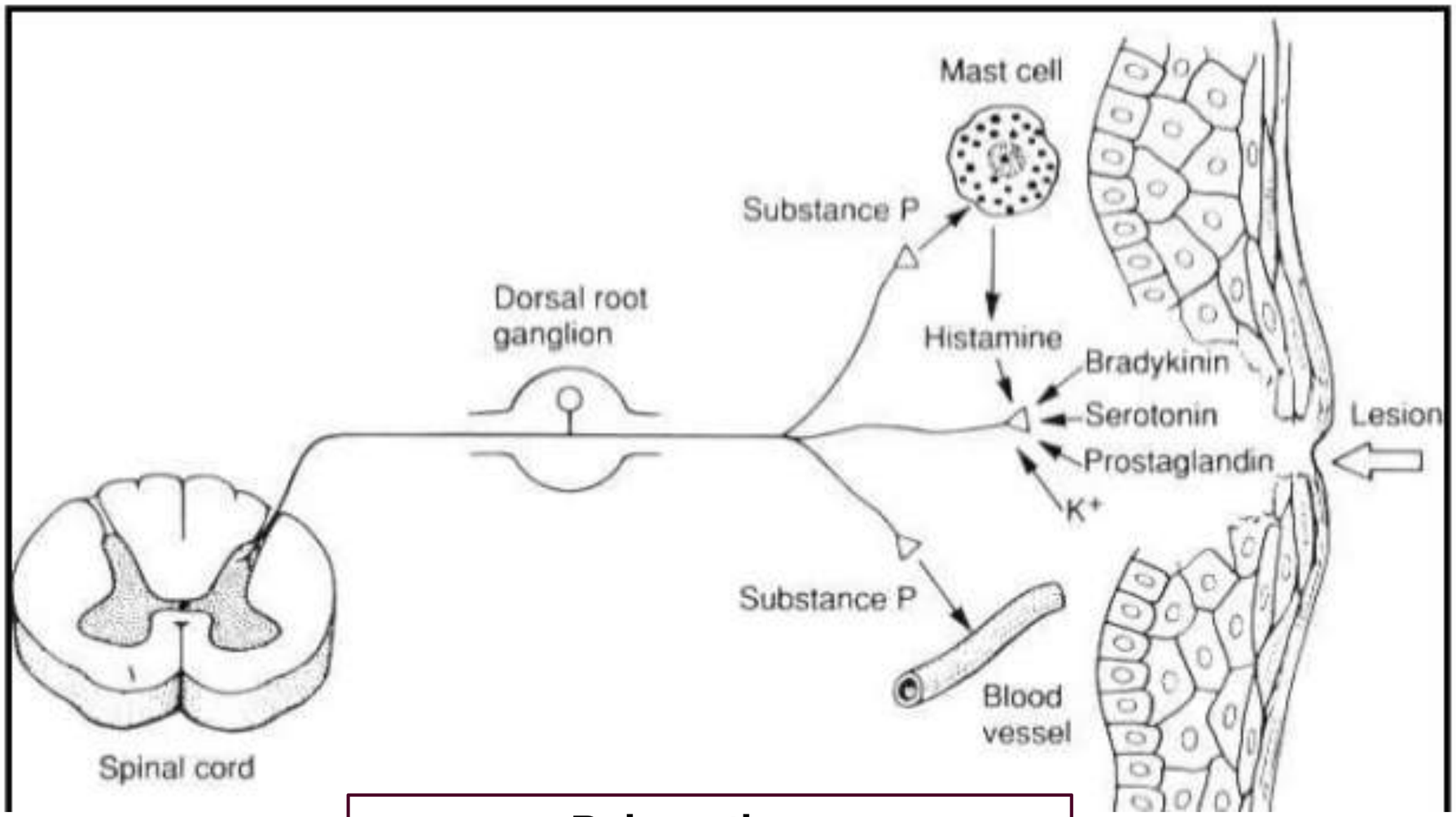
DR. MARWAH WALEED SH.

Orofacial Pain

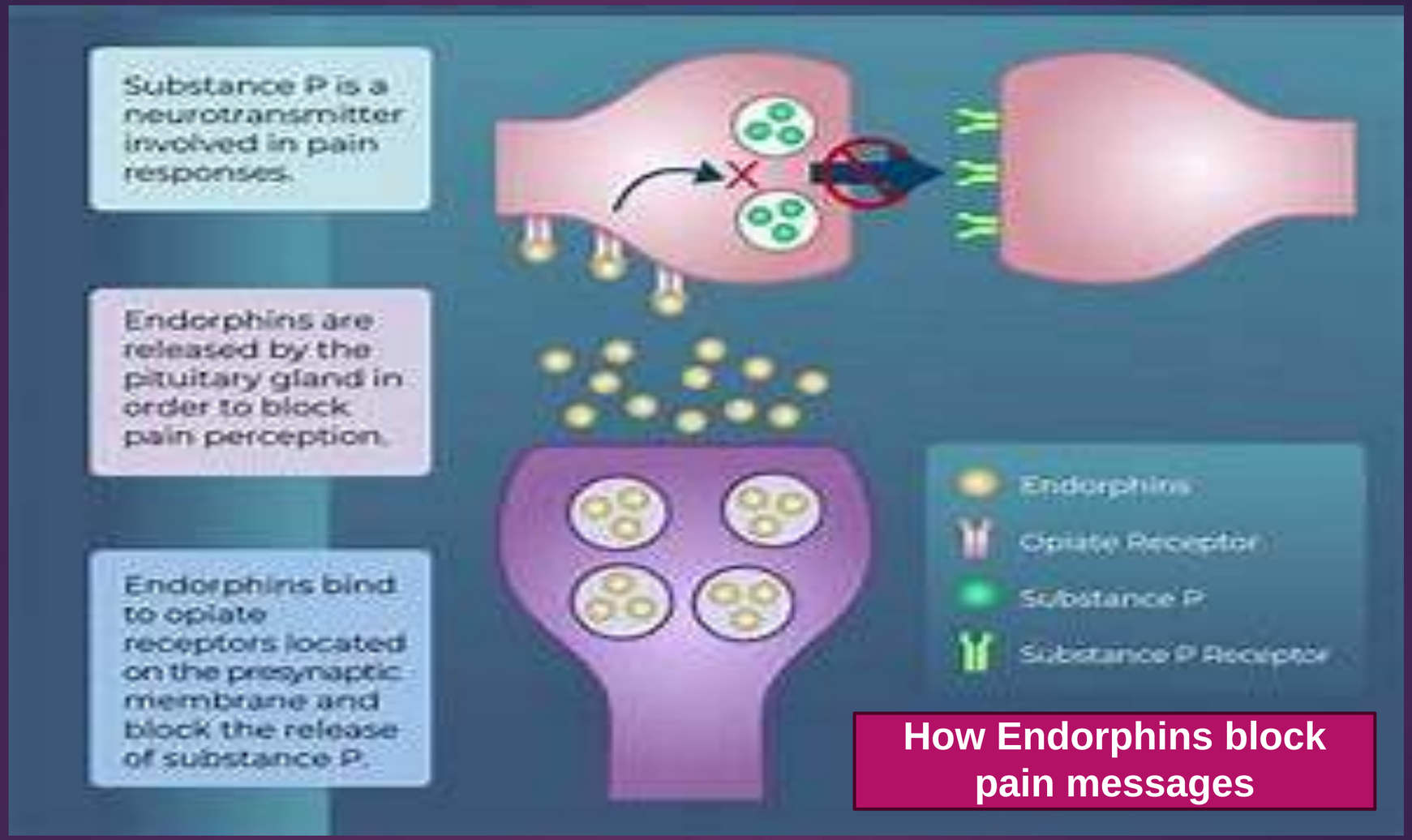
- **Pain: -** is a sensation of suffering resulting from a noxious stimulus, physical disorder, or mental derangement. Pain is, an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- Acute pain resulting from injury will generally initiate a reflex withdrawal thus ensuring minimal or no tissue damage (nociceptive pain).
- **Allodynia**: the injured region becomes sensitive to even light touch ,it refers to central pain sensitization (increased **response** of neurons) following normally **non-painful**, often repetitive, stimulation. **Allodynia** can lead to the triggering of a pain **response** from stimuli which **do not normally provoke pain**.
- **Hyperalgesia:** over reactive to painful stimuli ,An increased response to a stimulus that is normally **painful**, at the site of injury or inflammation. ... **Primary hyperalgesia** results from the direct effects of injury to skin and nerve tissue, whereas **secondary hyperalgesia** involves the increased pain sensitivity of the surrounding tissue.

What are the four phases of the pain pathway?

- Nociceptive **pain** occurs in 5 **phases**: 1) Transduction, 2) Conduction, 3) Transmission, **4**) Modulation, 5) Perception. Transduction begins when peripheral terminals of nociceptive C fibers and A-delta (Aδ) fibers are depolarized by noxious mechanical, thermal, or chemical energy.
- The spinal cord carries the **pain** message from its receptors all the way up to the **brain**, where it is received by the thalamus and sent to the cerebral cortex, the **part of the brain** that **processes** the message.
- Cellular damage and inflammation increase concentrations of other **chemical mediators** such as histamine, bradykinin, and prostaglandins in the area surrounding functional **pain** units
- **Endorphin and enkephalin** are the body's natural painkillers. ... **Enkephalins** block pain signals **in the** spinal cord. **Endorphins** are thought to block pain principally at the brain stem. Both are morphine-like substances whose functions are similar to those of opium-based drugs.



Pain pathway



How Endorphins block pain messages

CLINICAL EVALUATION OF PAIN

- **A-** Onset of pain: A pain of brief duration from its onset to the request for treatment can suggest inflammatory somatic pain and exclude a chronic condition.
- **B-** Localization of the pain: Somatic pain of the oral and perioral region nearly always arises from the affected site . Inability of the patient to localize pain may indicate somatic pain originating from deep tissues or the pain is not somatic, radiation of pain is the sensation of spreading to the adjacent areas from the primary source which may suggest a **neurogenic** component to the problem.
- **C-** Characters of pain: These could be sharp, dull, aching, burning, stabbing, throbbing, pulsating. The severity of pain can be graded as mild, moderate or severe based on its disruption of normal daily activities like sleeping, eating, working.
- **D-** Course of pain: The course of pain often suggests possible causes. Steady increase in the severity of pain is typical of a progressive acute inflammation produced by a bacterial infection. Periods of relief followed by recurrences is a pattern of pain often caused by chronic periapical lesions that episodically undergo acute exacerbations.
- **E-** Factors that alter pain: certain agents or conditions can alter pain nature. Application of ice can soothe pain from most superficial inflammatory causes, and moist heat usually relieves the deeper discomfort of muscle spasm.
- **F-** Associated findings: Certain systemic conditions can cause or influence the nature of pain, and a variety of drugs can accentuate pain perception. Emotional stress may exacerbate somatic pain or suggest psychogenic nature.

Orofacial Pain

- **Acute OFP**: is primarily associated with the teeth and their supporting structures. Most frequently, dental pain is due to dental caries, although a broken filling or tooth- abrasion may also cause dental sensitivity. Other oral pains are usually periodontal or gingival in origin.
- **Chronic orofacial pain (COFP):** is a term used to describe painful regional syndromes with a chronic, unremitting pattern.
- • The trigeminal nerve (CN V),, is the dominant nerve that relays sensory impulses from the orofacial area to the central nervous system
- • The facial (CN VII), glossopharyngeal (CNIX), and vagus (CN X) nerves and the upper cervical nerves (C2 and C3) also relay sensory information from the face and surrounding area.

Possible causes of Facial Pain:

1. Dental pain
2. TMJ
3. Neuropathic pain (neuralgias)
4. Pathology in related structures (salivary gland , sinus ,eyes , cervical spine, nasopharynx)
5. Vascular disorder (headaches)
6. Intracranial lesions (neoplasm, MS)
7. Referred pain (angina pectoris.)
8. Psychogenic facial pain.

COFP may be subdivided into three main symptomatic classes

- **1- Musculoskeletal**
- **2- Neuropathic**
- **3- Neurovascular**

*Musculoskeletal entities are dealt with Temporomandibular Disorders.

Differential Diagnosis of Orofacial Pain

1- Intracranial pain disorders: Neoplasm, aneurysm, abscess, hemorrhage, hematoma, and edema.

2- Primary headache disorders (neurovascular disorders) Migraine, migraine variants, cluster headache, paroxysmal hemicrania, cranial arteritis and tension-type headache.

3- Neurogenic pain disorders: Paroxysmal neuralgias (trigeminal, glossopharyngeal, nervus intermedius), or Continuous pain disorders (neuritis, post herpetic neuralgia, post-traumatic and postsurgical neuralgia)

4- Intraoral pain disorders Dental pulp, periodontium, mucogingival tissues, tongue.

5- Temporomandibular disorders Masticatory muscle, temporomandibular joint.

6- Associated structures Ears, eyes, nose, paranasal sinuses, throat, lymph nodes, salivary glands and neck.

Intracranial pain disorders (ICP)

*If the cause is intra-cranial; more than one division may be involved. Classic signs of **intracranial pressure** include a headache and/or the **feeling** of increased **pressure** when lying down and relieved **pressure** when standing. vision changes, changes in behavior, and seizures can also occur.

Clinical features of raised I.C.P

1.Brain swelling can be caused by a number of injuries and conditions, including:

2. Headache.

3. Impairment of conscious level.

4. Papilloedema

5. Nausea, vomiting

6. Raised arterial pressure

7. Bradycardia

- Traumatic injury to the head
- Not having enough red blood cells or hemoglobin (anemia)
- CSF buildup in the brain (hydrocephalus)
- Brain bleeding (hemorrhage)
- Brain inflammation (encephalitis).
- Brain tissue inflammation (meningitis)
- High blood pressure (hypertension)
- Collection of infected pus in the brain (abscess)
- Brain tumor

Diagnostic Tests of OFP

Any test to select is guided by history & physical examination:

- 1. CT and/or MRI (to rule out intracranial pathology)
- 2. TMJ radiography
- 3. Diagnostic occlusal appliance
- 4. Cervical spine films
- 5. Lab. (ESR ,C- reactive protein)
- 6. Biopsy
- 7. VAS (visual analog scale)

CHRONIC OROFACIAL PAIN (CFP)

1- Neuropathic Orofacial Pain.

2-Musculoskeletal

1.Neuropathic Orofacial Pain

- **Neuropathic pain** is **pain** caused by damage or disease affecting the somatosensory nervous system. **Neuropathic pain** may be associated with abnormal sensations called dysesthesia or **pain** from normally **non-painful** stimuli (allodynia). It may have continuous and/or episodic (paroxysmal) components.
- Neuropathic OFP includes a number of clinical entities; the most common are :- Trigeminal Neuralgia (TN), glossopharyngeal neuralgia (GN) , geniculate neuralgia, Painful posttraumatic neuropathies, burning mouth syndrome (BMS), facial postherpetic neuropathy and central poststroke pain.

2-Neurovascular Pain:

- It arising from neuronal firing of nociceptors associated with intracranial blood vessels and dura. For this reason, these pain disorders were historically referred to as ‘vascular pain’, but further research has identified both peripheral and central aspects of the nervous system are playing crucial roles in the initiation and perpetuation of these pains .This brought about a change in nomenclature regarding headache, which are now referred to as ‘neurovascular.
- Cluster headache (CH), migraine, paroxysmal hemicrania (PH), cranial arteritis , tension-type headache

Neuralgias

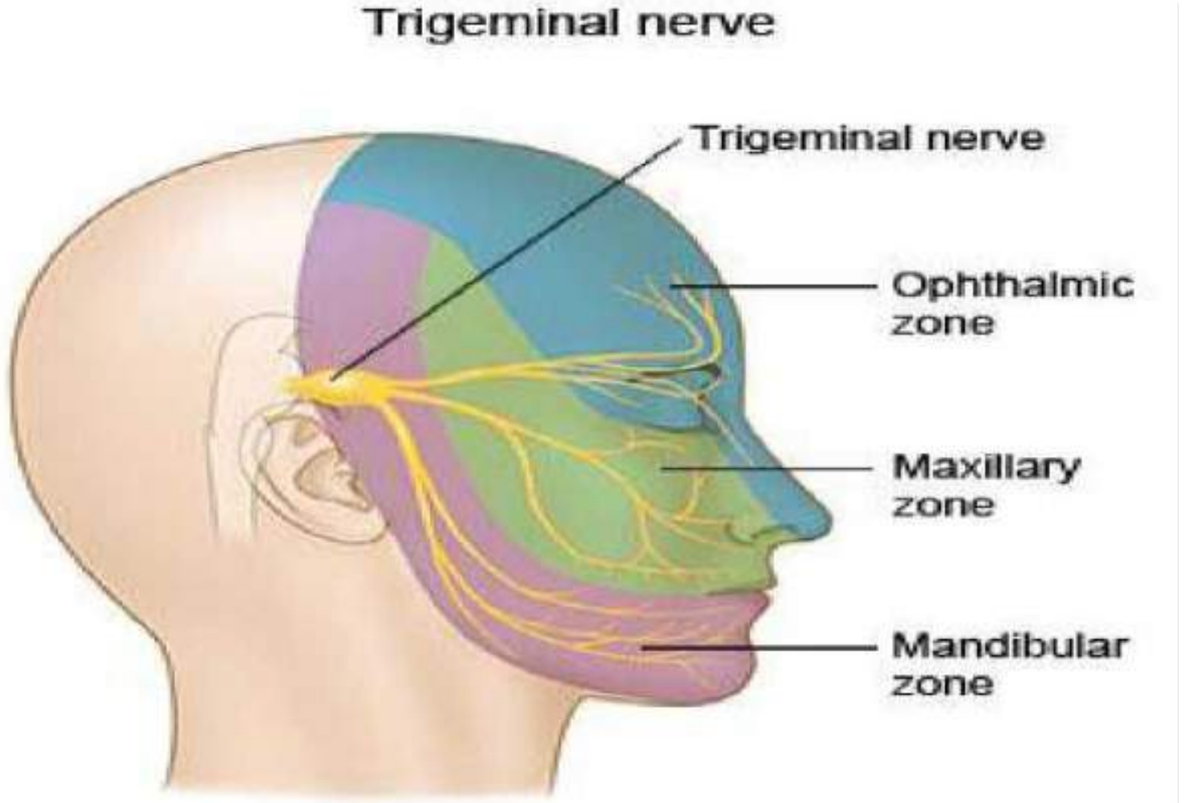
- The classic neuralgias that affect the craniofacial region are a unique group of neurological disorders involving the cranial nerves and are characterized by :
- (a) Brief episodes of shooting
- (b) Trigger zones on the skin or mucosa that precipitate painful attacks when touched
- (c) pain-free periods between attacks and refractory periods immediately after an attack, during which a new episode cannot be triggered.

Trigeminal Neuralgia:

- **Sever recurrent shooting pain, sharp, stabbing or electrical lasting within seconds or minutes and provoked by talking, eating or touching specific areas called the "trigger zone", short-lasting, unilateral facial pain.**
- Characterized by **sever paroxysmal pain** in one or more branches of trigeminal nerve. Usually affecting the **middle aged and elderly** and often **women** are more affected than men. The most common sites involved are the mandibular mental area and the maxillary canine area. The ophthalmic distribution of the trigeminal nerve is **rarely** affected. There is a period of remission, but the condition tends to recur or persist throughout the patient's life. The pain can be also an early manifestation of **disseminated sclerosis** .TN is characterized by **spontaneous remissions** lasting weeks to years but approximately 20% of TN patients suffer daily attacks.

Trigeminal Neuralgia:

- **1- Classical**: unrelated to pathology and most probably caused by neurovascular compression of the trigeminal nerve root, (>85%) of TN.
- **2- Secondary:** these are related to a variety of pathologies including tumors, cysts, viral infection, trauma, and systemic diseases such as multiple sclerosis.



Types of Trigeminal Neuralgia:

- **Trigeminal neuralgia, type 1**, (TN1): facial pain spontaneous onset > 50% limited to the duration of an episode of pain as temporary pain.
- **Trigeminal neuralgia, type 2**, (TN2): facial pain of spontaneous onset > 50% as a constant pain.

Trigeminal Neuralgia:

There are two attack-related phenomena that are particular to TN:

- **Latency** refers to the short period of time between stimulation of a trigger area and pain onset.
- **A refractory period** occurs following an attack and during this time pain may not be initiated.
- Attacks begin and end abruptly, lasting from a fraction of a second up to 2 minutes. Longer attacks, increasing with disease duration.
- Most paroxysms occur during waking hours but may awaken the patient **(hence the name tic douloureux).**
- Pain paroxysms are usually accompanied by spasm of the ipsilateral facial muscles.

Trigeminal Neuralgia:

Etiology : Mostly, atherosclerotic blood vessel (usually **the superior cerebellar artery**) pressing on and grooving the root of the trigeminal nerve. This pressure results in focal demyelination and hyper excitability of nerve fibers.10% of cases have detectable underlying pathology such as:

- 1- Tumors of the cerebellopontine angle
- 2- Demyelinating plaque of multiple sclerosis
- 3- Vascular malformation.
- 4- Idiopathic TN.

Trigeminal Neuralgia:

Pretrigeminal Neuralgia (PTN).

- An early form of TN, has been reported in 18% of TN patients characterized by a **dull continuous pain** (days to years) in one of the jaws. As PTN progresses it becomes more typical with characteristic flashes of pain. Thermal stimuli may cause triggering at a relatively higher rate, and a throbbing quality to PTN pain is sometimes present mimicking dental pathology.
- PTN is however highly responsive to carbamazepine, and careful dental assessment should help differentiate it.

Trigeminal Neuralgia:

Diagnosis:

- The diagnosis of TN is usually based on the history of shooting pain along a branch of the trigeminal nerve, precipitated by touching a trigger zone, and possibly examination that demonstrates the shooting pain.
- MRI of the brain is indicated to rule out tumors, multiple sclerosis, and vascular malformations.

Trigeminal Neuralgia:

Treatment:

- **1- Anticonvulsant**; Carbamazepine (Tegretol) remains the drug of choice for TN. Initial low-dose therapy (100 mg with food) and a slow increase (byl00-200 mg) on alternate days will minimize side effects. Titration to final dose (800-1200 mg/d) should continue slowly based on response and side effects.
- Patients receiving carbamazepine must have periodic hematologic laboratory evaluations because serious life-threatening blood dyscrasias occur. Monitoring of hepatic and renal function is also recommended.

Trigeminal Neuralgia:

Main side effects of Carbamazepine:

- a- Transient elevation in liver enzymes may occur b- Transient leucopenia
- c- Aplastic anemia is a serious effect that may occur. d- Hyponatremia.
- e- Skin rashes occur in patients and may signal the onset of antiepileptic drug hypersensitivity syndrome. This is a life-threatening syndrome (fever, rash, and lymphadenopathy) associated with some antiepileptic drugs.
- **2. Muscle relaxant(Baclofen):** has a strong synergistic effect with carbamazepine. Newer anticonvulsants have fewer side effects as **Lamotrigine** is effective, and gabapentin may be useful in selected TN cases.

Trigeminal Neuralgia:

- **2-Surgery:** is directed peripherally or centrally at the trigeminal ganglion or nerve root. Better prognosis when carried out on patients with typical CTN; has the best prognosis when performed within seven years of TN onset.

A. Peripheral Procedures

- Peripheral neurectomy carries the danger of inducing traumatic neuropathic pain and is not recommended.
- Cryotherapy of peripheral branches may give pain relief for six months. Pain recurrence is at the original site, repeated cryotherapy often produces better results.

Trigeminal Neuralgia:

B. Central Procedures

- Percutaneous Trigeminal Rhizotomy
- Microvascular decompression of the nerve root at the brainstem Gamma Knife
- Alcohol injections have been used but are painful and cause fibrosis. Alcohol may induce herpes zoster (HZ) reactivation ,bony necrosis and post injection neuropathic pain.
- Peripheral glycerol injection, success seems short term.
- **Complications**; dysesthesia ,hypertension, , and hyperesthesia ,headache ,ocular dysesthesia, masseter weakness hyperalgesia and attack of paroxysmal pain.

Glossopharyngeal neuralgia (GN):

- **Etiology:** The most common causes **are intracranial or extra cranial tumors and vascular abnormalities that compress CN IX.**
- GN is characterized by a milder natural history with most patients going into remission.

Glossopharyngeal neuralgia (GN):

The glossopharyngeal (IX) nerve has two main sensory branches:

- 1.**Pharyngeal-GN**, the pharynx or posterior tongue-base are involved. Pain radiates to the inner ear or the angle of the mandible, and may include the eye, nose, maxilla, or shoulder and even the tip of the tongue.
- 2.**Tympanic- GN**, pain predominates in the ear but may radiate to the pharynx.

Glossopharyngeal neuralgia (GN):

Clinical Features:

- A. paroxysmal, mostly unilateral, severe pain that is sharp, stabbing, shooting, or lancinating . Patients often feel a scratching or foreign body sensation in the throat. Pain attacks last from a fraction of a second up to 2 minutes.
- Trigger areas are in the tonsillar region and posterior pharynx, and these display a refractory period. Swallowing, chewing, talking, coughing and/or yawning, sneezing, clearing the throat, and rubbing the ear activate these areas. Frequency is around 5-12 every hour, and attacks may occur in clusters lasting weeks to months, then relapse for up to several years.
- GN may induce uncontrollable coughing, seizures, and cardiac arrhythmias, particularly bradycardia, and syncope.

Glossopharyngeal neuralgia (GN):

Pathologies Mimicking GN:

- 1- A significant association between symptomatic GN and multiple sclerosis.
- 2- Regional diseases such as infectious or inflammatory processes.
- 3- Tonsillar carcinoma.
- 4- Other regional tumors (tongue, oropharyngeal).
- 5- Cerebellopontine angle or pontine lesion.
- 6- Pathophysiology of GN : is uncertain but is considered to be secondary to compression of the nerve root by a blood vessel.

Glossopharyngeal neuralgia (GN):

Diagnosis: GN cases demonstrate nerve compression on MRI.

- On surgical exposure, and nerve biopsy shows variable myelin damage and patches of demyelinated axons.
- The application of topical anesthetic to the pharyngeal mucosa eliminates glossopharyngeal nerve pain and can aid in its diagnosis.

Treatment

- Carbamazepine is usually successful. Alternatives include baclofen, gabapentin, lamotrigine, and phenytoin.
- Permanent neurological deficits are rare and may include mild hoarseness and/or dysphagia, or facial nerve paresis.

Facial Pain Associated With Herpes Zoster

1. **Post herpetic neuralgia:**
2. **Acute Herpes Zoster**

Facial Pain Associated With Herpes Zoster

Etiology and Pathogenesis:

- Herpes zoster (shingles) is caused by the reactivation of latent varicella-zoster virus infection that results in both pain and vesicular lesions along the course of the affected nerve (dermatomal).
- In a majority of cases, the pain of herpes zoster resolves within a month after the lesions heal. Pain that persists longer than a month is classified as post herpetic neuralgia (PHN), although some authors do not make the diagnosis of PHN until the pain has persisted for longer than 3 or even 6 months.

Facial Pain Associated With Herpes Zoster

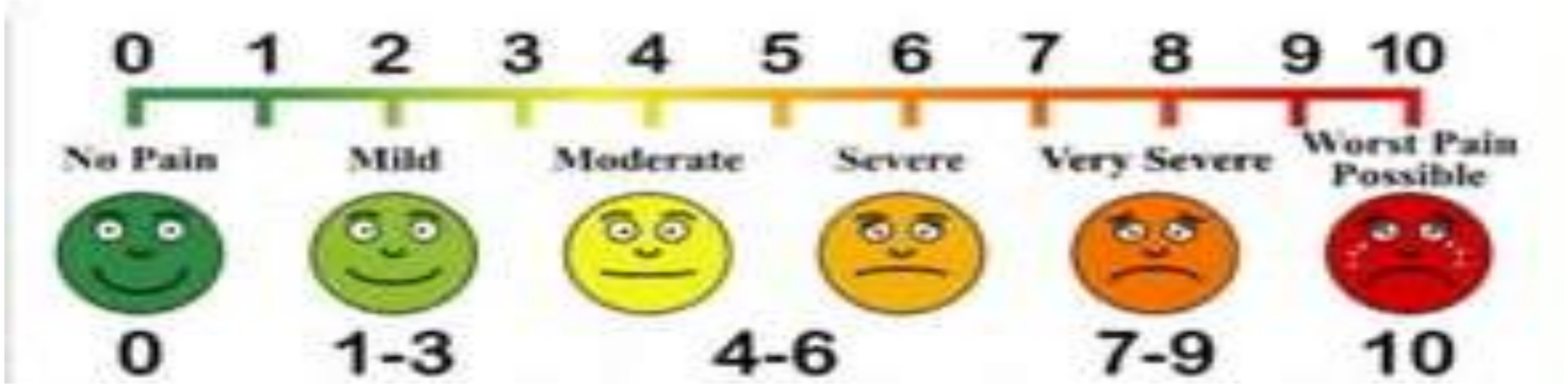
- **Diagnosis** may be obtained by identification of viral DNA from vesicular fluid employing the polymerase chain reaction.
- Trigeminal and cervical nerves are involved in up to a quarter of cases. The ophthalmic branch is affected in more than 80% of the trigeminal cases, particularly in elderly males, and may cause sight-threatening keratitis.
- The vesicles and pain are dermatomal and unilateral and may appear intraorally when the maxillary or mandibular branches of the trigeminal nerve are affected.

Facial Pain Associated With Herpes Zoster

Clinical Features:

- A prodrome of regional pain, itching and malaise.
- Pain precedes typical vesicular eruption by <7 days, usually 2-3 days.
- The dermatomal vesicular or herpetic eruption will rupture and “dry out” over 7-10 days, but complete healing may last up to one month.
- Accompanying pain is moderate to severe visual analog scal (VAS 6) and may persist for three to six months.

Visual Analogue Scale(VAS) score



Facial Pain Associated With Herpes Zoster

Treatment of shingles:

- Antiviral should be initiated within 72 hours from onset of rash, and will significantly decrease rash duration, pain severity, and the incidence of PHN. This is particularly effective in patients >50 years old.
- Fever and pain should be controlled initially by mild analgesics; central analgesics may be used (amitriptyline or gabapentin). . Amitriptyline may reduce the incidence of PHN.
- Use of glucocorticoids is controversial, but may help reduce acute pain; they should always be used together with antivirals.

Post herpetic neuralgia(PHN)

Clinical Features of PHN:

- Persisting or recurring >3 months after the acute HZ stage. Patients relate a previous herpetic (dermatomal) eruption.
- Fluctuations from moderate back ground pain to excruciating, superimposed lancinating pains.
- Pain quality is burning, throbbing, stabbing, shooting, or sharp. Burning pain is significantly higher in patients not treated with antivirals for acute HZ. Itching is very common and prominent in trigeminal dermatomes.
- Pale, Red/purple scars that are usually hypoesthesia or anesthetic.
- Paresthesia, hyperesthesia, and allodynia, months to years after the zoster lesions have healed.

Post herpetic neuralgia(PHN)

Treatment:

- Ophthalmic PHN has the worst prognosis.
- Tricyclic antidepressant (TCA) drugs, gabapentin and pregabalin (lyrica) ,tramadol.
- Invasive therapies include epidural and intrathecal steroids and a variety of neurosurgical techniques may provide relief.
- Use of antiviral famciclovir 500 mg 3 times daily for 7-10 days or Acyclovir 200mg 5times 7-10 days.
- Short course of systemic corticosteroid during the active phase of the disease.
- Topical anesthetic agents, such as lidocaine, or analgesics.
- Tricyclic antidepressants such as triptyline ,nortriptyline, is a well method of reducing the chronic burning pain of PHN.

Nervous intermedius (geniculate) neuralgia

- Uncommon paroxysmal neuralgia of CN VII resulting from herpes zoster infection of geniculate ganglion and nervous intermedius of CN VII.
- Pain in the ear and (less frequently) the anterior tongue or soft palate.
- GN may be caused by compression of somatic sensory branch of cranial nerve VII which goes through the nervus intermedius.
- GN may also develop following herpes zoster oticus (Ramsay Hunt syndrome), caused by reactivation of herpes zoster virus that has previously caused chickenpox in the patient.
- where cold sores occur on the ear drum or ear ,and sometimes on the roof of the mouth or tongue. This may also be associated with facial paresis (weakness), tinnitus, vertigo and deafness. Disorders of lacrimation, salivation and/or taste sometimes accompany the pain.
- The location of pain (external auditory canal and a small area on the soft palate and the posterior auricular region).

Nervous intermedius (geniculate) neuralgia

Treatment:

- Short course (2 to 3 weeks of high-dose steroid therapy is beneficial).
- Acyclovir significantly reduces the duration of the pain 200mg 5 times daily for 10-14 days.
- Patients with geniculate neuralgia are also treated with carbamazepine and antidepressants.
- Patients who do not respond to these medications may undergo surgery to section the nervus intermedius.

Burning Mouth Syndrome (BMS)

*BMS is characterized by resistance to a wide range of treatments and most challenging. A poorly understood pain condition that is most probably neuropathic.

- **(Stomatodynia)** is characterized by a burning mucosal pain with no significant physical signs and is common in postmenopausal women.
- **BMS may be sub classified into:-**
- 1- **Primary or idiopathic BMS** for which a neuropathological cause is likely.
- 2- **Secondary BMS (SBMS)** resulting from local or systemic pathological conditions.

Burning Mouth Syndrome (BMS)

Clinical Features

- The primary location is the tongue, usually the anterior 2/3. Hard palate, lips, and gingiva are frequently involved. Pain is most commonly described as burning or hot and intensity varies from mild to severe.
- BMS is typically of spontaneous onset and lasts from months to several years. Pain pattern may be irregular, but some patients may complain that pain increases toward the end of the day.
- Although a chronic unremitting pattern is usual, partial remission has been reported in about one half to two-thirds of patients, six to seven years after onset. Spontaneous remission is very rare.
- Common aggravating factors include personal stressors, fatigue, and specific foods (acidic, hot, or spicy). More than two-thirds of the patients complain of altered taste sensation (dysgeusia) as metallic taste.
- Abnormal sensations, such as feeling of dry mouth, are common but true hyposalivation is less common and should be considered.

Burning Mouth Syndrome (BMS)

- Oral and perioral burning sensation as a result of local or systemic factors or diseases is classified as BMS.
- 1- **Local factors** and diseases known to induce SBMS include oral candidiasis, lichen planus and allergies.
- 2- **Systemic disorders** that induce SBMS include hormonal changes, deficiencies of vitamin B12, folic acid or iron, diabetes mellitus, side effects of medications, and autoimmune diseases.

Burning Mouth Syndrome (BMS)

Treatment

- **Topical therapies** may be effective and are useful in elderly, medically compromised patients. as Clonazepam (tranquilizers) /1mg three times daily.
- **Systemic therapies** include paroxetine **(antidepressant)** (20 mg/d) and sertraline (50 mg/d) or other selective serotonin reuptake inhibitors (SSRIs). These may reduce pain and improve anxiety and depression.
- A combination **of alpha-lipoic acid (600 mg/d) and gabapentin (300 mg/d)** results in greater improvement of the burning symptoms compared to these medications taken alone.
- Pharmacotherapy-resistant BMS has benefit from **cognitive behavioral therapy.**

Painful Posttraumatic Trigeminal Neuropathy (PTTN)

- Chronic pain following negligible nerve trauma (root canal therapy, injury to nerve bundles, such as in fractures of the facial skeleton, dental implant surgery l%-8% ,orthognathic jaw surgery 5%-30%.
- Third molar extractions may lead to disturbed sensation in the lingual or inferior alveolar nerve for varying periods. Patient complaints of tongue dysesthesia after injury may remain in a small group of patients (0.5%).
- Persistent pain after successful root canal therapy may occur; also surgical root therapy may resulted in chronic neuropathic pain.

Painful Posttraumatic Trigeminal Neuropathy (PTTN)

Clinical Features:

- Chronic pain issues are possible risk factor. The presence and duration of pain in the tooth, tenderness to percussion, female gender, previous painful treatment in the orofacial region.
- Pain is unilateral and occurs in the area of injury, or at the distal dermatome of an injured nerve. Initially pain may be precisely located to the dermatome of the affected nerve. Pain is of moderate-to-severe intensity (VAS 5-9), usually burning in quality but also stabbing during exacerbations.
- Positive or negative local neurological signs include clinically demonstrable sensory dysfunction, usually allodynia, hyperalgesia, or paresthesia.
- Most cases are continuous, but some report superimposed paroxysmal pain attacks.
- Short-lasting pain with associated mechanical trigger areas, mimicking TN. Rarely, a subjective feeling of swelling, foreign body, hot or cold, local redness or flushing.

Painful Posttraumatic Trigeminal Neuropathy (PTTN)

Treatment:

- **Topical anesthetics:** for the management of painful neuropathies. **Topical capsaicin** (active component of chili peppers) in patients with oral neuropathic pain, topical medication as single treatment or in combination with systemic medications can reduce the severity of orofacial neuropathic pain.
- **Systemic Pharmacotherapy:** Anti epilepsy Drugs AEDs and tricyclic antidepressant TCAs are most effective.
- Therapy of neuropathic pain improve quality of life, sleep, and mood. However, pain intensity is reduced in only a subset of responders and is usually accompanied by significant side effects, particularly at the higher doses often required in neuropathic pain.

Neurovascular Pain

Cluster Headache (CH)

- Distinct pain syndrome characterized by episodes of severe unilateral head pain occurring chiefly around the eye and accompanied by a number of autonomic signs (AS), with severe pain. CH typically appears between the ages of 20-29 years, and seems to affect men more than women.
- Episodic CH: commonly occurs at least once daily for a period of weeks, at the same time of day or night. Active periods (or “clusters” of 6-12 weeks) are followed by a temporary remission that may last from weeks to years.
- **Chronic CH:** repeated attacks recur over more than a year without remission or with remission periods lasting less than one month.
- CH active periods are seasonal, occurring around spring or autumn.

Cluster Headache (CH)

Clinical Features:

- Periorbital or ocular pain. In **“upper CH”** the forehead, temporal, and parietal regions are involved, whereas in **“lower CH”** the temporal and suboccipital regions are affected with radiation to the teeth, jaws, neck, and cheeks. Pain is unilateral and in 20% of cases may change sides.
- Severity (8-10) on a visual analog scale. Quality is nonspecific and is variably described as throbbing or boring, burning, stabbing or a “stabbing” feeling in the eye (a hot metal rod in or around the eye).
- CH attacks last 15-180 minutes reaching peak intensity very rapidly—within 3 minutes (up to 9-10 minutes). Longer attacks lasting from 3 to 48 hours are rare and frequency is one every other day to 8/d. Pain is most usually accompanied by at least one ipsilateral autonomic sign (AS); conjunctival injection/lacrimation, nasal congestion/rhinorrhea, eyelid edema, forehead/facial sweating, miosis, and ptosis.

Cluster Headache (CH)

- The vast majority (>80%) of patients are markedly restless during an attack. Patients appear agitated; continually move around, particularly during more severe attacks; **in sharp contrast to the quiet-seeking behavior observed in migraine.**
- Nocturnal attacks that wake them. Pain typically awakens patients within 90 minutes coinciding with the onset of rapid eye movement sleep (Obstructive sleep apnea). Alcohol is a common precipitant of CH attacks.
- CH prodromes (days before attack) include AS, blurred vision, sensitivity to smells, nausea, dyspepsia, hunger, irritability, tiredness, tenseness, and mild pain or non-painful sensations in the area that subsequently becomes painful.
- Photophobia, phonophobia, nausea, and vomiting are reported in up to half of cases. It is important to note that phono- and photophobia are unilateral while in migraine these are bilateral.

Cluster Headache (CH)

Etiology: The cause of cluster headache is unknown. Dilation of blood vessels which in turn, was thought to create pressure on the trigeminal nerve.

- **1. Genetics :**Cluster headache may, but rarely, run in some families in an autosomal dominant inheritance pattern.
- **2.Tobacco smoking**
- **3.Hypothalamus** :A review suggests that the suprachiasmatic nucleus of the hypothalamus, which is the major biological clock in the human body.

Differential Diagnosis: is often misdiagnosed as dental or maxillary sinus pathology.

Cluster Headache (CH)

Treatment:

- Based on attack patterns, patients should avoid daytime naps, alcoholic beverages, and other triggers.
- Pharmacologic Treatment may be abortive, transitional, or preventative or prophylaxis.
- 1- Abortive symptomatic relief may be rapidly attained with oxygen inhalation. Subcutaneous sumatriptan (neuro active alkaloids)
- 2- Rapid transitional prophylaxis may be attained with corticosteroids that may be continued only for a limited period in selected patients.
- 3- Prophylactic or preventive treatment usually with verapamil (calcium channel blockers)and topiramate (anticonvulsant) as second-line therapy.
- Remission periods may increase with time beyond the age of 65-75 active CH is rare.

Paroxysmal Hemicrania (PH)

- Primary headache disorder belonging to the group of trigeminal autonomic cephalalgias(TACs). Patients typically experience intense lateralized headaches with pain primarily in the **ophthalmic trigeminal** distribution (V1) associated with superimposed ipsilateral cranial autonomic features.
- PH is rare with an estimated prevalence of 2-20 per 100,000.
- Mean age of onset is usually 34-41 years, but children aged 6 and adults aged 81 years have been reported .

Paroxysmal Hemicrania (PH)

Clinical Features:

- PH is a unilateral, severe orbital, or periorbital pain.
- Majority of attacks do not change sides, but strong pain may cross the midline and very rarely becomes bilateral.
- It may occur in temporal, periauricular, maxillary, and rarely occipital areas. Referral to the shoulder, neck, and arm is quite common.
- Patients usually report 8-30 attacks/24 h that last 2-30 minutes but may last nearly an hour. Pain onset is rapid and mostly peaks in less than 5 minutes. Quality is mostly sharp but may also be throbbing, stabbing, or boring.
- Accompanying ipsilateral AS:- include conjunctival injection / lacrimation, nasal congestion/rhinorrhea, eyelid edema, forehead/facial sweating, miosis (constricted pupil), and ptosis (droopy eyelid).
- AS may occur bilaterally but are more pronounced on the symptomatic side.

Paroxysmal Hemicrania (PH)

Treatment:

- Most cases respond to Indomethacin within 24 hours and this response to indomethacin is part of its classification criteria.
- Indomethacin should be initiated for 3 days at 75mg, followed, if needed, by 150 mg for a further 3 days is recommended.
- Prognosis in PH is good and long-term remission.

Migraine

- Migraine is the most common headaches, pain of the face and jaws.
- It may be triggered by foods such as nuts, chocolate, and red wine; stress; sleep deprivation; or hunger, menses, weather changes and alcohol.
- Migraine is more common in women. An episodic “sick” headache that interferes with normal daily activities.
- Nausea, vomiting, photophobia (aversion to light), phonophobia (aversion to sound), and osmophobia (aversion to odors). It may be preceded by an aura of neurological dysfunction, such as visual disturbances, vertigo, numbness, or weakness.
- The pain may be moderate. The lifetime prevalence of migraine is estimated to be near 35%.

Migraine

Etiology and Pathogenesis

1 Genetic: More than half of all migraineurs report having other family members who suffer from migraine

2- Vascular Theory : cerebral vasoconstriction and the headache by reactive vasodilation, which explained the throbbing quality of migraine and the relief of pain by ergots. It is now believed that the aura is caused by neuronal dysfunction rather than ischemia. Migrainous fortification spectra (an aura consisting of zigzag figures of bright luminous geometric lines and shapes) experienced by many patients corresponds to cortical changes in metabolism that begin in the visual cortex and spreads across the cortex at 2 -3 mm/min and continues as the headache phase begins.

Migraine

3- Neuronal Theory and the Trigeminovascular System :Migraine aura is believed to result from a slow-moving, spreading depression of cortical activity that liberates potassium and is preceded by a wave front of increased metabolic activity, suggesting that dysregulation of normal neuronal function .

4- Role of Serotonin and Dopamine Pharmacologic data point to a strong role of the neurotransmitter serotonin in migraine, the “triptan” class of drugs has renewed interest in the role of 5- hydroxytryptamine (5-HT) in migraine because of their ability to stimulate selectively a crucial subtypes of 5-HT receptors. Biologic, genetic, and pharmacologic evidence includes the following: (1) most migraine symptoms can be induced by dopamine, (2) there is dopamine receptor hypersensitivity in migraineurs, and (3) dopamine receptor antagonists are effective agents in treating migraine.

Migraine

Clinical Findings:

- **1- Migraine without aura (common migraine)**
- **2- Migraine with aura (classic migraine)**

Migraine

Classic migraine starts with a prodromal aura that is usually visual but that may also be sensory or motor (flashing lights or a localized area of depressed vision (scotoma), sensitivity to light, hemianesthesia, aphasia (impairment of language), or other neurologic symptoms may also be part of the aura, which commonly lasts from 20 to 30 minutes.

- The aura is followed by an increasingly severe unilateral throbbing headache that is frequently accompanied by nausea and vomiting.
- The patient characteristically lies down in a dark room and tries to fall asleep.
- Headaches characteristically last for hours up to 2 or 3 days.

Common migraine: Is not preceded by an aura, but patients may experience irritability or other mood changes. The pain of common migraine resembles the pain of classic migraine and is usually unilateral, pounding, and associated with sensitivity to light and noise. Nausea and vomiting are also common

Migraine

Treatment

- **Prophylactic or preventative therapy** :more than three migraines per month, careful assessment to determine common food triggers. Minimize reactions to the stress of everyday living by using relaxation techniques.
- Drug therapy may be used either prophylactically to prevent frequent headaches or acute attack.
- Drugs that are useful in aborting migraine include **ergotamine and sumatriptan**, which can be given orally, nasally, rectally or parenterally. Ergotamine Initial dose: Oral, Sublingual: 2 mg ergotamine in fixed combination with caffeine given as quickly as possible after the first symptom of headache. Additional 1 mg doses can be given every 30 minutes until the headache has been aborted or until a total dose of 6 mg has been reached or 10 mg/week. Side effects//hypertension and other cardiovascular complications.
- Drugs that are used to prevent migraine include propranolol, verapamil , and TCAs or monoamine oxidase inhibitors such as phenelzine for refractory cases.

Atypical Facial Pain (AFP)

- Is a persistent facial pain that does not follow any anatomical pattern, and not responding to any treatment .
- Constant dull aching pain without an apparent cause. Most frequently in women in the fourth and fifth decades of life.
- Unilateral, cross the midline in some cases, or involve both the maxilla and mandible and lancinating pains are rare.
- The patient frequently reports that the onset of pain coincided with a dental procedure such as oral surgery or an endodontic or restorative procedure.
- Patients also report seeking multiple dental procedures to treat the pain; these procedures may result in temporary relief.

Atypical Facial Pain (AFP)

MANAGEMENT :

- It is important that the symptoms are taken seriously
- Patients should be reassured that they do not have an undetected life-threatening disease and that they can be helped without invasive procedures.
- Consultation with other specialists such as otolaryngologists, neurologists, or psychiatrists.
- TCAs such as amitriptyline, nortriptyline, and doxepin, given in low to moderate doses, are often effective in reducing or (in some cases) eliminating the pain.
- Other recommended drugs include gabapentin and clonazepam.
- Topical desensitization with capsaicin, topical anesthetics, or topical doxepin.

- **Vascular Pain:**
- Pain originating from vascular structures may cause facial pain that can be misdiagnosed and mistaken for other oral disorders, including toothache or TMD.
- The pain is dull, pressing or throbbing.

CRANIAL ARTERITIS

- **Cranial arteritis (temporal arteritis, giant cell arteritis)** is an inflammatory disorder involving the medium-sized branches of the carotid arteries. The temporal artery is the most involved branch.
- Patients have a throbbing headache. accompanied by generalized symptoms including fever, malaise, and loss of appetite. Dull temporal pain, fatigue of the masticatory muscles, joint pain.

Etiology and Pathogenesis :

- Both cranial arteritis and polymyalgia rheumatica are caused by immune abnormalities that affect cytokines and T -lymphocytes, resulting in inflammatory infiltrates in the walls of arteries. This infiltrate is characterized by the formation of multinucleated giant cells. The underlying trigger of the inflammatory response is unknown.

CRANIAL ARTERITIS

Clinical features:

1. Woman ^50 years of age
2. Unilateral temporal headache
3. Jaw claudication
4. Associated with polymyalgia rheumatica
5. Constitutional symptoms
6. Tender temporal artery
7. Visual defects
8. Sudden, painless, monocular vision loss
9. Elevated ESR (50-1 OOJ
10. High-dose steroids when suspect dx
11. Temporal artery biopsy confirms dx Woman

CRANIAL ARTERITIS

Differential Diagnosis:

- Masticatory muscle myalgia
- Myofascial pain
- Temporomandibular disorder

CRANIAL ARTERITIS

Laboratory investigations:

- Elevated erythrocyte sedimentation rate (ESR) and anemia. Abnormal C-reactive protein may also be an important early finding.
- The most definitive diagnostic test is a biopsy specimen (from the involved temporal artery) that demonstrates the characteristic inflammatory infiltrate.

Treatment :

- Systemic corticosteroids: The initial dose ranges between 40 to 60 mg of prednisone per day, and the steroid is tapered once the signs of the disease are controlled.

Cardiac Toothache (referred pain)

The ESR may be used to help monitor disease status. Patients are maintained on systemic steroids for 1 to 2 years after symptoms resolve.

Adjuvant therapy with immunosuppressive drugs, such as cyclophosphamide, to reduce the complications of long-term corticosteroid therapy.

Refer pain to the shoulder, arm, the jaw and to the teeth. Associated with chest pain (substernal), Tooth ache increases with exercises and decreased with medication specific for the heart (nitroglycerin) is directed to the underlying heart problem, after dental evaluation.

When pain occurs after exertion, cardiogenic etiology should be suspected. If patients are experiencing a cardiogenic toothache give them an aspirin, and make sure they get to a hospital emergency room immediately.

Sinusitis and orofacial pain

Acute sinusitis, also called acute rhinosinusitis, is a short-term infection or inflammation of the membranes that line sinuses. It prevents mucus from draining from nose.

Symptoms of acute sinusitis include:

- Nasal congestion
- Thick, yellow, or green mucus discharge from the nose
- Sore throat
- Cough (usually worse at night)
- Drainage of mucus in the back throat (postnasal drip)
- Headache
- Pain, pressure, or tenderness behind eyes, nose, cheeks, or forehead
- Earache
- Toothache
- Bad breath
- Reduced sense of smell
- Reduced sense of taste
- Fever
- Fatigue.

Sinusitis and orofacial pain

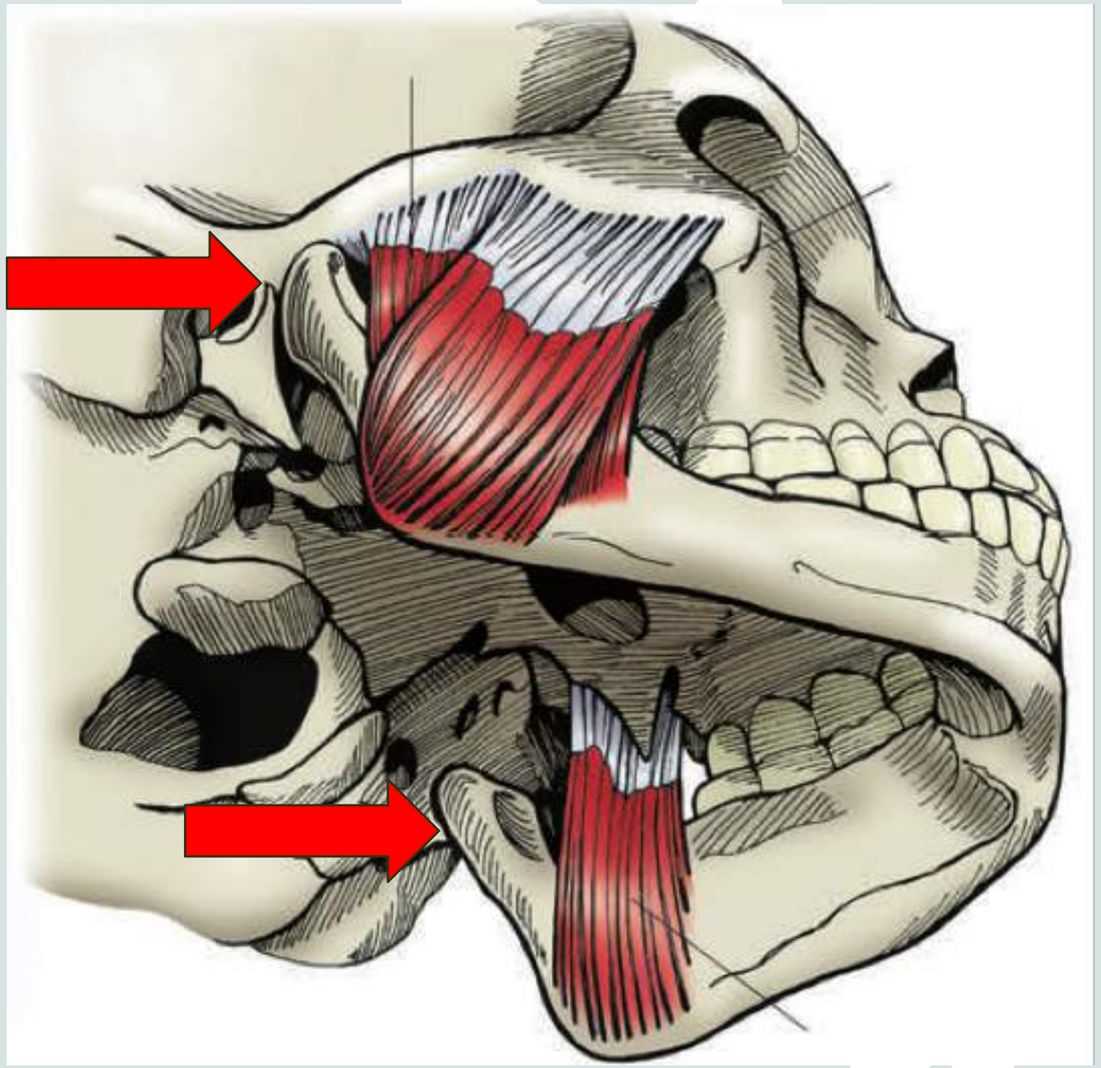
- Dull pain, aching or throbbing in several upper teeth, associated with pressure below the eyes and worsen by bending down, applying pressure in the sinuses, coughing, sneezing, chewing, cold, percussion, worsen the pain, with history of upper respiratory infection, nasal congestion, or sinus problem.
- Acute maxillary sinusitis and acute allergic sinusitis cause actual toothache pain in the maxillary teeth particularly when the roots of the teeth extend into or near the antrum. When fluid pressure caused by infection or inflammation builds up, the patient will experience tenderness in the cheekbone, facial swelling. It rarely involves just one tooth and should be suspected when multiple teeth test positive to biting and percussion tests.


THANK
YOU

Temporomandibular joint
Lec 7 part -1-

Dr. Marwah Waleed S.

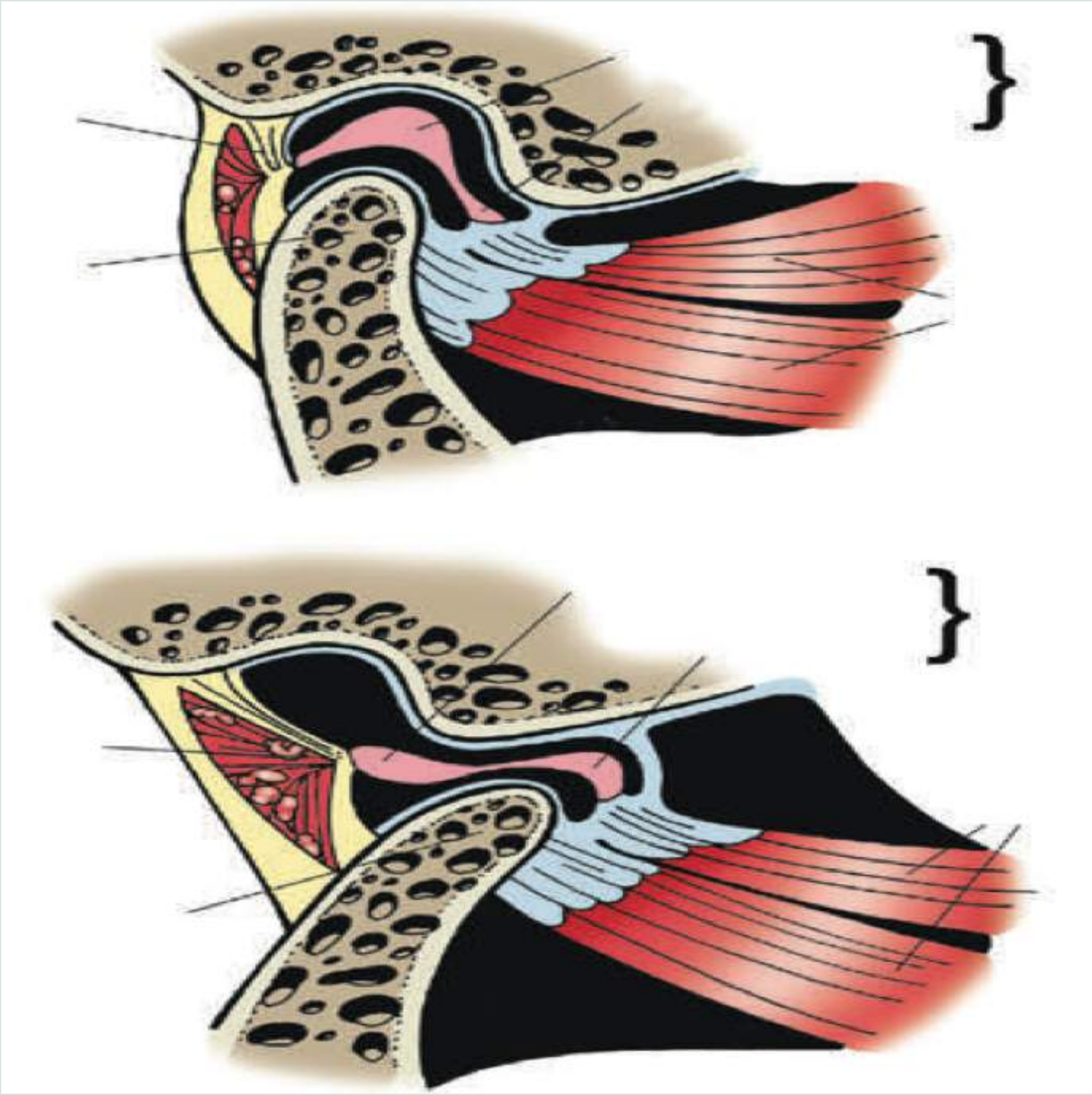
- The **temporomandibular joints** (**TMJ**) are the two joints connecting the jawbone to the skull. It is a bilateral synovial articulation between the temporal bone (glenoid fossa) of the skull (above) and the mandibular condyle (below).
- This joint is unique in that it is a bilateral joint that functions as one unit.



The Capsule:

is a dense fibrous membrane that surrounds the joint and incorporates the articular eminence. It attaches to the :

- articular eminence,
- the articular disc and
- the neck of the mandibular condyle.

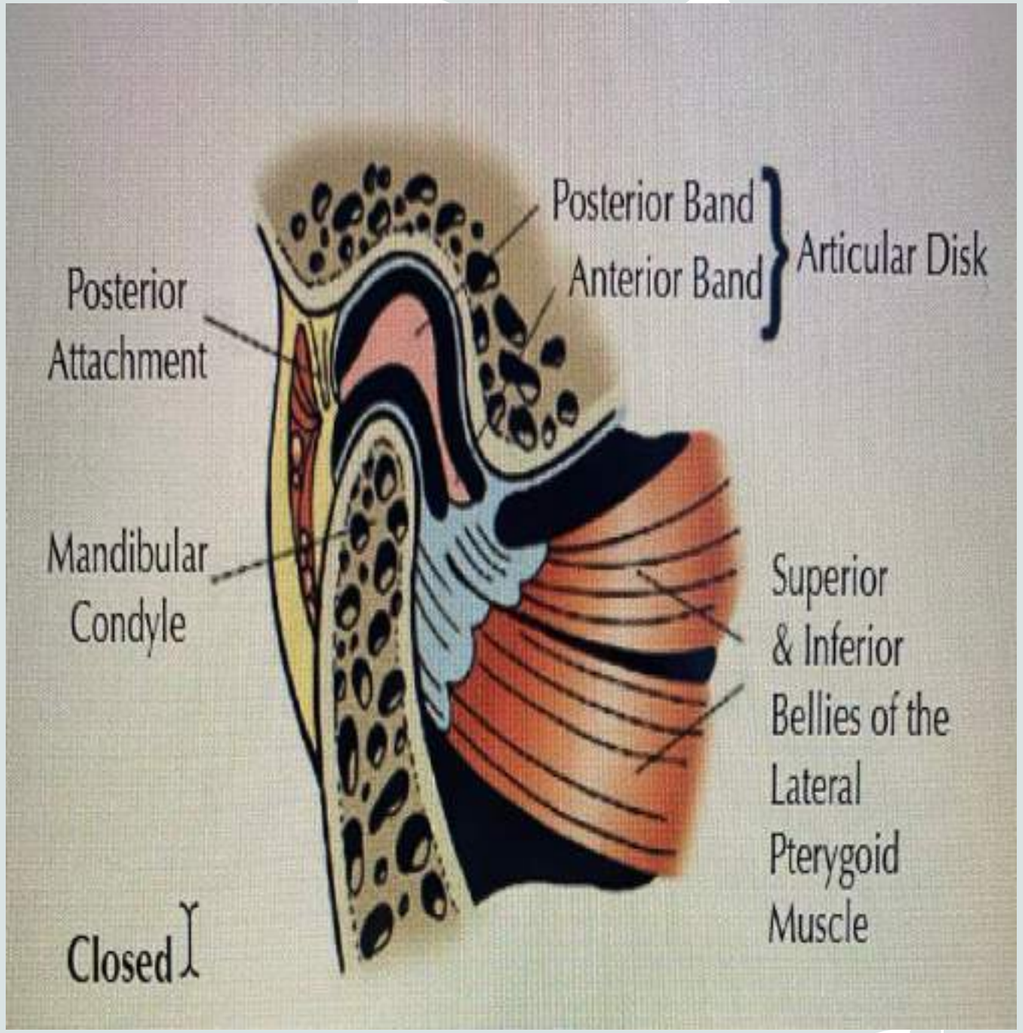


The articular disc: is composed of dense, biconcave and fibrocartilagenous tissue that divides each joint into two compartments, the lower and upper compartments. These two compartments are synovial cavities, which consists of an upper and a lower synovial cavity. The synovial membrane lining the joint capsule produces the synovial fluid that fills these cavities. The central area of the disc is avascular and lacks innervation, thus getting its nutrients from the surrounding synovial fluid. The central area is also thinner but of denser consistency than the peripheral region, which is thicker but has a more cushioned consistency. With age, the entire disc thins and may undergo addition of cartilage in the central part, changes that may lead to impaired movement of the joint. The disc functions as articular surfaces.

It attaches to the condyle medially and laterally.

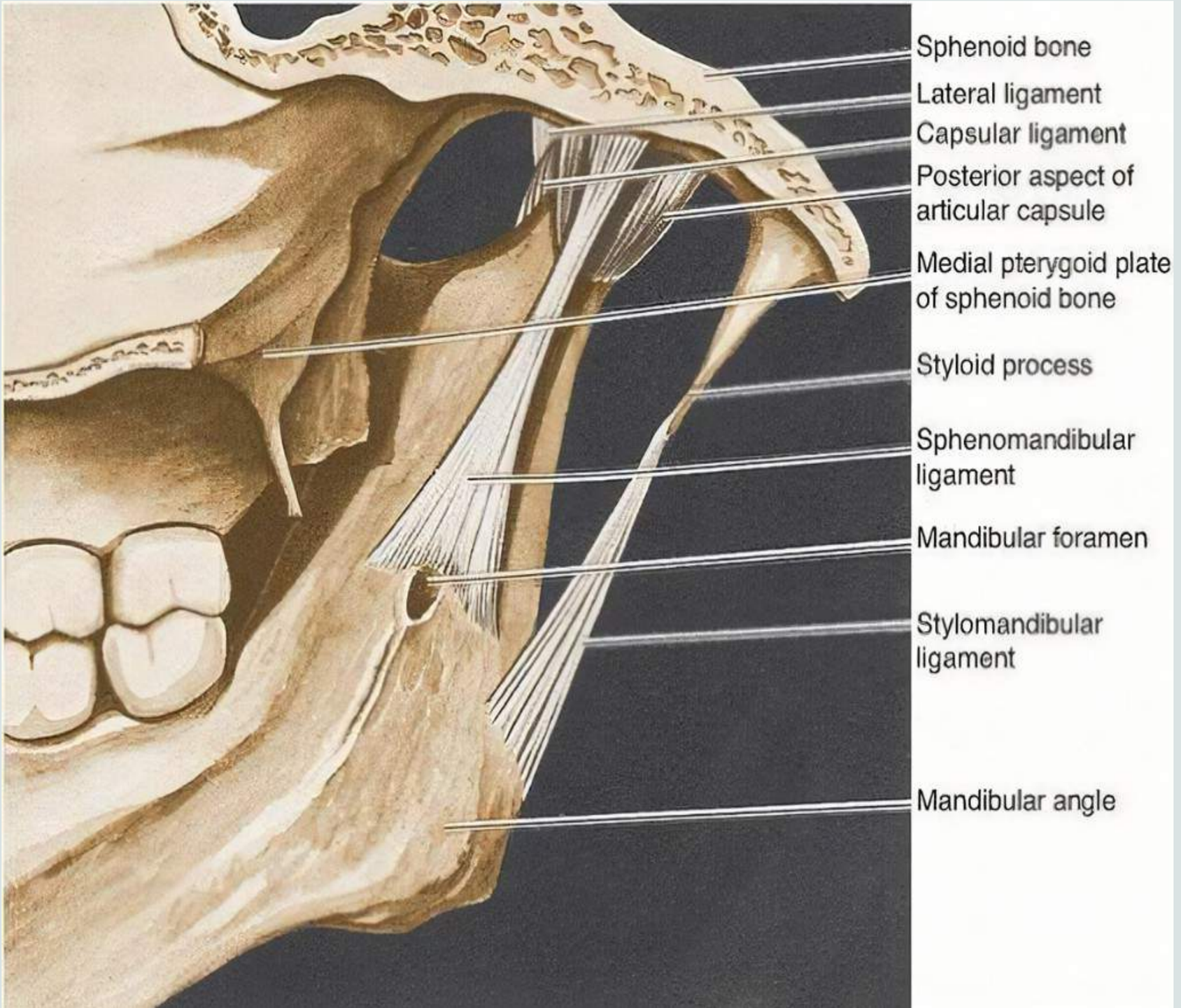
The anterior portion of the disc splits in the vertical dimension, coincident with the insertion of the superior head of the lateral pterygoid.

The posterior portion also splits in the vertical dimension, it referred to as the retrodiscal tissue. This piece of connective tissue is vascular and innervated, and in some cases of anterior disc displacement, the pain felt during movement of the mandible is due to the condyle compressing this area against the articular surface of the temporal bone.



Ligaments

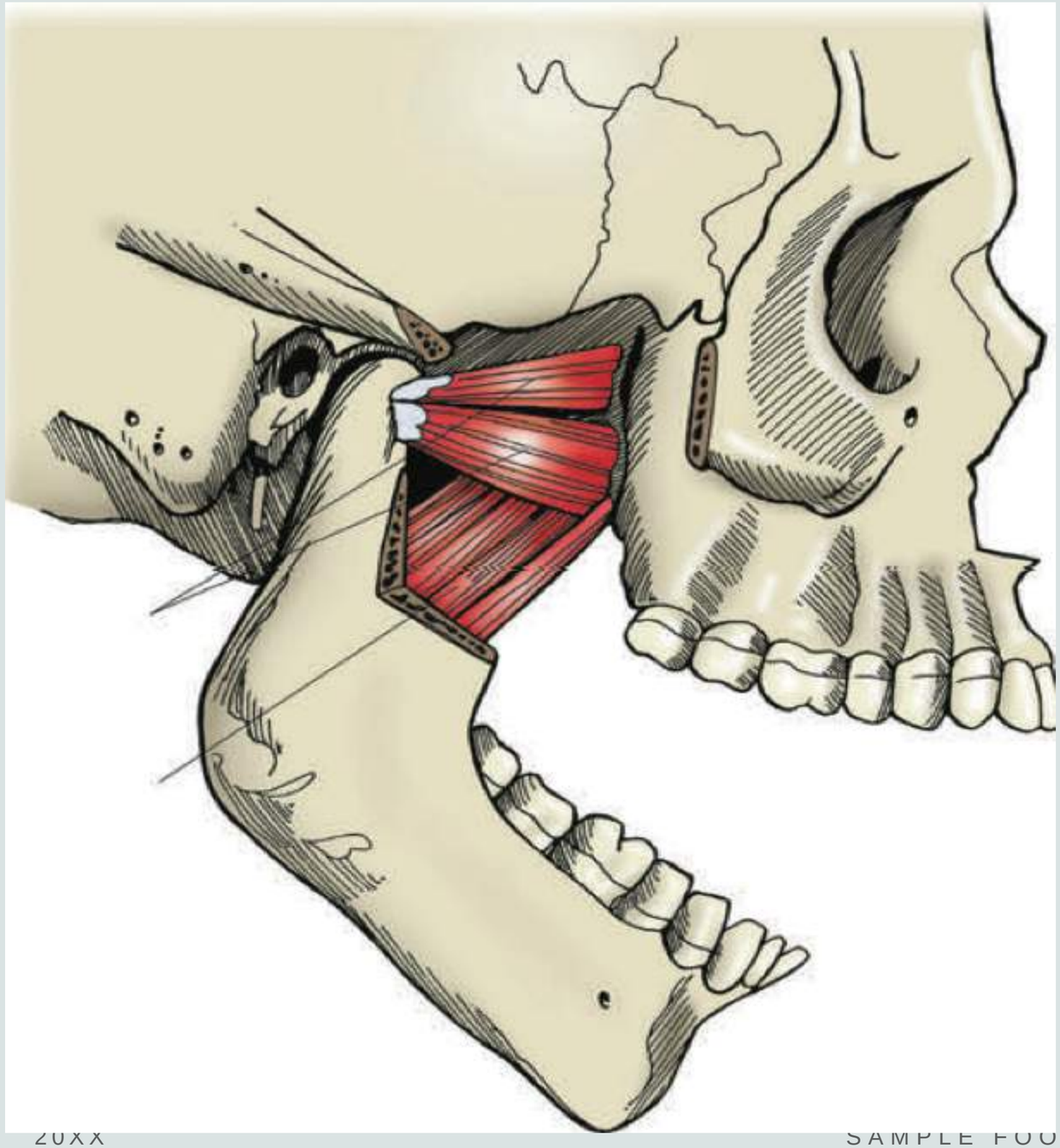
There are three ligaments associated with the temporomandibular joints: one major and two minor ligaments, which are important in that they define the farthest extents of movements (border) of the mandible.



Ligaments

The major ligament, the temporomandibular ligament, is actually thickened lateral portion of the capsule, and it has two parts: an outer oblique portion (OOP) and an inner horizontal portion (IHP). The base of this triangular ligament is attached to the zygomatic process of the temporal bone and the articular tubercle; its apex is fixed to the lateral side of the neck of the mandible. This ligament prevents the excessive retraction or moving backward of the mandible, a situation that might lead to problems with the joint.

The two minor ligaments, the stylomandibular and sphenomandibular ligaments are accessory and are not directly attached to any part of the joint.



The movement of the TMJ

Rotational movement: this is the initial movement of the jaw when the mouth opens.

Translational movement :the upper joint compartment formed by the articular disc and the temporal bone is involved, it is a gliding motion of the jaw as it is opened widely. The part of the mandible which mates to the under-surface of the disc is the condyle and the part of the temporal bone which mates to the upper surface of the disk is the articular fossa or glenoid fossa or mandibular fossa.

Etiological factors of the TMJ disorder

- There are numerous factors that can contribute to temporomandibular disorders.

- Factors that increase the risk of temporomandibular disorders are called “*Predisposing factors*” and those causing the onset of temporomandibular disorders are called “*Initiating factors*” and factors that interfere with healing or enhance the progression of temporomandibular disorder are called“*Perpetuating factors.*”

The most common factors include bruxism and orthopedic instability ,Macrotrauma and microtrauma, other factors like poor health and nutrition, joint laxity and exogenous estrogen. Psychosocial factors like stress.

Occlusion is the first and probably the most discussed etiologic factor of temporomandibular disorders. Today its role is widely considered as contributing by initiating, perpetuating or predisposing of temporomandibular joint disorders.

1.Initiating factors lead to the onset of the symptoms and are related primarily to trauma or adverse loading of the masticatory system.

2.In the perpetuating factors the following may be included:

a.Behavioral factors (grinding, clenching and abnormal head posture)

b.Social factors (could affect perception and influence of learned response to pain)

c.Emotional factors (depression and anxiety)

d.Cognitive factors (negative thoughts and attitudes which can make resolution of the illness more difficult).

The main occlusion effect include:

a. Open bite

b. Overjet greater than 6-7 mm

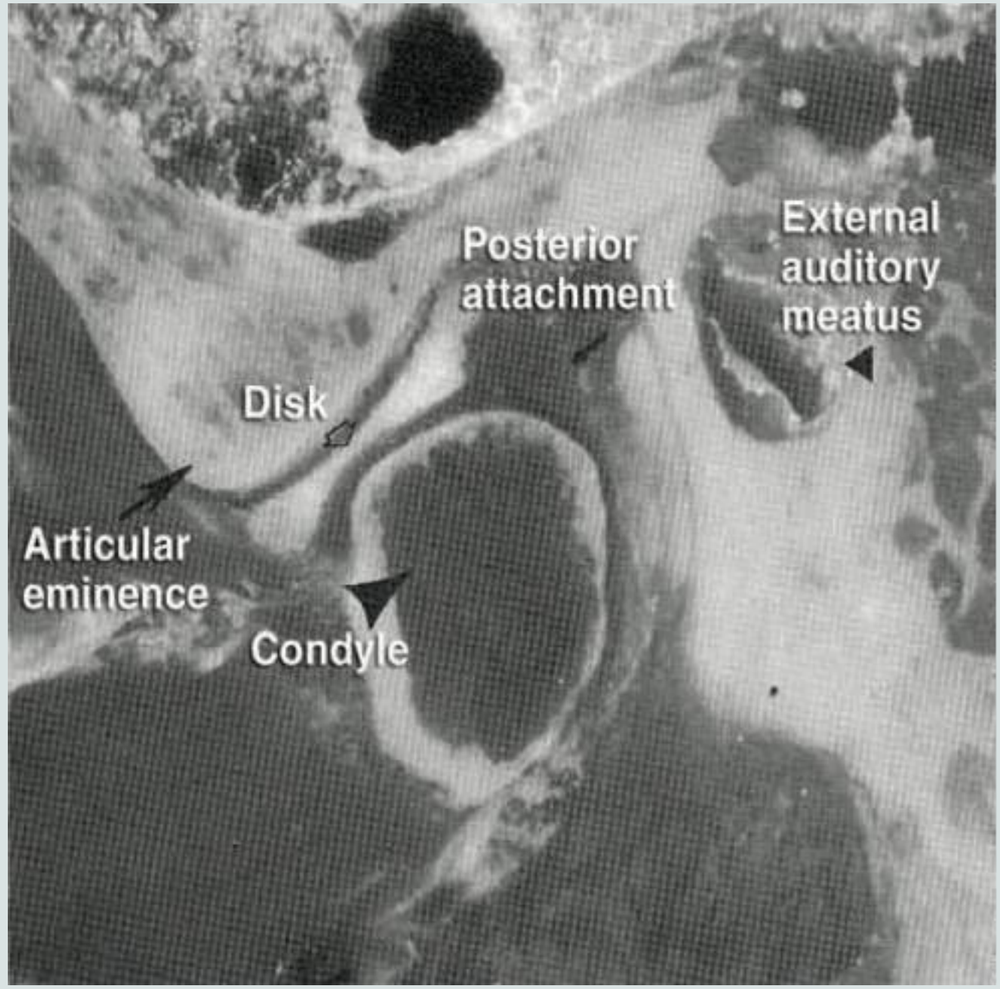
c. Retruded contact position/intercuspal position with sliding

greater than 4 mm

d. Unilateral lingual cross-bite

e. Five or more missing posterior teeth

f. Faulty restorations and ill-fitting prosthesis.



Iatrogenic injuries can act as both initiating as well as predisposing factors. This can occur during any dental procedure in which there is prolonged opening causes a functional imbalance between the temporomandibular joints, muscles and occlusion . TMD and systemic diseases it has been shown that infectious arthritis, traumatic arthritis, osteoarthritis, rheumatoid arthritis and secondary degenerative arthritis can affect the TMJ.

Symptoms

1. Pain or tenderness of the jaw
2. Pain in one or both of the temporomandibular joints
3. Aching pain in and around the ear
4. Difficulty chewing or pain while chewing
5. Aching facial pain
6. Locking of the joint, making it difficult to open or close the mouth TMJ disorders can also cause a clicking sound or grating sensation when open the mouth or chew. But if there's no pain or limitation of movement associated with the jaw clicking, don't need treatment for a TMJ disorder. TMJ can become tense or locked due to stress, misalignment, and teeth grinding. A locked jaw is a painful condition that can often cause other problems like headaches and neck or face soreness.

Symptoms

Trismus, also called **lockjaw**, is reduced opening of the jaws (limited jaw range of motion).

-It may be caused by spasm of the muscles of mastication, or a variety of other causes usually temporary trismus occurs much more frequently than permanent trismus.

-It is known to interfere with eating, speaking, and maintaining proper oral hygiene. This interference, specifically with the patient's ability to swallow properly, results in an increased risk of aspiration.

-In some instances, trismus presents with altered facial appearance. The condition may be distressing and painful for the patient. Examination and treatments requiring access to the oral cavity can be limited.

Hyper mobility, can result in excessive anterior movement of the jaw and the articular disc. This will result in deviation of the jaw away from the affected side. There are usually some clicking sounds in the TMJ and there may or may not be pain.

Hyper mobility may be related to connective tissue disorders such as Marfan syndrome or conditions such as Down's syndrome and cerebral palsy.

Long term hyper mobility can cause the articular disc to elongate and degenerate. The disc can then fail to reduce on closing, causing the TMJ to become stuck in an open position (Open Lock). This can often occur after opening the mouth to an extreme position, such as when singing or yawning or after a prolonged dental procedure.

DIAGNOSIS

The Research Diagnostic Criteria for TMD (RDC/TMD) most commonly used.

1.The diagnosis of TMD is based largely on history and physical examination findings.

2.The symptoms of TMD are often associated with jaw movement (e.g., opening and closing the mouth, chewing) and pain in the preauricular, masseter, or temple region.

3. Another source of orofacial pain should be suspected if pain is not affected by jaw movement.

4.Sounds of the jaw (e.g., clicking, popping, grating, crepitus) may occur with TMD.

5.Other symptoms may include dizziness or neck, eye, arm, or back pain.

6.Chronic TMD is defined by pain of more than three months' duration.

DIAGNOSIS

Single click during opening of the mouth may be associated with an anterior disk displacement.

Second click during closure of the mouth results in recapture of the displaced disk; this condition is referred to as disk displacement with reduction.

When disk displacement progresses and the patient is unable to fully open the mouth (i.e., the disk is blocking translation of the condyle), this condition is referred to as **closed lock.**

Crepitus is related to Physical examination findings that support the diagnosis of TMD may include—but are not limited to—abnormal mandibular movement, decreased range of motion, tenderness of masticatory muscles, pain with dynamic loading, signs of bruxism, and neck or shoulder muscle tenderness.

DIAGNOSIS

Clinicians should assess for malocclusion (e.g., acquired edentulism, hemifacial asymmetries, restorative occlusal rehabilitation), which can contribute to the manifestation of TMD.

Cranial nerve abnormalities should not be attributed to TMD. articular surface disruption, which often occurs in patients with osteoarthritis.

Reproducible tenderness to palpation of the TMJ is suggestive of intra-articular derangement. Tenderness of the masseter, temporalis, and surrounding neck muscles may distinguish myalgia, myofascial trigger points, or referred pain syndrome.

Deviation of the mandible toward the affected side during mouth opening may indicate anterior articular disk displacement

Thank you

TMJ Disorders Lec 7 part_2

Dr. Marwah Waleed Sh.

INTERNAL DERANGEMENTS OF THE TMJ

The most common is the **anterior misalignment or displacement** of the articular disk above the condyle.

Etiology:

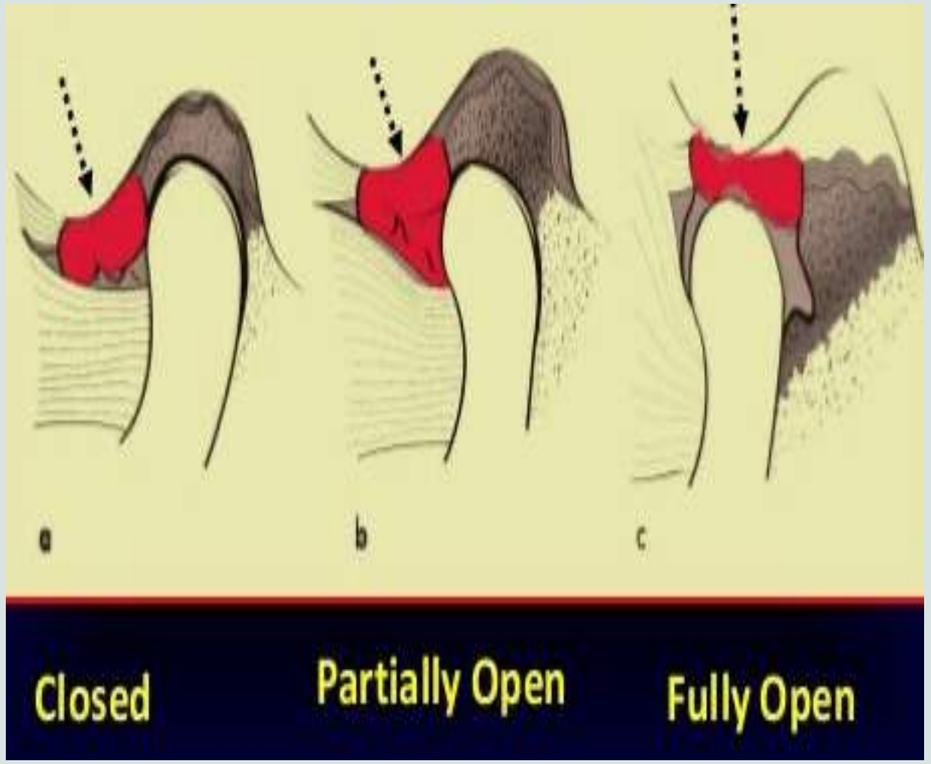
1. Abnormal jaw mechanics can be due to congenital or acquired asymmetries or to the sequelae of trauma or arthritis. If the disk remains **anterior**, the derangement is said to be **without reduction**.
2. Restricted jaw opening (locked jaw) and pain in the ear and around the temporomandibular joint may result when the disk returned to the head of the condyle, the derangement is said to be **with reduction.**

Symptoms: are localized joint pain and popping on jaw movement.

Diagnosis: is based on history and physical examination.

1.Disc displacement with reduction

- The articular disc has displaced **anterior to** the condylar head.
- It may also be displaced medially or laterally.
- When the mouth is **opened, the disc is re-situated** on the condylar head.
- The movement of the disc may result in a clicking, snapping, and/or popping sound.
- It should be heard by the patient at least once in the last 30 days and by the examining dentist during at least a third of the mandibular movements.



Because the disc reduces during condylar translation, range of motion is not limited. However, movements may not be as smooth as a normal TMJ because of the momentary sliding of the condyle on and off of the disc.

2.Disc displacement with reduction with intermittent locking

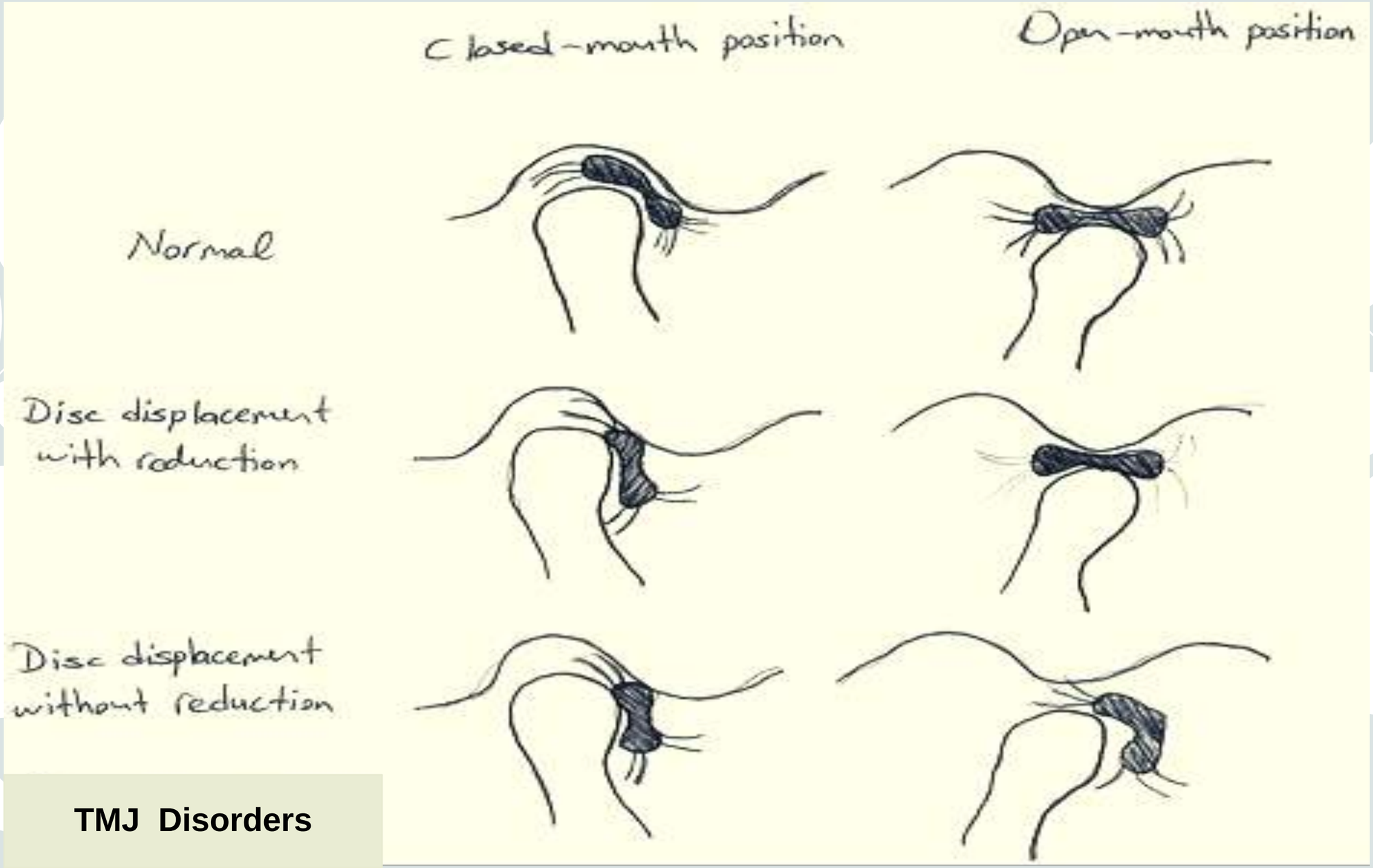
This condition is identical to disc displacement with reduction, with the additional feature of intermittent limited mandibular opening on the occasions that the disc does not reduce.

3. Disc displacement without reduction with limited opening

- The articular disc consistently does not reduce, resulting in limiting opening.
- Limited opening is defined as <40 mm between maxillary and mandibular incisor incisal edges with opening assisted by the dentist.
- This maximum assisted opening range must have factored in the vertical incisal overlap at maximum intercuspal position.

4. Disc displacement without reduction without limited opening

This condition is identical to the previous condition with the exception that mandibular movement is not limited. However, such limitation must have occurred in the past to the extent that eating was hindered. This condition typically follows the previous condition.

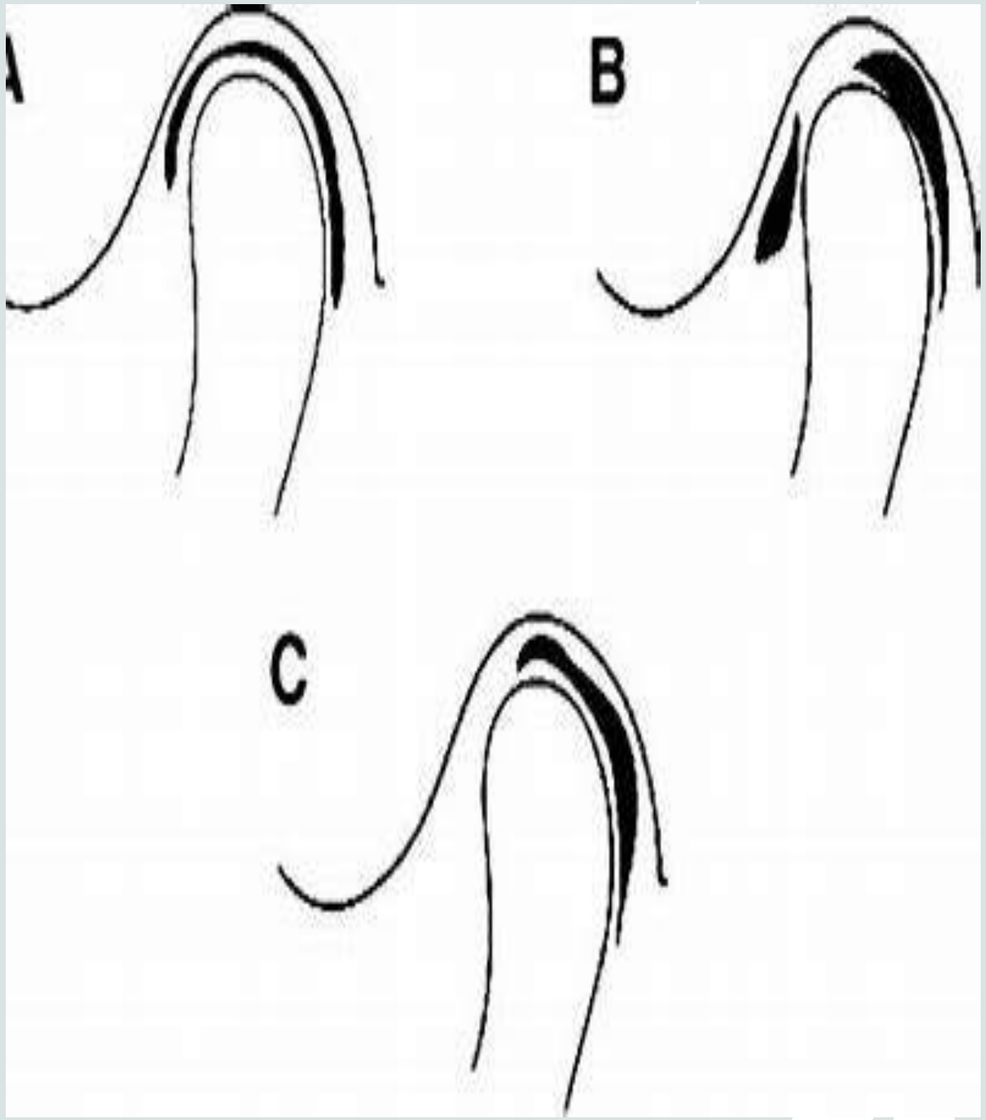


TMJ Disorders


PRESSURE ON THE BILAMMINAR AREA
AD WITH REDUCTION
AD WITHOUT REDUCTION
Pain!
Click!
Lock!

5. Posterior disc displacement

- (very rare in patients with internal derangement).
- Pain is present more often when the disc is perforated.
- Joint sounds occur more often in the thin disc type, with a click in approximately half of the cases.
- Open lock and TMJ luxation each occur roughly in TMJ.



Osteoarthritis (OA)

- **Chronic degeneration** of the various hard and soft tissues around the joint. The jaw joint can be the first joint to get the disease in OA , while in rheumatoid arthritis it is the last joint to be affected.
- This results in anatomical changes in the joint (Stress bearing joints of the body such as knee, hips, spine, and fingers).
- TMJ osteoarthritis affects the cartilage, subchondral bone, synovial membrane, and other hard and soft tissues causing changes such as TMJ remodeling, articular cartilage abrasion and deterioration , causing dysfunction in functional movements of the jaw and pain. **Diagnosis** is complicated in that there is a lack of correlation between damage and pain with radiographic evidence.

Osteoarthritis

- **Symptoms:** Pain on opening, limited movement to the **opposite side**, coarse grinding noise on function, history of clicking that has now stopped, and deviation on opening to the affected side.
- Mostly in women around the age of 35.
- Microtrauma usually from a maximal voluntary contraction (MVC) force or even a blow to the mandible.
- Facial asymmetry and tipped Curve of Wilson.
- Loss of condylar bone which traumatizes the posterior molar on the same side.
- Referral pain to the ear, pain on eating, talking, or function of the jaw joint, jaw locking, and pain in the front tooth of a bridge (due to torque forces on two molars).
- Flattened condyle, osteophytes on condyle(could be noticed by X ray findings).

6. Rheumatoid arthritis

- **Chronic, systemic**, autoimmune inflammatory disorder that is characterized by joint inflammation, erosive properties and **symmetric** multiple joint involvement.
- **Diagnosis:** Conventional radiographs **fail** to show the early lesions due to its limitations. More recently cone-beam computed tomography(CBCT) has been found to diagnose the early degenerative changes of TMJ.
- **Signs and symptoms:** TMJ sounds/noises, TMJ pain, facial pain, headaches, limited range of mandibular movement, change in occlusion, masticatory difficulty, earaches, tinnitus, vertigo, and neck, shoulder, and back pain.

Infection arthritis

Etiology: direct extension of adjacent infection or hematogenous spread of bloodborne organisms .

Signs and symptoms: Jaw movement is limited and painful. Local signs of infection associated with evidence of a systemic disease or with an adjacent infection. Fibrous adhesions, anterior disc displacement, muscle contracture, or more severe degeneration of the TMJ in the advanced stage.

Diagnosis: X-ray results are **negative** in the early stages but may show bone destruction later. If suppurative arthritis is suspected, the joint is aspirated to confirm the diagnosis and to identify the causative organism.

Treatment: includes antibiotics, proper hydration, pain control, and motion restriction. Parenteral penicillin G is the drug of choice. For methicillin-resistant *Staphylococcus aureus* (MRSA) infections, IV vancomycin is the antibiotic of choice.

traumatic arthritis

- Rarely, acute injury (eg, due to difficult tooth extraction or endotracheal intubation) may lead to arthritis of the TMJ.
- **Signs and symptoms**: Pain, tenderness, and limitation of motion occur.
- **Diagnosis** is based primarily on history. X-ray results are negative except when intra-articular edema or hemorrhage widens the joint space.
- **Treatment** includes NSAIDs, application of heat, a soft diet, and restriction of jaw movement.

Ankylosis

Etiology: trauma or infection, but it may be congenital or a result of rheumatoid arthritis.

Signs and symptoms: Chronic, painless limitation of motion occurs. When ankylosis leads to arrest of condylar growth, facial asymmetry is common.

Intra-articular (true) ankylosis

X-rays of the joint show loss of normal bony architecture . A late and rare finding; in some cases, it affects both sides. In severe cases, there is a loss of mandibular condylar support with resultant retrognathia.

Extra-articular (false) ankylosis

It caused by enlargement of the coronoid process, depressed fracture of the zygomatic arch, or scarring resulting from surgery, irradiation, or infection

Ankylosis

Congenital temporomandibular joint ankylosis

- Rare maxillofacial disorder. Significant reduction in mouth opening (i.e. from a few millimeters to a few centimeters).
- Facial dysmorphism (i.e. lateral deviation of the mandible and chin, lower facial asymmetry, retrognathia, micrognathia, dental malocclusion).
- Feeding and breathing difficulties.
- Developmental delay, hypotonia, seizures, and additional dysmorphic features.

IMAGING of TMJ

- The initial study should be plain radiography (transcranial and transmaxillary views) or panoramic radiography.
- Acute fractures, dislocations, and severe degenerative articular disease are often visible in these views.

Computed tomography is superior to plain radiography for evaluation of subtle bony morphology and, to detect bony abnormalities of the TMJ and in rare conditions such as synovial osteochondromatosis.

The followings could be detected by the CT.

- Internal disc derangement.
- Erosive arthritis .Osseous erosions are frequently seen in association with disc displacement.
- Idiopathic condylar resorption. A more severe form of condylar erosion associated with high grade internal derangement is recognized.
- Ankylosis.
- Osteoarthritis.
- Condylar fractures.
- Osteochondroma.

Magnetic resonance imaging(MRI) is the optimal modality for comprehensive joint evaluation in patients with signs and symptoms of TMD.

- The first step in MR imaging of the TMJ is to evaluate the articular disk, or meniscus, and its morphologic features and its location relative to the condyle in both closed- and open-mouth positions.
- Abnormal disk morphologic features, disk displacement, joint effusion, osteoarthritis, as well as new indirect MR imaging signs of dysfunction not attachment ,and also rupture of retrodiscal layers.

IMAGING of TMJ

Ultrasonography: (Advantages) a noninvasive, dynamic, low-cost technique to diagnose internal derangement of the TMJ , it is **indicated** when magnetic resonance imaging is not available.

Panoramic Radiography (OPG) :

Indications:

1. To detect the osseous abnormalities.
2. **Pain in front of the ears**
3. **Jaw clicking / locking**
4. **Reduced / Painful mouth opening**

Disadvantages:

1. They do not give useful information for non-bony elements such as cartilage or adjacent soft tissues, joint effusions, which are commonly associated with pain and disc displacements.
2. Superimposition of adjacent structures.
3. Limited value for diagnosis of temporomandibular joint dysfunction because mild degenerative disease.
4. Not recommended as a routine investigation in all patients who present with TMJ symptoms.

Treatment of the TMJ

A. Nonpharmacologic Management

- **Supportive patient education** is the recommended initial treatment for TMD.
- **Adjunctive measures** include jaw rest, soft diet, moist warm compresses, and passive stretching exercise.
- **Physical therapy** for improving symptoms associated with TMD. Techniques may be active or passive (e.g., scissor opening with fingers, use of medical devices) for improving muscle strength, coordination, relaxation, and range of motion. Specialized physical therapy options such as ultrasound, electrotherapy, or low-level laser therapy have been used in the management of TMD.
- **Acupuncture** is used increasingly in the treatment of myofascial TMD.
- **Behavior modifications** such as stress reduction, sleep hygiene, elimination of parafunctional habits (e.g., teeth grinding, pencil or ice chewing, teeth clenching), and avoidance of extreme mandibular movement (e.g., excessive opening during yawning, tooth brushing, and flossing).

B.Pharmacological Management

1. Nonsteroidal anti-inflammatory drugs (salicylates and cyclooxygenase inhibitors), Naproxen has proven benefit in reduction of pain.

2. Muscle relaxants can be prescribed with NSAIDs if there is evidence of a muscular component to TMD.

3.Tricyclic antidepressants (most commonly amitriptyline), desipramine (Norpramin), doxepin, and nortriptyline (Pamelor)—are used for the management of chronic TMD pain.

4. Benzodiazepines are also used, but are generally limited to two to four weeks in the initial phase of treatment ,diazepam [Valium], clonazepam [Klonopin], gabapentin [Neurontin]) may provide more benefit than shorter acting agents. Opioids are not recommended and, should be used for a short period for severe pain treatment.

C.Dental occlusal splinting and permanent occlusal adjustment

Goals of the treatment:

1. Creating neuromuscular harmony in the masticatory system with a removable appliances."

2. To improve jaw-muscle function

3. To relieve associated pain by creating a stable balanced occlusion.

Occluding splints
(stabilization splints)
*are specially fabricated to improve the alignment of the upper and lower teeth.

Non-occluding splints

(simple splints) primarily open the jaw ,and to release the muscle tension ,and prevent the teeth clenching. It is made of a soft –vinyl and are easier and cheaper to fabricate

D. Surgical treatment of the TMJ

Surgical intervention is appropriate only when:

1) There is identifiable pathology amenable to surgical intervention.

2) There is resultant loss of mechanical function

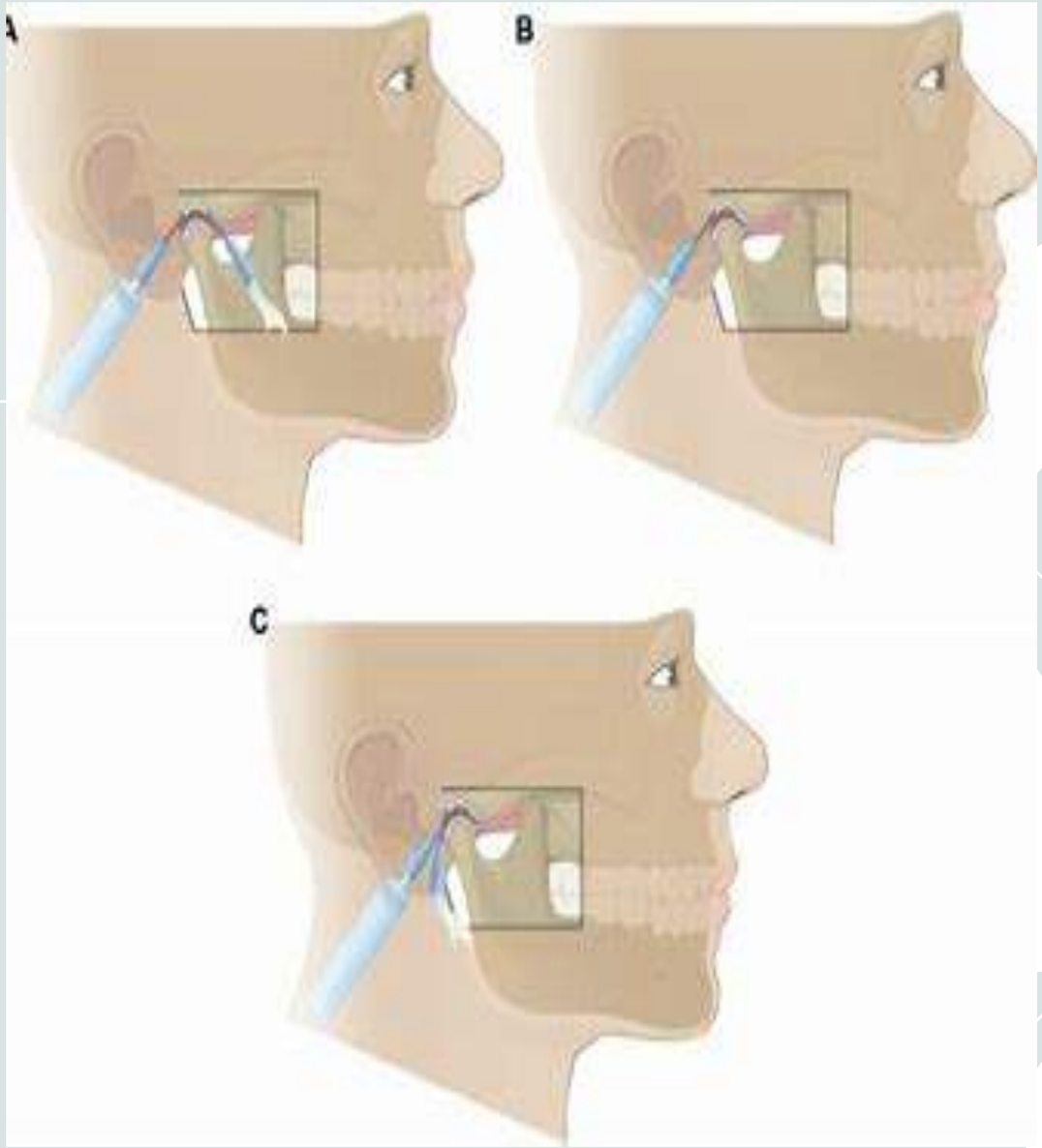
3) There is pain related to joint pathology

ARTHROCENTESIS

Minimally invasive surgical techniques used in the management of TMJD.

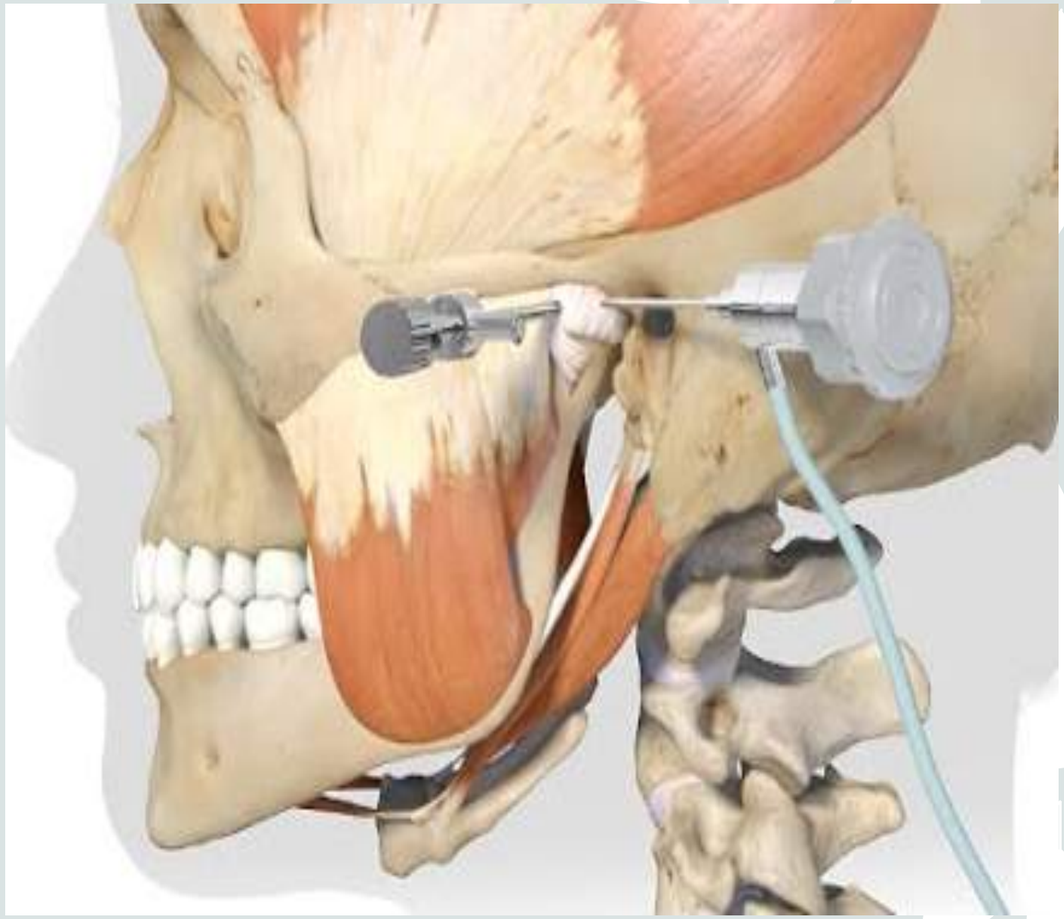
Arthrocentesis involves the placement of two needles into the superior joint space for the purpose of hydraulic distension then joint lavage.

In the **acute “closed lock” or in the painful self-reducing disc displacement disorder** arthrocentesis will help mobilize an entrapped disc and will remove nociceptive inflammatory mediators.



Arthroscopic surgery

- Arthroscopic surgery is considered a minimally invasive diagnostic and therapeutic procedure however it is usually done in the hospital out-patient setting.
- Most arthroscopic procedures are used for **diagnosis, lysis of adhesions and lavage of inflammatory mediators within the superior joint space.**



CONDYLOTOMY DERANGEMENT

- For the management of recurrent self-reducing disc displacement.
- Condylotomy is an osteotomy (**a controlled fracture**) performed through the condylar neck/vertical mandibular ramus.

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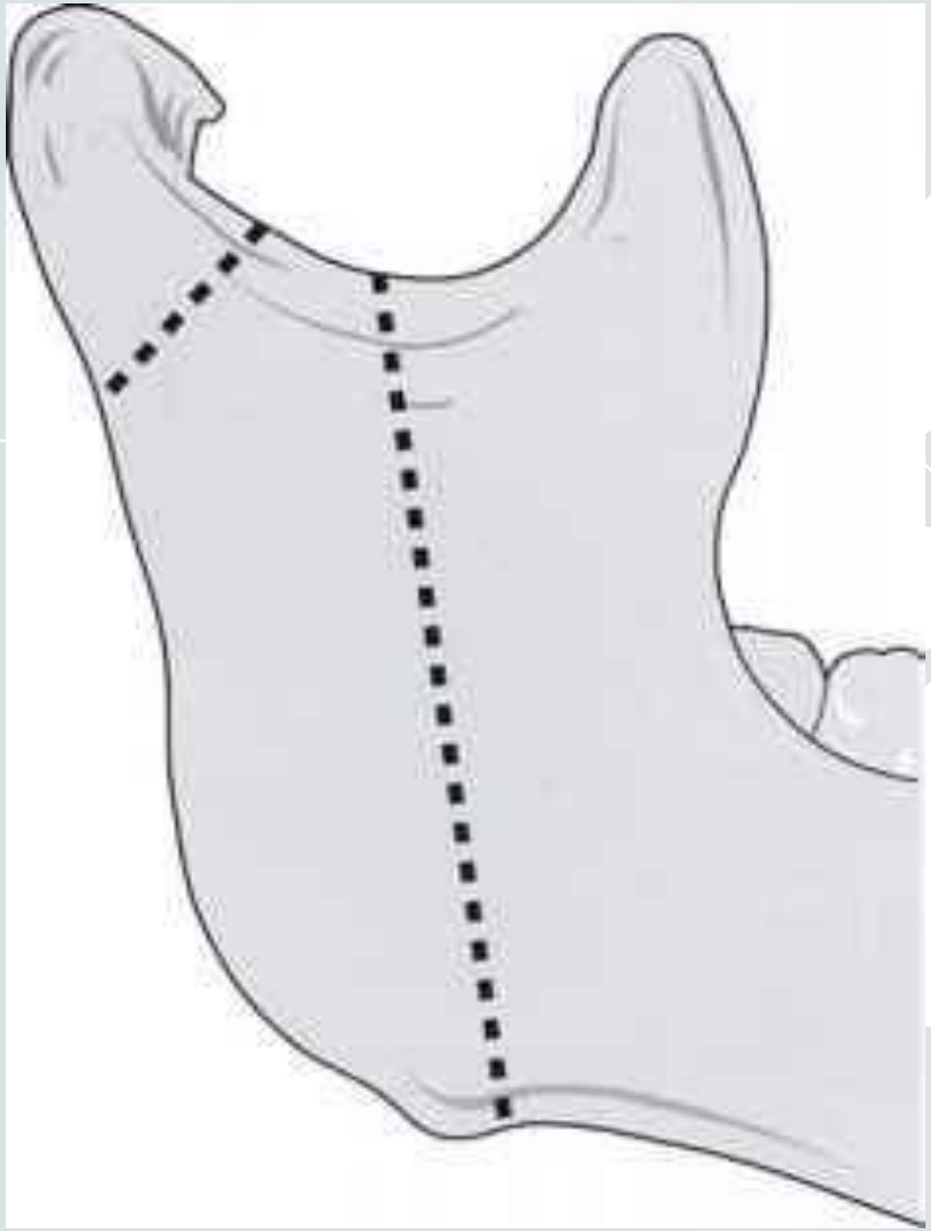
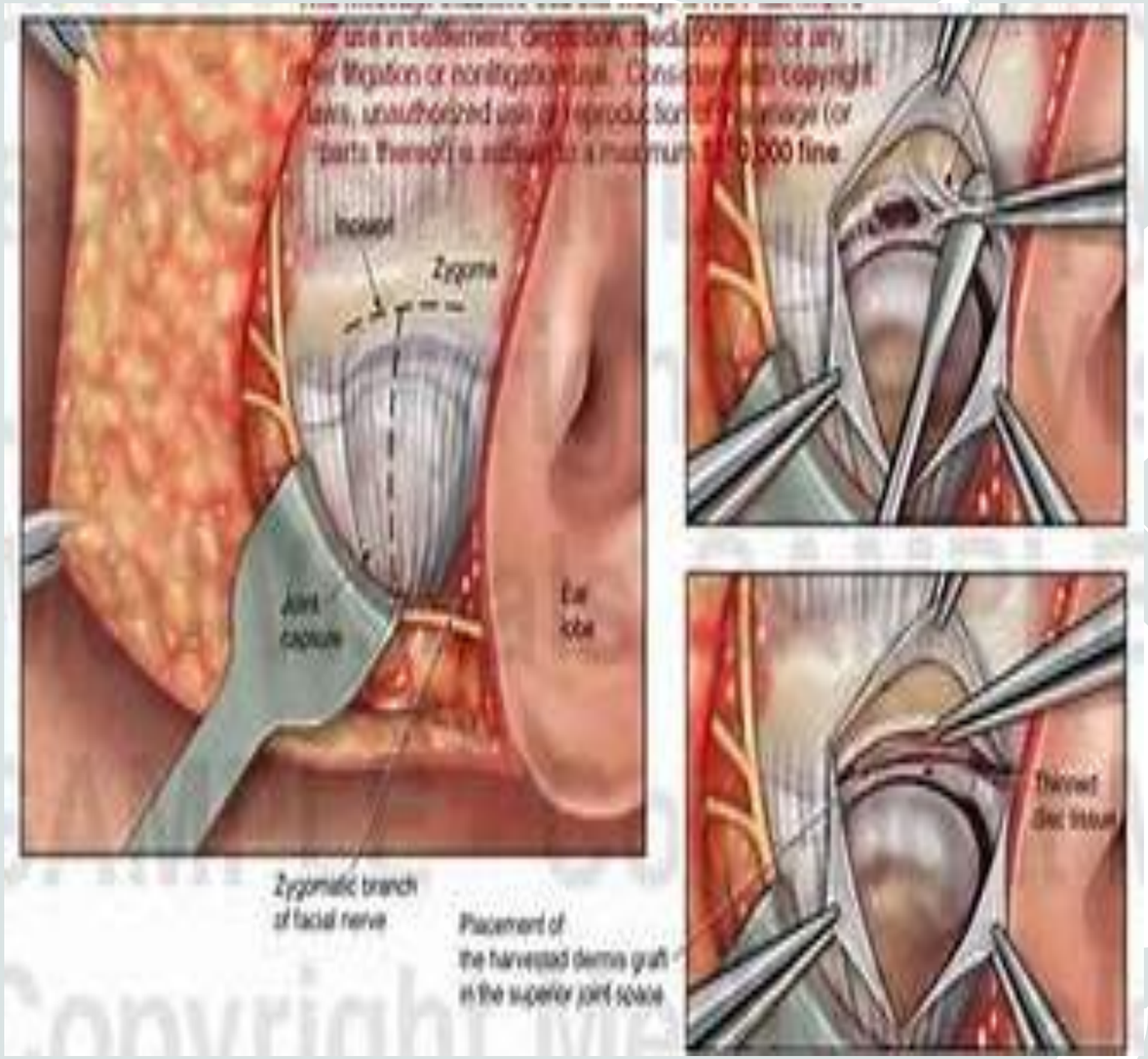


ARTHROPLASTY

- Arthroplasty refers to a group of TMJ surgical procedures approached with an incision directly into the joint itself.
- They **are indicated for** those patients with progressively debilitating internal derangement refractory to the non-surgical and minimally invasive techniques.



Thank you

ULCERATIVE, VESICULAR, AND BULLOUS LESIONS

Dr. Marwah Waleed Sh.

Dermatologic lesions are classified according to their clinical appearance

Frequently used terms that are applicable in the oral mucosa are:

- **1. Macules** Lesions that are **flush with the adjacent mucosa** and that are noticeable because of their **difference in color from normal** skin or mucosa. They may be **red due to increased vascularity or inflammation**, **or pigmented due to the presence of melanin**, **hemosiderin, and foreign materials** (including the breakdown products of medications).
- A good example in the oral cavity is the **melanotic macule.**
- **2. Papules**
- These are lesions **raised above the skin or mucosal surface that are smaller than 1.0 cm in diameter** (some use 0.5 cm for oral mucosal lesions).
- They may be slightly domed or flat-topped.
- Papules are seen in a wide variety of diseases, such as **the yellow-white papules of pseudomembranous candidiasis**.
- **3. Plaques** These are **raised lesions that are greater than 1 cm in diameter**; they are **essentially large papules.**
- **4. Nodules** These lesions are present within the dermis or mucosa. The lesions may also **protrude above the skin or mucosa forming a characteristic dome-shaped structure.** like **irritation fibroma.**

5. Vesicles.

These are small blisters containing clear fluid that are **less than 1 cm in diameter.**

6. Bullae.

These are elevated blisters containing clear fluid that are **greater than 1 cm** in diameter

7. Erosions. These **are red lesions** often caused by **the rupture of vesicles or bullae**, or **trauma**. May also **result from thinning or atrophy of the epithelium in inflammatory** diseases such as **lichen planus**. These should not be mistaken for ulcers that are covered with fibrin and are yellow although erosions may develop into ulcers.

8. Pustules. These are **blisters containing purulent material and appear yellow**.

9. Ulcers.

These are **well-circumscribed, sometimes depressed lesions** with an **epithelial defect** that is **covered by a fibrin clot**, resulting in a yellow-white appearance. e.g. aphthous

10. Purpura. reddish to purple discolorations caused by **blood from vessels leaking into the connective tissue.**

These lesions **do not blanch when pressure is applied and are classified by size** as **petechiae** (less than 0.3 cm), **purpura** (0.4–0.9 cm), or **ecchymoses** (greater than 1 cm)

Classification of Vesiculobullous and ulcerative diseases

- Acute Multiple Ulcers
- Chronic multiple Ulcers
- Recurrent Ulcers
- Single ulcers

1. The Patient with Acute Multiple Ulcers

The major diseases that cause acute multiple oral ulcers include:
Viral and bacterial stomatitis, allergic and hypersensitivity reactions (particularly erythema multiforme and contact allergic stomatitis), and lesions caused by medications (such as cancer chemotherapy)

1. Herpes Simplex Virus Infections
2. Varicella-Zoster Virus Infections
3. Cytomegalovirus Infections
4. Coxsackievirus Infection - CV Infections
5. Necrotizing Ulcerative Gingivitis and Necrotizing Ulcerative Periodontitis
6. Erythema Multiforme
7. Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis
8. Plasma Cell Stomatitis and Oral Hypersensitivity Reactions

1. Herpes Simplex Virus Infection

Etiology and Pathogenesis

- **The primary infection**, which occurs on initial contact with the virus, is acquired by inoculation of the mucosa, skin, and eye with infected secretions.

The virus then **travels** along the sensory nerve axons and establishes chronic, latent infection in the sensory ganglion (trigeminal ganglion).

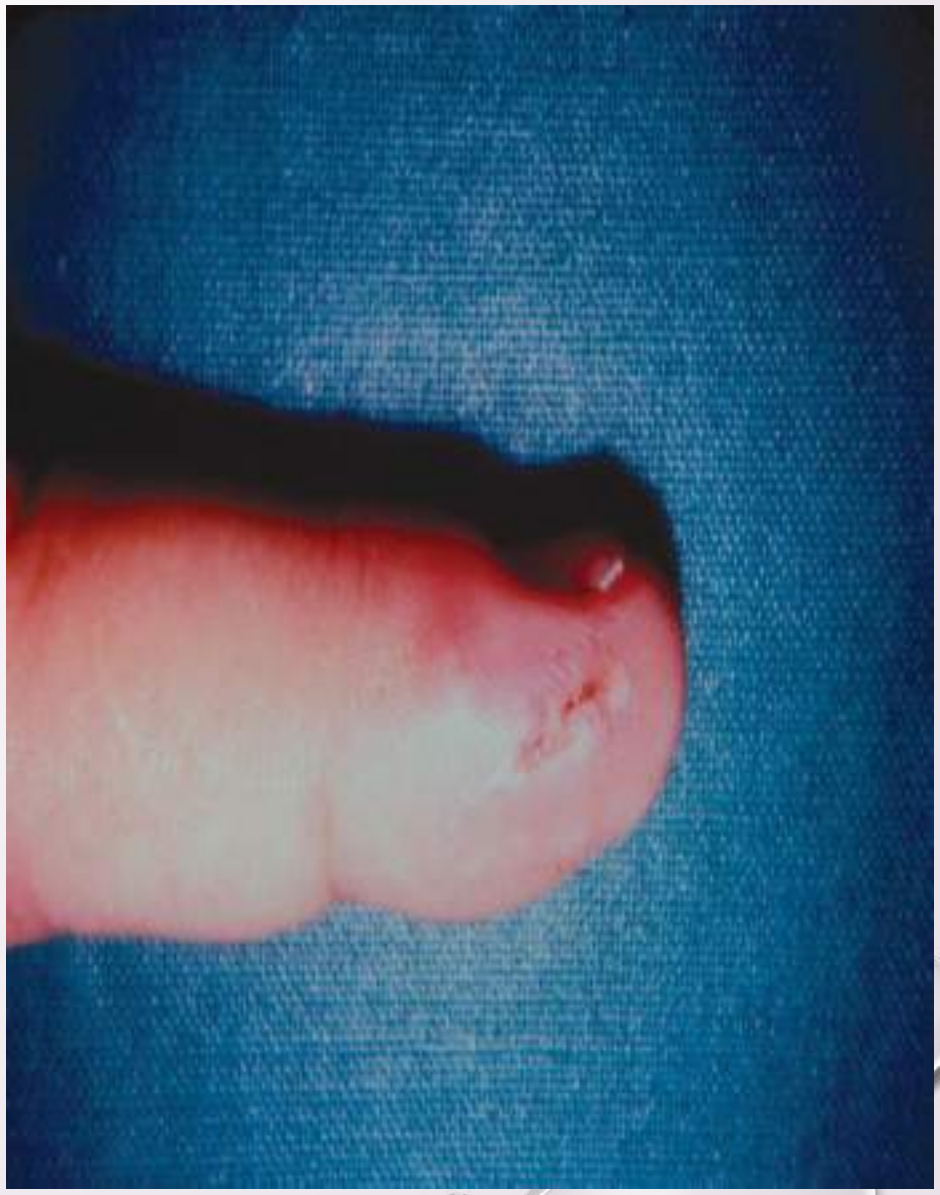
Extraneuronal latency (i.e., HSV remaining latent in cells other than neurons such as the epithelium) may play a role in recurrent lesions of the lips.

Recurrent HSV results when HSV **reactivates at latent sites** and travels centripetally to the mucosa or the skin, where it is directly cytopathic to epithelial cells, causing recrudescent HSV infection in the form of localized vesicles or ulcers.

The most common sites of infection are the **oral** and **genital** mucosa and the **eye.**

In general, infections above the waist are caused byHSV -1 and those below the waist by HSV- 2, although with changing sexual practices, it is not uncommon to culture HSV-2 from oral lesions and vice versa.

- HSV infection of the cornea (keratitis) is a major cause of blindness in the world.



- HSV-1 or -2 may cause **herpes whitlow**, an infection of the fingers when virus is inoculated into the fingers through a break in the skin .
- This was a common occupational hazard (including within the dental profession) before the widespread use of gloves.

Other HSV-1 infections include

Herpes gladiatorum (infections of the skin spread through the sport of wrestling), herpes encephalitis, HSV esophagitis,
HSV pneumonia and neonatal and disseminated infection.
HSV is an important etiologic agent in erythema multiforme,
HSV has been recovered in the endoneurial fluid of of patients with Bell palsy.

(**endoneurium** a layer of delicate connective tissue around the myelin sheath of each myelinated nerve fiber. Its component cells are called **endoneurial)**

However, varicella-zoster virus(VZV) has also been strongly implicated in the development of Bell palsy.

Treatment with antiviral therapy (especially with corticosteroids) within the first 48hours resulted in better outcomes further supporting the concept of herpesvirus involvement in the pathogenesis of Bell palsy.
However, a recent study showed that approximately 60% of cases of Bell palsy were associated with Human herpesvirus (HHV6), and only 13% with HSV**.**

Primary Gingivostomatitis

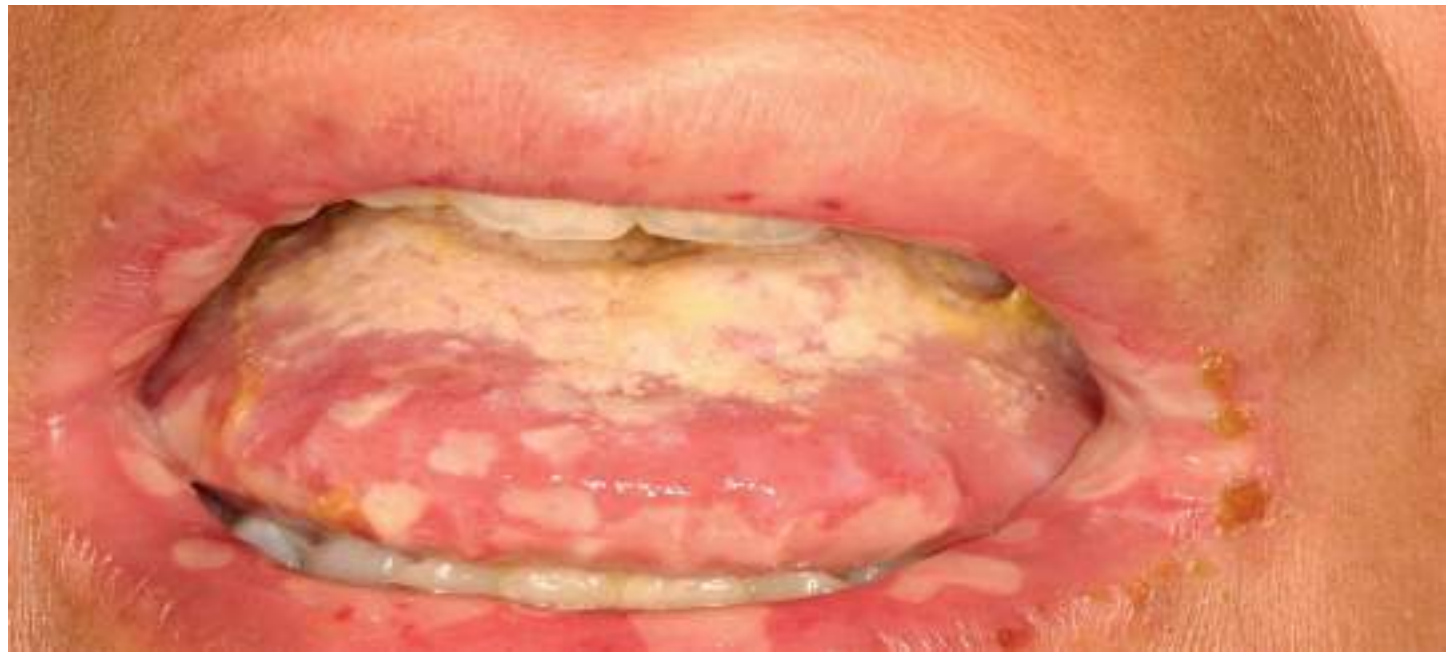
Clinical Manifestations

- The majority of primary HSV-1 infections are subclinical and generally occur in **children** and **teenagers**, and **young Adults**
- There is a one- to three-day viral prodrome of fever, loss of appetite, malaise, and myalgia that may also be accompanied by headache and nausea.
- Oral pain leads to poor oral intake, and patients may require hospitalization for hydration.
- The disease is self-limiting in otherwise normal patients and resolves within 10–14 days, typical for a viral illness.

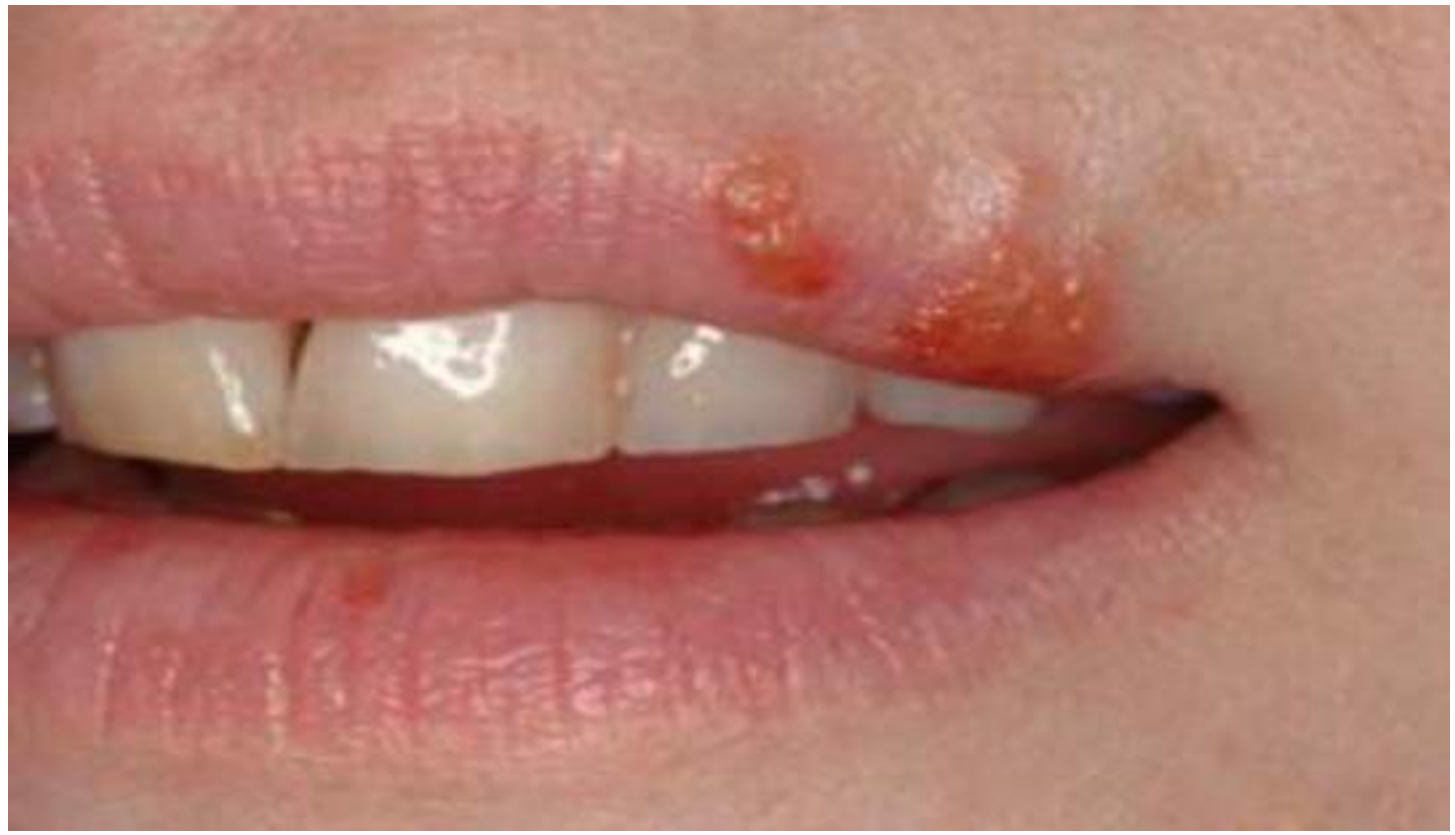
Oral Findings

- Within a few days of the prodrome, erythema and clusters of vesicles and/or ulcers appear on the keratinized mucosa of the hard palatal mucosa, attached gingiva and dorsum of the tongue, and the nonkeratinized mucosa of the buccal and labial mucosa, ventral tongue, and soft palate.
- Vesicles break rapidly down to form ulcers that are usually 1–5 mm and coalesce to form larger ulcers with scalloped borders and marked surrounding erythema.
- The gingiva is often erythematous, and the mouth is extremely painful, causing difficulty with eating.
- Pharyngitis causes swallowing difficulties.

- Primary HSV infection in adults follows a similar pattern.



Primary herpetic gingivostomatitis



Clustered vesicles of recrudescent herpes labialis on vermilion.

Recrudescent (renewing) Oral HSV Infection

❖ **Reactivation** of HSV may lead to asymptomatic shedding of HSV, in the saliva and other secretions, an important **risk factor** for transmission; it may also cause ulcers to form.

- Asymptomatic shedding of HSV is not associated with systemic signs and symptoms and occurs in 8-10% of patients following dental treatment.

❑ Reactivation of **HSV-1** on the oral mucosa is common and usually **asymptomatic**. However, **HSV-1** is rarely found in tears and nasal mucosa. Frequent oral **shedding** of **HSV-1** may increase the risk for transmitting the virus to both oral and genital mucosa of sexual partners

❖ The term **recrudescent HSV** should be used to refer to the actual ulcerations caused by reactivated virus.

❖ Fever, ultraviolet radiation, trauma, stress, and menstruation are important triggers for reactivation of HSV.

❖ Recrudescent HSV on the lips is called recurrent herpes labialis (RHL) and occurs in 20- 40% of the young adult population..

- These are associated with a prodrome **of itching, tingling, or burning** approximately 50% of the time, followed by the appearance of papules, vesicles, ulcers, crusting, and then resolution of lesions
- Pain is generally present only within the **first two days**.
- **There is a suggestion that patients who do not experience a prodrome develop lesions from extraneural latent HSV within the epithelium and these lesions are less responive to topical therapy.**

Recrudescent intraoral HSV (RIH) in the immunocompetent host

- Occurs chiefly on the **keratinized mucosa** of the hard palatal mucosa, attached gingiva, and dorsum of the Tongue
- They present as **1–5 mm** single or clustered painful ulcers with a bright erythematous border .
- One common presentation is the complaint of pain in the gingiva **one to two days** after a scaling and prophylaxis or other dental treatment.
- Lesions appear as **1–5 mm** painful vesicles but more often ulcers on the marginal gingiva.

HSV in Immunocompromised Patients

- In immunocompromised patients (such as those undergoing chemotherapy, who have undergone organ transplantation, or who have acquired immune deficiency syndrome [AIDS]),
- May occur at any site intraorally and may form ulcers that may be **several centimeters in size** and may **last several weeks or months** if undiagnosed and untreated
- SingleRecurrent intraoral herpes (RIH) ulcers are clinically indistinguishable from recurrent aphthous ulcers if they occur on a nonkeratinized site.
- These ulcers are painful and similar to those seen in immunocompetent patients **except** that they may be **larger** and often occur on **non-keratinized** sites.
- They appear slightly depressed with raised borders.
- The presence of 1–2 mm vesicles or satellite ulcers at the edges of the main ulcer is a helpful sign.

If undiagnosed and left untreated, RIH infection may disseminate to other sites and cause severe infections in the immunocompromised population.

This is a particular problem in patients undergoing **hematopoietic stem cell transplantation**, where reactivation of HSV occurs in approximately 70% of patients.

Laboratory Diagnosis

HSV isolation by cell culture is the gold standard test for the diagnosis since it **grows readily in tissue culture**.
A **single swab** of the oral ulcers is performed.
More recently, **polymerase chain reaction (PCR)** from **swabs** has been shown to detect HSV antigen **3 to 4 times** more often than culture **real-time PCR** has also been shown to be highly sensitive and specific.

- Primary HSV infection is associated with elevated immunoglobulin **(Ig)M** titers that occur **within days**, followed several weeks later by permanent **IgG** titers, that indicate previous infection but confer no protection against reactivation.

- **Recurrent infection** is associated with a rise in **IgG antibody titer** in acute and convalescent sera, but a four-fold rise (a criterion that indicates active infection) is seen in only 5% of patients.

- The assay for HSV IgM is not particularly reliable for diagnostic purposes, and overall, the use of serology alone to diagnose recurrent infection is not advised.

HSV lesions **are not generally biopsied** because the clinical appearance and history are characteristic, and infection is readily confirmed with a culture or cytology specimen when necessary.

Management

Primary HSV Infection

Management is directed toward

1. Pain control,
2. Supportive care,
3. Definitive treatment.

In the past, healthy patients with primary herpetic gingivostomatitis were treated only with hydration and supportive measures.

However, since the **acyclovir family** of drugs is inexpensive, safe, and readily available, it is appropriate to treat even primary infections definitively because it **reduces viral shedding and infectivity.**

- Acyclovir **inhibits viral replication** and is activated by virally produced **thymidine kinase**.

As such, it has little activity against non-virally infected cells.

The use of acyclovir at **15 mg/kg five times a day in children** reduces the duration of fever, reduces HSV shedding, stops the progress of lesions, improves oral intake, and reduces the incidence of hospital admissions.

- **Valacyclovir, a prodrug of acyclovir, has 3 to 5 times the bioavailability of acyclovir and, together with famciclovir, is now widely used.**

Recrudescent HSV

Recurrent herpes labialis can often be suppressed by reducing tissue damage, such as using sunscreen.

Although RHL is self-limiting, the use of topical antiviral medications reduces shedding, infectivity, pain, and the size and duration of lesions.

Topical antiviral medications such as **5% acyclovir cream**, **1% penciclovir** cream, and **10% docosanol** cream are efficacious if applied **5 to 8 times a day at the first prodrome or sign of a lesion.**

Systemic therapy with valacyclovir (2 g every 12 hours for one day) or famciclovir (1500 mg single dose) are both effective in treating active lesions of RHL

For intraoral lesions, treatment is with 500–1000 mg valacyclovir three times a day or 400–800 mg of acyclovir for 7–10 days.

Suppression of HSV infection in patients who develop **Frequent Episodes, Large Lesions, Or Erythema Multiforme** is effected with variable doses of acyclovir, valacyclovir, and famciclovir.

Similar **suppressive regimens** can be used for patients susceptible to recrudescent HSV **after dental procedures**.

HSV in Immunocompromised Patients

- HSV infections should be treated with systemic antivirals to prevent dissemination to other sites (e.g., HSV esophagitis) or systemically.
- The primary pathogen for herpes encephalitis&herpes pneumonitis is HSV-1.
- For patients undergoing hematopoietic cell transplantation, antiviral therapy such as acyclovir or valacyclovir at suppressive doses should be initiated for all patients who are HSV seropositive (acyclovir 400 mg three times a day or 500 mg valacyclovir twice a day).
- Acyclovir-resistant HSV is most frequently seen in this group of patients, where the virally derived thymidine kinase that activates acyclovir **is mutated**.
- In such cases, foscarnet or cidofovir is effective.

- **The dosage of the acyclovir family should be adjusted for Age and Renal Health**.

- A number of vaccines and new therapies against HSV are currently under development.

2. Varicella-Zoster Virus Infection

Etiology and Pathogenesis

- Primary infection with varicella zoster virus (VZV), an α-herpesvirus, leads to varicella **(chicken pox).**
- The virus then becomes latent, usually in the **dorsal root ganglia or ganglia of the cranial nerves.**
- **Reactivation** produces herpes zoster infection (HZI), commonly called **shingles.**
- The incidence of HZI **increases with age** and the degree of **immunosuppression**. this increases to **10 per 1000** in those older than the age of 75 years.
- **Therefore, it is not uncommon to see HZI**
- **in the elderly**,
- **in patients undergoing cancer chemotherapy**,
- **in patients on chronic immunosuppressive drug therapy and in patients with AIDS**.

As with HSV, this virus is cytopathic to the epithelial cells of the skin and mucosa, causing blisters and ulcers.

Transmission is usually by the respiratory route, with an incubation period of **2 to 3 weeks.**

Post herpetic neuralgia, **a morbid sequela of HZI, is a neuropathy resulting from peripheral and central nervous system injury.**

Clinical Findings

- ✔ **Primary VZV infection** generally occurs in the **first two decades of life**.
- ✔ The disease begins with a low-grade fever, malaise, and the development of an intensely pruritic, maculopapular rash, followed by vesicles that have been described as "**dewdrop-like."**
- ✔ These vesicles turn cloudy and pustular, burst, and scab, with the crusts falling off after one to two weeks.
- ✔ Lesions begin on the trunk and face and spread centrifugally.
- ✔ Central nervous system involvement may result in cerebellar ataxia and encephalitis.
- ✔ Other complications of varicella include **pneumonia**, **myocarditis**, and **hepatitis**.

- Immunocompromised hosts usually experience more severe disease with more blisters, a prolonged course, and, not infrequently, involvement of the lungs, central nervous system, and liver; **there is a significantly higher mortality rate.**
- Secondary bacterial infection by gram-positive cocci may have severe septic consequences.

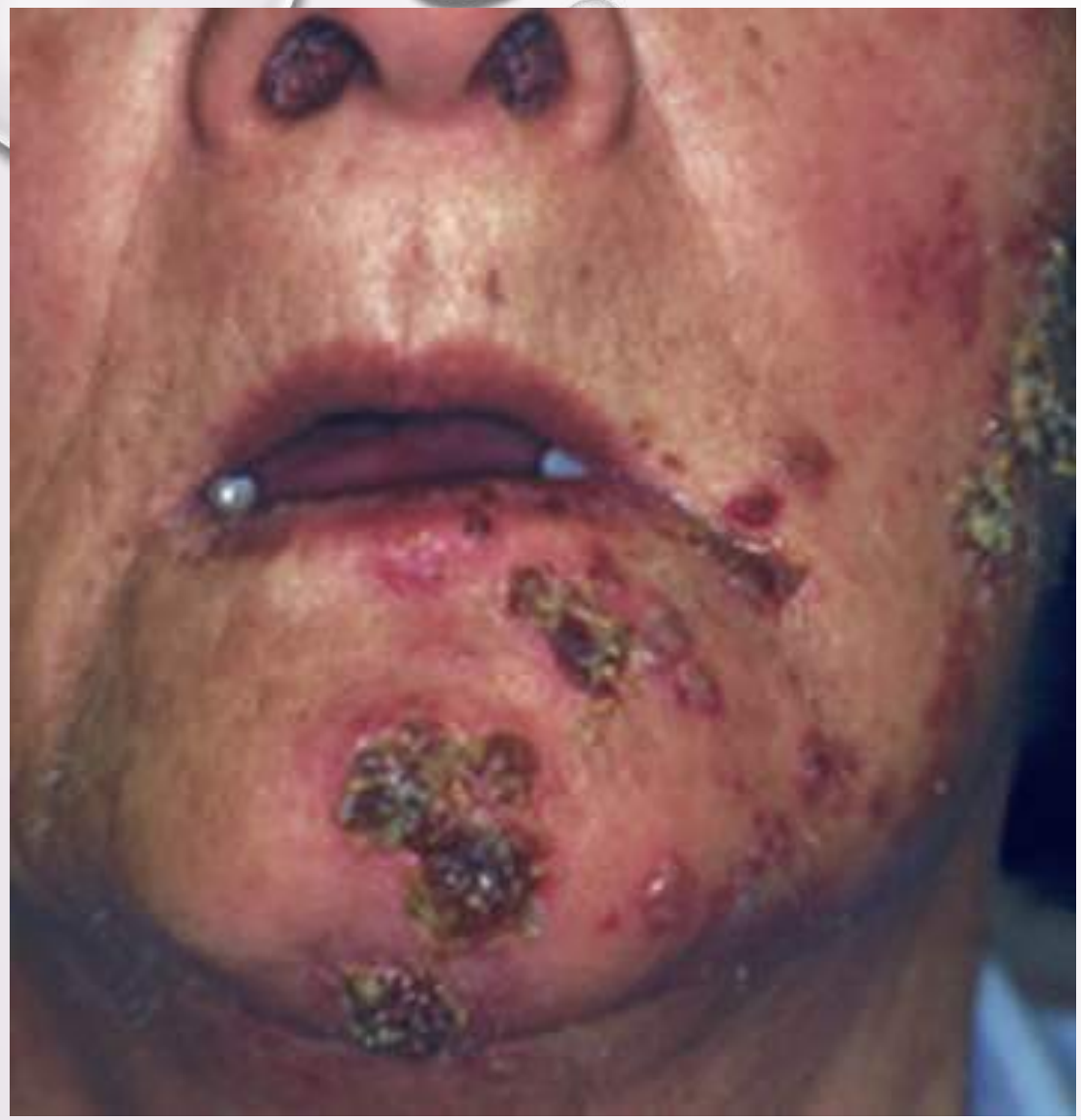
HZI of the skin (shingles) occurs in adults and starts with a prodrome of deep, aching, or burning pain. There is usually little to no fever or lymphadenopathy. This is followed within **2 to 4 days** by the appearance of **crops of vesicles** in a dermatomal or “zosteriform” pattern. This pattern describes the unilateral, linear, and clustered distribution of the vesicles, ulcers, and scabs in a dermatome supplied by one nerve.

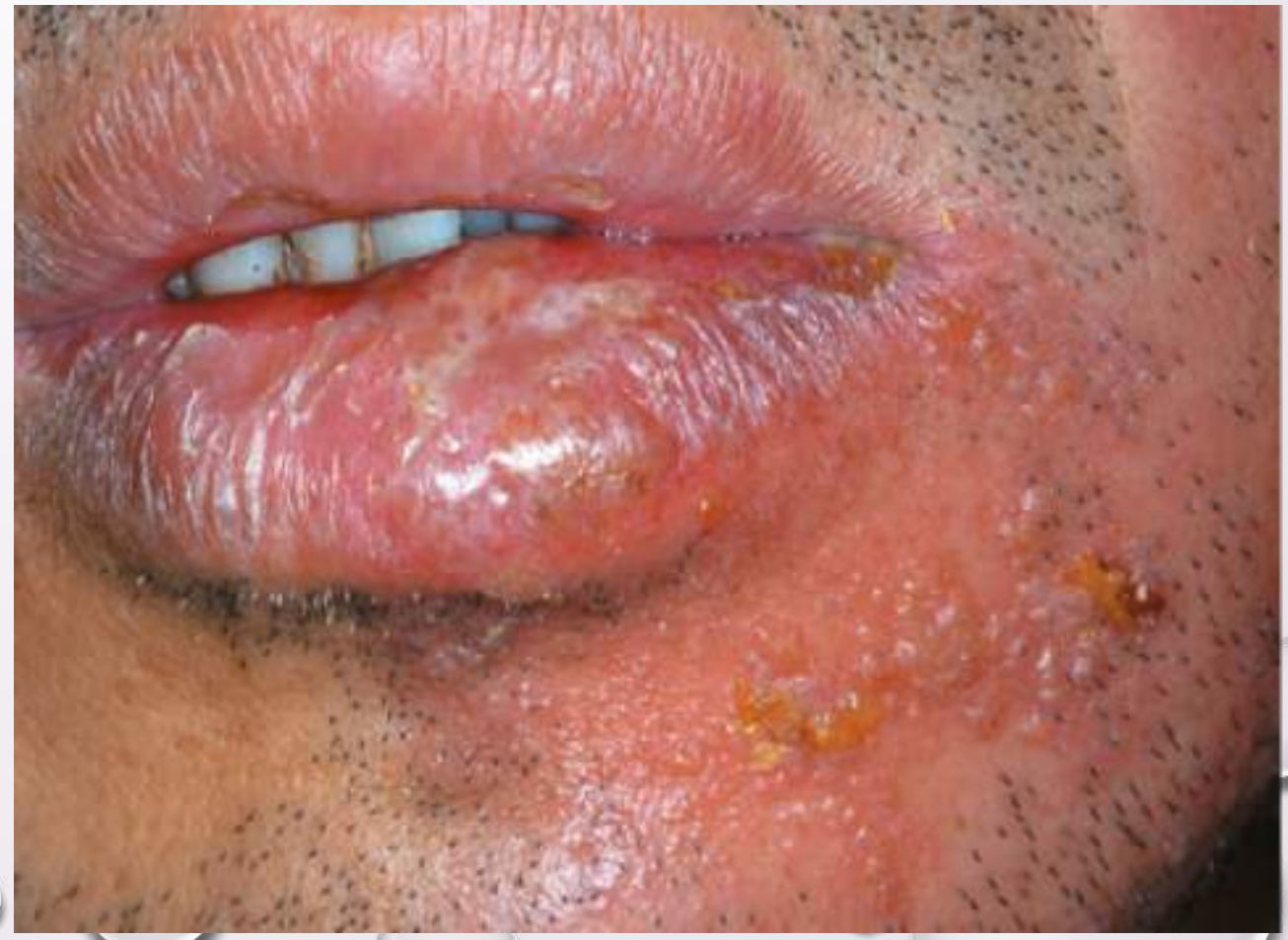
Thoracic/lumbar dermatomes are the most frequently involved, **followed by the craniofacial area.**

Lesions heal within **2 to 4 weeks,** often with **scarring and hypopigmentation**. Occasionally, HZI may occur without the appearance of dermatomal lesions (zoster sine eruptione or zoster sine herpete), which makes the diagnosis of this condition challenging; these patients often present with facial palsy.

- VZV has been detected in up to 20% of patients with Bell palsy.
- A serious and occasional side effect of HZI is **acute retinal necrosis**.

- One of the most important complications of HZI is **postherpetic neuralgia**, defined as pain that remains for 120 days after the onset of the acute rash





- patients older than age 50, up to 70% developed postherpetic neuralgia and up to 50% have debilitating pain, usually of a sharp, stabbing, burning or gnawing nature lasting more than one month.

- Some unfortunate patients experience pain for **years**.

- Predisposing factors include older age, prodromal pain, and more severe clinical disease during the acute rash phase.

- **Immunocompromised patients** often experience more severe VZI that may appear atypical, be bilateral, and involve multiple dermatomes; retinitis, pneumonitis, and encephalitis have been reported as complications in this patient population.

- **On rare occasions, HZI may involve not just the dorsal root ganglion but also the anterior horn cells, leading to paralysis.**

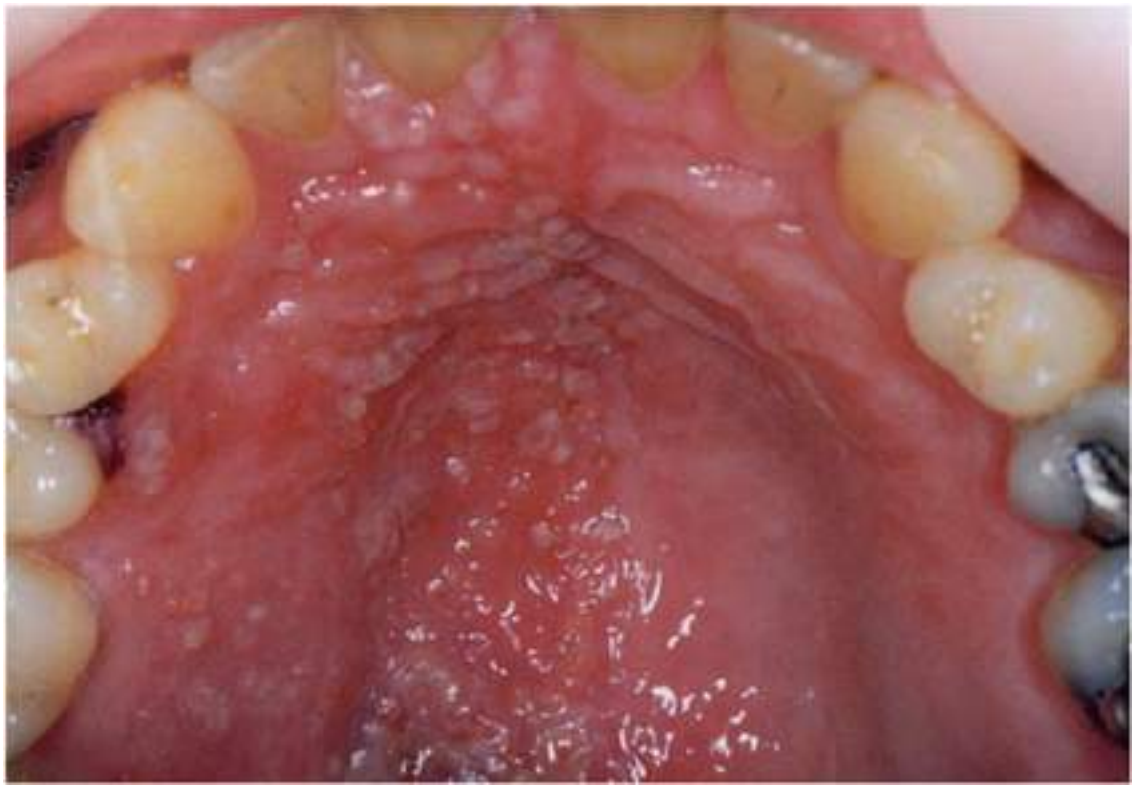
Oral Manifestations

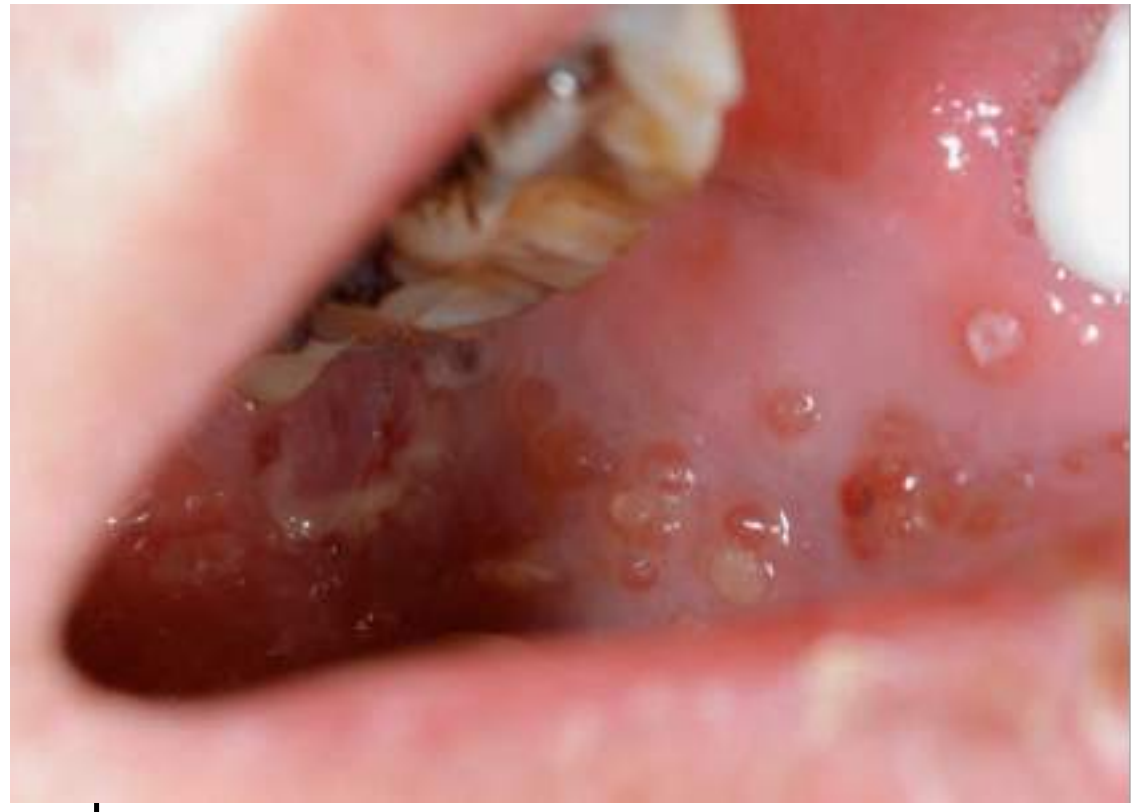
- Primary VZV infection presents as acute-onset ulcerations in the mouth that often pale
- In recurrent VZV infection, the ophthalmic division of the trigeminal (V) nerve is the cranial nerve **most often affected** (herpes zoster ophthalmicus);
- Corneal involvement may lead to blindness.
- Involvement of this nerve (V) leads to lesions on the upper eyelid, forehead, and scalp with V1; midface and upper lip with V2; and lower face and lower lip with V3 . With the involvement of V2, patients experience a prodrome of pain, burning, and tenderness, usually on the palate on one side.

- This is followed **several days later** by the appearance of painful, clustered 1–5 mm ulcers (rarely vesicles, which break down quickly) on the hard palatal mucosa or even buccal gingiva, in a distinctive unilateral distribution.

- These ulcers heal within **10–14 days**, and post herpeticneuralgia **in the oral cavity is uncommon.** Involvement of V results in blisters and ulcers on the mandibular gingiva and tongue.

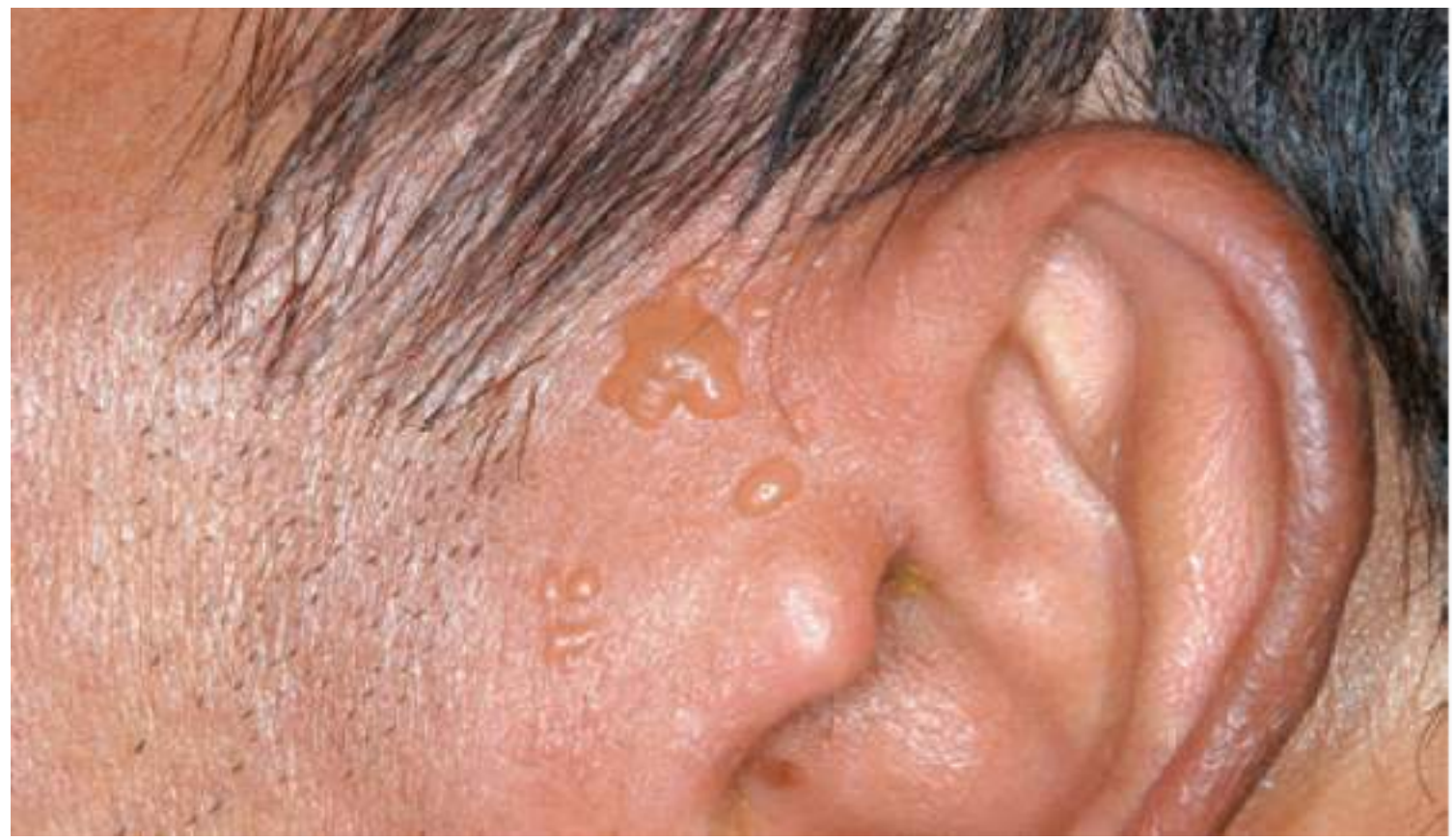
- An uncommon complication of HZI involving the geniculate ganglion:
- is Ramsay Hunt syndrome. Patients develop Bell palsy, vesicles of the external ear, and loss of taste sensation in the anterior two-thirds of the tongue
- HZI has been reported to cause **resorption** and **exfoliation of teeth** and **osteonecrosis of the jawbones**, especially in patients with **HIV disease**





Palatal lesions of herpes zoster involving the second division of the trigeminal nerve.

Ramsay Hunt syndrome



Laboratory Findings

As with HSV infection, an oral swab for viral isolation using cell culture is still the best way to confirm a diagnosis of VZV infection, although VZV is more difficult to culture, but this does not distinguish between HSV and VZV.

Direct fluorescent antibody testing using a smear has greater sensitivity. This test uses a **smear** obtained by scraping the lesion and staining it with antibody against VZV conjugated to a fluorescent compound.

The use of PCR and real-time PCR to detect viral antigen is expensive and highly sensitive, but the presence of VZV antigen does not always equate with active infection.

In HZI, there is inflammation of peripheral nerves leading to demyelination and **wallerian degeneration**, as well as degeneration of the dorsal horn cells of the spinal cord.

Management

Management of oral lesions of varicella and HZI is directed toward

- pain control (particularly, the prevention of postherpetic neuralgia),
- supportive care,
- hydration
- definitive treatment to minimize the risk for dissemination, particularly in immunocompromised patients.

➤ **Aspirin use**, especially in children with VZV infection or influenza, may be associated with the development of **Reye syndrome**, which is potentially fatal, and is contraindicated; characterized by fatty degeneration of the liver and encephalopathy.

➤ **ibuprofen is the preferred analgesic**.

Treatment of primary VZV infection includes the use of :

- Acyclovir (800 mg five times a day).
- This reduces infectivity, severity of lesions, and hospitalization for complications. However, acyclovir has poor bioavailability.
- Valacyclovir (1000 mg 3 times a day)

or Famciclovir (500 mg) 3 times a day) **for 7 days** is effective in treating HZI and should be started **within 72 hours of disease onset**.

- These drugs also reduce the incidence of postherpetic neuralgia compared with acyclovir.

The first line of treatment for postherpetic neuralgia is

- Gabapentin,
- 5% lidocaine patch,
- and 0.025%–0.8% topical capsaicin,

The second line of treatment is with tricyclic antidepressants and corticosteroids

- The use of **corticosteroids and antiviral** therapy together in an attempt to reduce post herpetic neuralgia has not proved effective, although early treatment with **famciclovir or valacyclovir** may prevent it.

Other modalities of treatment in Case reports suggest that

- Botulinum toxin may provide relief.
- Attenuated vaccine for the prevention of VZV infection has been shown to reduce the incidence of varicella outbreaks. But because it establishes **latency** may be associated with increased zoster incidence

Vaccination of older adults using:

- ZostavaxTM (live, attenuated virus),
- or ShingrixTM (recombinant VZV antigen) reduces incidence of HZI significantly and the latter, post-herpetic neuralgia.

The use of recombinant virus in a vaccine is more appropriate for use in **immunocompromised hosts**.

Recombinant virus : When viruses of **two different parent strains** coinfect the same host cell and interact during replication to generate virus **progeny** that have some genes from both parents.

3. CYTOMEGALOVIRUS INFECTION

Etiology and Pathogenesis

- **Transmission** is by direct transfer of infected white blood cells through intimate contact and through blood products. **In organ transplant recipients, CMV in the donor organ leads to CMV infection in the recipient**.
  - ❖**Risk for exposure** increases with age, low socio-economic status, and crowded living conditions.
  - ❖**Primary infection** may be asymptomatic **or** cause an infectious mononucleosis–like disease.
  - ❖Manifestations of infection and disease are most evident in the **immunocompromised** population.
  - ❖It is the most common cause of **pneumonia** within the first 120 days after hematopoietic stem cell transplantation.
  - ❖Once exposed to CMV, this virus establishes latency within the **connective tissue cells, such as the endothelium of blood vessels, mononuclear cells, and white blood cells.**
  - ❖CMV within endothelial cells may contribute to vascular inflammation, vascular occlusion, and end-organ damage.
  - ❖50–100% of the adult population has been exposed world-wide.

Clinical Findings

Primary CMV infection presents similarly to other viral infections with fever, malaise, and leucopenia and organ-specific findings such as gastroenteritis (most common), pneumonitis, retinitis and hepatitis, and even thromboembolism.

•Presents similarly to infectious mononucleosis with marked lymphocytosis;

▪**Unlike** the more common EBV-associated infectious mononucleosis, there is fever but little lymphadenopathy or splenomegaly.

▪**Serious complications include** meningoencephalitis, myocarditis, and thrombocytopenia.

•Approximately **90%** of patients with AIDS have circulating antibodies against CMV.

➤In these patients, CMV tends to involve the eye (CMV retinitis that may result in blindness if untreated), gastrointestinal tract (CMV enteritis), and mucocutaneous sites, especially perianal and perigenital areas.

•There is growing evidence that CMV infection is associated with Guillain-Barré syndrome especially after renal transplantation (immune system damage the nerves causes muscle weakness and sometimes paralysis).

Oral Manifestations

➤CMV infection in the mouth in the immunocompromised patient tends to present as **a single large ulcer** and **less** often as **multiple ulcers**

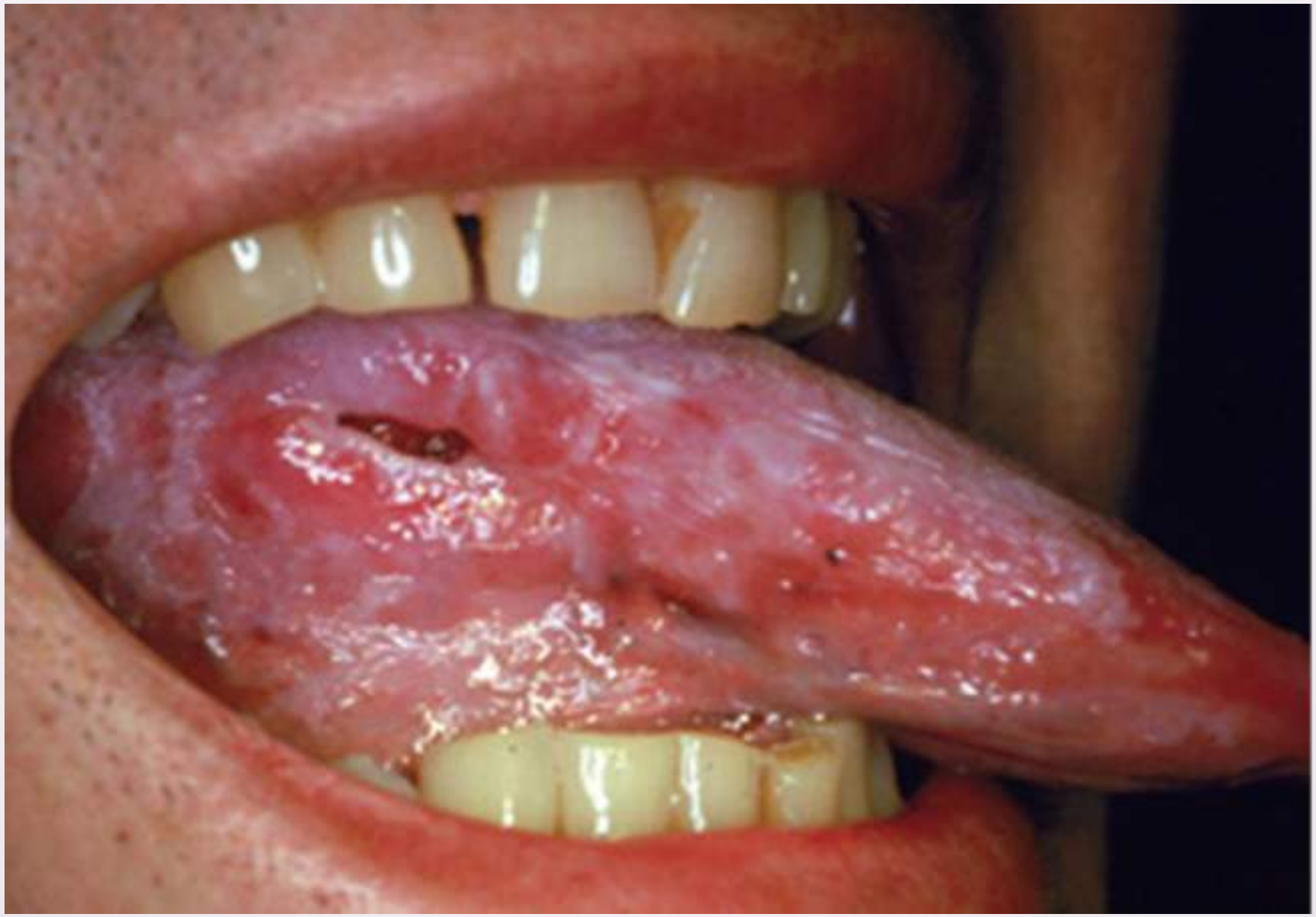
➤They are usually painful and may have been present for weeks or months.

➤Any site may be involved.

➤ **Up to one-third** of such ulcers are coinfected with other viruses of the herpes family, especially HSV and VZV.

➤There have been **occasional reports** of mandibular osteomyelitis and tooth exfoliation associated with CMV and VZV infection.

➤Both viruses are associated with **vasculopathy and thrombosis**, which may be the underlying **etiopathogenesis.**



Cytomegalovirus ulcer on a background of hairy leukoplakia in a patient with AIDS

Management

- Pain is managed with **topical anesthetics** and **systemic analgesics** as needed, with appropriate **dietary modifications and good hydration**.
- CMV infection is treated with **ganciclovir 5 mg/kg - IV twice daily, valganciclovir** (a valine ester and oral prodrug of ganciclovir with approximately 10-fold bioavailability of ganciclovir) 900 mg twice daily.
- **A CMV vaccine is currently under development stage, with expectation that it will be available in the next 5 to 10 years**

4. Coxsackievirus Infection

- Coxsackie (CV), RNA virus, has several sero-types including enterovirus A, B, C, or D; CV A and B virus, are the most.
- More than **90% of infections** caused by the **nonpolio enteroviruses** are either asymptomatic or result in nonspecific febrile illness.
- The viruses replicate extensively in the lower gastrointestinal tract, and less so in the oropharynx, from where they shed.

➤**Transmission** is therefore primarily by the **fecal-oral route**, although some shedding occurs **in the upper respiratory tract**.

➤**Enterovirus infection is implicated in aseptic meningitis, acute encephalitis, acute paralysis, ocular infections, pleurodynia, myopericarditis, and respiratory illness.**

➤**Enteroviruses in particular B1, has been implicated in the pathogenesis of type 1 insulin-dependent diabetes mellitus.**

Coxsackievirus infections In the oral cavity leads to three disease entities:

1.Hand, Foot and Mouth disease (HFM disease),

2.Herpangina

3. Lymphonodular pharyngitis.

HFM disease:-

- As with many CV infections, including herpangina, tends to be **seasonal** (usually summer), occurs in epidemic clusters, and has high transmission rates.
- Atypical HFM disease exhibits widespread oral and skin involvement and onychomadesis (separation of the nail plate from the nail bed) and is caused by **CVA6**.

Clinical Findings

- **Children younger than 10 years** are usually afflicted, and outbreaks usually occur in epidemics in summer.
- Patients develop fever, headache, and myalgia that usually last only 1 to 3 days.
- Patients have a low-grade fever, emesis, and sore mouth; 75 to 100% of patients have a skin rash, especially on the **hands and feet (dorsa, palms, and soles) and 30% on the buttocks.**

Oral Manifestations

- Patients are febrile and complain of a sore mouth and throat.
- Lesions begin as erythematous macules that become vesicles and quickly break down to ulcers.
- Lesions are usually located on the tongue, hard and soft palate, and buccal mucosa but can present on any oral mucosal surface.

Herpangina;- The word herpangina derives from herpes, meaning —vesicular eruption, and angina, meaning —inflammation of the throat. CVA (serotypes 1–10, 16, and 22) are the most common viruses isolated from this disease.

Oral Manifestations

- The first oral symptoms of herpangina are **sore mouth and throat** and **pain on swallowing**.
- There may be erythema of the oropharynx, soft palate, and tonsillar pillars. Lesions are usually located on the tongue, hard and soft palate, and buccal mucosa but can present on any oral mucosal surface
- Small vesicles form, but these rapidly break down to 2–4 mm ulcers and these persist for 5 -10 days.
- **Lymphonodular pharyngitis;-** is considered a variant of herpangina and is associated with **CVA- serotype10**. Patients report a **sore throat**, but rather than presenting with vesicles that break down to ulcers, patients develop **diffuse small nodules in the oropharynx (likely lymphoid hyperplasia) in the oropharynx.**

Laboratory Tests

- Diagnosis is usually made on clinical findings, and culture and biopsies are rarely necessary for diagnosis.
- CV infections may be diagnosed by culture (usually from the throat or stools), but real-time PCR is now employed for typing.

Management

- **CV** infections are self-limiting, Unless complications arises or the patient is immunocompromised, and the management is directed toward:
- Control of fever and mouth pain, supportive care, and limiting contact with others to prevent spread of the infection.

- **Effective antiviral agents for CV are not available, but vaccines are under development** .

5. Necrotizing Ulcerative Gingivitis & Periodontitis

- Previously known as acute necrotizing ulcerative gingivitis and its more severe counterpart, NUP, were reclassified in 2017 by the American Academy of Periodontics under the category of —**Necrotizing Periodontal Disease**.
  - Acute ulcerative-inflammatory conditions of the gingiva and periodontium; that are associated with polymicrobial infection.
  - It was called —trench mouthǁ since it was frequent among the soldiers in the trenches.
  - **Both with strong associations** with immune suppression (especially AIDS), debilitation, smoking, stress, poor oral hygiene, local trauma & contaminated food supply.
  - **Diabetes** may also be a risk factor.
  - It is unclear if NUG is an indication of NUP, but they are often seen in patients with AIDS.
  - Both NUP and Noma thrive in communities characterized by a large low-socioeconomic class and extreme poverty.

Etiology and Pathogenesis

- **Treponema species,** Prevotella intermedia, **Fusobacterium** nucleatum, are the most common.

❑ Gingiva and adjacent tissues is most probably involved.

❑Patients show reduced **neutrophil chemotaxis and phagocytosis**, resulting in **poor control of infection.**

❑Some have identified herpesviruses within the crevicular fluid, but such viruses shed readily in oral secretions, particularly in areas where there is tissue destruction.

❑If there is underlying systemic illness, NUG and NUP can spread rapidly from the gingiva to the periodontium and into the soft tissues, giving rise to **cancrum oris, noma, or orofacial gangrene.**

❑This is particularly in children who are malnourished and live in poverty and is seen frequently in Africa.

- **Fusobacterium necrophorum** is likely to play an important role in the progression of NUP to cancrum oris because this organism produces a **dermonecrotic toxin**, **hemolysin**, **leukotoxin**, and **proteolytic enzymes**, all leading to extensive tissue destruction. It may also **stimulate** the growth of Prevotella Intermedia.

Clinical Findings

•NUG and NUP may or may not be associated with fever and malaise, although submandibular lymphadenopathy is usually present.

▪**Noma** generally is accompanied by **fluctuating fever, marked anemia, high white cell count, general debilitation, and a recent history of some other systemic illness, such as measles**

Oral Manifestations

❑NUG has a rapid and acute onset.

❑The first symptoms include **excessive salivation**, **a metallic taste**, and **sensitivity of the gingiva**.

❑This rapidly develops into extremely painful and erythematous gingiva with scattered **punched-out ulcerations**, usually on the interdental papillae, although any part are of the marginal gingiva may be affected .

❑There is accompanying **malodor**, and there may be gingival **bleeding**.

➤Because of the **pain** associated with the gingivitis, there is usually abundant buildup of dental **plaque** around the teeth because it may be too painful to perform **effective oral hygiene**.

➤**Risk factors// immunocompromised** and **neutropenic** are prone to developing such lesions.

➤In patients with **AIDS**, the prevalence of NUP is approximately **6%** and is strongly predictive of a **CD4 count less than 200 cell/mm**, leading to **osteonecrosis or necrosis** of the soft tissues

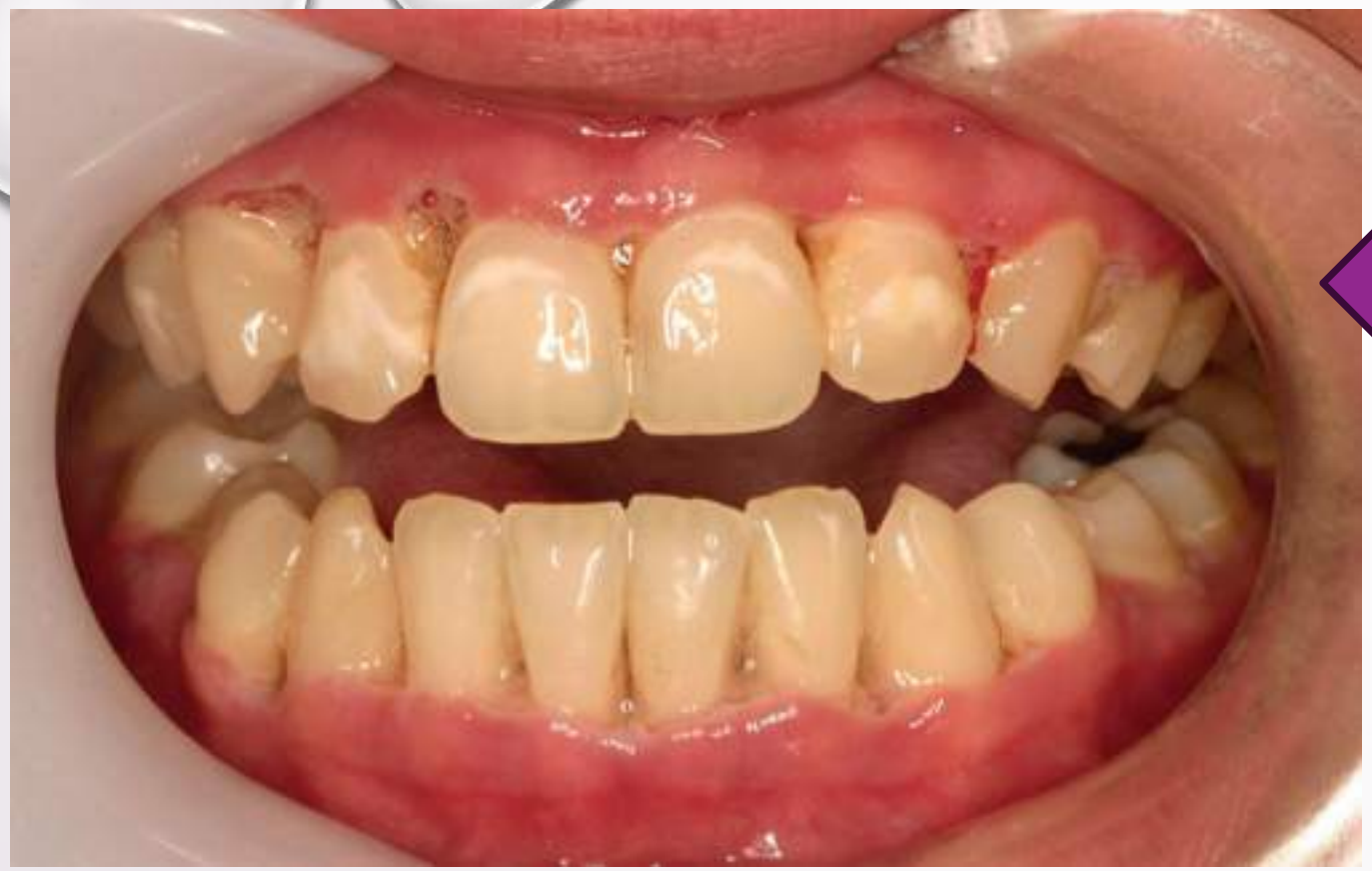
➤In patients who have **severe immunodeficiency or are malnourished**, NUG and NUP may **progress** to **Noma.** The overlying skin becomes discolored, and perforation of the skin follows.

➤The **orofacial lesions cone shaped**, with the base of the cone within the oral cavity and the tip at the skin aspect.

➤There is sloughing of the oral mucosa followed by sequestration of the exposed, necrotic bone and teeth.

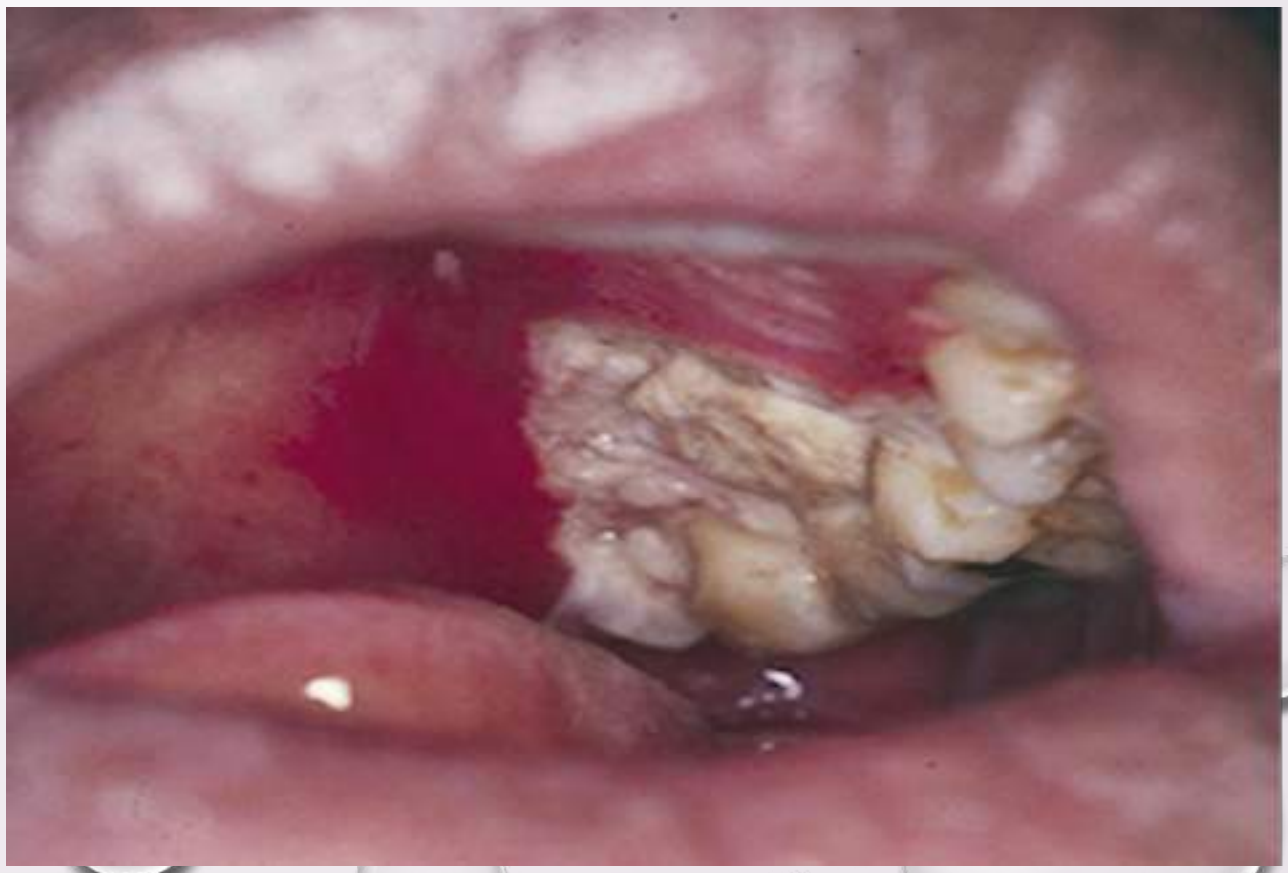
➤Without treatment, the **mortality rate is 70 –90%.**

➤**Laboratory Testing:** Secretions from the **gingival sulcus** grow mixed flora but it will be positive by culture or PCR for Treponema species, Prevotella intermedia, Fusobacterium nucleatum, and other bacteria.



Necrotizing ulcerative gingivitis with typical punched out, necrotic and ulcerated interdental papillae.

Necrotizing ulcerative periodontitis with osteonecrosis in a patient with AIDS.



Management

- **Gentle debridement** to remove as much of the **debris and plaque** as possible; this is best accomplished with **topical anesthesia** during the first few visits.
- The use of **chlorhexidin**e mouthrinse led to resolution in **>90%** of cases.
- Patients with more extensive disease and/or systemic symptoms may require **antibiotics active against gram-negative anaerobes**, such as β-lactams; such as penicillin derivatives, cephalosporins. **Interestingly, metronidazole**, which has little activity against spirochetes, also is effective.
- Once the **acutely painful episodes** have resolved, **scaling and root planing** to completely remove all residual plaque and calculus are indicated.
- **Periodontal surgery** may be necessary to correct gingival and periodontal defects.
- It may be appropriate to test the patient for **HIV** or other immunosuppressive conditions, such as blood dyscrasia.
- **Cases of Noma** need aggressive treatment with nutritional supplementation, antibiotics, and tissue debridement.

6. Erythema Multiforme(EM)

- Is an acute, self-limited, inflammatory mucocutaneous disease that manifests on the **skin and often oral mucosa**, although other mucosal surfaces, such as **the genitalia**, may also be involved.
- It represents a **hypersensitivity reaction** to infectious agents or medications.
- EM is classified as **EM minor** if there **is less than 10%** of skin involvement and there is **minimal to no mucous membrane** involvement.
- ✔ whereas **EM major** has **more extensive** but still characteristic skin involvement, with the oral mucosa and other mucous membranes affected.
- ✔However, there is likely a subset of EM that affects the **oral mucosa only without skin involvemen**t. Historically, fulminant forms EM were labeled Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN [Lyell disease]).

Etiology and Pathogenesis

➤EM is a hypersensitivity reaction, and the most common inciting factors are infection, particularly with **HSV**.

➤**Drug reactions** to **NSAIDS, anticonvulsants**, or other drugs play a smaller role.

➤Cases of oral EM **precipitated by benzoic acid**, **a food preservative, have been reported.**

➤Studies show that recurrent EM is associated with **HSV infection** in 65–70% of cases, both by history of HSV infection **1-3 weeks before** onset of EM,

➤Using PCR techniques, HSV gene products have been identified in 71–81% of cases of recurrent EM. For non-recurrent EM, this falls to 27%.

➤**Cytotoxic T cells, natural killer cells, and/or cytokines destroy the epithelial cells**.

➤More recently, it has been suggested that CD34+ cells, Langerhans cell precursors, carry fragments of HSV DNA to the skin where it incites EM.

Clinical Findings

- EM affects ages 20 and 40 years, with 20% occurring in children.
- Patients with **recurrent EM** have an average of **six episodes a year** (range 2–24), with a mean duration of 9.5 years; remission occurred in 20% of cases.
- Episodes usually last **several weeks**.
- There may be a **prodrome** of fever, malaise, headache, sore throat, rhinorrhea, and cough.
- These symptoms suggest **a viral** (especially respiratory tract) infection, and this is not surprising since infectious agents are known to trigger EM.
- Skin lesions appear rapidly over a **few days** and begin **as red macules that become papular, starting primarily in the hands and moving centripetally toward the trunk in a symmetric distribution.**
- The most common sites of involvement are the **upper extremities, face, & neck.**
- The skin lesions may take several forms—hence the term multiforme.
- The classic skin lesion consists called typical —targe or —iris lesion that is pathognomonic of EM; variants are called —atypical target lesions.
- The skin may feel **itchy and burnt.**
- **Post inflammatory hyperpigmentation** is common in dark-skinned individuals and may be **worsened by sun exposure**

Oral Findings

❖The oral findings in EM range from **mild erythema and erosion to large painful ulcerations,**

❖**Severe, large ulcers,** causing difficulty in eating, drinking, and swallowing,

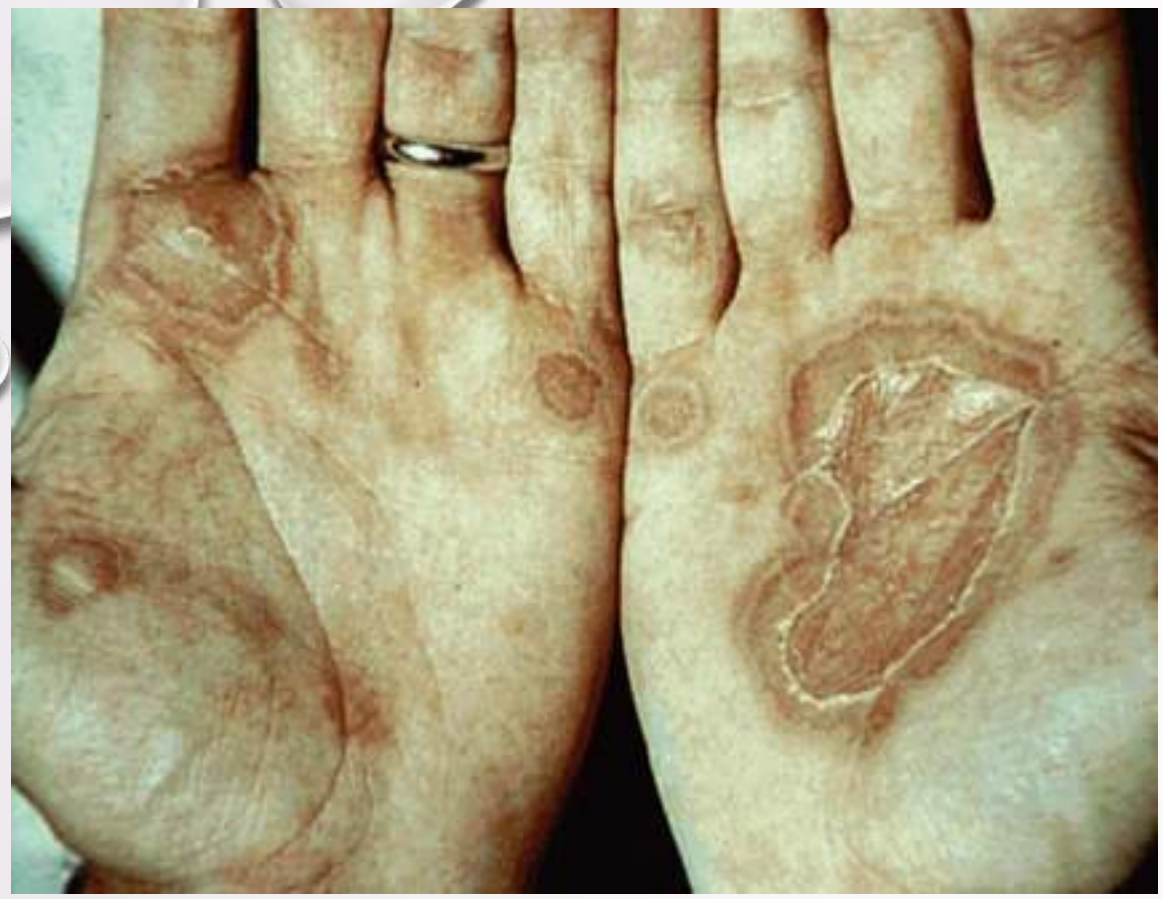
❖Patients with severe EM **may drool blood-tinged saliva.**

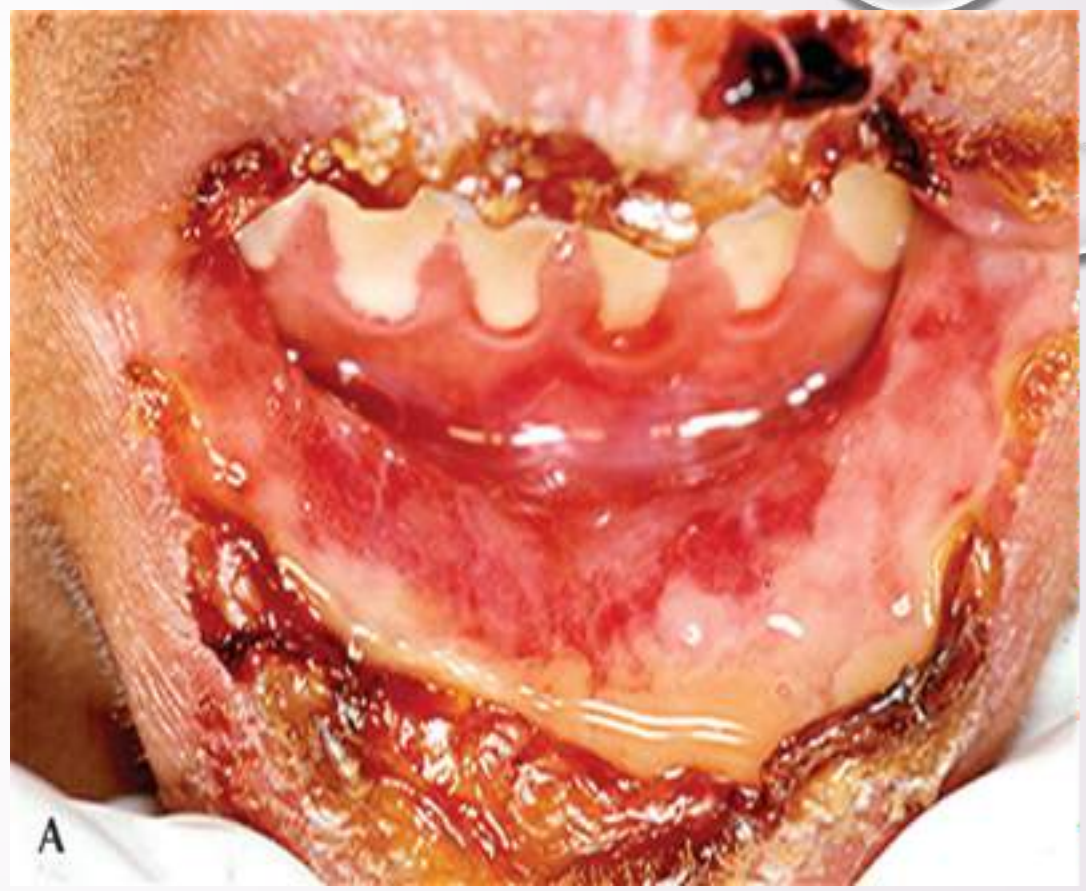
❖ **Extensive lip** involvement with inflammation, ulceration, and crusting is common.

❖Oral lesions are present in 23–70% of patients with recurrent EM.

❖The most affected sites are the **lips** (36%), **buccal mucosa** (31%), **tongue** (22%), and **labial mucosa** (19%), **Genital** 25% and **ocular** sites are 17%.

❖**Crusting and bleeding** of the lips are common, but not always present

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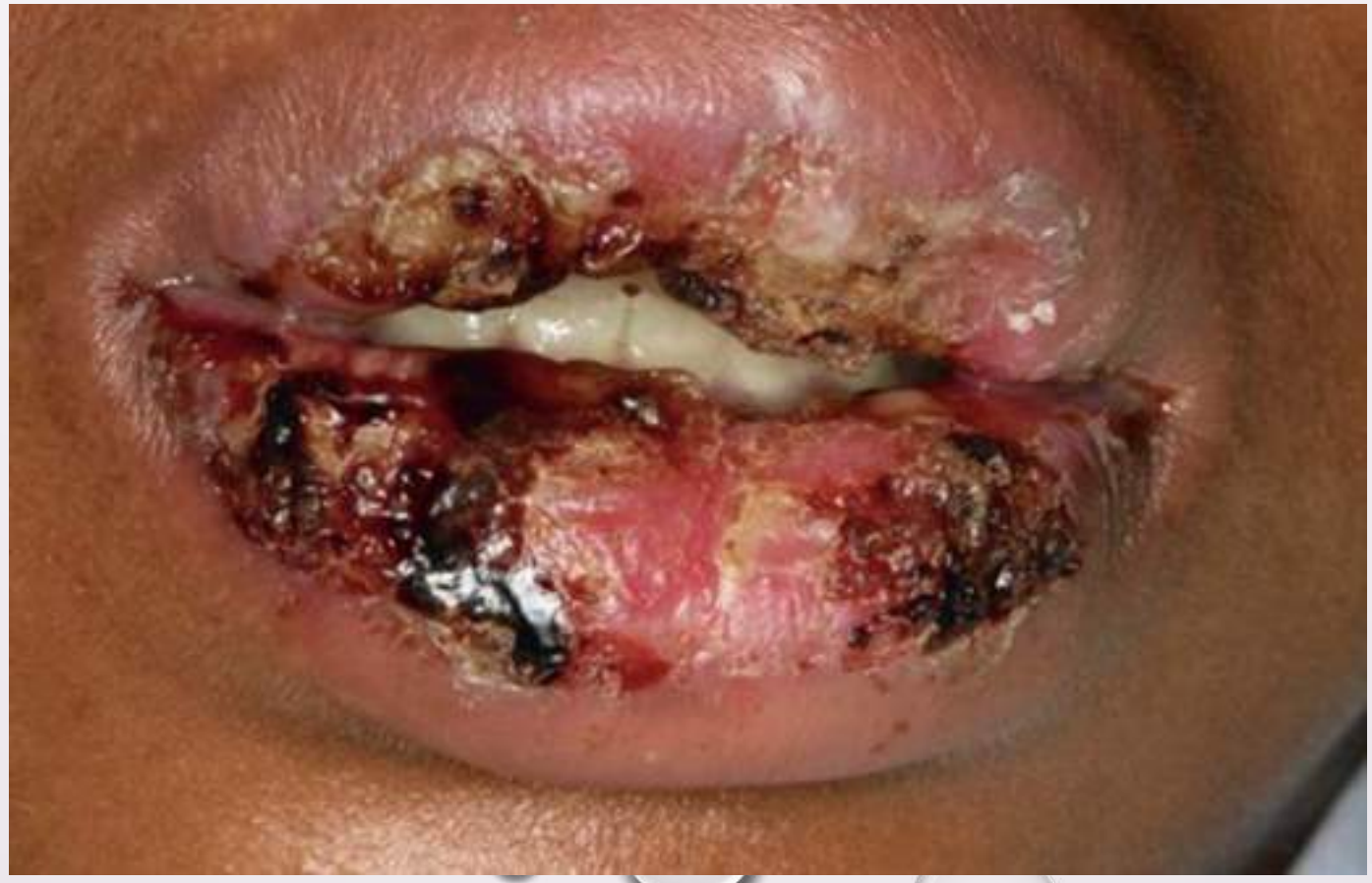


Management

✔Mild oral EM can be managed with systemic or topical analgesics **for pain** and supportive care since the disease is self-limiting and resolves within a few weeks.

✔ More severe cases are usually managed with systemic corticosteroids

✔**Topical steroids** may also help resolve lesions.

✔Cases suspected of having **HSV-associated EM** should be treated with **antiviral medications.**

✔Treatment with acyclovir at the first sign of disease in recurrent EM controls disease in approximately **half of patients.**

✔Other treatment modalities include **dapsone, hydroxychloroquin, mycophenolate mofetil, azathioprine, colchicines, methotrexate, and intravenous immunoglobulin.**

✔Continuous acyclovir at 400 mg twice a day prevents development of EM in most patients with HSV-associated disease, whereas EM not related to HSV responded well to azathioprine (100–150 mg/d).

✔Other studies have also shown good suppression of recurrent HSV-associated EM using **500 mg of valacyclovir twice a day** or 250 mg of famciclovir twice daily.

✔**Dapsone** (100–150 mg/d) and antimalarials are partially successful in suppressing recurrent outbreaks

7. Stevens-Johnson Syndrome & Toxic Epidermal Necrolysis

- Both are rare **severe necrolytic mucocutaneous** disorders resulting from **hypersensitivity to medications** and are clinically and etiopathogenetically distinct from EM.
- Although all three are hypersensitivity reactions and give rise to oral bullae, erosions, ulcers, and crusted lips, the skin lesions of SJS and TEN are **different** from EM.
- They are **more severe** and tend to arise on **the chest** rather than the extremities on **erythematous and purpuric macules; these lesions are called —atypical targets.**
- **SJS** is much more likely to be associated with medication use and Mycoplasma pneumoniae infection (especially in children) and **rarely** with HSV infection.
- Some cases of **Mycoplasma pneumonia** are associated with EM.
- The more common inciting drugs include **antibacterial sulfonamides, penicillin, anticonvulsants, and NSAIDs in children**, and **allopurinol, oxicams, and nevirapine in adults**.
- In Han Chinese, development of SJS/TEN to **the aromatic anticonvulsants; carbamazepine, phenytoin**

✔The mucosal surfaces of the **eye, genitalia, and mouth** are almost always severely affected by SJS/TEN, always with skin involvement.

✔ The typical oral manifestation is extensive oral ulceration with hemorrhagic crusts on the vermilion and oral and other mucosal surfaces. **Diagnosis:**

- SJS is made if there **is less than 10%** of body surface involvement,
- SJS-TEN overlap syndrome **if 10–30%** of body surface is involved
- TEN **if >30%** is involved.

✔The mortality rate of SJS is 1–5% and TEN are 25–35%.

➤**Histopathologically**, most of the disease is localized in the epidermis, presumably this being the site where the medication or its metabolite is bound, with less inflammation in the dermis.

➤**Because of the severity of this condition**, treatment is generally with **intensive supportive care** because **of loss of skin barrier**, **intravenous immunoglobulin, systemic steroids, cyclosporine, plasmapheresis, cyclophosphamide, and TNF-α inhibitor.**

➤Because of the strong genetic associations with **h**uman **l**eukocyte **a**ntigen (HLA) haplotypes, such severe cutaneous adverse reactions may be substantially reduced by **pharmacogenetic screening** (history of medications).

8. Plasma Cell Stomatitis(PCS) & Oral Hypersensitivity Reactions

Etiology and Pathogenesis:

Oral hypersensitivity reactions may take the following forms:

1.Acute onset of ulcers such as in oral EM

2. Red and white reticulated lesions of a lichenoid hypersensitivity reaction

3. Fixed drug eruption

4.Marked erosions and erythema especially on the gingiva with or without ulceration called plasma cell stomatitis (PCS).

5. Swelling of the lips/angioedema

6. Oral allergy syndrome that presents mainly with symptoms of itching with or without swelling of the oral structures and oropharynx.

- **PCS** is a hypersensitivity reaction that was likely a contact stomatitis to a component of chewing gum, and these are all likely caused by a sensitizing contactant, whether the contactant is identified. These include khat (Catha edulis),components of toothpaste, mint candies, and household cleaners.

- Because of the intense **plasma cell infiltration**, it is believed that this is a B cell–mediated disorder, with T cells augmenting the response.
- The terms **mucous membrane plasmacytosis** and **plasma cell orofacial mucositis** are used because there may be involvement of the **upper respiratory tract.**
- Some believe that this is caused by components of plaque bacteria.
- **Clinical Findings**

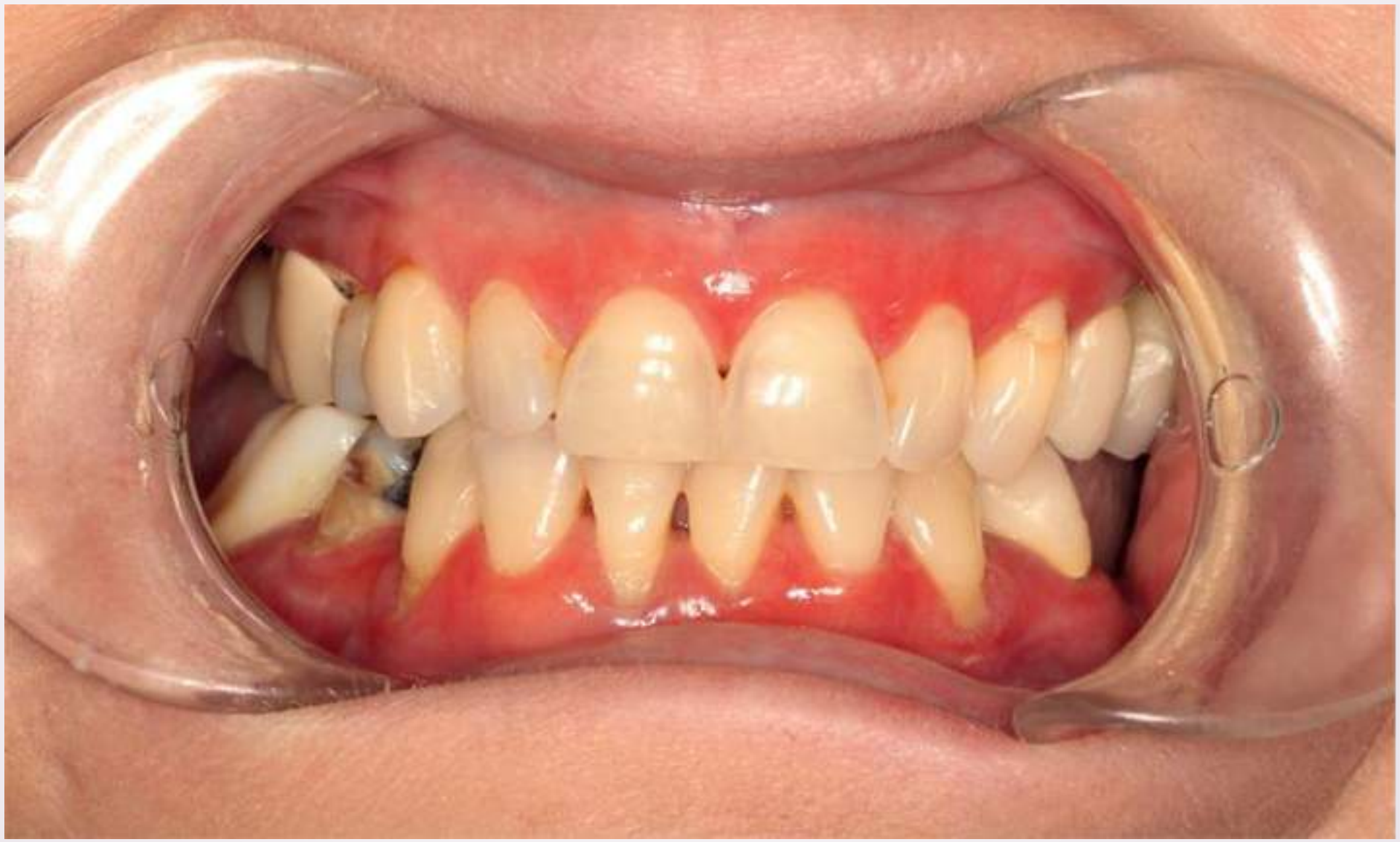
•PCS occurs **within days** of exposure to the contactant, with most signs and symptoms limited to the oral cavity.

•**Some lesions may affect the periorificial tissues or the oropharynx, leading to upper airway symptoms of hoarseness, dysphagia, and mild airway obstruction.**

•Endoscopy may reveal **erythematous and thickened mucosa, often with a cobblestoning pattern from the edema.** An obvious allergen/contactant is not always identified.

Oral Manifestations

- PCS occurs within **a few days** of exposure.
- It presents as brightly **erythematous macular areas** of the oral cavity, almost always involving **the marginal and attached gingiva or alveolar mucosa and often involving other soft tissues, such as the maxillary and mandibular sulcus or buccal mucosa.**
- Ulcers may be present & there may be epithelial **sloughing and desquamation.**
- The gingiva may also be **swollen and edematous**.
- Patients may complain of **pain and sensitivity & bleeding of the gingiva on brushing.**
- **Angular cheilitis with fissuring** and **dry atrophic lips have been reported.**
- Some cases reported as PCS consisted of **a very localized area** of **erythematous gingiva**, usually around a single tooth and measuring usually <1 cm. .



Plasma cell gingivitis presenting as desquamative gingivitis.

Laboratory Findings

✔**A biopsy** is the most useful diagnostic test for this condition. Patch testing to identify an allergen. **A biopsy** of the gingiva in PCS shows parakeratosis, epithelial hyperplasia, neutrophilic exocytosis, and numerous spongiotic pustules in the absence of Candida.

✔**The most significant finding is dense sheets of plasma cells in the lamina propria; many dilated capillaries lie close to the surface, accounting for the marked erythema.**

✔Eosinophils are **not seen** usually.

✔**Immunoperoxidase stains** will invariably show the plasma cell infiltrate to be polyclonal, typical for a reactive/inflammatory process, and not monoclonal, which typifies neoplastic lesions.

Management

- **PCS** is self-limiting and will generally, but not always, regress if the contactant is identified and removed.
- **Pain control and anti-inflammatory agents** may be helpful during the healing process.
- **Topical steroids** may help reduce inflammation and speed healing.
- Some lesions have resolved with **intralesional triamcinolone injections**, although the gingiva is a particularly difficult location for such injections.
- Cases have also responded well to **prednisone.**
- **Gingivectomies** may be needed to recontour lesions that are long-standing and more fibrotic.
- Improvement with **2% fusidic acid** may be seen.

The Patient with Recurring Oral Ulcers

- Recurring oral ulcers are among the most common problems seen by **clinicians** who manage diseases of the **oral mucosa**.
- Several diseases that should be included in the differential diagnosis of a patient with a history of recurring ulcers of the mouth, including:

1.Recurrent aphthous stomatitis(RAS)
2. Behçet Disease(Behçet syndrome)
3.Recrudescent HSV infection.
4. Recurrent oral EM.

1. Recurrent Aphthous Stomatitis

➤RAS is a common disorder characterized by recurring ulcers confined to the oral mucosa in patients with **no other signs of systemic disease**.

➤RAS is considered a diagnosis of exclusion since **Hematologic deficiencies, immune disorders, and connective tissue diseases** may cause oral aphthous-like ulcers clinically like RAS.

➤These ulcers **resolve** when the underlying systemic condition resolves.

➤RAS **affects** approximately **20%** of the general population, but when **specific ethnic or socioeconomic groups** are studied, the incidence ranges from **5 to 50%.**

➤RAS is classified according to **clinical characteristics**: **minor** ulcers, **major** ulcers and **herpetiform**.

➤There are cases in which a clear distinction between minor and major ulcers is blurred, particularly in patients who **experience severe discomfort from continuous episodes of ulcers**. These lesions have been referred to as **“severe” minor ulcers**

Etiology and Pathogenesis

✔It was once assumed that RAS was a form of recurrent HSV infection, and there are still clinicians who mistakenly call RAS "herpes."

✔Many studies done during the **past 40 years** have confirmed that RAS is not caused by HSV.

➤The major **factors presently linked** to RAS include **genetic factors**, **hematologic** or **immunologic abnormalities**, and **local factors**(trauma and smoking).

➤There is increasing evidence **linking local immune dysfunction** to RAS

➤During the past 30 years, research has suggested a relationship between RAS and lymphocytotoxicity, antibody-dependent cell-mediated cytotoxicity, defects in lymphocyte cell subpopulations, and an alteration in the **CD4 to CD8 lymphocyte ratio.**

➤More recent research has centered on dysfunction of **the mucosal cytokine network.**

➤Further evidence for the **inherited nature** of this disorder results from studies in which genetically specific human leukocyte antigens (HLAs) have been identified in patients with RAS, particularly in certain ethnic groups.

➤Recent studies **linking minor RAS to genetic factors associated with immune function**.

❑**Hematologic deficiency**, particularly of **serum iron, folate, or vitamin B_{12}, appears to be an etiologic factor in 5%–10% patients** with aphthous-like ulcers although these sometimes occur on keratinized mucosa. **Aphthous-like ulcers may also be seen in celiac disease**.

❑It was initially reported in the 1960s that there is a **negative correlation between RAS and a history of smoking**, and many clinicians have reported that RAS is exacerbated when patients stop smoking.

➤A study measuring **a nicotine metabolite** present in the blood of smokers confirmed that the incidence of RAS is significantly lower among smokers. The nicotine metabolites are believed to **decrease levels of proinflammatory** cytokines and **increase anti-inflammatory cytokines**.

➤Other factors that have been reported associated with RAS include anxiety, periods of psychological stress, localized trauma to the mucosa, menstruation, upper respiratory infections, and food allergy.

Oral Findings

•**The first episodes** of RAS most frequently begin during the second decade of life.

•The lesions are confined to the oral mucosa and begin with prodromal burning or the sensation of a small bump in the mucosa from **2 to 48 hours** before an ulcer appears.

• During this initial period, a localized area of erythema develops.

• **Within hours**, a small white papule forms, ulcerates, and gradually enlarges over the **next 48–72 hours**.

• The individual lesions are round, symmetric, and shallow (similar to viral ulcers), but no tissue tags are present from ruptured vesicles, which helps distinguish RAS from diseases that start as vesicles, such as pemphigus, and pemphigoid.

➤Multiple lesions are often present, but the number, size, and frequency vary considerably.
➤The buccal and labial mucosae are most commonly involved.
➤Lesions rarely occur on the heavily keratinized palatal mucosa or gingiva.
➤In mild RAS, the lesions reach a size of 0.3–1.0 cm and begin healing within a few days.
➤Healing without scarring is usually complete in 10–14 days.
➤**Most patients with RAS have between one and six lesions at each episode and experience several episodes a year.**
➤The disease is an annoyance for the majority of patients with mild RAS, but it can be painfully disabling for patients with severe RAS and RAS major.

➤Patients with major ulcers develop deep lesions that are larger than 1 cm in diameter and last for weeks to months

➤In the most severe cases, large portions of the oral mucosa may be covered with large deep ulcers that can become confluent, and are extremely painful, interfering with speech and eating. These patients may require hospitalization for intravenous feeding and treatment with **systemic corticosteroids.**

➤The lesions may **last for months** and sometimes be misdiagnosed as squamous cell carcinoma, granulomatous disease, or blistering disease. The lesions heal slowly and leave scars that may result in decreased mobility of the uvula and tongue.

➤**The least common variant of RAS** is the herpetiform type, which tends to occur in adults. The patient presents with more than 10 small punctate ulcers, measuring <5 mm, scattered over large portions of the oral mucosa.

Laboratory Findings

Laboratory investigation should be ordered when patients do not follow the usual pattern of RAS, for example,

- when episodes of RAS become more severe,
- begin past the age of 40,
- or are accompanied by other signs and symptoms. **Biopsies are only indicated** when it is necessary to exclude other diseases, particularly granulomatous diseases such as Crohn disease, sarcoidosis, or blistering diseases such as pemphigus or pemphigoid.

Patients with severe minor aphthae or major aphthous ulcers should be investigated for systemic disorders, including:
connective tissue diseases and hematologic abnormalities, such as reduced levels of serum iron, folate, vitamin B12, and ferritin.
Patients with abnormalities in these values should be referred to an internist for further management.
HIV-infected patients, particularly those with CD4 counts below 100/mm_3, may develop major aphthous ulcers, and, occasionally, such oral ulcers are the presenting sign of AIDS.
Biopsies reveal only a superficial ulcer covered by a fibrinous exudate with granulation tissue at the base and a mixed acute and chronic inflammatory infiltrate.

Management

- Pain relief with a topical anesthetic agent such as benzocaine or lidocaine.
- In more severe cases, the use of a high-potency topical steroid preparation, such as fluocinonide, betamethasone, or clobetasol, placed directly on the lesion, shortens healing time and reduces the size of the ulcers. The effectiveness of the topical steroid is partially based on good instruction and patient compliance regarding proper use.
- The **steroid gel** should be applied directly to the lesion after meals and at bedtime two to three times a day or mixed with an adhesive such as Orabase™ prior to application.
- Larger lesions can be treated by placing **a gauze sponge** containing the topical steroid on the ulcer and leaving it in place for 15–30 minutes to allow for longer contact of the medication.

Other topical preparations that have been shown to decrease the healing time of RAS lesions include **amlexanox paste** and a **topical tetracycline or doxycycline**, which can be used either as a mouthrinse or applied as a paste directly to the lesions. **Intralesional steroid injections** can be used to treat large indolent major RAS lesions. It should be emphasized that no available topical therapy reduces the frequency of new lesions. When patients with major aphthae or severe cases of multiple minor aphthae do not improve sufficiently with topical therapy, use of systemic therapy should be considered. Drugs that have been reported to reduce the number of ulcers in selected cases of major aphthae include colchicine, pentoxifylline, dapsone, short bursts of systemic steroids, and thalidomide. Each of these drugs has the potential for side effects, and the clinician must weigh the potential benefits versus the risks.

Thalidomide, a drug originally marketed as a nonaddicting hypnotic in the 1950s, was withdrawn from the market in the early 1960s due to its association with multiple, severe, deforming, and life-threatening birth defects Thalidomide has significant anti-inflammatory and immunomodulatory properties and is useful in treating a number of diseases, including erythema nodosum leprosum, discoid lupus erythematosus, graftvs- host disease, multiple myeloma, and Behçet disease. The drug has also been shown to reduce both the incidence and severity of major RAS in both HIV-positive and HIV-negative patients. The use of thalidomide for RAS should be reserved for management of severe major RAS where other less toxic therapies, including high-potency topical steroids, colchicine, and pentoxifylline**, have failed to control**

Women during childbearing years owing to the potential for severe life-threatening and deforming birth defects. All clinicians prescribing thalidomide in the United States must be registered in the (Risk Evaluation Mitigation Strategy) program for thalidomide and patients receiving the drug must be thoroughly counseled regarding effective birth control methods that must be used whenever thalidomide is prescribed. For example, two methods of birth control must be used, and the patient must have a pregnancy test monthly. Other side effects of thalidomide include peripheral neuropathy, gastrointestinal complaints, drowsiness and deep vein thrombosis. Monitoring patients taking long-term thalidomide for the development of peripheral neuropathy with periodic nerve conduction studies is also recommended.

2. Behçet Syndrome

Was initially described by the Turkish dermatologist Hulusi Behçet as **a triad of** symptoms including **recurring oral ulcers, recurring genital ulcers, and eye involvement.**

➤BD is now understood to be a **multisystem disorder** with many possible manifestations.

➤BD is more **severe** in **younger patients** and patients with **eye and GI** involvement.

Etiology and Pathogenesis

BD is a systemic vasculitis characterized by hyperactivity of neutrophils with enhanced chemotaxis and elevated proinflammatory cytokines IL-8 and IL-17, with TNF-α playing a major role in the pathogenesis. The HLA-B51 genotype is most frequently linked to BD, especially in patients with severe forms of the disease in Asia.

Clinical Manifestations

1.The highest incidence is in young adults 25 and 40 years , with the oral mucosa as the most common site of involvement.

2. The genital area is the second most common site of involvement and presents as ulcers of the scrotum and penis in males and ulcers of the labia in females.

3.The eye lesions consist of uveitis, retinal vasculitis, vascular occlusion, optic atrophy, and conjunctivitis.

4. Blindness is a common complication of the disease, and periodic evaluation by an ophthalmologist is necessary.

▪**Systemic** involvement occurs in over 50% of patients with BD.

• Skin lesions resembling erythema nodosum or large pustular lesions occur in over 50% of patients with BD.

•These lesions may be precipitated by **trauma**, and it is common for patients with BD to have a cutaneous hyperreactivity to intracutaneous injection or a needlestick (pathergy).

• **Arthritis** occurs in greater than 40% of patients and most frequently affects the knees, ankles, wrists, and elbows(red and swollen)

- In some patients, central nervous system involvement is the most distressing component of the disease (brainstem syndrome, involvement of the cranial nerves, or neurologic degeneration resembling multiple sclerosis that can be visualized by magnetic resonance imaging of the brain)
- Other reported signs of BD include thrombophlebitis, intestinal ulceration, venous thrombosis, and renal, cardiac, and pulmonary disease.
  - Both pulmonary involvement and cardiac involvement are believed to be secondary to vasculitis. Involvement of large vessels is life threatening because of the risk of arterial occlusion or aneurysms.

BD in children, which most frequently presents 9 and 10 years, has similar manifestations to the adult form of the disease, but **oral ulcers are a more common** presenting sign in children, whereas uveitis is less common. **Oral lesions** are seen **more than 95% of children** with BD. A variant of BD, characterized by mouth and genital ulcers with inflamed cartilage, is associated with relapsing polychondritis.

Oral Findings

- The most common site of involvement of BD is the oral mucosa.
- **Recurring oral ulcers appear** in more than 90% of patients; these lesions cannot be distinguished either clinically or histologically from RAS.
- Some patients experience **mild** recurring oral lesions; others have deep, **large**, scarring lesions characteristic of major RAS.
- These lesions may appear anywhere on the oral or pharyngeal mucosa

Laboratory Findings BD is a clinical diagnosis based up the criteria described above. Laboratory tests are used to rule out other diseases, such as connective tissue (lupus erythematosus) and hematologic diseases causing severe neutropenia

Management

The management of BD depends on the severity and the sites of involvement.

➤ Patients with sight-threatening eye involvement or central nervous system lesions require more aggressive therapy with drugs, with a higher potential for serious side effects.

1.Azathioprine and other immunosuppressive drugs combined with prednisone have been shown to reduce **ocular disease** as well as **oral and genital** involvement.

2.Pentoxifylline, which has fewer side effects than immunosuppressive drugs or systemic steroids, has also been reported to be effective in decreasing disease activity, particularly of oral and genital lesions. 3. Dapsone, colchicine, and thalidomide have also been used effectively to treat mucosal lesions of BD. 4. Therapy with monoclonal antibodies such as infliximab and etanercept are playing an increasing role in therapy of BD particularly in patients who do not respond to anti-inflammatory and immunosuppressive drugs.

The Patient With Chronic Multiple Ulcers

1.Pemphigus Vulgaris
2.Paraneoplastic pemphigus PNPP
3.Pemphigus Vegetans
4.Subepithelial Bullous Dermatoses
5.Bullous Pemphigoid
6.Mucous Membrane Pemphigoid (Cicatricial Pemphigoid)
7. Linear IgA disease(LAD) and Chronic Bullous Disease of Childhood
8. Epidermolysis bullosa acquisita(EBA)

Pemphigus

- Pemphigus includes a group of autoimmune, potentially life-threatening diseases that cause blisters and erosions of the skin and mucous membranes, characterized by **intraepithelial acantholysis.** The predisposition to develop the **autoantibodies** that cause pemphigus is genetically determined, but the triggering mechanism that initiates the immune response is unknown **Desmoglein 1** (DSG1), a glucoprotein adhesion molecule, is primarily found in the skin, whereas **desmoglein 3** (DSG3) is chiefly detected in mucosal epithelium and individuals genetically susceptible to pemphigus harbor desmoglein reactive B and T cells. The **immune reaction** against these **glycoproteins** causes a loss of cell-to-cell adhesion, resulting in the separation of cells and the formation of **intraepithelial bullae.**

Pemphigus Vulgaris

Etiology and Pathogenesis

✔It is the most common form of pemphigus, accounting for more than 80% of cases.

✔ The underlying mechanism responsible for causing the intraepithelial lesion of PV is the **binding** of IgG autoantibodies to DSG3, a transmembrane glycoprotein adhesion molecule present on desmosomes.

✔The loss of this glycoprotein results in loss of cell- to-cell adhesion resulting in intra-epithelial blisters.

✔Patients with PV mainly involving the mucosa have antibodies primarily against DSG3, but patients with PV involving both the skin and mucosa will have antibodies against both DSG3 and DSG1.

✔PV has been reported coexisting with other autoimmune

✔Several cases of pemphigus have been reported in patients with other autoimmune disorders or those with neoplasms such as lymphoma. **Death occurs most frequently in elderly patients and in patients requiring high doses of corticosteroids** who develop infections and bacterial septicemia, most notably from Staphylococcus aureus.

➤A characteristic sign of the disease may be obtained by applying pressure to an intact bulla.

➤In patients with PV, the bulla enlarges by extending to an apparently normal surface.

➤Another characteristic sign of the disease is that pressure to an apparently normal area results in the formation of a new lesion. **This phenomenon, called the Nikolsky sign, results from the upper layer of the skin pulling away from the basal layer**.

➤Any mucosal and skin surface may be involved, and in severe cases, the conjunctival, pharyngeal, and laryngeal mucosa may be involved, along with extensive skin lesions.

➤ Patients with oral lesions of pemphigus may also have esophageal lesions, and if esophageal symptoms are present, endoscopic examination should be performed to determine the severity of the lesions.

Oral Findings

1.Up to 80- 90% of patients with PV develop oral lesions sometime during the course of the disease, and in 60% of cases, the oral lesions are the first sign.

2. The oral lesions may begin as the classic bulla on a non inflamed base; more frequently, the clinician sees shallow irregular erosions and ulcers because the bullae rapidly break.

3.A thin layer of epithelium peels away in an irregular pattern, leaving a denuded base.

4. The edges of the lesion continue to extend peripherally over a period of weeks until they involve large portions of the oral mucosa.

5.Most commonly, the lesions start on the buccal mucosa, often in areas of trauma along the occlusal plane. The palatal mucosa and gingiva are other common sites of involvement. It is common for the oral lesions to be present for months before the skin lesions appear.

6. Frequently, however, the initial diagnosis is missed, and the lesions are misdiagnosed as HSV infection or candidiasis.

7. The average time from the disease onset to diagnosis may often take over five months, and coexisting candidiasis may mask the typical clinical picture of the pemphigus lesions.

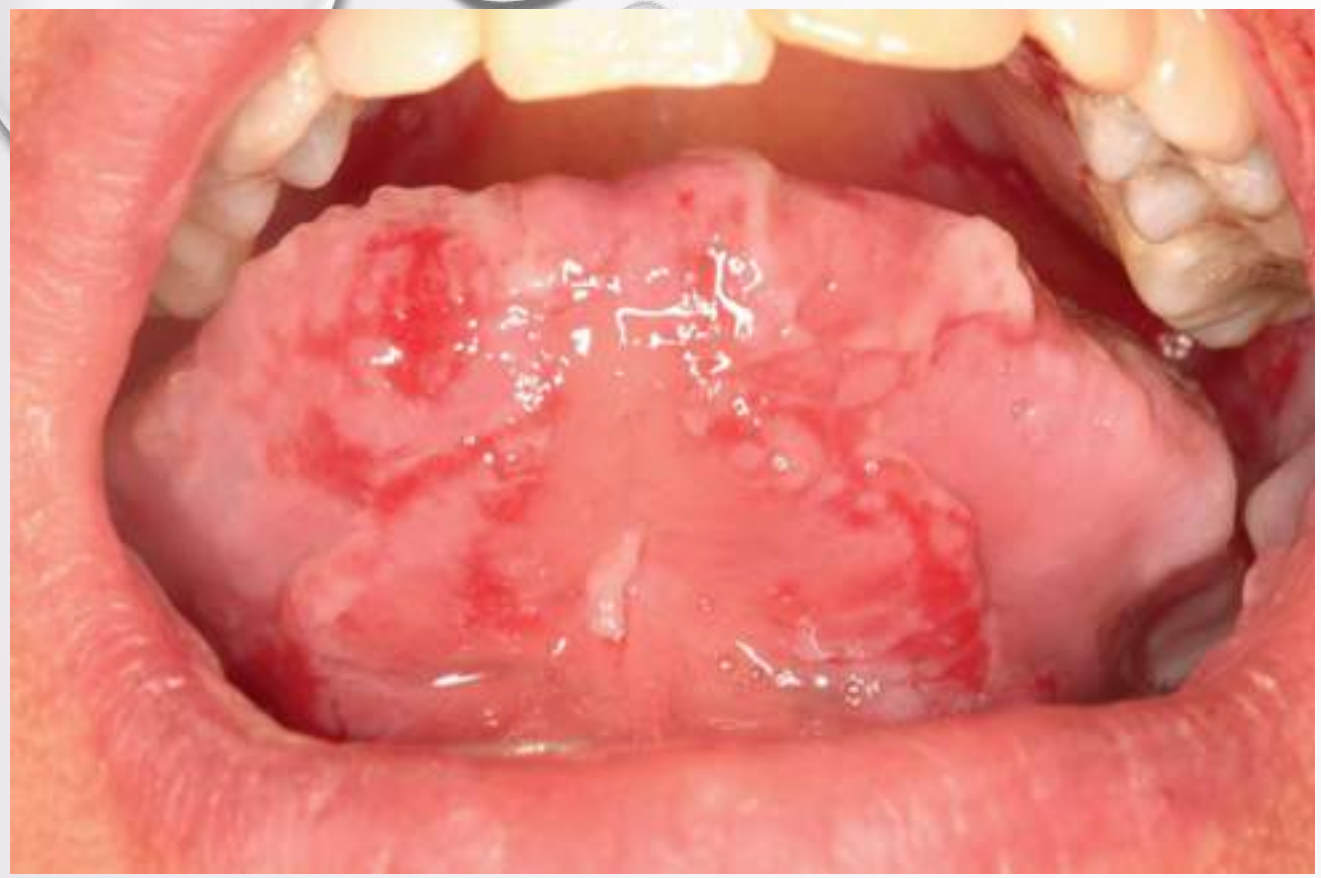
8. There is a small subgroup of pemphigus patients whose disease remains confined to the oral mucosa.

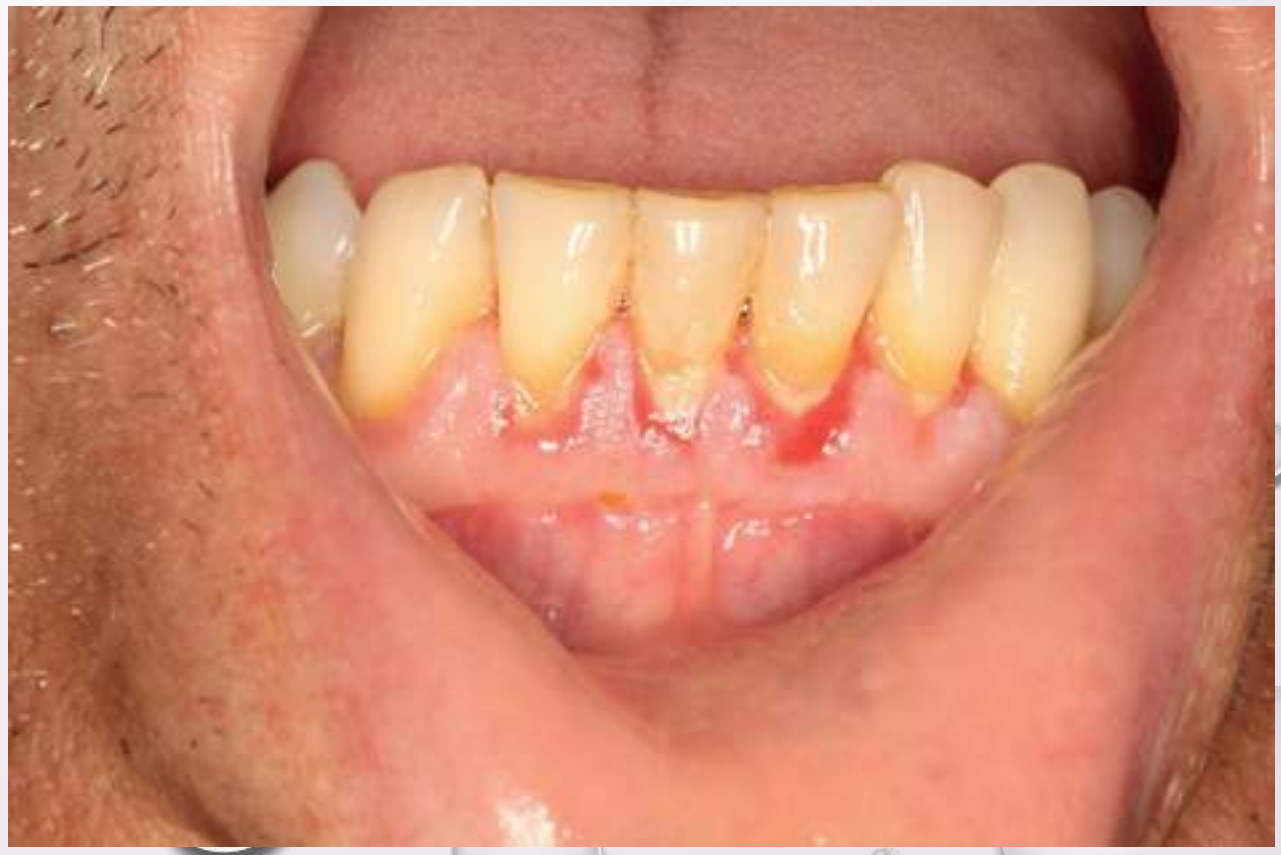
9.These patients often have negative results on indirect and direct immuno-fluorescence testing.

Laboratory Findings and Pathology

PV is diagnosed by biopsy and biopsies are best done on **intact vesicles and bullae less than 24 hours old**. However, because intact lesions are rare on the oral mucosa, the biopsy specimen should be taken from the advancing edge of the lesion, where areas of characteristic suprabasilar acantholysis may be observed by the pathologist.

- Specimens taken from the center of a denuded area are nonspecific histologically.
- Sometimes more than one biopsy is necessary before the correct diagnosis is rendered.





Management

➤Early diagnosis, lower doses of medication can be used for shorter periods of time to control the disease.

➤Management varies according to several factors, including the severity of the disease and the speed at which the disease **progresses**.

➤The mainstay of treatment remains high doses of systemic corticosteroids, usually given in dosages of **1–2 mg/kg/d**.

➤When substantial doses of steroids must be used for long periods, adjuvant therapy is recommended to reduce the steroid dose and their potential serious complications.

➤The most commonly used adjuvants are immunosuppressive drugs such as mycophenolate mofetil, azathioprine, cyclophosphamide, and cyclophosphamide pulse therapy.

➤Prednisone is used initially to bring the disease under control, and once this is achieved, the dose of prednisone is decreased to the lowest possible maintenance levels.

➤Patients with only oral involvement also may need lower doses of prednisone for shorter periods, so the clinician should weigh the potential benefits of adding adjuvant therapy against the risks of long- term immunosuppression, such as blood dyscrasias and an increased risk of malignancy.

- Most studies of PV of **the skin** show a decreased mortality rate when adjuvant therapy is given along with prednisone.
- The need for systemic steroids may be lowered further in cases of oral PV by combining topical with systemic steroid therapy, either by allowing the prednisone tablets to dissolve slowly in the mouth before swallowing or by using high-potency topical steroid creams.
- **Dapsone** has been shown to be effective.
- Recalcitrant cases are treated with rituximab and intravenous immunoglobulins.

Rituximab is presently being used and evaluated as a **first line treatment** although some studies demonstrated a high rate of infection.

Bullous Pemphigoid

Etiology and Pathogenesis ❖BP is the most common of the subepithelial blistering diseases,

❖ Occurs chiefly in adults older than the age of 60 years; it is self-limited and may last from a **few months to five years**.

❖BP may be a cause of death in older debilitated individuals.

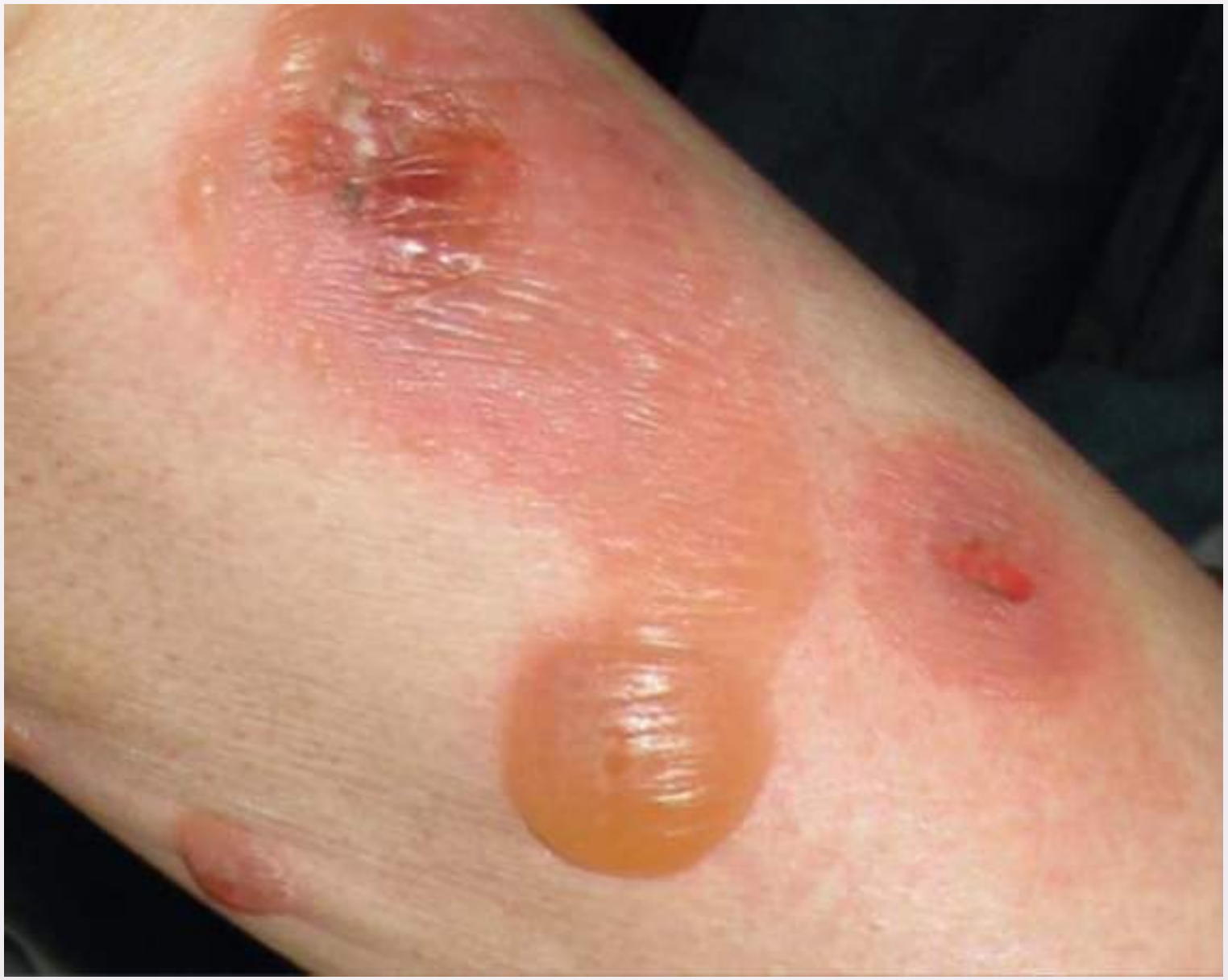
❖A thorough evaluation for an underlying malignancy is recommended for patients with severe or recalcitrant BP.

- **BP is an autoimmune disease caused by the binding of autoantibodies to specific antigens found in the lamina lucida region of the basement membrane on the hemidesmosomes of epithelial basal cells. These antigens are glycoproteins referred to as BP antigens, BP 180 and BP 230.**

❖Binding of antibody to antigen activates both **leukocytes and complement**, causing localized damage to the basement membrane, resulting in vesicle formation in the **subepithelial region**.

Clinical Manifestations

- The characteristic skin lesion of BP is a tense blister on an inflamed base accompanied by urticarial plaques in the scalp, abdomen, extremities, axilla, and groin.
- **Pruritus** is a common feature of the skin lesions
- The disease is self-limiting but can last for months to years without therapy.
- Patients with BP may experience one episode or recurrent bouts of lesions.
- Unlike pemphigus, BP is rarely life threatening since the bullae do not continue to extend at the periphery to form large denuded areas,
- Death from sepsis or cardiovascular disease secondary to long-term steroid use has been reported to be high in groups of sick elderly patients.



Bullous Pemphigoid

Oral Findings

- Oral involvement occurs in 10–20% of BP patients.
- The oral lesions of BP are smaller, more slowly, and less painful than in PV; the often-extensive labial involvement seen in PV is not present.

➤ Desquamative gingivitis has also been reported as the most common oral manifestation of BP, and the gingival lesions may be the only site of oral involvement.

➤ **The gingival lesions** consist of generalized edema, inflammation, and desquamation with localized areas of discrete vesicle formation.

➤The oral lesions are clinically and histologically indistinguishable from oral lesions of MMP.

Laboratory Findings

Routine histology of a biopsy specimen demonstrates **separation** of **the epithelium** from the **connective tissue at the basement membrane zone** and an inflammatory infiltrate that is usually rich in **eosinophils**, particularly in skin biopsies

Management

- ✔Localized oral lesions of BP may be treated with high-potency topical steroids, such as clobetasol or betamethasone, whereas patients with more extensive disease require use of systemic corticosteroids alone or combined with immunosuppressive drugs such as **azathioprine**, **cyclophosphamide, mycophenolate, or rituximab**.
- ✔Patients with **moderate levels** of disease may minimize the use of systemic steroids by the use of **dapsone or tetracycline, doxycycline, or minocycline, which may be combined with niacinamide**.

Mucous Membrane Pemphigoid –MMP

(Cicatricial Pemphigoid)

Etiology and Pathogenesis

✔Is a chronic autoimmune subepithelial disease that primarily affects the mucous membranes of patients older than the age of 50 years, resulting in mucosal blistering, ulceration, and subsequent scarring in some organs.

✔The disease **occurs twice as frequently in women**.

➤The primary lesion of MMP occurs when autoantibodies directed against proteins in the basement membrane zone, acting with complement (C3), cause a subepithelial split and subsequent vesicle formation.

➤ Antibodies against basement membrane antigens have been identified in cases of MMP.

✔The antigens are most frequently present in the **lamina lucida** portion of the basement membrane, but the **lamina densa** may be the primary site of involvement in some cases.

Oral Findings

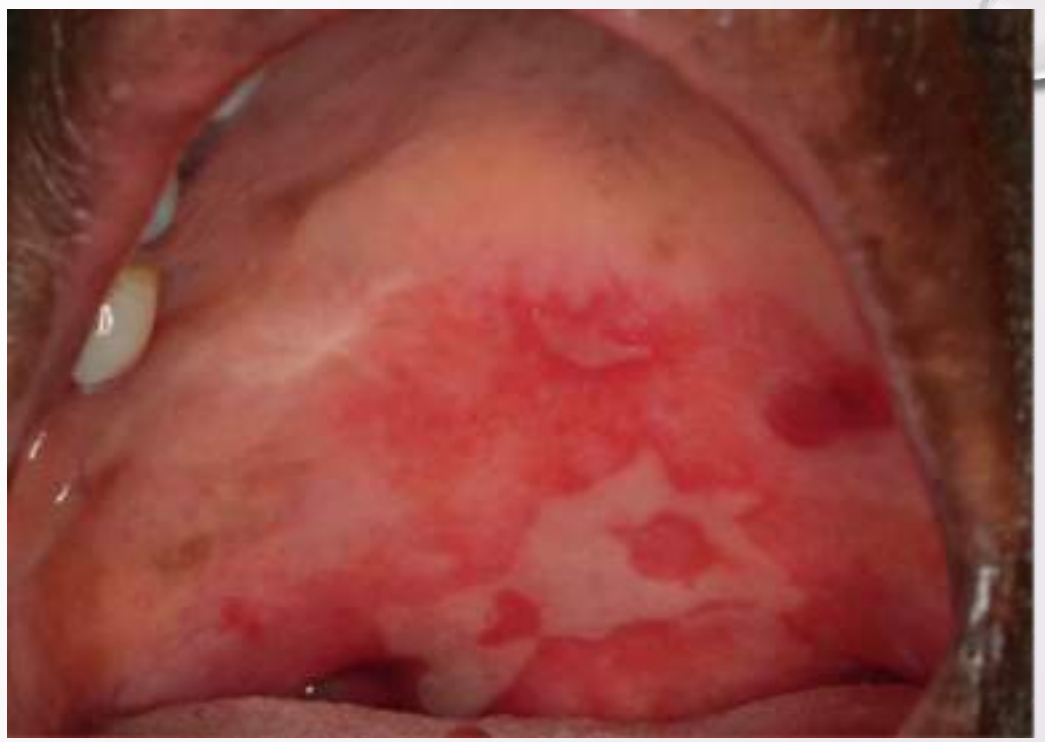
✔Oral lesions occur in more than 90% of patients.

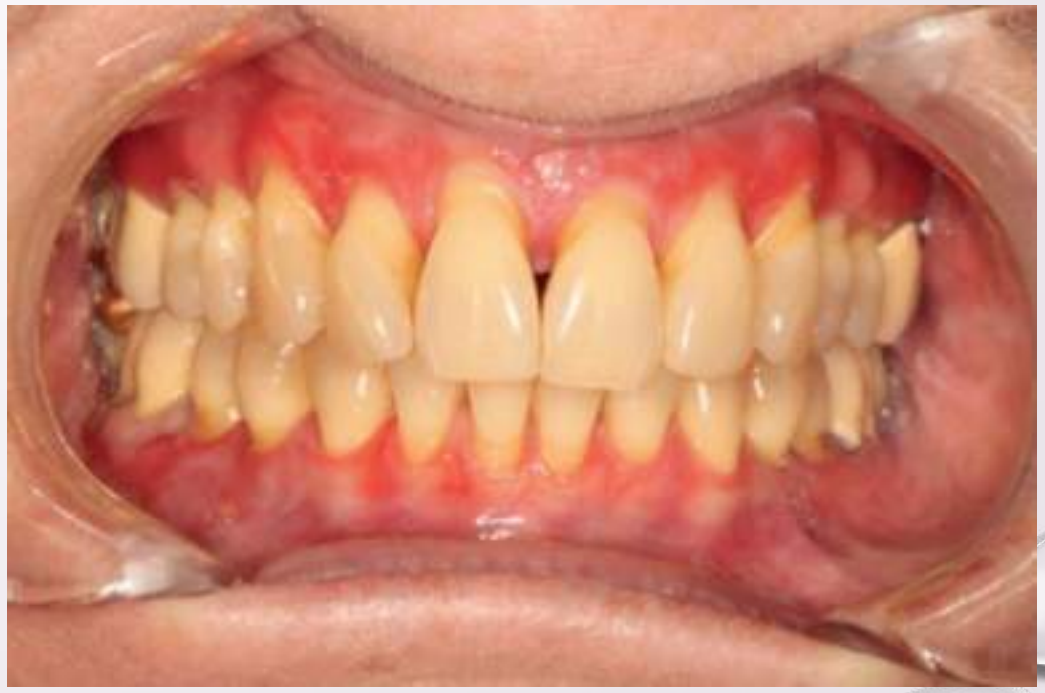
✔Desquamative gingivitis is the most common manifestation and may be the only manifestation of the disease appearing bright red.

✔**Since these desquamative lesions resemble the lesions of erosive lichen planus and PV, all cases of desquamative gingivitis should be biopsied and studied with both routine histology and DIF for definitive diagnosis**.

✔Lesions may present as intact vesicles of the gingival or other mucosal surfaces, but more frequently they appear as nonspecific- appearing erythema and erosions.

✔Unlike ocular pemphigoid, oral MMP rarely results in scarring.





Laboratory Findings Patients with suspected MMP should have biopsy specimens taken for both routine and DIF studies. **The specimen for routine histology and DIF should be taken from the edge of an ulcer, vesicle, or erythema and tissue**. Histopathology reveals subepithelial clefting with preservation of basal cells and variable inflammation

Management

Management of MMP depends on the severity of symptoms and site of involvement.

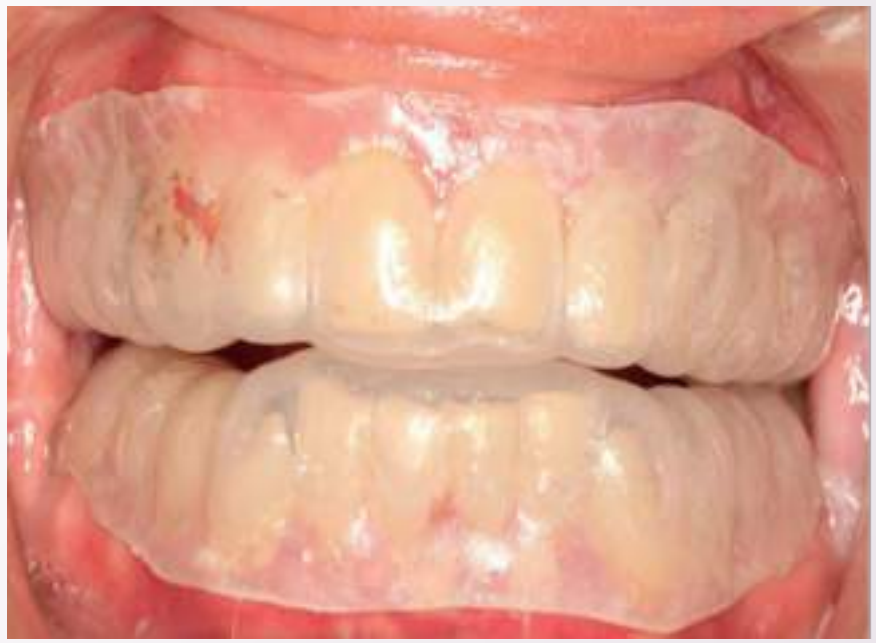
➤ When the lesions are confined to the oral mucosa, use of systemic corticosteroids should only be considered for short periods for severe outbreaks until steroid-sparing therapy can be instituted.

➤ Unlike PV, MMP rarely a fatal disease, and long-term use of systemic steroids for oral lesion involvement alone is seldom indicated.

➤Patients with **mild oral disease** may be treated with **topical and intralesional steroids.**

Steroid-sparing therapy Because the disease can persist throughout a patient's lifetime and To control and minimizing toxicities related to immunosuppression agents, steroid-sparing agents in the management of patients with autoimmune bullous diseases is important.

- **Desquamative gingivitis** Can often be managed with topical steroids in a soft dental splint that covers the gingiva, although the clinician using topical steroids over large areas of mucosa must closely monitor the patient for side effects such as candidiasis and effects of systemic absorption



➤ When **topical or intralesional therapy is not** successful, use of a tetracycline, such as doxycycline or minocycline is often helpful in controlling desquamative gingivitis and other oral lesions.

➤ When there are severe oral lesions, conjunctival or laryngeal involvement, **dapsone therapy** is recommended as the next choice before considering long-term systemic steroids, immunosuppressive drug therapy or rituximab.

Since **dapsone** causes hemolysis and methemoglobinemia, **glucose-6-phosphate dehydrogenase** deficiency must be ruled out, and the patient's hemoglobin must be closely monitored

Epidermolysis Bullosa Acquisita

Patients with EBA have **IgG autoantibodies directed against type VII collagen, a** component of the anchoring fibrils of the basement membrane. **There are two forms of EBA: The classic form**, which results in a lesion of the basement membrane with little inflammation, **or the inflammatory form**, which includes a significant infiltration of neutrophils. **Clinical Manifestations** The clinical course of EBA can resemble BP or MMP with **widespread skin lesions or primary involvement of the oral mucosa, genital mucosa, conjunctiva, and larynx**. **Oral lesions** present as erythema, erosion, ulcers and desquamative gingivitis.

Management

oDepending on the extent and severity of the clinical lesions.

oThe **classic form** of the disease tends to be resistant to treatment, whereas the inflammatory form often responds well to **dapsone**.

oSystemic corticosteroids, immunosuppressive or intravenous IG may be required to control the lesions in severe widespread EBA

Patient with Single Ulcers

1.Traumatic Injuries Causing Solitary Ulcerations

2.Traumatic Ulcerative Granuloma (Eosinophilic Ulcer of Tongue)

3. Infectious Ulcers

Traumatic Injuries Causing Solitary Ulcerations

Etiology and Pathogenesis

- Single mucosal ulcers may be caused by
  - direct physical/ mechanical,
  - thermal,
  - chemical trauma to the mucosa
  - or even vascular compromise, causing tissue damage and ulceration.

Acute bite injuries, an example of direct physical/ mechanical trauma, occur often in the oral mucosa **Traumatic injuries** may also result from malocclusion, ill-fitting dental prostheses, overzealous toothbrushing and flossing, self-injurious habits, and oral piercings. **Thermal injuries** including electrical burns are infrequently seen in children who inadvertently chew on electrical wiring. More commonly, thermal burns occur on the palatal mucosa from ingesting hot foods and beverages (such as hot pizza or coffee). An iatrogenic cause of thermal injury is from a heated dental instrument Chemical trauma is caused by patients or dentists placing noxious and caustic substances directly on the mucosa or chewing medications formulated to be swallowed (such as aspirin or oral bisphosphonates) may also lead to severe oral ulcers.

➤Mouthwashes or other oral care products with high alcoholic content, hydrogen peroxide, or phenols used too frequently or undiluted can cause mucosal ulcerations

➤Some over-the-counter medications for treating aphthous ulcers contain high concentrations of silver nitrate, phenols, or sulfuric acid and should be used with caution.

➤ Ulcers have also resulted in the use of denture cleansers as an oral rinse.

➤Prolonged contact of methacrylate monomer on the mucosa may also lead to necrosis of the mucosa.

➤**Necrosis of the bone** and mucosa has been reported from chemicals used in endodontics if these are pushed **past the apices** of teeth.

Vascular compromise leads to oral ulcers and two main patterns are identified.

➤**Necrotizing sialometaplasia** where there is local infarction of the salivary gland tissue leading to overlying ulceration, exfoliation of the necrotic tissue, and healing. Many etiologies have been identified including vasoconstrictors, sustained pressure and bulimia and the most common location for this condition is the hard palatal mucosa although any location that contains salivary glands may be affected.

➤ **Another is systemic vasculitis,** where inflammation of vessels leads to thrombosis and infarction. Tongue necrosis is a particularly well-documented aspect of giant cell (temporal) arteritis.

Management

1.Smaller lesions heal on their own once the irritant is removed.
2. Pain can be achieved with topical anesthetics (viscous lidocaine).
3.Topical steroids or intra-lesional steroid injections may be useful..
4.Dentists also should be more aware of taking protective measures when using caustic substances and heated instruments.
5.Electrical burns are generally deep and more extensive and healing often results in scarring and contracture. If the corners of the mouth are involved, microstomia may result. Children benefit from the use of microstomia prevention devices during this healing period, although surgical correction may still be required to restore function and esthetics. Antibiotics may be necessary to prevent a secondary infection since these burns often take several weeks to heal. **Necrotizing sialometaplasia** heals on its own while ulcers of vasculitic origin will generally require treatment with systemic corticosteroids.

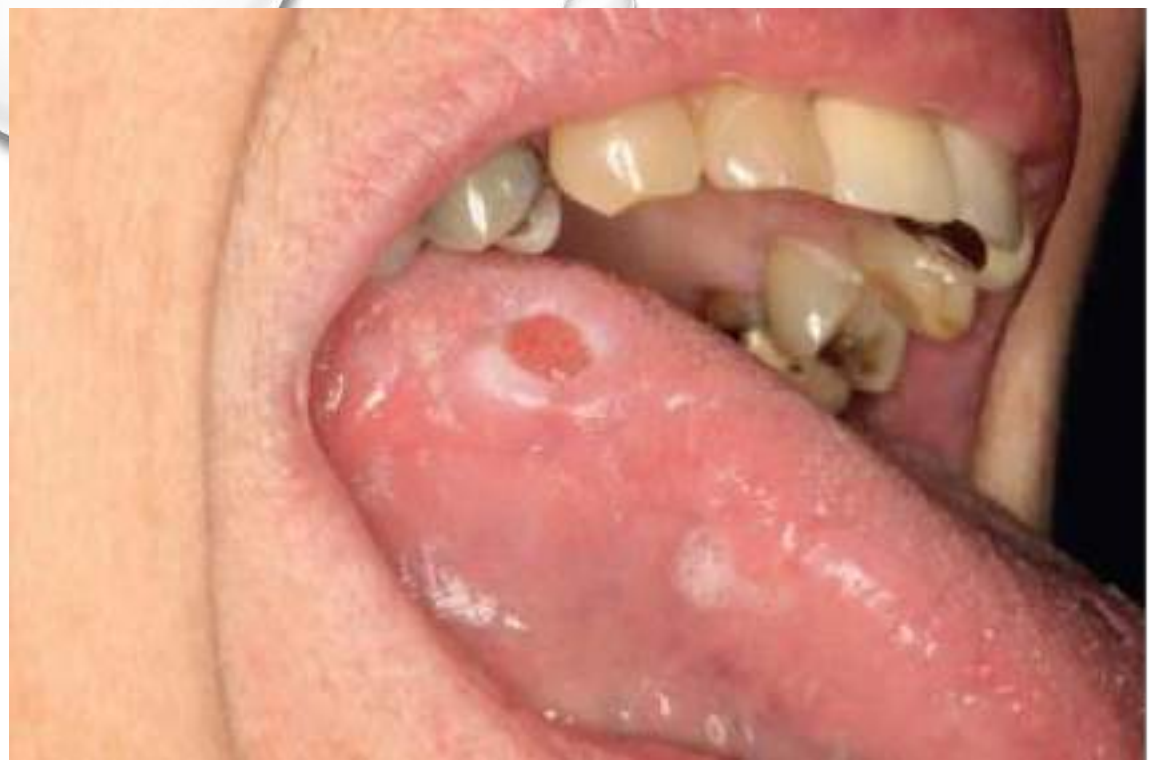
Traumatic Ulcerative Granuloma (Eosinophilic Ulcer of Tongue)

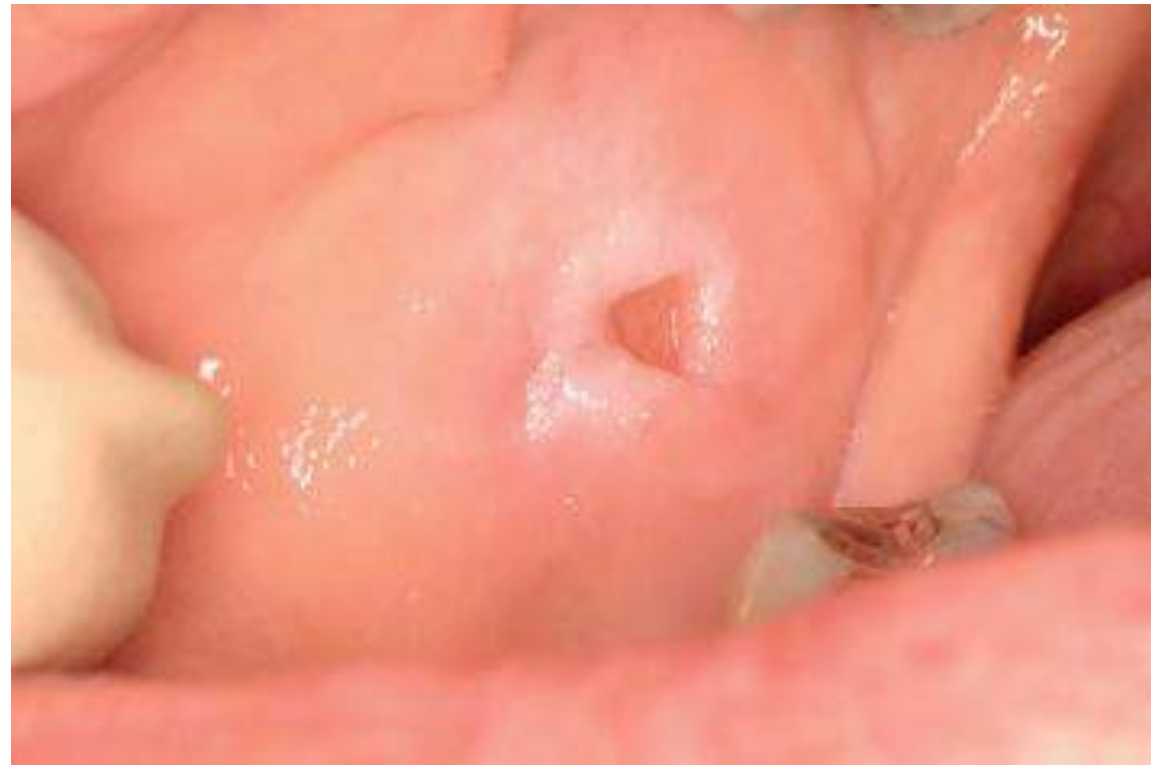
Etiology and Pathogenesis

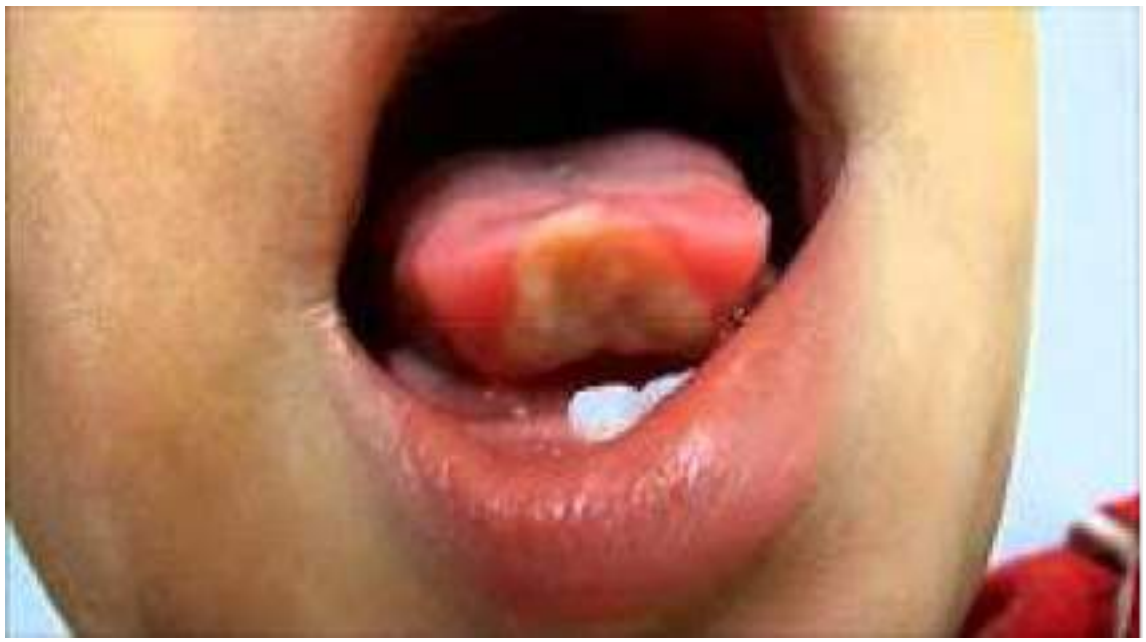
- This ulcerative condition of the oral cavity is considered traumatic in nature, although less than 50% of patients recall a history of trauma.

. It is likely that the penetrating nature of the inflammation results in myositis that leads to chronicity.

- other acute or chronic ulcerative conditions left untreated may become deep and penetrating.
- Similar lesions are seen on the ventral tongue in infants caused by the tongue rasping against newly erupted primary incisors, a condition known as **Riga–Fede disease**.
- Patients with familial dysautonomia and other conditions, such as Riley–Day syndrome and Lesch–Nyhan syndrome, who have congenital incapacity to sense pain often also develop similar ulcerative and necrotic ulcers because they are unaware of the self-inflicted injury.







Clinical Manifestations

Bimodal age distribution

➤First two years of life associated with erupting primary dentition.

➤Adults in the fifth and sixth decades.

Oral Findings

❖**In children**, the ulcers are always on the anterior ventral or dorsal tongue associated with erupting mandibular or maxillary incisors, respectively.

❖**The tongue** is the site of involvement in approximately 60% of adult cases, usually on the posterior and lateral aspects.

❖An ulcer develops that may not be painful in two-thirds of cases and may persist for months.

❖A history of trauma is 20–50% of cases.

❖The ulcer generally appears cleanly punched out, with surrounding erythema and keratosis if present for weeks or months.

➤A single, chronic, painless ulcer with induration raises the suspicion for squamous cell carcinoma (especially if it is on the tongue), salivary gland malignancy or lymphoma.

Management

1.A careful history is important to rule out continued trauma to the site.

2.Intralesional steroid injections performed over a few weeks will often resolve these lesions.

3.Wound debridement also often leads to complete resolution, in 1/3 of cases

4.The use of a nightguard on the lower teeth may help reduce nighttime trauma.

Infections Causing Solitary Ulcers

1.Viral infections such as CMV and EBV of the herpes family may cause single ulcers that **last for weeks or months** in the immunocompromised or immunosenescent patient

2.The deep mycoses were uncommon causes of oral lesions prior to HIV infection, myelosuppressive cancer chemotherapy, and immunosuppressive drug therapy.

3.The dentist must consider this group of diseases in the differential diagnosis whenever **isolated ulcerative oral lesions develop in known or suspected immunosuppressed patients.** If there is reactive epithelial hyperplasia to the organism, lesions may appear as fungating masses resembling squamous cell carcinoma. Biopsy of suspected lesions, accompanied by a request for appropriate stains, is necessary for early diagnosis. Newer molecular-based diagnostic tests are also available.

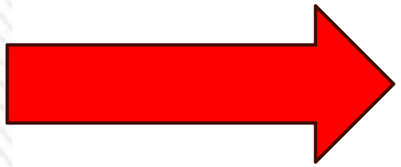

Thank You

Red and White Lesions of the Oral Mucosa

PART-1

Dr. Marwah Waleed

Oral mucosal lesions may be classified according to different characteristics



❒ Infectious Diseases

Oral Candidiasis

Oral Hairy Leukoplakia

❒ Oral Potentially Malignant Disorders

Oral Leukoplakia

Proliferative Verrucous leukoplakia

Oral Erythroplakia

Oral Submucous Fibrosis

❒ Immunopathologic Diseases

Oral Lichen Planus

Oral Disease Severity Scoring

Oral Lichenoid Drug Eruptions

Lichenoid Reactions of Graft-versus-Host Disease

Lupus Erythematosus

❒ Allergic Reactions

Oral Lichenoid Contact Reactions

Reactions to Dentifrice and Chlorhexidine

❒ Toxic Reactions

Reactions to Smokeless Tobacco

Smoker's Keratosis

Smoker's Palate

❒ Reactions To Mechanical Trauma

Morsicatio (Mucosal Nibbling)

Frictional Hyperkeratosis

❒ Other Red And White Lesions

Benign Migratory Glossitis (Geographic Tongue)

Leukoedema

White Sponge Nevus

Hairy Tongue

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

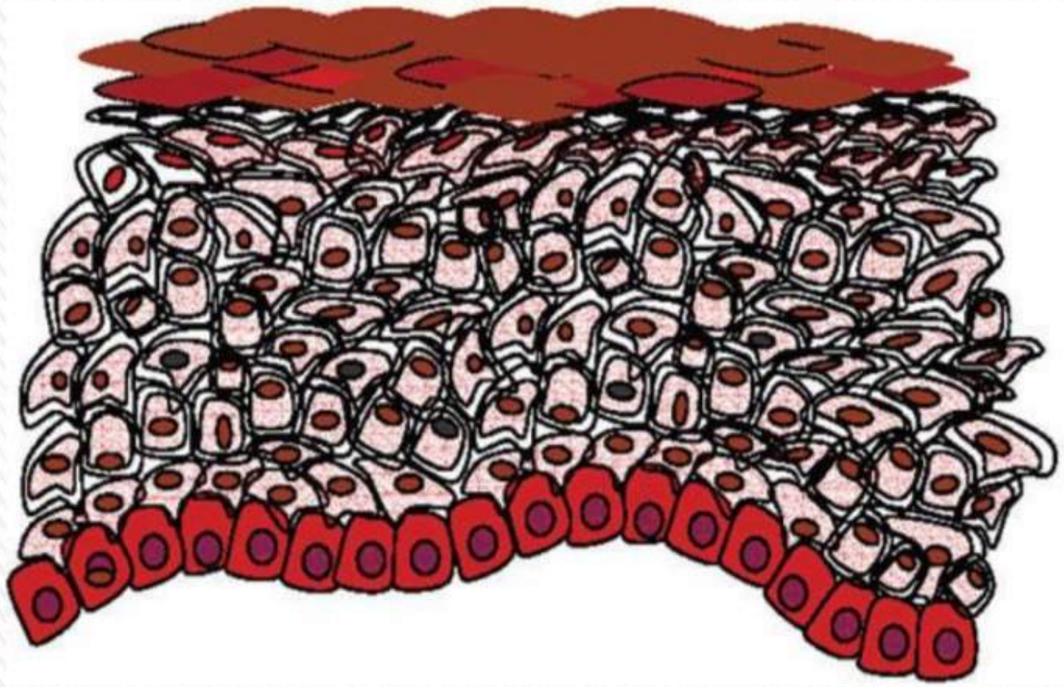
- The oral epithelium may be stimulated to an increased production of keratin (**hyperkeratosis**)
- An abnormal but benign thickening of stratum spinosum (**acanthosis**)
- Intra- and extracellular accumulation of fluid in the epithelium may also result in **clinical whitening**.
- **Microbes,** particularly **fungi**, can produce whitish pseudo-membranes sloughed epithelial consisting of sloughed epithelial cells ,neutrophils, and fungal mycelium, that loosely attached to the oral mucosa.

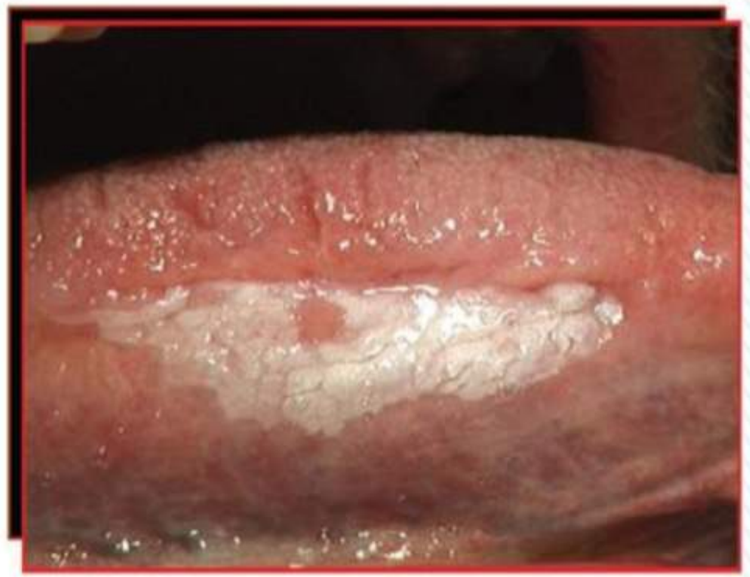
White lesions of oral mucosa are white because of several possible structural occurrences.

1) Increased thickness of the corneal layer (in keratinized epithelium).
2) Keratinization of epithelium that does not normally contain a corneal layer (nonkeratinized epithelium).Both (1) and (2) manifest as hyperkeratosis
3) Formation of abnormal keratin.
4) Epithelial edema: intra- and extracellular accumulation of fluid in the epithelium may also result in clinical whitening.
5) Abnormal keratinization occurring prematurely within individual cells or groups below the stratum granulosum (dyskeratosis often also contains hyperkeratosis).
6) Subepithelial superficial fibrosis, which with its decreased vascularity network causes a diffuse whitish appearance.

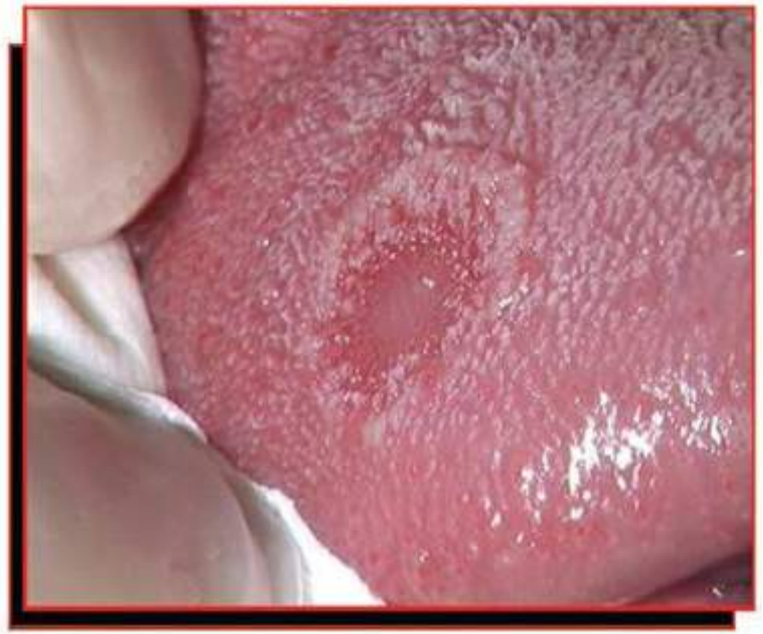
- **Any overall epithelial thickening (acanthosis) itself does not seem to cause whiteness**

Hyperkeratosis



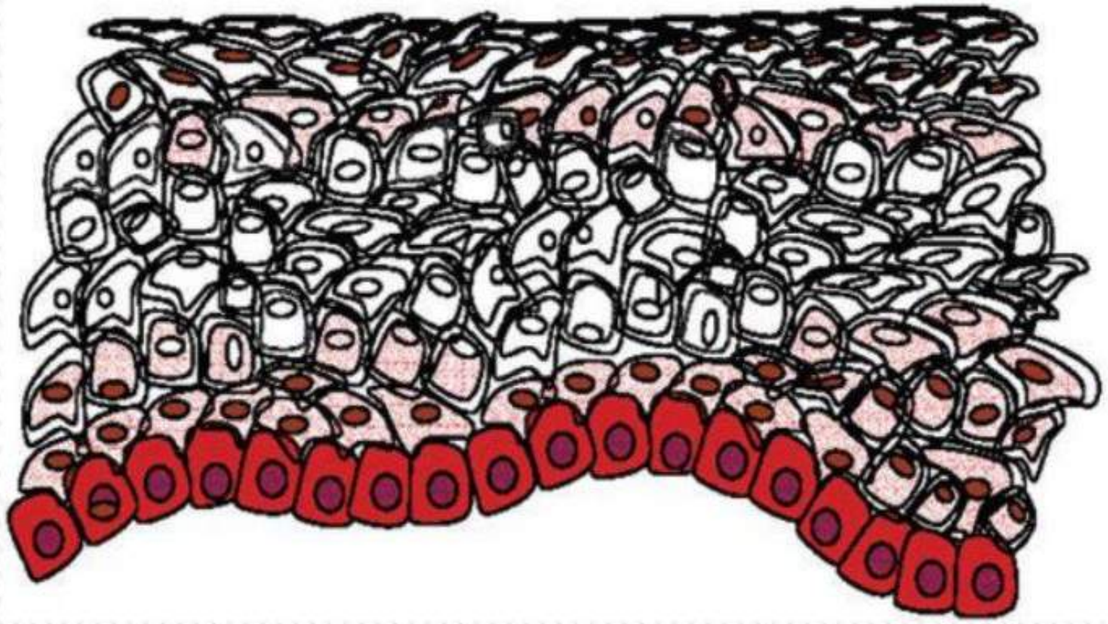


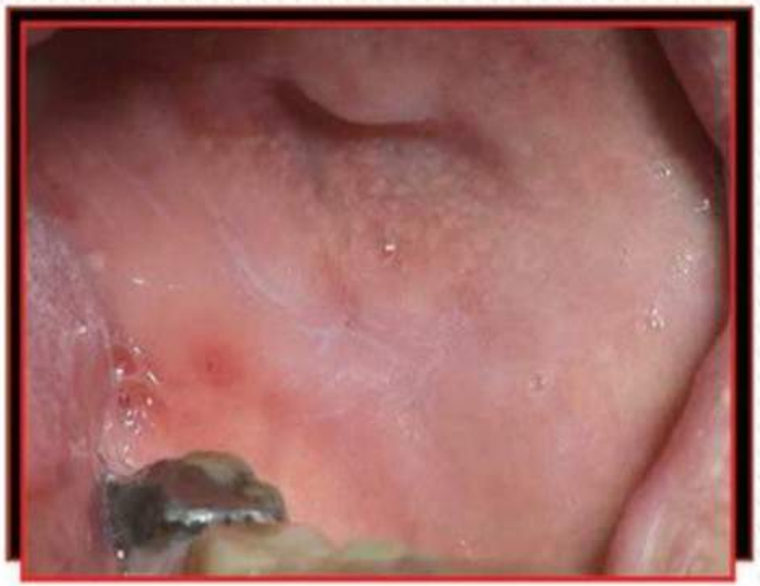
Mechanisms leading to a white appearance of the oral mucosa due to an increased production of keratin (hyperkeratosis).



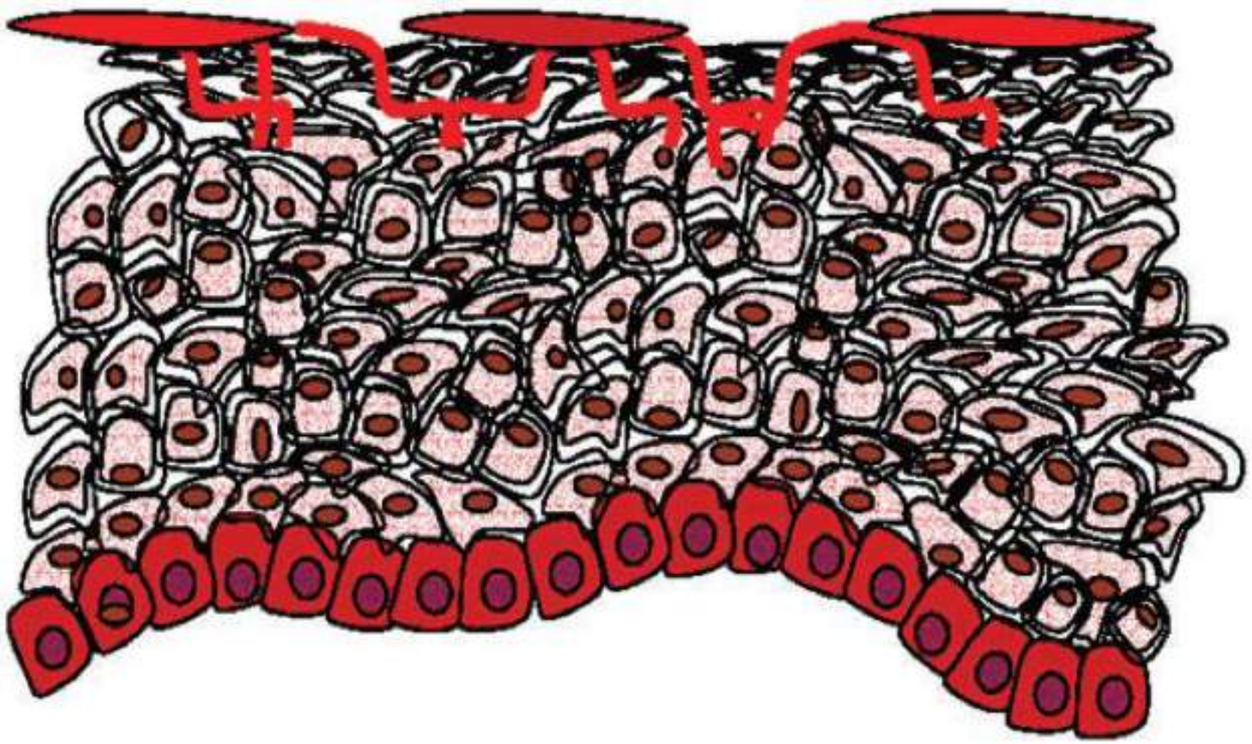
Mechanisms leading to a white appearance of the oral mucosa due to an abnormal but benign thickening of stratum spinosum (acanthosis).

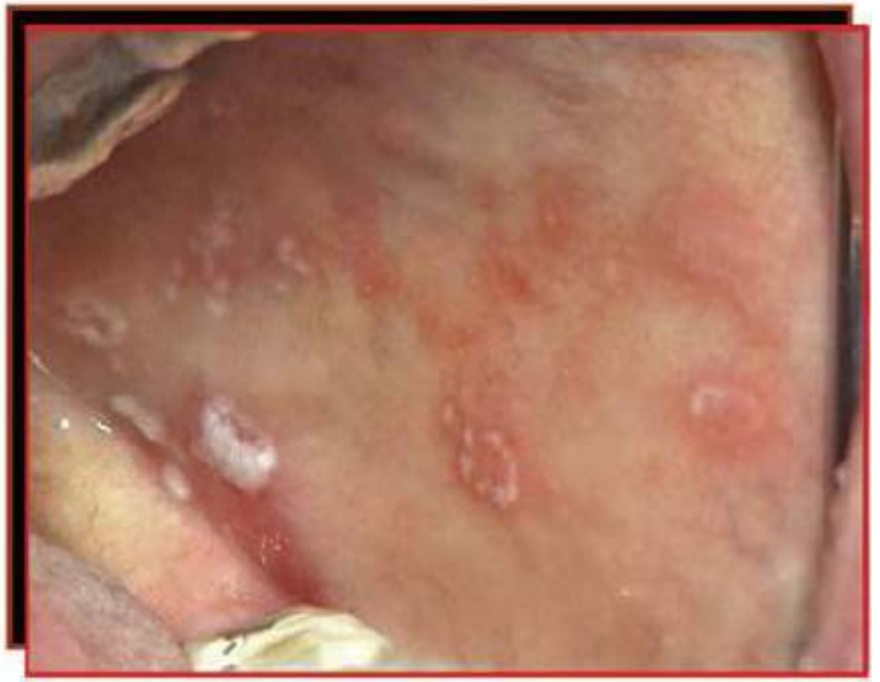
(Leukodema)





Mechanisms leading to a transparent white appearance of the oral mucosa due to intra- and extracellular accumulation of fluid in the epithelium

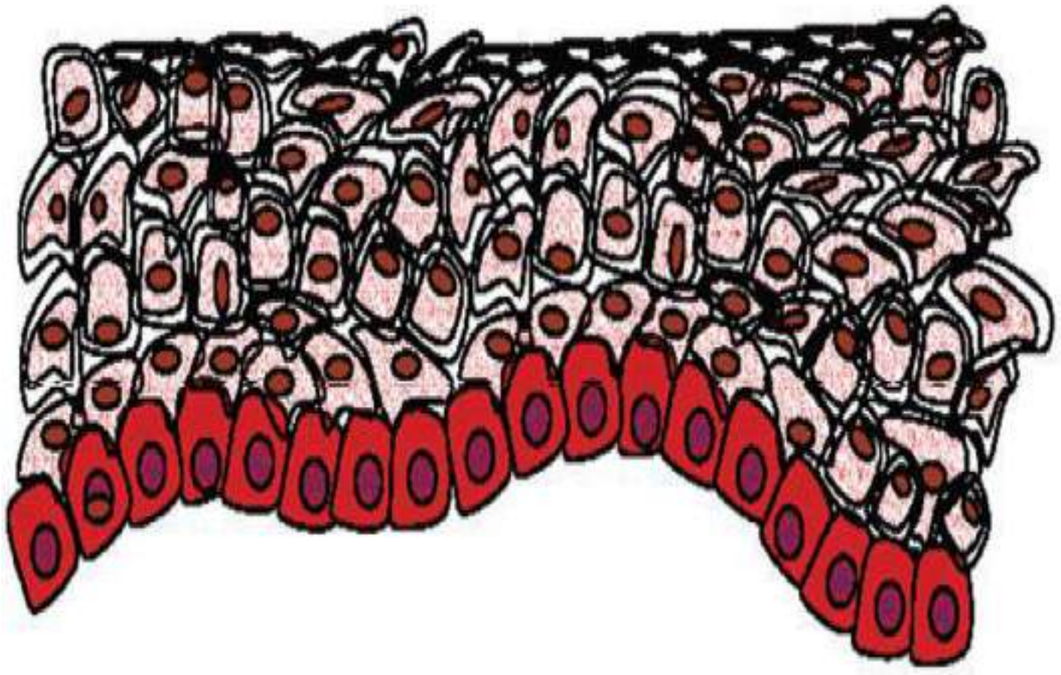


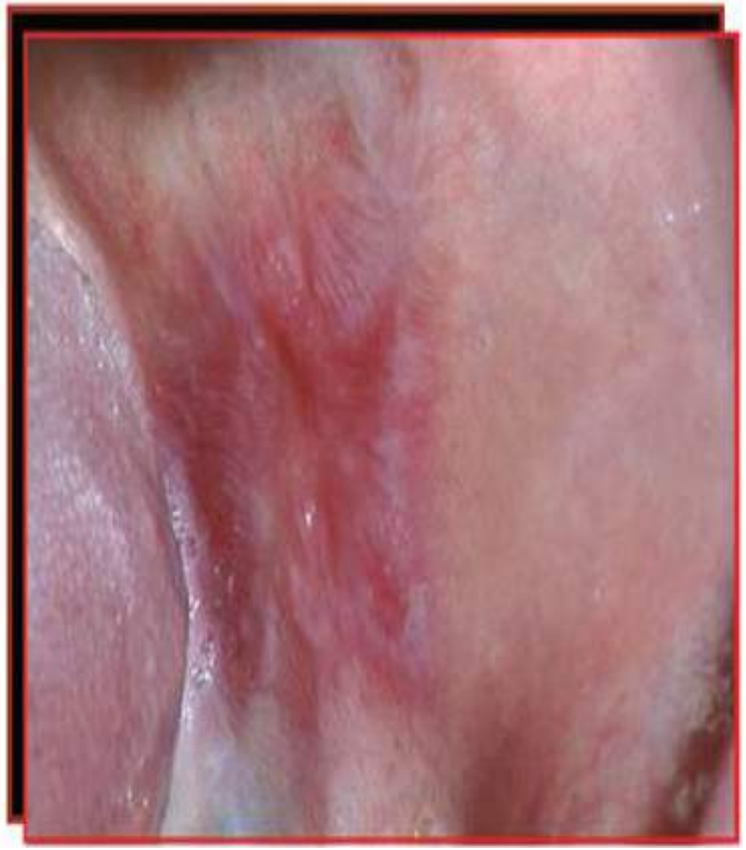


Mechanisms of a white appearance of the oral mucosa due to microbes, particularly fungi, which can produce whitish pseudomembranes consisting of sloughed epithelial cells, fungal mycelium, and neutrophils, which are loosely attached to the oral mucosa (plaques).

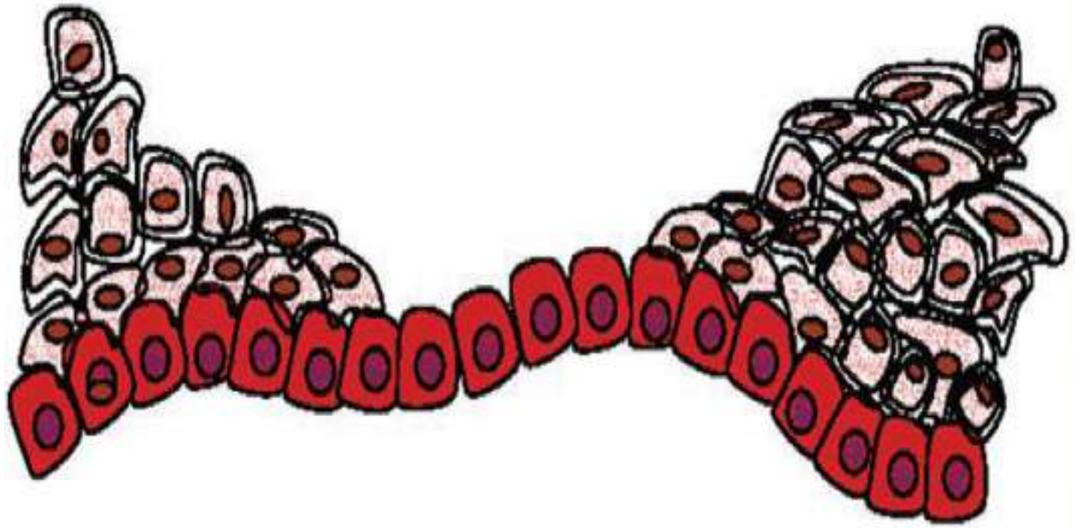
A red lesion of the oral mucosa may develop because of:

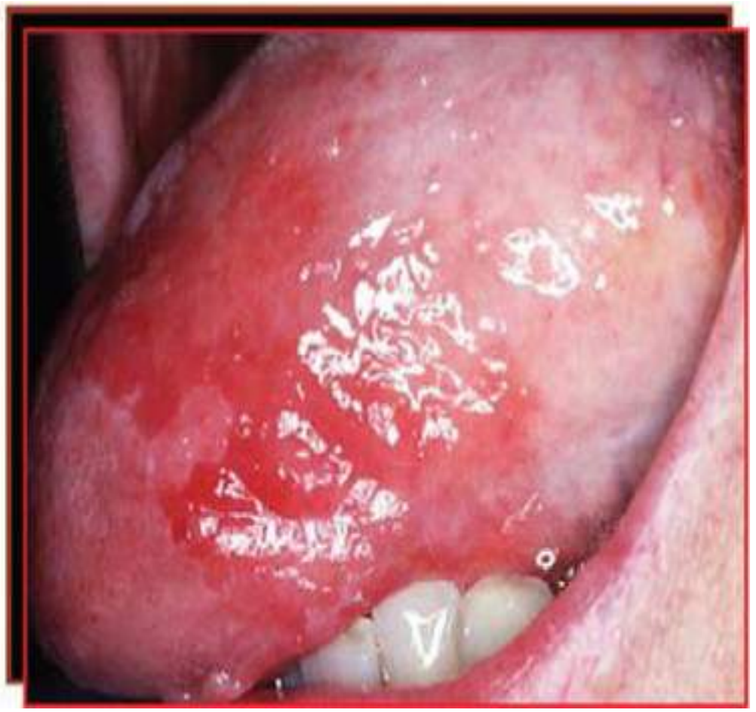
- Atrophic epithelium characterized by a reduction in the number of epithelial cells
- Loss of the superficial cell layers (superficial erosion)
- Increased vascularization due to proliferation of vessels
- Redness or erythema may further be caused by dilatation of vessels associated with inflammation of the oral mucosa,
- Reduced epithelial keratinization, and, importantly, cellular proliferation signifying a possible malignancy.





Mechanisms leading to a red appearance of the oral mucosa; a red lesion of the oral mucosa may develop as the result of an atrophic epithelium (atrophy).





Mechanisms leading to a red appearance of the oral mucosa characterized by a reduction in the number of epithelial cells or increased vascularization; that is, dilatation of vessels and/or proliferation of vessels.

Main clinical characteristics of red or white lesions.

- Is pain present?
- Are lesions single or multiple?
- Are lesions bilateral or unilateral?
- Is the distribution of lesions linked to mucosal type?
- Are lesion borders defined or indistinct?
- Date of onset
- Are lesions associated with changes of the skin?
- Duration of lesion
- Any changes in shape, size, or texture with time?
- Any previous response to therapy?
- What makes the pain or the lesions worse?
- Have lesions healed and recurred?

Infectious Diseases

Oral Candidiasis

- Affecting the **opportunistic infection.**
- Oral candidiasis is the most prevalent oral mucosa. In several cases, the lesions are caused by Candida albican.
- **The pathogenesis** is not fully understood, but several predisposing factors have been shown to convert C. albicans from the normal commensal flora (saprophytic stage) to a pathogenic organism (parasitic stage).
- C. albicans is usually a weak pathogen, **affecting the very young, the very old, the very sick.** Most candidal infections only affect mucosal linings, but rare systemic manifestations may have a fatal course.
- Oral candidiasis is divided into **primary and secondary** infections .The primary infections are restricted to the oral and perioral sites, whereas secondary infections are accompanied by systemic mucocutaneous manifestations

Etiology and Pathogenesis

- **C. albicans, C. tropicalis, and C. glabrata** comprise together over 80% of the species isolated from human candidal infections
- To invade the mucosal lining, the microorganisms must adhere to the epithelial surface; therefore, candidal strains with **better adhesion** potential are more virulent than strains with **poorer adhesion** ability.
- The yeasts' penetration of the epithelial cells is facilitated by their **production of lipases** and for the yeasts to remain within the epithelium, they **must overcome constant desquamation of surface** epithelial cells.

Predisposing Factors for Oral Candidiasis and Candida-Associated Lesions

Local Factors:

- Lack of saliva (medications causing dry mouth, autoimmune diseases, head and neck radiotherapy),
- Denture wearing,
- Topical steroid use,
- Use of antibiotics
- Immunosuppressive medications

Systemic conditions including

Diabetes, Immunosuppressive diseases-HIV Impaired health status
Chemotherapy Endocrine disorders Anemia - Hematinic deficiencies

- Rare systemic manifestations of candidal infections may have a fatal course and are major causes of morbidity and mortality, causing variety of diseases from mucosal infections to deep tissue disease, which may lead toward candidemia and organ involvement.

Classification of oral candidiasis:

Pseudomembranous—acute → Thrush

Pseudomembranous—chronic → With inhalers

Erythematous—acute atrophic → After antibiotic therapy

Erythematous—chronic atrophic → Denture stomatitis; in HIV

Chronic hyperplastic (nodular and plaque-like subtypes) → Candidal leukoplakia, median rhomboid glossitis

Candida-associated lesion → Denture stomatitis; angular cheilitis

Candidiasis affecting extraoral sites and conditions predisposing to candidiasis

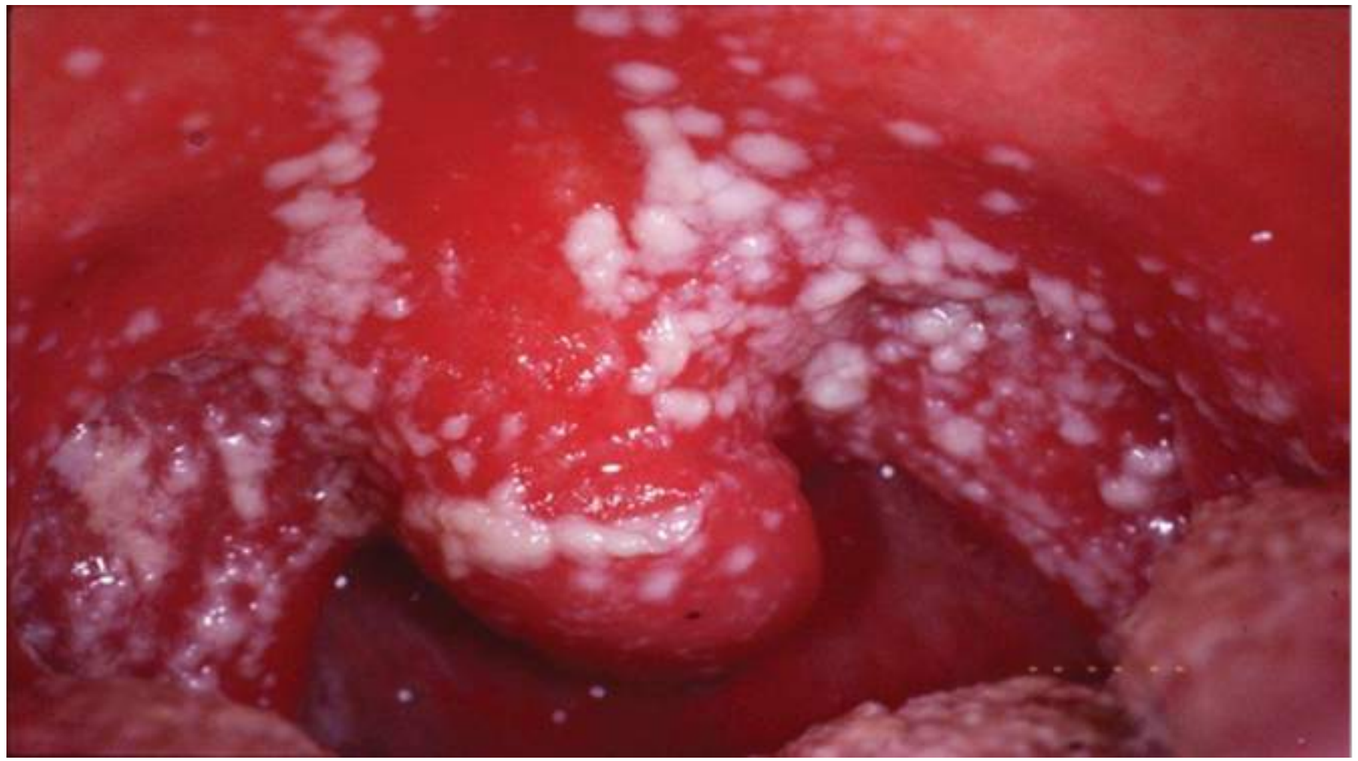
- Familial chronic mucocutaneous candidiasis
- Diffuse chronic mucocutaneous candidiasis
- Erythematous candidiasis endocrinopathy syndrome
- Chronic severe combined immunodeficiency
- DiGeorge syndrome
- Chronic granulomatous disease
- HIV disease

Epidemiology:

- Large geographic variations
- Candidal strains are more frequently isolated from **women**.
- A seasonal variation has been observed, with an increase during **summer** months.
- **Hospitalized patients** have a higher prevalence of the yeasts.
- In healthy individuals, **blood group O** and non-secretion of blood group antigens are separate and cumulative risk factors for oral carriage of C. albicans.
- In **complete denture-wearers**, the prevalence of denture stomatitis has been reported as nearly 70%.
- Candidiasis is frequently **over-reported** in those without experience of the normal anatomy of the oral cavity. Thus, even slight elongation of the filiform papillae on the dorsum of he tongue may be erroneously diagnosed as candidiasis.

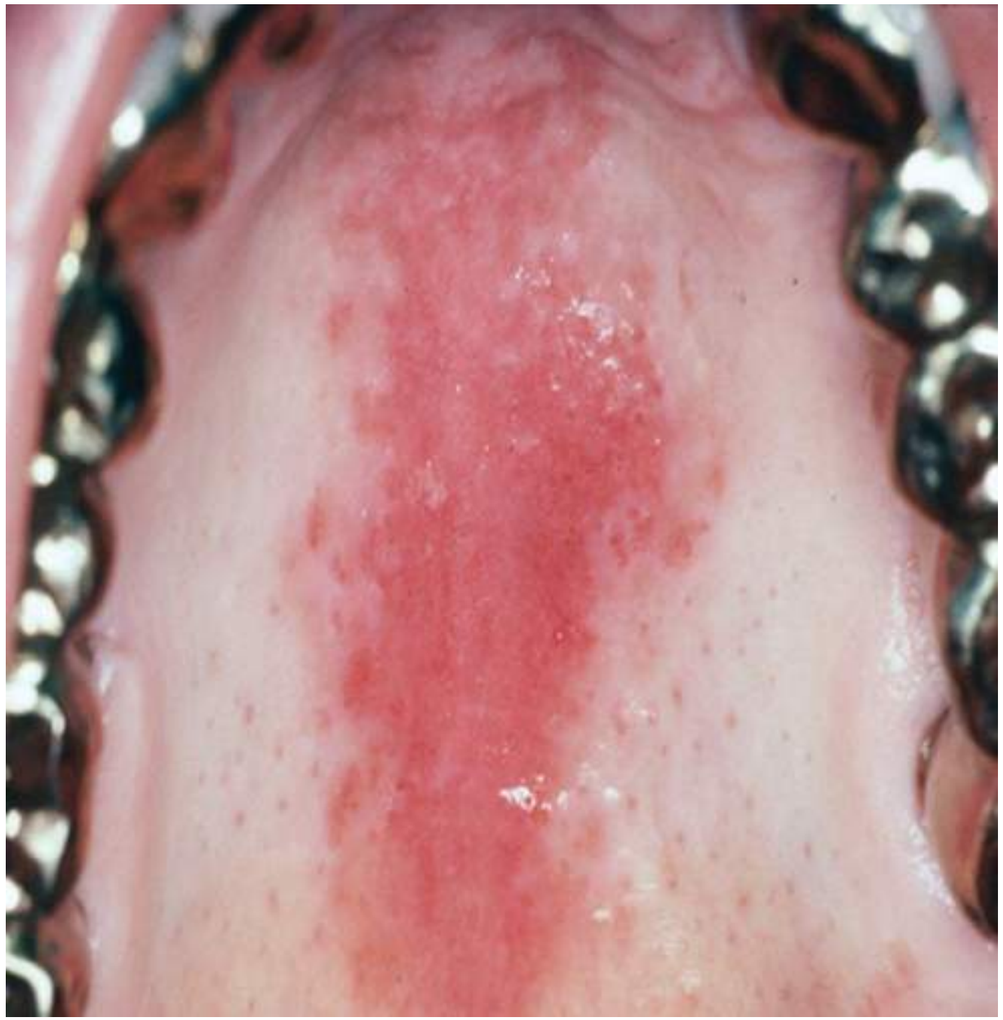
Pseudomembranous Candidiasis

- Acute form of pseudomembranous candidiasis (thrush) is grouped with the primary oral candidiasis. The infection predominantly affects patients taking **antibiotics, immunosuppressant agents, or having a disease that suppresses the immune system**.



Erythematous Candidiasis

- Erythematous atrophic oral candidiasis can reflect **atrophy** surface may not just has a diffuse border. The lesion has increased vascularization, to distinguish it from sharper demarcation that usually present in **erythroplakia**.
- The infection is predominantly seen in the **palate** and the **dorsum of the tongue** of patients who are using **inhalation steroids.**
- Other predisposing factors that can cause erythematous candidiasis are **smoking** and treatment with **broad-spectrum antibiotics**.



Chronic Plaque-Type and Nodular Candidiasis

- Replaces the older term, candidal leukoplakia.

oA **white irremovable plaque**

oCharacterizes the typical clinical presentation, which may be indistinguishable from **oral leukoplakia**

oA positive correlation between oral candidiasis and **moderate to severe epithelial dysplasia.**

oBoth the chronic plaque-type and the nodular type of oral candidiasis associated with malignant transformation. Carcinogenesis is unclear.

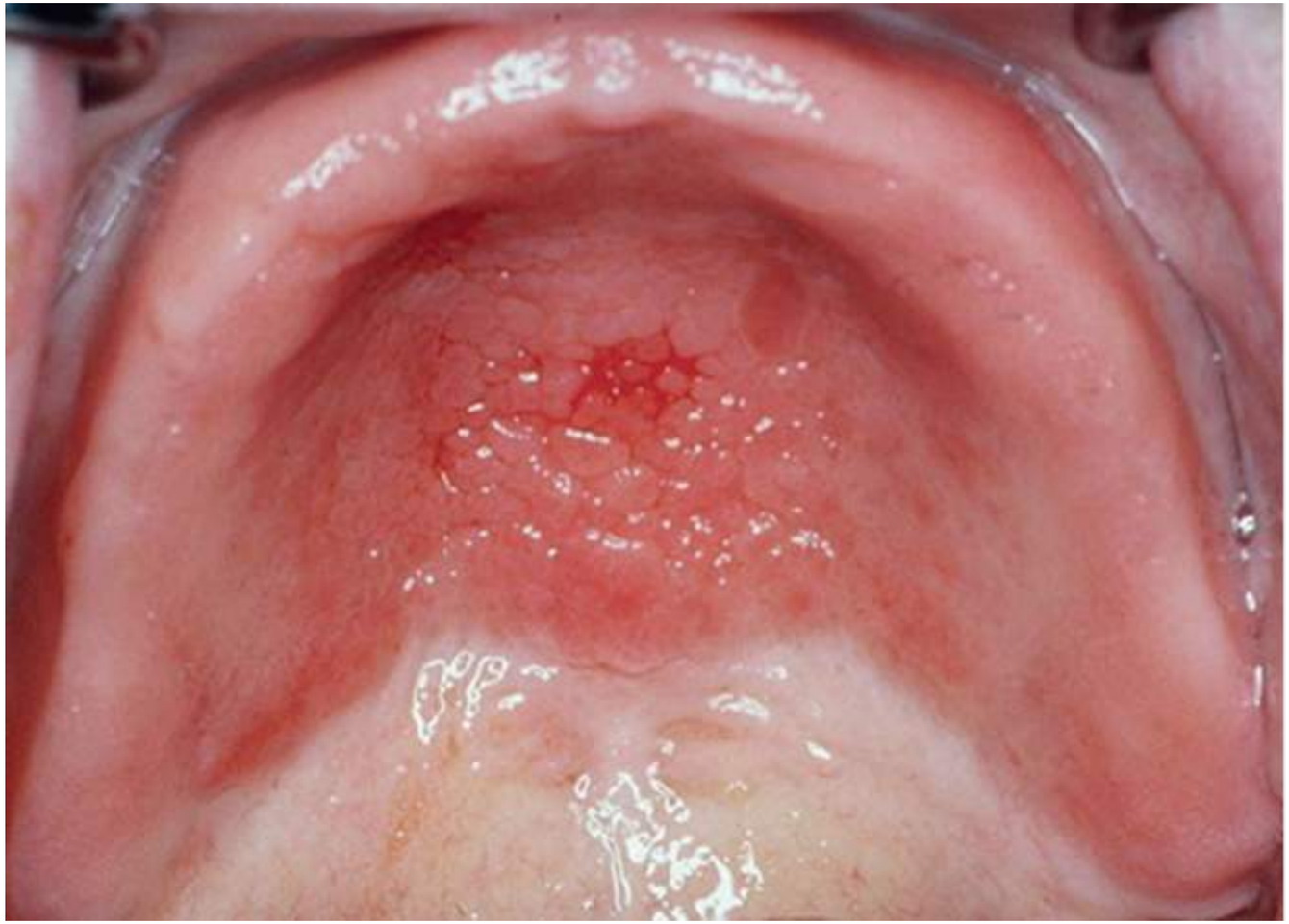
o It has been hypothesized that yeast may act through its capacity to catalyze **nitrosamin** production .

Denture Stomatitis

- The denture serves as a **vehicle that accumulates sloughed epithelial cells and protects the microorganisms from physical influences such as salivary flow.**
- The microflora is complex and may, in addition to C. albicans contain bacteria from several genera, such as **streptococcus-, Veillonella-, Lactobacillus-, Prevotella-Actinomyces-strains.**
- It is not known to what extent these bacteria participate in the pathogenesis of denture stomatitis

Denture stomatitis is classified into three different types:

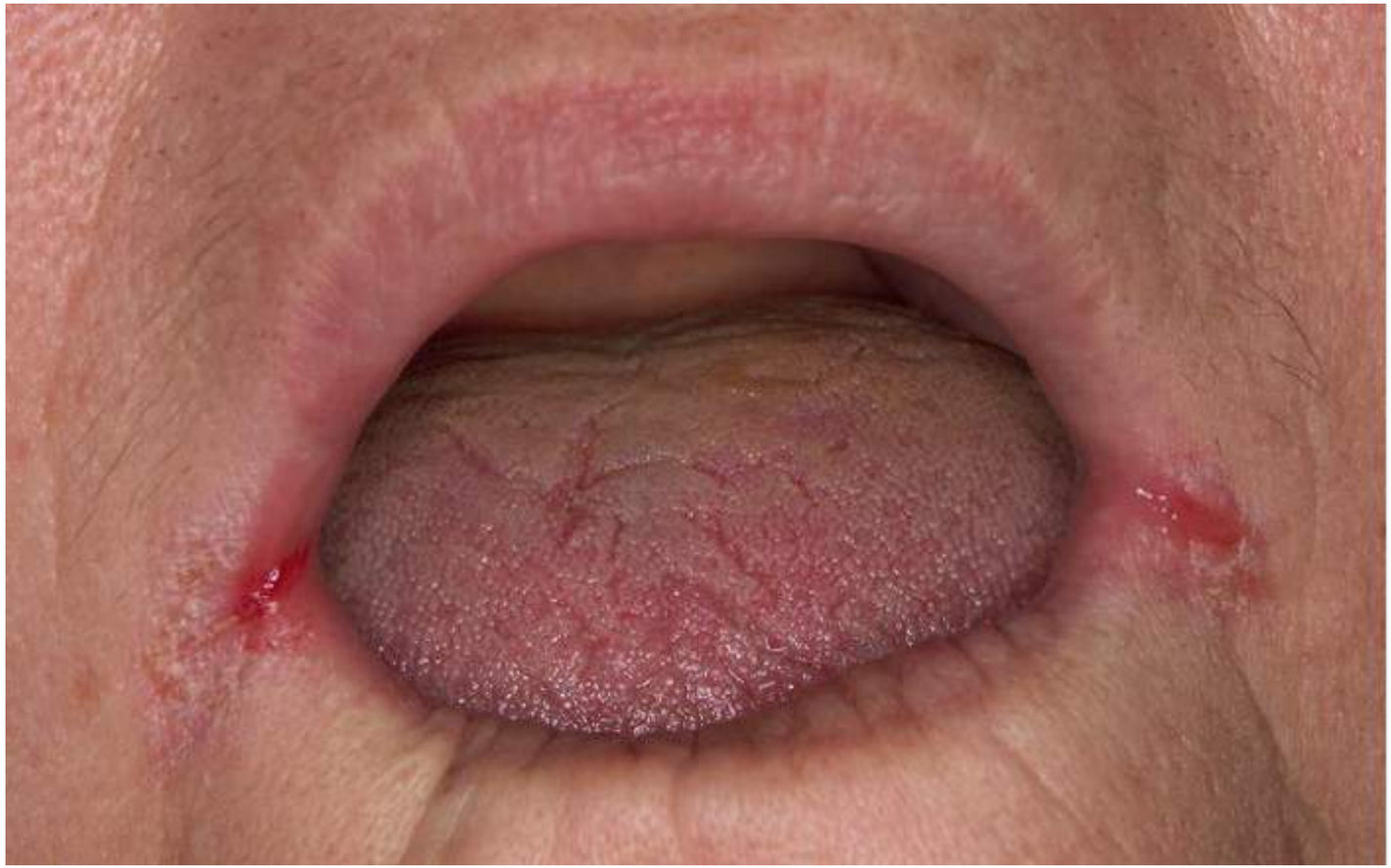
- **Type I** is limited to erythematous sites caused by trauma from the denture.
- **Type II** affects a major part of the denture-covered mucosa.
- **Type III** has a granular mucosa (reactive proliferation of underlying fibrous tissue) in addition to the features of type II.



Chronic atrophic candidiasis (denture stomatitis) type III with a granular mucosa in the central part of the palate

Angular Cheilitis

- Angular cheilitis presents as **infected fissures of the commissures of the mouth, often surrounded by erythema.**
- The lesions are frequently infected with both **Candida albicans and Staphylococcus aureus.**
- Loss of vertical dimention , iron deficiencies, and deficiency of Vitamin B 12 have been associated with this disorder.
- Dry skin may promote the development of fissures in the commissures, **allowing invasion** by the microorganisms.
- 30% of patients with denture stomatitis also have angular cheilitis, but this infection is only seen in 10% of denture-wearing



Candida-induced bilateral angular cheilitis. Treatment must include the intraoral Candida reservoir.

Median Rhomboid Glossitis

❖Clinically characterized by an erythematous lesion in **the center of the posterior part of the dorsum of the tongue;**

❖An oval configuration. This area of erythema results from atrophy of the filiform papillae and the surface may be lobulated.

❖The etiology is not fully clarified, but the lesion frequently shows a mixed **bacterial/fungal microflora.**

❖Biopsies yield candidal hyphae in more than 85% of the lesions.

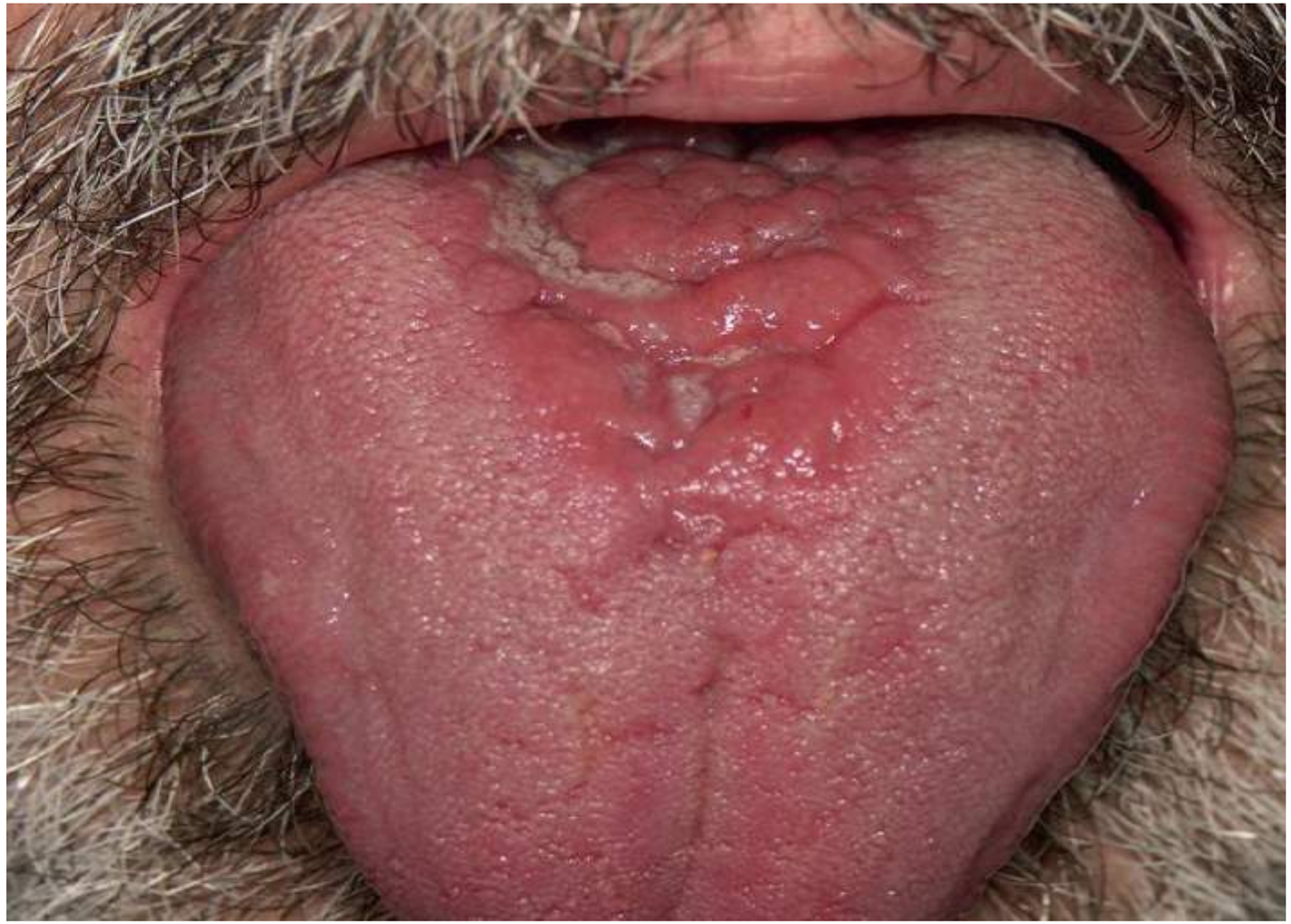
❖**Smokers** and denture-wearers have an increased risk of developing median rhomboid glossitis

❖**Patients using inhalation steroids**.

❖Sometimes a concurrent erythematous lesion may be observed in the palatal mucosa **(kissing lesions).**

❖Median rhomboid glossitis is **asymptomatic**, and management is restricted to a reduction of predisposing factors.

❖The lesion does not entail any increased risk for malignant transformation



Median rhomboid glossitis apparently arising from the junction of the posterior third and anterior two-thirds of the tongue. Histology confirmed chronic hyperplastic candidiasis.

Oral Candidiasis Associated with HIV

- More than **90%** of acquired immune deficiency syndrome (AIDS) patients have had oral candidiasis during their HIV infection, and the infection is considered a portent of AIDS development
- **The most common types of oral candidiasis in conjunction with HIV are** Pseudomembranous candidiasis, Erythematous candidiasis, Angular cheilitis, and chronic plaque-like candidiasis.
- As a result of the highly active antiretroviral therapy (HAART), the prevalence of oral candidiasis has **decreased** substantially.

Chronic mucocutaneous candidiasis (CMC)

➤Involves a heterogeneous group of disorders, which, in addition to oral candidiasis, also affect the **skin**, typically the **nail** and other mucosal linings, such as the **genital mucosa**.

➤The **face and scalp** may be involved.

➤Approximately 90% of the patients with CMC also present with oral candidiasis.

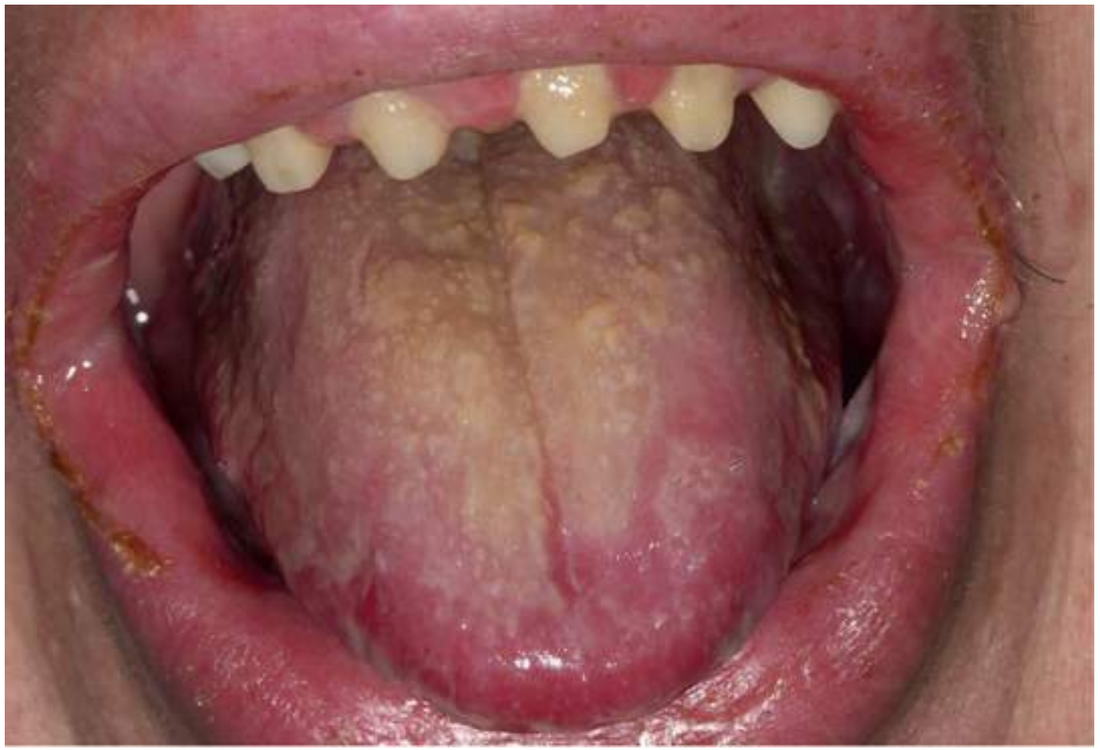
➤The oral manifestations may involve the tongue, and lesions are seen in conjunction with fissures.

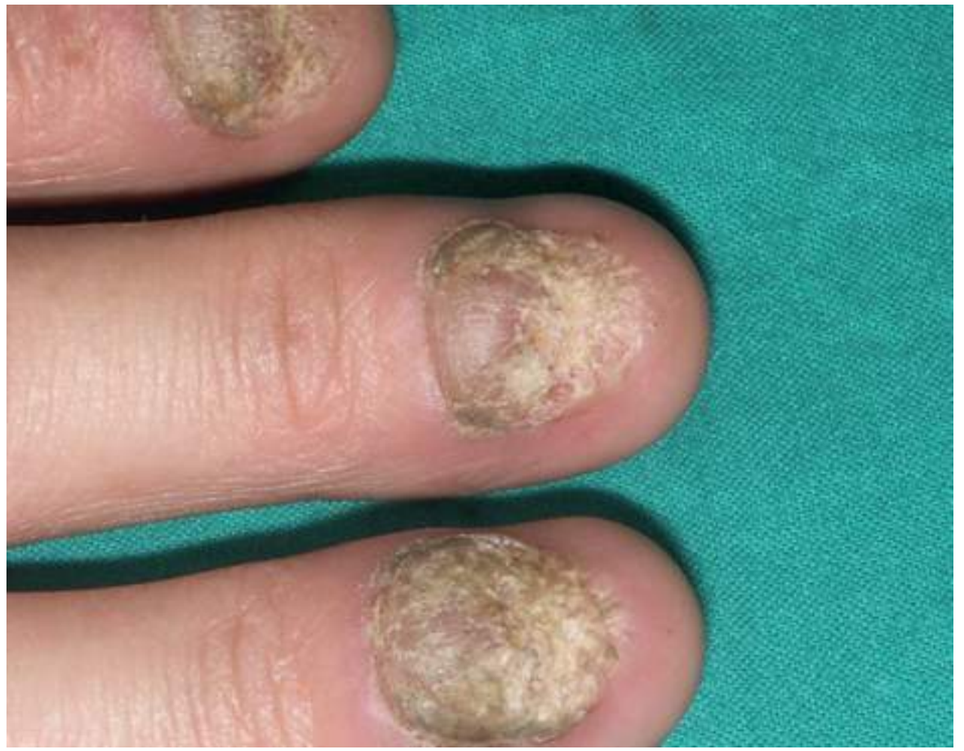
➤CMC can occur as part of endocrine disorders, including hyperparathyroidism and Addison's disease.

➤Recent studies revealed that an impairment of interleukin- 17 (IL-17) immunity underlies the development of CMC

➤T-helper 17 cells produce IL-17 and play an important role in host mucosal immunity to Candida.

- **Impaired phagocytic function by neutrophilic granulocytes and macrophages caused by myeloperoxidase (MPO) deficiency (oxidative stress plays a key role in the release of MPO from these cells)**
- **Severe combined immunodeficiency** (SCID) syndrome is characterized by a defect in the function of the cell-mediated arm of the immune system.
- Patients with this disorder frequently contract disseminated candidal infections.
- **Thymoma i**s a neoplasm of thymic epithelial cells that also entails systemic candidiasis. Thus, both the native and adaptive immune systems are critical to prevent development of systemic mucocutaneous candidiasis





Chronic candidiasis of (A) dorsum of tongue and (B) fingernails of a patient with chronic mucocutaneous candidiasis

Diagnosis and Laboratory Findings

- The presence of candidal microorganisms as a member of the commensal flora **complicates** the discrimination of the normal state from infection.
- The detection of yeast organisms in the form of hyphae- or pseudohyphae-like structures is usually considered a sign of infection .
- To increase the sensitivity, a second scrape can be transferred to a transport medium followed by caltivation.
- Techniques are primarily used in parallel with other **culture.**
- **Salivary** diagnostic methods to obtain an adequate quantification of candidal usually **oral candidiasis clinical signs of** organisms.

- In chronic plaque-type and nodular candidiasis, cultivation techniques must be supplemented by a histopathologic examination. This examination is primarily performed to identify the presence of **organisms by candidal** invading and to identify **epithelial dysplasia**.
- **PAS staining Smears (cytology) Swabs Culture of saliva (or saline rinses) for cfu/Ml.**
- **Oral candidiasisRoutine tests for patients with suspected**
- **Biopsies Hematology Full blood picture, liver function tests Hematinics (iron/ferritin, folate, vitamin B12) Immunology, endocrinology.**
- Candida cells can be found in 60% of people in numbers of up to 500 cfu/mL as **normal commensals**. /mL cfu000 ,10over increase to , these numbers may **indicate infection.** However, and any increase to over 1000 cfu/Ml may be seen in candidal infections.

Management:

- **Antifungal** treatment for fungal infections. Treatment will not always be successful unless the clinician addresses **the predisposing factors.** Local factors are often easy to identify but sometimes not possible to reduce or eradicate.

➤Elimination or reduction of predisposing factors should always be the first goal for treatment

➤This involves improved denture hygiene, not to use the denture while sleeping.

➤**In smokers**, cessation of the habit may result in **disappearance** of the infection even without antifungal treatment.

➤Antifungal drugs belong to the groups of **polyenes or azoles** in **first choices**are usually the **B Polyenes such as nystatin and amphotericin** treatment of primary oral candidiasis and are both well tolerated.

- Different solutions ,including alkaline peroxides, alkaline hypochlorites, acids, disinfectants, and enzymes which seems to be most effective against candidal strains.
- Chlorhexidine may also be used **but can discolor the denture and also counteracts the effect of nystatin.**

➤The denture hygiene is important to remove nutrients, including desquamated epithelial cells, which may serve as a **source of nitrogen** essential for the growth of the yeasts.

➤Denture cleaning also disturbs the maturity of a microbial environment established under the denture.

➤**Porosities** in the denture can harbor microorganisms, which may not be removed by physical cleaning, the denture should b**e stored in antimicrobial solutions during the night**

➤**Systemic azoles** may be used for deeply seated primary candidiasis, such as **chronic hyperplastic candidiasis**, granular with **median rhomboid glossitis** , and **denture stomatitis.**

➤Topical treatment with **azoles** such as **miconazole** is the treatment of choice for **angular cheilitis** often infected by **both S. aureus and candidal strains. (biostatic effect on S. aureus in and fungistatic effect).**

➤If angular cheilitis comprises an erythema surrounding the fissure, a may be required to suppress the inflammation. Mild **steroid ointment**

➤To prevent recurrences, patients to apply a **moisturizing cream**, which may prevent new fissure formation.

➤**Type III denture stomatitis** may be treated with **surgical excision** to eradicate microorganisms present in the deeper fissures of the granular tissue. If this is not sufficient, continuous treatment with topical antifungal drugs should be considered.

There are several disadvantages with the use of azoles:

➤They are known to interact with warfarin, leading to an increased bleeding propensity.

➤Topical application as the azoles **are fully or partly resorbed from the GIT**.

➤**Development of resistance** is particularly compelling for **fluconazole** in individuals with HIV disease. In such cases, **ketoconazole and itraconazole** have been recommended as alternatives.

➤The **azoles** are also used in the treatment of secondary oral candidiasis associated with systemic predisposing factors and for systemic candidiasis.

Prognosis of oral candidiasis

- Good prognosis when the predisposing factors reduced or eliminated.
- Nodular candidiasis and chronic plaque type been suggested to be associated with an increased risk malignant transformation compared with leukoplakia infected with candidal strains.

Oral Hairy Leukoplakia(OHL)

❖Is the second most common **HIV-associated oral mucosal lesion**. HL has been used as a marker of disease activity since the lesion is associated **with low CD4+ T-lymphocyte counts.**

❖The lesion is not pathognomonic for HIV disease since other states of immune deficiencies, such as caused by immunosuppressive agents.

❑Is strongly associated with **Epstein-Barr virus (EBV) and with low levels of CD4+ T lymphocytes.**

❖ **Antiviral medication**, which prevents EBV replication, is curative

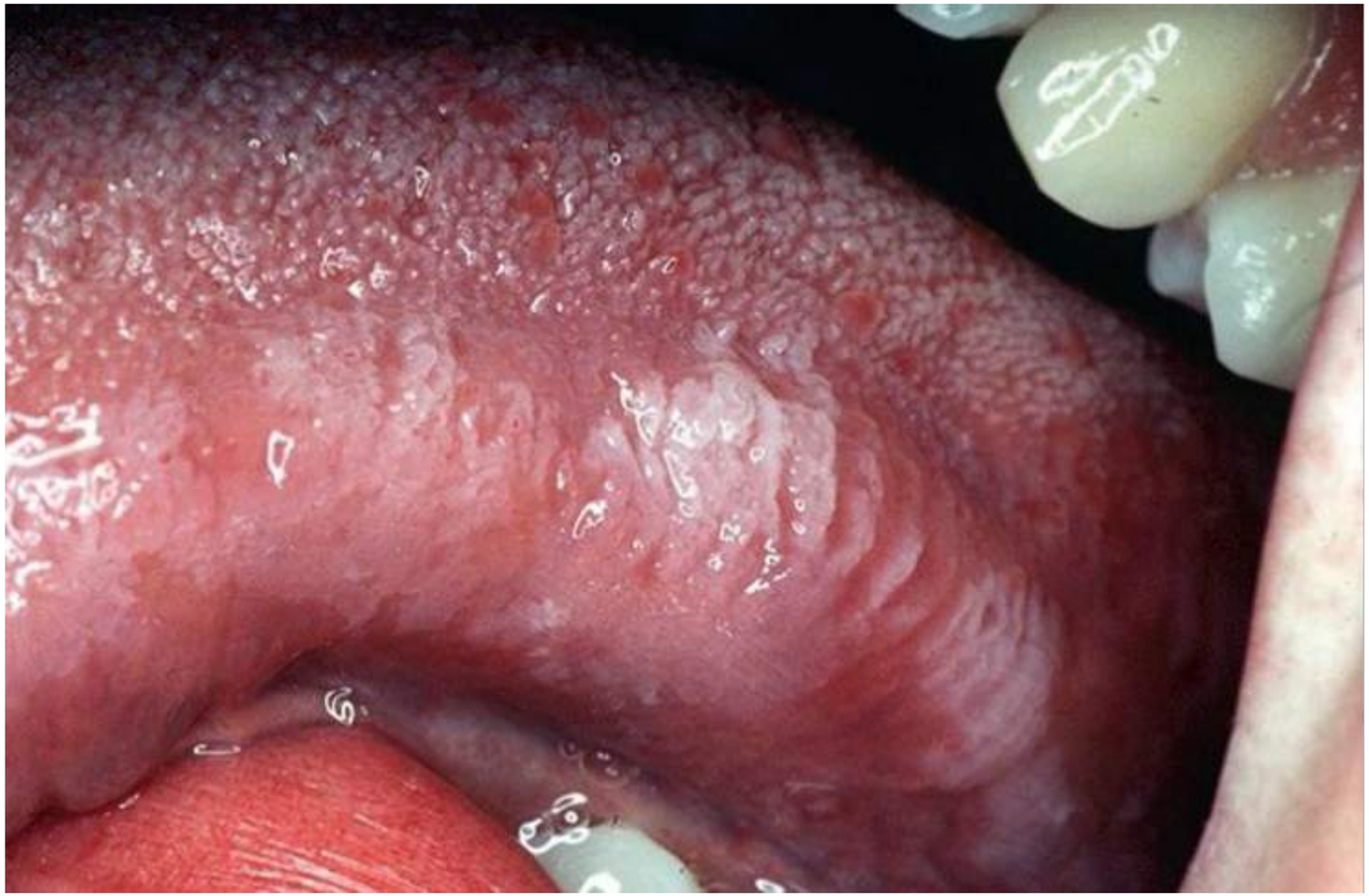
❑ In **AIDS,** the prevalence may be as high as 80%.

❑ In children the prevalence is **lower** compared with adults (2%).

❑ Is more frequently in **men**, but the reason for this predisposition is not known.

❑ A correlation between **smoking** and OHL has also been observed

❑ Immunosuppressive medications and cancer chemotherapy, have also been associated with OHL .



Hairy leukoplakia at the left lateral border of tongue in an AIDS patient showing vertical keratotic corrugations.

Clinical Findings

✔Is frequently encountered on the lateral borders of the tongue but may also be observed on the dorsum and in the buccal mucosa

✔is asymptomatic, although symptoms may be present when the lesion is **superinfected with candidal strains**

✔**it is important to always consider mucosal lesion whenever the border of the tongue is affected by white lesions, particularly in immunocompromised patients**

Diagnosis: **A diagnosis of OHL is usually based on can be performed to EBV detection of histopathologic examination and confirm the clinical diagnosis**

Management

➤It can be treated successfully with **antiviral medication**, but this is not often indicated as this disorder is **not associated with adverse symptoms**.

➤The disorder may show spontaneous regression.

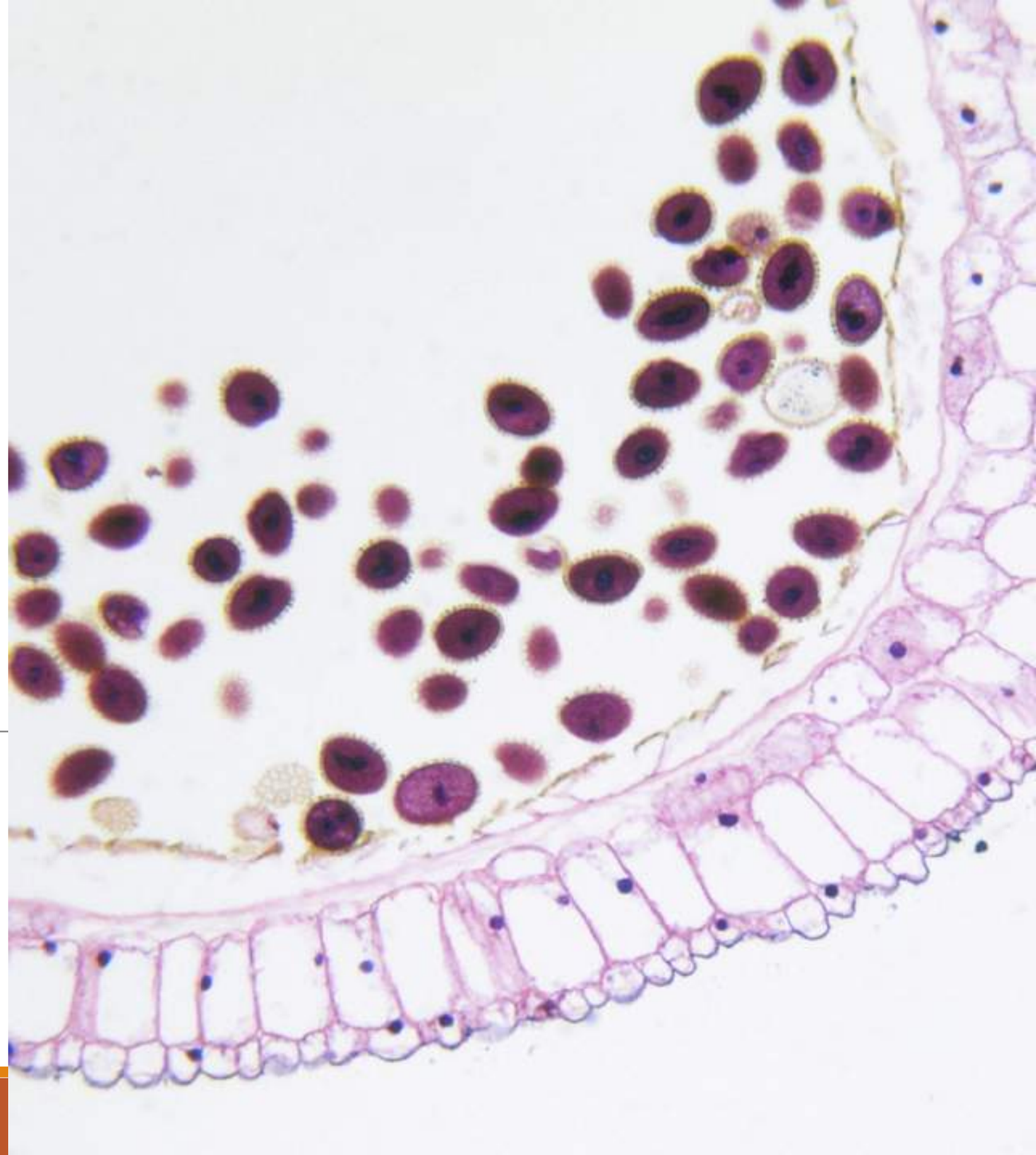
➤OHL is not related to increased risk of malignant transformation

Medication with Antiretroviral therapy(ART) has reduced the number of OHL to a few percent in HIV-infected patients

Red and White Lesions of the Oral Mucosa

PART -2

Dr. Marwah Waleed



Oral Potentially Malignant Disorders (PMD)

The development of oral leukoplakia and erythroplakia as potentially malignant lesions, involve different genetic events. **Pathogenesis**; the markers of genetic defect is differently expressed.

❖Following a **series of mutations,** a malignant transformation may occur. For example: Carcinogens such as **tobacco** may induce hyperkeratinization, tobacco-associated leukoplakia; which is reversible following cessation, but at some stage, mutations will lead to an unrestrained proliferation and cell division.

Oral Leukoplakia

is a white plaque of questionable risk for malignant transformation having excluded other known white lesions or disorders that carry no increased risk for cancer. Leukoplakia is thus a diagnosis of exclusion. Leukoplakia is idiopathic.

➤Smoking is recognized as an etiological or exacerbating factor and smoker's keratosis may regress when the irritant is removed.

❖**The prevalence** Oral Leukoplakia according a comprehensive global review points 1.5 - 2.6%

❖Most oral leukoplakias are seen in patients beyond the age of 50 and infrequently encountered below the age of 30.

❖Leukoplakias are more common in men but a slight majority for women has been found in some studies.

It can be divided into:

: **Homogeneous type** characterized as a white, often well-demarcated plaque with an identical reaction pattern throughout the entire lesion. **Non-homogeneous type**

Non-homogeneous type combined appearance of white and red areas, also been called **erythroleukoplakia** and **speckled leukoplakia.**

❖Oral leukoplakia may be found at all sites of the oral cavity

❖**Non-smokers** have a higher percentage of leukoplakias **at the border of the tongue compared with smokers.**

The floor of the mouth and the lateral borders of the tongue have been considered high-risk sites for malignant transformation

❑These sites have also been found to have a higher frequency of loss of heterozygosity compared with low-risk sites. The relative importance of one versus the other is that leukoplakia is **very common** and **can sometimes** transform into cancer, whereas erythroplakia is rather **uncommon** but **frequently represents a precursor to cancer**.

❑However, the distinction between high- and low-risk sites has been questioned leaving: ➤The size of the lesion ➤Homogenous/non-homogenous pattern being for the prognosis

❑**Hairy leukoplakia** is not considered a true leukoplakia, since the etiology and infective agent (EBV) are known, and the risk of malignant transformation appears to be almost nonexistent.

Oral erythroplakia

Erythroplakia is a **fiery red patch** that cannot be characterized clinically or pathologically as any other definable disease.

Oral erythroplakia Is not as common as oral leukoplakia, and the prevalence has been estimated to be in the range of 0.02 – 0.1%.

❖The gender distribution is reported to be equal.

Erythroplakia is usually asymptomatic, although some patients may experience a burning sensation with food intake.

A special form of erythroplakia has been reported in India , predominantly practiced (reverse smoking of chutta) Which require exclusion of other similar-looking lesions of known causes or mechanisms.

Diagnosis

- The provisional diagnosis is based on the clinical observation of a white or red patch that is not explained by a definable cause, such as **trauma**.

- If trauma is suspected, the cause, such as a sharp tooth or restoration, should be eliminated.

- **If healing does not occur in two weeks, a tissue biopsy is essential to rule out malignancy**

➤It has been reported that **91%** of histologically assessed erythroplakias showed invasive carcinoma or carcinoma in situ, and in **9%** there was moderate to severe dysplasia. Another study showed that severe dysplasia and frank carcinoma in 75% and mild to moderate dysplasia in 25%.

➤Any **red mucosal lesion** without an apparent local cause or not fitting into other known red lesions and not regressing following removal of possible cause or two weeks of treatment, should be considered a cancer unless histologically proven otherwise.

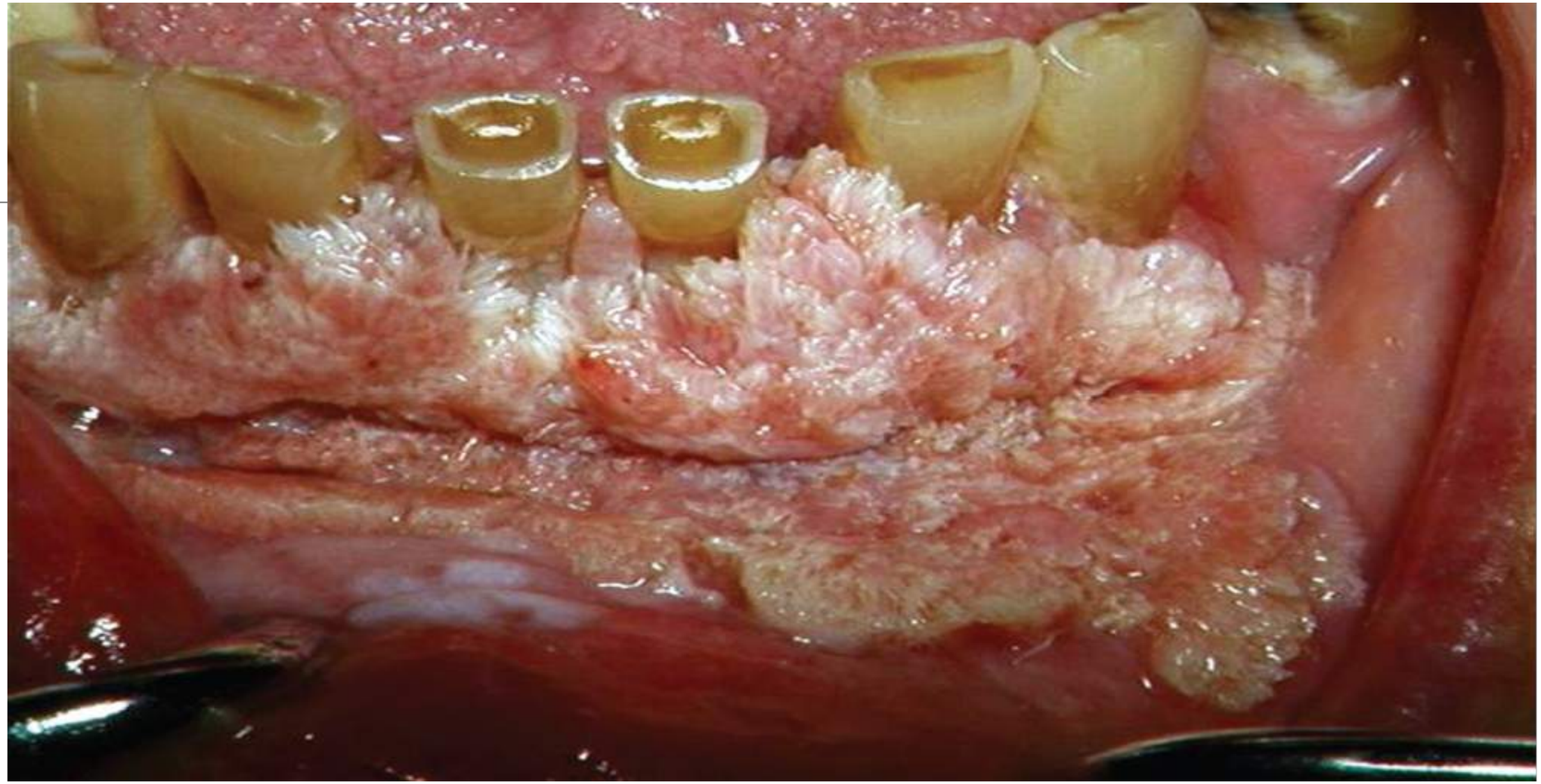
Proliferative verrucous leukoplakia(PVL)

White component is dominated by papillary projections similar to oral papilloma,is referred to **verrucous or verruciform oral leukoplakia.**

- PVL is seen in **older women**, and the **lower gingiva.**
- The malignant potential is **very high** and verrucous carcinoma or squamous cell carcinoma may be present at the primary examination. It is highly aggressive and high recurrence rate.
- Similar to what is seen in oral papillomas, the PVL has been suspected to have a **viral etiology.**

Diagnosis: can not be established at a single consultation.

Histologically: may appear benign but clinically it behaves as malignancy with spreading leukoplakia often gingivally.



A proliferative verrucous leukoplakia in an 80-year-old woman

Erythroplakia and Oral Leukoplakia pathology

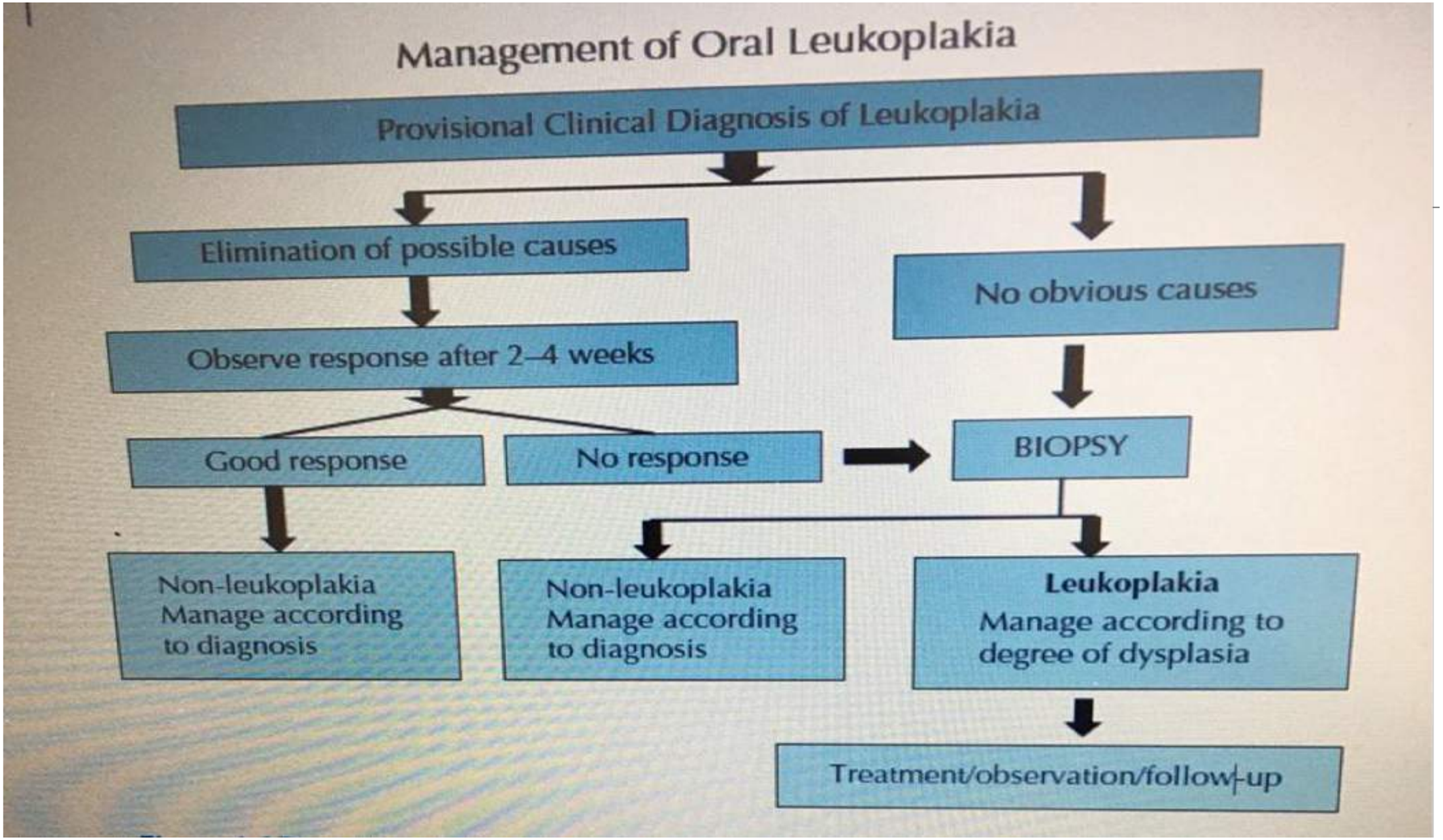
Epithelial dysplasia may be found in homogeneous leukoplakia , but is more frequently seen in **non-homogeneous leukoplakias and in erythroplakias.**

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

- The prevalence of dysplasia in oral leukoplakias varies from 1-30%, presumably due to various lifestyle.

- Since alcohol and smoking are well established risk factors for oral squamous cell carcinomas, measures should be taken to influence the patients to discontinue such habits.

- **Cold-knife surgical excision, as well as laser surgery**, is widely used to eradicate leukoplakias and erythroplakias but will not prevent all premalignant lesions from malignant development.


Management of Oral Leukoplakia
Provisional Clinical Diagnosis of Leukoplakia
Elimination of possible causes
Observe response after 2–4 weeks
Good response
No response
No obvious causes
BIOPSY
Non-leukoplakia
Manage according
to diagnosis
Non-leukoplakia
Manage according
to diagnosis
Leukoplakia
Manage according to
degree of dysplasia
Treatment/observation/follow-up

• **Squamous cell carcinomas are almost equally prevalent in patients subjected and not subjected to surgery.**• This may be explained by genetic defects even in clinically normal mucosa surrounding the removed lesion and is supported by a concept of **Field of Cancerization. It is referred to as genetic instabilities in the epithelium tof several extra lesional sites that may lead to SCC**.

• **Surgery** will remain the treatment of choice for erythroplakias and oral leukoplakia.

• **Malignant transformation of oral leukoplakias; up 20% over 30 years depending on site and habits. Homogeneous leukoplakias** are associated with a decreased risk for malignant transformation than **nonhomogeneous and erythroplakias**, and lesions not exceeding **200 mm2** appear to have a better prognosis than **larger** lesions.

➤A general recommendation is to reexamine the premalignant site irrespective of surgical excision every **three months** for **the first year**.

➤ If the lesion does not relapse or change in reaction pattern, the follow-up intervals may be extended to **once every six months**.

➤New biopsies should be taken if new clinical features emerge.

➤**Following five years** of no relapse, self-examination may be a reasonable approach.

Oral Submucous Fibrosis

- Is a chronic disease affecting the oral mucosa, pharynx and the upper two-thirds of the esophagus.

- **Areca nuts** in **the etiology behind oral submucous fibrosis.**
- Areca nut–derived products are commonly used in ASIA. There is **dose dependence** between **areca quid** chewing habit and the development of this oral mucosal disorder.

- Areca nuts **contain alkaloids, coline** seems to be a primary etiologic factor. **Arecoline** has the capacity to modulate **matrix metalloproteinases**, **lysyl oxidases**, and **collagenases**, all affecting the metabolism of collagen, which leads to an **increased fibrosis**. A **decrease** in water retaining proteoglycans will occur in favor of **increased** **collagen type I** production.
- Genetic predisposition of importance for the etiology. **Polymorphism of the gene**, which is coding for **tumor necrosis factor α** (TNF-α), has been reported.
- **Fibroblasts are stimulated by TNF-α**,participating in the development of fibrosis.

- Abnormalities of other cytokines of importance are transforming growth factor β and interferon-γ, which may lead to increased production and decreased degradation of collagen.
- Oral complications are most observed: on the **lips, buccal mucosa, retro molar area, and soft palatal mucosa.**
  - The global incidence estimated at 2.5 million individuals.
  - Individuals in less than 20 years old seem to be affected more commonly.

Clinical Findings

➤The **First Signs** are **eythematous lesions, sometimes in conjunction with petechiae, pigmentations,and vesicles.**

➤Followed by a **paler mucosa**, (white marbling)

➤The most prominent clinical characteristics include **fibrotic bands located beneath an atrophic epithelium.**

➤Increased fibrosis eventually interferes with **speech, tongue mobility, and a decreased ability to open the mouth.**

➤**The atrophic epithelium may cause inability to eat hot and spicy food**.

Diagnosis

- The diagnosis is based on the clinical features and the patients report of areca chewing habit.
- **An international consensus has been reached that one of the following clinical characteristics should be present:**

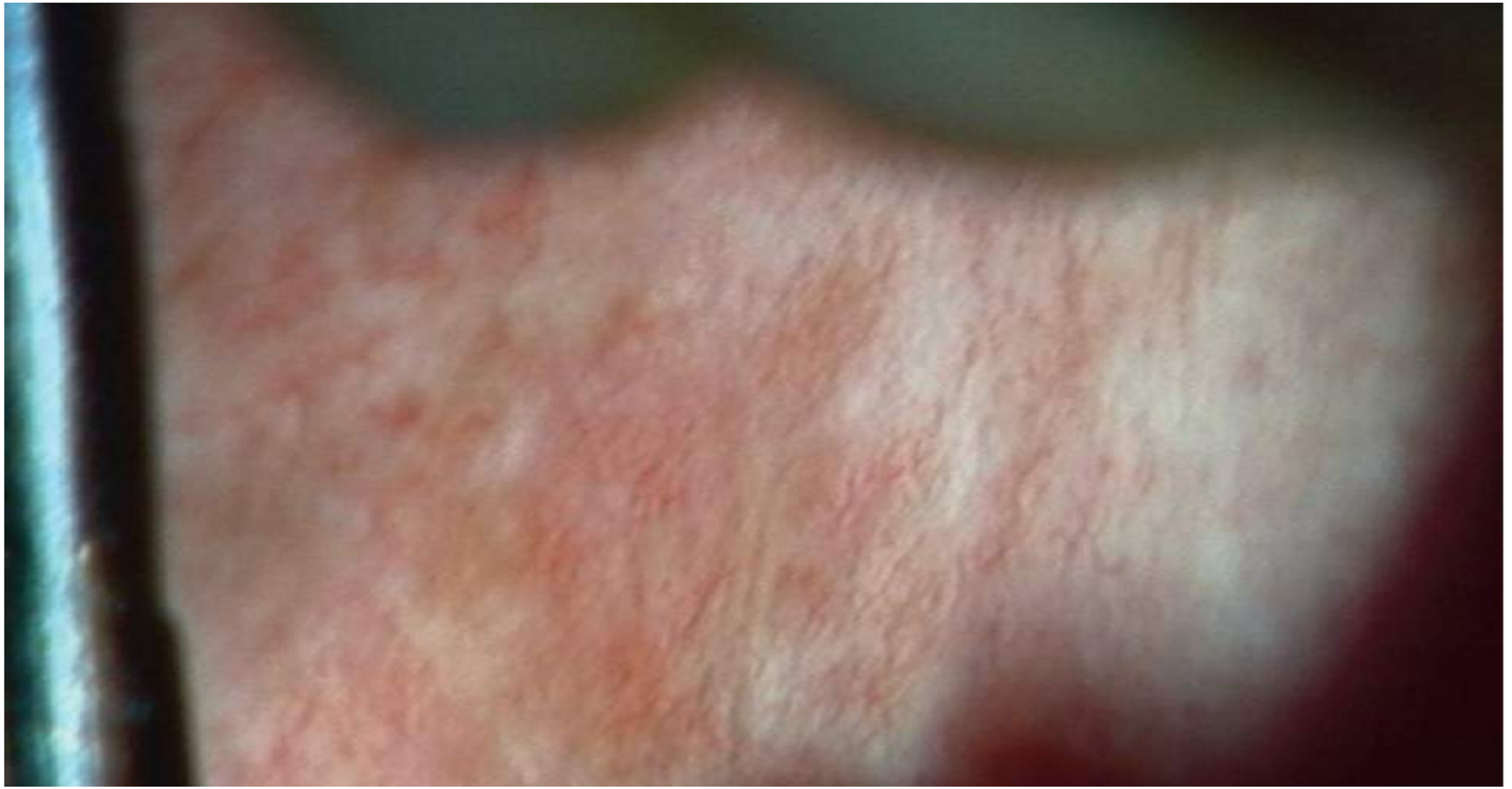
1. **Palpable fibrous bands**
2. **Mucosal texture feels tough and leathery**
3. **Blanching of mucosa together with histological features (Atrophic epithelium with loss of rete ridges and juxta-epithelial hyalinization of lamina propria).**

Management

- Products derived from areca nuts are carcinogenic, regardless of concomitant use of tobacco products.
- Cessation of the chewing habits . If this is successfully implemented, early lesions have a good prognosis as they may regress.
- Several treatment strategies have been tried, such as:

- **Topical and systemic steroids,**
- **Hyaluronic acid, interferon γ,**
- **Supplement of vitamins and nutrients, Repeated dilatation with physical devices, and surgery**.

- None of these treatments have reached general acceptance and the long-term results are uncertain.
- **Malignant transformation** of oral submucous fibrosis has **0.7–1.3%** per annum and the incidence over a 10-year period at approximately 8%.
- **Epithelial dysplasia** in OSMF tissues appeared to vary from 7- 25%.



Marble-like appearance of the right buccal mucosa in a patient with submucous fibrosis

Immunopathologic Diseases

Lichen Planus:

- It is a family of lesions with different etiologies with a common clinical and histologic appearance.
- **Neither clinical nor histopathologic** features enable discrimination between different lichenoid reactions but may be used to distinguish **them** from other pathologic conditions of the oral mucosa.

- **Skin and mucous membranes** are most involved. In addition to oral mucosa, other mucous membranes (e.g., genitals in women, esophagus, rectal area) as well as scalp and nails can be affected.

  This group include the following disorders:

  - **Oral lichen planus**
  - **Oral lichenoid contact reactions**
  - **Oral lichenoid drug eruptions**
  - **Oral lichenoid reactions of graft-versus-host disease (GVHD)**

Oral Lichen Planus

✔The etiology is not known

✔It has become evident that the **immune system** has a primary role in the development of this disease. This is supported by the **histopathologic characteristics of a subepithelial band–formed infiltrate(in the lamina propria) dominated by T lymphocytes and macrophages and the degeneration of basal cells known as liquefaction degeneration.**

- ✔ **Cytotoxic CD8+ T lymphocytes** are responsible for **apoptosis** of the keratinocytes in the basal cell layer. ✔These features can be interpreted as an expression of the cell-mediated arm of the immune system being involved in the pathogenesis of OLP through **T-lymphocyte cytotoxicity directed against antigens expressed by the basal cell layer**.

✔It is not possible to identify a single etiologic factor behind OLP. Other factors, such as **stress**. It is not unusual that patients report that they have been exposed to negative social events months before the onset of the disease.

➤During recent years, an association between OLP and **hepatitis C virus (HCV) has been described , possibly geographically based.**
➤OLP prevalence is also enhanced in those with **thyroid diseases**.
➤Prevalence OLP have been reported and vary from 0.5 – 2.2%
➤Among referred patients, **women** is higher than that of men,
➤The condition usually occurs in people **older than 40 years, the mean age of onset being 53 years.** ➤It is very rarely encountered in children,
➤Does not seem to have a hereditary predisposition.

Clinical Oral Findings:

- Some have long periods of **remission**, while others have frequent **exacerbations** and are not very responsive to treatment.
- OLP may contain both red and white elements which can be a part of the following clinical types:**(Reticular,Papular,Plaque-like,Bullous,Erythematous ,Ulcerative).**
- **OLP confined to the gingiva may be entirely erythematous, with no reticular or papular elements present.**

- **Different clinical manifestations of OLP** is related to the magnitude of the **subepithelial inflammation**. **A mild degree** of inflammation provoke the epithelium to produce **hyperkeratosis**, whereas **more intense inflammation** will lead to **partial or complete deterioration of the epithelium**.

➤Typically, OLP is bilateral (symmetric) and can appear both white and red, depending on disease activity

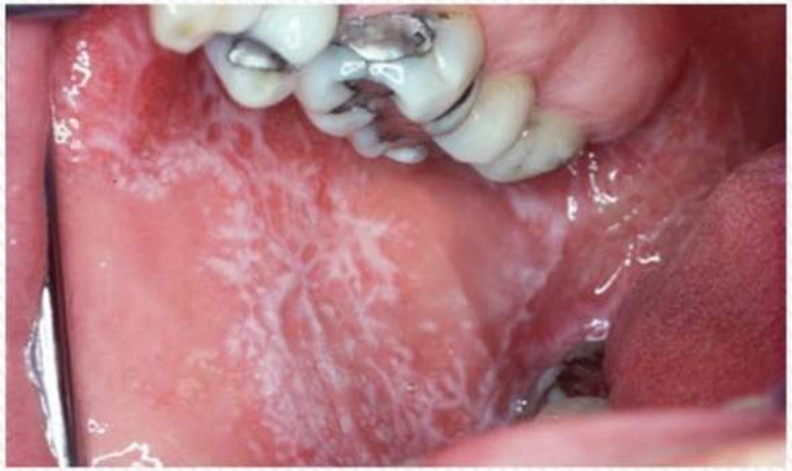
➤Hyperkeratotic white striations **Wickham's striae**, which are a **hallmark** of the condition.

❑**Reticular, papular, and plaque-like** are **asymptomatic**, although the patient may experience a **feeling of roughness**.

❑The **bullous** form is very unusual but may appear as bullous structures surrounded by a reticular network.

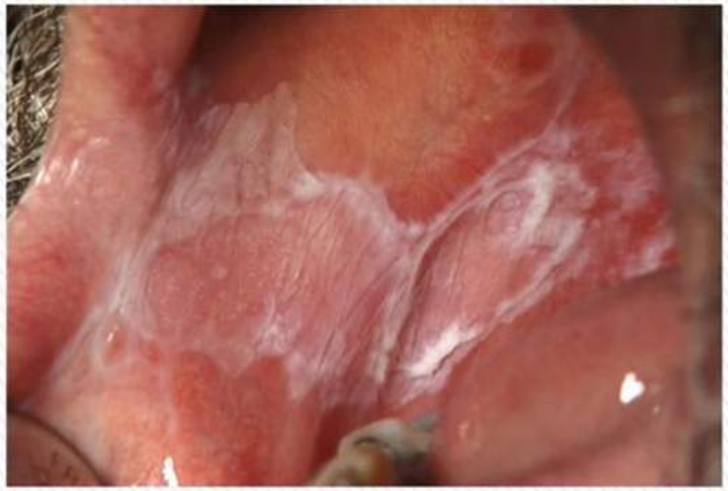
❑**Erythematous** (atrophic) OLP: **Homogeneous red area** in the buccal mucosa or in the palate, striae are frequently seen in the periphery of the lesion.

❑**Ulcerative** lesions are the **most disabling** form of OLP. **Fibrin-coated ulcers** are surrounded by an erythematous zone with white striae in the periphery.

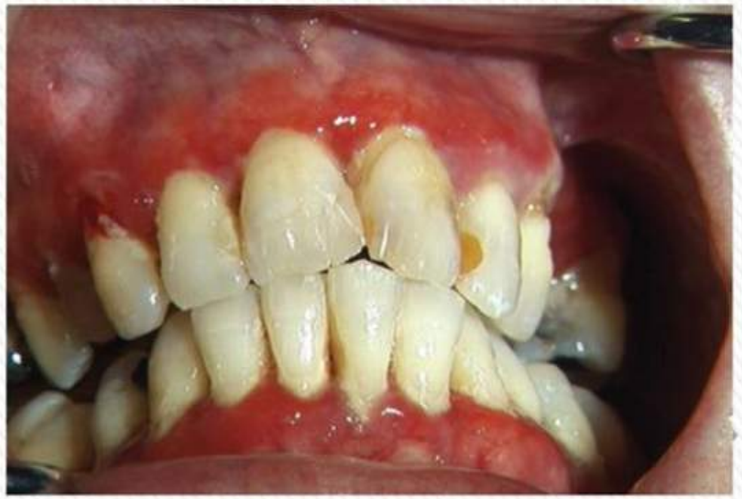


A reticular

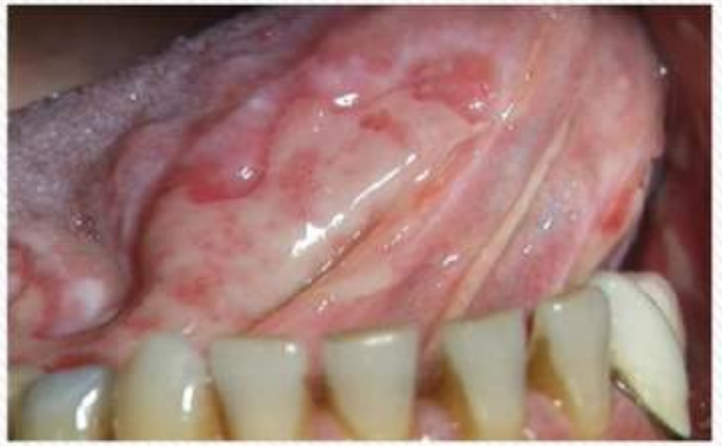
Papular



A plaque-like



Erythematous



Ulcerative

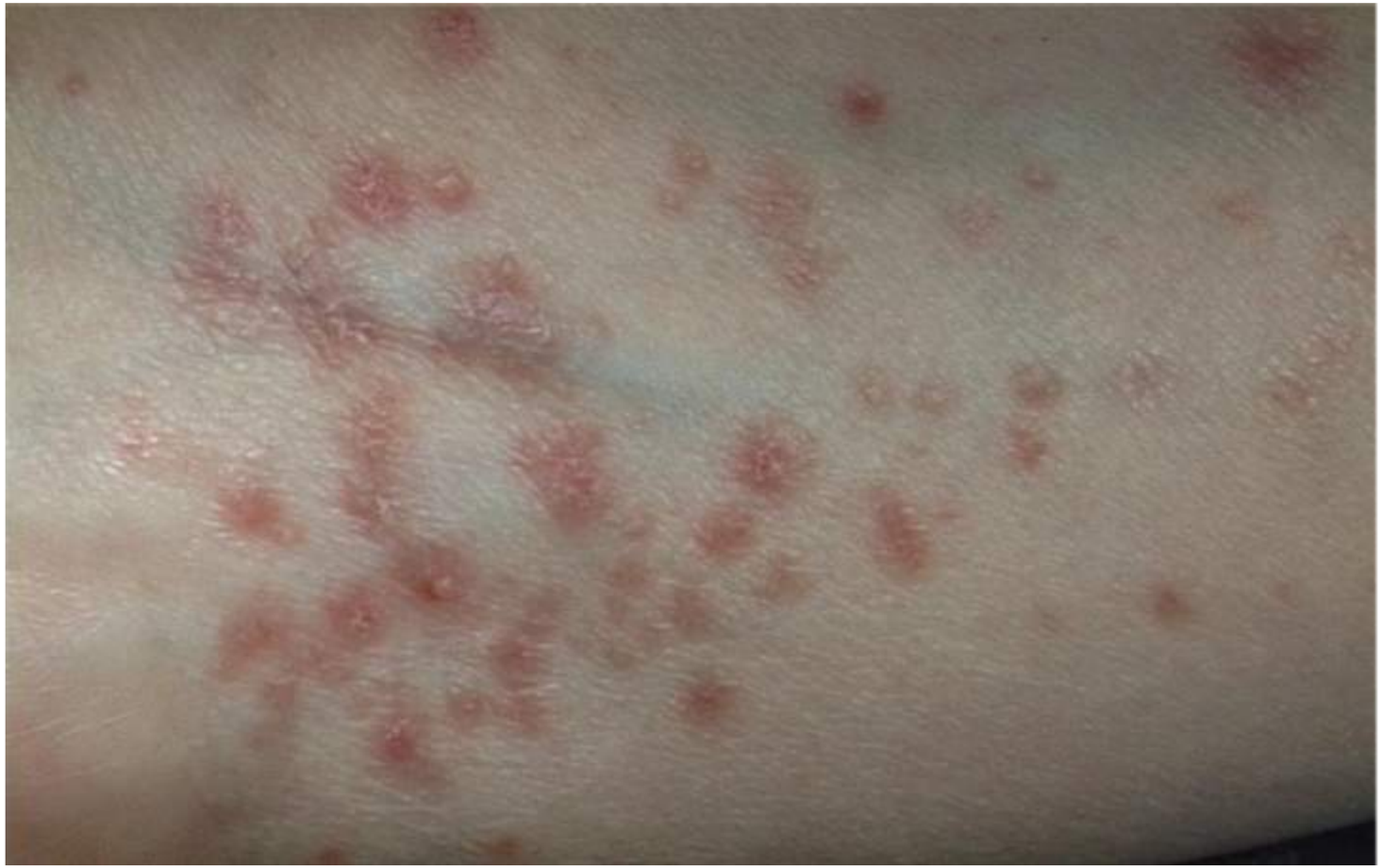
Clinical Manifestation

❖Cutaneous lesions may be seen in approximately15% with classic appearance **of pruritic erythematous flat topped skin lesions**.

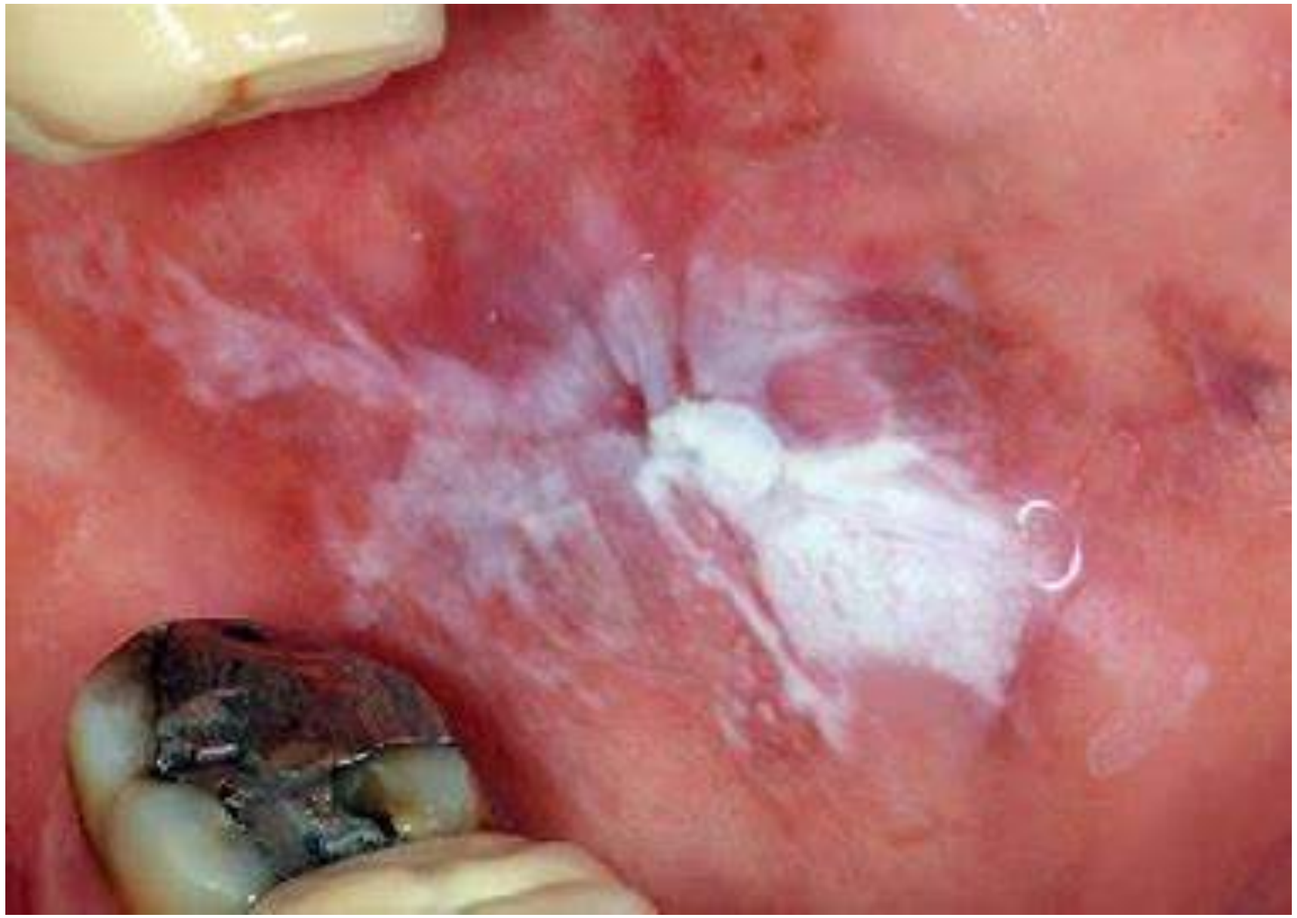
- The predilection sites are the trunk and flexor surfaces of arms and legs.

❖ The **most frequent** extra-oral mucosal site involved is the genital mucosa; in 20% of women with OLP. Symptoms including burning, pain, vaginal discharge,

❖Following intense scratching of the lesions, trauma may aggravate the disease, which is referred to as a **Koebner phenomenon** (appearance of new skin lesions on previously unaffected skin secondary to trauma). This phenomenon may also be of relevance for OLP, which is continuously exposed to physical trauma during mastication and brushing.

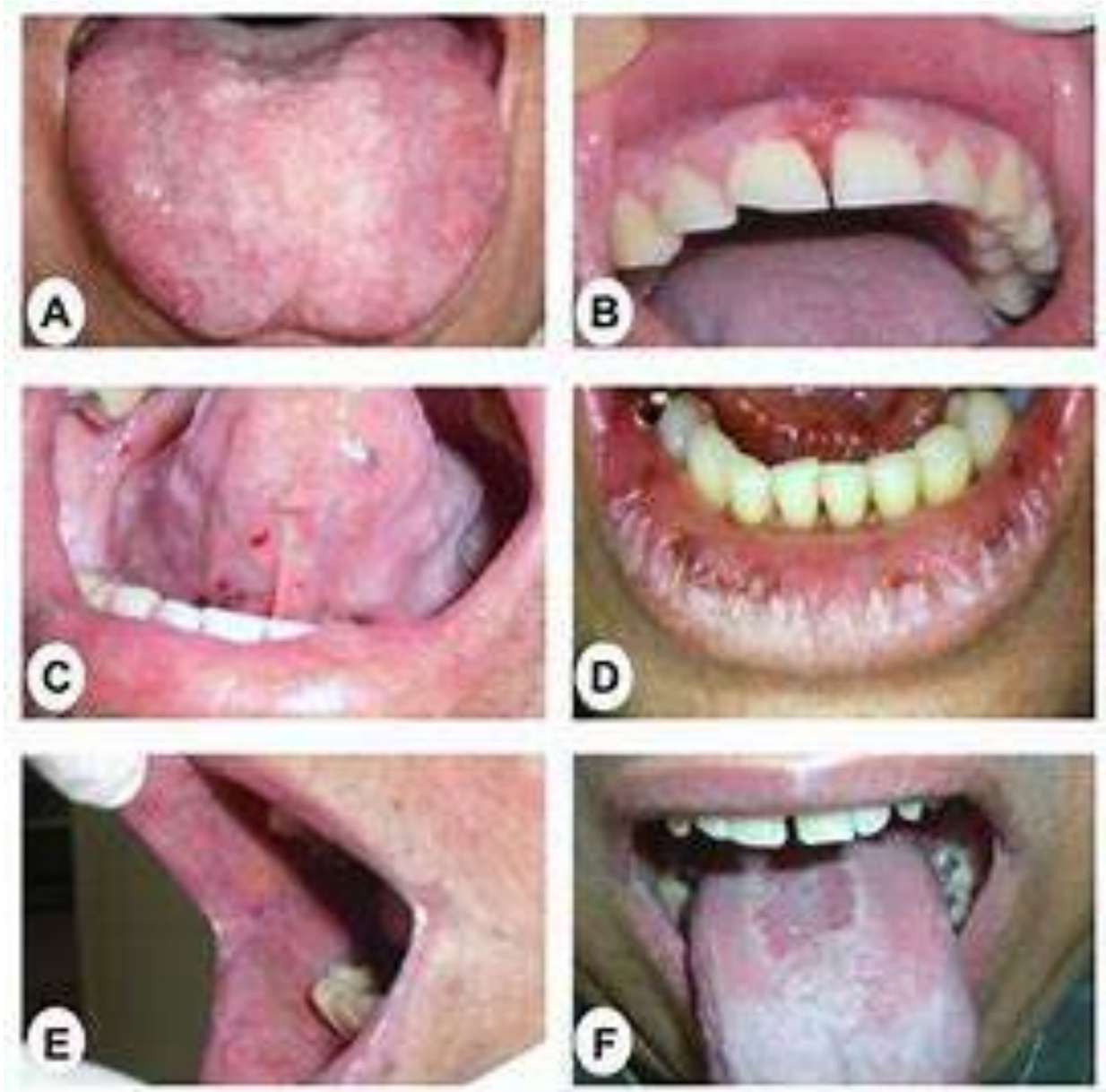


Cutaneous lichen planus on the flexor side of the fore arm.



Lichenoid contact reactions

- To **dental materials**, which are most often detected on the buccal mucosa and the lateral borders of the tongue.
- **OLP** , on the other hand, usually displays a **more general involvement.**



Oral graft- versus host disease (OGVHD)

- Has the same clinical appearance as OLP, but the lesion is usually more generalized.

The **lichenoid reactions** are frequently seen simultaneously with other characteristics, such as xerostomia and the presence of localized skin involvement and liver dysfunction.

Oral lichenoid drug eruptions

- Have **the same** clinical and histopathologic characteristics as OLP.

➤The patient's disease history may give some indication as to which **drug** is involved, but lichenoid drug eruptions **may not start when the drug was first introduced**. **Withdrawal** of the drug are the most reliable way for diagnosis.

➤An OLDE may not develop for several months after a new drug is started.

➤It may also take **several weeks** before an OLDE disappears following withdrawal. The delay between exclusion of the offending drug and regression of the lesion indicates that the drug molecule has sensitized the epithelium, which may persist regardless of drug withdrawal.

- Examples of drugs which have been associated with lichenoid reactions. **Angiotensin-converting enzyme inhibitors, Antimalarials(Barbiturates Colchicine, Dapsone, Gold, Hydroxychloroquine), Metformin, Nonsteroidal anti-inflammatory drugs, Penicillamine, Phenothiazines, Phenytoin, Sulfonamide, Tetracyclines.**

Oral and genital lichen planus

- No relationship seems to exist between the degree of severity in the oral and genital sites. Genital LP has been reported in males, but the association with OLP is not as frequent as for women.
- Esophageal lichen planus has been described to occur simultaneously with OLP in some patients, the main complaint being dysphagia

Diagnosis

➤Papules or reticular components must be present. **These pathognomonic** components may exist together with plaque-like, erythematous, bullous, or ulcerative lesions.

➤**In patients with gingival erythematous lesions**, it may be difficult to find striae or papules. A biopsy is usually required for an accurate diagnosis of this type of OLP.

➤It is important that the biopsy is taken as far as possible from the **gingival pocket** to avoid inflammatory changes due to periodontal disease.

Oral mucosal lesions that do not belong to the group a lichenoid reactions may sometimes comprise a differential diagnostic problem:

1.Discoid lupus erythematosus (DLE) shows white radiating striae sometimes resembling OLP. The striae in DLE are **typically more prominent, with a more marked hyperkeratinization, and the striae may abruptly terminate against a sharp demarcation**

- Histopathologic criteria for lupus erythematosus (LE) is different from those of OLP.

2. **Plaque-like OLP** is discriminated from **homogeneous oral leukoplakia** as the latter is not featured with papular or reticular elements.

3. Erythematous OLP of the gingiva exhibits a similar clinical presentation as mucous membrane pemphigoid.

- In **pemphigoid** lesions, the epithelium is easily detached from the connective tissue by a probe or a gentle searing force **(Nikolsky's phenomenon). A biopsy** for routine histology and direct immunofluorescence are required for an accurate differential diagnosis.

4. Ulcerating conditions such as erythema multiform and adverse reactions to non-steroidalanti-inflammatory drugs (NSAIDs) may be difficult to distinguish from **ulcerative OLP**. The former lesions, however, do not typically appear with reticular or papular elements in the periphery of the ulcerations.

Management

- Since the etiology behind OLP is unknown, basic conditions for development of preventive therapies are lacking.
- Current therapies are directed **against: (1) Immune mechanisms using immunosuppressives; (2) the cellular inflammatory response using anti-inflammatories; and (3) reducing or eliminating symptoms**

➤Careful oral hygiene to reduce biofilm-associated supplementary inflammation is extremely important in OLP patients with symptoms.

➤Several topical drugs have been suggested, including steroids, retinoids, and ultraviolet phototherapy.

➤Topical steroids: **clobetasol propionate** as a **potent steroids,** the primary treatment of choice in favor of **Triamcinolone acetonide** such as **intermediate steroids.**

➤**Cyclosporine** may be considered a **second choice**.

➤**Tacrolimus** should only be used by experts when symptomatic OLP lesions are recalcitrant to topical steroids.

Topical steroids

- Mouth rinse or a gel are preferred and often easier for the patient to administer than a paste. Two to four times a day for one to two months, **followed by tapering during the following eight weeks until a maintenance dose of two to three times a week is reached.**
- Fungal infection may emerge, and a parallel treatment with **antifungal drugs** may be necessary
- **For more widespread lesions** , betamethasone is more useful. **Dexamethasone 0,5 mg/5 mL rinse can be applied three times** a day for three minutes, gradually decreasing the number of applications following the improvement.

➤**Adhesive pastes** consisting of pectin, gelatin, and carboxymethyl cellulose containing topical steroids (e.g., triamcinolone) have been formulated for use on moist oral mucosal surfaces.

➤**Ointments** containing steroids can also be effective, but as they are hydrophobic, they require drying of the mucosal surface before application.

- **Topical application** of **cyclosporine and tacrolimus** has been suggested as a substitute topical therapy in OLP patients who develop candidiasis Cyclosporine has been reported to be less effective than clobetasol propionate. No adverse effects related to these two drugs have been reported, except for a **temporary burning sensation following the use of cyclosporine.**

Systemic Therapy

Systemic steroids used to control symptoms from recalcitrant lesions.

- A dose of 0.5–1 mg/kg prednisolone daily for seven days has been suggested, followed by a reduction of 5 mg each subsequent day. Maintenance dose with topical steroids may be commenced during tapering of systemic steroids.
- However, **before switching to systemic steroids**, the use of peri or intralesional steroids should be considered.Usually, 0.2–0.5 mL of 40 mg/mL methyl prednisolone or triamcinolone suspension is injected around and under the erosive lesion of OLP.

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Management of Erythematous OLP of the gingiva:

- it is critical to remove both **sub- and supragingival plaque and calculus**.

If a **microbial plaque–induced gingivitis,** make the lesion more resistant to pharmacologic treatment.

- Thus, oral hygiene should be optimized prior to the beginning of steroid treatment. Once the hygiene treatment is complete, some patients experience a decrease in or even elimination of symptoms and steroid treatment is no longer justified.
- If symptoms persist, **steroid gels** in **prefabricated plastic trays** may be used for **30 minutes** at each application to increase the concentration of steroids in the gingival tissue.

Drug-Induced Lichenoid Reactions management:

✔ Not conjugated with severe life-threatening reactions such as toxic epidermal necrolysis.

✔Discontinuance of the drug and symptomatic treatment with topical steroids are often sufficient.

✔The patient should be properly educated about the responsible drug to prevent future REACTION.

Management of Lichenoid Reactions of GVHD:

- The major cause of GVHD is **allogeneic hematopoietic cell.** Oral lichenoid reactions as part of GVHD may be seen both in acute and chronic GVHD transplantation
- Clinically are indistinguishable from OLP, that is, reticulum, erythema, and ulcerations, but lichenoid reactions associated with GVHD are typically associated with a more widespread involvement.
- It **is not possible** to distinguish between OLP and oral GVHD based on clinical and histopathologic features.
- **Topical steroid** preparations, such as fluocinonide and clobetasol gel.
- Opportunistic infections such as **candidiasis** should always be considered in immunosuppressed patients.
- The development of **secondary malignancies** has been recognized as a potentially serious complication of GVHD.
- Patients with a history of oral GVHD should therefore be examined for oral malignancies as part of the **medical follow-up**

Malignant transformation of OLP

- A recent systematic review pooled 7806 of OLP patients from 16 follow up studies on the risk of malignant transformation showed a wide variations of (0,03% to 1,3%).
- Patients thus need to be realistically informed about a small but increased risk of developing oral carcinoma.
- No clear relationship with the clinical phenotype has emerged and the site and the severity seems to be important.

Red and White Lesions of the Oral Mucosa

PART -3

Dr. Marwah Waleed

Lupus Erythematosus (LE)

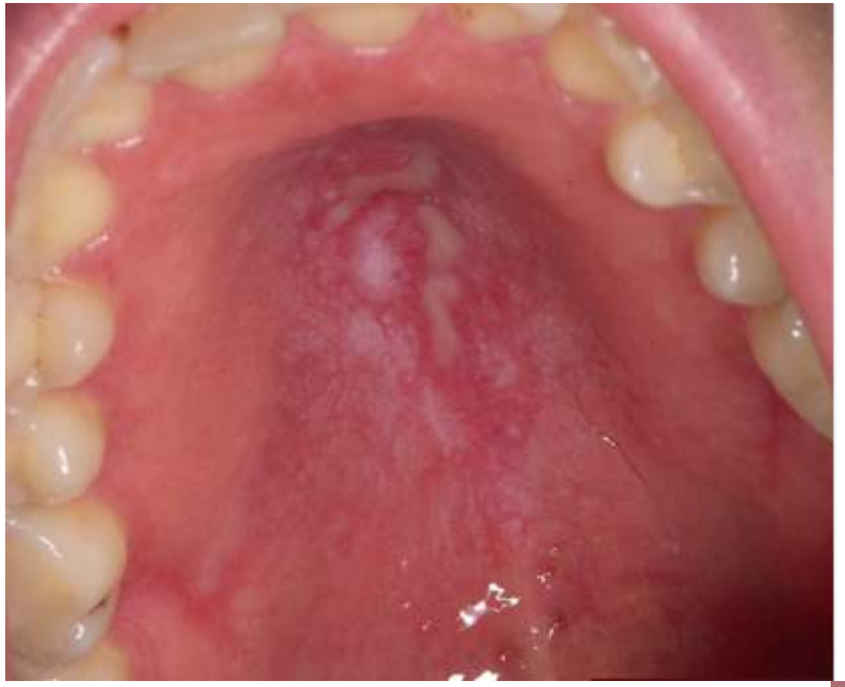
- Innate and adaptive (B and T lymphocytes) arms of the immune system participating in LE.

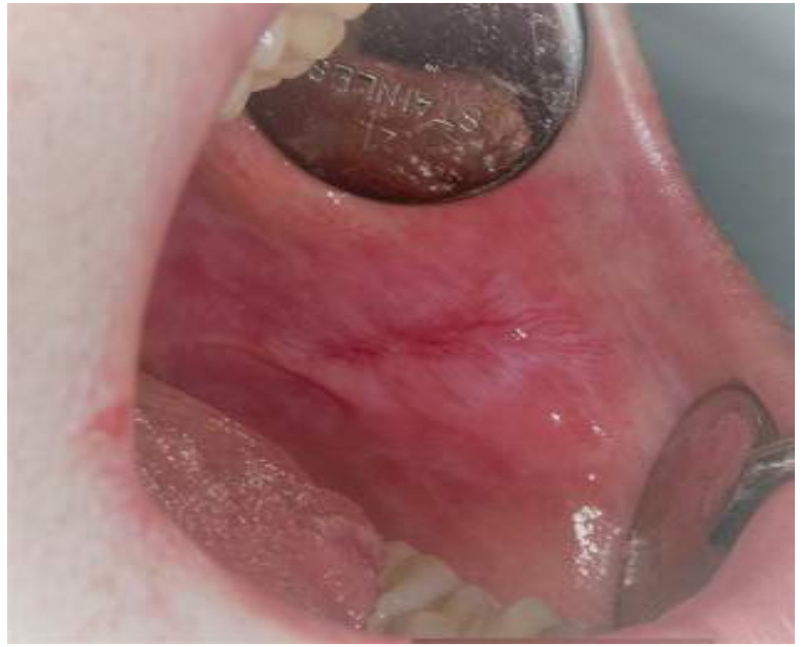
?❖**Environmental factors** as **sun exposure**, **medications, chemical substance**s, and **hormones** are aggravating factors of this disease.

❖**A genetic predisposition** is supported by an elevated risk for siblings to develop LE

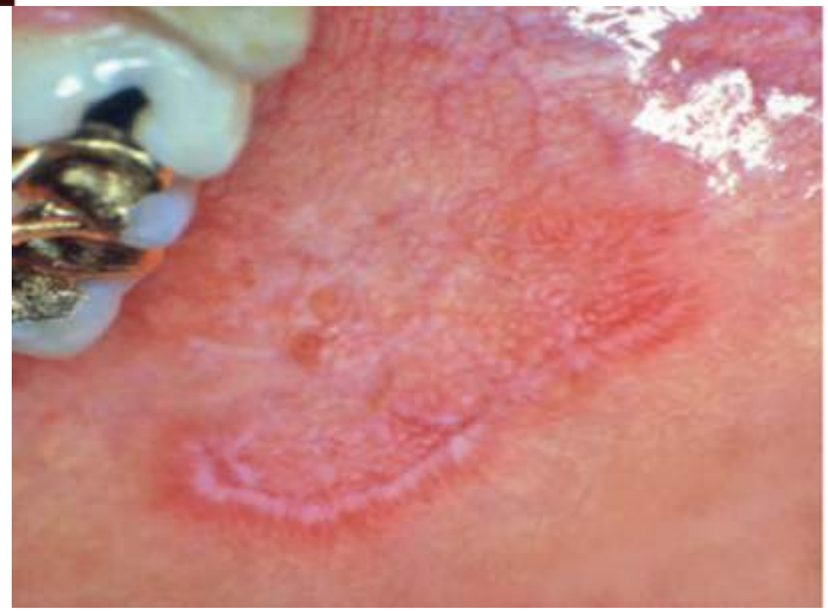
❖**Hydralazine, methyldopa, chlorpromazine, isoniazid, quinidine, and procainamide** have been associated with the onset of SLE.

❖SLE predominantly affects **women** of reproductive age (20–40 years)and decreases during the menopause. Hormones may participitate in the pathogenesis of LE as well as the fact that the disease can be precipitated by hormonal drugs.





Discoid lupus erythematosus lesions



- 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 **hard palate buccal mucosa, and gingiva**.
- The tongue also can be involved, lesions in the palatal mucosa can be dominated by erythematous lesions and white structures **may not** be observed.
- The typical oral DLE lesion is **a well-demarcated lesion with a mixed center and with a brush border of fine striae around the lesion. They are usually asymmetric or scattered, in contrast to OLP.**
- **Oral mucosa lesions compatible with LE may be the first sign of the disease.**
- The classic categorization of LE into SLE and DLE has during recent years been supplemented with **acute cutaneous lupus erythematosus and subacute cutaneous lupus erythematosus**.

Diagnosis

- The typical DLE diagnosis comprises well-demarcated cutaneous lesions with round or oval erythematous plaques with scales and follicular plugging.
- These lesions may form butterfly-like rashes over the cheeks and nose, known as a **malar rash**.

- Diagnosis **for SLE according to American college of rheumatology**(**Four or more of the following criteria):**

1. Malar
2. Discoid lesions
3. Photosensitivity
4. Presence of oral ulcers
5. Non-erosive arthritis of two joints or more
6. Serositis
7. Renal disorder
8. Neurologic disorder (seizures or psychosis)
9. Hematologic disorder (hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia)
10.Immunologic disorder (anti-DNA, anti-Smith, or antiphospholipid antibodies

Laboratory Findings

1.**Antinuclear antibodies** (patients with other rheumatologic diseases, such as Sjogren's syndrome and rheumatoid arthritis)

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

3.Direct immunohistochemistry to reveal **granular deposition of IgM, IgG, IgA, and C3 (lupus band test)**

- Oral mucosal lesions seen in conjunction with different types of Lupus Erythematosus are clinically and histopathologically indistinguishable.
- **Liquefaction degeneration** may also be present, which may result in diagnostic problems in relation to OLP.
- **Oral LE** lesions would **respond less rapidly than OLP** to the usual topical steroid treatment. **This also may be helpful in distinguishing between LE and OLP**.

Management

✔The oral lesions may respond to **systematic treatment**.

✔When symptomatic intraoral lesions are present, topical steroids should be considered

✔**Two to three times a day followed by a tapering during the next six to nine weeks of Clobetasol propionate gel 0.05%, Betamethasone dipropionate 0.05%, or Fluticasone propionate spray 50 µg aqueous solution.**

✔**Opportunistic oral** infections can also originate the immunologic defects, which are part of the pathogenesis.

✔Another **complication** of the drugs used in treatment of LE is mucosal ulceration caused by **frequent exploitation of NSAIDs**.

- **Oral mucosal lesions often mirror the disease activity. They may regress spontaneously but can also persist for months or even years.The overall objective is to use a minimum of steroids to obtain relief.**

ALLERGIC REACTIONS

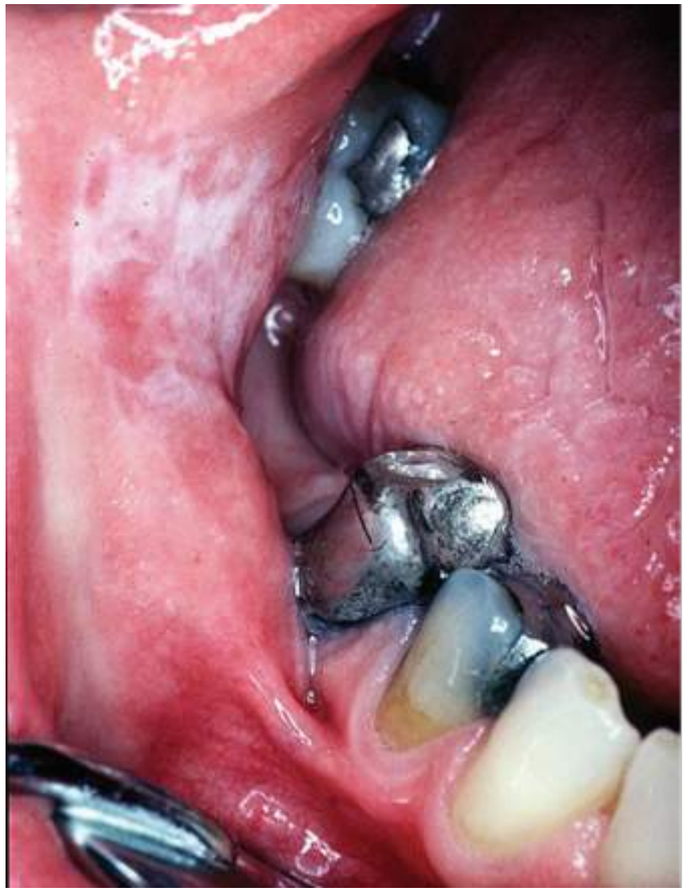
Oral Lichenoid Contact Reactions

➤Due to a delayed hypersensitivity reaction to constituents derived from dental materials.

➤ The majority of patients are **patch test positive to mercury (Hg),** which lends support to LCR being an allergic reaction.

➤Although **Hg** is usually considered the primary etiologic factor, other **amalgam constituents may also initiate LCR.**

➤Other filling materials such as **gold, composites, and glass ionomers** may also generate reactions.



CLINICAL FINDINGS

0 Oral Lichenoid Contact Reactions are a type of **delayed hypersensitivity reaction** to constituents derived from dental predominantly amalgam fillings materials.

0 Clinically, LCRs display the same reaction patterns as seen in **OLP, that is, reticulum, papules, plaque, erythema, and ulcers.**

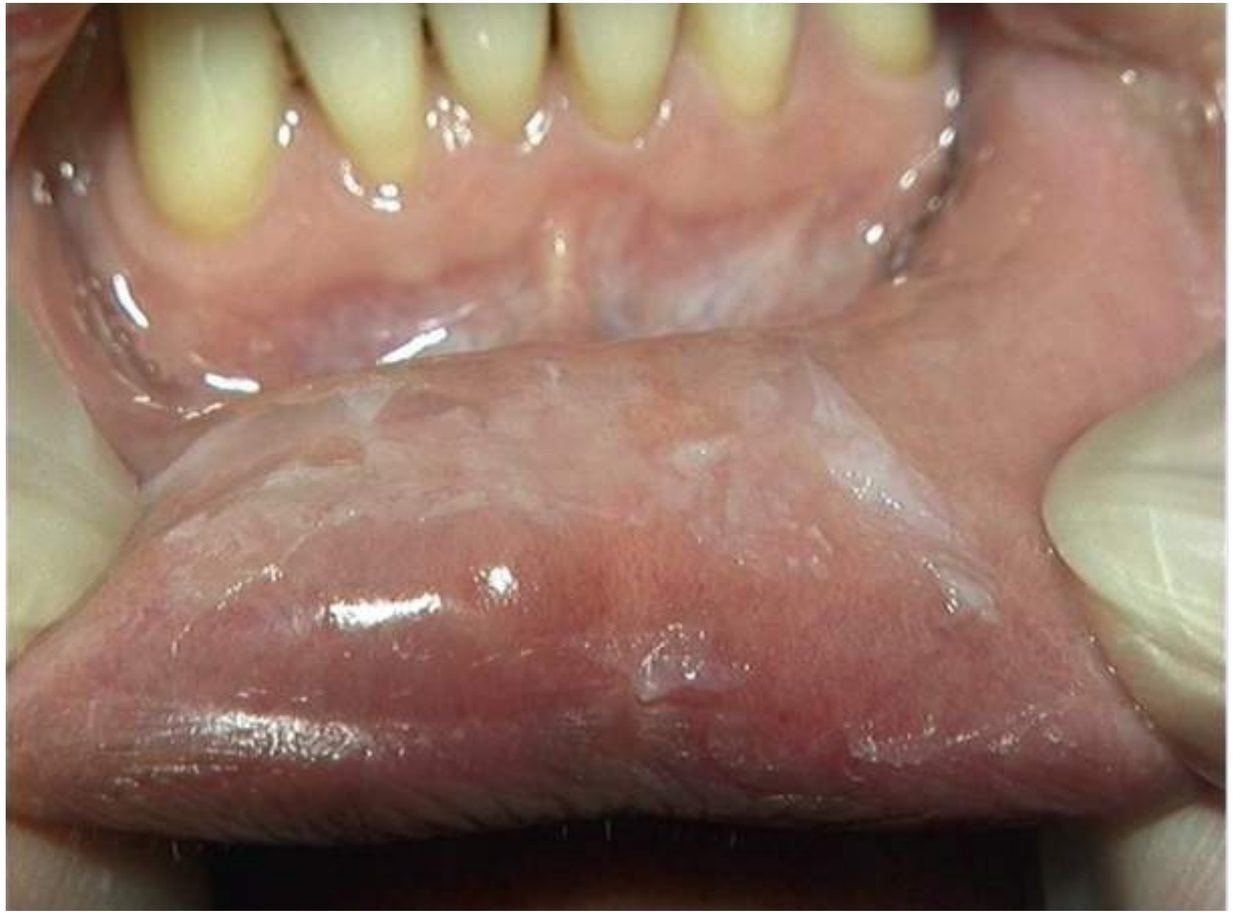
O Diagnosis: The most apparent clinical difference between OLP and LCR is the **extension of the lesions. (Histologically is as like as OLP).**

oThe majority of LCRs are confined to sites that are regularly in contact with dental materials, such as the **buccal mucosa** and the **border of the tongue**

O Management: Most of this type of LCR **resolve** following treatment with chlorhexidine and removal of the causative dental materials.

Reactions to Dentifrice and Chlorhexidine

- **Delayed hypersensitivity** reactions to toothpastes and mouthwashes have been reported, but such reactions are rare.
- **Cinnamon or preservatives flavor additives such as carvone** and these flavoring constituents may also be used in **chewing** gum can produce **gingivostomatitis.**
- The clinical manifestations include **fiery red edematous gingiva,** which may include both ulcerations and white lesions.
- Similar lesions may involve other sites, such as the **labial, buccal, and tongue mucosae.**
- The clinical manifestation are characteristic and form the basis of the diagnosis, which is supported by healing of the lesions after **withdrawal of the allergen-containing agent**
- **Dentifrice** may also cause a disturbed desquamation, which clinically can be observed as **thin veils of scaling keratin.**



Hypersensitivity reaction to dentifrice resulting in desquamation of the superficial epithelial layers

TOXIC REACTIONS

Reactions to Smokeless Tobacco

- Nonhomogeneous group of compounds used with different intraoral application methods.
- Three different geographic areas are of special interest: **South Asia, United States, and Scandinavia.**

Tobacco is often used in combination with betel leaf in India, sliced areca nut, which increases the toxicity of the compound. There is a definitive association between this form of smokeless tobacco and oral cancer .

In Scandinavia and US: ST can be divided into three different groups: **chewing tobacco**, ***moist snuff, and dry snuff***. All three are different regarding composition, manufacturing procedures, and type of consumers. The clinical picture varies in relation to the type, brand, frequency, and duration of use of moist snuff .

➤ **The mildest form, of the lesion wrinkles at the site of application.**

❑Whereas **high consumers** may display a white and **leathery lesion with ulcerations. Hyperkeratinization, acanthosis, and epithelial vacuolizations together with different degrees of subepithelial inflammation.**

❖**Gingival retractions** are the most common adverse.

- These retractions are **irreversible,** whereas the mucosal lesion usually **regresses** within a couple of months.

➤Oral mucosal lesions are less frequently observed in association with chewing tobacco compared with moist snuff.

➤A difference between lesions caused by **smokeless tobacco and oral leukoplakia** is the **epithelial dysplasia in oral leukoplakia.**

- **The carcinogenic potential** of smokeless tobacco has been a subject of considerable debate, however, no doubt that smokeless tobacco products contain **nitrosamines,polycyclic hydrocarbons, aldehydes heavy metals which all have a potential to cause harm**.

Smoker’s Keratosis

➤Moderate to heavy tobacco smoking, especially cigarettes but also cannabis, can give rise to reactive keratosis anywhere in the oral cavity, but especially in the palate and sublingually

➤Persistence of the lesion after cessation of smoking confirms a sublingual leucoplakia, which must be biopsied due to the high risk of malignant transformation.

Smoker palate

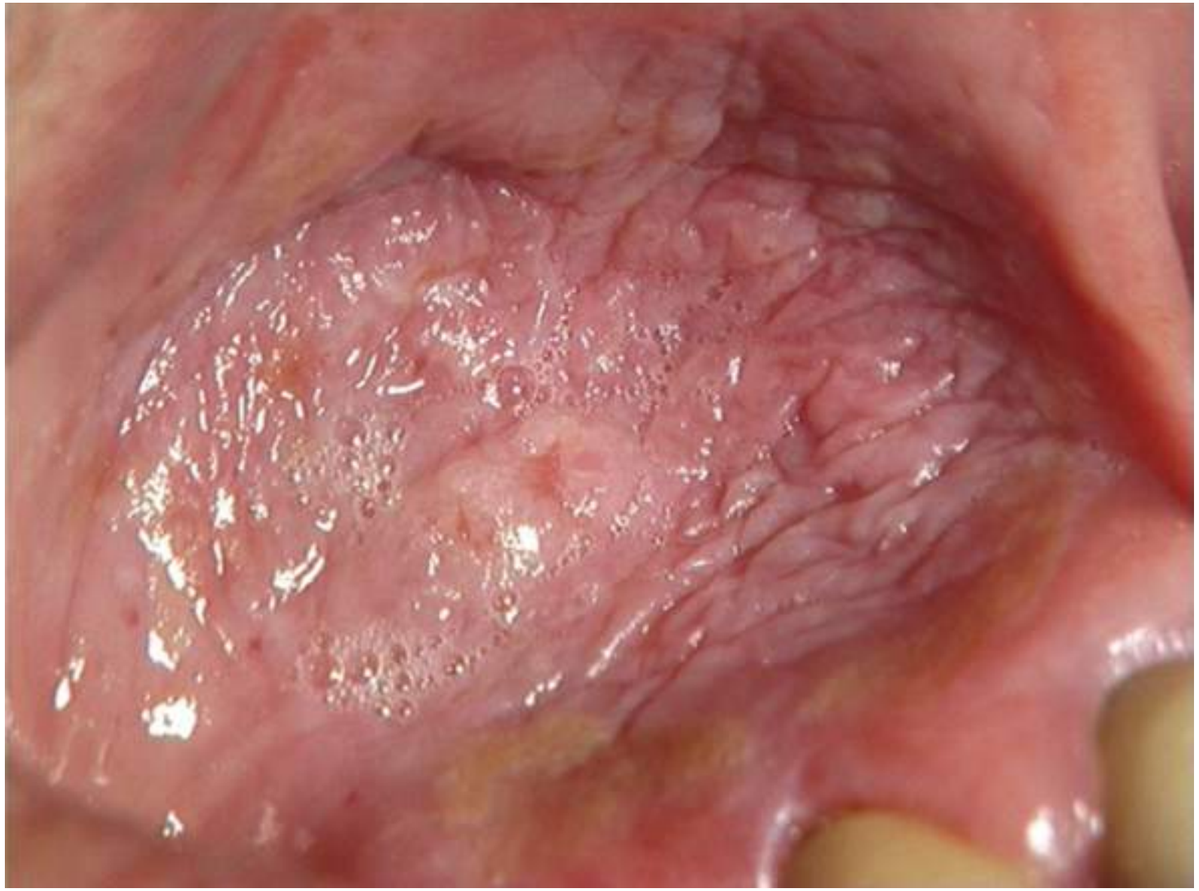
The most common effects of smoking are presented clinically as:

- **Dark brown pigmentations (smoker's melanosis)** and as
- **White leathered lesions (nicotine stomatitis)** or **smoker's palate**.

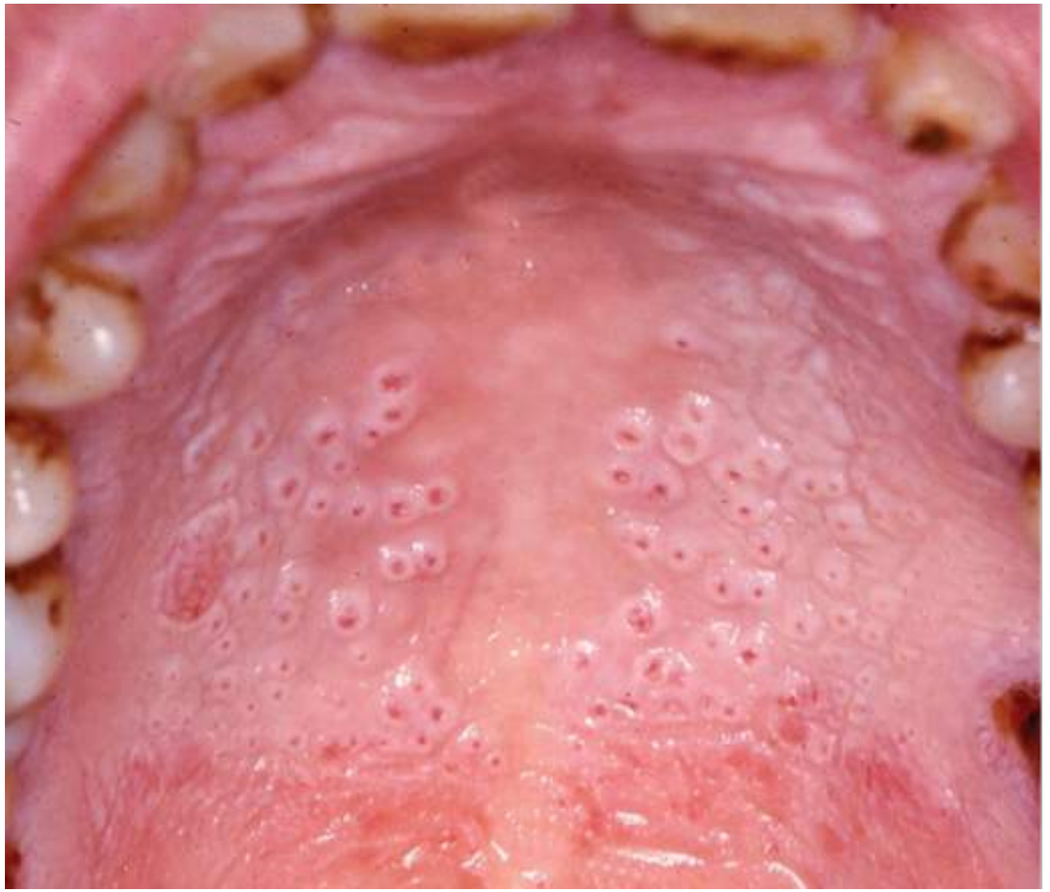
- **In smoker's palate:** an erythematous irritation is initially, followed by a whitish palatal mucosa reflecting **hyperkeratosis, as a part of this lesion red dots can be seen representing an accessory salivary minor salivary gland ,**which can be enlarged and display **metaplasia**.
- **Prevalence of smoker's palate is 2.5%–0.1%**, more prevalent in men.

High prevalence in consumers of **pipe tobacco and cigarettes** and among individuals who practice **inverse smoking**.

- The etiology is due to high temperature rather than the chemical composition of the smoke, although there is a synergistic effect of the two.



Lesion associated with the use of Swedish snuff.



Smoker’s palate with pronounced orifices of the accessory salivary glands

Reactions To Mechanical Trauma

Morsicatio (Mucosal Nibbling)

❖Parafunctional behavior (habitual chewing) is done unconsciously.

❖ Morsicatio is most frequently seen in the **buccal and lip mucosa** and never encountered in areas that are not possible to traumatize

❖Typically, morsicatio does not entail ulcerations but encompasses an **asymptomatic shredded area.**

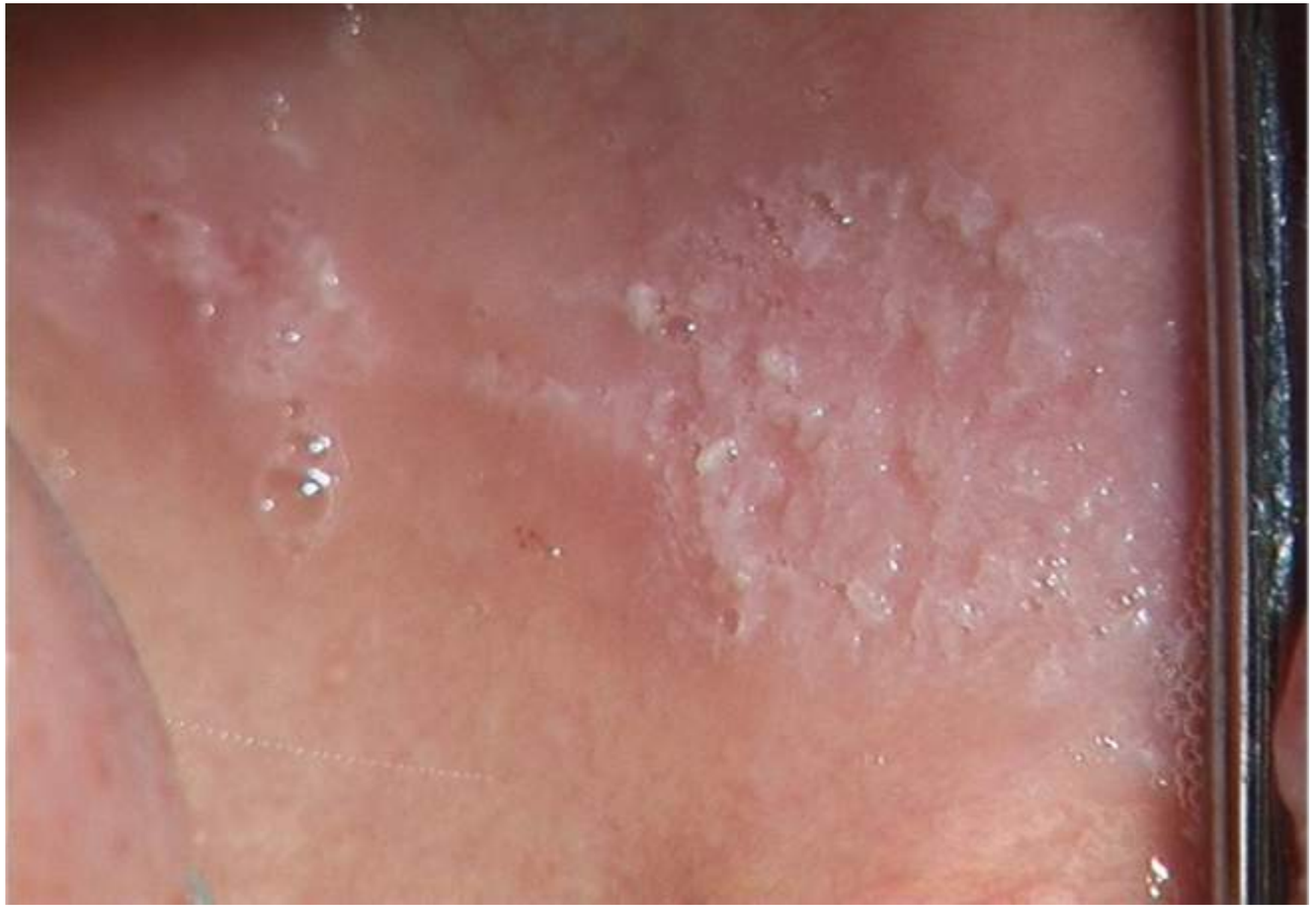
❖In cases of more extensive destruction of oral tissues by habitual chewing in **psychiatric disorders.**

❖ The prevalence has been reported to be in the range of 0.5%- 1%

❖ Morsicatio is three times more common among **women**

Management:

- The patient should be informed about the habit and motivate the patient for stopping. The condition does not involve malignant potential.



Morsicatio of the retrocommissural area.

Frictional Hyperkeratosis

Oral frictional hyperkeratosis is typically clinically characterized by a white lesion without any red elements

➤Oral mucosa subjected to **increased friction** caused by food intake **.** Or **increased abrasion**, which stimulates the epithelium to respond with an increased production of keratin

➤The reaction can be regarded as a **physiologic response** to minor trauma.

➤**Smoking and alcohol** consumption have been reported as predisposing factors. Prevalence has been reported to be in the range of 2%–7%.

❑Frictional hyperkeratosis is often seen in **edentulous areas** of the alveolar ridge.

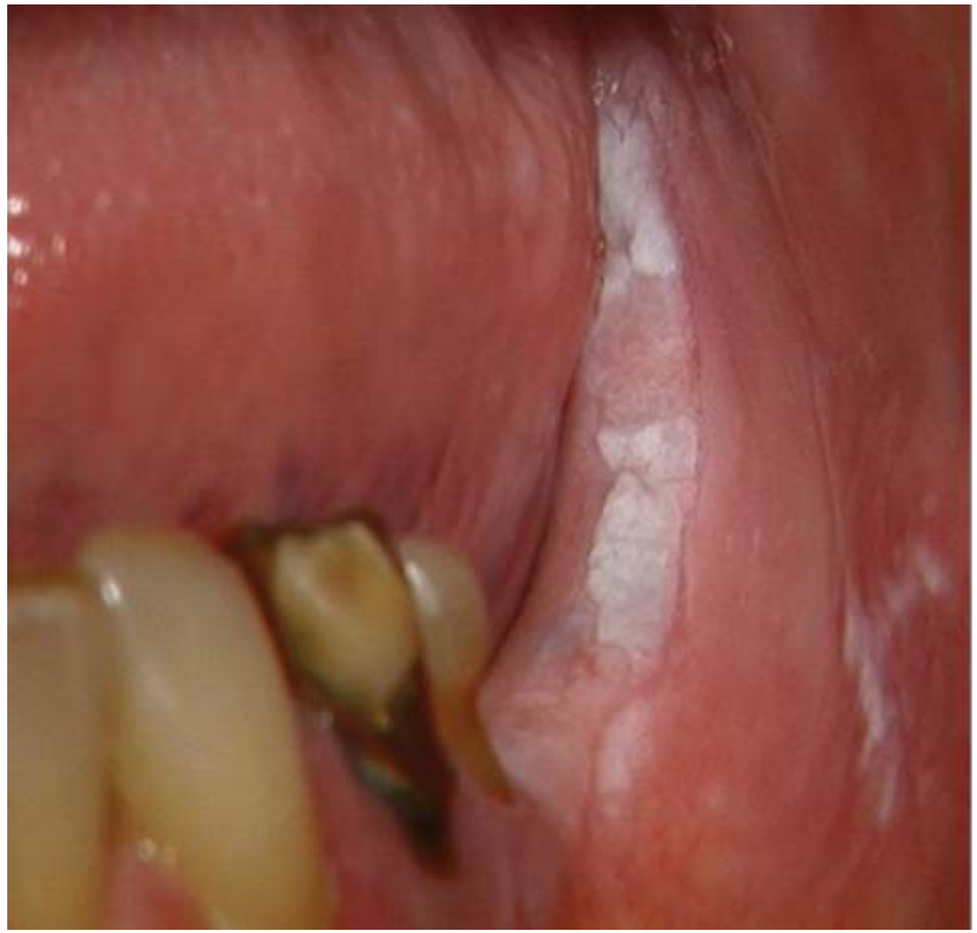
➤**Asymptomatic** but can cause **anxiety** to the patient (supposed as a malignant or premalignant lesion)

Diagnosis:

- Based on clinical findings. It is **asymptomatic**.
- It is doubtful, and the **biopsy** should be taken to exclude premalignant.
- To differentiate it from leukoplakia, the causative factors should be eliminated.

Management

- No surgical intervention is indicated.
- No malignant nature of the lesions
- Attempts to reduce predisposing factors are sufficient



Frictional keratosis of the edentulous alveolar ridge.

Other Red And White Lesions

Benign Migratory Glossitis, Geographic Tongue (erythema margin), Leukoedema, White Sponge Nevus ,Hairy Tongue.

•**, Geographic Tongue (erythema margin):** Is an annular lesion affecting the dorsum and margin of the **tongue**. Clinically: White, yellow, or gray slightly peripheral zone

•**ONE of the most prevalent oral mucosal lesions**, 1%–2.5%.

•Heredity has been reported, suggesting the involvement of genetic factors. •The gender distribution equal.

✔**Circumferentially migrating** and leaves an erythematous area behind, reflecting atrophy of the filiform papillae.

▪The peripheral zone **disappears** after some time, and healing of the depapillated and erythematous area starts. The lesion may commence at different starting points, the peripheral zones **fuse, and the typical clinical features of a geographic tongue emerge.**

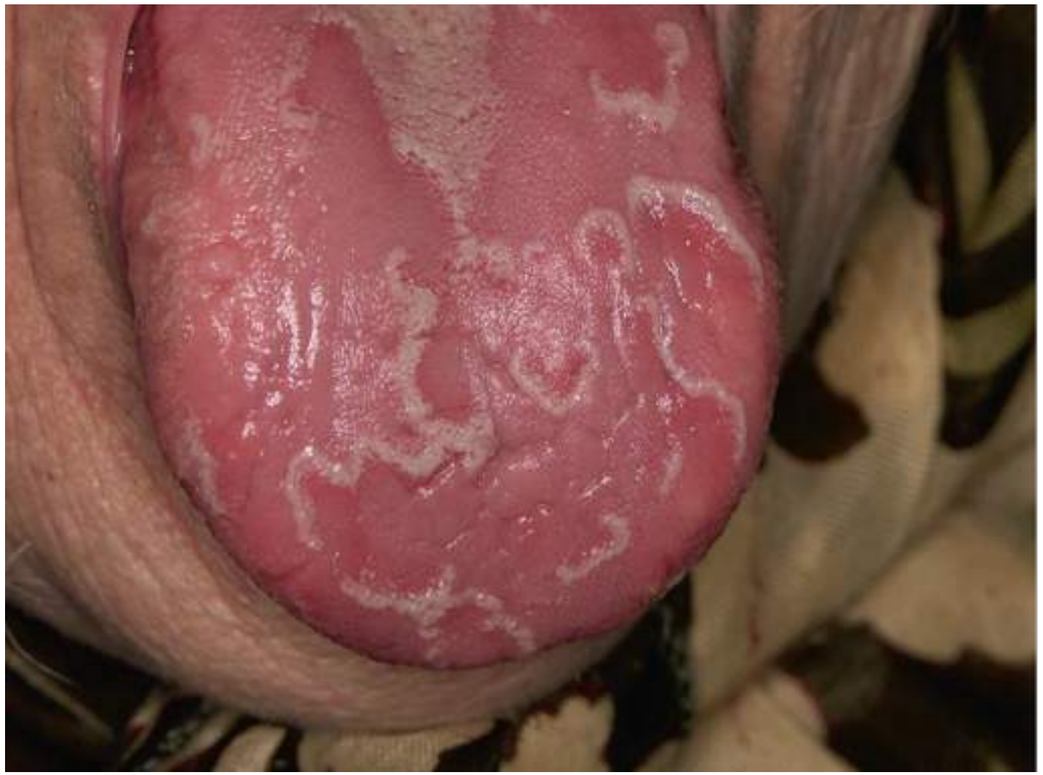
❑Disappearance of the peripheral zone may indicate that the mucosa is recovering.

- GT is characterized by a period of **exacerbation and remission**, Asymptomatic disorder but. Some patient may experience a sensation.
- **A parafunctional habit** revealed by indentation of lateral border of the tongue, may be a contributing factor to the symptoms.
- Patients often report that their lesions are aggravating during periods of stress. Geographic tongue and fissured tongue may be observed simultaneously. Most likely, **fissured tongue** should be interpreted as an **end stage of geographic tongue** in some patients

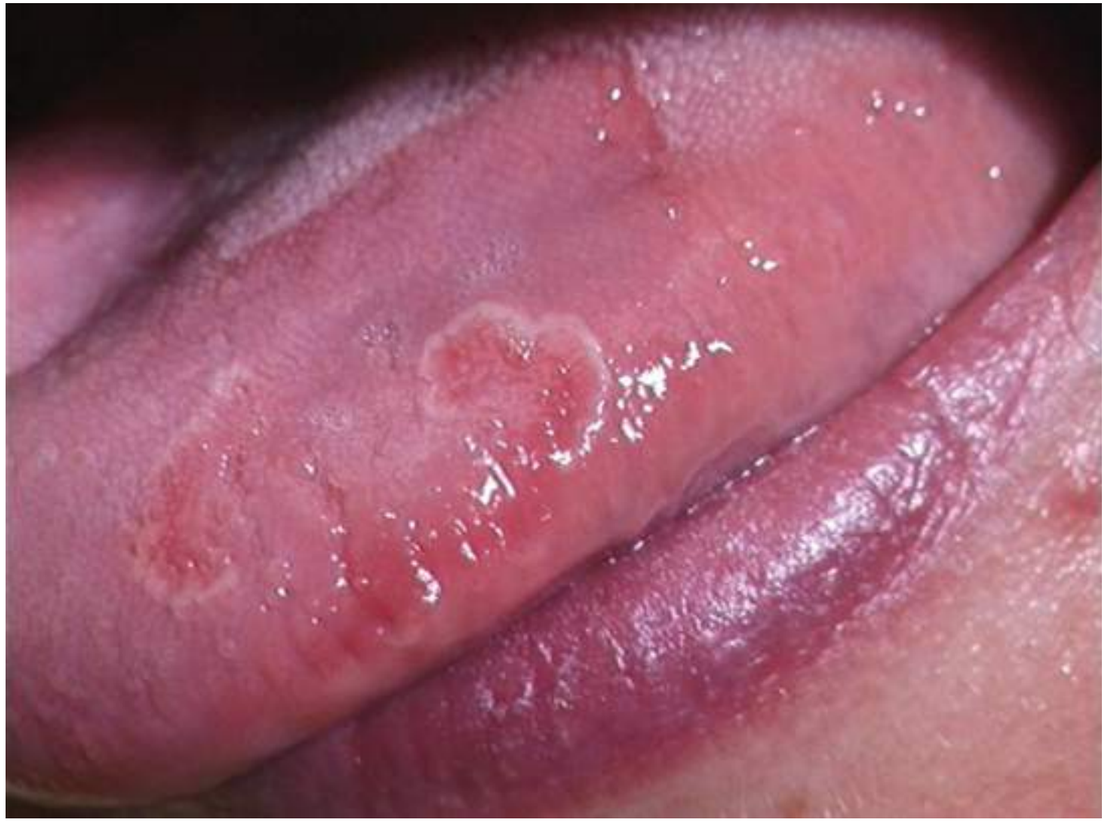
- A similar clinical presentation for geographic stomatitis as a part for **Reiter's disease**, in addition to conjunctivitis arthritis, uveitis and urethritis.
- Reiter's disease is originated from a **gastroenteral or urogenital infection**.
- An **increased prevalence** of geographic tongue has been seen in generalized Pustular psoriasis.
- A **negative** relationship with smoking was revealed.

Management:

- **No special treatment** is requir. If symptoms are reported, **topical anesthetics** may be used to obtain temporary relief.
- **Antihistamines**, anxiolytic drugs, or steroids, but none of these has been systematically evaluated.
- Geographic tongue may regress, but it is not possible to predict when and to which patient this may happen.
- The prevalence of the disease seems to **decrease with age**.

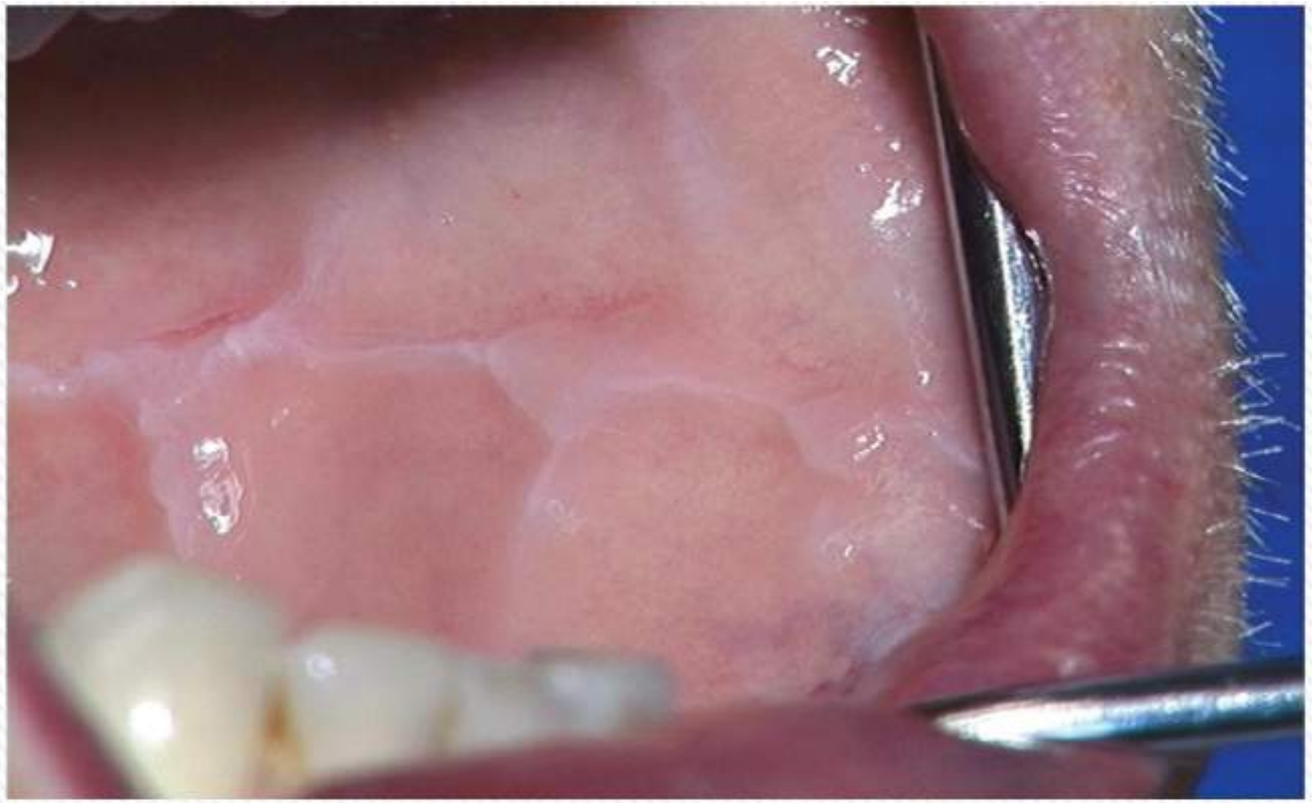


Geographic tongue



Leukoedema

- **Edematous mucosa with a whiteish, often apparently translucent appearance**
- **The etiology of leukoedema is not clear**
- Leukoedema is a white and veil-like alteration of the oral mucosa that is merely **considered a normal variant**.
- The condition is often bilaterally in the **buccal mucosa** and sometimes at the borders of the tongue.
- Leukoedema **is less clinically** evident after stretching the mucosa but reappears after this manipulation is discontinued.
- The prevalence in Caucasians has been estimated at 50%. The lesion is even **more prevalent in the black population**.
- Leukoedema is accompanied by mucosal folds. The condition is asymptomatic and has no malignant potential.
- The clinical features of leukoedema are **quite different** from oral keratosis, such as leukoplakia, **as the demarcation is diffuse and gentle stretching results in a temporary disappearance**



Leukoedema

The distribution between sexes has been found to be equal.

Treatment

There is no demand for TT as the condition is non-symptomatic and has no complications, including premalignant features.

White Sponge Nevus

❖Mutations in genes that are coding for epithelial keratin of the types K4 and K13.

❖It has been listed as an **autosomal dominant disorder(rare disorder)** by the National Institutes of Health, a prevalence below 1 in 200,000 .

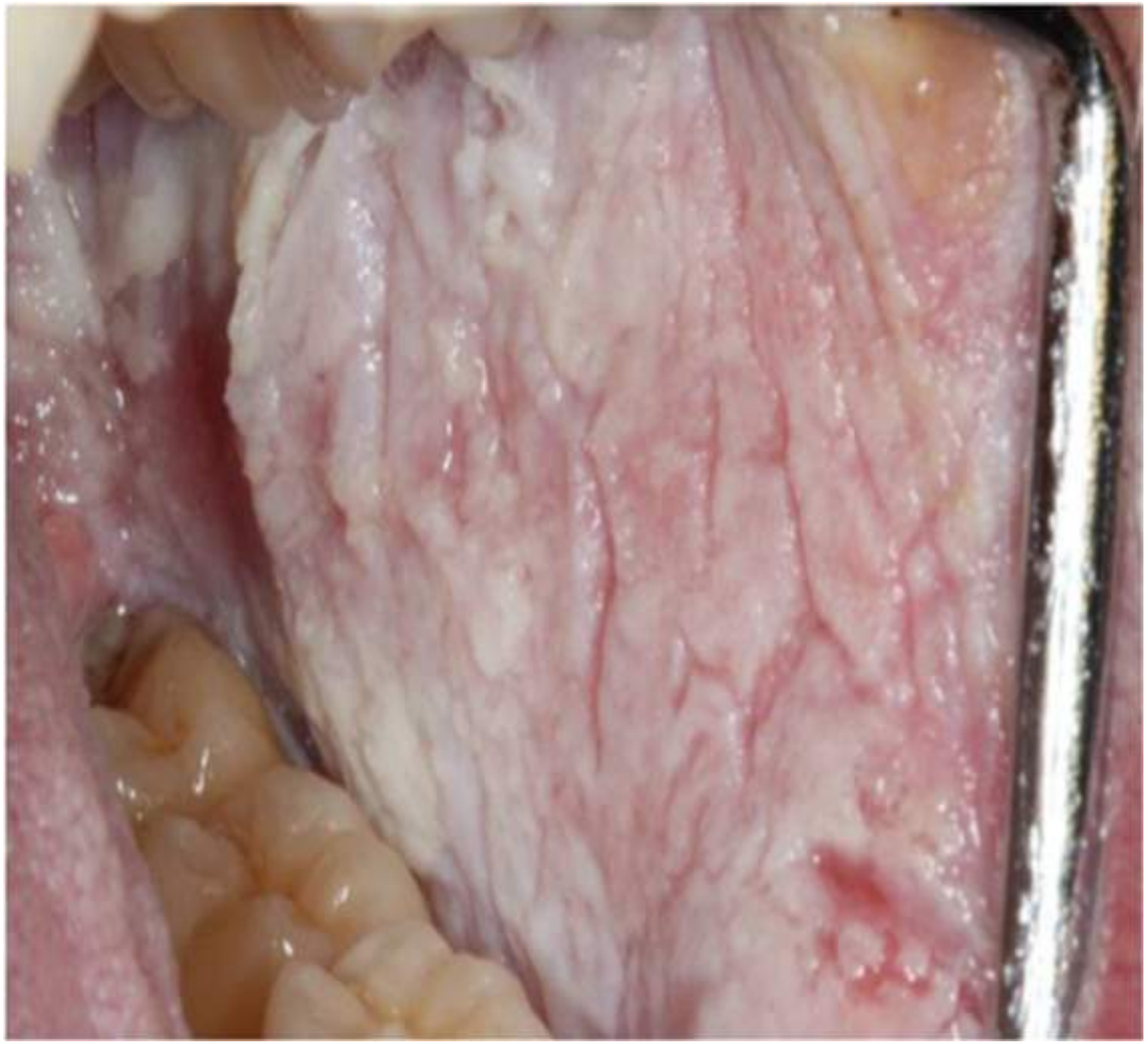
❖The clinical appearance usually commences during **adolescence.**

❖Gender distribution, **equal**.

- **The typical clinical appearance** is a white lesion with an elevated and irregular surface comprising fissures or plaque formations
- The most affected sites are the **buccal mucosa,** but the lesion may also be encountered in other areas of the oral cavity covered by parakeratinized or non-keratinized epithelium.
- The disorder may also involve extraoral sites, **esophagus and anogenital mucosa.**
- Although the lesion does not entail any symptoms, it may cause dysphagia when the esophagus is involved

Management:

- White sponge nevus does not entail any symptoms, and no treatment is therefore required.
- **Systemic antibiotics was used** to resolve the disorder, but with non-consistent results. The recurrence rate is considerable.
- **Totally a White sponge nevus is .benign condition.**
- **Diagnosis:** A differential diagnostic problem for other oral dyskeratoses, such as plaque **type candidiasis** and oral **leukoplakia.** The hallmark microscopic feature of this disorder is pronounced.



Hairy Tongue

The etiology of hairy tongue is unknown in most cases .

It is related to several **predisposing factors** :

- Neglected oral hygiene(in hospitalized patients)
- A shift in the microflora,
- Antibiotics and
- Immunosuppressive drugs,
- Oral candidiasis,
- Excessive alcohol consumption,
- Oral inactivity (in hospitalized patients)
- And therapeutic radiation.
- Also associated with smoking habits

Clinically:

➤Hairy tongue is characterized by an **impaired desquamation of the filiform papilla**, which leads to the hairy-like

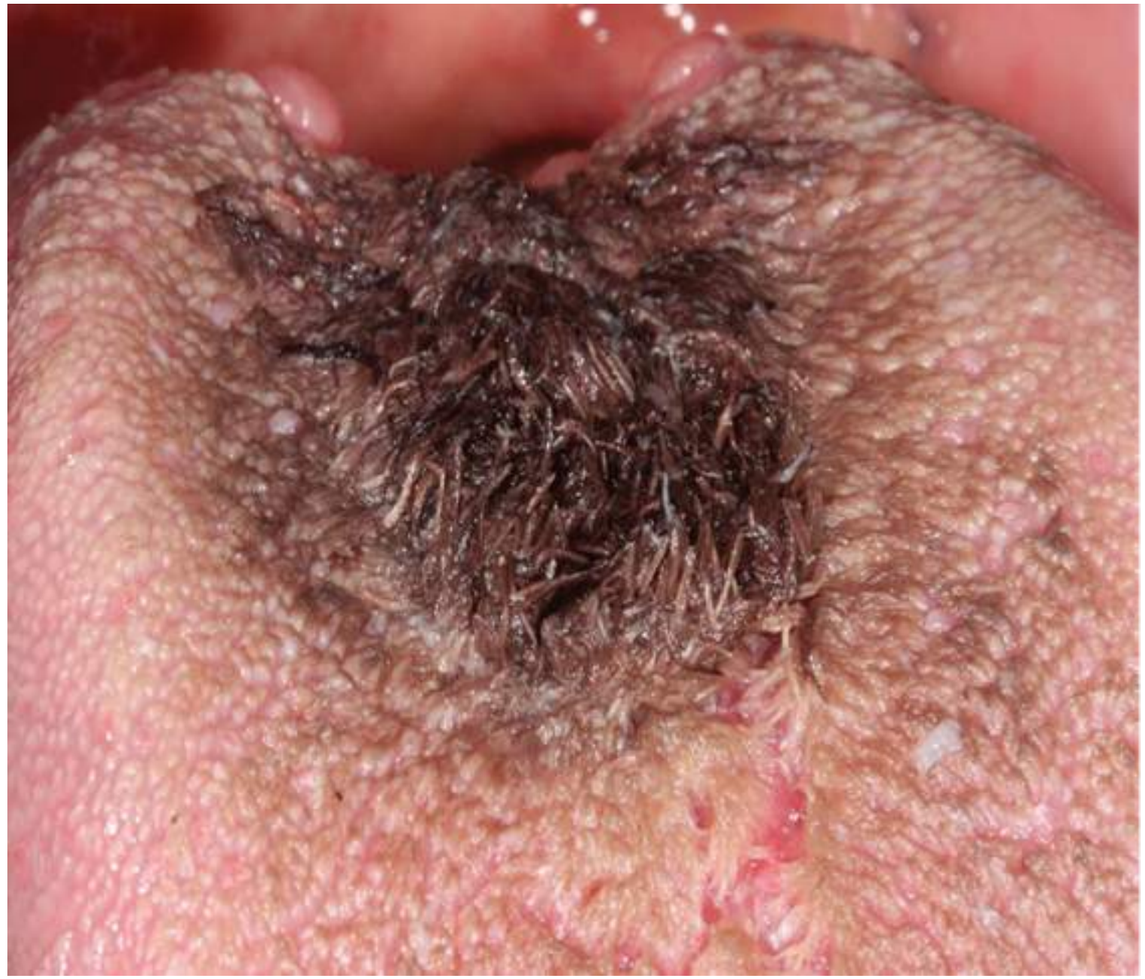
➤The elongated papillae **must reach lengths more than 3 mm** to be classified as “hairy,” although lengths of more **than just 15 mm** have been reported in hairy tongue.

➤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 microflora**.

➤Patients experience both **physical discomfort and esthetic embarrassment** related to the lengths of the filiform papillae

Diagnosis: is based on the clinical appearance.



Management

oThe treatment of hairy tongue is focused on reduction or elimination of **predisposing factors and removal of the elongated filiform papillae.**

oThe patients should be instructed on how to use **devices developed to scrape the tongue**.

o The use of **food** constituents with an **abrasive effect** may also be used to prevent recurrences.

o Attempts have been made with **tretinoin (retinin acid- vitamin A**) but this treatment has not reached any widespread acceptance.

oPatients should be informed about the benign and noncontagious nature of hairy tongue

Dr. Marwah Waleed Sh.

Diagnostic Aids for Early detection

- Early detection of potentially malignant and malignant lesions is associated with improved treatment outcomes and a reduction in morbidity of treatment.

- Patient history, thorough head and neck and intraoral examinations, is an essential issue.
- The definitive test for diagnosis remains tissue biopsy.

- Several aids to the oral examination have been suggested , including:
- Light technologies,
- Vital tissue staining using toluidine blue (TB),
- Computer-assisted cytology of oral brush biopsy specimens.

- Additional markers based on **blood or saliva samples** are also under investigation for use in early detection, diagnosis, and surveillance for recurrence.

- **These techniques** are adjunctive aids for screening and tools for early detection and **are not** a replacement for surgical tissue sample collection and histopathologic diagnosis.

Possible warning signs

1)Lump or thickening of oral soft tissue

2)Soreness or “lump” in throat

3)Difficulty chewing or swallowing

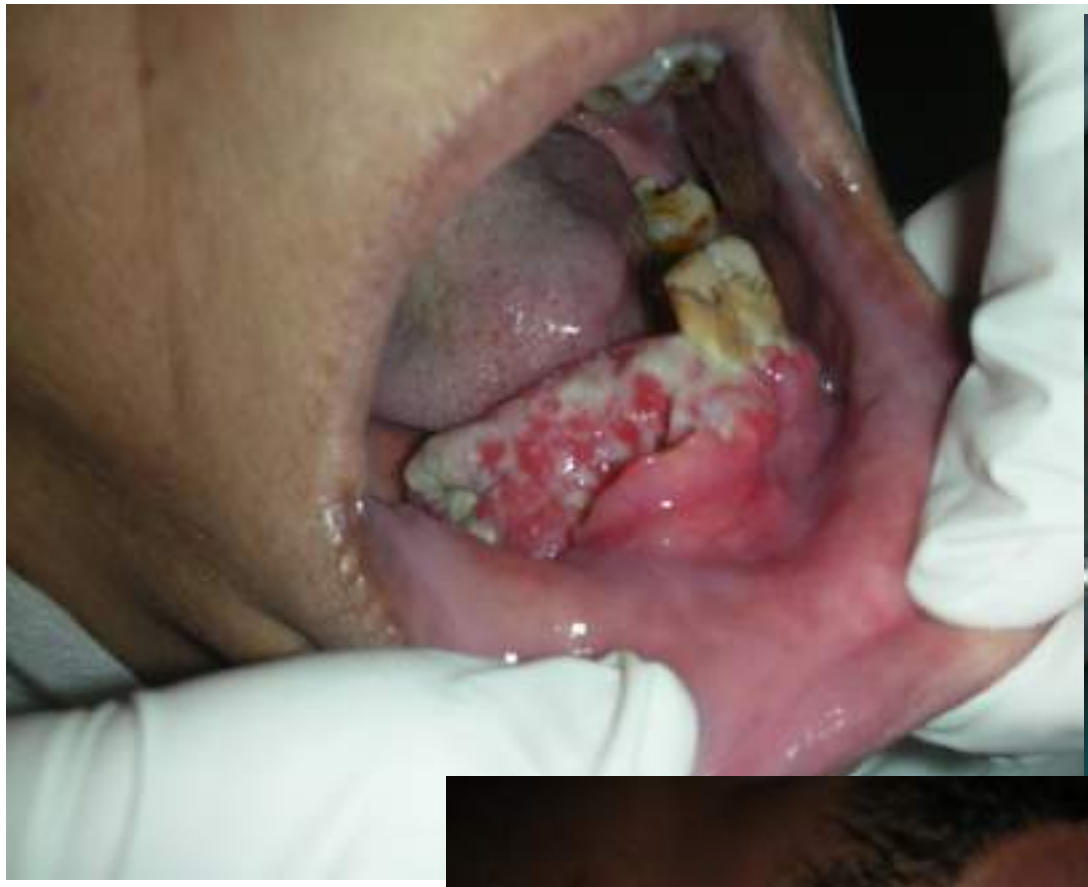
4)Ear pain

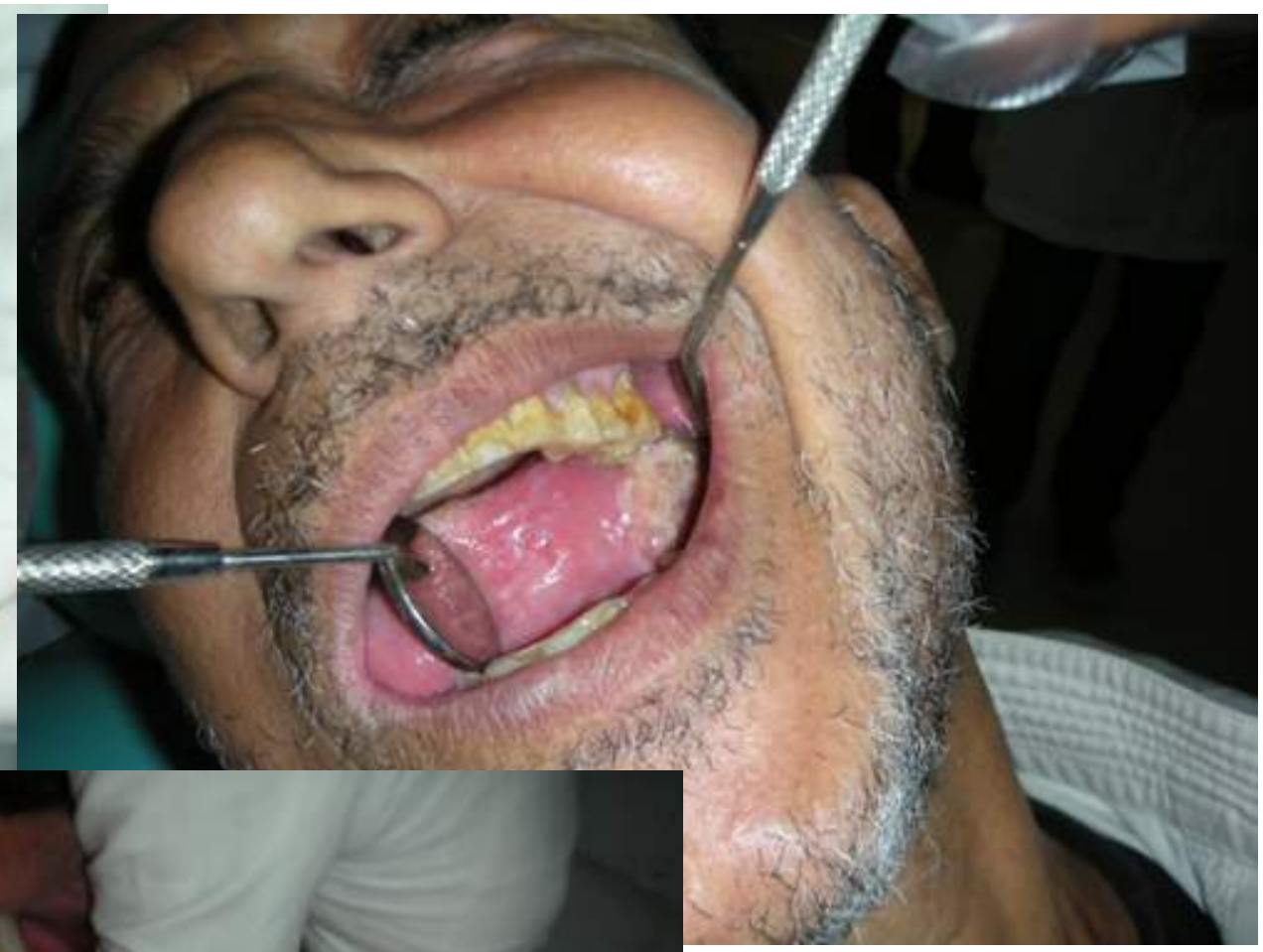
5)Difficulty moving jaw or tongue

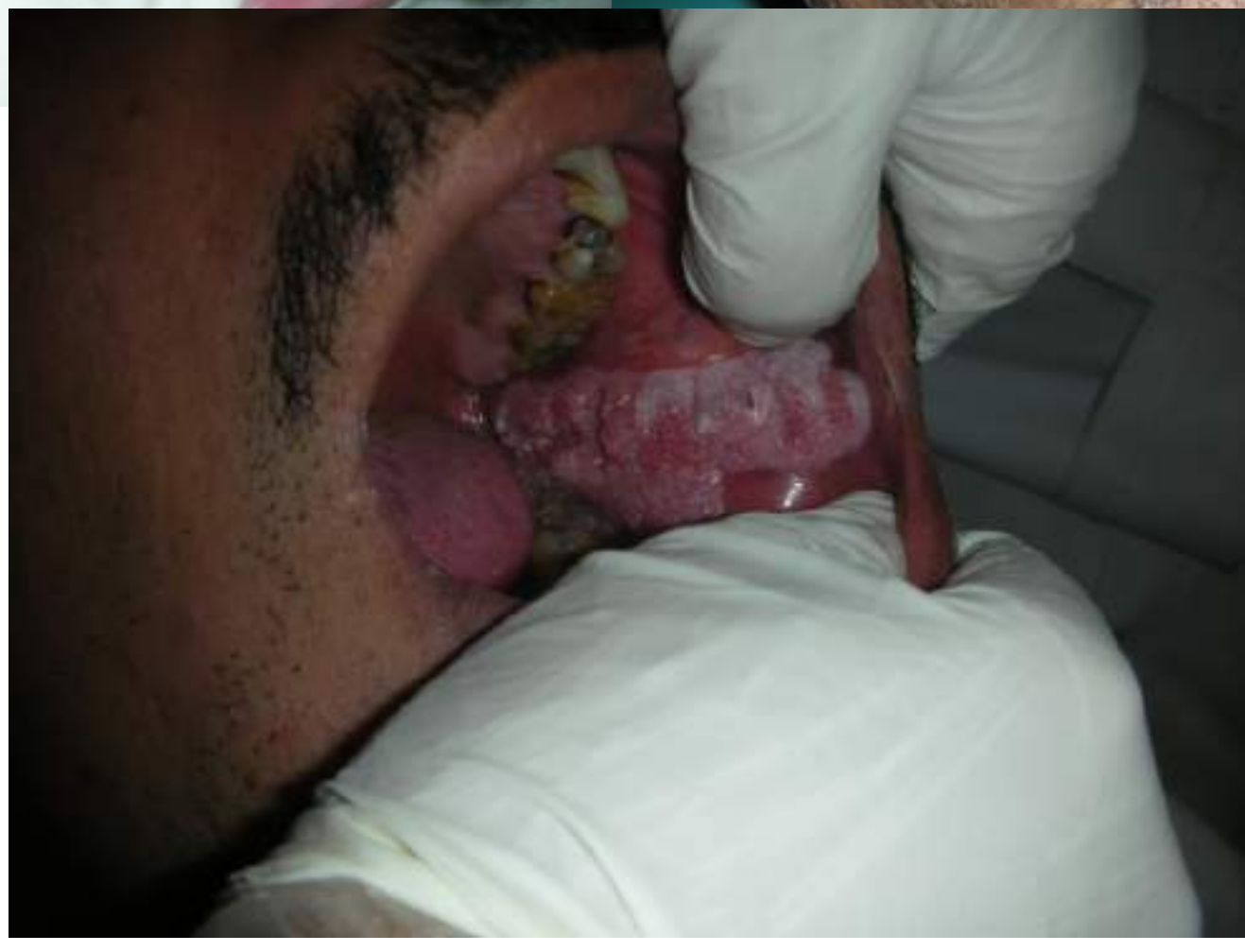
6)Hoarseness

7)Numbness of tongue or mouth

8)Swelling of the jaw







Adjunctive Diagnostic Aids And Screening Tools

1. Toluidine Blue (TB)

- Vital staining with TB may be used as an adjunctive aid in assessing potentially malignant oral mucosal lesions.
- TB is a metachromatic dye, which has an affinity to bind with DNA.
- TB staining has been correlated with loss of heterozygosity (LOH) profiles in tissue biopsies.
- TB can be applied directly to suspicious lesions or used as an oral rinse.
- The assessment of dye uptake depends on clinical judgment and experience
- Positive retention of TB (particularly in areas of leukoplakia, erythroplakia , and uptake in a peripheral pattern of an ulcer) may indicate the **need** for biopsy or assist in identifying the **site** of biopsy.

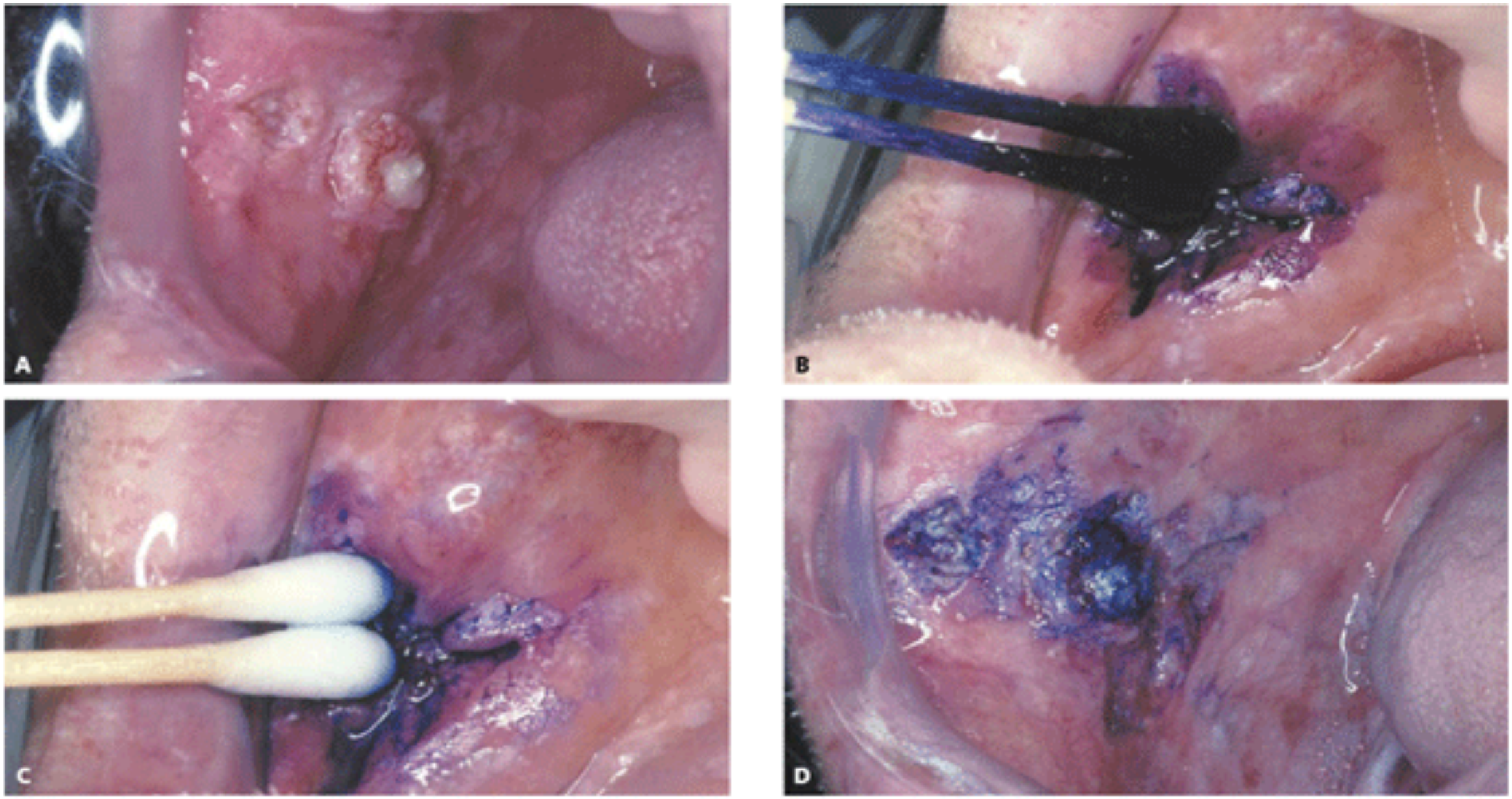


Figure 20–20 Toluidine blue staining technique: *A*, squamous cell carcinoma and leukoplakia, buccal mucosa; *B*, applying 1% aqueous toluidine blue stain; *C*, after water rinse, decolorize with 1% acetic acid; and *D*, dye retention in area of carcinoma and surrounding dysplasia.

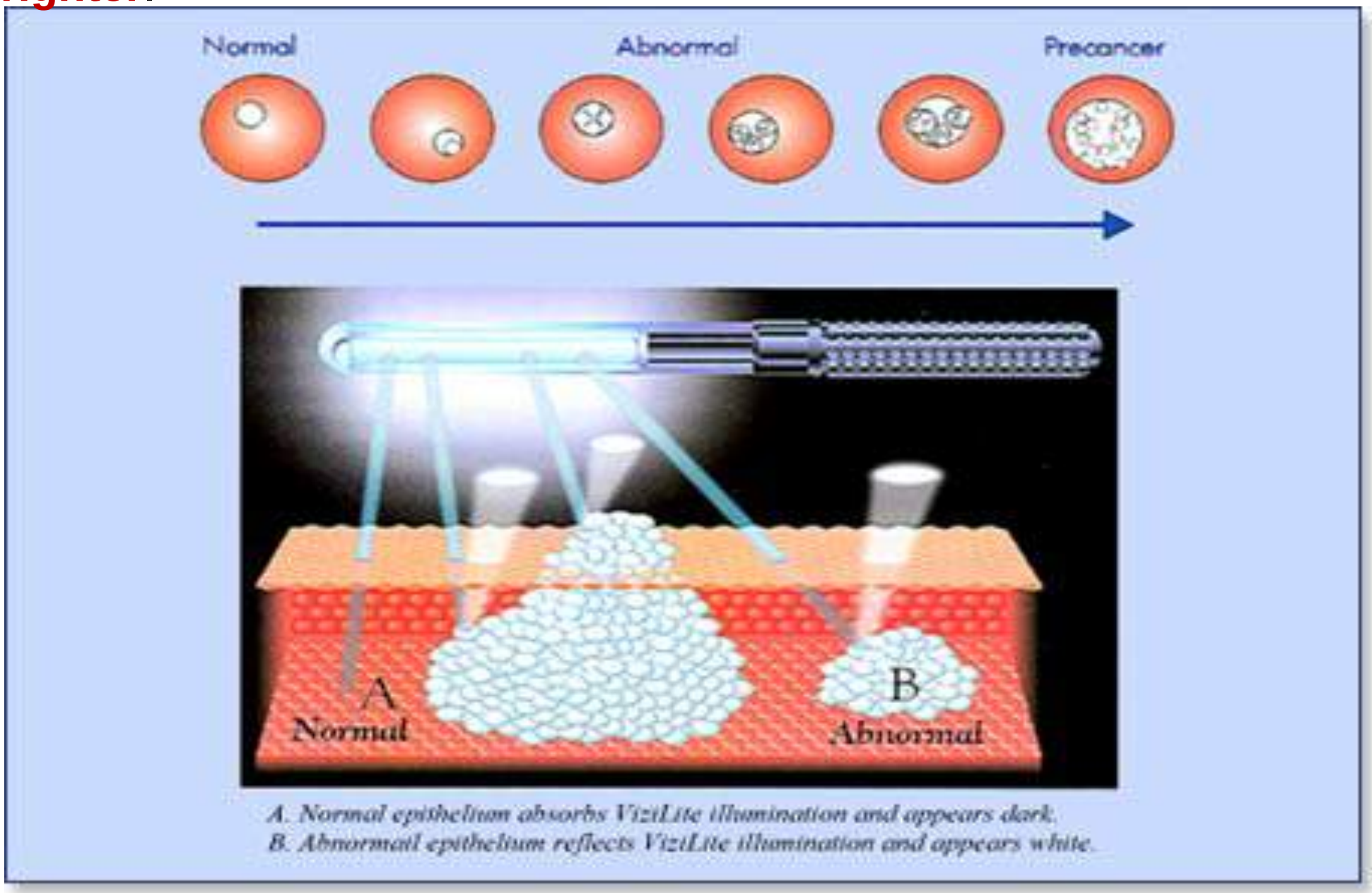
Fig 1

Essentials of Oral Medicine. 2001-BC Decker by Silverman, Eversole and Truelove.
Permission was kindly granted by the three authors for its use in this publication.

- **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.
- In post-radiotherapy follow-up, the retention of TB may assist in distinguishing Non-healing ulcers and persistent or recurrent disease.
- TB is currently **proved by** the US Food and Drug Administration (FDA) as an adjunctive marking aid, and **not marketed** as a stand-alone diagnostic tool.
- TB has been suggested by the Council on Scientific Affairs of the American Dental Association **for use** in high-risk patients and high-risk clinical settings by experienced providers.
- **No guidance** was possible for use in **the general practice** setting due to the lack of clinical study in these settings.

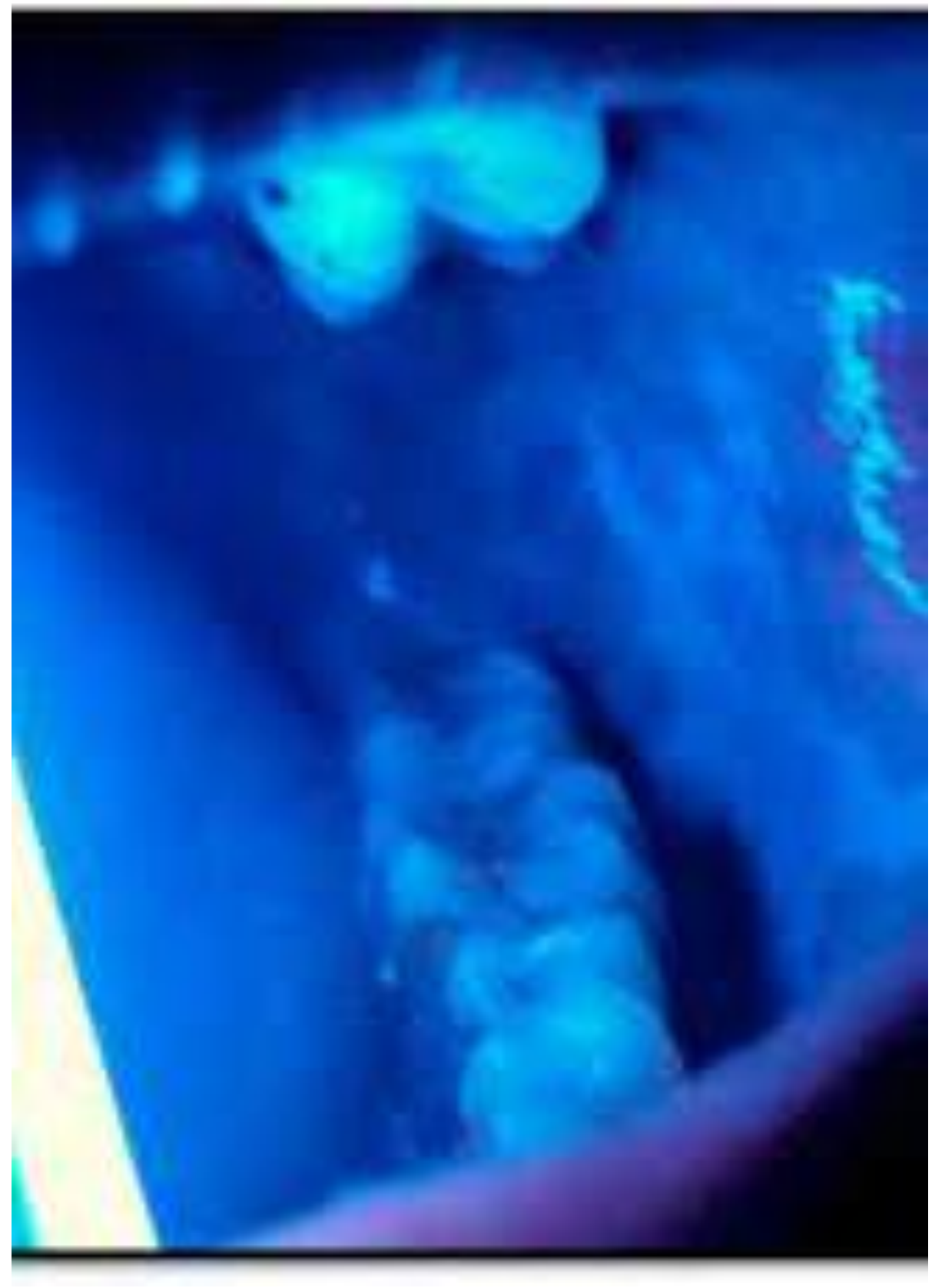
Visualization Adjunctive Tools

2.ViziLite: **Chemiluminescent devices** generate **light based on chemical reactions**. The suspected area of mucosa appears **brighter**.



A. Normal epithelium absorbs ViziLite illumination and appears dark.
B. Abnormal epithelium reflects ViziLite illumination and appears white.

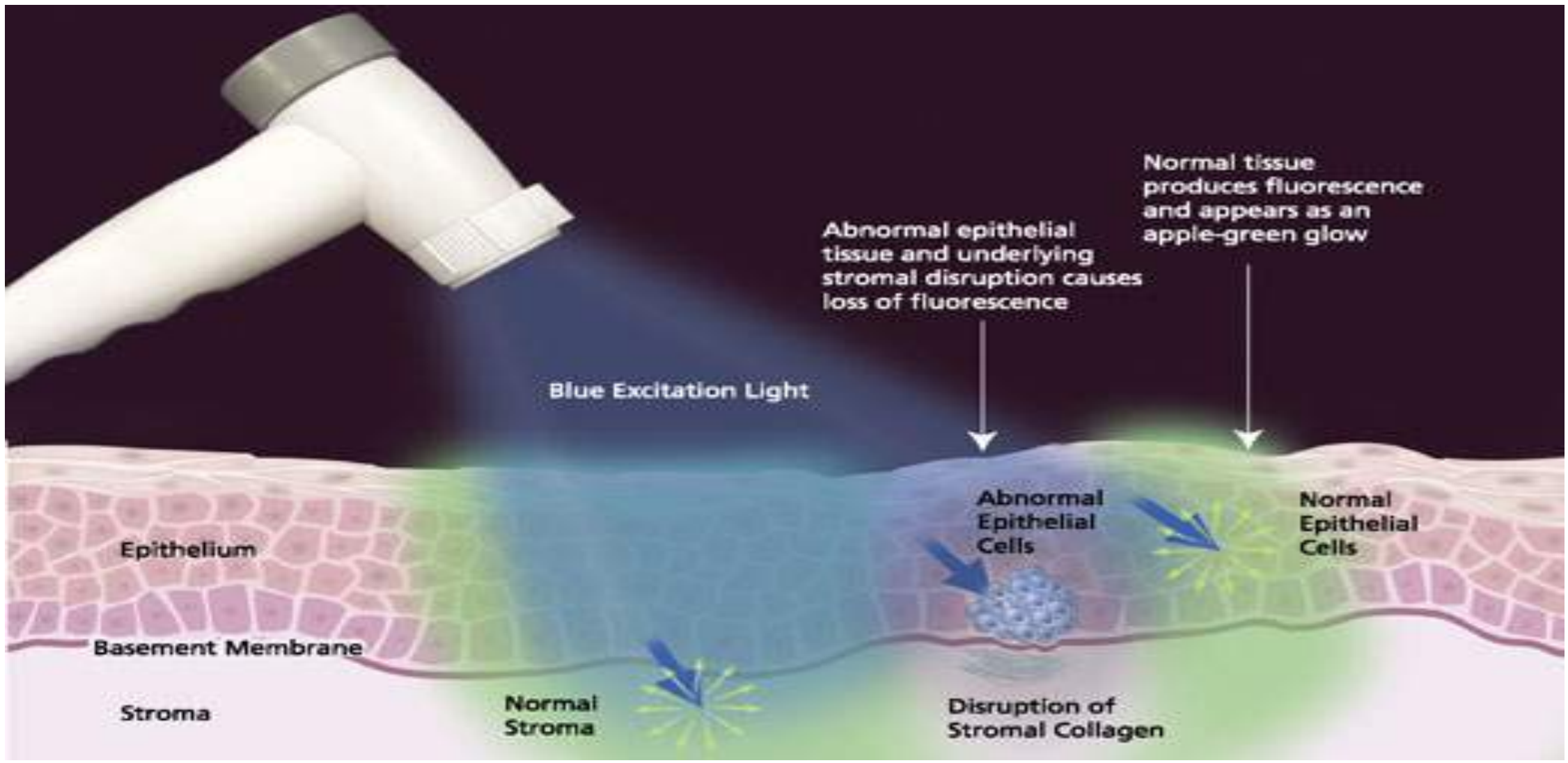
Figure 1: Vizilite illumination of malignant ulcer on lateral border of



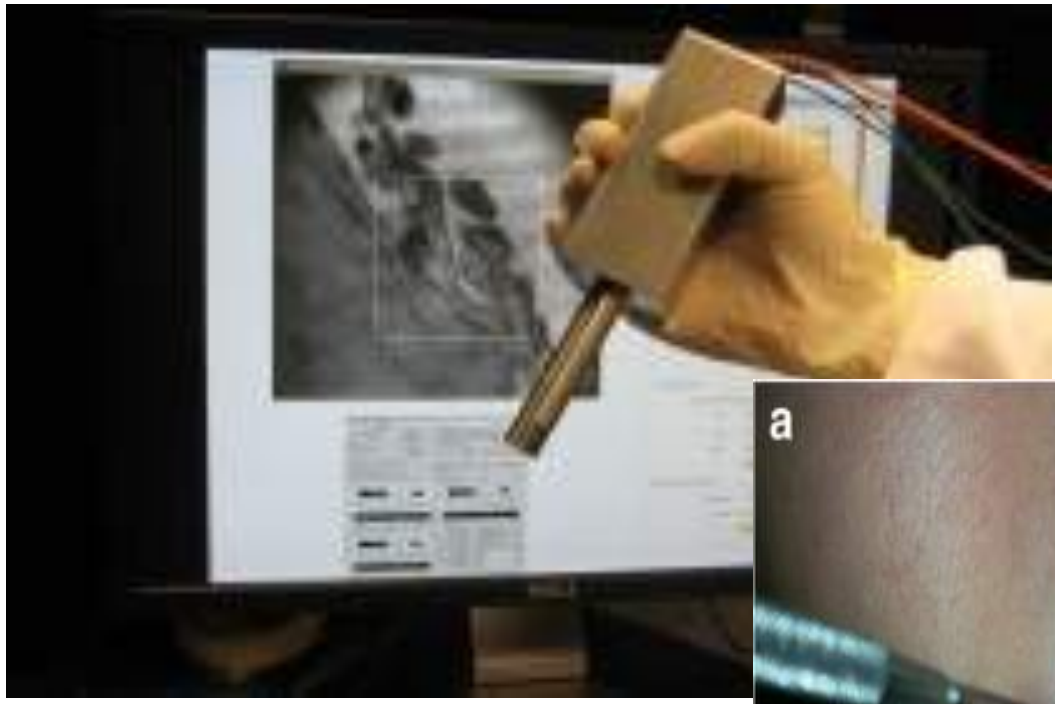
3. VELscope

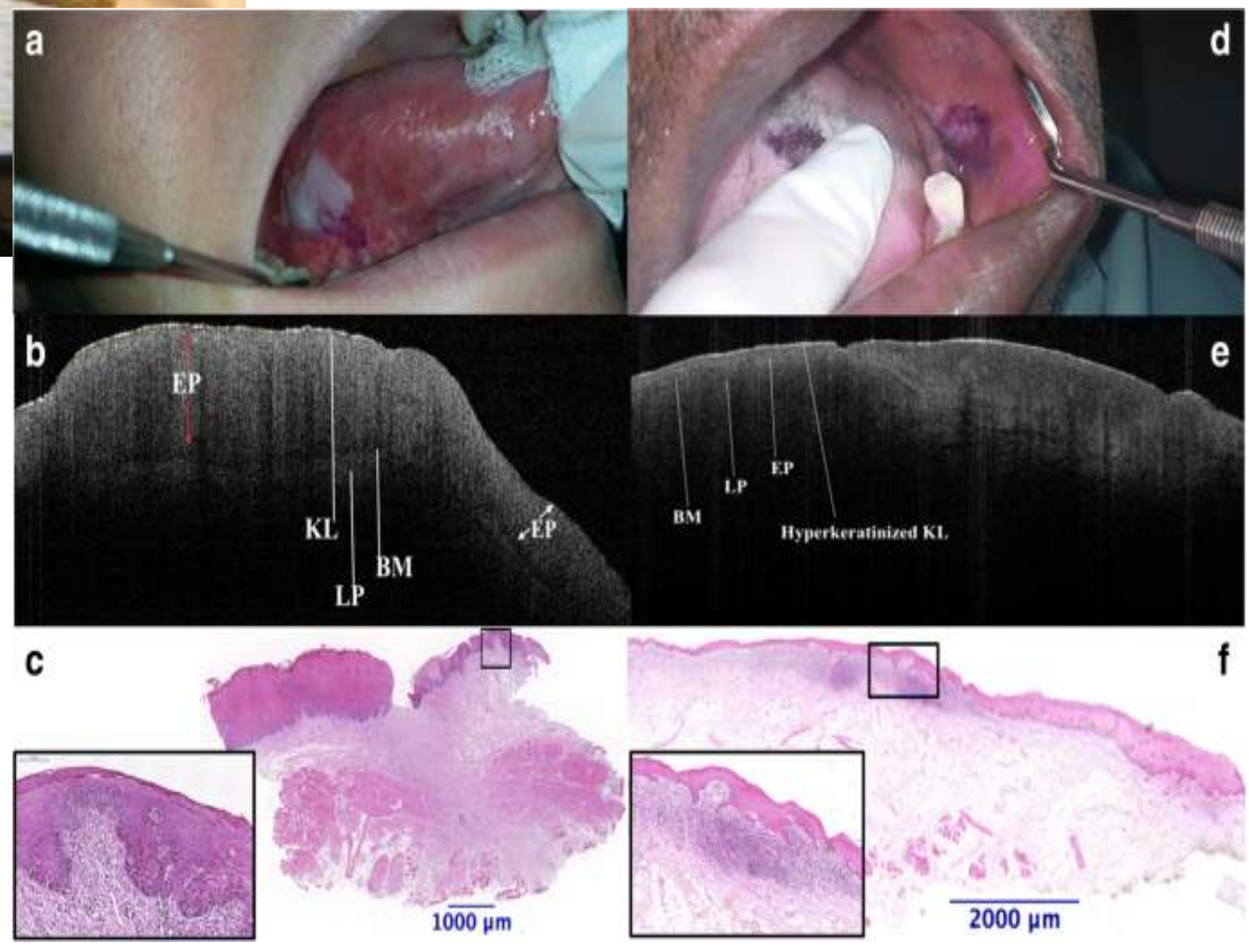
- A hand-held device that emits blue light and is useful as aid for detection of potentially malignant lesions.
- It produce different fluorescence in normal and abnormal surfaces **generate fluorescent light using a light emitting diode(LED) source**, sometimes combined with **optical filtration of a viewfinder**, to enhance natural tissue fluorescence.

- When using the **fluorescence light**, the suspected area shows **loss of fluorescence, which appears dark.**
- **Oral cavity fluorescence**, using **blue light excitation**, is thought to represent the tissue structure, metabolic activity, presence of hemoglobin, vessel dilatation, and possibly inflammation.
- Localized modification in these factors may change the reflective features of the tissue.



- There is no consensus regarding the sensitivity and specificity of these devices, and their ability to detect early disease.
- Nonetheless, **fluorescence** has been shown to provide evidence on lesion margins in patients with known **malignant lesions**.
- There is an increasing interest in the use of confocal microscopy and optical coherent tomography systems to provide tissue diagnosis in real time, noninvasively, and in situ.
- Such diagnostic approach is available in **dermatology** and anticipated to be developed for oral mucosal application in the future.

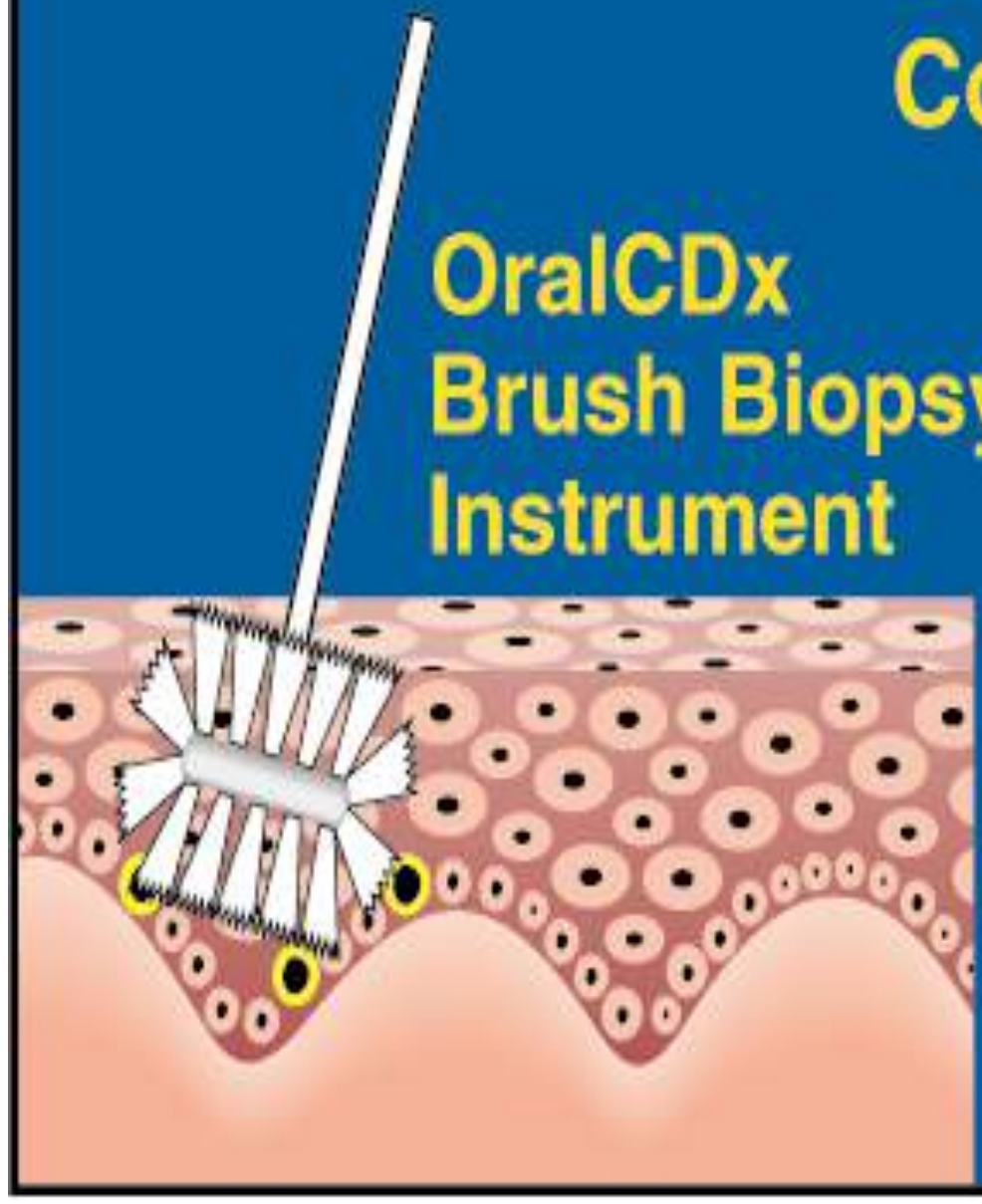



a
d
b
EP
KL
LP
BM
EP
e
EP
LP
BM
Hyperkeratinized KL
c
1000 µm
f
2000 µm

4.Cytology

- **OralCDx** is used to assess cellular morphology.
- The introduction of a brush designed to sample the entire thickness of the oral epithelium improved interest in cytology for oral disease.
- **Cyto-brush** was combined with a **computer- assisted** analysis of the cytologic sample, assessing the cell morphology and keratinization.
- The final diagnosis was made by a pathologist based on the standard histomorphological criteria.
- Further developments in cytology include **molecular** evaluation of exfoliated cells for molecular markers of dysplasia or carcinoma to improve the diagnostic and prognostic value.
- **Liquid-based cytology** has renewed some interest in this noninvasive technique, as it may improve its sensitivity and specificity.

BRUSH BIOPSY
Complete Transepithelial Tissue Sample

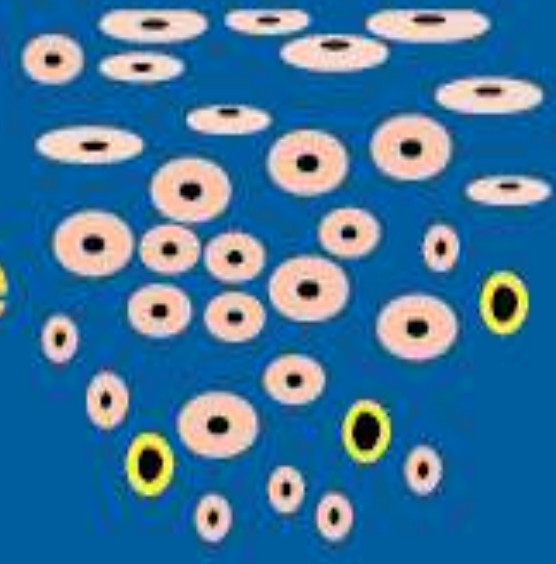


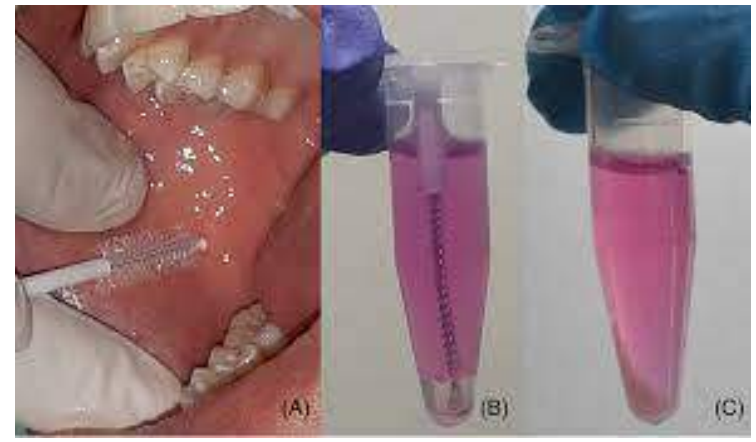
Superficial

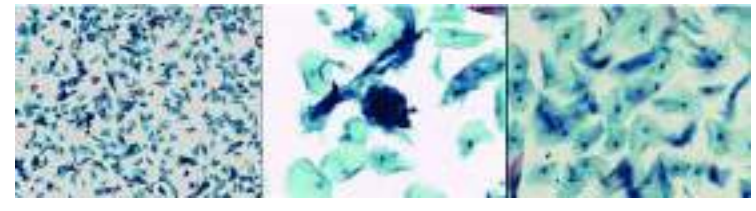
Intermediate

Basal

SPECIMEN




(A)
(B)
(C)



5.Molecular Analysis

- Molecular markers obtained from tissue specimens have been explained HNSCC HPV-negative and HPV-positive cancers arising from different anatomic locations as well as genomic profiles, molecular characteristics, and therefore clinical prognosis.
- HNSCC. HPV-positive tumors often demonstrate mutations in genes E6 and E7, TP53/RB1.
- Alterations in HPV-negative tumor genes commonly noted were TP53,EGFR.

*Head and neck squamous cell carcinoma (HNSCC).

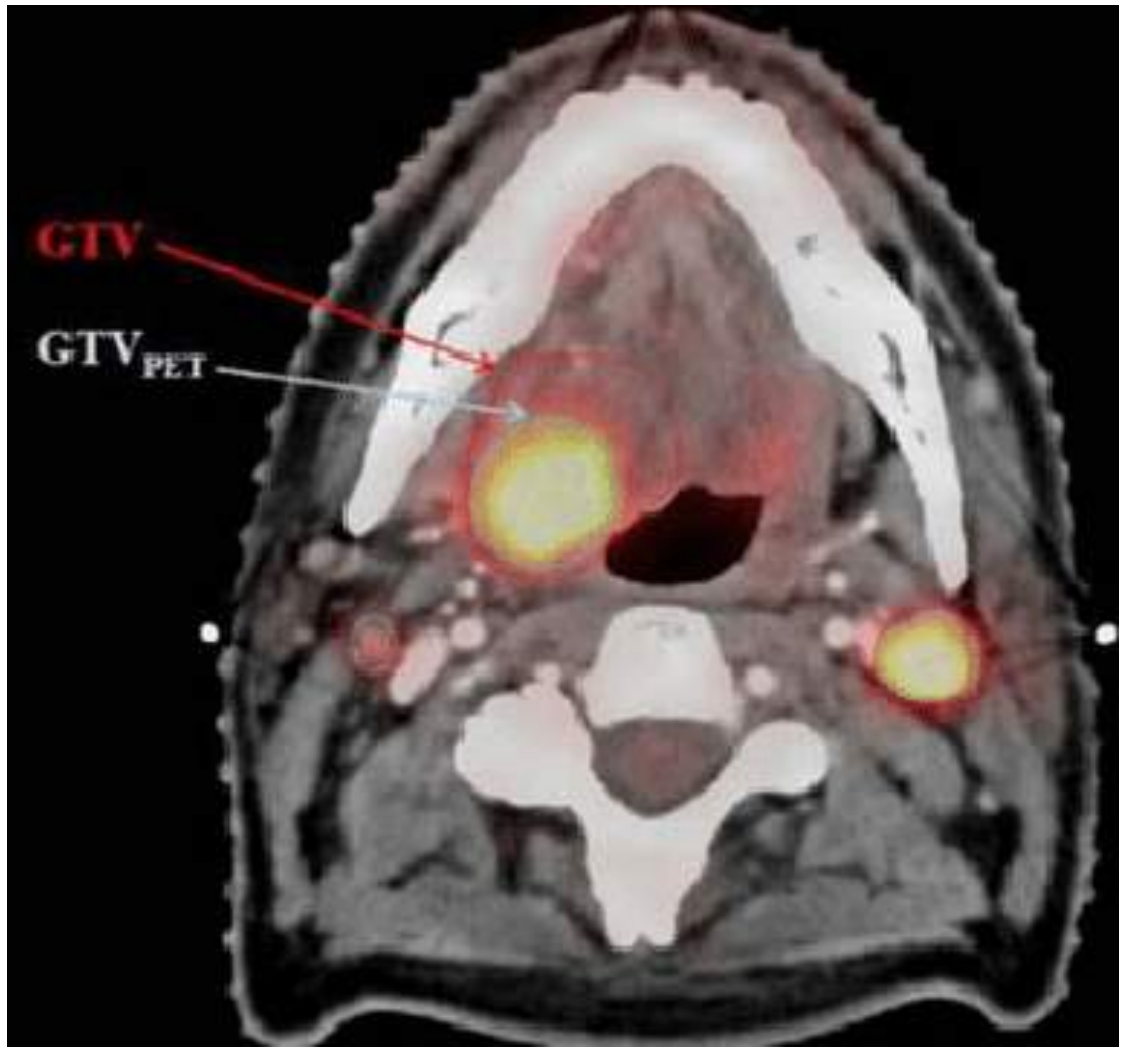
6.Imaging

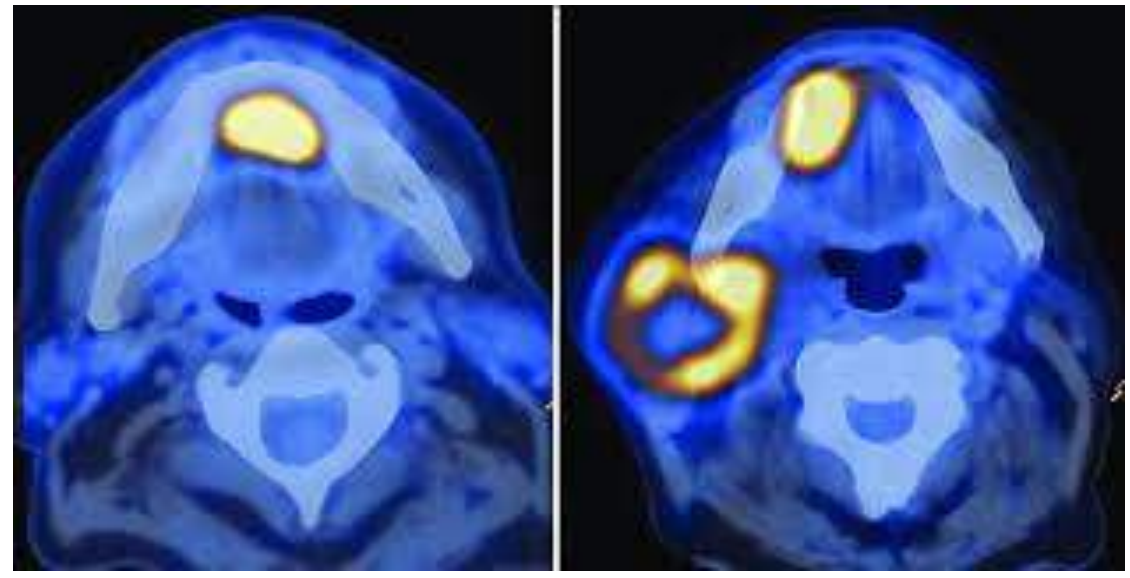
- Routine radiology, computed tomography (CT), nuclear scintiscanning ,magnetic resonance imaging, and ultrasonography can provide evidence of bone involvement or can indicate the extent of some soft tissue lesions.

- The selection of the appropriate imaging modality is dependent on the **type and location** of the suspected tumor.

Positron emission tomography (PET)

- is a type of nuclear medicine procedure that measures metabolic activity of the cells of body tissues. PET using the radiolabeled **glucose analog 18-fluorodeoxyglucose** offers a functional imaging approach for the entire body.
- PET is a combination of **nuclear medicine** and **biochemical analysis**.
- Used mostly in patients with brain or heart conditions and cancer.
- PET differs from other nuclear medicine examinations, in that PET detects **metabolism** within body tissues, whereas other types of nuclear medicine examinations detect the **amount of a radioactive substance** collected in body tissue in a certain location to examine the tissue's function.
- PET is most often used by oncologists, neurologists, neurosurgeons, cardiologists, and PET may also be used in conjunction with other diagnostic tests.

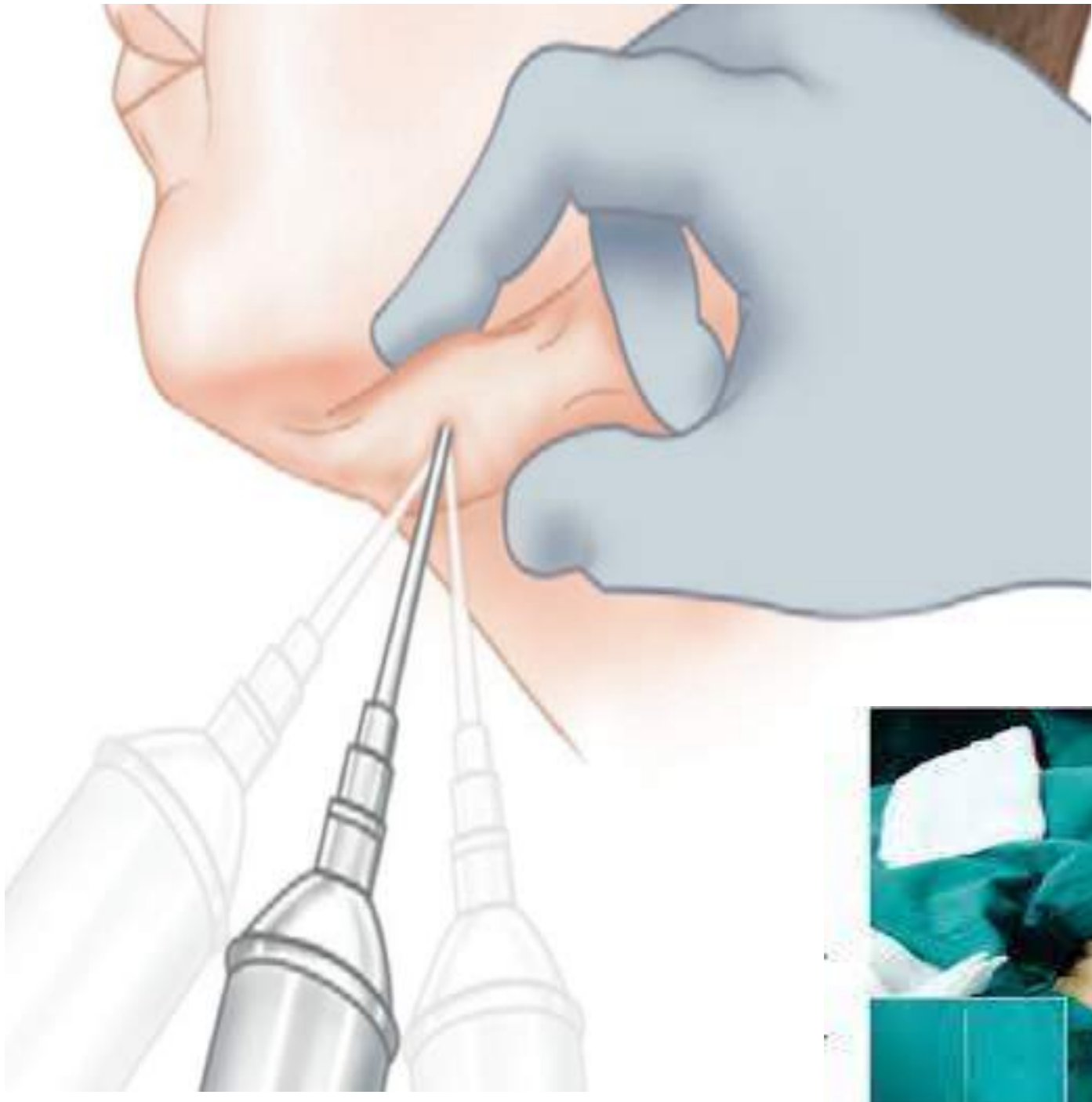

GTV
GTV PET



7.Acquisition of a Tissue Specimen

- In addition to standard surgical biopsy techniques, tissue can be acquired for histopathology by using fine-needle aspiration (FNA) or core needle biopsy (CNB).
- **Indications:**

1. Enlarged lymph nodes when open biopsy not recommended; in such cases, FNA biopsy should be considered.
2. FNA/CNB also may aid in the **evaluation of suspicious masses** in other areas of the head and neck, including mass that involve salivary glands, tongue, and palate.
3. When there is contraindication for conventional biopsy (e.g., thrombocytopenia). **Ultrasound** may assist in guiding FNA/CNB.



Treatment

- The principal objective of treatment is to cure the patient of cancer with the least possible morbidity.
- The choice of treatment depends on cell type and 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, and the presence or absence of metastases.
- Treatment decisions are also impacted by appraisal of the ability to preserve oropharyngeal function, including speech, swallowing, and esthetics, as well as the medical and mental status of the patient.
- Current trends in treatment plan recommendations consider the patient's personal preference, ability and willingness to tolerate therapeutic modalities based on cultural, individual,and sychosocial-motivated beliefs and attitudes.

- First-line definitive therapy may include **surgery, radiation therapy**, with or without chemotherapy/targeted therapy, Immunotherapy as an adjunct to principal therapeutic modalities for curative intent for oral and oropharyngeal carcinoma. In general, the **larger the primary tumor** and the **more advanced** the disease, the more multimodality treatment is recommended.
- Often the combined treatment includes all three modalities: radiotherapy, surgery, and chemotherapy.
- Continuing study of clinical outcomes, shed new light on the preferred combined treatment protocol.
- Treating patients with head and neck cancer note that **All** patients need access to multidisciplinary team.

a. SURGICAL ONCOLOGY

Indications:

1. Early or localized oral cancer.
2. Tumors involving bone, and when the side effects of surgery are expected to be less significant than those associated with radiation.
3. Tumors that lack sensitivity to radiation.
4. Recurrent tumor in areas that have previously received radiotherapy.
5. Surgery also may be used in palliative cases to **reduce the bulk of the tumor** and to promote drainage from a blocked cavity (e.g., antrum).

- Despite advances in radiation therapy, chemotherapy, targeted therapy,and immunotherapy, the backbone of treatment for resectable malignant tumors of the oral cavity remains upfront **surgery** with tailored adjuvant therapy.

- Surgical excision of dysplastic and malignant lesions can be accomplished with laser therapy . It is well tolerated and usually decreases the period of hospitalization and may have similar outcomes as traditional surgical interventions.
- However, laser therapy has the **disadvantage** of limiting the assessment of the margins for histopathologic confirmation.
- The **most important technological** advances in ablative head and neck cancer surgery is **robotic-assisted surgery.** The surgical robot is introduced through the oral cavity with the aid of a suspended retractor. Just like endoscopic techniques, robotic-assisted surgery allows for minimally **invasive approaches**.

b. Radiation Therapy

- Radiation therapy may be administered as a **single** modality, or as part of a **combined** radiation surgery and/or chemotherapy management, or for palliation.
- Radiotherapy with intent to cure causes early and late toxicities.
- In palliative care, radiation may provide symptomatic relief from pain, bleeding, ulceration, and oropharyngeal obstruction.
- Hyperfractionation of radiation (usually twice daily dosing) is one of the strategies to increase intensity of treatment to increase tumoricidal effects, which results in more severe acute effects.
- High-dose re-irradiation is offered as safe treatment and may be considered in case of recurrent or second primary head and neck cancer, particularly when safe surgery is not feasible.
- Radiation kills cells by interaction with water molecules in the cells, producing charged molecules that interact with biochemical processes in the cells and by causing direct damage to DNA.

- The affected cells may die or remain incapable of division.
- Due to a greater potential for cell repair in normal tissue than in malignant cells and a greater susceptibility to radiation due to the **higher growth fraction of cancer cells, a differential effect is achieved.**

- To achieve therapeutic effects, radiation therapy is delivered in daily fractions for a planned number of days.
- **The biologic effect** of radiation depends on the **dose per fraction, the number of fractions per day, the total treatment time, the total dose of radiation, and the radiation used (electron, neutron, proton).**

- **Radiation therapy has the advantage** of treating the disease in situ and avoiding the need for the removal of tissue and may be the treatment of choice for **T1 and T2 tumors**, particularly in the base of the tongue and oropharynx.

- Radiation may be administered to a **localized lesion** by using implant techniques (brachytherapy) or to a region of the head and neck by using external beam radiation.

- **The biologic effect** of radiation depends on the **dose per fraction, the number of fractions per day, the total treatment time, the total dose of radiation, and the radiation used (electron, neutron, proton).**

Cancer Treatment Planning is determined by

1. The tumor site and size,
2. Relation to vital structures,
3. The volume to be radiated,
4. Radiation technology available,
5. The number of treatment fractions,
6. The total number of days of treatment,
7. The tolerance of the patient.

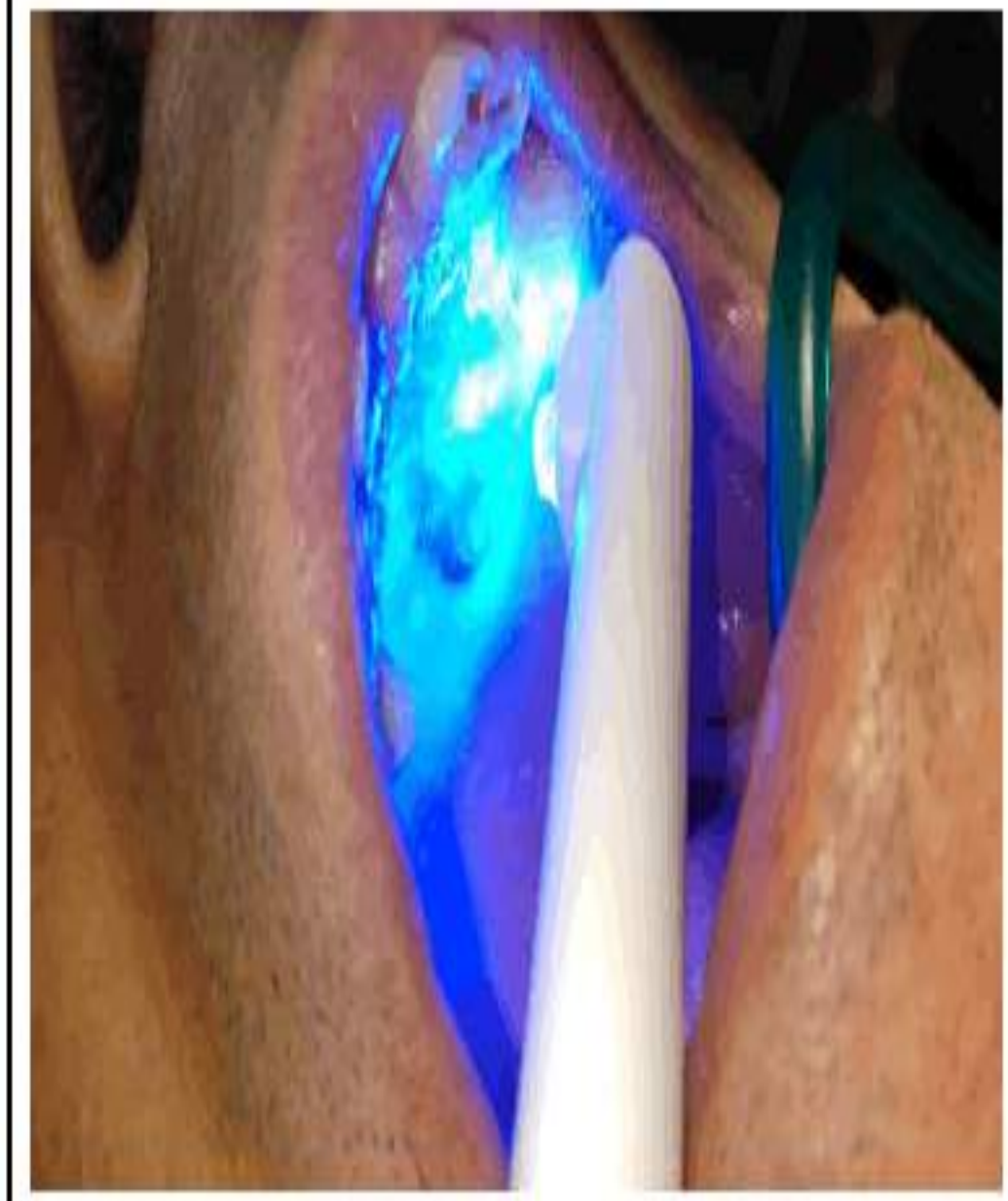
c. Cytotoxic Chemotherapy

- Chemotherapy may be used as induction therapy prior to local therapies, concurrent chemoradiotherapy (CCRT), and adjuvant chemotherapy after local treatment.

- The objective of induction chemotherapy is to **promote initial tumor reduction and to provide early treatment of micrometastases due to the recognition that local control.**
- The principal agents that have been studied alone or in combination in head and neck cancer are **taxol and derivatives, platinum derivatives (cisplatin and carboplatin), 5-fluorouracil, and hydroxyurea,** although hydroxyurea is rarely used in current protocols.

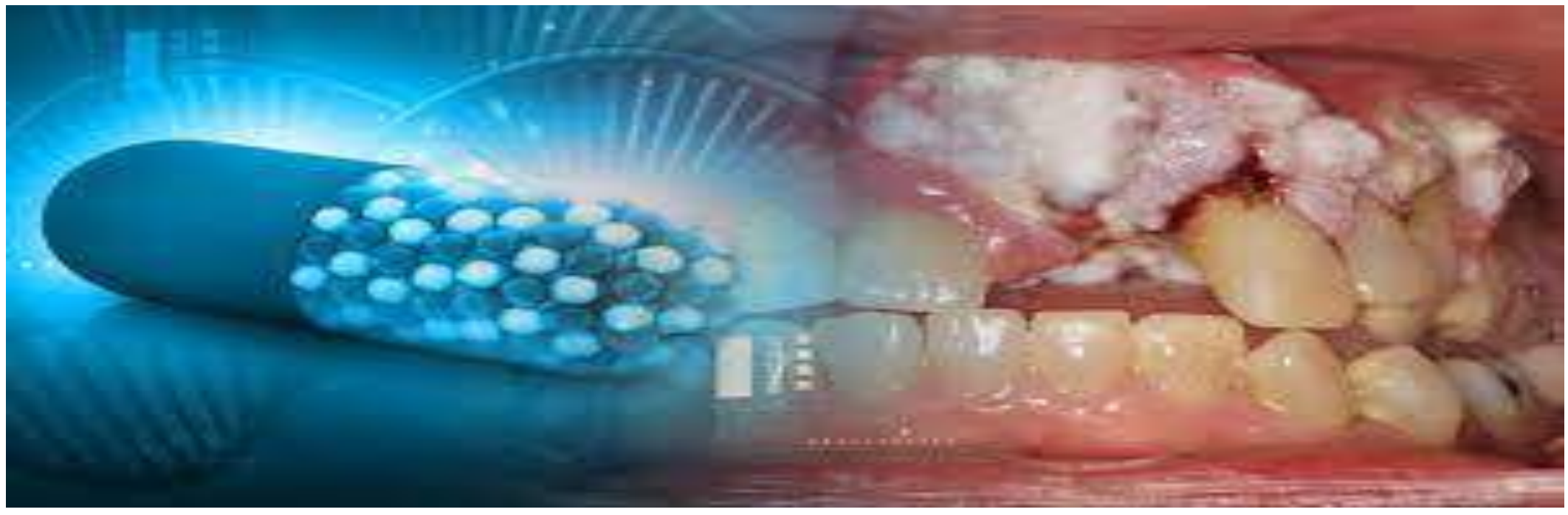
d. Photodynamic Therapy

- Light over a tissue that initially absorbed exogenous sensitizer.
- The sensitizing agent may be delivered systemically or topically and then after it selectively accumulates in target tissue.
- The subsequent light delivery to the target tissue results in cellular destruction.
- Due to the focused cellular destruction, the complications and disfigurement associated with this treatment are relatively small.
- Although photodynamic therapy in oral cancer has some encouraging preliminary results, it **is not accepted routine treatment**.



Gene Therapy

- Gene therapy is being studied with the objective of **reversing dysplasia** in oral epithelial lesions.
- The modalities evaluated include suicide gene therapy, immunotherapy, oncolytic virus therapy, inhibition of tumor angiogenesis, gene deletion therapy, and antisense RNA.
- Considering the high rate of mutation in p53 in oral cancer, gene therapy focused on *p53* gene, mostly with adenoviral vectors, shows promise.



e. Immunotherapy

- Immunotherapy offers the potential for additional approaches to management, alone or in combination with other therapies.
- Clinical practice guidelines for management of malignant melanoma and other cancers are approaching.
- Recurrent or metastatic SCC has limited treatment options and immunotherapy offers an intervention that may improve overall survival for these patients.
- **Keytruda** may be used with the chemotherapy medicines **fluorouracil** and a **platinum** as first treatment when head and neck cancer has spread or returned and cannot be removed by surgery.

Prognosis

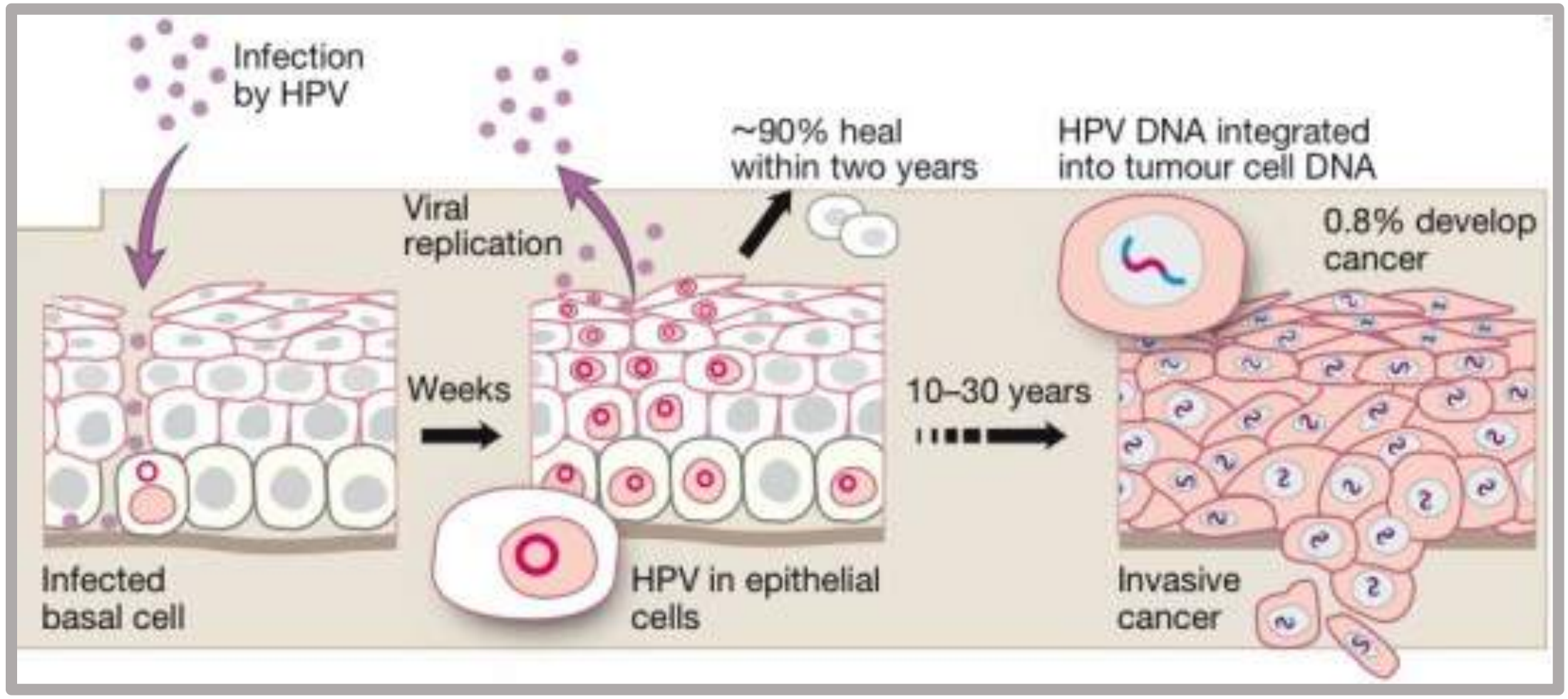
- The most important factors influencing survival in patients with oral and oropharyngeal cancer are the **presence of HPV** and the **stage** of disease at diagnosis.
- Unfortunately, the majority of oral cancers continue to be diagnosed at advanced stages, after becoming symptomatic.

- Cancers positive for HPV, particularly type 16, have a better prognosis compared to HPV-negative tumors.

- Locoregional causes of **death** from head and neck cancer may be due to erosion of major vessels, erosion of the cranial base, nutritional compromise, cachexia, and secondary infection of the respiratory tract.

- Overall survival in **younger** patients is **better** reflects that a more complex medical background and comorbidities in **older** patients

Etiologic role for this virus is strengthened by the fact **that HPV E6 protein is known to bind to and inactivate the p53 tumor suppressor gene**, possibly allowing chromosomal instability and subsequent neoplastic growth. HPV-16 has also been shown by to produce obviously **dysplastic epithelial cells** in differentiating tissue cultures which are otherwise sterile.



Human Papillomavirus Vaccine

- Human papillomavirus is known to have 19 different oncovirus strains.
- These are known to cause cervical, vaginal, vulvar, anal, penile, and head and neck cancers.
- Current vaccination is expected to prevent 90% of these cancers.
- The vaccine can be given to children (boys and girls) age 9 to adults aged 45.


كل عام وانتم بخير
Ramzan
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Pigmented Lesions of the Oral Mucosa

Dr. Marwah Waleed Sh.

Classification of pigmented lesions

A. Endogenous Pigmentation

- **Focal Melanocytic Pigmentation** 1. Freckle/Ephelis 2. Oral/Labial Melanotic Macule 3. Oral Melanoacanthoma 4. Melanocytic Nevus 5. Malignant Melanoma
- **Multifocal/Diffuse Pigmentation** 1. Physiologic Pigmentation
- 2. Drug-Induced Melanosis 3. Smoker's Melanosis 4.Postinflammatory (Inflammatory) Hyperpigmentation
- 5. Melasma (Chloasma)
- **Melanosis Associated with Systemic or Genetic Disease** 1.Hypoadrenocorticism (Adrenal Insufficiency or Addison's Disease) 2. Cushing's Syndrome/Cushing's Disease 3. Hyperthyroidism (Graves' Disease) 4. Primary Biliary Cirrhosis 5. Vitamin B12 (Cobalamin) Deficiency 6. Peutz–Jeghers Syndrome 7. Café au Lait Pigmentation 8. HIV/AIDS-Associated Melanosis
- **Idiopathic Pigmentation** 1. Laugier–Hunziker Pigmentation Treatment of Mucocutaneous Melanosis
- **Depigmentation** 1. Vitiligo
- **Hemoglobin and Iron-Associated Pigmentation** 1. Ecchymosis 2. Purpura/Petechiae 3. Hemochromatosis

B. Exogenous Pigmentation

1.Amalgam Tattoo
2.Graphite Tattoos
3.Ornamental Tattoos
4.Medicinal Metal-Induced Pigmentation
5.Heavy Metal Pigmentation
6.Drug-Induced Pigmentation
7.Hairy Tongue

- Healthy oral soft tissues present a typical pink to red hue with slight topographical variations of color. This chromatic range is due to the interaction of several tissues that compose the mucosal lining:
- **•The presence or absence of keratin on the surface epithelium.**
- **•The quantity, superficial or deep location of blood vessels in the subjacent stroma.**
- **•The existence of lobules of adipocytes.**
- **•The absence of melanin pigmentation in the basal cell layer of the epithelium.**

✔Although oral and perioral pigmentation may be physiologic in nature, particularly in individuals with **dark skin** complexion, **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 attributed 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.**

- ➤**Hemoglobin, hemosiderin, and melanin** represent the most common endogenous sources of mucosal color change.

- ➤Sub mucosal collection of hemoglobin or hemosiderin, produced by extravasation and/or lysis of red blood cells, may impart a **red, blue, or brown** transient appearance to the oral mucosa.

- **Melanin,** which is synthesized by **melanocytes** and **nevus cells**, may **appear brown, blue,** or **black**, depending on the **amount** of melanin and its **location** within the tissue (superficial / deep).

1. Exogenous pigmentations

- Are usually associated with traumatic or iatrogenic events that result in the deposition of foreign material directly into the mucosal tissues.

- In some cases, the substances may be ingested, absorbed, and distributed hematogenously into connective tissues, particularly in areas subject to **chronic inflammation, such as the gingiva**. In other instances, these **ingested substances** can actually **stimulate melanin** production, thus precipitating the **color change**.

- **Chromogenic bacteria** can also produce oral pigmentation, usually resulting in discoloration of the **dorsal tongue**.

- **Certain foods**, **drinks, and confectionaries** can also result in exogenous pigmentation. However, in most cases, the discoloration can be easily reversed.

The manifestation of oral pigmentation is quite variable,

- ➤To obtain an **accurate diagnosis**, thorough social, family, medical, and dental histories are required, and **various diagnostic procedures** (colonoscopy) and laboratory tests, including **biopsy**, may be necessary.
- ➤**Lesions** that are associated with mucosal discoloration but are **vascular in origin**, including developmental, hamartomatous, and neoplastic lesions (hemangioma, lymphangioma, angiosarcoma, Kaposi's sarcoma).
- It should be noted that these entities are frequently considered in the differential diagnosis of both macular and mass-forming pigmented lesions.

2.Endogenous Pigmentation

- **Melanin** is a pigment **derivative of tyrosine and is synthesized by melanocytes,** which typically reside in the basal cell layer of the epithelium.
- **Keratinocytes** 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.**
- ➤They also act as scavengers in protecting against various cytotoxic intermediates. **The role of melanocytes in oral epithelium is not clear.**
- **Melanin** is synthesized within specialized structures known as **melanosomes**.
- Melanin is composed of **eumelanin,** which is a **brown-black** pigment, and **pheomelanin**, which has a **red-yellow** color.

- **The term melanosis is frequently used to describe diffuse hyperpigmentation.**

- ?➤**Overproduction of melanin** may be caused by a variety of **mechanisms**, the most common of which is related to **increased sun exposure**.
- ?➤Intra-orally, 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), **post inflammatory** changes, and **genetic or autoimmune disease**. Therefore, the presence or absence of systemic signs and symptoms, including cutaneous hyperpigmentation, is of great importance to explain the cause of oral pigmentation.
- If the etiology of the pigmentation cannot be clinically ascertained, **a tissue biopsy** is warranted for definitive diagnosis.
- This is critical because malignant melanoma may present with a **misleadingly** benign clinical appearance.

- **Diascopy, radiography,** and **blood tests**, may be necessary for definitive diagnosis of oral pigmentation. **Dermascopy,** also known as **epiluminescence microscopy**, can be useful in the diagnosis of melanocytic lesions.
- **The dermascopy** is used in the evaluation of labial and anterior lingual pigmentation. This noninvasive technique is performed using a handheld surface microscope using incident light and oil immersion.
- **A more advanced method** using a **binocular stereo microscopes**. This diagnostic technique has been shown to be effective in discriminating **melanocytic** from **non melanocytic** lesions and **benign** versus **malignant** melanocytic processes.

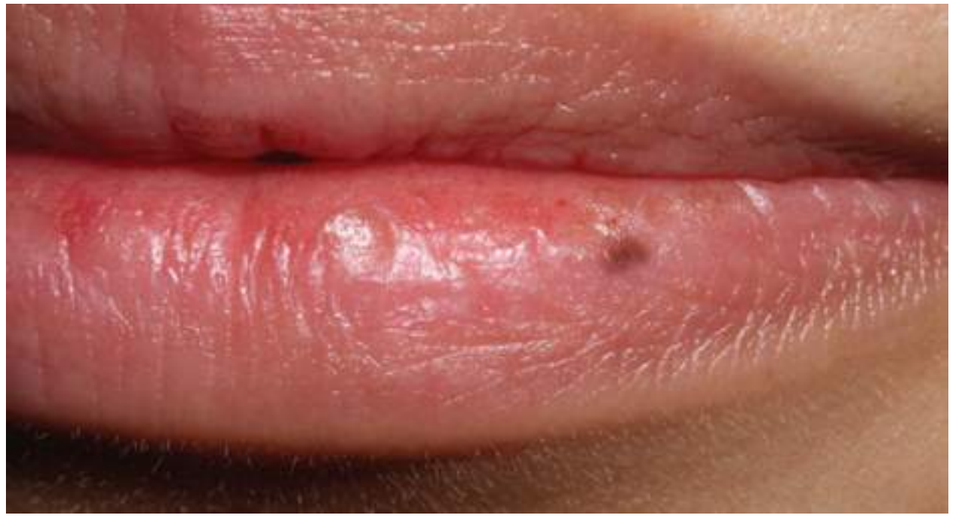
Dermascopy

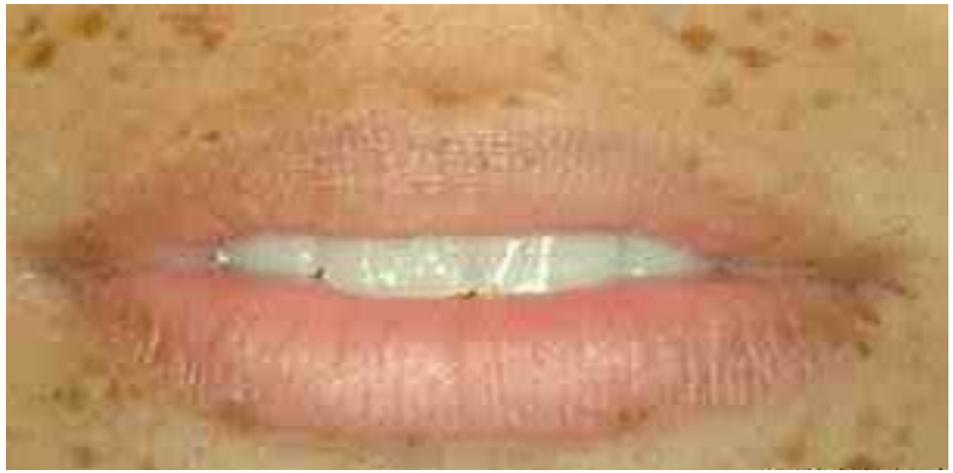
Binocular stereo microscopes

Focal Melanocytic Pigmentation

Freckle/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 observed in light-skinned individuals and are quite prevalent in red- or light blond–haired individuals.





- **Freckles** are thought to be **developmental** in origin Polymorphisms in the **MC1R gene** are strongly associated with the development of childhood freckles. Another putative freckles-predisposition gene has also been mapped to **chromosome 4q32–q34.**

- **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 fall and winter months.
- The increase in pigmentation is merely 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.

MELANOTIC MACULES

- Melanotic macules develop more frequently in **females**, usually in the lower lip (labial melanotic macule) and gingiva. 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**.
- 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 **innocent** lesion, does not represent a melanocytic proliferation, and **does not recur** following surgical removal

Pathology:

- Microscopically, melanotic macules are characterized by the presence of abundant melanin pigment in the basal cell layer without an associated increase in the number of melanocytes. The pigmentation is often accentuated at the tips of the rete pegs, and melanin incontinence into the subjacent lamina propria is commonly encountered.

Differential Diagnosis:

- The differential diagnosis may include melanocytic nevus, malignant melanoma, amalgam tattoo, and focal ecchymosis. If such pigmented lesions are present after a two-week period, ecchymosis can usually be ruled out, and a biopsy specimen should be obtained to secure a definitive diagnosis.
- Since oral mucosal malignant melanomas have no defining clinical characteristics, a biopsy of any persistent solitary pigmented lesion is always warranted.

Oral Melanoacanthoma

Etiology and Pathogenesis

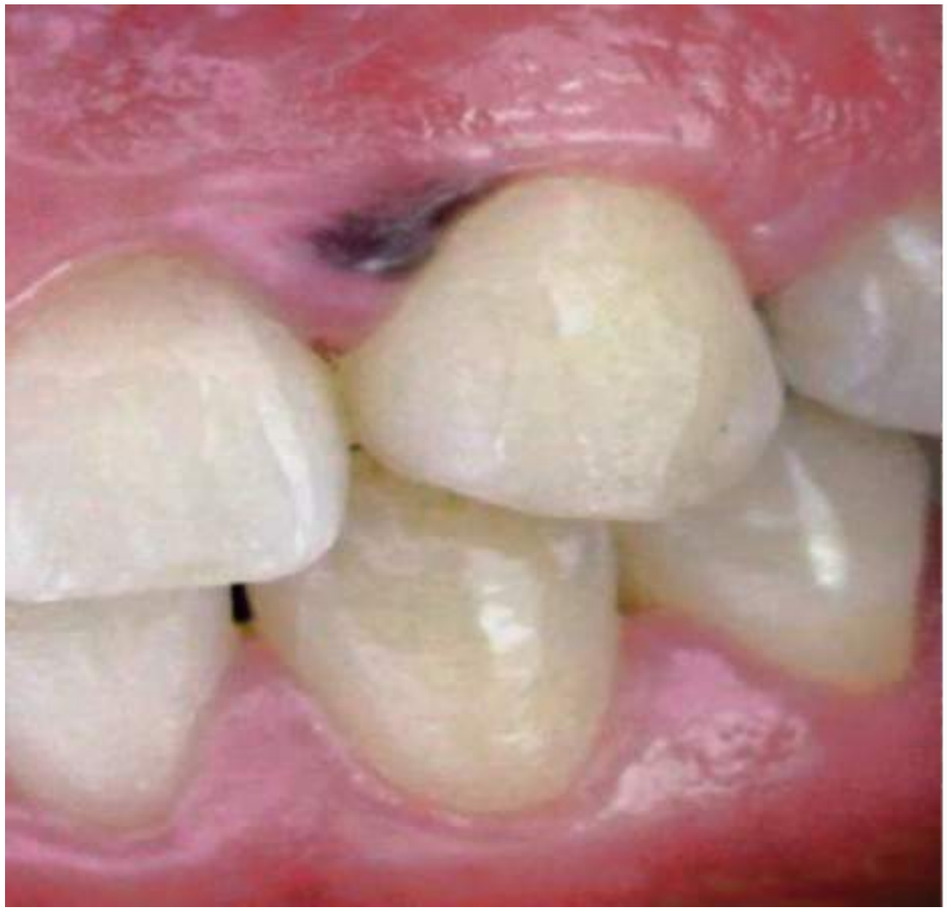
✔It is another **unusual, benign, melanocytic** lesion that is **unique to the mucosal tissues.**

✔ Oral melanoacanthoma is an innocent melanocytic lesion that may spontaneously resolve, with or without surgical intervention.

✔Although the term melanoacanthoma may imply a neoplastic process, the oral lesion is actually **reactive in nature**.

✔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. The biopsy procedure itself may lead to spontaneous regression of the lesion. The underlying source of the **irritation** should be eliminated to minimize recurrence



Clinical Features

- Oral melanoacanthoma usually presents as a **rapidly enlarging**, ill-defined, darkly pigmented macular or plaque-like lesion, and mostly develop in **black females**.
- Although, lesions may present over a wide age range, the majority occur between the third and fourth decades of life.
- Typically, melanoacanthoma presents as a solitary lesion; however, bilateral and multifocal lesions have been reported.
- It is generally asymptomatic; however, pain has been reported.
- Although any mucosal surface may be involved, close to 50% of melanoacanthomas arise on the **buccal mucosa**.
- 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.

Pathology:

Microscopically, oral melanoacanthomas are characterized by a proliferation of benign, dendritic melanocytes throughout the full thickness of an acanthotic and spongiotic epithelium. A mild lymphocytic infiltrate with exocytosis is also characteristic. Occasional eosinophils may be observed.

Diagnosis: Because oral melanoacanthoma may resemble other melanocytic lesions, such as pigmented nevus, melanotic macule, and melanoma, a biopsy is warranted to obtain a definitive diagnosis.

Melanocytic Nevus

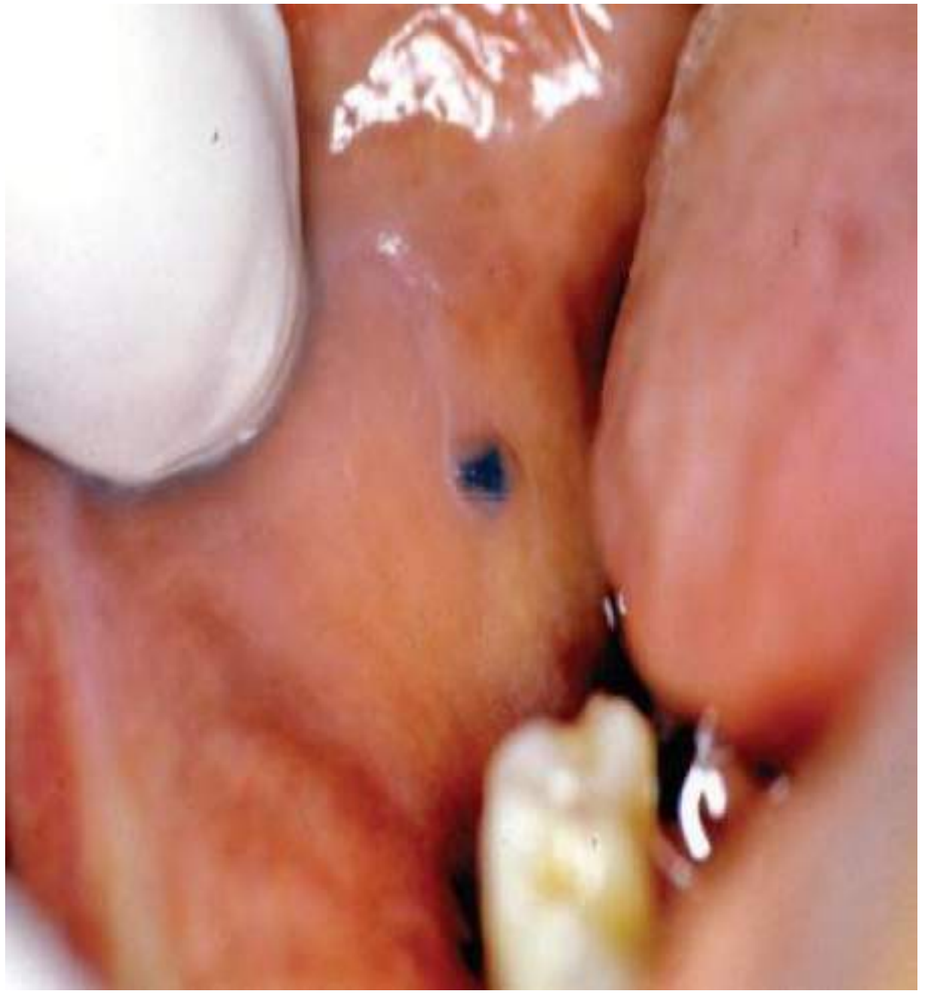
Etiology and Pathogenesis

➤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.

➤Compound nevi are less common, and the junctional nevus and combined nevus (a nevus composed of two different cell types) are infrequently identified.



- In fact, there is still debate as to whether “nevus cells” are a distinct cell type derived from the neural crest or if they are simply a unique or immature form of melanocyte. The lesional nevus cells are cytologically and biologically distinct from the melanocytes that colonize the basal cell layer of the epidermis and oral epithelium.
- Most nevic cells tend to be round, ovoid, or spindle shaped. Nevus cells to closely approximate one another, if not aggregate in clusters, and their ability to migrate into and/or within the submucosal tissues. **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.
- A**ge- and location-dependent** differences in the presentation, number, and distribution of nevi.

- Most melanocytic nevi are acquired , some may present as congenital lesions (including in the oral cavity).
- **Familial atypical multiple mole 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** and **Noonan's syndrome**; and congenital nevi are typical of **Neurocutaneous melanosis.**

Clinical Features

- 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**.
- Oral melanocytic nevi are rare, typically present as solitary lesions, and may be more common in female.

➤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 show 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.

Pathology

- Transformation of an oral nevus to malignancy has not been well documented in the literature.
- **It is advised that all oral nevi, regardless of histologic type, be completely removed as they may still represent a potential precursor of malignant melanoma.**

Diagnosis :**Biopsy is necessary** for diagnostic confirmation .

- **Complete and conservative surgical excision is the treatment of choice for oral lesions.** Recurrence has rarely been reported.
- **Laser** and intense pulse light therapies have been used successfully for the treatment of cutaneous nevi.

Malignant Melanoma

Etiology and Pathogenesis

- 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.

Clinical Features

➤**Cutaneous melanoma** is most common among **white populations** that live in the **Sunbelt** regions of the world, mortality rates are higher in blacks and Hispanics.

➤M**ales older than 45 years**.

➤Male predilection, but melanoma is one of the most commonly occurring cancers **in women of child-bearing age**.

➤**No significantly increased incidence of melanoma in pregnancy**, and there is no difference in survival rates between pregnant and non pregnant women with the disease

➤**Melanomas may develop either de novo or, much less commonly, arise from an existing melanocytic nevus.**

➤ On the **facial skin**, the **malar region** is a common site for melanoma since this area is **subject to significant solar exposure**.

➤**The clinical characteristics of cutaneous melanoma are best described by the ABCDE** criteria: **A**symmetry, irregular **B**orders, **C**olor variegation, **D**iameter greater than 6 mm, and **E**volution or surface elevation. This criteria differentiating cutaneous melanoma from other focally, pigmented melanocytic lesions.

➤**There are four main clinicopathologic subtypes of melanoma that include :**

- 1) Superficial spreading melanoma,.
- 2) Lentigo maligna melanoma.
- 3) Acral lentiginous melanoma.
- 4) Nodular melanoma.
- In the first three subtypes, the initial growth is characterized by radial extension of the tumor cells (**radial growth phase**). In this pattern, the melanocytic tumor cells spread laterally and therefore superficially. These lesions have a **good prognosis** if they are detected early and treated before the appearance of nodular lesions, which indicates invasion into the deeper connective tissue (i.e., a **vertical growth phase**). The development of nodularity in a previously macular lesion is often a warning sign.

➤**The prognosis of melanoma** can be determined by Breslow’s tumor thickness criteria or Clark’s level of invasion.

➤Surface ulceration, vascular or lymphatic invasion, neurotropism, high mitotic index, and absence of lymphocytes infiltrating the tumor are all associated with a **poor prognosis.**

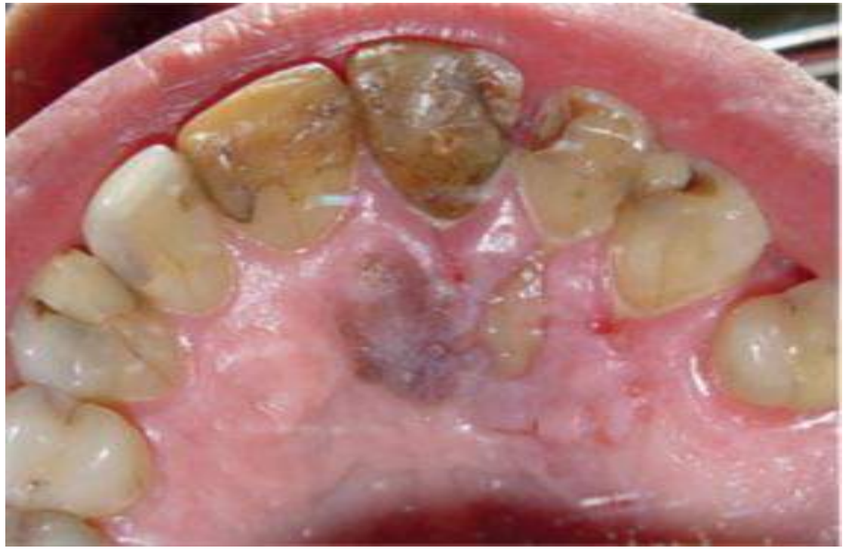
- Oral mucosal malignant melanoma is associated with a very poor prognosis. The palate shows the worst prognosis compared to other intraoral sites.

➤ In addition, various clinical parameters, including tumor site, age of the patient (>60 years), gender (male), and regional or distant metastasis, also are predictive of **poor prognosis**.

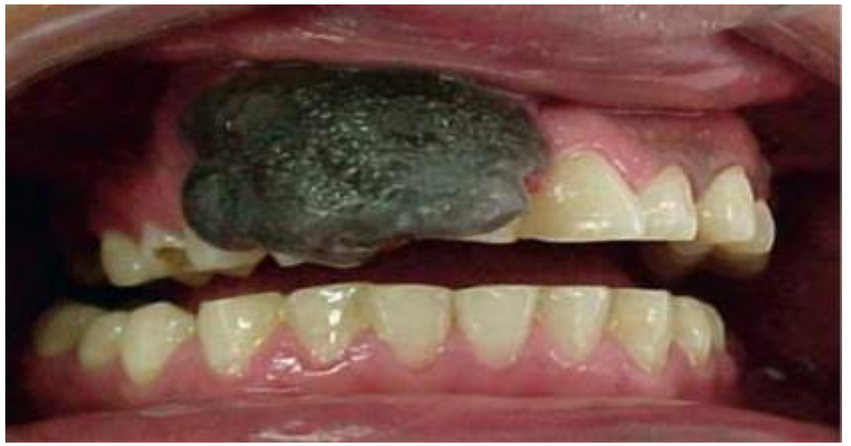
➤ The five-year survival rate of patients with metastatic melanoma is less than 15%. **The 10-year-survival rate is 0%..**

- **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.
- Unlike the cutaneous variant, which has distinct and well-recognized risk factors associated with its development, the etiology of oral melanoma remains unknown.
- **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/alveolar crest** 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 show 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.



Malignant melanoma exhibiting macular involvement of the anterior hard palate



Malignant melanoma presenting as a mass on the maxillary gingiva

➤**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 and could include melanocytic nevus, oral melanotic macule, and amalgam tattoo, as well as various vascular lesions and other soft tissue neoplasms.

➤ **Diagnosis:** Biopsy of any persistent solitary pigmented lesion is always warranted. Determination whether the lesion is **a primary neoplasm** or **a metastasis from a distant site.**

Management

- For primary oral melanomas, **ablative surgery** with wide margins remains the treatment of choice.
- Adjuvant **radiation therapy** may also be necessary. It remains unclear whether radiation therapy is beneficial for the treatment of oral mucosal melanoma.
- Computed tomography and magnetic resonance imaging studies should be undertaken to explore metastases to the regional lymph nodes.
- A variety of **chemotherapeutic and immunotherapeutic strategies** are often used if metastases are identified or for palliation.
- Adjuvant **interferon-α-2B** therapy for the treatment of primary cutaneous melanomas greater than 4 mm in thickness.
- Unusual side effects of chemotherapy and immunotherapy may include the onset of autoimmunity.
- The appearance of autoantibodies and clinical manifestations of autoimmune disease, including **vitiligo**, have been associated with statistically significant improvements in overall survival rates for patients with cutaneous melanoma.

Multifocal/Diffuse Pigmentation

1. Physiologic Pigmentation

- Physiologic pigmentation is the **most common** multifocal or diffuse oral mucosal pigmentation.
- Dark-complexioned individuals, including blacks, Asians, and Latinos, frequently show patchy to generalized hyperpigmentation of the oral mucosal tissues.
- The pigment is restricted to the gingiva , melanosis of other mucosal surfaces is not uncommon.
- The pigment is typically **first** observed during childhood and **does not** develop de novo in the adult.
- The **sudden or gradual onset** of diffuse mucosal pigmentation in adulthood, even in darker-skinned patients, should **alert** the clinician to consider a **pathological genesis**.

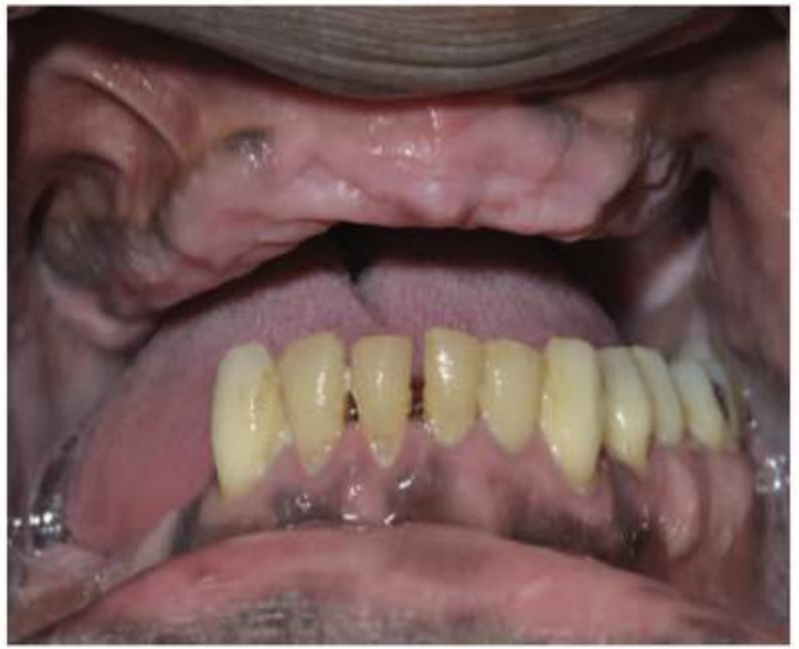
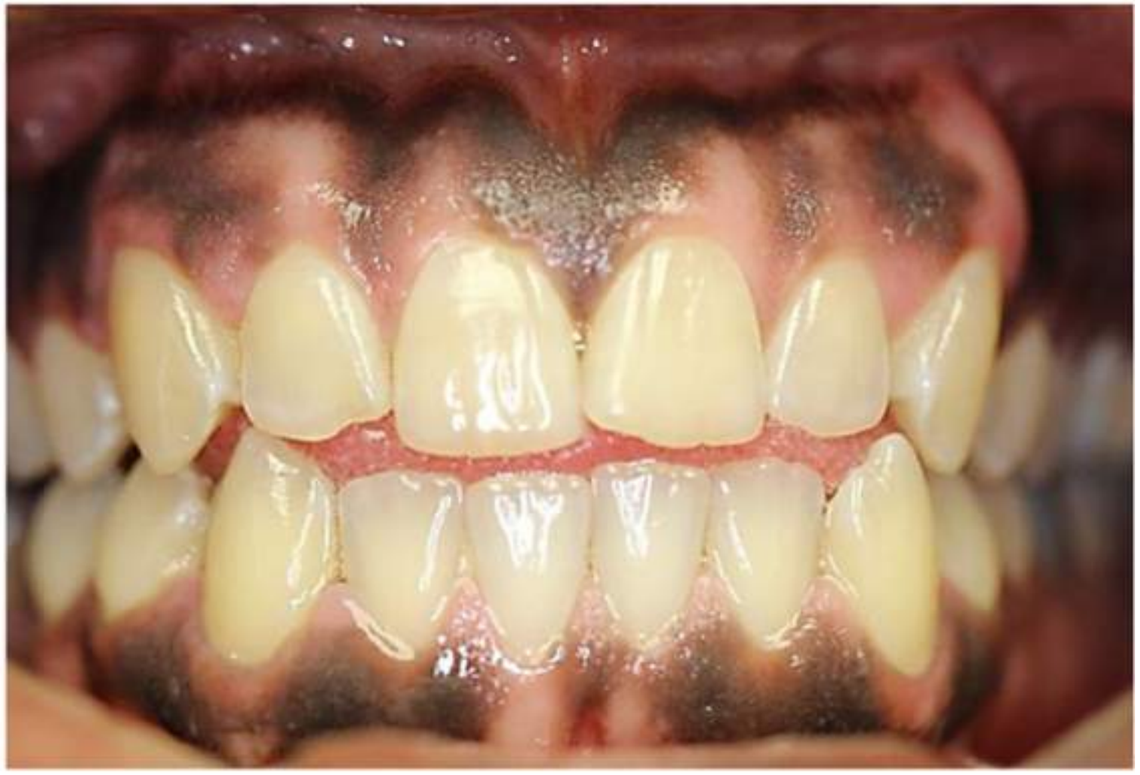
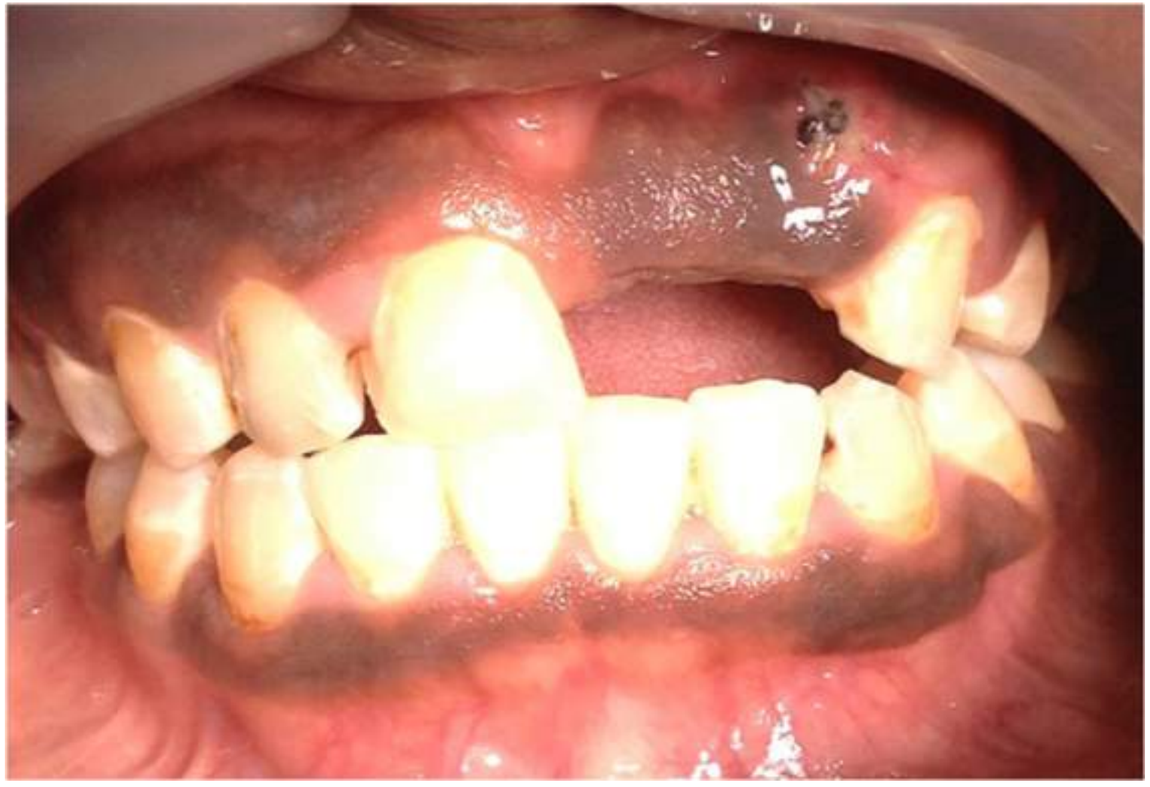


Figure 5-14 Physiologic pigmentation of the maxillary and mandibular gingiva. Note the patchy distribution of the pigment. *Source:* Courtesy of Dr. Christine Chu, private practice, New York, USA.



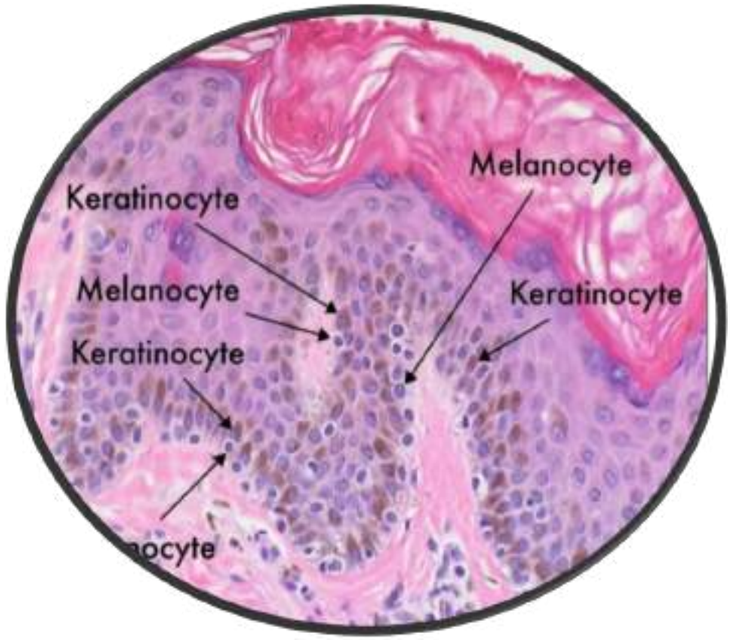


Differential diagnosis:

- May include idiopathic, drug-induced, or smoking-induced melanosis.
- Hyperpigmentation associated with endocrinopathy, and other systemic disease should also be considered.

A thorough history and laboratory tests are necessary to obtain a precise diagnosis.

- **Microscopically, physiologic pigmentation is characterized by the presence of increased amounts of melanin pigment within the basal cell layer.**
- The appearance of brown - black discoloration, even **intraorally**, can be esthetically displeasing to some patients.
- Surgical intervention may be necessary:
- Gingivectomy
- Laser therapy
- Cryosurgery has been reported to effectively remove oral mucosal pigmentation. However, with all these modalities, the pigmentation may eventually recur. **The cause of the re-pigmentation remains unclear**.



2.Drug-Induced Melanosis

Etiology and Pathogenesis

- Medications may induce a variety of different forms of mucocutaneous pigmentation, including melanosis.
- Pigmentation that is caused by the soft tissue deposition of drug metabolites or complexes and pigment associated with deposition of **lipofuscin or iron**.
- The chief drugs implicated in drug-induced melanosis are the **antimalarials**, including chloroquine, hydroxychloroquine, and **quinacrine**; used for the treatment of autoimmune disease.
- Other common classes of medications that induce melanosis include the **phenothiazines**, such as **chlorpromazine**, **oral contraceptives**, and **cytotoxic medications** (cyclophosphamide and busulfan).

Clinical Features

- 10–20% of all cases of acquired melanocytic pigmentation may be drug induced.
- **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 medications may even be associated with a specific pattern of pigmentation.
- The lesions are flat and without any evidence of nodularity or swelling.
- Sun exposure may exacerbate cutaneous drug-induced pigmentation.

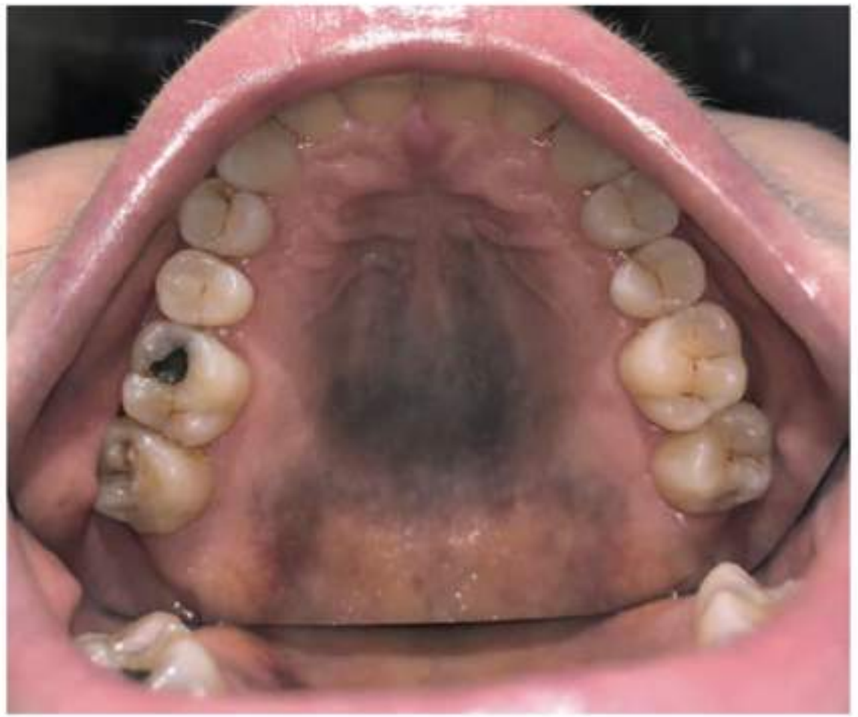
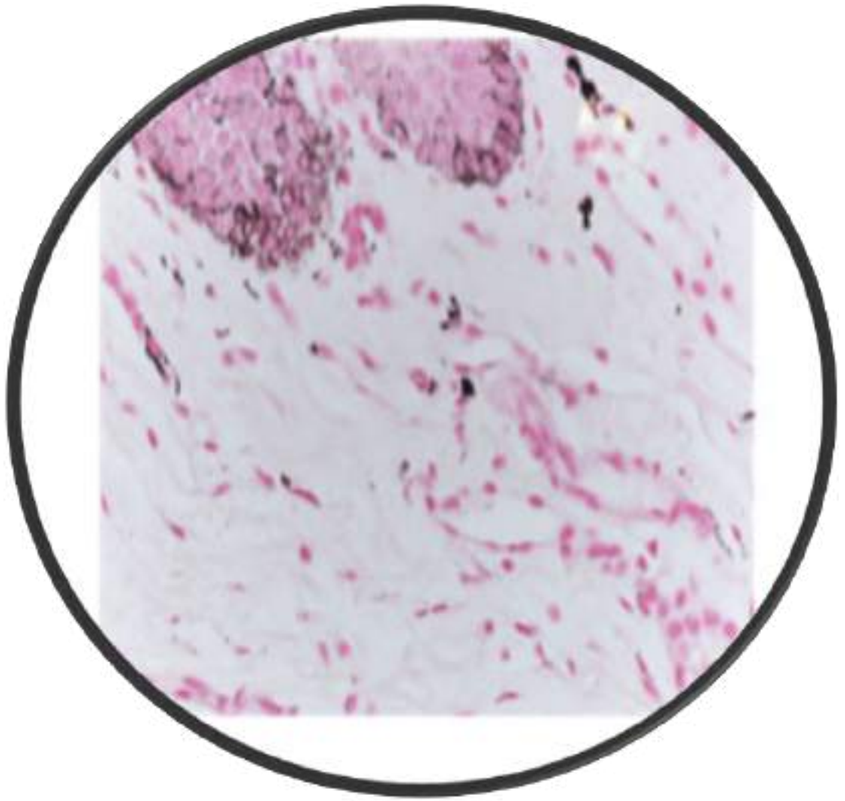


Figure 5-16 Imatinib-induced pigmentation of the palate. A 65-year-old white female treated with imatinib for gastrointestinal stromal tumor. Courtesy of Dr. Suman Sra, private practice, San Jose, CA, USA.

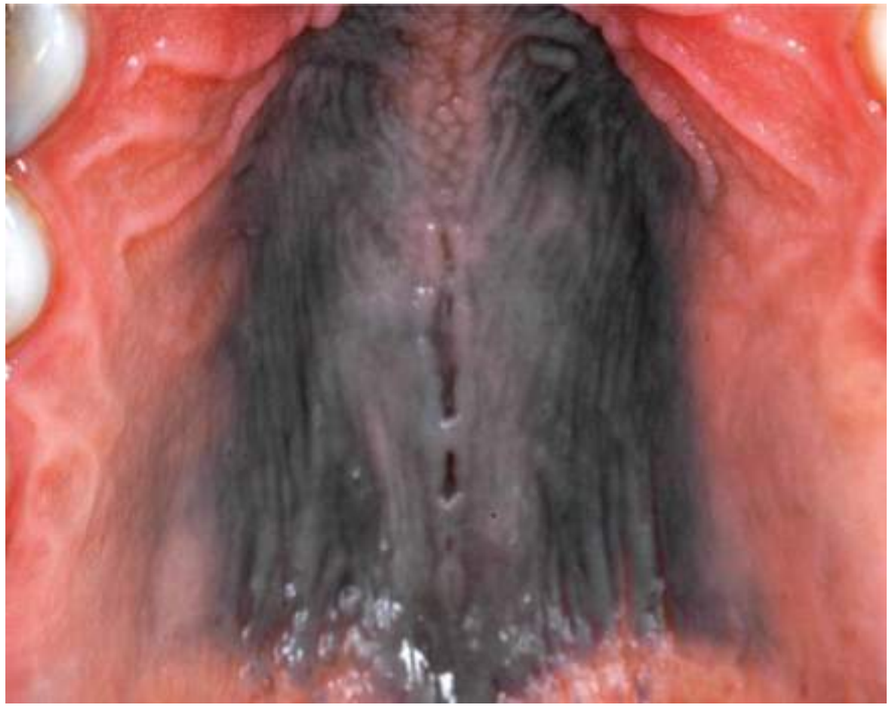
Pathology

- Microscopically, there is usually evidence of basilar hyperpigmentation and melanin incontinence without a concomitant increase in the number of melanocytes.
- The mechanisms by which melanin synthesis is increased remain unknown;
- **One theory** is that the drugs or drug metabolites stimulate melanogenesis.
- **Alternatively**, some drugs, including chloroquine and chlorpromazine, have been shown to physically bind melanin.
- This complexation of melanin and drugs within melanocytes may contribute to the adverse mucocutaneous effects.



Diagnosis

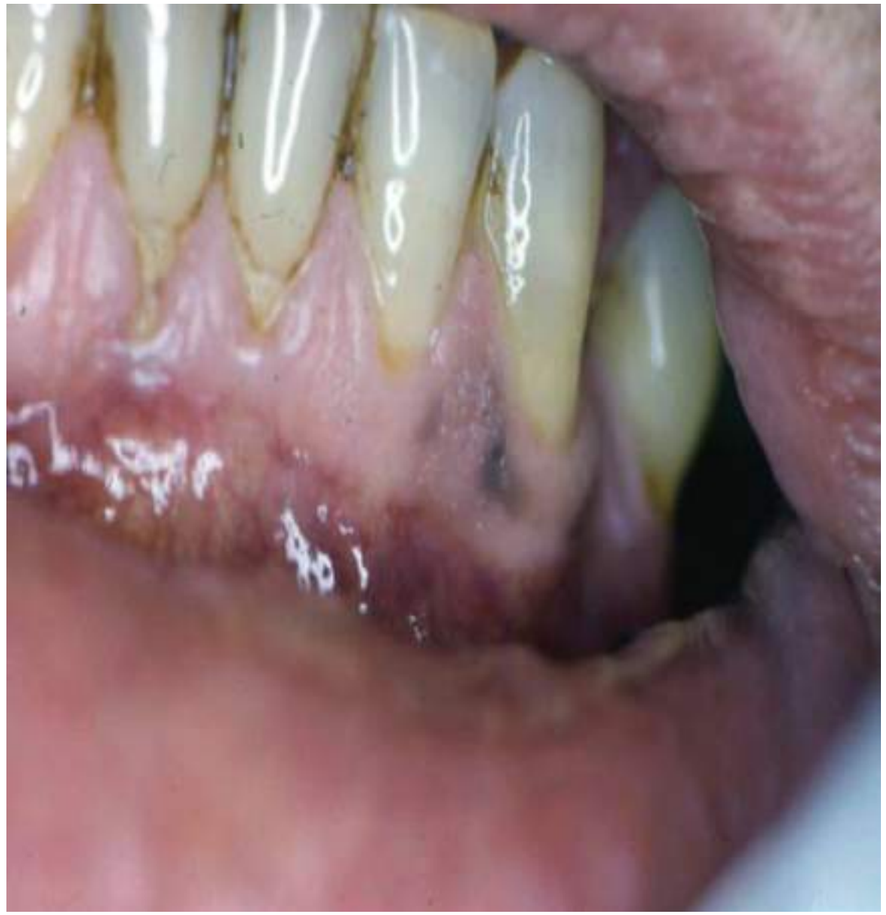
- If the **onset of the melanosis** can be chronologically and accurately associated with the use of a specific medication; within several weeks or months before development of the pigmentation, then no further intervention is warranted.
- In most cases, the discoloration tends to disappear within a few months after the drug is discontinued.
- Pigmentation associated with hormone therapy may tend to persist for longer periods of time, despite discontinuation of the medications.
- Differential diagnosis includes other causes of diffuse mucosal pigmentation. **Laboratory tests may be necessary to rule out an underlying endocrinopathy.**



Drug-induced pigmentation of the palate in a patient who was taking quinacrine for the treatment of discoid lupus erythematosus.

3. Smoker’s Melanosis

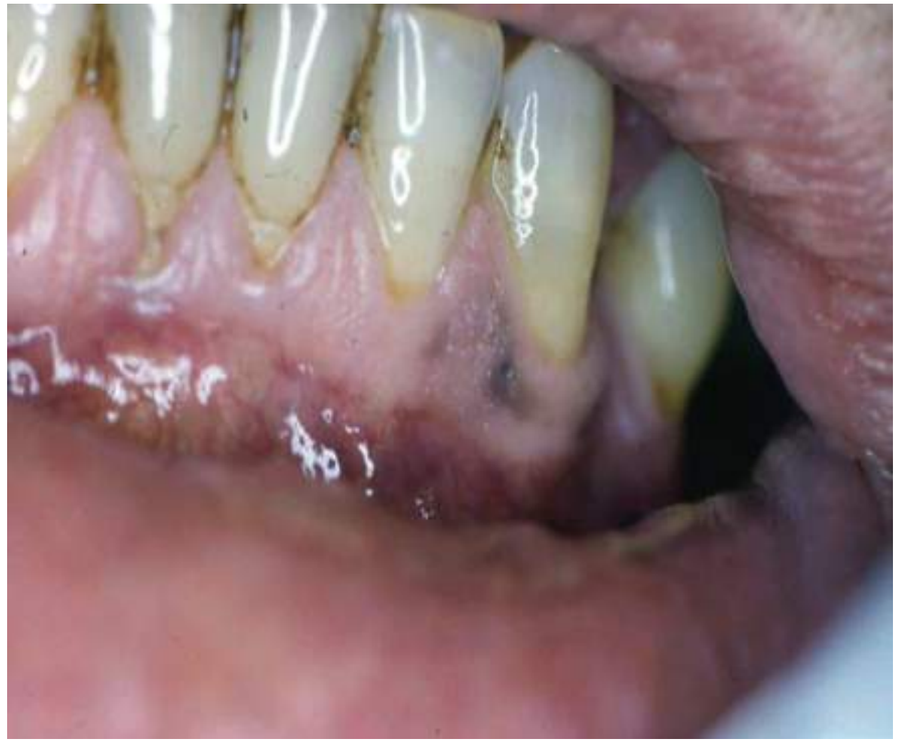
- **Diffuse melanosis** of the anterior vestibular maxillary and mandibular gingivae, buccal mucosa, lateral tongue, palate, and floor of the mouth is occasionally seen among cigarette smokers.
- Most smokers (including heavy smokers) usually fail to show such changes.
- However, in certain individuals, melanin synthesis may be stimulated by tobacco smoke products.
- 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 . The mechanism by which smoking induces the pigmentation remains unknown. **Smokeless tobacco** (snuff) does not appear to be associated with an increase in oral melanosis.



Smoker’s melanosis. The attached mandibular left gingiva shows pigmented macules on the side where the patient places the cigarette to smoke.

- It is possible that one or more of the chemical compounds incorporated within cigarettes, rather than the actual tobacco, may be causative.
- Another possibility is that the heat of the smoke may stimulate the pigmentation.
- **Passive smoking in children may result in increased gingival pigmentation**.
- Oral melanosis increases prominently during the first year of smoking.
- A reduction in smoking may lead to disappearing of the pigmentation.
- Smoker’s melanosis is not a preneoplastic condition.
- **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.
- **Alcoholic melanosis** may be associated with a higher risk of cancers of the upper aerodigestive tract.

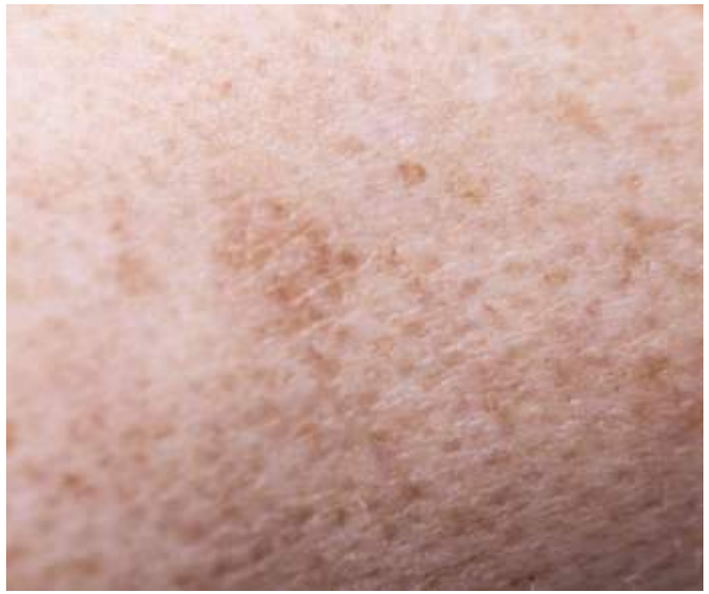
- **Oral submucous fibrosis**: Diffuse or patchy melanotic pigmentation. Unlike smoker’s melanosis, oral submucous fibrosis is a preneoplastic condition caused by habitual chewing of areca (betel) nut. This custom is common in some East Asian cultures. In addition to the melanosis, increased fibrosis of the oral soft.



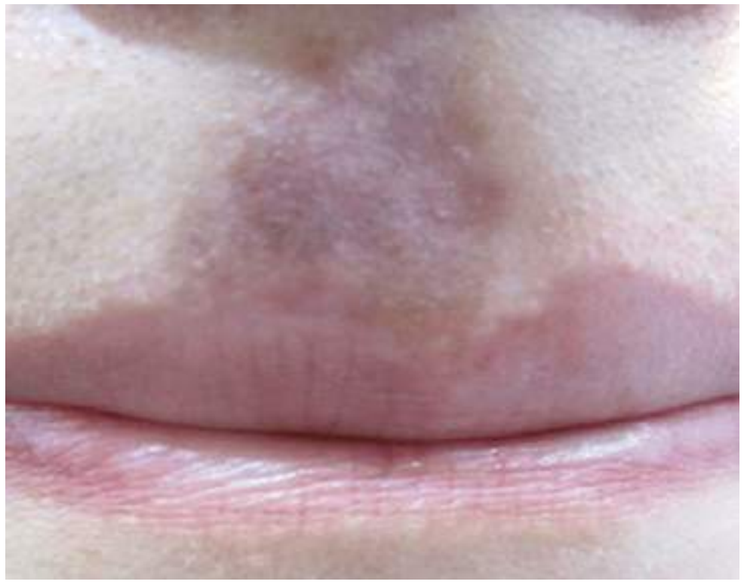
4.Postinflammatory (Inflammatory) Hyperpigmentation

- It is a well-recognized phenomenon that tends to develop more commonly in **dark-complexioned** 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.
- Postinflammatory pigmentation may also develop in the oral cavity.
- In rare cases, the mucosa overlying a non melanocytic malignancy may become pigmented.
- **Oral pigmentation** has also been described in patients with **lichen planus**. This phenomenon has been described in various races, including Caucasians.

- There is also evidence of basilar hyperpigmentation and melanin incontinence.
- Upon resolution of the lichenoid lesion, in most cases, the pigmentation eventually subside.
- It is unclear whether lichen planus– associated pigmentation should be appropriately characterized as postinflammatory or inflammatory pigmentation.
- In addition, spontaneous postsurgical healing pigmentation of palatal donor sites for free gingival grafts has been reported.



Post-Inflammatory Hyperpigmentation and Acne
By Angela Palmer Updated on March 01, 2022
Medically reviewed by Leah Ansell, MD



Lee, Ye & Shin, Ho & Noh, Tai-Kyung & Choi, Kwang-Ho & Chang, Sung-Eun. (2017). Treatment of Melasma and Post-Inflammatory Hyperpigmentation by a Picosecond 755-nm Alexandrite Laser in Asian Patients. Annals of Dermatology. 29. 779. 10.5021/ad.2017.29.6.779.

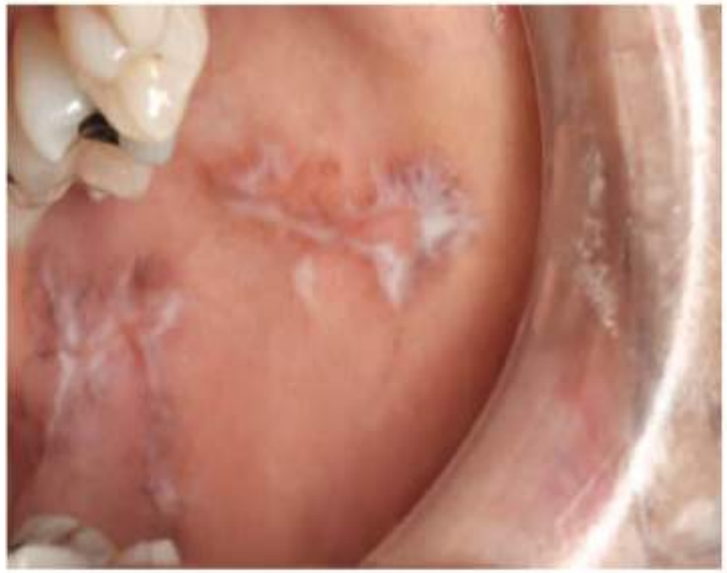
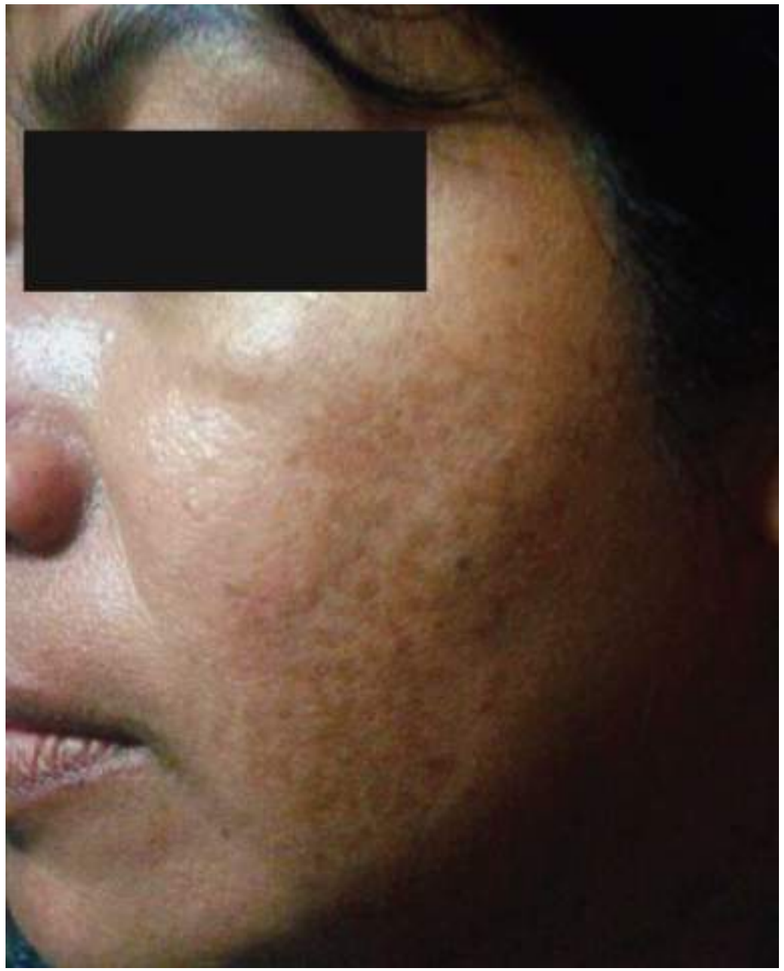


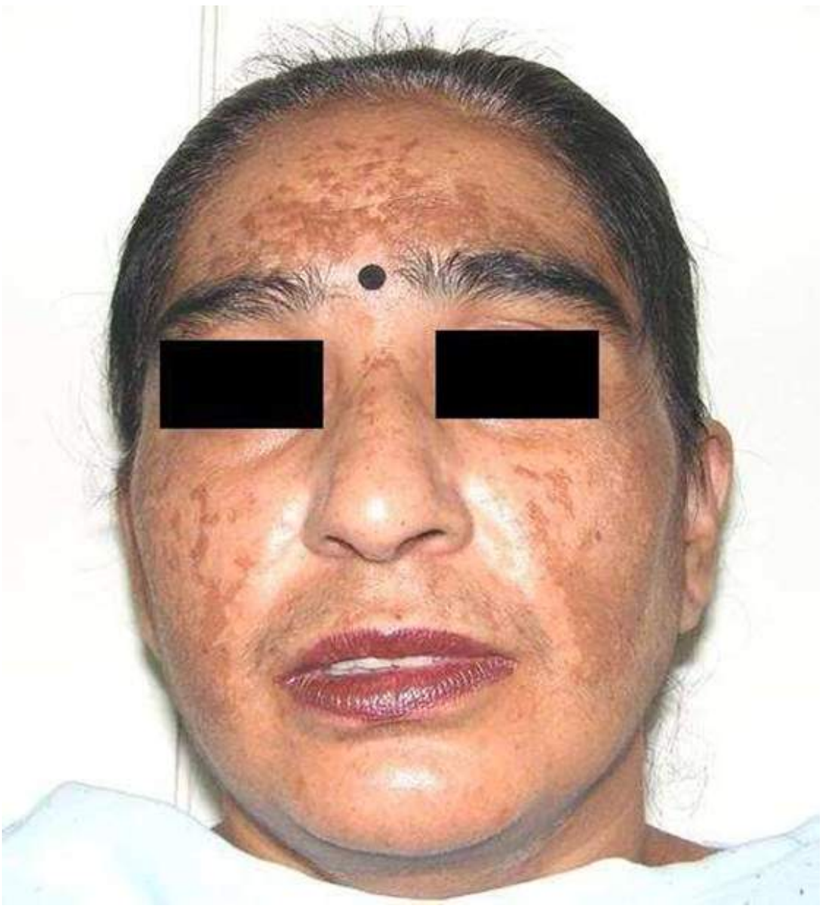
Figure 5-18 Lichen planus–associated pigment. Classic-appearing Wickham's striae and surrounding pigmentation are seen in this Caucasian patient with biopsy-proven lichen planus. *Source:* Courtesy of Dr. Carl Allen. The Ohio State University, Columbus, OH, USA.

5.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 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.
- The term melasma has been used to describe any form of generalized **facial hyperpigmentation**, including those related to postinflammatory changes and medication use.



- This term is most appropriately used to describe the pigmentary changes associated with sun exposure and hormonal factors, including pregnancy and 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.
- In most cases, it is the combination of estrogen and progesterone that induces the pigment.
- Estrogen replacement therapy alone, without progesterone, does not precipitate melasma.
- **In idiopathic cases**, significantly elevated levels of luteinizing hormone have been identified in both sexes, with associated decreases in serum estradiol (in women) and testosterone (in males).



Melasma: Treatment strategy
December 2011Journal of Cosmetic and Laser Therapy
13(6):265-79
DOI:10.3109/14764172.2011.630088

- Various thyroid abnormalities, including hypothyroidism, may also play a role in the pathogenesis of pregnancy- and non-pregnancy-associated melasma.
- A biopsy typically reveals basilar melanosis with no increase in the number of melanocytes. However, the melanocytes that are present may be larger than those in the adjacent normally pigmented areas.
- Melasma may spontaneously resolve after **parturition, cessation of the exogenous hormones, or regulation of endogenous sex hormone levels.**
- A successful therapeutic approach for the treatment of melasma consists in the topical administration of a triple combination product (4% hydroquinone, 0.05% tretinoin, and 0.01% fluocinolone acetonide) along with photoprotection (SPF 30 sunscreen).

Pigmented Lesions of the Oral Mucosa

Part-2

Dr. Marwah Waleed Sh.

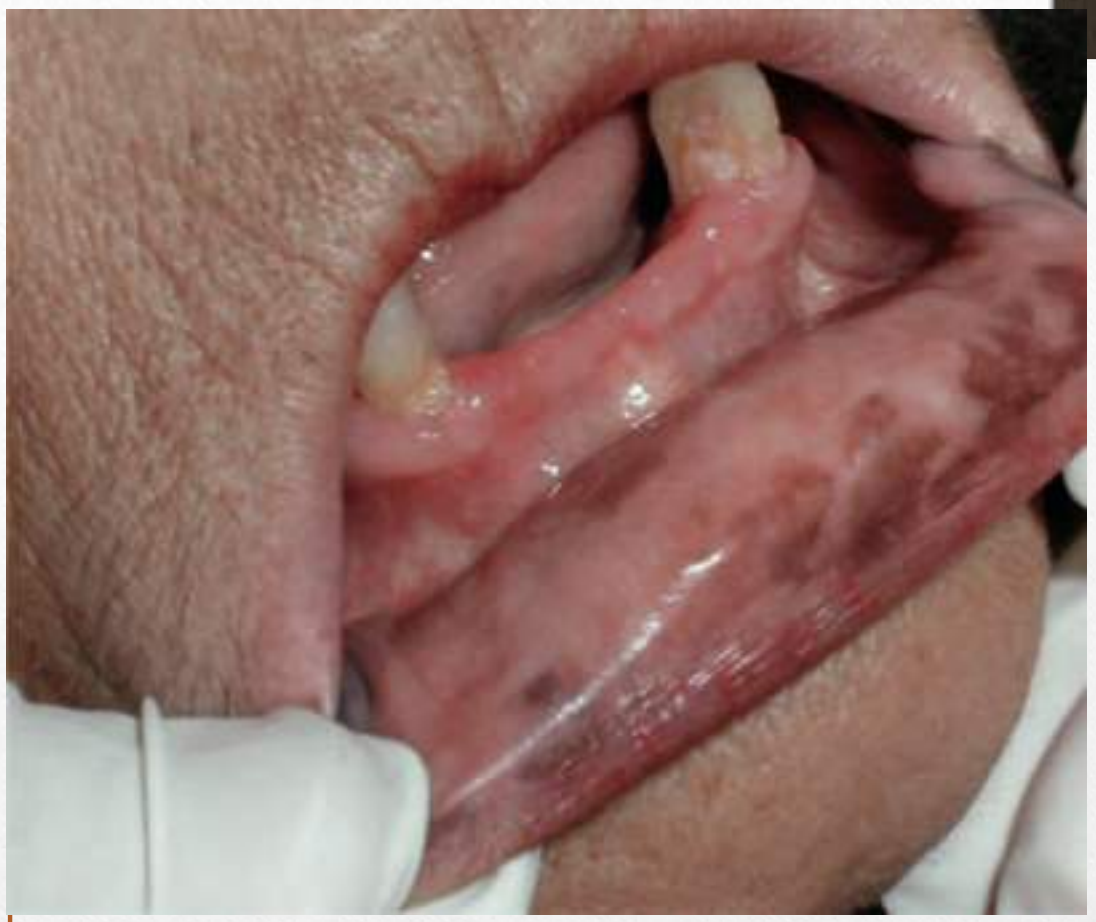
Melanosis Associated with Systemic or Genetic Disease

Hypoadrenocorticism (Adrenal Insufficiency or Addison's Disease)

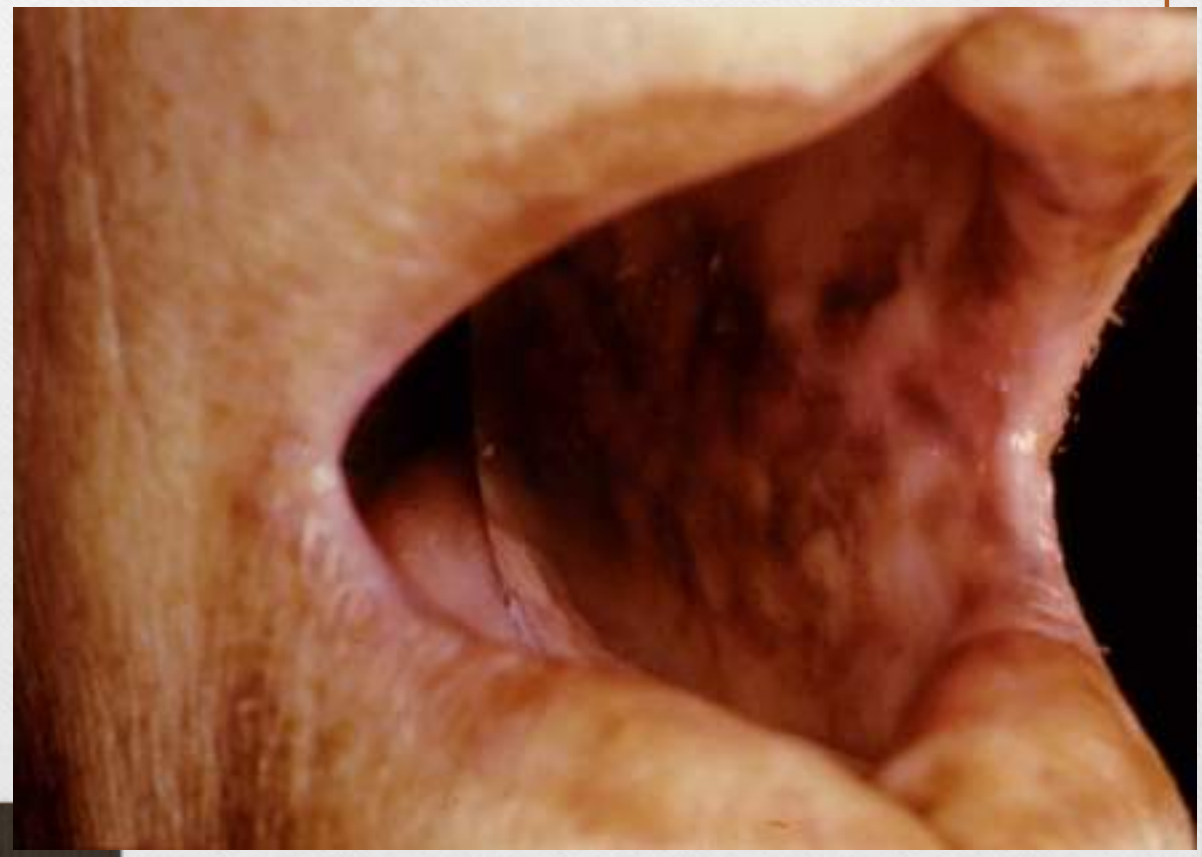
Etiology and Pathogenesis

- It is a potentially life-threatening disease, as much for its systemic complications as its under-diagnosis.
- In adults, autoimmune disease represents one of the most common causes where most patients show the presence of circulating autoantibodies to steroidogenic enzyme 21-hydroxylase.
- 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 result is essentially the same; that is, a decrease in endogenous corticosteroid levels.



Addison’s disease; Patchy brown areas of pigmentations in the labial and buccal mucosa of an individual with Addison’s disease.



- 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 α-melanocyte-stimulating hormone (α-MSH) also increase**.
- At the molecular level, this is explained by the fact that the precursor **proopiomelanocortin gene** contains the sequences of both the ACTH and α-MSH genes.
- During processing of the progenitor hormone, the ACTH and α-MSH genes may be cleaved independently of one another, thus creating two distinct hormones.
- However, the α-MSH sequence is actually, contained within a portion of the ACTH gene; in fact, the first 13 amino acids of the ACTH hormone are identical to α-MSH.

- Apart from the wide range of tissues and organs that these hormones act upon, both α-MSH and ACTH are also thought to have stimulatory effects on **melanocytes**.
- However, the exact mechanism by which melanin synthesis increases remains unclear.

  - 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

Diagnosis

- ✔ The diagnosis of oral addison pigmentation requires a clinicopathologic correlation.
- ✔ Endocrinopathic disease should be suspected whenever **oral melanosis** is accompanied by **cutaneous bronzing**.
- ✔ An oral biopsy typically shows increased melanin in the basal cell layer with melanin incontinence.
- ➤ **Thus, the differential diagnosis**, including **physiologic** and **drug-induced pigmentation**.

Laboratory tests, including:

- ➤ Evaluation of serum cortisol and electrolyte levels, are necessary to make a diagnosis of addisonian hyperpigmentation.
- ➤ **Serum cortisol levels of less than 100 nmol/L at 9:00 a.m**, is a diagnostic of deficiency.
- ➤ **Hyponatremia and hyperkalemia** are frequently associated with adrenal insufficiency.

Treatment

- Treatment consists of **exogenous steroid replacement** therapy with glucocorticoids and mineralocorticoids.
- There is evidence supporting the use of adrenal androgens such as **dehydroepiandrosterone** to improve the quality of life of patients with Addison's disease.
- With appropriate therapy, the pigmentation will eventually resolve.

Cushing's Syndrome/Cushing's Disease

Etiology and Pathogenesis

- 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 because 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, including small cell carcinoma of the lung.
  - Recently, Cushing's syndrome has been described in patients with activating, germline mutations in the ACTH receptor.

Clinical Features

- 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 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

Diagnosis

Three main tests are used for the diagnosis of Cushing's syndrome:

- Low-dose dexamethasone suppression test,
- Midnight plasma cortisol,
- And 24-hour urinary free cortisol.

The pigmentation often resolves following appropriate surgical, radiation, or drug therapy for the specific source of the endocrinopathy.

Pasireotide (a somatostatin analog) has been approved for the treatment of Cushing's syndrome.

Hyperthyroidism (Graves' Disease)

- Melanosis is a common consequence of hyperthyroidism (Graves' disease), especially in **dark-skinned** individuals.
- At least **40%** of black patients with thyrotoxicosis may present with mucocutaneous hyperpigmentation.
- In contrast, melanosis is very rarely observed in Caucasian patients with the disease.

The pigmentation tends to resolve following treatment of the thyroid abnormality.

Primary Biliary Cirrhosis

- It develops mainly in middle-aged women.
- The disease results from damage to small **intrahepatic bile ducts**.
- Diffuse mucocutaneous hyperpigmentation may be one of the earliest manifestations of primary biliary cirrhosis.
- Up to 47% of patients with this condition develop diffuse melanosis.
- This uncommon disease is of unknown etiology, although it is thought to be autoimmune in nature as evidenced by the presence of **antimitochondrial antibodies**.

Primary biliary cirrhosis may also be a source of generalized nonmelanocytic mucocutaneous discoloration.

- **Jaundice is usually an end-stage complication of primary biliary cirrhosis.**

- However, jaundice may also be associated with a variety of other etiologies, including liver cirrhosis, hepatitis, neoplasia, gallstones, congenital disorders, and infection.

- Jaundice is caused by excessive levels of serum bilirubin (a breakdown product of hemoglobin).
- Hyperbilirubinemia often induces a yellowish discoloration of the skin, eyes, and mucous membranes.
- Treatment of the underlying disease will lead to resolution of jaundice.

- **A differential diagnosis** should include **carotenemia** (excessive -carotene levels) and **lycopenemia** (excessive lycopene, a compound found within tomatoes and other fruits and vegetables).
- However, the oral mucosal tissues are **not affected** in either of these latter conditions.

- **A person has an earlier stage (stage 1 or 2), their life expectancy is normal.**

- **If a person with advanced symptoms with an advanced stage, the average life expectancy is about 10-15 years.**

Vitamin B 12 (Cobalamin) Deficiency

Vitamin B12 deficiency may be associated with a variety of systemic manifestations, including megaloblastic anemia, various neurologic signs and symptoms, and various cutaneous and oral manifestations, including a generalized burning sensation, erythema, and atrophy of the mucosal tissue.

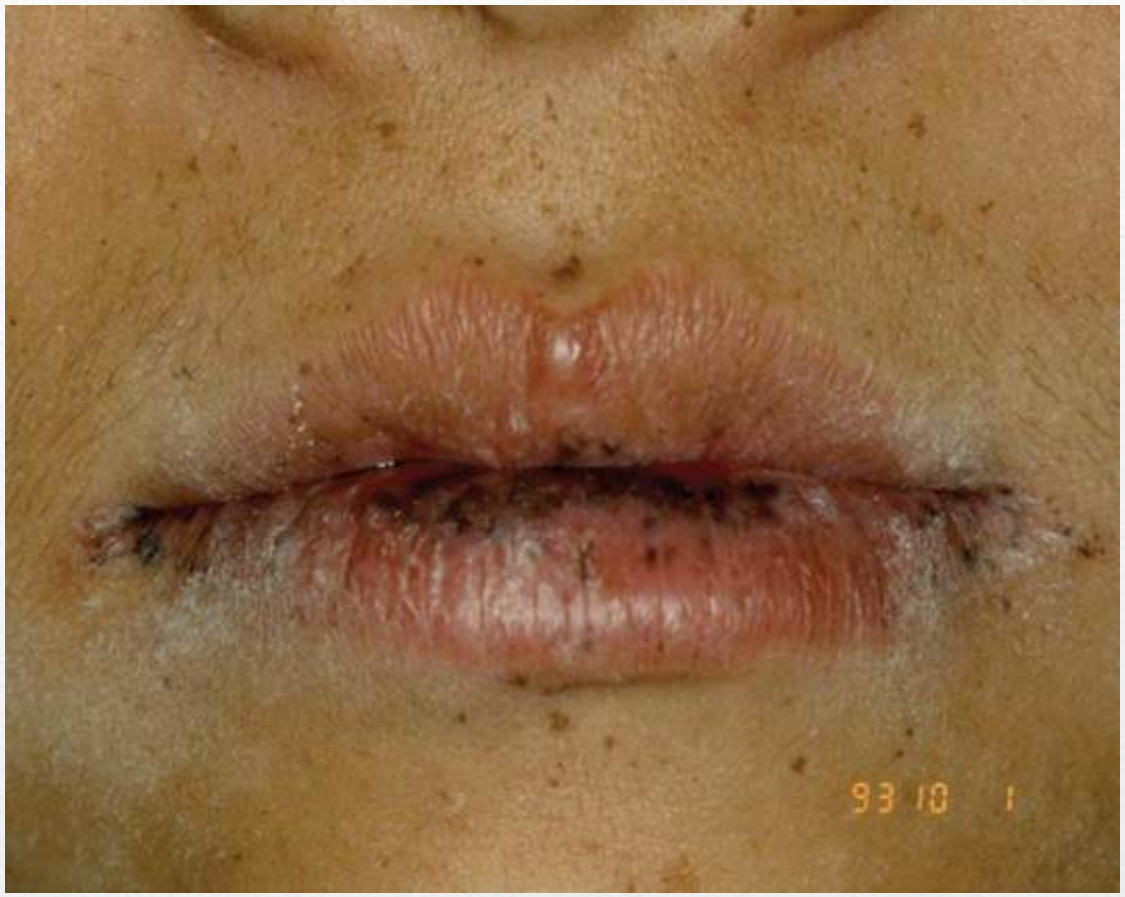
- Diffuse mucocutaneous hyperpigmentation is a rare, and poorly recognized, complication of vitamin B12 deficiency.

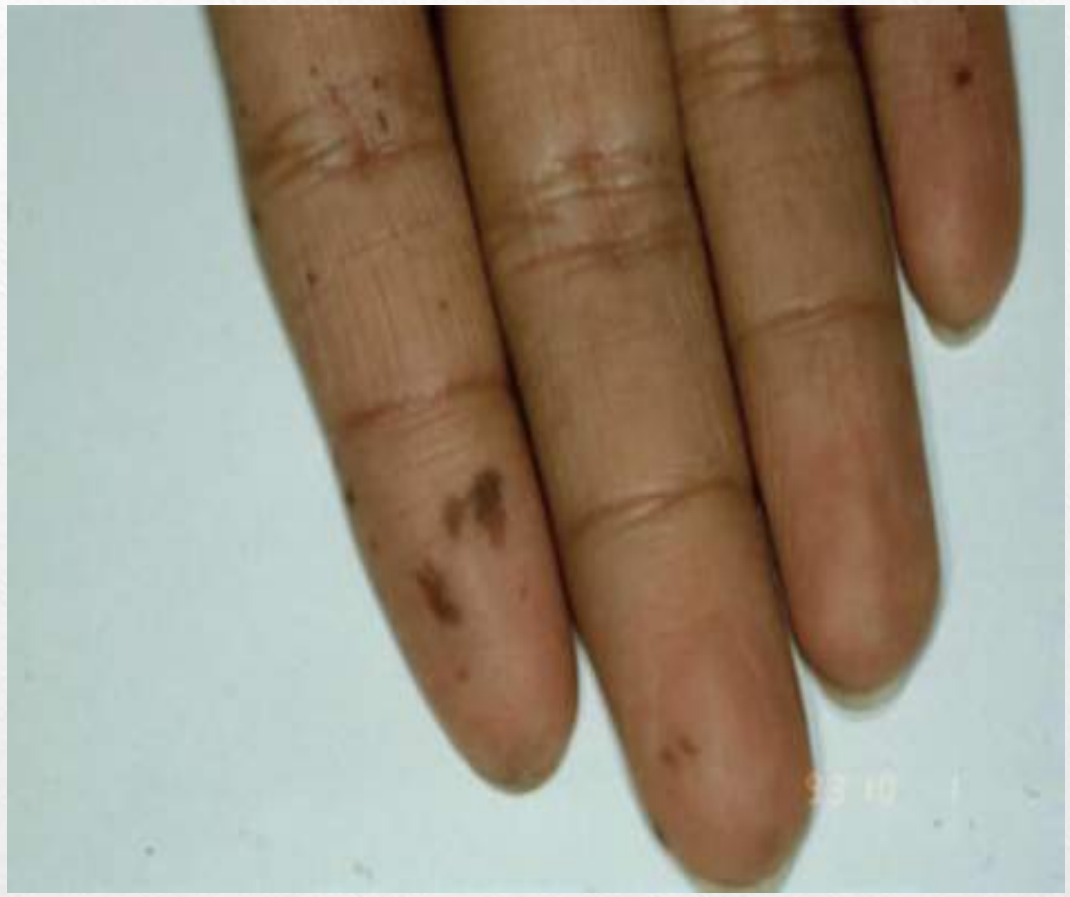
- This hyperpigmentation is suggestive of Addison's disease.
- The pigmentation resolves following restoration of vitamin B12 levels.

Peutz–Jeghers Syndrome

- Peutz–Jeghers syndrome is **an autosomal dominant disease** that is associated with mutations in the **STK11/LKB1 tumor suppressor gene.**

- 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





Histologically These lesions show increased basilar melanin without an increase in the number of melanocytes. The medical management for Peutz–Jeghers syndrome consists in surveillance and treatment of hamartomatous polyps.

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.** Including neurofibromatosis type I, McCune–Albright syndrome, and Noonan's syndrome.

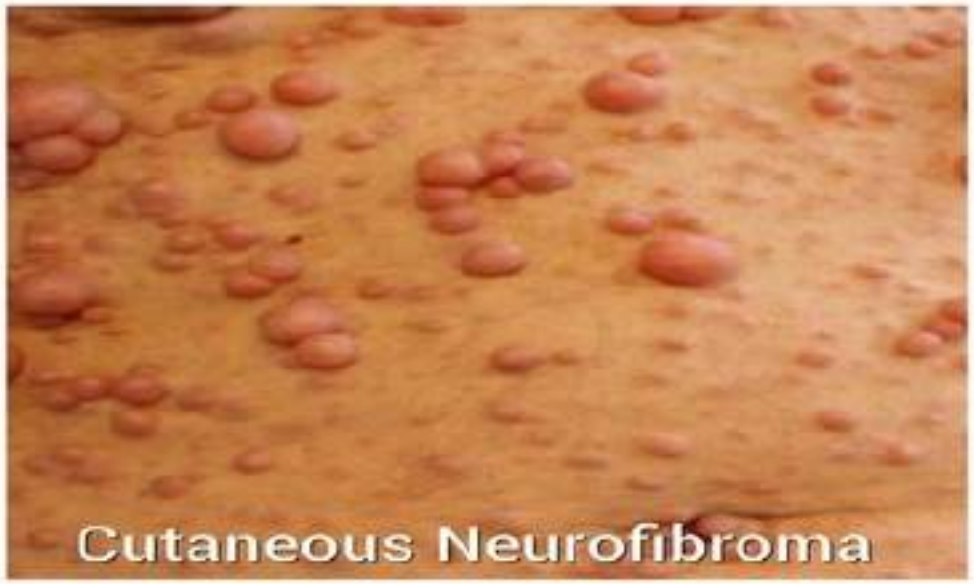
❖

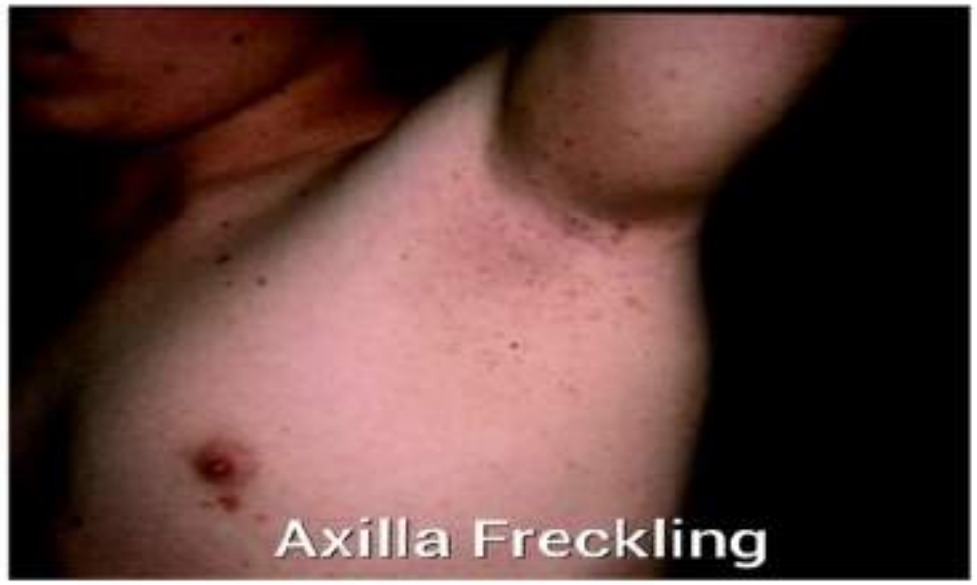
❖It is typically present as **tan- or brown-colored, irregularly shaped macules of variable size;** anywhere on the skin, although unusual, examples of similar-appearing oral macular pigmentation have been described in some patients.

❖**Neurofibromatosis type I** is an autosomal dominant disease caused by a mutation or a deletion of the NF1 gene localized in chromosome 17, it is associated with the development of multiple neurofibromas of various histologic subtypes.

❖**Microscopically,** when compared with adjacent uninvolved skin, genetic café au lait spots exhibit **basilar melanosis** without a concomitant increase in the number of melanocytes. The **melanocytes** that are present demonstrate giant melanosomes (macromelanosomes) that may be visible under light microscopy. In contrast, when compared with similar-appearing lesions in otherwise normal patients, genetic café au lait spots do exhibit increased numbers of melanocytes.

❖ Axillary and/ or inguinal freckling (Crowe's sign) and pigmented lesions of the iris (Lisch nodules) are also highly characteristic of neurofibromatosis type I.





HIV/AIDS-Associated Melanosis

- Diffuse or multifocal mucocutaneous pigmentation has been frequently described in HIV-seropositive including antifungal and antiretroviral drugs, or as a result of adrenocortical destruction by virulent infectious organisms.

- Melanesia has also been identified in some patients, including newly diagnosed patients, with no history of adrenocortical disease or medication intake.

In these patients, the cause of the hyperpigmentation is undetermined.

Recent studies suggest that melanosis may be an actual, potentially

late-stage, clinical manifestation of HIV/ AIDS

- A significant correlation between mucocutaneous pigment and **CD4 counts cells/µLf200.**

Studies have also shown that the immune dysregulation associated with HIV/AIDS leads to increased secretion of α-MSH from the anterior pituitary gland, which may also stimulate increased melanin synthesis.

- HIV/AIDS patients may present with a history of progressive hyperpigmentation of the skin, nails, and mucous membranes.
- The pigmentation resembles most of the other forms of diffuse melanosis.
- The buccal mucosa is the most frequently affected site, but the gingiva, palate, and tongue may also be involved.

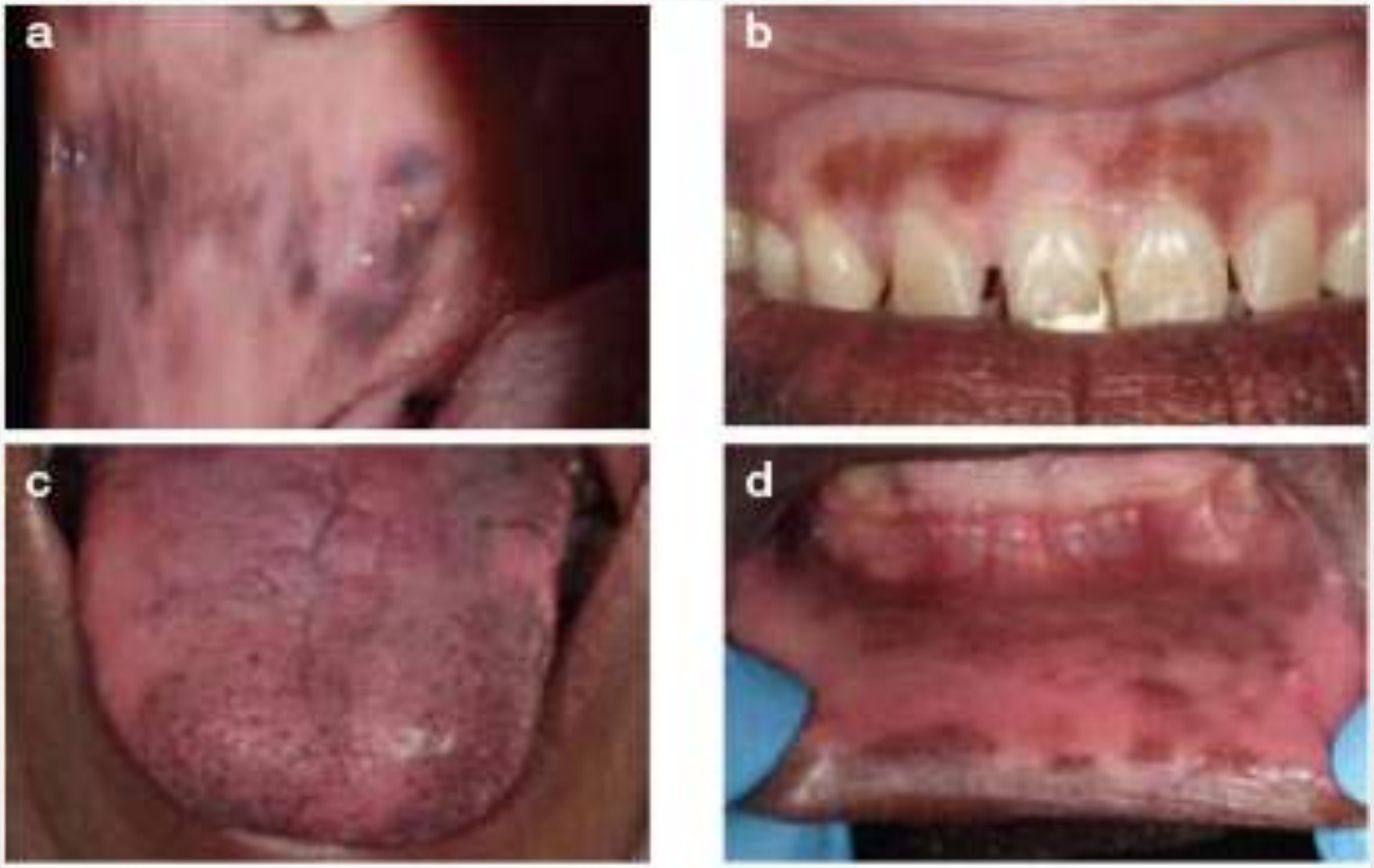


Figure 1a: Irregular, non-homogenous pigmented maculae on the buccal mucosa of a 68-year-old HIV-seropositive female on highly active antiretroviral therapy (HAART) with a CD4+ T cell count of 107 cells/mm³. She had been diagnosed

Treatment of Mucocutaneous Melanosis

- ✔ In general, focally pigmented lesions warrant removal, for both diagnostic and therapeutic purposes.
- ✔ However, apart from those cases associated with neoplasia, surgical intervention is less of an option for the treatment of multifocal or diffuse pigmentation.
- ✔ Drug-induced melanosis and other examples of exogenously stimulated generalized pigmentation may spontaneously subside after withdrawal of the offending substance.

In other cases, the discoloration may be persistent, if not permanent. In such cases, the cosmetic disfigurement may result in significant social, psychological, and emotional stress.

- ✔ Different thickness flap, gingivectomy, cryotherapy, electrosurgery, bur abrasion, and scraping with a scalpel have been successfully used to treat gingival pigmentation.

- ✔ Laser therapy has also proven to be an effective modality for use in the treatment of bothersome oral pigmentation. However, the beneficial effects may only be temporary, with recurrence of at least partial pigmentation in upward of 20% of treated patients.

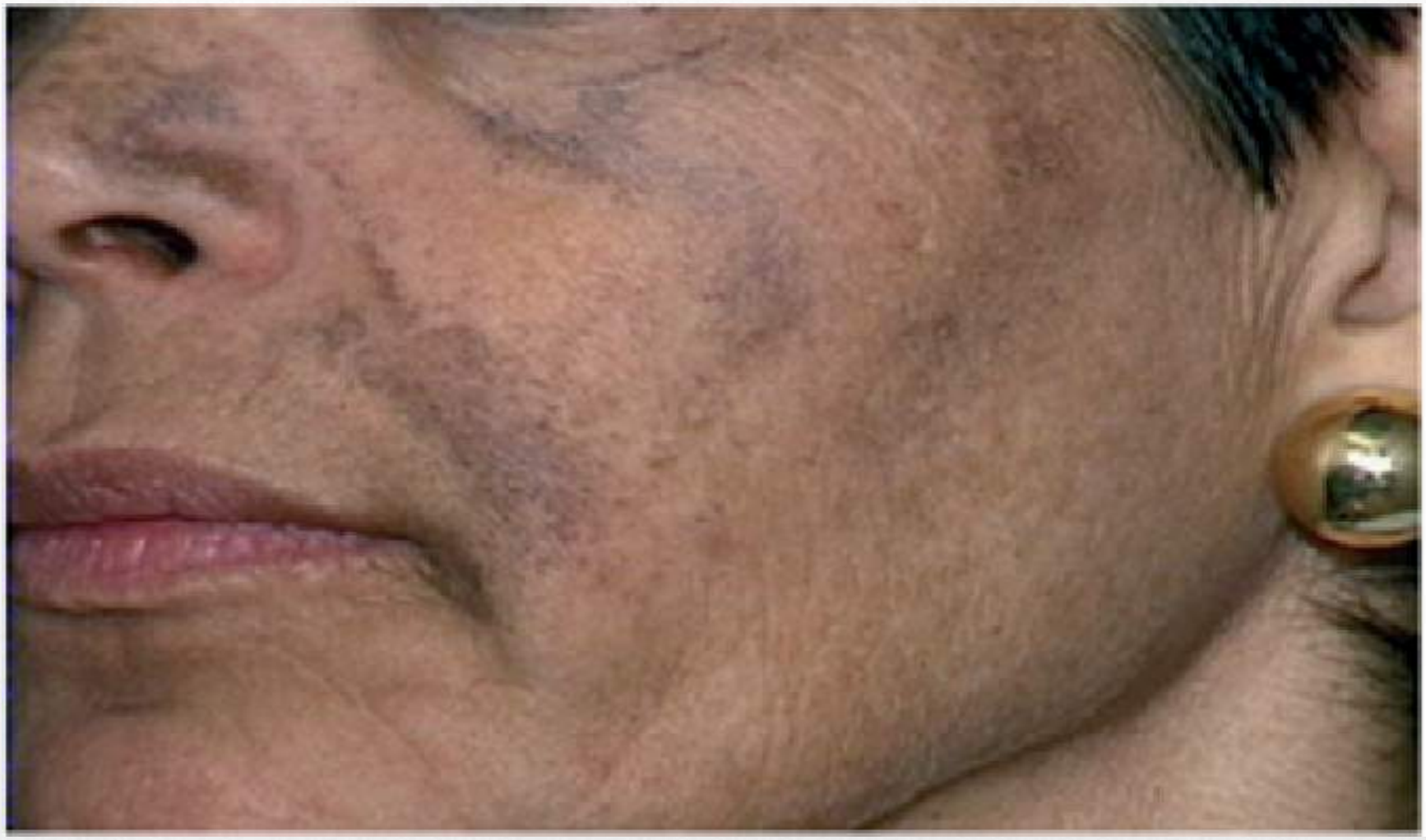
- ✔ However, first-line therapy remains the application of topical medications that is, bleaching creams.
- ✔ Although single agents such as azelaic acid or hydroquinone have been used, more commonly, dual- or triple-combination therapy is recommended.

A combination of 4% hydroquinone (0.05%) retinoic acid (0.01%) fluocinolone acetonide has proven to be effective in greater than 90% of patients.

Exogenous ochronosis

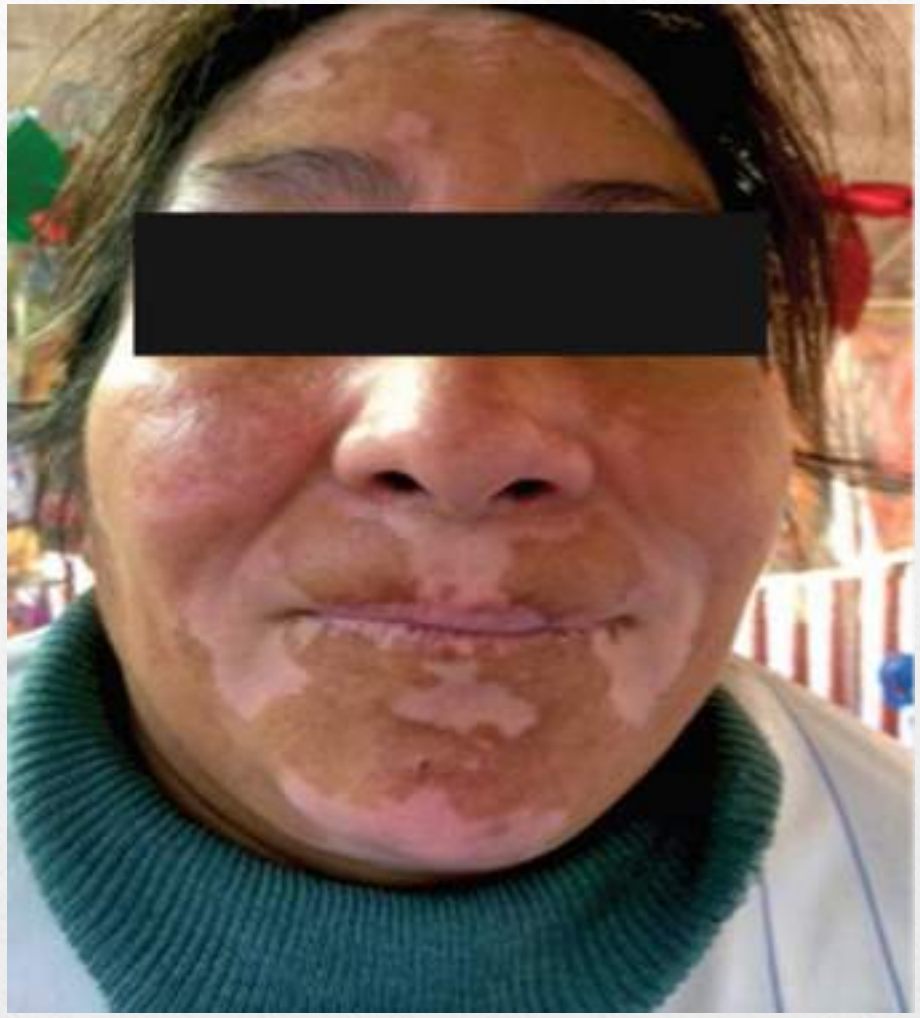
- Intense cutaneous hyperpigmentation with or without atrophic striae and coarsening of the skin or formation of numerous coalesced, black papules.

- ❖This phenomenon is more commonly observed in **black** individuals, usually female, who have undergone long-term bleaching therapy.
- ❖The intense color changes develop in the areas where the cream was applied (frequently on the face) and are related to the accumulation of a yellow-brown pigmented substance (not melanin) in the dermis.
- ❖ This pigmentation may be permanent.
- ❖Q-switched Nd: YAG laser therapy appears to be effective in reducing the dyschromia associated with exogenous ochronosis.
- ❖ Finally, there are several substances, including novel tyrosinase inhibitors that have demonstrable skin-lightening effects in animal models. However, these chemicals remain largely experimental and have not yet been proven to be effective in humans.



Slate-gray patches on the nose, malar eminence, and nasolabial fold consistent with exogenous ochronosis.

Depigmentation(Vitiligo)



Vitiligo is a relatively common, acquired, autoimmune disease that is associated with hypomelanosis.

- ✓ Vitiligo affects 0.5–2 % of the world population with no gender or racial preference.
- ✔ Although the precise etiology remains unknown, autoimmunity, cytotoxicity, genetics, and alterations from metabolic or oxidative stress have been implicated in this condition where the result is a destruction of the melanocytes.

A recent study has identified a single-nucleotide polymorphism in a vitiligo-susceptibility gene that is also associated with susceptibility to other autoimmune diseases, including diabetes type 1, systemic lupus erythematosus, and rheumatoid arthritis.

Clinical Features

- The classification for vitiligo has been recently revised, and now this condition is segregated into nonsegmental vitiligo, segmental vitiligo, and unclassified/undetermined vitiligo.
- Multiple **achromic patches** with remitting-relapsing course are seen in nonsegmental vitiligo.
- **Segmental vitiligo** shows a characteristic dermatomeric distribution of the achromic patches with a rapid onset that is usually not progressive.
- The onset of vitiligo may occur at any age, but more frequently during the second and third decade of life.
- The depigmentation is more apparent in patients who have a darker skin tone. Yet the disease occurs in all races.
- Vitiligo may also arise in patients undergoing immunotherapy for the treatment of malignant melanoma.
- Studies suggest that this phenomenon may be associated with a better prognosis for this group of patients.
- ✔Vitiligo rarely affects the intraoral mucosal tissues. However, hypomelanosis of the inner and outer surfaces of the lips and perioral skin may be seen in up to 20% of patients.

Pathology

Microscopically, there is a destruction of melanocytes by antigen-specific T cells and complete loss of melanin pigmentation in the basal cell layer. The use of histochemical stains such as Fontana-Masson will confirm the absence of melanin.

Management

In most cases, the objective of therapeutic intervention is to stimulate repigmentation.

Topical corticosteroids, topical calcineurin inhibitors, ultraviolet B narrow band, and psoralen and ultraviolet A exposure have proven to be effective nonsurgical therapies.

In rare cases, small foci of normal pigmented skin may be contained within otherwise diffuse areas of hypomelanosis.

Thus, to create a unified skin color, cutaneous bleaching may be considered.

➤From the standpoint of therapy, labial vitiligo is more resistant to the typical treatments used for cutaneous vitiligo. Due to a **lack of hair follicles**, the lips do not have a reservoir of melanocytes that can be stimulated to produce pigment.

➤ Thus, surgical intervention may be the only option to achieve an esthetic result.

➤Autologous epithelial grafts have been used successfully, with patients often reporting a more acceptable cosmetic appearance.

➤Split-thickness skin grafts have been reported as having the highest repigmentation success rate.

➤ Punch grafting and micropigmentation (whereby an exogenous brown pigment is injected into the lip, much like a tattoo) have also been reported.

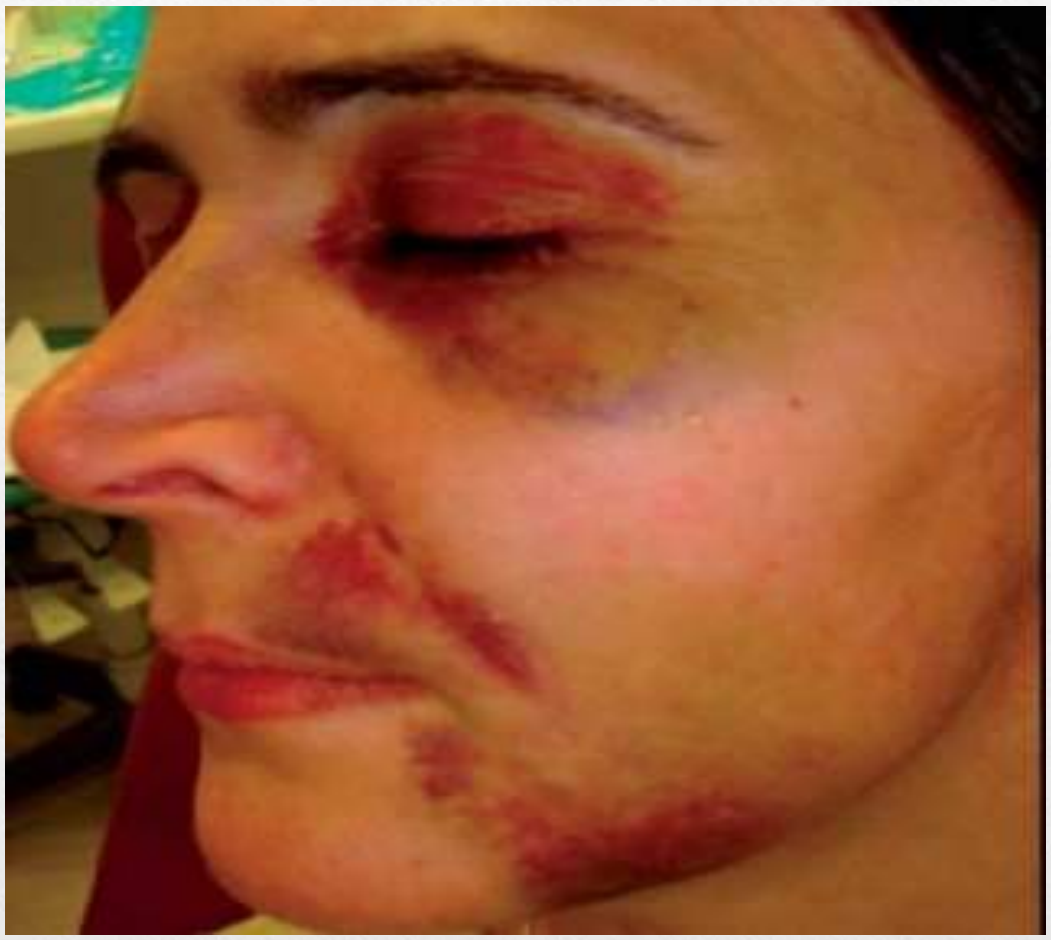
➤In rare instances, surgical intervention may stimulate spontaneous repigmentation of vitiligenous lesions elsewhere on the body.

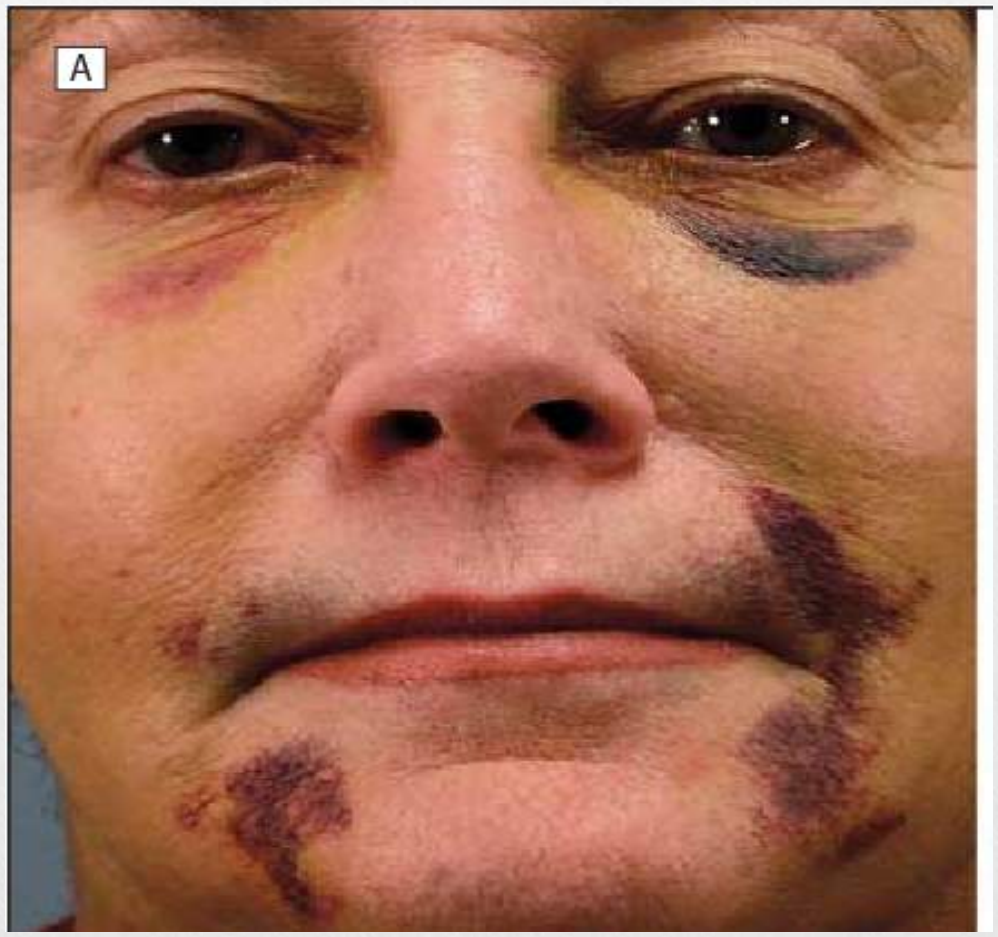
Hemoglobin and Iron associated Pigmentation

Ecchymosis

- Traumatic ecchymosis is common on the lips and face yet 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 connective tissue will appear as a bright red macule or as a swelling if a hematoma forms.
- The lesion will assume a brown discoloration **within a few days, after the hemoglobin is degraded to hemosiderin.**
- **The differential diagnosis** must include other focally pigmented lesions.
- If the patient recalls an episode of trauma, however, the lesion should be observed for two weeks, by which time it should resolve.
- Patients taking anticoagulants 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, in patients with leukemia, and in patients with end-stage renal disease who are undergoing dialysis treatment.
- **Laboratory tests**, including bleeding time, prothrombin time, partial thromboplastin time, and international normalization ratio, should be obtained in instances of spontaneous ecchymoses to explore defects in the coagulation pathways.





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 2–4 mm collections of extravasated blood.

Oral purpura/petechiae may develop because of trauma, 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.

➤**Within two weeks**, the lesions should resolve. Failure to do so should produce suspicion of a hemorrhagic diathesis, a persistent infectious disease, or other systemic disease, and **laboratory investigations** must be undertaken.

Hemochromatosis

¬It is a chronic, progressive disease characterized by excessive iron deposition (usually in the form of hemosiderin) in the liver and other organs and tissues.

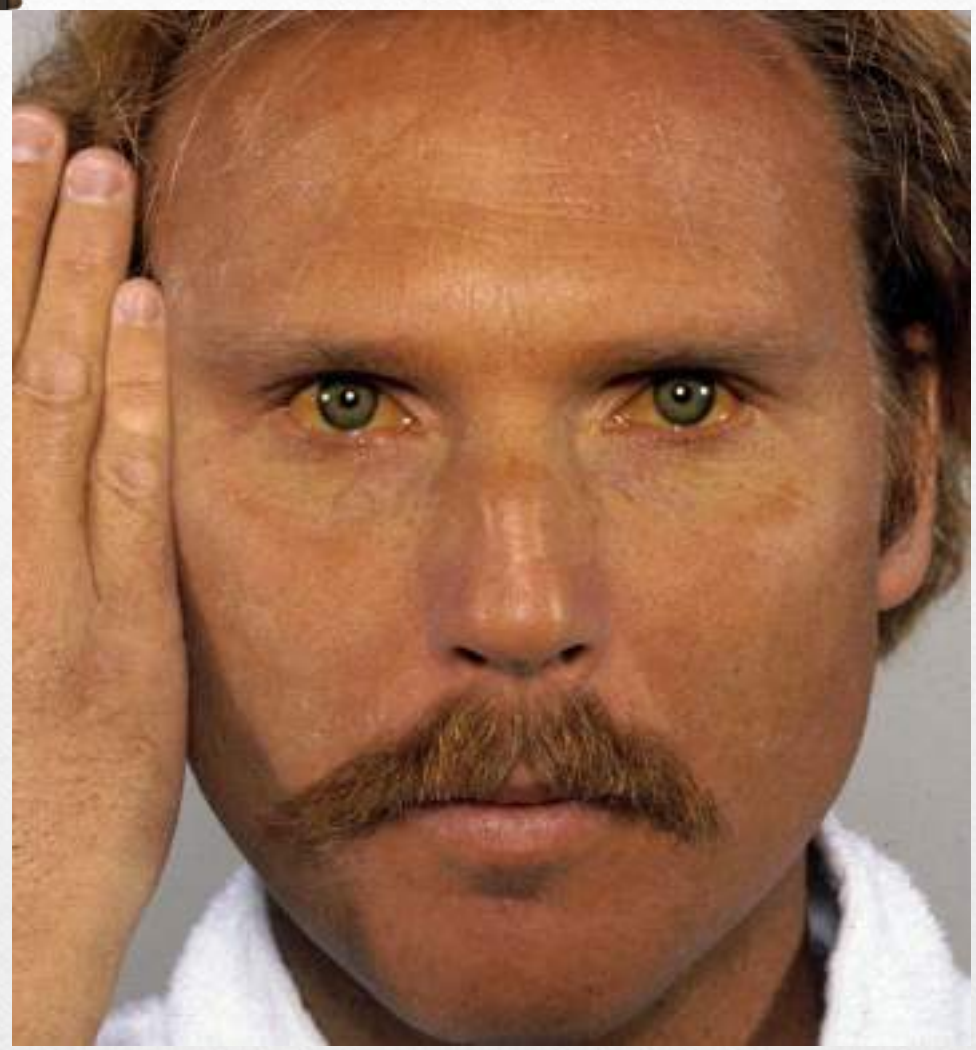
¬Idiopathic, neonatal, blood transfusion, and heritable forms of this disease are recognized. **Complications of hemochromatosis** may include liver cirrhosis, diabetes, anemia, heart failure, hypertension, and bronzing of the skin.

¬The **cutaneous pigmentation** is seen in over 90% of affected patients, regardless of the etiology of the disease.

¬The primary oral manifestation of hemochromatosis is ablue-gray to brown pigmentation affecting mainly the palate and gingiva.

¬Early in the course of disease, the pigmentation may be more commonly a result of basilar melanosis rather than iron-associated pigment.

¬**Iron deposition** within the adrenal cortex may lead to hypoadrenocorticism and ACTH hypersecretion, with the associated Addisonian -type changes.



- In the later stages of hemochromatosis, the pigmentation is usually a result of hemosiderosis and melanosis. **A lower labial gland biopsy has been shown to be an easy and effective method for the diagnosis of hemochromatosis**. Increased melanin pigment may be seen in the basal cell layer, whereas golden or brown-colored hemosiderin can be seen diffusely scattered throughout the submucosal and salivary gland tissues.

Exogenous Pigmentation

(Amalgam Tattoo)

- The most common pigmented lesion in the oral mucosa is amalgam tattoo. These are iatrogenic in origin and typically a consequence of the accidental deposition of amalgam restorative material into the submucosal tissue.

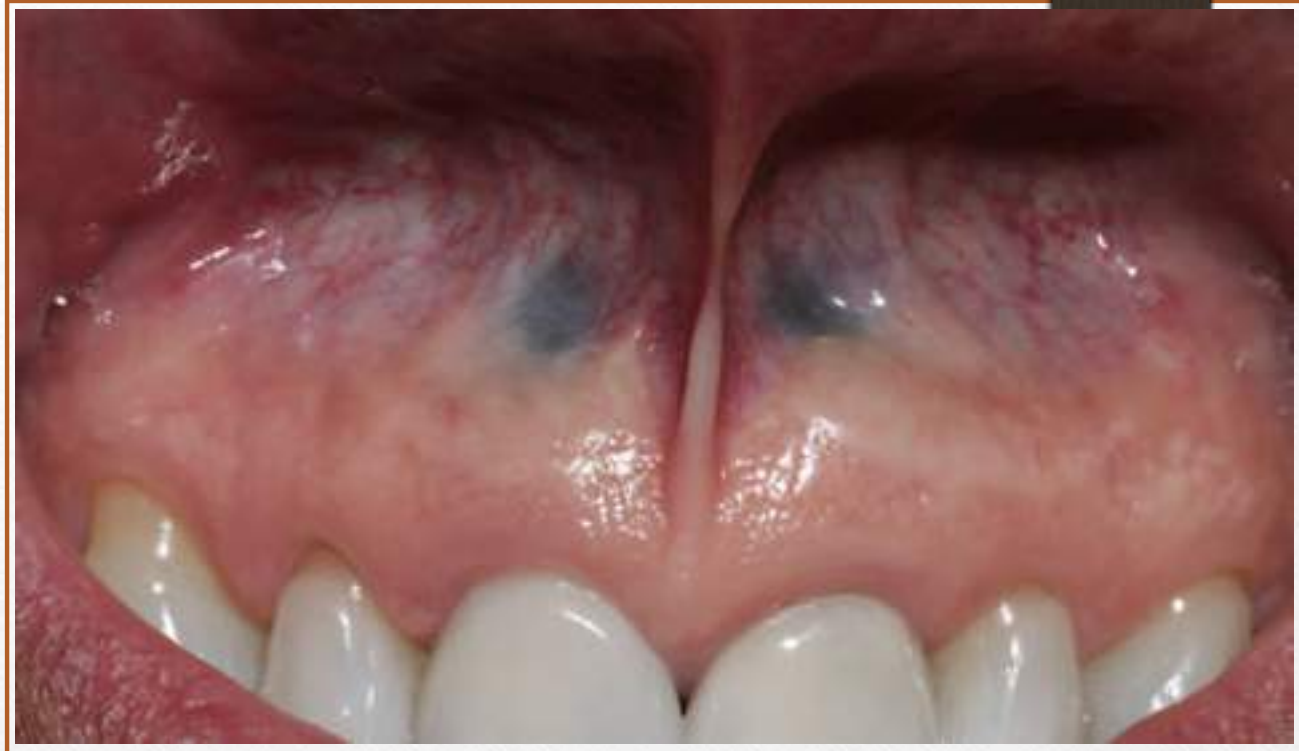
Clinical Features

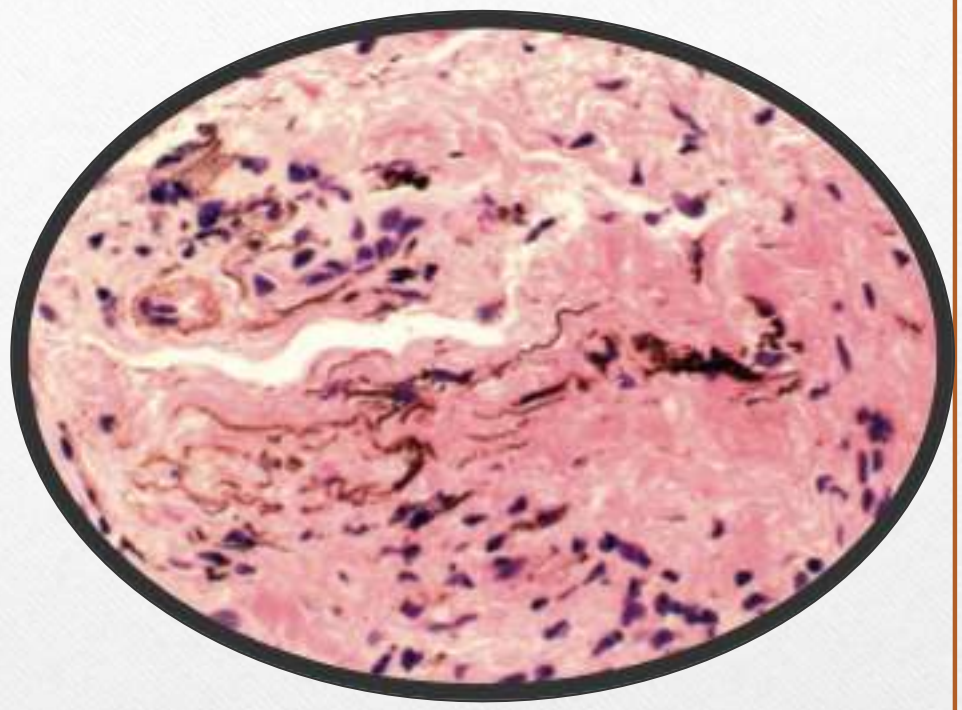
▪Amalgam tattoos may be found in up to 1–3% of the general population. The lesions are typically small, asymptomatic, macular, and bluish gray or even black in appearance.

▪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 area 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

▪**Amalgam tattoo of the head and neck skin** may occur in **dentists** and represents an occupational hazard resulting from failure to use facial protective barriers.





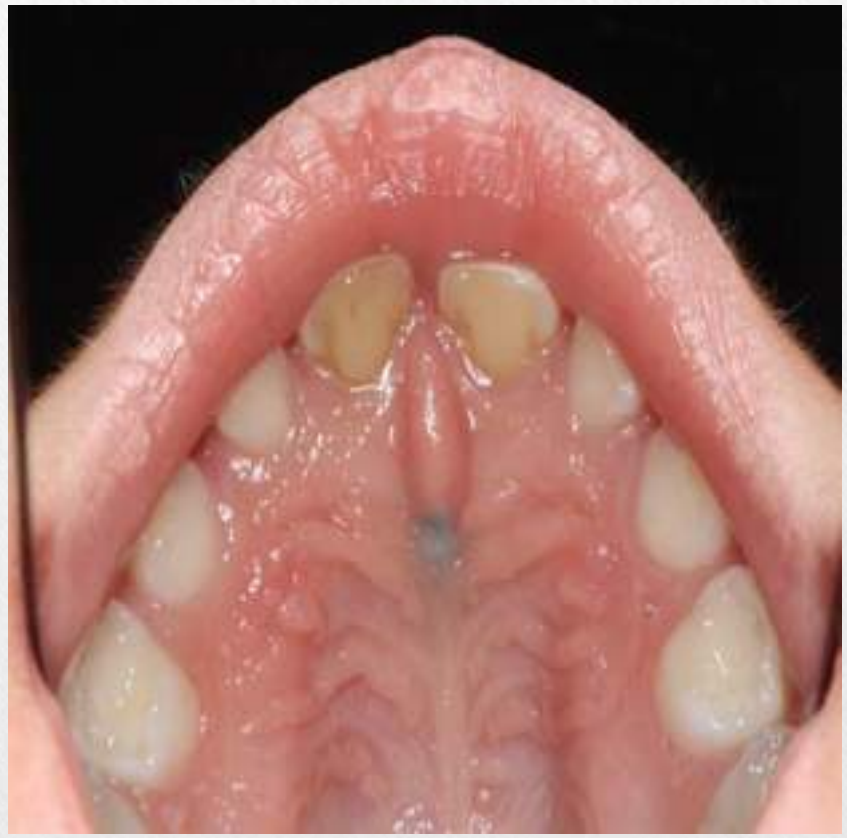
Microscopically, amalgam tattoos show a fine brown granular stippling of collagen fibers, with a particular affinity for vessel walls and nerve fibers with little or no inflammation. In some cases, large aggregates of black material may be seen and could result in a **foreign body–type giant cell granulomatous inflammation**. However, a mild to moderate lymphocytic inflammatory infiltrate is more commonly seen.

Management

- The amalgam particles are sometimes they are large enough to be identified on dental radiographs. In some patients, the focal argyrosis may compromise esthetics; thus, surgical removal may be warranted.
- Amalgam tattoos are innocent, their removal is not always necessary, particularly when they can be documented radiographically. In the absence of radiographic evidence of amalgam, if the lesion is not in proximity to a restored tooth, or if the lesion suddenly appears, a biopsy is warranted.
- A typical differential diagnosis **includes melanotic macule, nevus, and melanoma.** Pigmentation associated with other dental restorative materials has also been described. Metal components from almost all forms of **cast alloy material** can be detected in the adjacent tissues. **Titanium** has been associated with pigmentation of the skin, specifically in areas around **orthopedic implants.** Thus, it is possible that **dental implants** may also be a potential source of exogenous oral pigmentation.

Graphite Tattoos

- Graphite tattoos are an unusual source of focal exogenous pigmentation.
- They are most seen on the palate and gingiva 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. **Microscopically,** graphite particles resemble those of amalgam. When the graphite tattoo involves areas of cosmetic concern, removal of the lesion and a subsequent autogenous connective tissue graft provide a highly esthetic outcome.

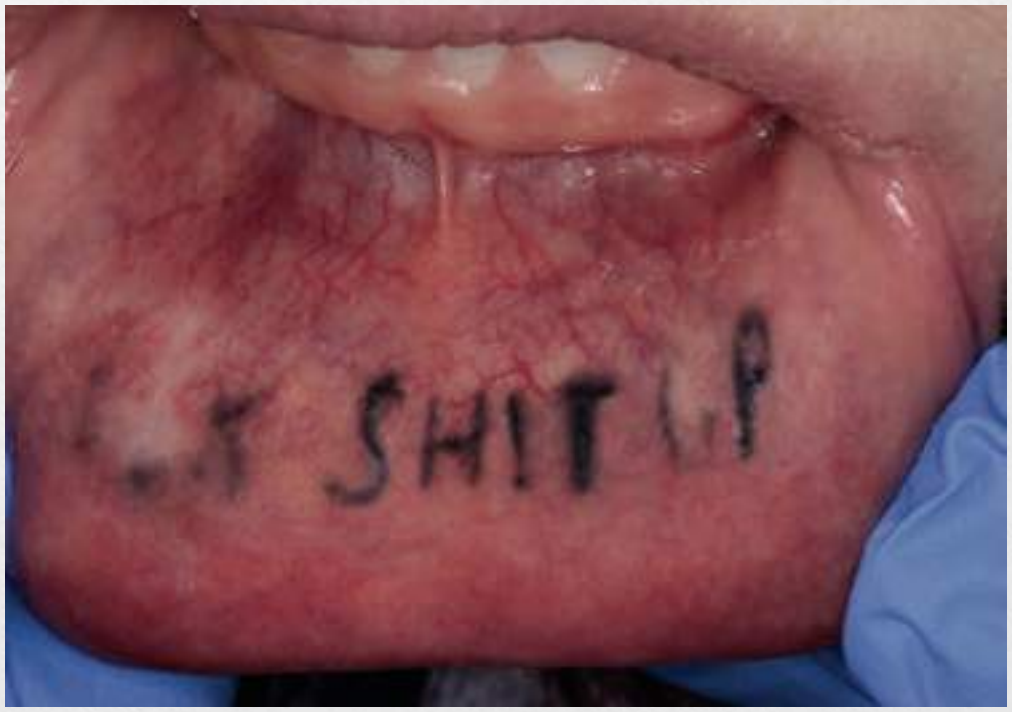


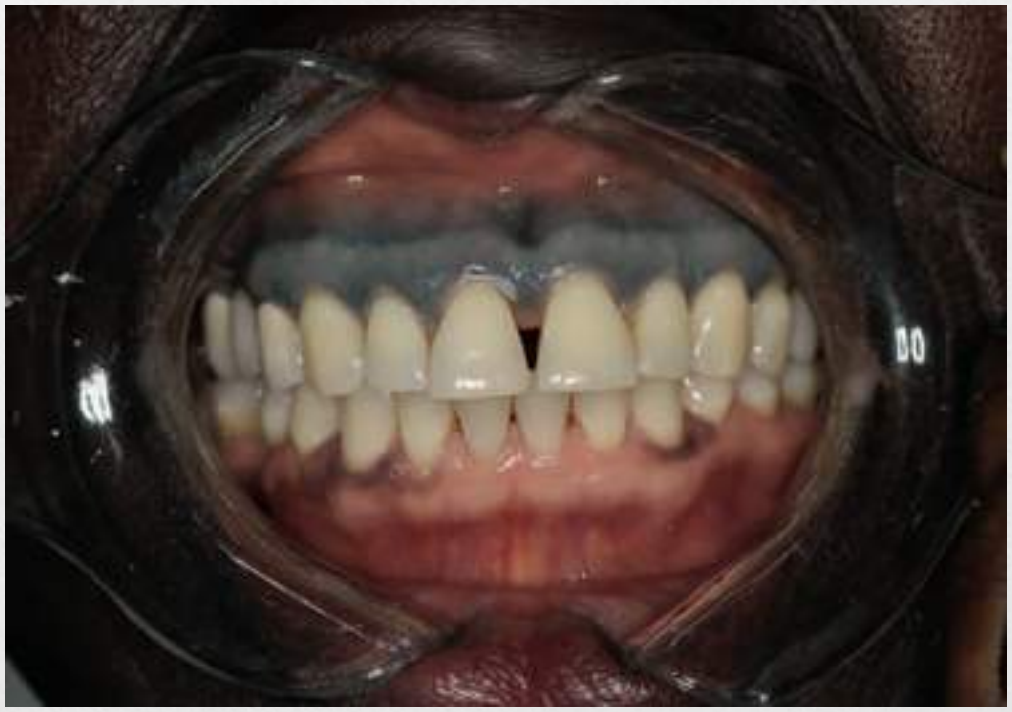
Ornamental Tattoos

➤Mucosal tattoos in the form of lettering or complicated artwork are becoming increasingly common phenomena.

➤Amateur tattoo inks are permanent and consist of simple, carbon particles originating from a variety of sources, including burnt wood, plastic, or paper, and from a variety of inks, such as India ink, pen ink, and plant-derived matter.

➤Q-Switched laser therapy has been used successfully to remove tattoos of the oral mucosa.





Medicinal Metal-Induced Pigmentation

➤Variety of metallic compounds have been used for the treatment of various systemic diseases.

➤Fortunately, with the advent of methotrexate for the treatment of rheumatoid arthritis, gold therapy is in less demand.

➤Colloidal silver is another metal-based substance that has been historically used for its beneficial health effects.

➤Although its medical use has been significantly reduced, it has become widely available among patients using "complementary and alternative medicine therapies."

➤ 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 both cases, the pigmentation may be **persistent**, if not permanent, even following discontinuation of the substance.

➤However, oral lichenoid eruptions have been associated with systemic **gold therapy**.

➤**Silver nitrate and zinc oxide**; Silver nitrate cautery has been used to treat recurrent aphthous stomatitis, and zinc oxide is a common component of sunblock creams. Both substances have been associated **with focal mucocutaneous pigmentation.**

➤Using of zinc oxide containing sunblock in severely chaffed lips may result in the development of hyperpigmentation.

➤Medicinal silver-associated pigment appears as **brown or black** particulate matter dispersed throughout the connective tissue.

➤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.

➤**Black tongue** induced by bismuth subsalicylate is caused by deposition of actual pigment (bismuth sulfide), without any other lingual changes.

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➤Discontinuation of the antacid and cleansing of the tongue are curative.

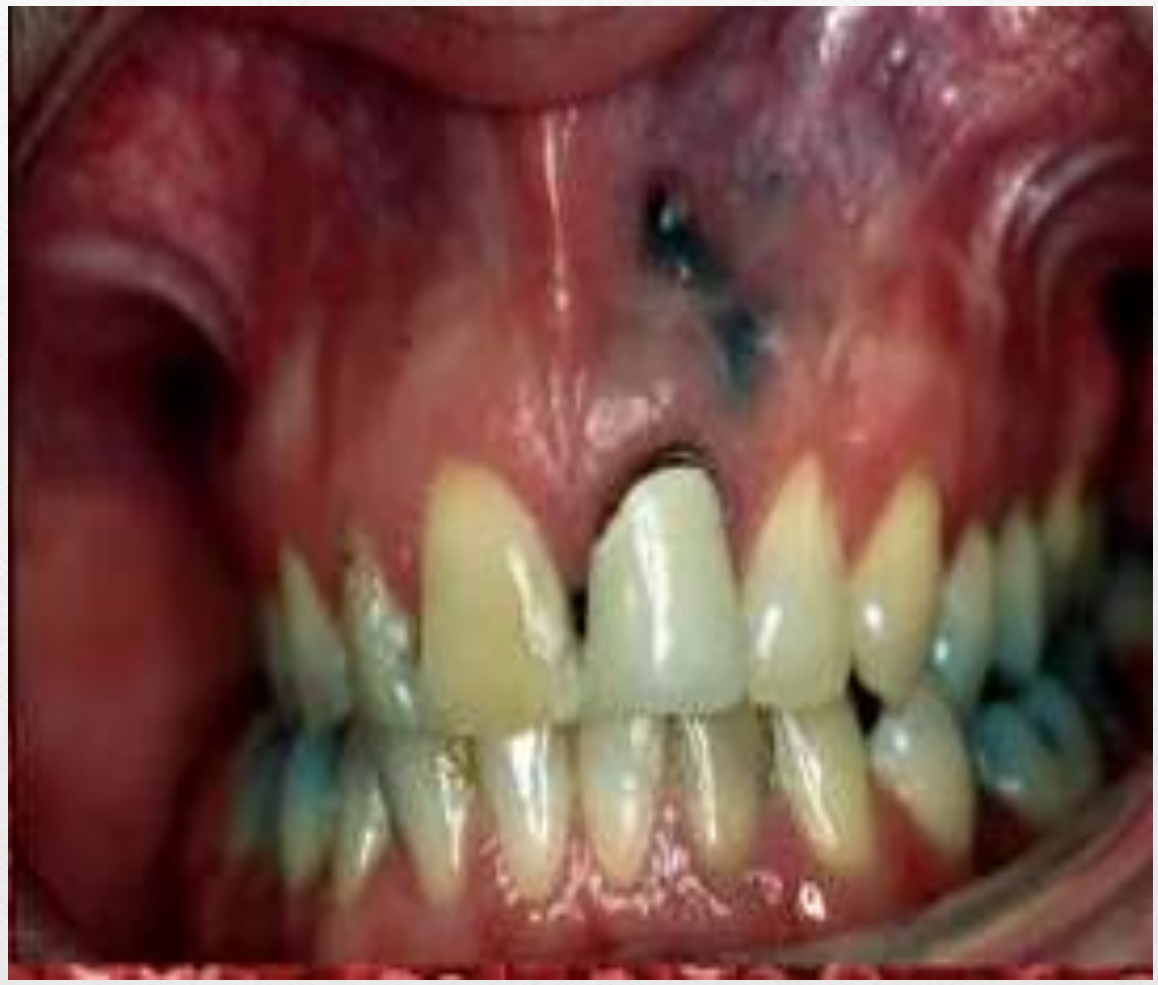
➤It should be noted that typical black hairy tongue may also be attributed to the use of bismuth subsalicylate.

Heavy Metal Pigmentation

❖Diffuse oral pigmentation may be associated with ingestion of heavy metals.

❖Yet 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.



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, although 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.

➤In addition, **roots show a green color**, whereas developing roots tend to be **black**.

➤Minocycline can also induce actual pigmentation of the oral soft tissues, as well as the skin and nails.

➤Minocycline-induced soft tissue pigmentation may appear **gray, brown, or black**. Often the pigmentation is patchy or diffuse in its presentation. Although a biopsy may reveal basilar melanosis, more commonly, aggregates of fine brown or golden particles are identified within the submucosal tissue.

➤ The particles are often intracellular and contained within macrophages.

➤It is likely that the particulate substance represents an actual precipitated drug metabolite rather than true melanin.

➤The mucosal discoloration produced by minocycline often subsides within months after discontinuation of the medication.

➤Alexandrite755- nm laser therapy is used with acceptable esthetic effect.

➤The bone pigment may persist for longer periods of time, if not indefinitely.

➤**Methacycline,** another tetracycline derivative that is no longer widely used in clinical practice, can also produce a similar form of pigmentation.

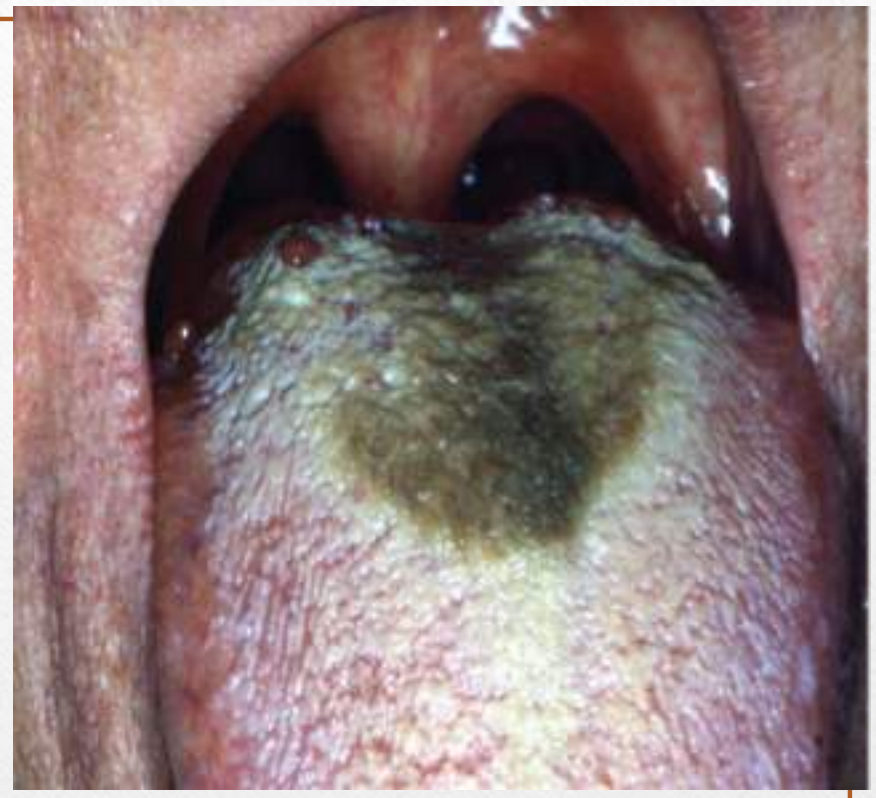
➤Imatinib (a tyrosine kinase inhibitor) used for the treatment of (chronic myeloid leukemia) has the potential to **induce mucosal pigmentation.**

- Minocycline induced pigmentation

Hairy Tongue

- Common condition of unknown etiology.
- The change in oral flora associated with chronic antibiotic therapy may be causative in some patients.
- The discoloration involves the dorsal tongue, particularly the middle and posterior one-third.
- **Rarely** children are affected.
- The filiform papillae are elongated, sometimes markedly, and have the appearance of fine hairs. The hyperplastic papillae then become pigmented by the colonization of chromogenic bacteria, which can impart a variety of colors, including white, green, brown, or black. Various foods, drinks, and confectionaries can contribute to the diffuse discoloration.
- **Smoking of tobacco or crack cocaine** has been associated with black hairy tongue.

Microscopically, the filiform papillae can be seen as extremely elongated and hyperplastic with hyperkeratosis. Superficial microbial colonization of the papillae is a prominent feature. There are no additional pathologic findings in the remaining epithelium or in the connective tissue.



Treatments consist of having the patient brush the tongue, or use a tongue scraper, and limit the ingestion of color-forming foods and drinks until the discoloration resolves.

- Rare examples of black hairy tongue have also been linked to the use of psychotropic medications.
- Black hairy tongue has also been associated with other pharmacos such as tetracycline, linezolid, olanzapine, bismuth, and erlotinib.

Benign Lesions of Oral Cavity and the Jaws

Lecture 1 & 2
Dr. Marwah Waleed Sh.

Learning Objectives

- **To provides an overview of the etiology and pathogenesis, epidemiology, clinical and histopathologic manifestations, differential diagnosis, applicable laboratory findings, and management of nonmalignant growths and tumors of the oral cavity and the jaws.**

- VARIANTS OF NORMAL
  - Tori/Exostoses
  - Unencapsulated Lymphoid Aggregates
  - Fordyce Spots
- BENIGN SOFT TISSUE LESIONS
- INFLAMMATORY/REACTIVE EXOPHYTIC SOFT TISSUE LESIONS
  - Irritation Fibroma
  - Fibrous Inflammatory Hyperplasias/Epulis Fissuratum
  - Inflammatory Papillary Hyperplasia
  - Pyogenic Granuloma and Pregnancy Tumor
  - Peripheral Ossifying or Cementifying Fibroma
  - Peripheral Giant Cell Granuloma
  - Nodular Fasciitis
  - Proliferative Myositis and Focal Myositis
  - Reactive Gingival Enlargement
- BENIGN SOFT TISSUE TUMORS
  - Epithelial Tumors
  - Vascular Anomalies
  - Neurogenic Tumors
  - Lipoma
  - Tumors of Muscle
- BENIGN HARD TISSUE LESIONS
- BENIGN FIBRO-OSSEOUS LESIONS
  - Fibrous Dysplasia
  - Ossifying Fibroma
  - Cemento-Osseous Dysplasias
- LANGERHANS CELL HISTIOCYTOSIS (HISTIOCYTOSIS X)
- GIANT CELL LESIONS OF BONE
  - Central Giant Cell Granuloma (Central Giant Cell Lesion)
  - Aneurysmal Bone Cyst
  - Cherubism
- PAGET'S DISEASE OF BONE (OSTEITIS DEFORMANS)
- CYSTS OF THE JAWS AND ADJACENT SOFT TISSUES
  - Odontogenic Cysts
  - Nonodontogenic Cysts
  - Pseudocysts
- ODONTOGENIC TUMORS
  - Epithelial Odontogenic Tumors
  - Mesenchymal Odontogenic Tumors
  - Mixed Odontogenic Tumors
- BENIGN NONODONTOGENIC TUMORS OF THE JAWS
  - Osteomas and Gardner Syndrome
  - Osteoblastoma and Osteoid Osteoma
  - Chondroma and Chondromyxoid Fibroma
  - Desmoplastic Fibroma

1-Variant of normal

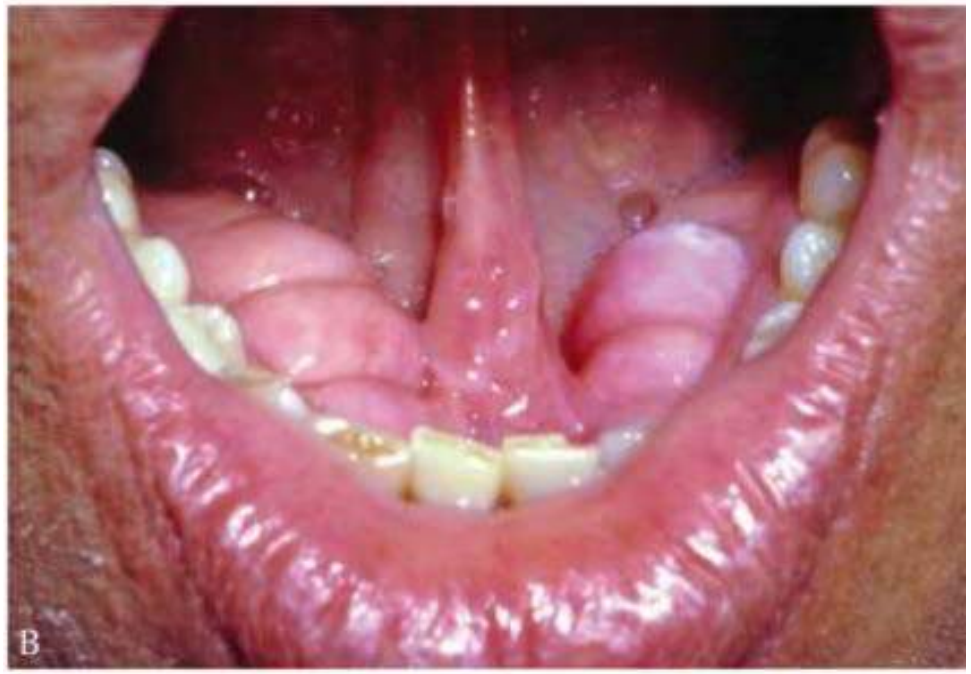
- Tori/Exostoses

Etiology and Pathogenesis

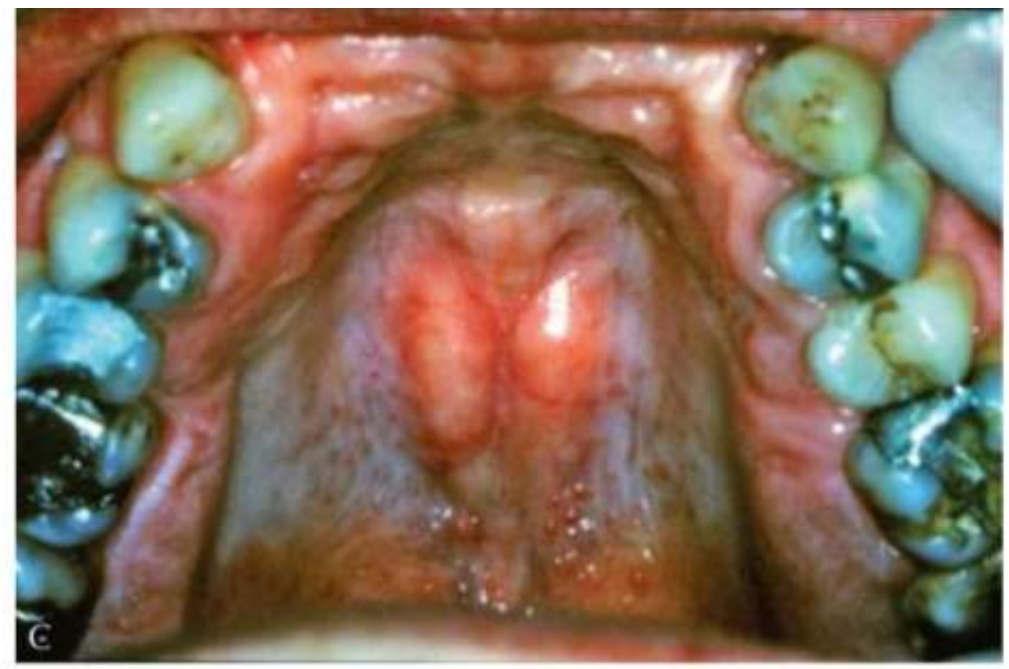
Tori and exostoses are considered to be normal structural variants. Their etiology is multifactorial and poorly defined, although genetics is a dominant factor. There is no strong evidence to either support or refute bruxism or other parafunctional habits as causes.

Clinical and Histologic Manifestations

Tori manifest as localized nodular enlargements of the cortical bone of the midline of the palate (torus palatinus), the lingual aspect of the mandible (torus mandibularis), and the buccal aspects of either jaws. Other than the torus palatinus, exostoses have a bilateral presentation. They are typically small, although rarely they may become sufficiently large to interfere with oral function. Histologically, tori consist of layers of dense cortical bone covered by periosteum and a thin overlying layer of epithelium with minimal rete peg development.



Mandibular tori (torus mandibularis)



Maxillary tori (torus palatinus)

Management

No management is required unless tori pose a functional problem such as a mechanical problem in the construction of dentures, or if they become frequently traumatized as a result of their prominent position and the resulting traumatic ulcers are slow to heal. In such cases, surgical removal is indicated.

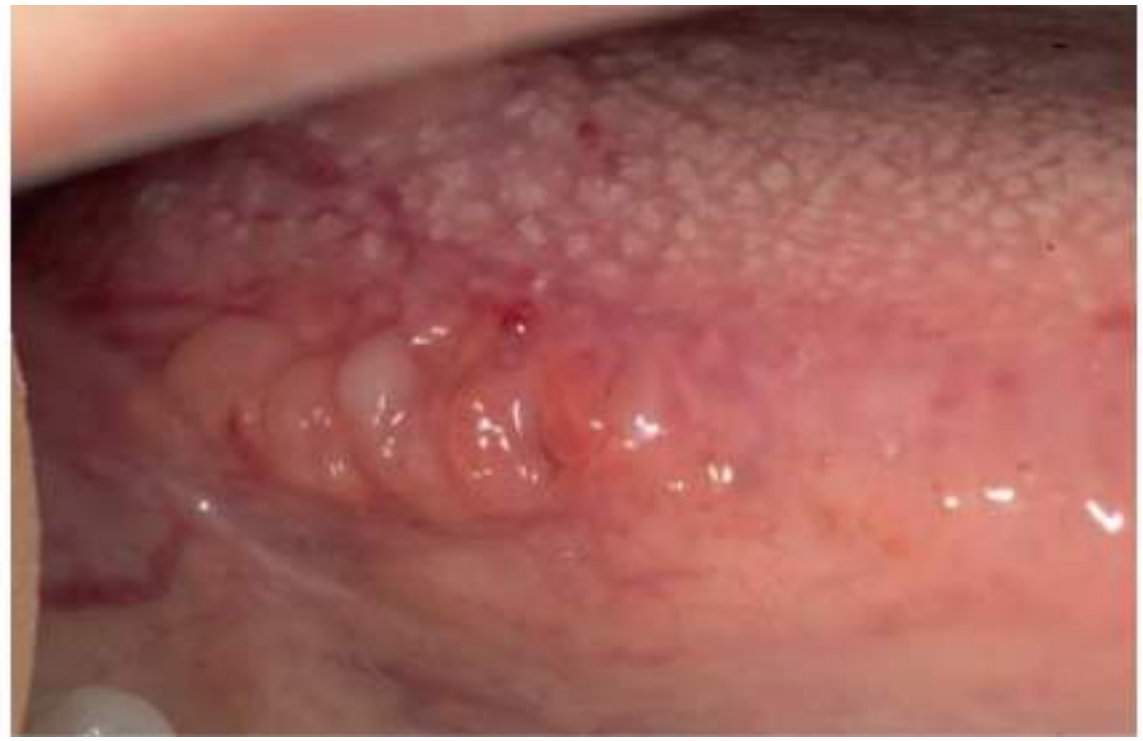
➢ Unencapsulated Lymphoid Aggregates

Etiology and Pathogenesis

These are normal structures, distinct from the palatine and lingual tonsils, and comprise part of Waldeyer's ring, They may increase in size as a result of benign (reactive) processes or due to lymphoid neoplasms (i.e., lymphomas).

Clinical Manifestations

They may be located on the posterolateral aspects of the tongue , anterior tonsillar pillar, posterior pharyngeal wall, soft palate, and dorsal tongue. Histologic criteria based on architectural, cytologic, and immunologic features of the lymphoid aggregate have been described.



Unencapsulated Lymphoid Aggregates

Management

No management is required unless these aggregates demonstrate unilateral and progressive enlargement, in which case a biopsy is indicated to rule out malignancy.

➢Fordyce Spots (granules)

Etiology and Pathogenesis

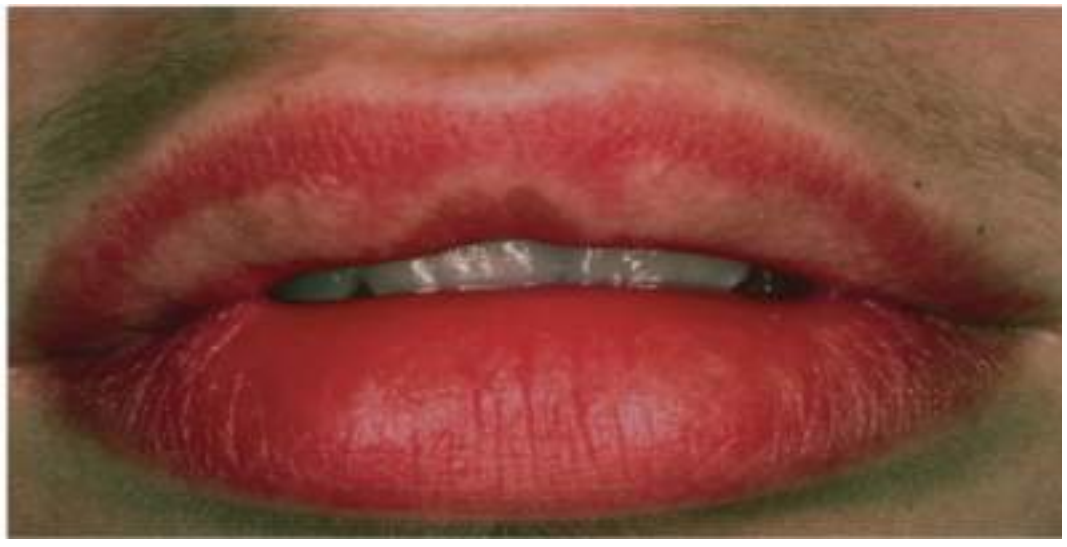
These are ectopic sebaceous glands and it is unclear why some individuals develop them. The link between hyperlipidemia and Fordyce spots has not been substantiated.

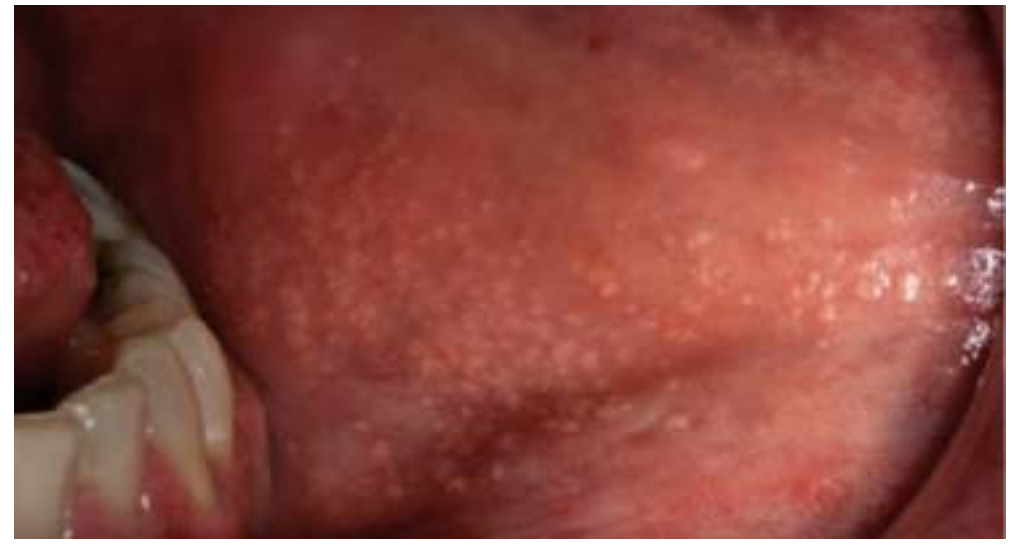
Clinical Manifestations

The most common locations for Fordyce spots are the buccal mucosae and lip vermillion.

Management

Typically no treatment is required. There are surgical options for patients with a high concentration of labial Fordyce spots deemed esthetically obtrusive.





Fordyce spots in buccal mucosae and lip vermillion

2-BENIGN SOFT TISSUE LESIONS

INFLAMMATORY/REACTIVE EXOPHYTIC SOFT TISSUE LESIONS

The term **inflammatory/reactive soft tissue tumors** is used to describe a large range of commonly occurring exophytic lesions of the oral mucosa that histologically represent inflamed fibrous and granulation tissue.

The majority of these occur peripherally on the oral mucosal surfaces that may be subject to masticatory trauma (i.e., as the result of chronic trauma from ill-fitting dentures, biting, or contact with fractured teeth), related to the chronic inflammatory stimuli (i.e., overhanging restorations, calculus), or in some lesions the levels of circulating hormones or medications play a role. The number and size of these reactive hyperplastic lesions vary depending on the degree to which one or more of the components of the inflammatory reaction and healing response are exaggerated. Some are predominantly epithelial overgrowths with only scanty connective tissue stroma; others are fibromatous, with a thin epithelial covering, and may exhibit either angiomatous, desmoplastic (collagenous), or fibroblastic features.

➢ Irritation Fibroma

Etiology and Pathogenesis Irritation fibromas develop following trauma, such as a cheek or lip bite.

Clinical Manifestations they are usually asymptomatic and may occur as either pedunculated or sessile (broad-based) pink nodules on any surface of the oral mucosa, but most commonly involving the buccal or labial mucosae . The majority are rarely >1 cm in diameter.

Management An excisional biopsy is indicated except when the procedure would produce marked deformity; in such a case, incisional biopsy to establish the diagnosis is mandatory. The irritant, if present, should also be eliminated when the lesion is excised to reduce the risk for recurrence.

Irritation Fibroma

Other Solitary Fibrous Lesions

Pulp polyps are analogous to a fibroma. They occur when the pulpal connective tissue proliferates through a large carious pulpal exposure and fills the cavity in the tooth with a mushroom-shaped polyp that is connected by a stalk to the pulp chamber . Masticatory pressure may lead to keratinization of the epithelium covering these lesions. Pulp polyps contain few sensory nerve fibers and are remarkably insensitive. The crowns of teeth affected by pulp polyps are usually so badly destroyed by caries that endodontic treatment is not feasible.

Giant cell fibromas comprise a small subset(<5%) of solitary fibrous lesions. Their etiology is unknown, and these exophytic lesions are typically smaller than the irritation fibroma, They most often involve the gingivae.

➢ Fibrous Inflammatory Hyperplasias/Epulis Fissuratum

Etiology and Pathogenesis

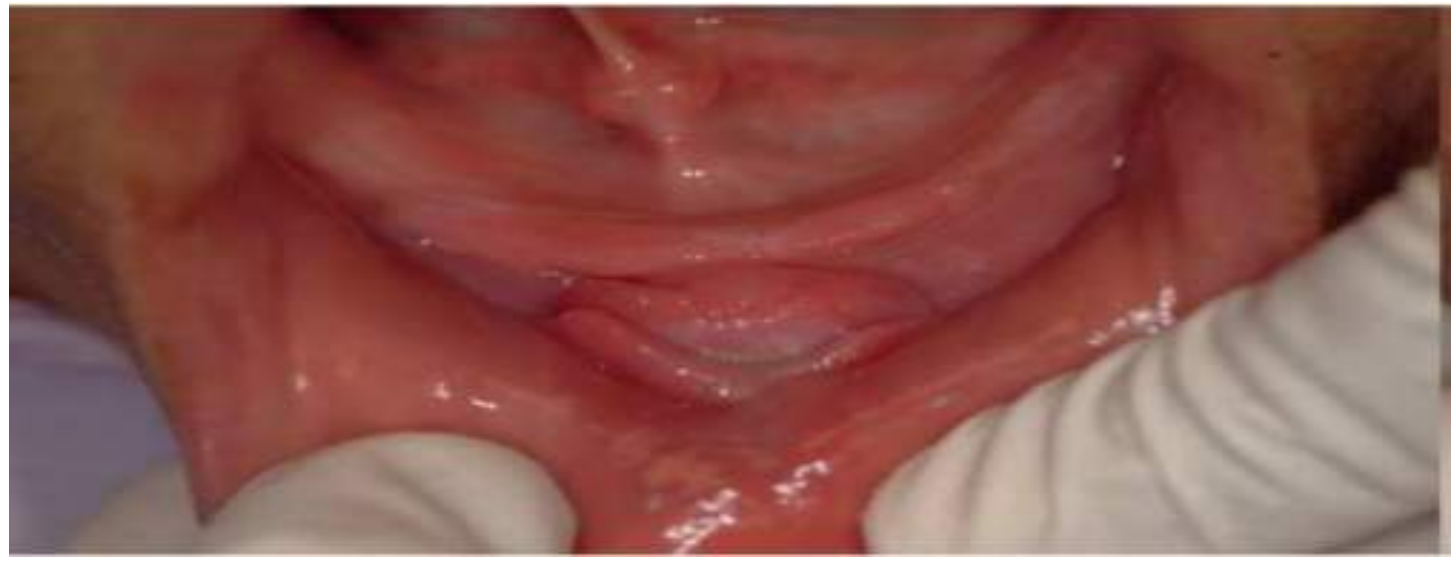
These are reactive inflammatory lesions associated with the periphery of ill-fitting dentures. They have no malignant potential.

Clinical and Histologic Manifestations

The growth is often split by the edge of the denture, resulting in a fissure, one part of the lesion lying under the denture and the other part lying between the lip or cheek and the outer denture surface Histologically they resemble the irritation fibroma.

Management

Many such hyperplastic growths will become less edematous and inflamed following the removal of the associated chronic irritant, but they rarely resolve entirely. In the preparation of the mouth to receive dentures, these lesions are excised (i.e., by conventional scalpel or laser excision) to prevent further irritation and to ensure a soft tissue seal for the denture periphery.



Epulis Fissuratum

➢Inflammatory Papillary Hyperplasia

Etiology and Pathogenesis

The exact pathogenesis is unclear, but this condition is usually associated with chronic denture irritation and denture stomatitis due to chronic candidal infection.

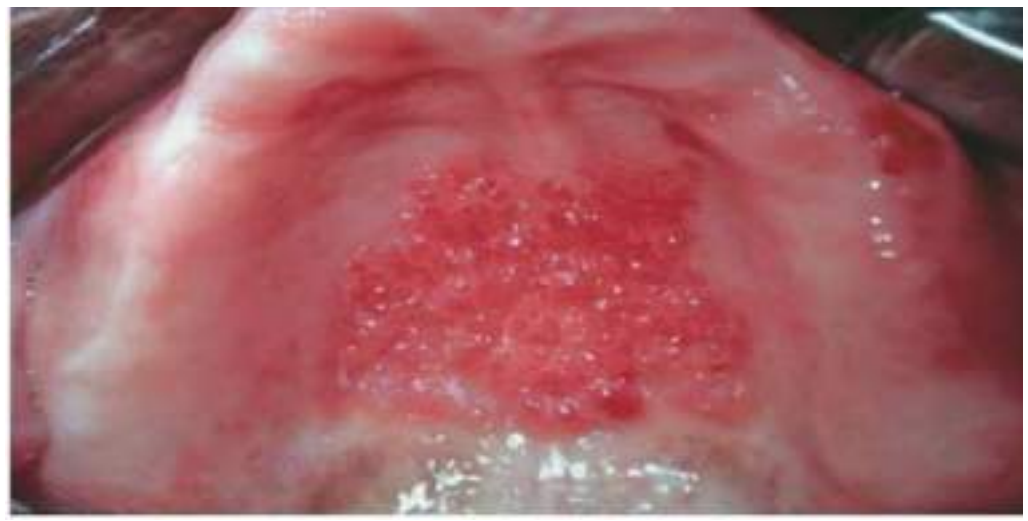
Clinical Manifestations

This condition develops on the central hard palate, with a characteristic red to scarlet lesion demonstrating swollen and

of an overripe berry . Such lesions are friable, and often bleed with minimal trauma.

Management

Mild cases may be treated successfully by topical or systemic antifungals alone; otherwise, papillary hyperplasia may be surgically excised or removed by electrocautery, cryosurgery, or laser surgery. The old denture or a palatal splint can be used as a postoperative surgical dressing, followed by fabrication of a new denture.



Inflammatory Papillary Hyperplasia

➤ Pyogenic Granuloma and Pregnancy Tumor

Etiology and Pathogenesis

The etiology of pyogenic granulomas is thought to be in response to chronic irritation. Their propensity for involving the gingival margin supports this etiology and suggests that calculus, food materials, and overhanging dental restoration margins are important irritants that should be eliminated when the lesion is excised. Hormones play a role in the etiology of the lesion in the setting of pregnancy (where the lesion is named a pregnancy tumor), although local irritation is also an important etiologic factor.

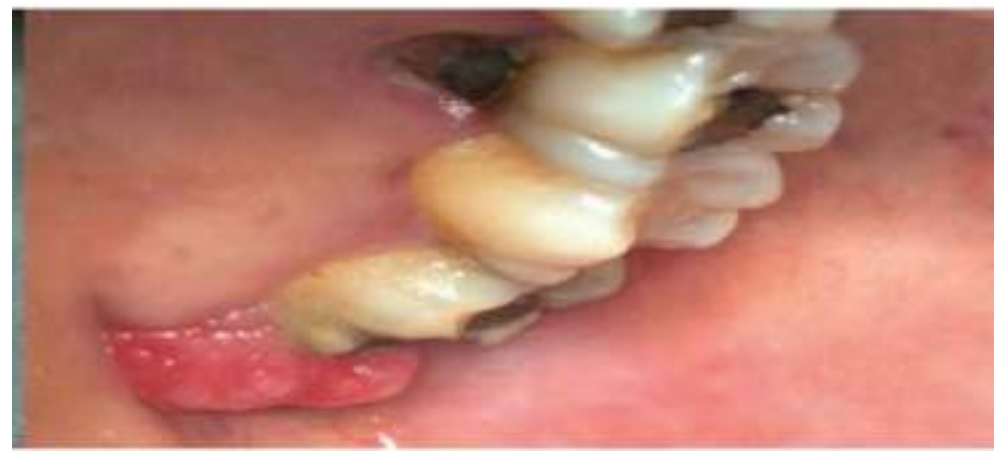
Clinical and Histologic Manifestations

Pyogenic granulomas typically present as solitary hemorrhagic, often pedunculated, nodules of variable size that occur most frequently on the gingiva , although they may occur on any mucosal surface. Their friable, hemorrhagic, and frequently ulcerated appearance correlates with their histologic structure,

demonstrating proliferating endothelial tissue, much of which is canalized into a rich vascular network with minimal collagenous support. Neutrophils, as well as chronic inflammatory cells, are consistently present throughout the edematous stroma, and form into microabscesses .

Management

Surgical excision and successful removal of the associated irritant are associated with a low rate of recurrence. Scrupulous oral hygiene can prevent pregnancy tumors.



Pyogenic granuloma

➢ Peripheral Ossifying or Cementifying Fibroma

Etiology and Pathogenesis

This is a reactive lesion of unclear etiology, most likely related to local trauma/irritation.

Epidemiology

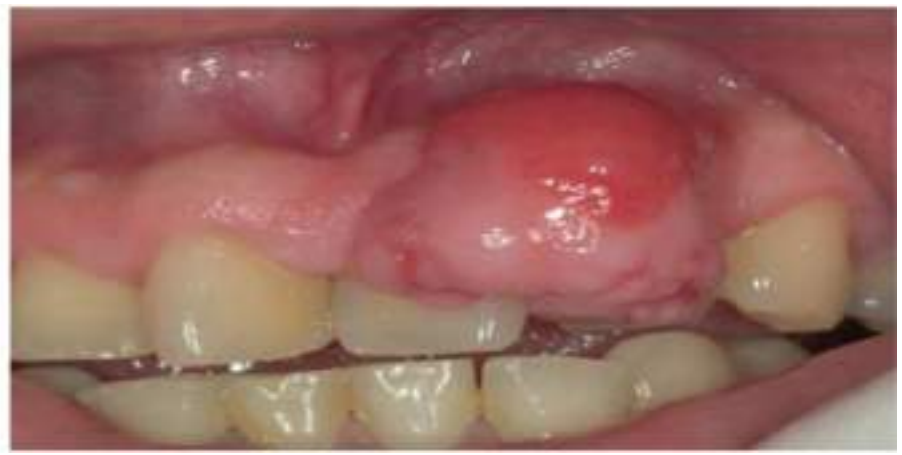
These lesions occur in teenagers and young adults and are more common in women.

Clinical/Histologic Manifestations

They occur exclusively on the gingiva, typically located in the interdental papilla region , and vary in presentation from pale pink to cherry red. This reactive proliferation is named because of the histologic evidence of calcifications that are seen in the context of a hypercellular fibroblastic stroma.

Management

Treatment should include the elimination of sub gingival irritants and periodontal pockets, as well as excision of the gingival growth.



Peripheral Ossifying Fibroma

- **Peripheral Giant Cell Granuloma**

Etiology and Pathogenesis

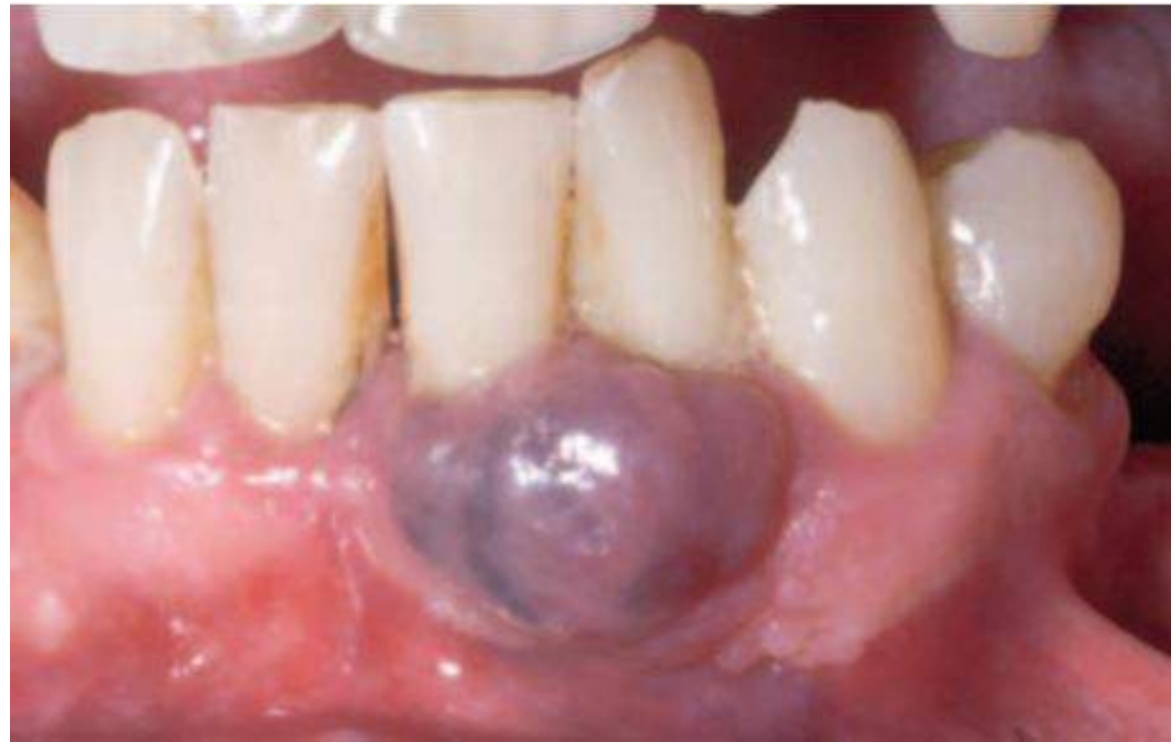
This is a reactive lesion of unclear etiology, most likely related to local trauma/irritation. It is the soft tissue counter part to the central giant cell granuloma.

Clinical and Histologic Manifestations

Giant cell granulomas are solitary and occur either as a peripheral exophytic lesion found exclusively on the gingiva or as a centrally located lesion within the jaw, skull, or other facial bones .

Management

Peripheral giant cell granuloma is treated identically to the other reactive gingival lesions, by surgical excision and the elimination of local factors contributing to gingival/periodontal disease



Peripheral Giant Cell Granuloma

- **Nodular Fasciitis**

Etiology and Pathogenesis

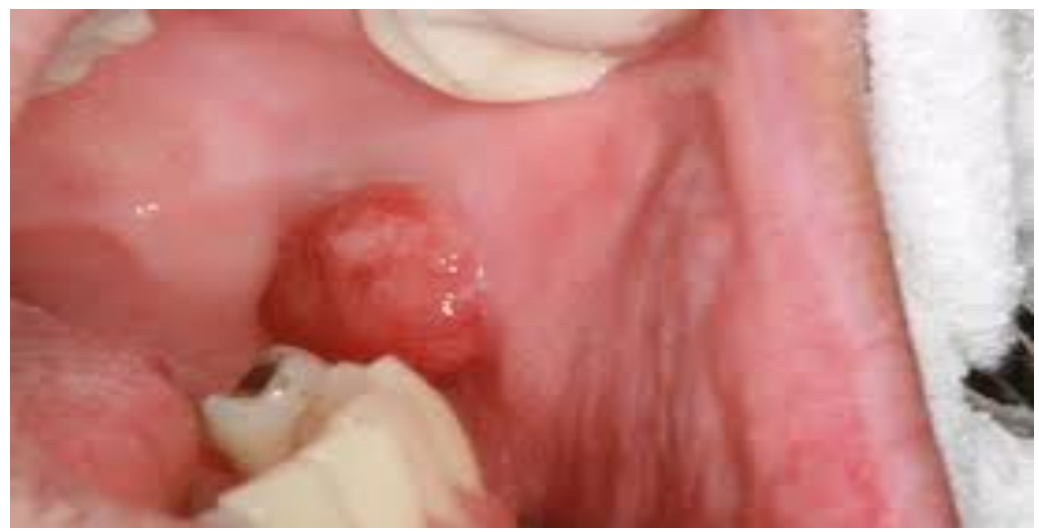
This is a reactive proliferation of myofibroblasts and although the etiology is unknown, trauma is a likely factor.

Clinical and Histopathologic Manifestations

The most common oral site is the buccal mucosa and most have an exophytic presentation. Nodular fasciitis has distinctive microscopic features revealing the myofibroblast as the predominant cell type.

Management Conservative surgical excision and submission for histology.

Nodular Fasciitis



➢ Proliferative Myositis and Focal Myositis

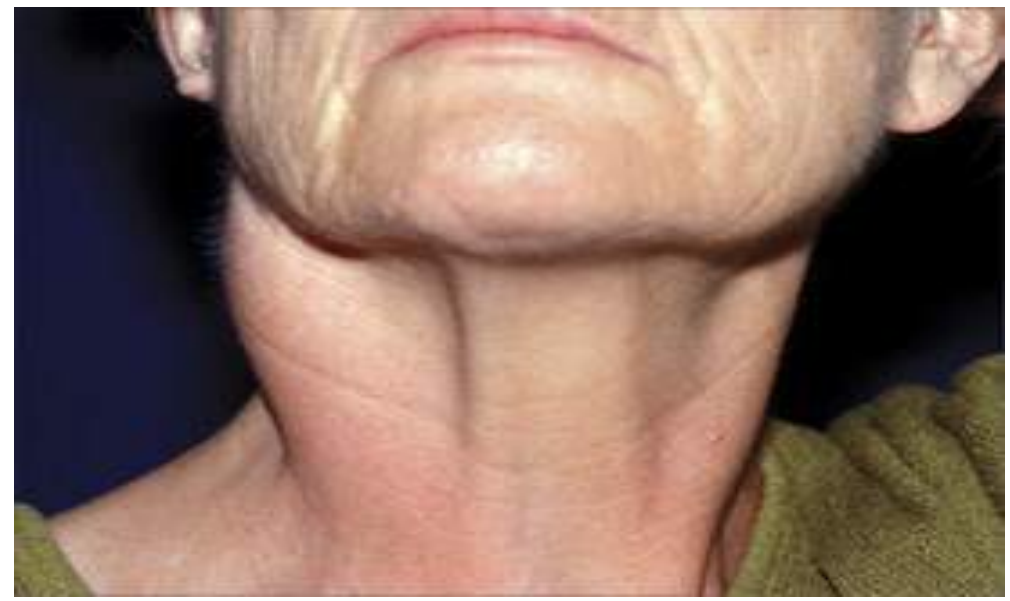
Etiology and Pathogenesis

These entities are reactive fibroblastic lesions that infiltrate around individual muscle fibers.

Clinical Manifestations

Lesions most frequently involve the tongue and other neck and jaw muscles. Despite the nomenclature, these lesions do not show histologic signs of inflammation.

Management Conservative surgical excision and submission for histopathology



Proliferative Myositis

➤ Reactive Gingival Enlargement

Gingival enlargement or overgrowth is usually caused by local inflammatory conditions such as poor oral hygiene, food impaction, or mouth breathing. Systemic conditions such as hormonal changes or drug therapy may also cause or contribute to the severity of gingival enlargement.

Histologically, there are a number of explanations for gingival enlargement hypertrophy (an increase in cell size), hyperplasia (an actual increase in cell number), edema, vascular engorgement, the presence of an inflammatory cell infiltrate, or an increase in dense fibrous connective tissue.

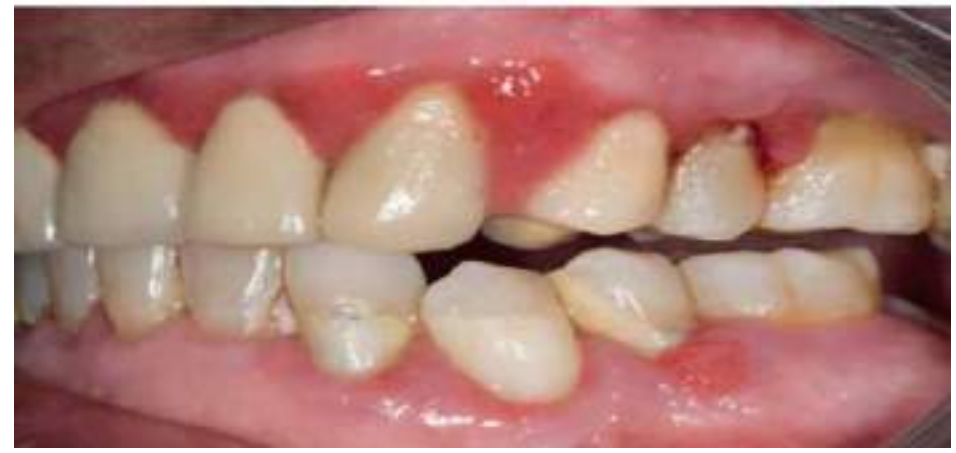
➢ Inflammatory Gingival Enlargement

Etiology and Pathogenesis

Inflammatory gingival enlargement occurs in sites where there has been chronic suboptimal oral hygiene with heavy biofilm accumulation, supragingival calculus formation, impaction of food, or the presence of aggravating factors such as orthodontic appliances, mouth breathing, hormonal changes, or other systemic diseases. Gingival enlargement primarily affecting the maxillary anterior region may be observed in mouth breathers, and hormonal changes (such as during pregnancy or puberty) may exaggerate the local immune response to local factors and contribute to gingival enlargement.

Clinical and Histologic Manifestations

The clinical diagnosis of inflammatory gingival enlargement is a glossy edematous bright red or purplish color, pitting edema, and a tendency to hemorrhage on slight provocation. A malodor ,Pseudopockets formed by gingival enlargement ,firm, resilient, and pink gingivae that do not bleed readily.



Inflammatory gingival enlargement secondary to local factors

Management Treatment of inflammatory gingival enlargement begins with the establishment of excellent oral hygiene, together with the elimination of all local and/or systemic predisposing factors if possible.

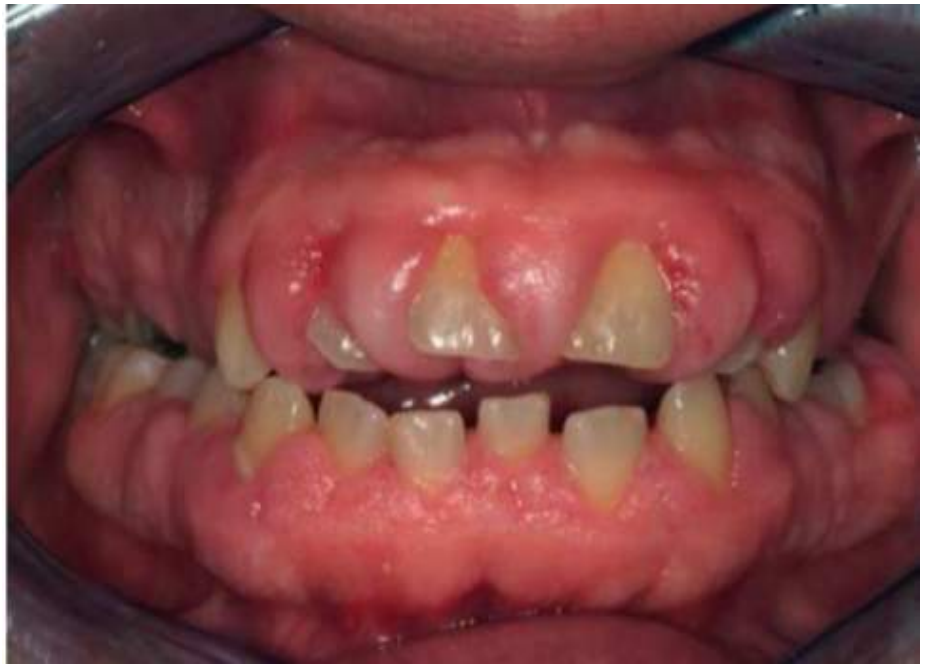
➢ Drug-Induced Gingival Enlargement

Etiology and Pathogenesis

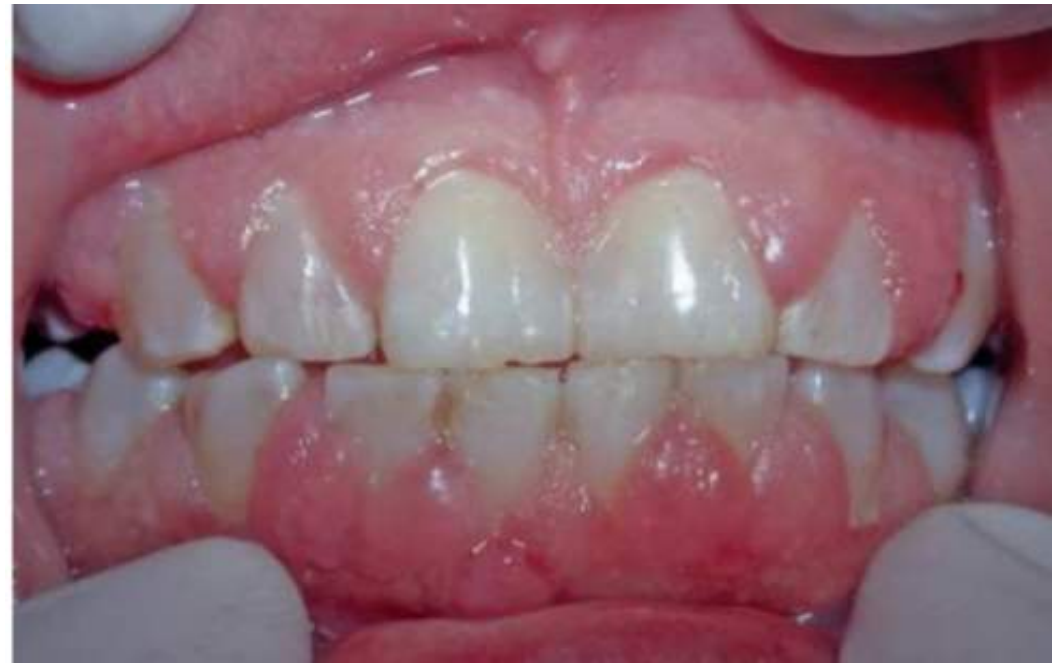
Drug-induced gingival enlargement is most commonly associated with the administration of anticonvulsants (principally phenytoin), cyclosporine, and calcium channel blocking agents (principally nifedipine). the extent of inflammation and fibrosis is largely influenced by the drug type, dosing, and duration. These drugs likely exert their influence by the dysregulation of cytokines and growth factors, and also differentially affect the response of innate and adaptive immune systems.

Clinical Manifestations

There is a characteristic clinical appearance of drug-induced gingival enlargement. After approximately one month of use of the drug, interdental papillae enlargement begins, usually in the anterior regions, and enlargement may become more extensive, leading to gingival disfigurement and associated esthetic and functional complications.



Gingival enlargement secondary to longstanding phenytoin use



Gingival enlargement secondary to longstanding cyclosporine use

Management

Prevention

through optimal oral hygiene is essential to minimize the severity of enlargement. The most predictable treatment is either the withdrawal or change of medication and there are a variety of new-generation anticonvulsants, immunosuppressants, and antihypertensive available. Tacrolimus has been shown to be an effective replacement for cyclosporine and does not seem to cause gingival enlargement.

Nonsurgical treatments such as professional gingival debridement and topical or systemic antimicrobials may ameliorate gingival enlargement.

Surgical management is reserved for severe cases, although recurrence is common. Laser ablation gingivectomy may offer an advantage over conventional surgery since procedures are faster and there is improved hemostasis and more rapid healing.

Other Causes of Gingival Enlargement

Although strictly reactive, gingival enlargement may rarely be the result of genetic predisposition.

1-Hereditary gingivofibromatosis is linked to both autosomal dominant and recessive patterns of inheritance, and genetic heterogeneity and variable expressivity contribute to the difficulty encountered in assigning this diagnosis to a specific syndrome.

2-_____ may be present at birth or may become apparent only with the eruption of the deciduous or permanent dentitions.

Enlargement

3-Patients with acute myelogenous leukemia may present with gingival leukemic infiltrates .

4-Others include von Recklinghausen's neurofibromatosis , Wegener's granulomatosis, sarcoidosis, Crohn's disease, primary amyloidosis, Kaposi's sarcoma, acromegaly, and lymphoma.

3-BENIGN SOFT TISSUE TUMORS

Oral mucosal benign tumors comprise lesions that are formed from epithelium, fibrous connective tissue, adipose tissue, nerve, and muscle. Benign proliferations of blood vessels and lymphatic vessels resemble neoplasms, but do not have unlimited growth potential and therefore are more appropriately considered hamartomatous proliferations.

❖ Epithelial

A-Human Papillomavirus-Induced Growths

Etiology and Pathogenesis

These growths are not true neoplasms, but rather virally induced tissue proliferations. There are almost 200 human papillomavirus (HPV) genotypes, of which at least 30 have been detected in oral lesions. Much attention has been focused on the relationship between oncogenic genotypes (predominantly HP 16) and oropharyngeal carcinogenesis.

The virus infects the basal cell layer of the epithelium following mucosal trauma, there is integration of the viral genome, and proliferation of the epithelium leading to the development of a clinically visible lesion or lesions. The virus is most often transmitted by direct contact with another infected person, although such a history may not be evident, suggesting transmission by autoinoculation or casual contact. Lesions associated with sexual contact (referred to as condyloma acuminatum).

Clinical and Histologic Manifestations

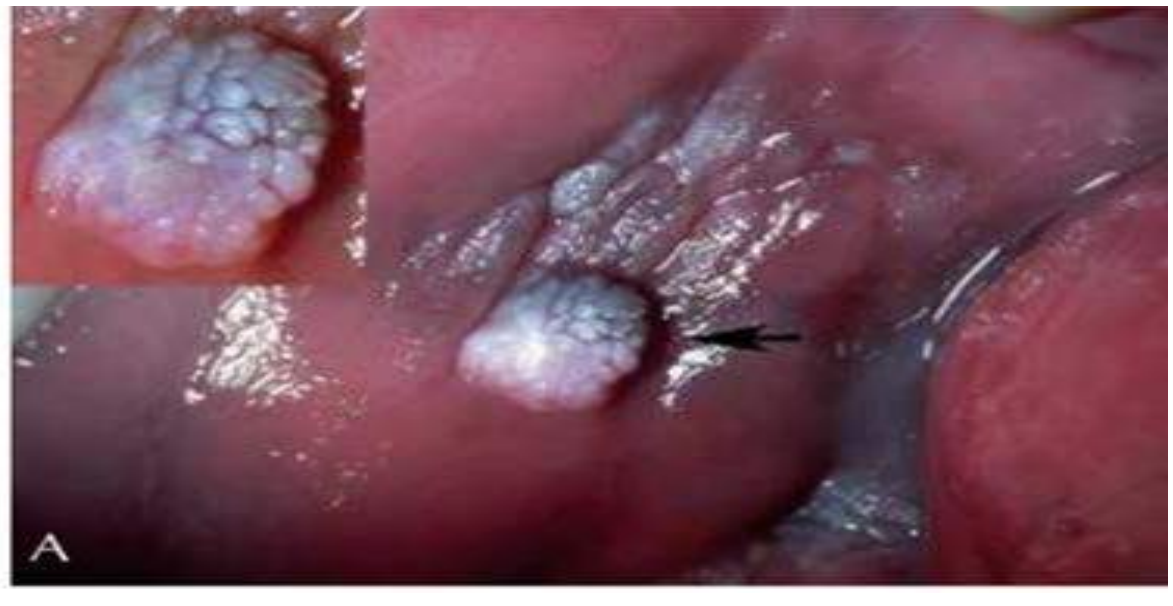
Viral papillomas most commonly present as an isolated small growth (<1 cm diameter) on the palate, ranging in color from white to pink, their surface is papillary/verrucous, and they are pedunculated more often than sessile. Condyloma accuminata are typically larger in size than viral papillomas, are often flat-topped, and may present as a single main growth associated with smaller satellite lesions.

The common wart, verruca vulgaris, is generally found on the skin (sometimes in association with similar skin lesions, often on the fingers). When involving the oral cavity, these warts are similar in appearance to viral papillomas and they tend to involve the lips, gingivae, and hard palate .

Focal epithelial hyperplasia (FEH) (Heck's disease) is characterized by numerous soft, well-circumscribed, comparatively flat, and sessile papules distributed throughout the oral mucosa. Histologically, FE is characterized by nondyskeratotic nodular acanthosis, which forms the basis of the papules, and a subepithelial lymphocytic infiltration. Intraoral papillomatosis, often florid, has been found in a small subset of HIV-infected patients .

Management

Oral viral papillomas and warts are clinically similar, and local excision is desirable. Care should be exercised when removing HPV-induced oral growths with electrocautery or laser, as there exists the possibility of aerosolizing viral particles. Due to the widespread manifestations, florid disease is challenging to manage surgically, and there is no current evidence-based medical management.



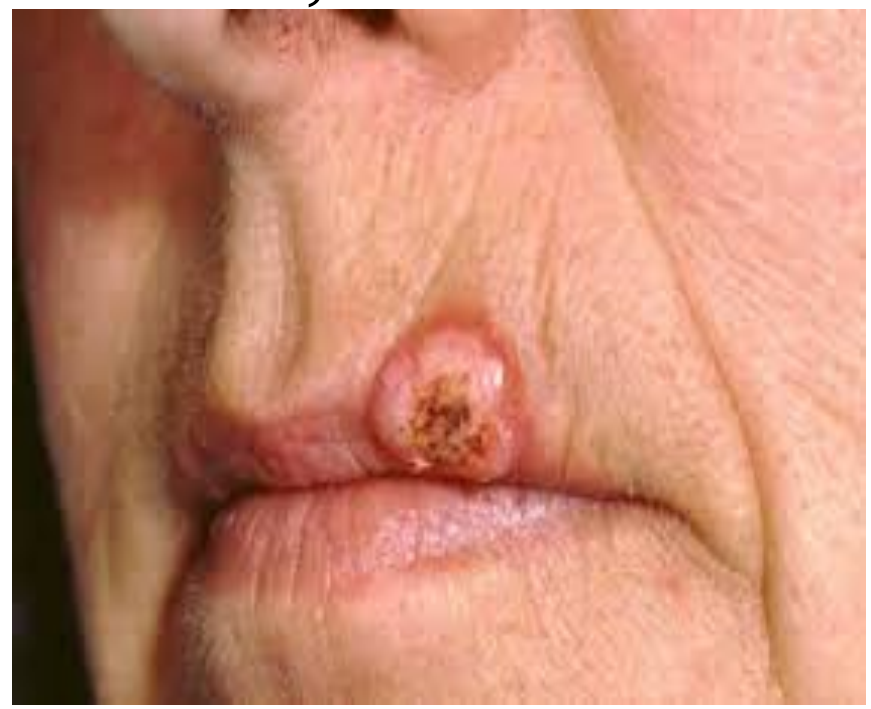
viral papillomas

B-Keratoacanthoma

Etiology and Pathogenesis The rapid growth of a keratoacanthoma may be quite frightening, to the point where it is often mistakenly diagnosed as squamous or basal cell carcinoma.

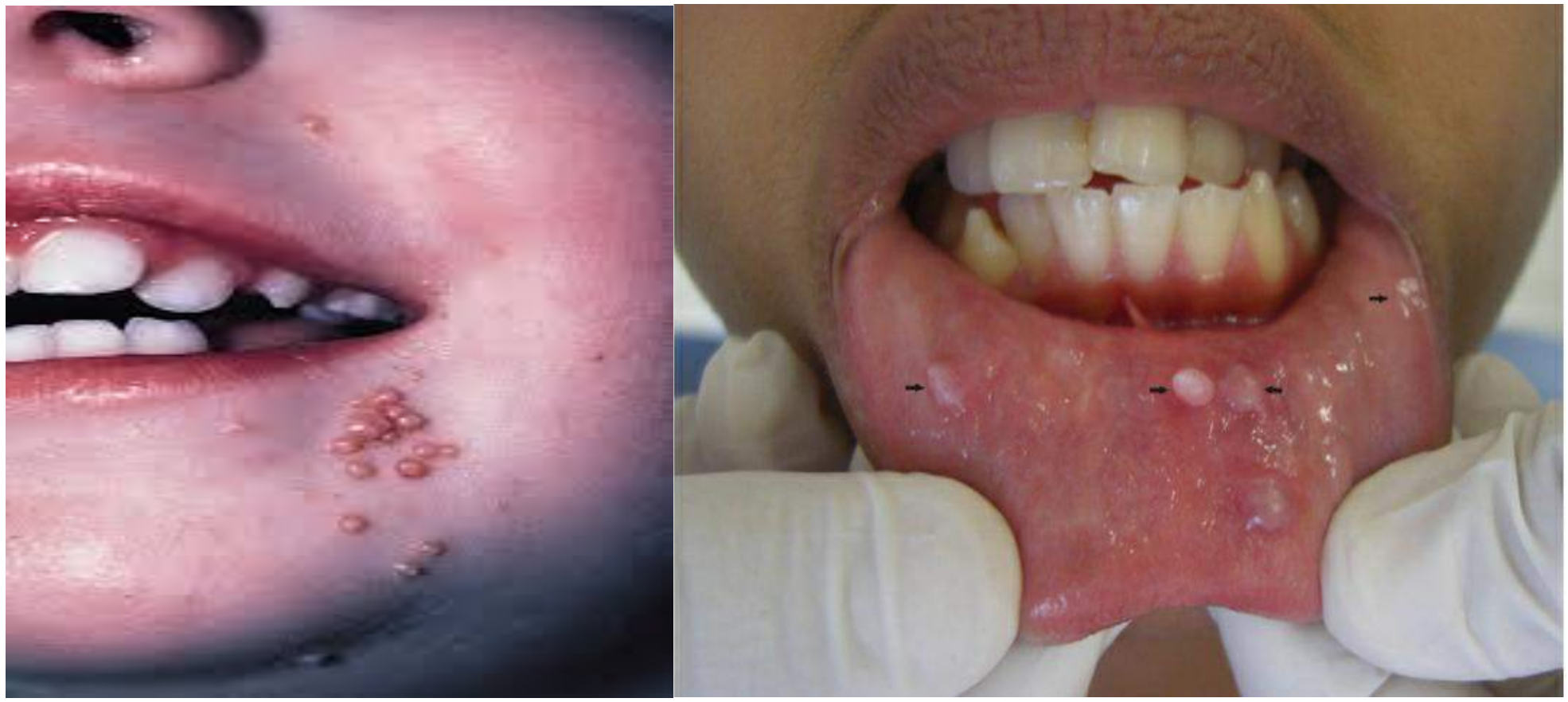
Clinical and Histologic Manifestations The usual location is on the upper lip, where they are dome- like, sharply demarcated, appear fixed to the surrounding tissue, and are usually capped by thick keratin.

Management Occasionally, the lesion matures, exfoliates, and heals spontaneously. In most cases, however, treatment of this lesion is conservative excision.



Keratoacanthoma

Other Benign Epithelial Growths **Molluscum contagiosum** is a dermatologic infection caused by a poxvirus that is acquired by direct skin contact. Both intraoral and labial lesions of molluscum contagiosum occur, predominantly in HIV-infected patients, and these are characterized by clusters of tiny firm papules.



Molluscum contagiosum

❖ Vascular Anomalies

These entities have been classified using standardized terminology developed by the International Society for the Study of Vascular Anomalies and may be subdivided into vascular tumors and vascular malformations.

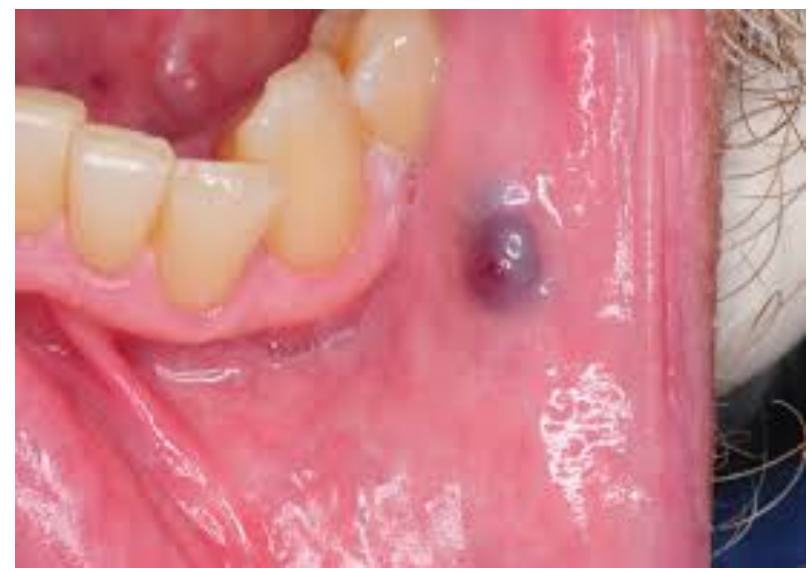
A-Hemangiomas

Etiology and Pathogenesis

Hemangiomas of the head and neck are vascular tumors and true endothelial cell neoplasms. They appear a few weeks after birth and grow rapidly, and in most cases undergo involution over time, with residual telangiectasia, fatty, or scar tissue apparent in approximately 50% of patients.

Clinical and Histologic Manifestations They have been described in almost all head and neck locations in a variety of presentations: superficial and deep, small and large, most commonly as solitary lesions but also as multiple lesions. Small lesions may be clinicall and histologically indistinguishable from pyogenic granulomas and superficial venous varicosities.

Managemen t Given the propensity for involution, surgery should only be considered for those that do not involute, are esthetically obtrusive, or bleed easily.



Hemangiomas

B-Capillary, Venous, and Arterial Malformations

Vascular Malformations

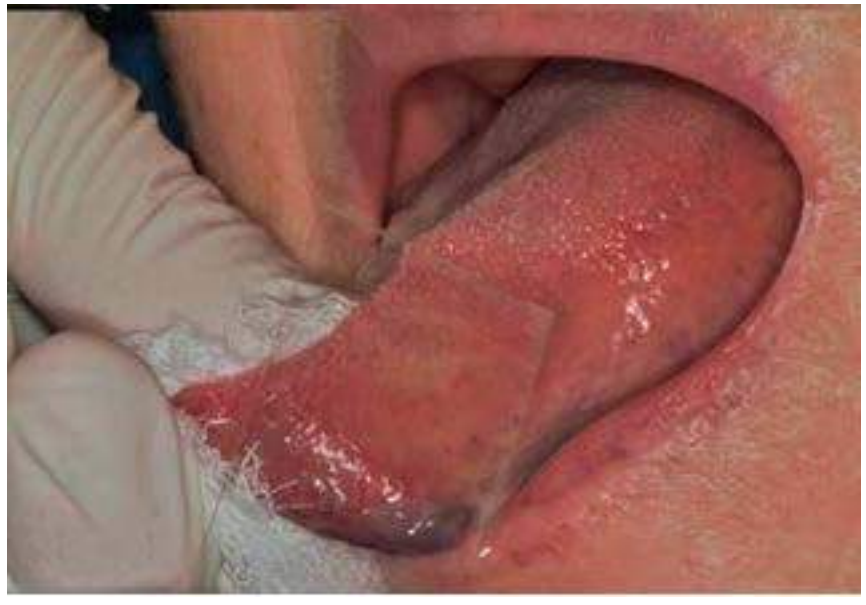
Etiology and Pathogenesis

These malformations are classified depending on the vessel type involved or flow types: arterial and arteriovenous (high flow), capillary , or venous (low flow). They are structural aberrations in components of the vascular apparatus and may be clinically apparent at birth, grow slowly proportional to the growth of the child (characterized by hypertrophy), and never involute

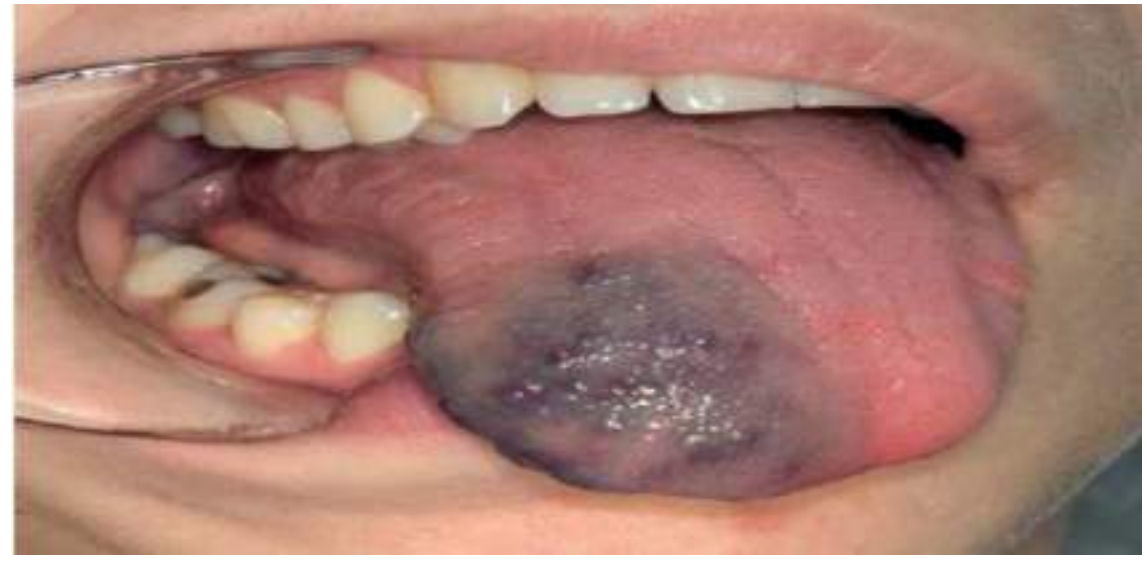
Arterial and arteriovenous malformations may first develop following hormonal changes (such as puberty), infections, or trauma. Venous malformations can sometimes appear first in early adulthood.

Clinical Manifestations

Arterial or arteriovenous malformations may be firm, pulsatile, and warm. Venous malformations are soft and easily compressible. Diascopy is the technique of applying pressure to a suspected vascular lesion to visualize the evacuation of coloration and may facilitate the differentiation of a small vascular lesion from non blanchable red or pigmented lesions.



Diascopy



Vascular malformation involving the tongue

Management

Care should be taken in performing biopsies or excising all vascular lesions, as they have a tendency for uncontrolled hemorrhage and the extent of the lesion is unknown, since only a small portion may be evident in the mouth. Therefore, identification of the precise anatomic location and depth of tissue extent is warranted before treatment, particularly for the high-flow lesions. A number of imaging modalities may be indicated, including ultrasound, contrast-enhanced magnetic resonance imaging or computed tomography (CT), and dynamic MR angiography. Treatment modalities (alone or in combination) for peripheral vascular malformations depend on the type of malformation and include sirolimus, sclerotherapy, embolization, or surgical excision/resection using electrocoagulation.

C-Lymphatic Malformations

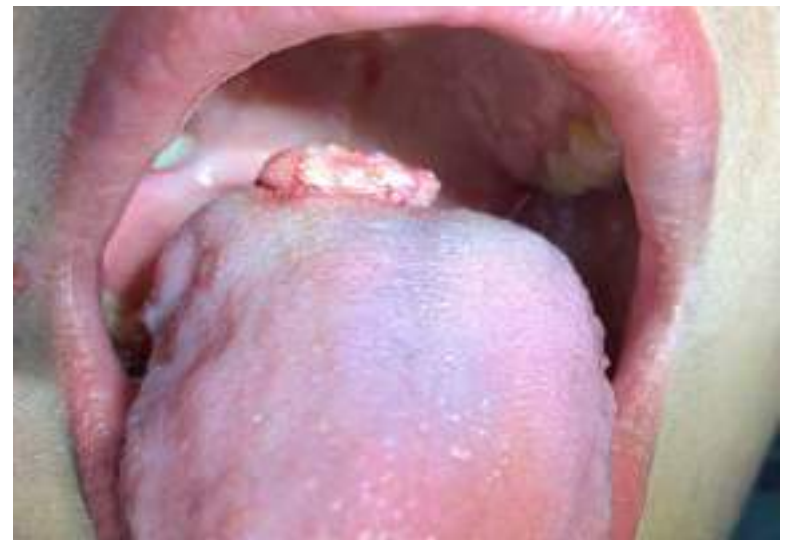
Etiology and Pathogenesis

Macrocystic, microcystic, or mixed cystic lymphatic malformations may be localized or regional, and they are characterized by an abnormal proliferation of lymphatic vessels. The most common extra oral and intraoral sites are the neck (predominantly in the posterior triangle) and tongue, respectively. The vast majority (80–90%) of lymphangiomas arise within the first two years of life and are an important cause of congenital macroglossia.

Clinical and Histologic Manifestations Clinically, lymphangiomas are a slow-growing and painless soft tissue mass. Frequently they are without a clear anatomic outline, dissecting tissue planes, and can be more extensive than anticipated. Occasionally, they may undergo a rapid increase in size secondary to inflammation from an infection or hemorrhage from trauma.

Large lymphangiomas may become life-threatening if they compromise the airway or vital blood vessels, and those spreading into and distending the neck are macrocystic and are referred to as cystic hygromas. Abnormalities of the tongue mucosa overlying a lymphatic malformation may give the appearance of a localized glossitis and may draw attention to the presence of a lesion buried deep in the tongue.

Management treatment of lymphatic malformations is dictated by their type, anatomic site, and extent of infiltration into surrounding structures. Sclerotherapy, bleomycin, or doxycycline) is advocated over surgical excision in most cases.



Lymphatic Malformations

❖ Neurogenic Tumors

A Traumatic Neuroma

Etiology and Pathogenesis

A traumatic neuroma is a reactive lesion caused by injury to a peripheral nerve. When a nerve and its sheath are damaged, the proximal end of the damaged nerve proliferates into a mass of nerve and Schwann cells mixed with dense fibrous scar tissue. In the oral cavity, injury to a nerve may occur from injection of local anesthesia, surgery, or other sources of trauma.

Clinical Manifestations

Traumatic neuromas in the oral cavity may occur in any location where a nerve is damaged, and the mental foramen area, tongue, and lower lip are the most common sites. Traumatic neuromas may lead to either reduced sensation or, in approximately 20% of cases elicit discomfort.

The discomfort range from pain on palpation or pressure from an overlying denture (in the case of a neuroma involving the mental foramen area) to severe and constant pain.

Management

Traumatic neuromas are treated by surgical excision and recurrence is rare.

Neurogenic tumor involving the right lateral tongue

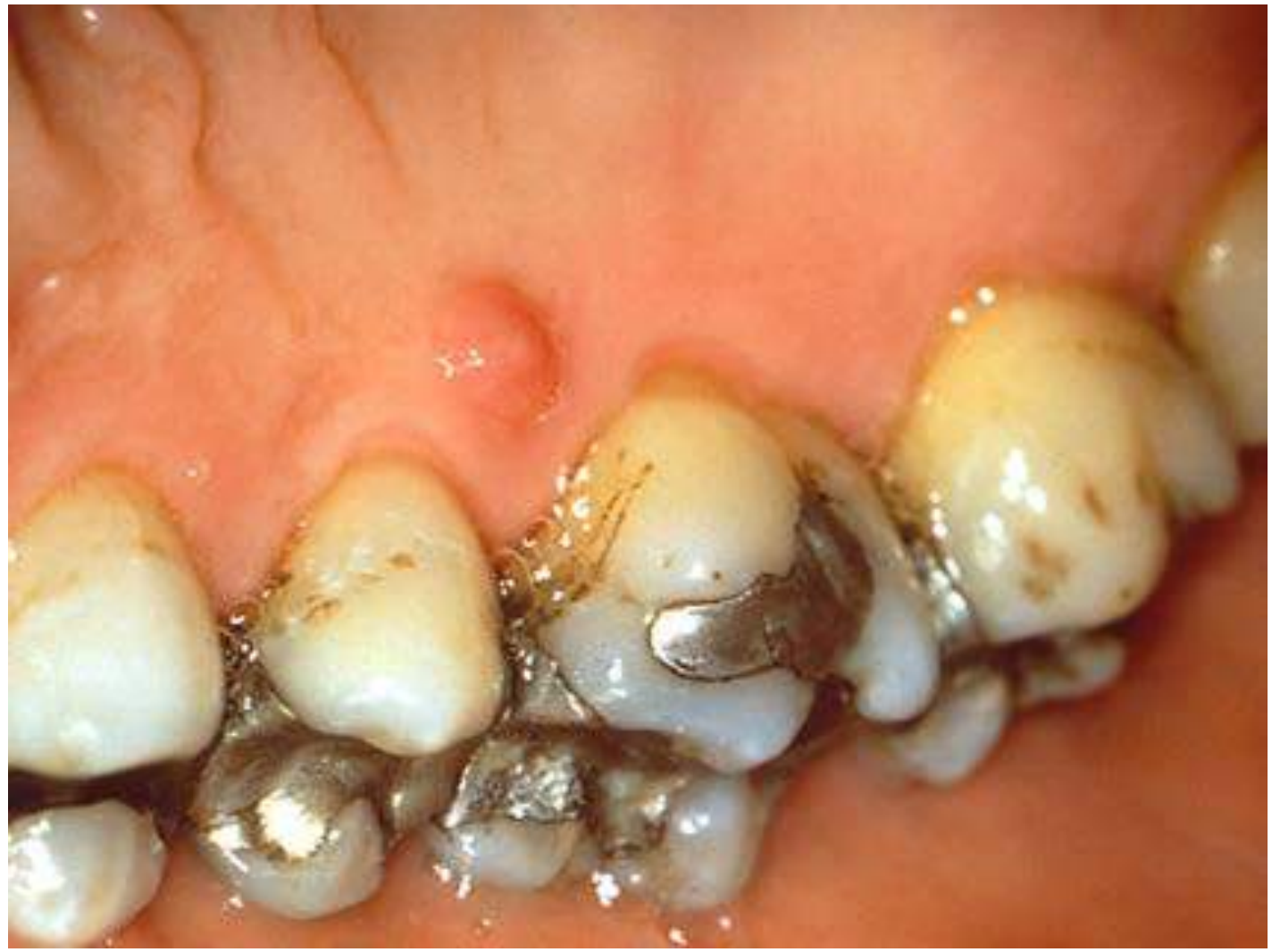
B-Palisaded Encapsulated Neuroma

Etiology and Pathogenesis

This is considered a reactive neoplasm, likely in response to trauma.

Clinical and Histologic Manifestations

The lesions are solitary, a feature that distinguishes them from the neuromas in Multiple Endocrine Neoplasia (MEN) syndrome . They are typically painless and the most common location is the hard palate. Histologically, there is a well-circumscribed, partially encapsulated nodule composed of spindle-shaped cells exhibiting areas of nuclear palisading, often admixed with axons. They contain Schwann cells, perineural cells, and axons.



Palisaded Encapsulated Neuroma

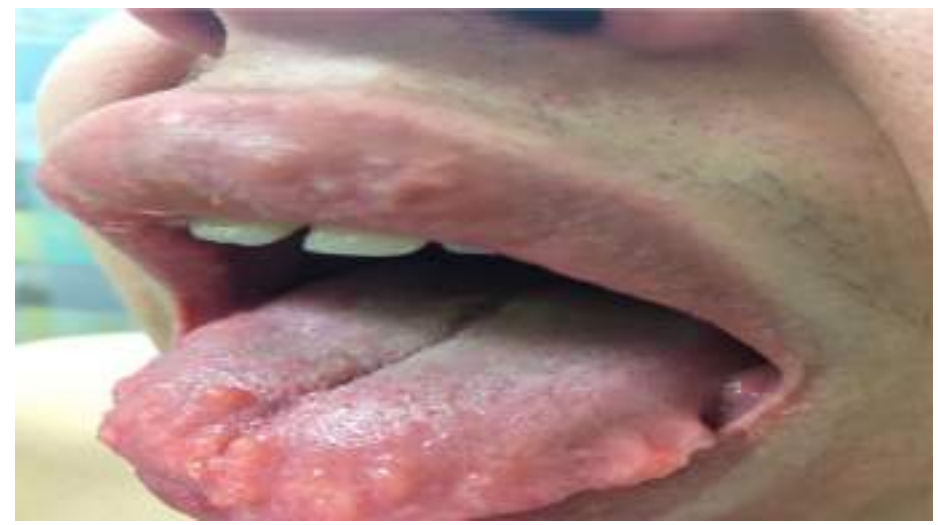
Management

Palisaded encapsulated neuromas are treated by surgical excision and recurrence is rare

C-Oral Mucosal Neuromas and Multiple Endocrine Neoplasia 2B (MEN 2B)

MEN 2B is caused by inherited mutations in the Met918Thr RET gene and characterized by tumors or hyperplasias of neuroendocrine tissues. Patients with ME 2B present with a characteristic phenotype that includes medullary thyroid carcinoma pheochromocytoma, prominent corneal nerve fibers, a "Marfanoid" body habitus, enlarged lips, and neuromas on the eyelids and oral mucosal tissues.

Management includes prophylactic total thyroidectomy, ideally before the age of 1 year.



Mucosal Neuroma

D-Neurofibroma and Schwannoma (aka Neurilemmoma)

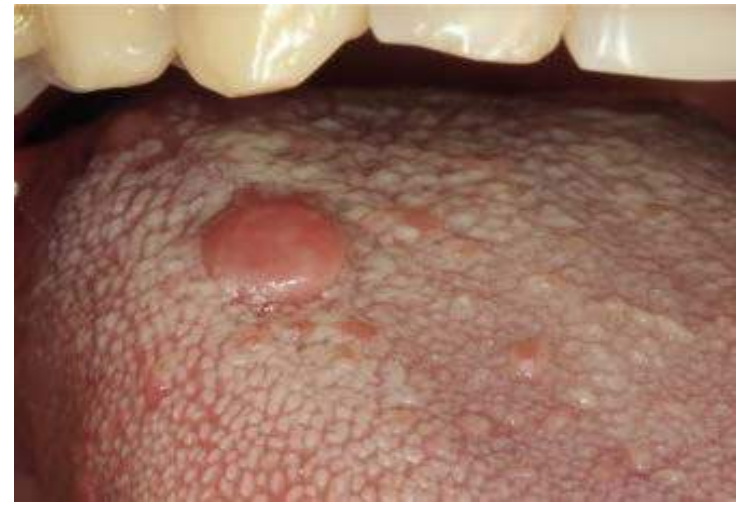
Etiology and Pathogenesis

These are benign tumors derived from the tissue that envelops nerves and includes Schwann cells and fibroblast.

Clinical and Histologic Manifestations

They are typically asymptomatic and the tongue is the most common intraoral location . Microscopic examination of a neurofibroma reveals a fairly well-delineated but diffuse proliferation of spindle-shaped Schwann cells

Management The treatment for a neurofibroma or schwannoma is surgical excision.



Neurofibroma

E-Granular Cell

Tumor

Etiology and Pathogenesis

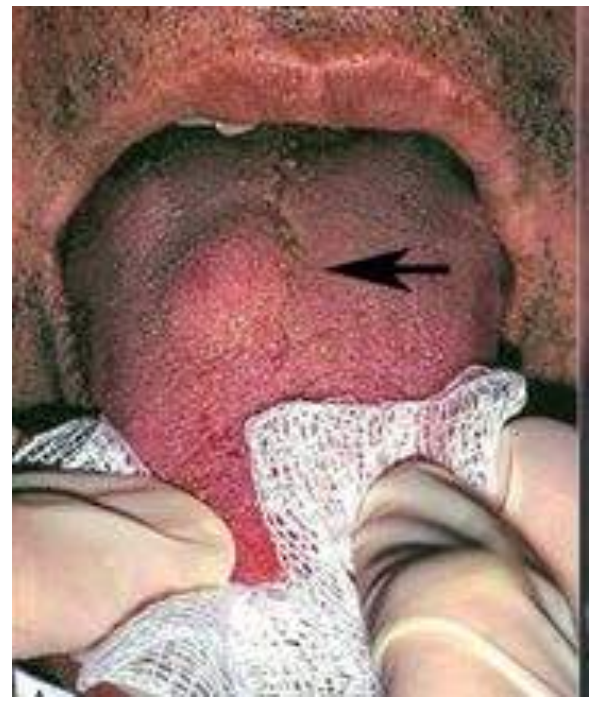
The pathogenesis of this tumor has not been established, but most evidence suggests that it is reactive and arises from Schwann cells or their primitive mesenchymal precursors.

Clinical and Histologic Manifestations

The granular cell tumor most often occurs on the dorsal tongue , followed by the buccal and labial mucosae. Other intraoral sites include the palate , gingiva, and floor of the mouth. The tumor appears as a painless, often yellowish, nonulcerated nodule. The granular cell tumor is a benign tumor composed of large oval-shaped cells with a granular cytoplasm.

Managemen t

This tumor is treated by conservative surgical excision and does not recur.



Granular Cell Tumor

F-Melanotic Neuroectodermal Tumor of Infancy

Etiology and Pathogenesis

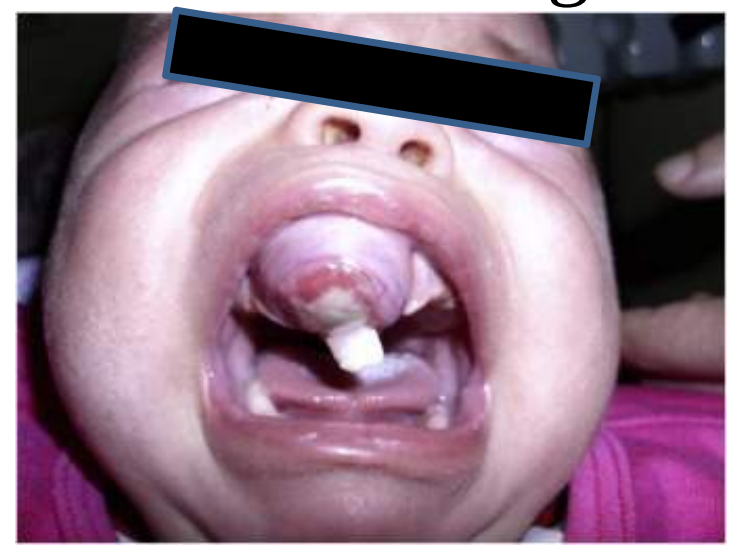
Melanotic neuroectodermal tumor of infancy is a benign neoplasm originating from neural crest cells that almost always occurs during the first year of life.

Clinical and Histologic Manifestations

The tumor most commonly occurs in the maxilla, followed by the skull, mandible, and brain. The tumor presents as a rapidly enlarging mass that destroys bone and may exhibit blue-black pigmentation. Histologically, the tumor is composed of collections of cells that resemble melanocytes.

Laboratory Findings High levels of urinary vanillylmandelic acid often found in patients with this tumor.

Management Conservative surgical removal is usually adequate, but this tumor has a high recurrence rate and malignant transformation has been reported rarely.



Melanotic Neuroectodermal Tumor

❖Lipom

Etiology and Pathogenesis

The lipoma is a benign mesenchymal tumor of mature adipocytes.

Epidemiolog

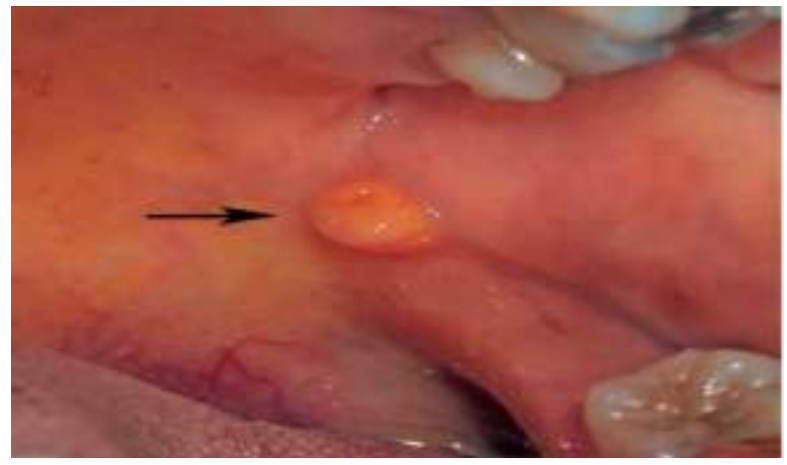
Lipomas involving the oral cavity are rare (<3% of lipomas). They occur in individuals over 40 years of age, and appear without any sex predilection

Clinical and Histologic Manifestations

The majority of oral lipomas are found on the buccal mucosa and tongue. When occurring in the superficial soft tissue, the lipoma appears as a yellow/orange mass with a thin epithelial surface, demonstrating a delicate pattern of blood vessels.

Differential Diagnosis The yellow/orange color is pathognomic. Other yellowish entities include abscess, sialolith, lymphoepithelial cyst,or granular cell tumor .

Managemen t The lipoma is treated by conservative surgical excision and generally does not recur. Intramuscular lipomas have a somewhat higher recurrence rate because they are more difficult to remove completely.



Lipoma involving the buccal mucosa

❖ Tumors of Muscle

Etiology and Pathogenesis

These are benign neoplasms of striated (rhabdomyoma) and smooth (leiomyoma) muscle.

Epidemiology

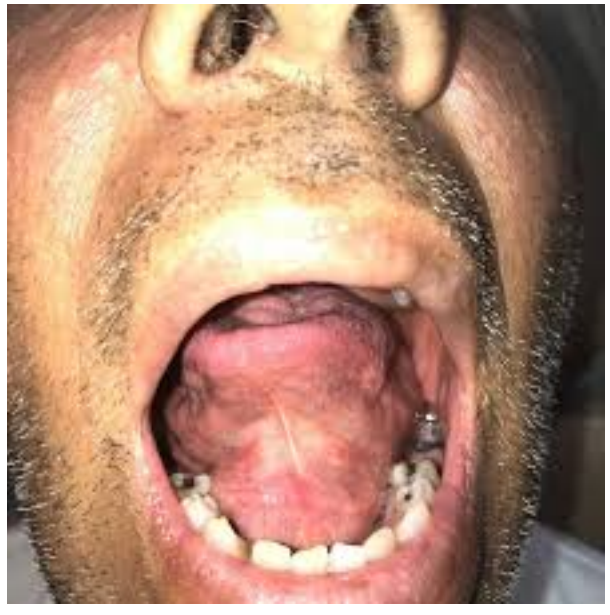
Tumors of muscle are exceedingly rare in the oral cavity.

Clinical Manifestations

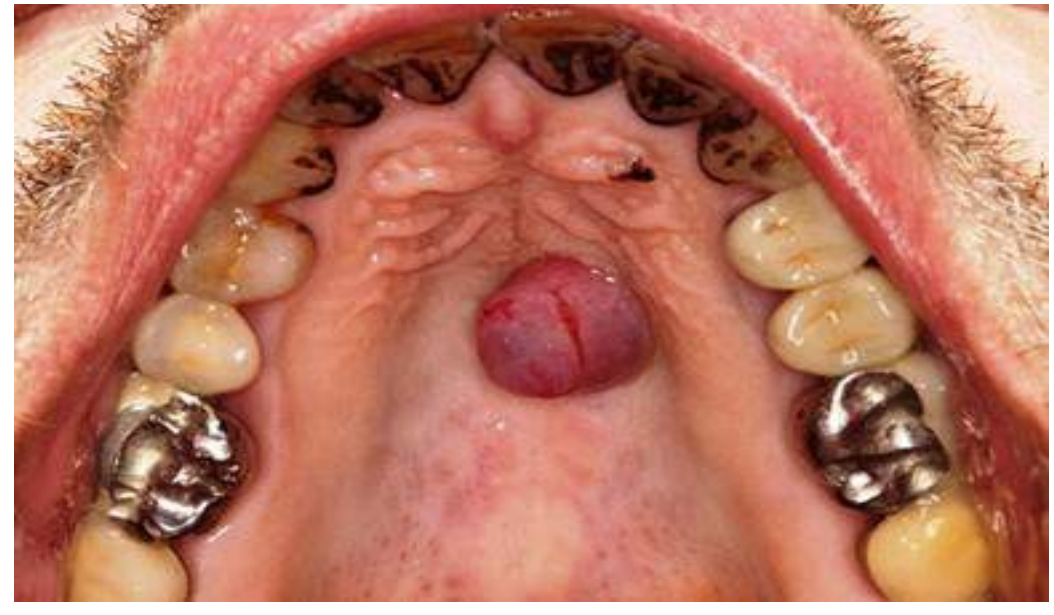
Oral rhabdomyomas have been reported to occur almost exclusively on the tongue. The vascular leiomyoma (angioleiomyoma) is the least rare of the leiomyoma variants and solitary lesions have been reported to involve multiple oral sites.

Management

Treatment is local surgical excision, and recurrence is rare



rhabdomyoma



angioleiomyoma

3-BENIGN HARD TISSUE

❖BENIGN FIBRO-OSSEOUS LESIONS

A-Fibrous Dysplasia

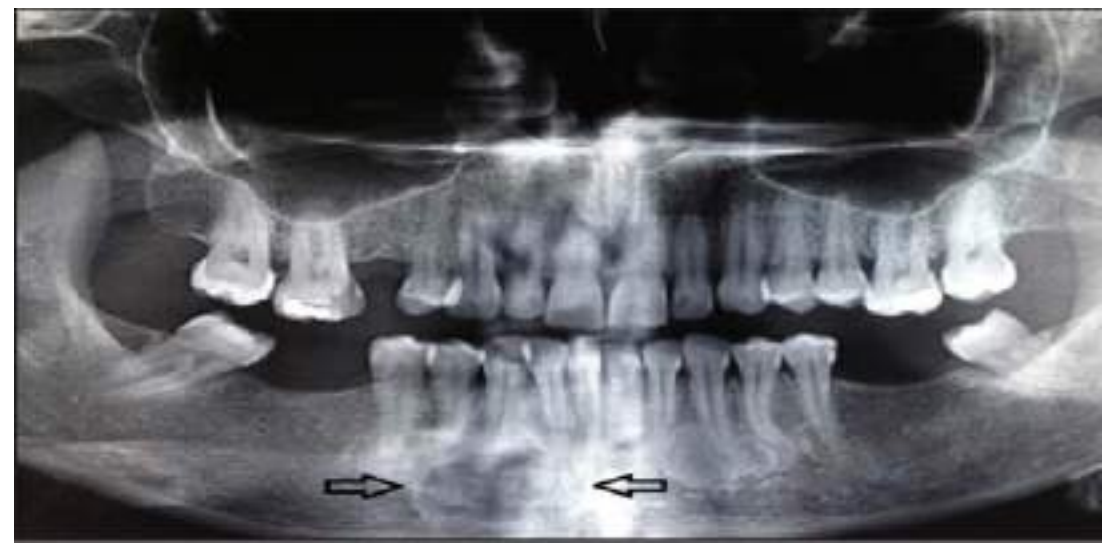
Fibrous dysplasia is a condition that is characterized by the replacement of normal bone with fibro-osseous tissue.

Etiology and Pathogenesis

The pathogenesis is related to GNAS (guanine nucleotide binding protein, alpha stimulating) gene mutation.

Clinical and Histologic Manifestations

Radiographically, fibrous dysplasia classically presents with a "ground glass" appearance and may have varying degrees of radiopacity and lucency depending on the amount of calcified material present. The abnormal bone merges with the adjacent normal bone, which leads to a lack of circumscription or delineation of these lesions. Biopsy of involved bone reveals a tissue that is often described clinically as "gritty" or "sandy." Several forms of fibrous dysplasia have been described. The monostotic form, characterized by the involvement of a single bone, is the most common form.



Fibrous dysplasia

Polyostotic forms are characterized by the involvement of more than one bone and include different types:

(1) craniofacial fibrous dysplasia, in which the maxilla and adjacent bones are involved.

(2) Jaffe's type (or Jaffe–Lichtenstein type), in which there is multiple bone involvement along with an irregular macular melanin pigmentation of the skin (café au lait spots).

(3) rare cases in children (McCune–Albright syndrome or Albright syndrome), in which there is severe, progressive bone involvement with café au lait skin pigmentation and endocrine abnormalities such as precocious puberty.

Laboratory Findings

An elevation in serum alkaline phosphatase may be seen in patients with extensive polyostotic disease.

Management

In most cases, once diagnosis has been confirmed, management with close monitoring or with superficial recontouring of the lesion is sufficient. Curettage is sometimes used for large radiolucent lesions. bisphosphonates has had some use in limiting bone loss. The clinical problems associated with fibrous dysplasia of bone are related to the site and extent of involvement. In the long bones, deformity and fractures are common complications that often lead to the initial diagnosis. In the jaws and other parts of the craniofacial skeleton, involvement of adjacent structures such as the cranial sinuses, cranial nerves, and ocular contents can lead to serious complications in addition to cosmetic and functional problems. Intracranial lesions arising from the cranial bones may produce seizures and electroencephalographic changes.

B-Ossifying Fibroma

Etiology and Pathogenesis

Ossifyin fibroma is a slow-growing, well-circumscribed, benign tumor of bone that probably arises from cells of the periodontal ligament.

Clinical, Radiographic, and Histologic Manifestations

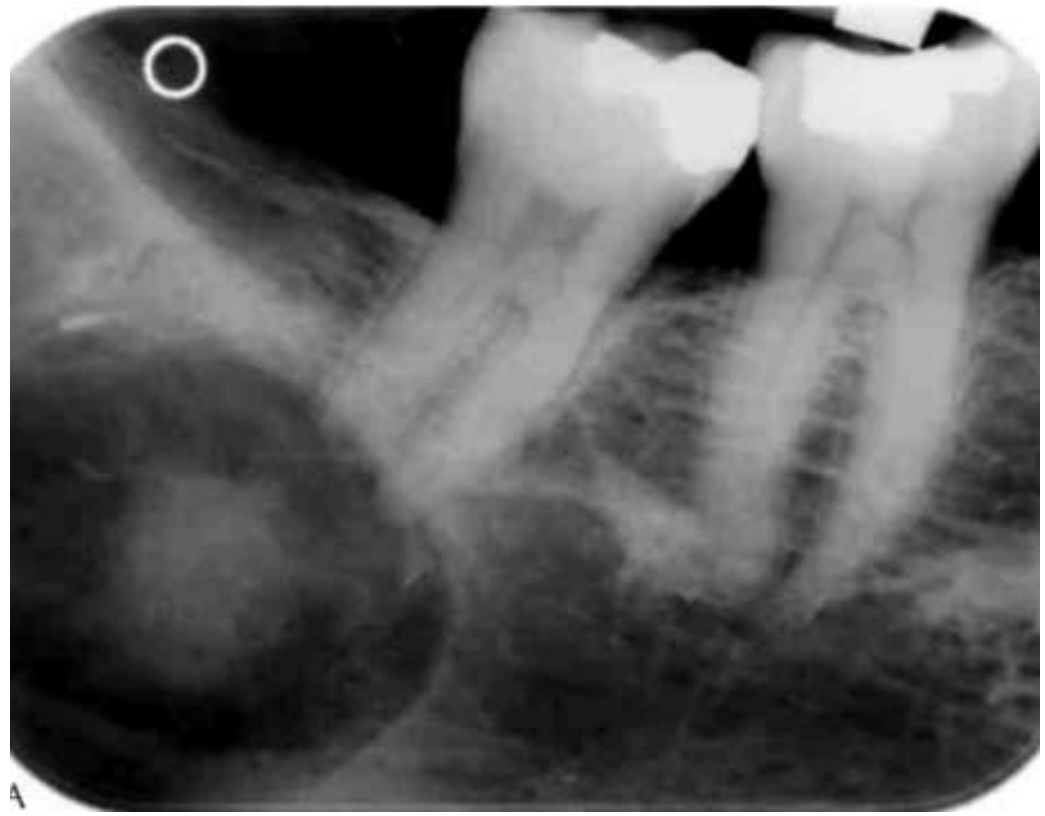
Radiographically, the tumor has a well-circumscribed margin The ossifying fibroma is a benign fibro-osseous lesion that is histologically composed of cellular fibrous connective tissue containing varying amounts of osteoid, rounded cementoid calcifications and irregularly shaped bone trabeculae.

Management

Treatment involves conservative surgical excision of the tumor.

Juvenile Ossifying Fibroma

Juvenile ossifying fibroma is a controversial lesion that is separated from ossifying fibroma based on the patient's age (most are children and young adults), location of lesion, and clinical behavior. This tumor exhibits more aggressive behavior and a greater propensity for recurrence than ossifying fibroma.



Ossifying Fibroma

C-Cemento-Osseous Dysplasias

Etiology and Pathogenesis

The lesions begin as radiolucencies that become more radiopaque with time; large calcified masses become a characteristic histologic feature. Three forms of this dysplastic process involving bone of the jaws are described:

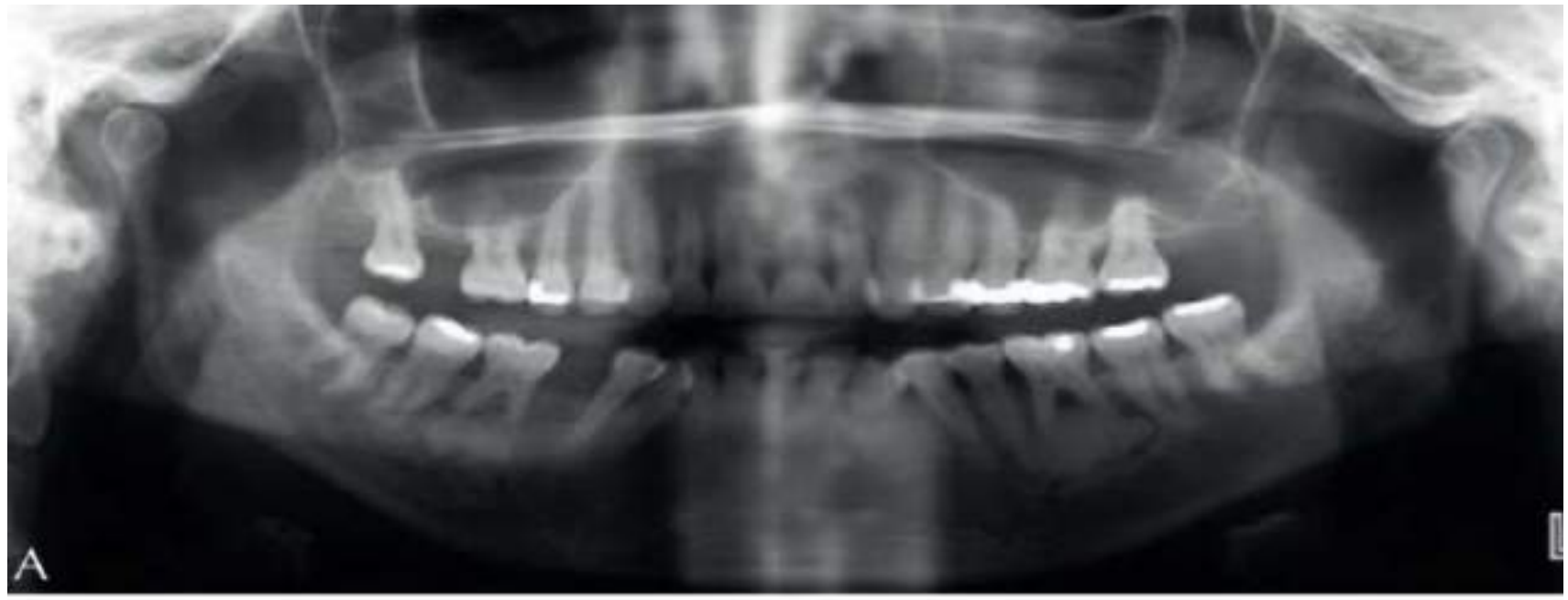
1-periapical cemento-osseous dysplasia

2- focal cemento-osseous dysplasia

3-florid cemento-osseous dysplasia.

Clinical and Histopathologic Manifestations

Periapical and florid types are generally most appropriately diagnosed on the basis of the clinical and radiographic features. The focal type requires a biopsy to establish a definitive diagnosis. Periapical cemento-osseous dysplasia, previously called cementoma, is a lesion that occurs at the apical aspect of vital mandibular anterior teeth. The condition is asymptomatic and does not require treatment. Focal cemento-osseous dysplasia differs from the periapical form since it occurs at the apical aspect of posterior teeth. Florid cemento-osseous dysplasia presents as an exuberant form of cemento-osseous dysplasia, involving more than one and often multiple quadrants of the maxilla and mandible.



Florid cemento-osseous dysplasia

Management

Surgery (e.g., extractions, placement of implants) should be avoided due to potential poor healing and the increased risk of osteomyelitis associated with the affected bone, especially once the bone is sclerotic. Asymptomatic patients should be counseled and followed regularly for prophylactic dental care. This will help to eliminate odontogenic or periodontal disease and any associated surgical intervention.

4-Langerhans cell histiocytosis (Histiocytosis X)

Etiology and Pathogenesis

Langerhans cell histiocytosis, formerly called histiocytosis X, comprises a group of conditions that are characterized histologically by a monoclonal proliferation of large mononuclear cells accompanied by a prominent eosinophilic infiltrate. The mononuclear cells have been identified as Langerhans cells. Historically, the clinical spectrum of Langerhans cell histiocytosis includes

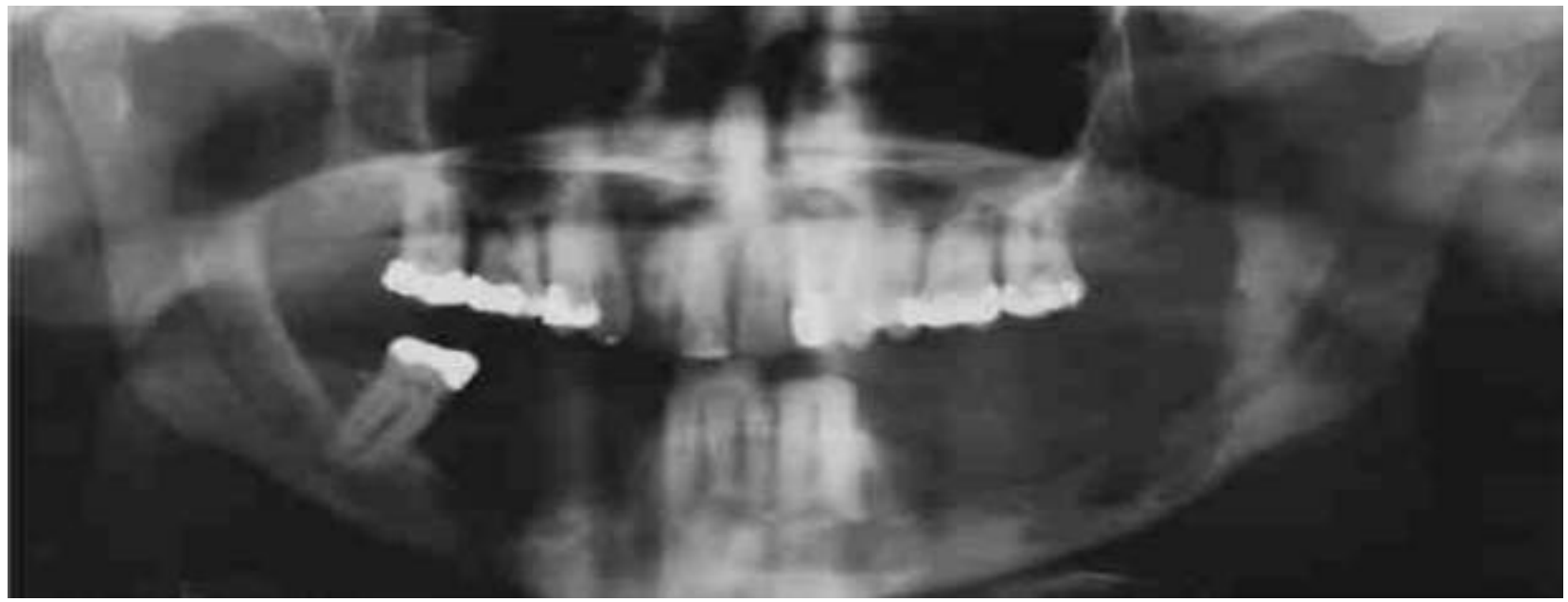
(1) single or multiple bone lesions with no visceral involvement (eosinophilic granuloma).

(2) a chronic disseminated form that includes the classic Hand–Schüller–Christian triad of skull lesions, exophthalmos, and diabetes insipidus.

(3) an acute disseminated form (Letterer–Siwe disease) that affects multiple organs and has a poor prognosis.

Clinical, Radiographic, and Histologic Manifestations

Single or multiple eosinophilic granulomas with no systemic or visceral involvement are the most common presentation. Both the maxilla and the mandible may be affected in Langerhans cell histiocytosis, both with and without systemic involvement. Early lesions present radiographically as well-defined, noncorticated radiolucencies. With time, the lesions enlarge and coalesce with one another, resulting in more bone destruction . Involvement of the alveolar process may mimic periodontal disease, but Langerhans cell histiocytosis starts at the mid-root level. The gingival soft tissues may also be involved, and this may resemble periapical or periodontal inflammatory disease.



Langerhans cell histiocytosis

Management

The treatment varies, based on the clinical presentation of the disease. Solitary eosinophilic granuloma may be treated by surgical curettage. Low-dose radiation therapy has been used successfully for lesions that are multiple, less accessible, or persistent. The older the patient with Langerhans cell histiocytosis and the less visceral involvement, the better the prognosis. Langerhans cell histiocytosis is a life-threatening disease in infants and very young children.

5-Giant cell lesions of bone

Giant cell lesions include the peripheral giant cell granuloma and the central giant cell granuloma, aneurysmal bone cyst, and cherubism . These conditions are all non-neoplastic lesions that are characterized by a similar histologic appearance. Common to all of them is the presence of numerous multinucleated giant cells in a background of mesenchymal cells that contain round to ovoid nuclei. Extravagated red blood cells and hemosiderin deposits are commonly found in these lesions, as are reactive bone trabeculae.

A-Central Giant Cell Granuloma (Central Giant Cell Lesion)

Etiology and Pathogenesis

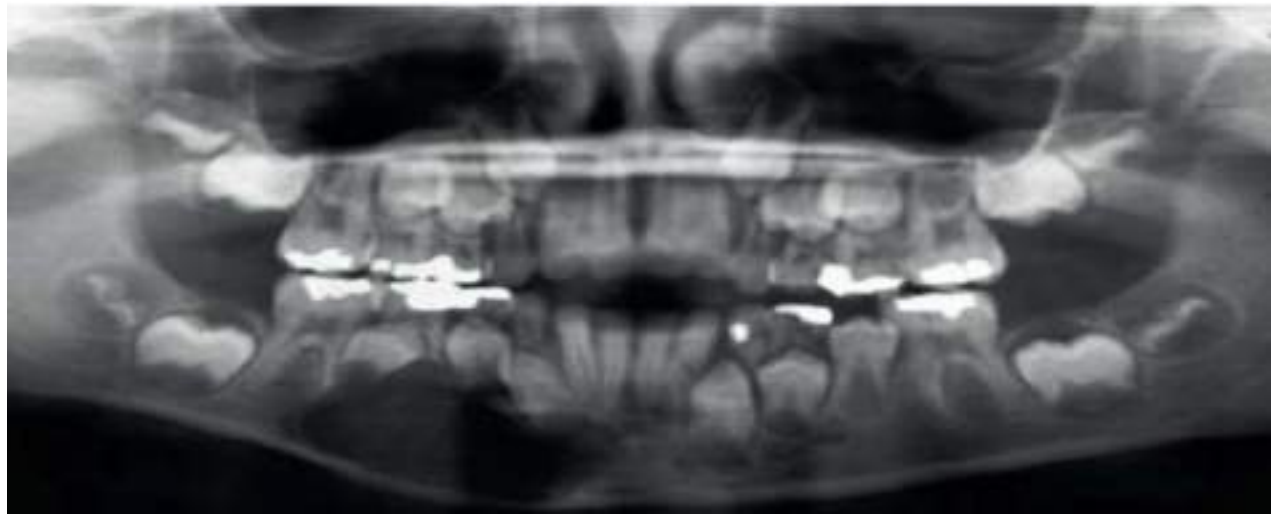
As already noted, the majority of these lesions are thought to be non-neoplastic.

Epidemiolog y

Central giant cell granuloma occurs more frequently in the mandible than the maxilla, generally anterior to the first molar, and often crossing the midline. Most central giant cell granulomas are diagnosed before age 30 years.

Clinical, Radiographic, and Histologic Manifestations

The radiographic features vary from small, well-circumscribed radiolucencies mimicking periapical inflammatory disease to large, destructive, multilocular radiolucencies . The lesions have been reported to perforate the corticle plate and extend into the soft tissue adjacent to the bone. Complaint of pain is an inconsistent feature of these lesions.



Central Giant Cell Granuloma

Laboratory Findings

The diagnosis of a central giant cell granuloma requires an evaluation for hyperparathyroidism Serum calcium, phosphorus, and alkaline phosphatase levels should be obtained prior to surgical removal of a giant cell granuloma, and if abnormal, parathyroid hormone (PTH) levels should be assessed. **Management** Treatment usually involves conservative curettage. Other treatment modalities include systemic calcitonin, Intralesional injections of corticosteroids, and denosumab.

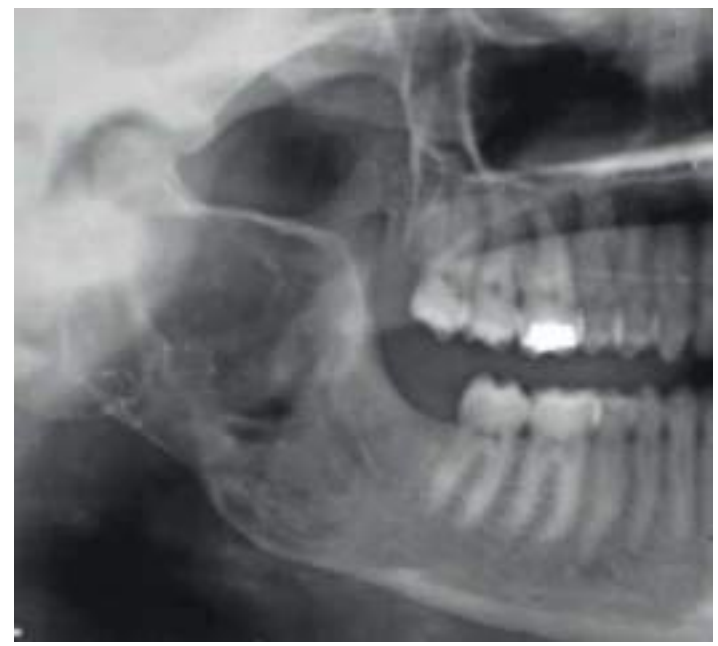
B-Aneurysmal Bone Cyst

Etiology and Pathogenesis The term aneurysmal bone cyst is a misnomer, since this lesion is not a true cyst and exhibits no epithelial lining. It does contain varying-sized blood-filled spaces.

Clinical, Radiographic, and Histologic Manifestations The clinical signs and symptoms are nonspecific. Pain has been reported and enlargement of the involved bone is common. The radiographic appearance varies from unilocular to multilocular.

Management Treatment depends on the size of the lesions and includes curettage, enucleation, and resection. Recurrence is attributed to incomplete removal.

aneurysmal bone cyst



C-

Etiology and Pathogenesis

Cherubism is inherited as an autosomal dominant trait with a penetrance of nearly 100% in males and 50–75% in females.

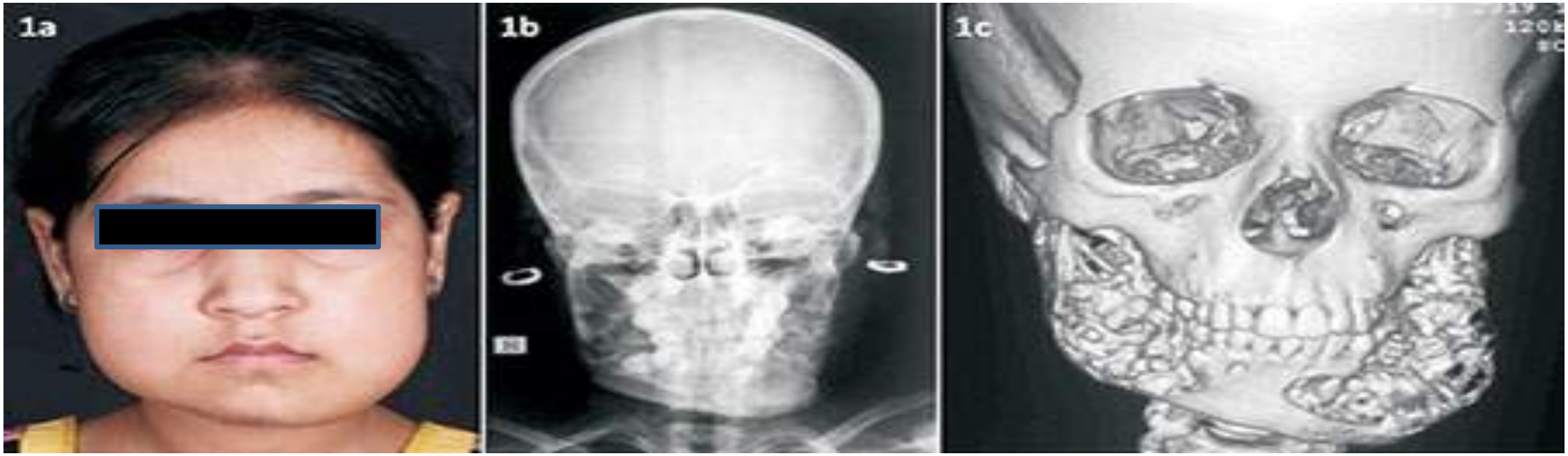
Epidemiology Cherubism is a rare disease that usually presents in early childhood.

Clinical, Radiographic, and Histologic

Manifestations characterized by bilateral painless swellings (mandible and maxilla) that cause fullness of the cheeks; firm, protuberant, intraoral, alveolar masses; and missing or displaced teeth. Submandibular lymphadenopathy is an early and constant feature that tends to subside after the age of 5 years and usually has regressed by the age of 12 years. Maxillary involvement can often produce a slightly upward turning of the child's eyes, revealing an abnormal amount of sclera beneath them. It was the upward "looking toward heaven" cast of the eyes combined with the characteristic facial chubbiness of these children that prompted the term cherubism.

The clinical appearance may vary from barely discernible posterior swellings of a single jaw to significant deformation from anterior and posterior expansion of both jaws, with concomitant difficulties in mastication, speech, swallowing, and respiration.

Disease activity declines with advancing age. Radiographically, the lesions are multiple well-defined multilocular radiolucencies in the mandible and maxilla. They are irregular in size and usually cause marked destruction of the alveolar bone.



Cherubis
m

Laboratory Findings

Serum calcium and phosphorus are within normal limits, but serum alkaline phosphatase may be elevated.

Management

A variety of treatments have been recommended: no active treatment and regular follow-up, extraction of teeth in the involved areas, surgical contouring of expanded lesions, or complete curettage.

6-Paget’s disease of bone(Osteitis deformans)

Etiology and Pathogenesis

The etiology of Paget’s disease is not well understood. The possibility of an infective viral etiology is suggested by the ultrastructural demonstration of intranuclear inclusions in the abnormal osteoclasts, both in Paget’s disease and in the cells of Paget’s disease–associated osteosarcoma.

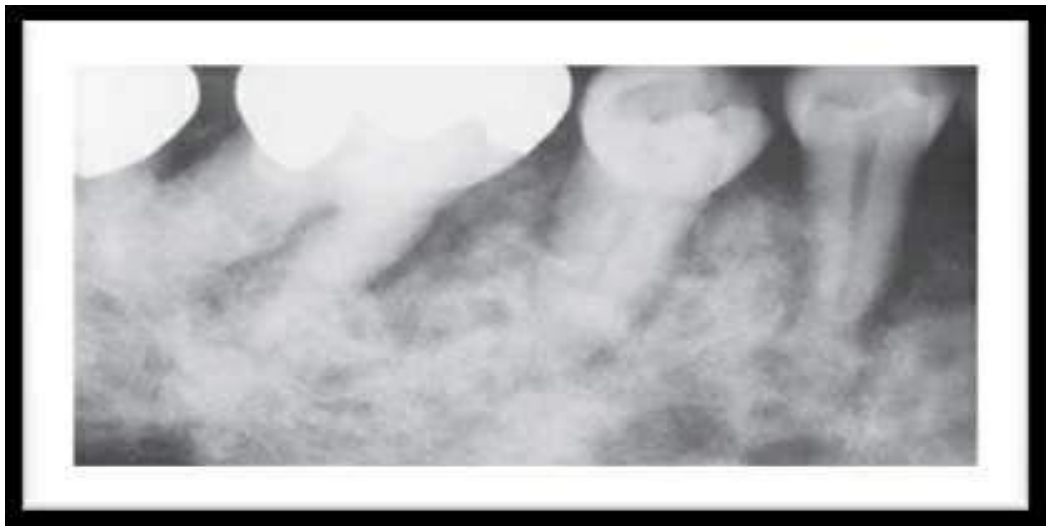
In recent years, genetic mutations affecting osteoclastogenesis, have been found in some cases of Paget's disease of bone.

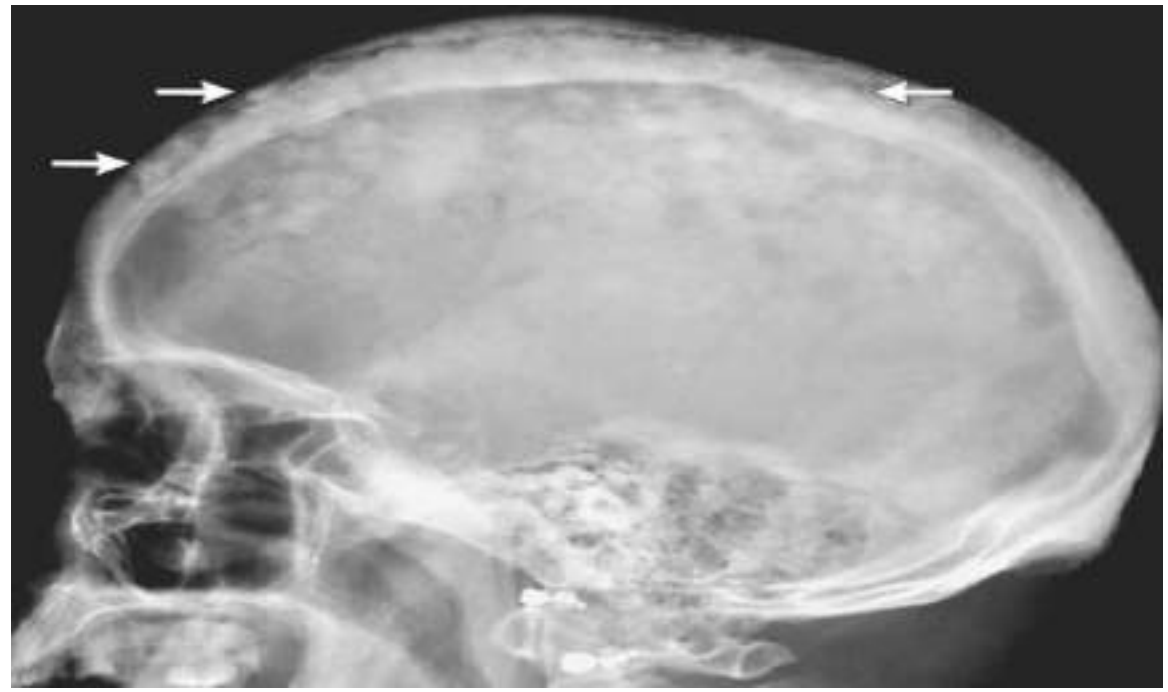
It has been reported that close to 30% of patients with Paget's disease have a first-degree relative who has also been affected. This supports the case that both genetic and environmental factors may be playing a role in the disease. About 40% of familial cases have been found to have a mutation of the SQSTM1 gene.

Clinical, Radiographic, and Histologic Manifestations

Paget's disease of bone is a chronic disease of the adult skeleton characterized by focal areas of excessive bone resorption followed by bone formation. Histologically, the involved bone demonstrates prominent reversal lines that result from the resorption and deposition of bone. There is also replacement of the normal bone marrow by vascular fibrous connective tissue.

Although some patients with Paget's disease have no symptoms, many experience considerable pain and deformity. The narrowing of skull foramina can cause ill- defined neuralgic pains, severe headache, dizziness, and deafness. The bony lesions of Paget's disease produce characteristic deformities of the skull, jaw, back, pelvis, and legs that are readily recognized both clinicall and radiographically. Enlargement of the affected bone is common. Irregular overgrowth of the maxilla may lead to the facial appearance described as "leontiasis ossea," and edentulous patients may complain that their dentures no longer fit. Radiographically, there are patchy radiolucent and radiopaque changes that have been described as a "cotton wool" appearance. Other radiographic findings of the jaw bones include loss of the lamina dura, root resorption, and hypercementosis.





cotton wool appearance of Paget’s disease

Laboratory Findings

Urinary levels of calcium and hydroxyproline (a measure of collagen metabolism) and serum alkaline phosphatase levels (a measure of osteoblastic activity) are useful for diagnosing Paget’s disease and for monitoring bone resorption and deposition during treatment.

Management

Craniofacial disorders, associated medical problems (e.g., cardiac failure, hypercalcemia), and the incidence of malignant transformation have encouraged the use of a variety of new treatments.These agents include

1-antibiotics (i.e., intravenous mithramycin, an effective inhibitor of osteoclastic activity).

2-hormones of human and animal origin (high- dose glucocorticoids and porcine, salmon, and human calcitonin administered subcutaneously or by nasal spray or suppository).

3-salts such as the diphosphonate etidronate (which effectively reduces bone resorption).

4- cytotoxic agents such as plicamycin and dactinomycin.

In addition to cosmetic issues, dental concerns include poor healing of dental extraction sites and excessive postsurgical bleeding from the highly vascular bone that is characteristic of this disease. Bone that exhibits unusually rapid change or enlargement suggests the possibility of malignant transformation. In view of the rarity of a giant cell tumor in the jaws except as a complication of Paget's disease, the finding of this lesion in a patient who is older than 40 years of age should raise the possibility of previously undiagnosed Paget's disease.

Neuromuscular Disorders

DEFINATION. 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. Causes 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.

Symptoms of muscle disease may include muscular weakness, rigidity, loss of muscular control, numbness, tingling, twitching, spasms, muscle pain and certain types of limb pain

Classification of neuromuscular disorders:

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

Cerebrovascular disease:-

Cerebrovascular disease includes all disorders that cause damage to the blood vessels supplying the brain, leading to impaired cerebral circulation thereby producing neurologic damage.

complete Stroke and –cerebrovascular accident (CVA) is a sudden impairment in cerebral circulation resulting in death or a focal neurologic deficit lasting more than 24 hours, are terms used to describe an acute neurologic injury resulting from a severe interruption in the flow of blood to the brain.

Complete cessation of the flow may render an irreversible cerebral infarct within a period of 3 or 4 minutes.

Neurologic events related to CVA include:

Transient ischemic attack (TIA):- defined as 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 reversible, acute, focal neurologic deficit due to transient and localized cerebral ischemia but resulting in neurologic deficits that last more than 24 hours

Symptoms of cerebrovascular disease

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 extraocular 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 according to the causes

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

1- Atherosclerosis(85%) .leading to cerebral ischemia and infarction result from ischemia due to atherosclerotic disease, thrombo embolic 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- Brain stem 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.

Thrombotic **strokes** may be preceded by one or more "mini-**strokes**," called transient ischemic attacks, or TIAs. ... Although usually mild and transient, the symptoms caused by a **TIA** are similar to those caused by a **stroke**. Another type of **stroke** that occurs in the small blood vessels in the brain is called a **lacunar infarct**

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.

Transient lschemic attack

A transient ischemic attack (TIA) is a sudden but reversible neurologic deficit that lasts from a few minutes to 24 hours. Approximately 30% of individuals with a history of TIA experience a completed stroke within a 5-year period. An important cause of transient cerebral ischemia is embolization a source is readily apparent in the heart or a major extracranial artery to the head.

Clinical manifestations

The symptoms of TIAs vary markedly among patients. Onset is abrupt and without warning, and recovery usually occurs rapidly, often within a few minutes.

During the attack, a wide variety of neurologic signs and symptoms can develop, depending on which site of the brain is affected by ischemia.

1- Repeated short periods of arm and hand weakness are associated with focal ischemia in the contralateral frontal lobe.

2- If the vertebrobasilar arterial system is involved, short episodes of dizziness, diplopia, dysarthria, facial paresthesia, and headache are common symptoms.

Treatment of TIA

Treatment of TIAs should be initiated as soon as the diagnosis is established and should be directed towards the:-

1- Correction of the immediate pathologic problem (e.g.,embolism).

2- Measures to control the primary underlying problem (e.g., hypertension or coagulopathy).

3- Anticoagulant therapy with either heparin or coumadin is often used.

4- Treatment with aspirin, however, significantly reduces the frequency of TIAs and the incidence of stroke in high-risk patients.

D.D. of CVA

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

Diagnosis

In addition to a thorough neurologic and cardiovascular examination, anatomic and functional brain imaging is central to the diagnosis of stroke. Time is of the essence for instituting treatment to manage acute stroke. Intracranial hemorrhage must be quickly excluded before life-saving thrombolytic therapy can begin. Although brain magnetic resonance imaging (MRI) provides greater anatomic detail and sensitivity for detection of early infarction, non contrast computed tomography (CT) scan is the first line of imaging.

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.

However, in the hospital, a series of blood tests to learn the cause of the stroke symptoms:

- Complete blood count (CBC)
- Serum electrolytes.
- Blood clotting tests.

- Heart attack tests.
- Thyroid tests. .
- Blood glucose. .
- Cholesterol tests. .
- C-reactive protein test and blood protein test

Treatment in general:-

The outcome of stroke and related TIAs 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).

Management of acute stroke includes medical therapy to reduce bleeding or thromboembolic occlusion, medical therapy to reduce brain edema and neurotoxicity/nerve injury, and surgical interventions (revascularization, hemorrhage control).

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 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.

The dentist should know that the risk increases of second stroke, during the first 90 days. Therefore optimal medical monitoring for the patients is necessary especially

in invasive dental treatment, with appropriate consideration for stress reduction, medication interactions and adverse effects, neurologic deficit management, also control of underlying cardiovascular/ cerbrovascular risk factors.

Use of antiplatelet and anticoagulant medications is common in patients with a history of stroke, TIA, and RIND. This includes oral aspirin; oral antiplatelet drugs such as subcutaneous low-molecular- weight heparin, and, less commonly, warfarin. These medications taken in therapeutic dosages, and for warfarin with an international normalized ratio ≤ 3.5, rarely require dose modification before routine dental and minor oral surgical treatment.

The dentist should know that the concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs) may increase the risk for bleeding, and their long-term use may reduce the protective effect of aspirin.

Stress reduction and confidence building for the patient during dental visits are important behavioral goals to make the patient comfortable and minimize anxiety-related elevation in blood pressure.

Pre- or perioperative inhalation- N2O-O2 or oral anxiolytic medication can aid in reducing treatment-related stress and anxiety.

Use of epinephrine-containing local anesthetics is not contraindicated, but they should be used judiciously and follow guidelines recommended for patients with cardiovascular disease; epinephrine-containing retraction cord should not be used. and blood pressure should be monitored at every visit

Important points of Oral Health Considerations:-

1. The medical management of stroke patients is often depend on anticoagulant therapy, the patient may have a predisposition to excessive bleeding. Therefore obtain current coagulation values (PT, INR ,APTT, bleeding time) is necessary for the dentist .
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.

, 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.

4. Patients with apraxia affecting the orofacial region may have impaired voluntary movements, such as protruding the tongue and expectorating during dental treatment
5. Careful history taking, checking of blood pressure prior to treatment, avoidance of lengthy appointments.

Patients taking warfarin or antiplatelet agents face an increased risk of bleeding due to dental procedures. But stopping these medications may put the patient at risk of a thrombotic event (e.g., DVT, stroke). Therefore, the risk of bleeding
must be weighed against the risk and consequences of thrombosis

Cavernous sinus thrombosis

Cavernous sinus thrombosis, usually secondary to dental, nasal, or ocular infections, is a rare but severe complication because of its possible fatal outcome.

Infections of the maxillary dentition may spread to the cavernous sinus through openings in the cranial bones or through emissary veins connecting the extra- and intra cranial systems.

Venous propagation begins with the facial vein and proceeds through the ophthalmic vein, which is an affluent of the cavernous sinus.

Signs and symptoms of cavernous sinus thrombosis

- Severe headache often accompanied by tearing
- Swelling, redness, or irritation around one or both eyes
- Drooping eyelids and inability to move the eye
- High fever
- Pain or numbness around the face or eyes
- Fatigue
- Vision loss or double vision
- Seizures
- Altered mental status that can range from confusion to coma
- seizures are rare.

In most cases, patients experience rapid swelling of the face and eyelids.

The classic neurologic signs of acute cavernous sinus thrombosis are:-

Exophthalmos, periorbital edema, retinal vein thrombosis, and involvement of the ophthalmic division of the trigeminal nerve , trochlear and abducent nerves, leading to ptosis, dilated pupils, and lack of corneal reflexes.

Cavernous sinus thrombosis is more common in people who take certain medications such as oral contraceptives or who have underlying health conditions such as uncontrolled diabetes or cancer that may increase their risk for blood clots

Treatment of cavernous sinus thrombosis:

Treatment consists of immediate antibiotic therapy and the removal of the source of infection whenever possible.

Staphylococcus aureus is the most common pathogen, identified in approximately 70% of cases and is the pathogen implicated in nearly all cases of facial infections and sphenoid sinusitis. Streptococci are cultured less commonly. Anaerobes are found occasionally, especially with sinus, dental, or tonsillar infections. Rarely, fungal infections from Aspergillus fumigatus or mucormycosis have been implicated.

Therefore, for most etiologies, empiric therapy should include:

- Vancomycin used until the actual culture results are available,plus
- A third-generation cephalosporin, such as ceftriaxone. In patients with documented true allergy to penicillin, a fluoroquinolone should be used instead.

- Intravenous metronidazole should be added if dental or sinus infection is suspected. Antifungal therapy has been advocated only in cases of biopsy-confirmed invasive fungal infection. However, in at-risk patients, antifungal treatment should be considered by the dentist as fungi may cause devastating neurological complications beyond cerebral venous thrombosis.

High doses of intravenous antibiotics are required because thrombus may limit penetration of antibiotics. Bacteria, sequestered within the thrombus, may not be killed until the dural sinuses have started to recanalize.

Antibiotics also need to be administered over an extended period, for at least 2 weeks beyond the time of clinical resolution. This aims to insure complete sterilization and prevent relapses.

The dentist have to take into consideration that concurrent supportive therapy is necessary alongside antibiotic treatment, and includes resuscitation, oxygen support, and local eye care.

Multiple sclerosis (MS)

Chronic neurologic disease 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 is 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 herpes virus 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

Pathophysiology of multiple sclerosis. an inflammatory demyelinating disease of the CNS in which activated immune cells invade the central nervous system and cause inflammation, neuro degeneration, and tissue damage. The underlying cause is currently unknown

Different cells are involved in the abnormal immune response. Two important types of immune cells are T cells and B cells. T cells become activated in the lymph system and in MS, enter the CNS through blood vessels

Clinical Manifestations

The dentist have to know 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 1month.
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

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
5. include an increase in total protein and mononuclear white blood cells.

Treatment.(the medication should be taken into consideration by the dentist)

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 3years. 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 andlesions

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.

Dentist should 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 tooth brushes and oral hygiene products with larger handles may be necessary for completing oral hygiene in patients with significant motor impairment.

The dentist should 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.

NEUROMUSCULAR DISEASES (second lecture)

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 common 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 65year

Clinical Manifestations

AD is a slowly progressive disorder represented by a continuum recognizes three stages of 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

The dentist have to know that 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 neuro degeneration (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-inflammatory, 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, temporomandibular 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.

Therefore 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.
The dentist should have information about the adverse effect of the medications used to treat AD which 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

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 –mask like facial appearance with infrequent blinking and lack of expression is caused by bradykinesis.
The dentist dealing with those patient should consider that 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 .knowing theses medication is important before start the dental 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 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 exposure to a viral infection. Viruses that have been linked to Bell's palsy include the virus that causes:

- Cold sores and genital herpes (herpessimplex)
- Chickenpox and shingles (herpeszoster)
- Mononucleosis(Epstein-Barr)
- Cytomegalovirusinfections
- Respiratory illnesses(adenovirus)
- German measles(rubella)
- Mumps (mumps virus)
- Flu (influenzaB)

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 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 and speed of the conduction of electrical impulses along a nerve.

Imaging scans. Magnetic resonance 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 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

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

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

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.
The dentist have to know that 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 andcortex.
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.

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 .all of the below medication have adverse effect on the dental treatment

- Antiepileptic drugs (AEDs)

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

- 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

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.

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

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
Dentist 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 oral ulceration .

Oral Medicine

SALIVARY GLAND DISEASES

The most common presenting complaints of a patient with salivary gland disease are oral dryness (xerostomia) or a glandular swelling or mass.

There are Major and Minor groups of Salivary Glands:

The Major groups of salivary glands which are consisting of three major glands, the parotid, submandular and sublingual glands. The parotid and submandular glands each drain into the mouth in a single long duct. The sublingual glands drain via many small ducts.

The major salivary glands can also be classified based on the dominant saliva- producing acinar cell type: serous, mucous, or a mix of serous and mucous cells. Serous cells produce a more watery, enzyme-rich saliva. Mucous cells secrete a more viscous fluid with plentiful salivary glycoproteins known as mucins.

The parotid gland is composed primarily of serous cells. submandibular gland are a mix of mucous and serous types ,while the sublingual and minor salivary glands are of the mucous type.

There are also between 600 and 1000 minor salivary glands named for the sites which they occupy (i.e., labial, buccal, lingual, palatal, retromolar).

In addition, there are three sets of minor salivary glands of the tongue:

1- the glands of Weber, found along the border of the lateral tongue 2- the glands of von Ebner, surrounding the circumvallate papillae

3- the glands of Blandin and Nuhn, also known as the anterior lingual glands, found in the anterior ventral tongue.

Parotid saliva is secreted through Stensen's ducts, the orifices of which are visible on the buccal mucosa in the vicinity of the maxillary first or second molar.

Submandibular gland saliva is secreted through the submandibular duct (Wharton's duct), which drains saliva from each submandibular gland and exits at the sublingual caruncles on either side of the lingual frenulum .

The sublingual glands are drained by 8-20 excretory ducts called the ducts of Rivinus. The largest of all, the sublingual duct (of Bartholin) joins the submandibular duct to drain through the sublingual caruncle. The sublingual caruncle is a small papilla near the midline of the floor of the mouth on each side of the lingual frenum. Most of the remaining small sublingual ducts open separately into the mouth on an elevated crest of mucous membrane

.

. Both sublingual glands unite anteriorly and form a single mass through a horseshoe configuration around the **lingual frenulum**. The superior aspect of this U-shape forms an elevated, elongate crest of mucous membrane called the **sublingual fold** (plica sublingualis). Each sublingual fold extends from a posterolateral position and traverses anteriorly to join the **sublingual papillae** at the midline bilateral to the lingual frenulum.

Whole saliva (WS; the mixed fluid contents of the oral cavity) is a hypotonic fluid relative to blood plasma and is composed of secretions from the major and minor salivary glands.

Saliva composed of greater than 99% water and less than 1% proteins and salts. WS may also contain variable amounts of gingival crevicular fluid, microorganisms, food debris, exfoliated mucosal cells, and mucus.

The most common presentation of salivary gland disease is xerostomia which is a subjective complaint of dry mouth.

Hyposalivation refers to a quantified reduced salivary flow rate and may or may not be accompanied by xerostomia.

Similarly, xerostomia may or may not be associated with hyposalivation and can be a result of, for example, a change in salivary composition to a greater mucous content.

Hypersalivation (ptyalism)

Refers to an increase in production of saliva and/or a decrease in oral clearance of saliva.

Salivary gland dysfunction is commonly used to indicate decreased salivary flow or another quantifiable alteration in salivary performance

Causes of salivary gland hypofunction include:-

1- Medications :xerogenic medications (including many antidepressants, Anticholinergics, antispasmodics, antihistamines, antihypertensives, sedatives, diuretics, and bronchodilators)

2- Other agents (e.g., caffeine, alcohol, cigarette smoking) irradiation to the head and neck (i.e., external and internal beam radiation therapy)

3- Systemic disease (e.g., diabetes mellitus)

4- Psychological conditions (e.g., depression)

5- Malnutrition (e.g., bulimia, dehydration)

6- Autoimmune disease (e.g., SS)

7- Other unspecified or undiagnosed conditions. (Anxiety)

List of Differential Diagnosis for Salivary Gland Hypofunction

- Autoimmune:- Chronic graft-versus-host disease ,Sjogren's syndrome Developmental :- Salivary gland aplasia Iatrogenic:
- External beam radiation, Internal beam radiation
- Postsurgical :- (adenectomy, ductal ligation),
- Botox injection Inflammatory:
- IgG4-related disease (Mikulicz's disease)
- Infectious:- Viral: CMV, HIV, hepatitis C
- Granulomatous: Tuberculosis Medication-
- Neoplastic :- Benign and malignant salivary gland tumors Nonneoplastic :- Sialolithiasis
- Systemic :- Anorexia nervosa, diabetes mellitus
- chronic alcoholism, sarcoidosis

Symptoms of Salivary Gland Dysfunction

Symptoms of salivary gland hypo function are related to

1- Decreased fluid in the oral cavity and this may have an effect on mucosal hydration and oral functions.

2- Patients may complain of dryness of all the oral mucosal surfaces, including the lips and throat, and difficulty chewing, swallowing, and speaking.

3- Other associated complaints may include oral pain, an oral burning sensation, chronic sore throat ,pain with swallowing.

4- The mucosa may be sensitive to spicy or coarse foods, limiting the patient's enjoyment of meals, which may compromise nutrition.

5- The need to sip liquids to swallow food, or difficulties in swallowing dry food have all been highly correlated with measurable decreases in secretory capacity.

Past and Present Medical History for the patient with salivary gland disorder

Over 400 drugs are reported to have dry mouth as a side effect, ex.individual that has recently started taking a tricyclic antidepressant.

If the past and present medical history reveals medical conditions like a patient who has received radiotherapy for a head and the neck malignancy.

A patient's report of eye, throat, nasal, skin, or a vaginal dryness, in addition to xerostomia, may be a significant indication of a systemic condition, such as Sjogren's syndrome.

Clinical Examination

Extra and intra oral examination: -

1- Signs of mucosal dryness:- Candidiasis, Enlargement of salivary gland. Viscous or scant secretions.

2- Enlargement can be associated with a variety of inflammatory, infectious, or neoplastic and other conditions

3- A cloudy exudates may be a sing of bacterial infection. The exudates should be cultured if it does not appear clear, particularly in the case of an enlarged gland.

4- Function of the facial nerve when evaluating parotid tumors.

5- Tumors of the minor salivary glands are usually smooth masses located on the hard or soft palate.

6- Ulceration of the overlying mucosa should raise suspicion of malignancy.

The parotid glands

The largest of the salivary glands, are positioned on the lateral aspect of the face overlying the posterior surface of the mandible, anteroinferiorly to the auricle.

A superficial and deep lobe based on the course of the facial nerve as it traverses the gland. Most benign tumors of the parotid gland are located within the superficial lobe and therefore are amenable to resection by superficial parotidectomy.

Because of its relationship to the parotid gland, it is important to document function of the facial nerve when evaluating parotid masses. Facial nerve paralysis is usually indicative of malignancy. Rarely, infection or rapidly growing benign tumors may cause facial nerve paralysis.

Other findings suggesting malignancy include

- Hardness.
- Fixation.
- Tenderness.
- Infiltration of surrounding structures - eg, facial nerve, local lymph nodes.
- Overlying skin ulceration.
- Cranial nerve palsy

Bilateral parotid gland masses are usually due to:-

- lymphadenopathy
- Warthin's tumors
- lymphoepithelial cysts (L ECs)
- enlarged lymph nodes in the setting of HIV
- SS
- rarely other salivary gland tumors such as the acinic cell adenocarcinoma.

Multiple painless masses within a single parotid gland may be due to:-

- Warthin's tumors
- lymph nodes
- metastatic disease

other benign and malignant tumors.

Tumors in the submandibular or sublingual glands usually present as painless, solitary, slow-growing mobile masses. Bimanual palpation, with one hand intraorally on the floor of the mouth and the other extraorally below the mandible, is necessary to evaluate the glands adequately.

Tumors of the minor salivary glands are usually smooth masses located most commonly on the hard or soft palate but may present anywhere minor salivary glands are present.

Salivary gland neoplasms arise most commonly in the parotid glands followed by the submandibular, sublingual, and minor salivary glands. The relative proportion of malignant

neoplasms is greater the smaller the gland: that is, a neoplasm in the parotid gland is more likely to be benign than one arising in a minor salivary gland imaging

methods of diagnosis

Radiography

lateral oblique and anteroposterior (AP) projections are used to visualize the parotid glands. A standard occlusal film can be placed intraorally adjacent to the parotid duct to visualize a stone close to the gland orifice.

It is useful particularly for the visualization of radiopaque sialoliths and the evaluation of bony destruction associated with malignant neoplasms and it can provide a background for interpretation of the sialogram.

Sialography:- The radiographic visualization of the parotid and submandibular salivary glands and ducts following retrograde instillation of soluble contrast material into the Stensen's or Wharton's ducts .

The ducts of the sublingual glands are too small for reliable injection of contrast medium. It provides the clearest visualization of the branching ducts and acinar end pieces.

It is the recommended method for evaluating intrinsic and acquired abnormalities of the ductal system:-

1- ductal stricture, 2- obstruction, 3- dilatation, 4- ruptures

5- for identifying and localizing sialoliths

The two contraindications to sialography are:-

1- Active infection

2- Allergy to contrast media

Oil-and water-based contrast media are available. (both containing iodine and therefore contraindicated in patients with iodine sensitivity) are available Radiographic views for sialography include panoramic, lateral oblique, AP.

Following the sialographic procedure, the patient should be instructed to massage the gland and/or to suck on lemon drops to promote the flow of saliva and contrast material out of the gland.

After approximately one hour. If a substantial amount of contrast material remains in the salivary gland, follow-up visits should be scheduled until the contrast material elutes or is fully resorbed.

Incomplete clearing can be due to:-

1. obstruction of salivary outflow

2. extraductal or extravasated contrast medium

3. collection of contrast material in abscess cavities

4. impaired secretory function

Sialography performed during active infection may lead to :

1- further irritate and potentially rupture the already inflamed gland.

2- the injection of contrast material might force bacteria throughout the ductal structure and worsen an infection.

The dentist should take into consideration that the iodine in the contrast media may induce an allergic reaction and can also interfere with thyroid function tests and with thyroid cancer evaluation by nuclear medicine (if these are done)

ULTRASONOGRAPHY (US)

Advantages,

1- initial evaluation of the salivary glands, especially in children and pregnant women

2- Evaluating for suspected sialolithiasis and salivary gland abscesses.

3- differentiating between intra-and extraglandular masses

4- used to distinguish focal from diffuse disease

5- assess adjacent vascular structures and vascularity

6- distinguish solid from cystic lesions,

7- guide fine needle aspiration biopsy (FNAB)

8- perform nodal staging

9- can correctly differentiate malignant lesions from benign in most of the cases Radionuclide Salivary Imaging

Scintigraphy with technetium (Tc) 99m pertechnetate is a dynamic and minimally invasive diagnostic test to assess salivary gland function and to determine abnormalities in gland up take and excretion.

Following intravenous injection,it will take up by the salivary gland transported through the glands, and then secreted into the oral cavity.

Only the parotid and submandibular glands are visualized distinctly, as well as the thyroid gland. It has been used to aid in the diagnosis of:-

1- ductal obstruction, 2- sialolithiasis, 3- gland aplasia,4- Bell's palsy, 5- sjogren's

syndrome.

computed tomography (CT)

The method of choice in patients suspicious for inflammatory disease (abscess, calculi, major salivary duct dilatation, and acute inflammation) or in patients with contraindication for MR imaging

- Superior to plain radiographs and US in detection of sialolithiasis
- Allows detection and assessment of extent of salivary gland tumors
- Helpful in the differential diagnosis of salivary gland tumors
- Helpful in assessment of deep lobe of parotid gland and the minor salivary glands
- Calcifications (pre-contrast) and enhancement pattern (post-contrast)
- Malignant tumor may mimic a benign tumor on CT scan
- Moderate accuracy (60-70%) in predicting the histological diagnosis of a lesion

CT provides definition of cystic walls, making it possible to distinguish fluid-filled masses from abscess.

For visualizing masses that are poorly defined on MRI.

For patients who are unable to lie still long enough for adequate MRI (pediatric, geriatric, claustrophobic, and mentally or physically challenged patients).

For patients for whom MRI is contraindicated.

The disadvantage of CT include:-

Radiation exposure , administration of iodine-containing contrast media for enhancement, and potential scatter from dental restoration.

Magnetic resonance imaging (MRI)

Provides images for evaluation salivary gland pathology, adjacent structure, and proximity to the facial nerve

- Non-invasive alternative to conventional/digital sialography
- Allows accurate assessment of salivary gland calculi and stenoses

Advantages

- Non-invasive
- No exposure to ionising radiation
- Does not require use of contrast material

The things that to be considered in this way

- False negative readings may occur in patients with very small calculi that are causing no ductal dilatation

- Inability to distinguish solid calculi from inspissated mucus and/or debris
- Distortion artefacts caused by dental amalgam may impair visualisation of calculi or
- stenoses near the main ductal orifice

Disadvantages

Expensive

Limited availability.

MRI is contraindicated for:

1. Patients with pacemakers or implants such as aneurismal bone clips. If the implant contains magnetic metal, an MRI can not be performed; however, dental implants are not magnetic and so are not contraindicated.

2. Patients who have difficulty maintaining a still position.

3. Patients with claustrophobia.

Cone Beam CT

Cone beam CT (CBCT) is increasingly being employed in dentomaxillo facial imaging since it provides high spatial resolution of osseous structures at a lower dose of radiation than conventional CT.

Using a cone-shaped x-ray beam and two-dimensional detectors, the CBCT scanner collects volume data by means of a single rotation taking 9-40 seconds

CBCT sialography provides several advantages over conventional sialography including:-

1- Three-dimensional reconstruction 2- allowing for manipulation of image rotation

3- Slice thickness 4- generation of various cross-sectional slices.

Overall, CBCT sialography appears to offer an improvement in imaging of salivary gland ductal system over conventional sialography.

Salivary gland biopsy

The labial minor salivary glands are most commonly biopsied since they provide the most accessible source of tissue, especially where SS is suspected .

SEROLOGIC EVALUATION

No single definitive laboratory test for the diagnosis of Sjogren Syndrome, a combination of abnormal test results is frequently observed:

Elevated erythrocyte sedimentation rate (ESR), mild normocytic anemia, leukopenia. **9**

Autoantibodies are present in the majority of SS cases:-

Elevated immunoglobulins (particularly IgG), : rheumatoid factor (RF), antinuclear antibodies (ANAs), and anti-SSA/Ro and anti-SSB/La are strongly indicative of SS.

The most proposed classification criteria for SS by the American College of Rheumatology (ACR) requires at least two of three criteria for case definition; one of which is a positive serum anti-SSA/Ro and/or anti-SSB/La or positive RF and ANA.

Disorder of the salivary gland

Developmental Abnormalities

- Complete absence (aplasia or agenesis) of salivary gland which is rare, although it

may occur together with other developmental defects

- Accessory ducts are common and do not require treatment

- Aberrant salivary glands are salivary tissues that develop at unusual anatomic sites.

Ectopic salivary glands have been reported in a variety of locations, including the

middle-ear, external auditory canal, neck, posterior mandible, anterior mandible, pituitary gland, and cerebellopontine angle. These are usually incidental findings and do not require intervention.

- The Stafne bone defect (SBD; also known as Stafne bone cyst):- is an asymptomatic depression of the lingual surface of the mandible often associated with ectopic salivary gland tissue. However, it is not a true cyst as there is no epithelial lining. The most common location of the SBD is in the region of the third molar inferior to the mandibular canal

- Diverticula

By definition, a diverticulum is a pouch or sac protruding from the wall of a duct. Diverticula in the ducts of the major salivary glands often lead to pooling of saliva and recurrent sialadenitis. Diagnosis by sialography. Patients with diverticula are encouraged to regularly milk the involved salivary gland and to promote salivary flow through the duct.

- Darier's Disease

Salivary duct abnormalities have been reported in Darier's disease (also known as dyskeratosis follicularis). Sialography of parotid glands in this condition revealed duct dilation, with periodic stricture affecting the main ducts. Symptoms of occasional obstructive sialadenitis have been reported.

Sialolithiasis (Salivary Stones)

Sialoliths (also termed salivary calculi or salivary stones) are typically calcified organic masses that form within the secretory system of the major salivary glands.

The etiologic factors favoring salivary stone formation may be classified into two groups:

1. Factors favoring saliva retention:

Irregularities in the duct system local inflammation dehydration ,Medications such as anticholinergics and diuretics

2.saliva composition .Calcium saturation

.Deficit of crystallization inhibitors such as phytate

.Bacterial infection also promotes sialolith formation due to an associated increase in salivary .pH favoring calcium phosphate supersaturation.

Although no causal relationship between tobacco smoking and an increased risk of sialolithiasis has been definitively shown, smoking is known to adversely affect the cytotoxic activity of saliva and salivary amylase.

Salivary stones occur most commonly in the submandibular glands (80%-90%), followed by the parotid (5%-15%) and sublingual (2%-5%) and only very rarely occur in the minor salivary glands.

The higher rate of sialolith formation in the submandibular gland is due to:

(1) the torturous course of Wharton's duct,

(2) the higher calcium and phosphate levels of the secretion contained within

(3) the dependent position of the submandibular glands that leaves them prone to stasis

(4) the increased mucoid nature of the secretion.

(5) since the submandibular and parotid glands' secretion is dependent on nervous stimulation, when there is an absence of stimulation, secretory inactivity increases the risk of stone development.

Clinical Presentation

Patients with sialoliths most commonly present with a history of acute, colicky pain and intermittent swelling of the affected major salivary gland during meals. The degree of symptoms is dependent on the extent of salivary duct obstruction and the presence of secondary infection.

Salivary gland swelling will be evident upon eating since the stone completely or partially blocks the flow of saliva resulting in salivary pooling within the gland ductal system.

Since the glands are encapsulated and there is little space for expansion, enlargement causes pain. Swelling will subside when salivary stimulation ceases and output decreases.

Stasis of saliva may lead to infection, fibrosis, and gland atrophy. If there is concurrent infection, there may be expressible suppurative or nonsuppurative drainage and erythema or warmth in the overlying skin.

Complications from sialoliths include:-

- Acute sialadenitis ductal - stricture ductal - dilatation Fistula and a sinus tract
- Ulceration in the tissue covering the stone in chronic cases.

Diagnosis

Plain film radiographs are helpful to visualize sialoliths; they, readily available, and result in minimal radiation exposure. Since small and poorly calcified stones may Not been readily identifiable, this modality is most useful in cases of suspected submandibular sialolithiasis, where an occlusal radiograph taken at 90° from the floor of the mouth is recommended. However, other calcified entities such as phleboliths (stones that lie within a blood vessel), calcified cervical lymphadenopathy, and arterial atherosclerosis of the lingual artery can also appear on these films.

Stones in the parotid gland can be more difficult to visualize for several reasons. Due to the Superimposition of other anatomic structures, sialoliths may be obscured and therefore the choice of radiographic views is important. An AP view of the face or an occlusal film placed intraorally adjacent to the duct may be useful in these cases.

Contrast sialography using iodinated contrast media may be used to visualize the parotid and submandibular ductal systems.

Sialography can also aid in differentiating calcified phleboliths from sialoliths since the former lie within a blood vessel, where as the latter occur within the ductal structure

Limitations of this modality include the use of ionizing radiation, dependence on successful ductal cannulation, pain during and after the procedure, and potential allergy to the contrast medium. The use of contrast sialography is also contraindicated in the presence of acute sialadenitis.

Ultrasound (US) is widely used as a first-line imaging modality to assess the presence of salivary gland calculi. Transoral sonography using an intraoral approach has been employed as an imaging modality in suspected sialolithiasis. US is noninvasive, less costly than other imaging, and may be able to visualize radiolucent calculi.

Treatment

During the acute phase of sialolithiasis, therapy is primarily supportive.

- Standard treatment during this phase often involves the use of analgesics, hydration, antibiotics, and antipyretics, as necessary.

- Use Sialogogues(a drug or substance that increases the flow rate of saliva e.g. chewing gum, pilocarpine, and cevimeline) ,
- massage and heat applied to the affected area may also be beneficial. Stones at or near the orifice of the duct can often be removed transorally by milking the gland
- deeper stones require intervention with conventional surgery or sialendoscopy placed to maintain patency of the duct.
- Extracorporeal shock wave lithotripsy (ESWL) also allows for fragmentation of large sialoliths of any size or location.

Extravasation and Retention Mucoceles

Mucocele is a clinical term that describes swelling caused by the accumulation of saliva at the site of a traumatized or obstructed minor salivary gland duct. Mucoceles can be classified histologically as extravasation types or retention types, the extravasation mucocele does not have an epithelial lining or a distinct border. The formation of an extravasation mucocele is believed to be the result of trauma to a minor salivary gland excretory duct. L aceration of the duct results in pooling of saliva in the adjacent submucosal tissue and consequent swelling.

The retention type mucocele is caused by obstruction of a minor salivary gland duct often by sialolith, periductal scaring, or tumor. The blockage of salivary flow results in the accumulation of saliva and dilation of the duct.

Clinical Presentation

Mucoceles often present as discrete, painless, smooth-surfaced swellings that can range from a few millimeters to a few centimeters in diameter. Superficial lesions frequently have a characteristic blue hue. While deeper lesions can be more diffuse, covered by normal-appearing mucosa without the distinctive blue color.

The lesions vary in size over time; superficial mucoceles are frequently traumatized, causing them to drain and deflate. Mucoceles that continue to be traumatized are most likely to recur and may develop surface ulceration.

Although the development of a bluish lesion after trauma is highly suggestive of a mucocele, other lesions (including salivary gland neoplasms, soft tissue neoplasms, vascular malformations, and vesiculobullous diseases) should be considered in the differential diagnosis.

Extravasation mucoceles most frequently occur on the lower lip, where trauma is common. The buccal mucosa, tongue, floor of the mouth, and retromolar region are other commonly traumatized areas where mucous extravasation may be found. These types of mucoceles are most commonly seen in children and teenagers.

Treatment

Conventional definitive surgical treatment of mucoceles involves removal of the entire lesion along with the feeder salivary glands and duct. Incomplete removal of the mucocele may result in recurrence.

Surgical management can be challenging since it can cause trauma to adjacent minor salivary glands and lead to the development of a new mucocele.

Alternative treatments that have been explored with varying degrees of success include electrosurgery, cryosurgery using liquid nitrogen, laser surgery and micromarsupialization, intralesional injections of corticosteroids, and sclerotherapy.

Ranula

A form of mucocele located in the floor of the mouth is known as a *ranula* .Ranulas are believed to arise from the sublingual gland Possible causes include:-

1- Mechanical trauma to its ducts of Rivinus, resulting in extravasation of saliva.

2- An obstructed salivary duct or a ductal aneurysm.

The predilection of ranulas in the sublingual glands has been thought to be due to the gland's continuous salivary secretion that precludes effective sealing of the mucous extravasation via fibrosis, in contrast to salivary secretion in the parotid and submandibular glands, which is dependent on gustatory stimulation. Ranulas are most common in the second decade of life and in females.

Oral ranula remains confined to the sublingual space. A congenital predisposition toward development of ranulas has been suggested,. In addition, particular anatomic variations of the ductal system of the sublingual gland may contribute to the formation of ranulas.

Clinical Presentation

The most common presentation of the "oral" ranula is a painless, slow-growing, fluctuant, movable mass located in the floor of the mouth . Usually, the lesion forms to one side of the lingual frenulum; however, if the lesion extends deep into the soft tissue, it can cross the midline.

As observed with mucoceles, superficial ranulas can have a typical bluish hue, but when the lesion is deeply seated, the overlying mucosa may have a normal appearance. The size of the lesions can vary, and larger lesions can cause deviation of the tongue.

Diagnosis

Imaging to diagnose an oral ranula may not be necessary due to its characteristic clinical appearance, but to rule out other cystic lesions (e.g., thyroglossal duct cyst, epidermoid cyst,

cystic hygroma), FNA, ultrasound, CT with contrast, and MRI have been used. Ultrasound has been recommended for oral ranulas.

Treatment

The most predictable method of eradicating both oral and plunging ranulas is to remove the associated sublingual gland because this will almost certainly eliminate recurrences.

Sublingual gland adenectomy combined with intraoral excision of the ranula is suggested for the simple ranula, other procedures used for the treatment of ranulas have included simple excision, marsupialization,

Injection of the sclerosing agent, silver nitrate, and botulinum toxin (BoNT) all with varying rates of success.

Postsurgical complications include:-lesion recurrence, sensory deficits of the tongue, and damage to Wharton's duct.

Frequency of recurrence is related to the surgical technique selected and has been reported as 67% with marsupialization, 58% with excision alone, and 1% with sublingual gland Excision.

Oral medicine

The second lecture of the salivary gland

prof dr fawaz aswad

Necrotizing Sialometaplasia (NS)

Description and Etiology

Necrotizing sialometaplasia (NS) is a benign, self-limiting, reactive inflammatory disorder of salivary tissue. NS can resemble a malignancy and its misdiagnosis has resulted in unnecessary radical surgery.

The etiology is unknown, although it likely represents a local ischemic event, infectious process, or perhaps an immune response to an unknown allergen. Development of NS has been associated with smoking, local injury, blunt force trauma, denture wear, and surgical procedures. It has been reported in pregnant patients and those with diabetes mellitus, sickle-cell disease, cocaine abuse, bulimia, and chronic vomiting. The incidence of NS appears to be higher in male patients and especially in those older than 40 years

Clinical Presentation

Necrotizing sialometaplasia (NS) has a spectrum of clinical presentations. Most commonly it presents as a painful, rapidly progressing swelling of the hard palate with central ulceration and peripheral erythema. The associated pain is often described as sharp in character and may

precede mucosal changes. Numbness or anesthesia in the associated area may be an early finding. The lesions are of rapid onset and range in size from 1 to 3 cm. Lesions occur predominantly on the palate; however, lesions can occur anywhere salivary gland tissue resides, including the lips, retromolar , buccal mucosa, tongue, nasal cavity, and maxillary sinus. Although the lesions are usually unilateral, bilateral cases have been reported. Lesion affecting the hard palate clinically resemble salivary gland malignancies particularly mucoepidermoid carcinoma and adenoid cystic carcinoma.

Rapid onset of NS may be a distinguishing feature. Lesions often occur shortly after an inciting event to the area such as oral surgical procedures, restorative dentistry, or administration of local anesthesia, but lesions also reported to develop weeks after a dental procedure or trauma. It is also not uncommon for lesions to develop in an individual with no history of trauma or oral habit

Diagnosis

Histopathologic diagnosis ,and a complete clinical history, medical history, and ideally, clinical photos should be submitted with the specimen.

Treatment

a self-limiting condition typically resolving within 3-12 weeks. During this time, supportive and symptomatic treatment is usually adequate. Appropriate analgesics combined with use of an antiseptic mouthwash such as 0.12% chlorhexidine gluconate have been recommended.

Surgical intervention is typically not required in cases of NS; however, there are reports of resolution following debridement for particularly large lesions and those secondarily infected

with bacterial species and Candida.

Cheilitis Glandularis

Description and Etiology

Cheilitis glandularis (CG) is a chronic inflammatory disorder affecting the minor salivary glands and their ducts in which thick saliva is secreted from dilated ductal openings. (CG) is characterized by superficial ulceration, painless crusting, swelling, and induration of the lip; a mucinous exudate is apparent at the ductal openings.

Although the etiology of (CG)is still undetermined, it has been suggested that it is an autosomal dominant hereditary disease. In addition, external factors (mainly UVrays) have been implicated as the condition occurs more frequently in fair-skinned adults and albino patients appear particularly prone to this condition. Additional proposed predisposing factors include poor oral hygiene, chronic exposure to sunlight and wind, smoking, and an immunocompromised state.

Occur in middle-aged and elderly men with only a few cases reported in women and children. it is associated with a relatively high incidence of squamous cell carcinoma of the lip. Although there may be a genetic susceptibility, no definitive cause has been established..

Clinical Presentation

Presents with a secretion of thick saliva secreted from dilated ostia of swollen labial minor salivary glands. This saliva often adheres to the vermilion causing discomfort to the patient. Edema and focal ulceration may also be present.

primarily affects the lower lip, but there are reports of upper lip and even palatal involvement.

Differential diagnosis (DD) of CG includes :- multiple mucocele, chronic sialadenitis of the minor salivary glands, factitious cheilitis, orofacial granulomatosis and actinic cheilitis.

Treatment

Treatment Elimination of potential predisposing factors and the use of lip balms, emollients, and sunscreens for those with excessive exposure to the sun and wind are advised. Conservative treatment of CG may involve using topical, intralesional or systemic steroids, systemic anticholinergics, systemic antihistamines, and/or antibiotics.

Refractory cases require surgical intervention such as cryosurgery, vermillionectomy, and/or labial mucosal stripping. Several reports documented the development of squamous cell carcinoma in areas affected by CG, therefore some call CG a premalignant lesion.

External Beam Radiation-Induced Pathology Description and Etiology

External beam radiation therapy is standard treatment for head and neck cancers, and the salivary glands are often within the field of radiation. Although therapeutic dosages for cancer are typically in excess of 65 Gy, permanent salivary gland damage and symptoms of oral dryness can develop after only 24-26 Gy.

The etiopathogenesis of radiation-induced salivary gland destruction is multifactorial, including programmed cell death (apoptosis) in conjunction with production of reactive oxygen species and other cytotoxic products. Radiation-associated impaired blood flow may also contribute to the destruction of glandular acinar and ductal cells.

Clinical Presentation

Acute effects on salivary function can be recognized within a week of initiating radiotherapy, with symptoms of oral dryness and thick, viscous saliva developing by the end of the second week.

Oral mucositis is a very common consequence of treatment and can become severe enough to alter the radiation therapy regimen.

Mucositis appears as a sloughing of the oral mucosa with erythema and ulceration. The pain associated with mucositis is described as a burning.

Mucositis generally persists throughout radiotherapy, peaks at the end of the irradiation, and continues for one to three weeks after cessation of treatment.

By the end of a typical six- to seven-week course of radiotherapy, salivary gland function is nearly absent. Hypofunction remains at a steady rate postradiation, with only small increases to two years post-radiotherapy (post-RT).

This can be permanent if the major salivary glands receive more than 24-26 GY Permanent xerostomia and oral complications of salivary hypofunction impair a patient's quality of life

Signs and symptoms of radiation-associated xerostomia include a burning sensation of the tongue, Assuring of the tongue and lips, new and recurrent dental caries, difficulty in wearing oral prostheses, and increased thirst.

Additional sequelae of radiation-induced salivary dysfunction include candidiasis, microbial infections, plaque retention, Gingivitis, difficulty in speaking and tasting, dysphagia, and mucosal pain.

Internal Radiation-Induced Pathology_

Radioactive iodine (RAI) is the standard treatment in cases of papillary and follicular thyroid carcinomas following thyroidectomy or in cases of suspected or known metastases.

A significant portion of the RAI taken up by thyroid tissue is concentrated and secreted through the salivary gland tissue resulting in radiation exposure of the salivary parenchyma and possible damage. Standard doses of RAI often cause obstructive duct symptoms, while hyposalivation from Parenchymal damage is usually observed with larger or repeated doses of RAI.

Acute risks associated with RAI include ageusia, salivary gland swelling, and pain, while longterm side effects include recurrent sialadenitis with xerostomia, stomatitis, and dental caries. In some circumstances, RAI treatment may lead to glandular fibrosis and permanent salivary gland hypofunction.

Clinical Presentation

The glandular effect of RAI can be mild to severe. Patients may be asymptomatic or may complain of parotid gland swelling (usually bilaterally), pain, xerostomia, and decreased salivary gland function almost immediately after treatment.

RAI-induced salivary gland injury is irreversible; however, residual functioning salivary gland tissue is often present and responsive to therapy.

Following administration of 131 I, patients should undergo an aggressive salivary stimulation routine that includes sugar-free lozenges, sour candies, and gums to stimulate salivary flow. This will aid in clearing the 131 I from the salivary glands and potentially decrease salivary gland damage. Stimulation of salivary flow by these means, however, should not be initiated within the first 24 hours after 131 I therapy as this has been shown to potentially increase the salivary gland side effects of the RAI.

Pilocarpine and cevimeline used before and after RAI treatment may decrease transit time through the salivary glands, thereby diminishing exposure.

Allergic Sialadenitis

Enlargement of the salivary glands has been associated with exposures to various pharmaceutical agents and allergens .It is unclear whether all of the reported cases are true allergic reaction or whether some represent secondary infections resulting from medication that reduced salivary output.

Compounds associated with allergic Sialadenitis

- Ethambutol.
- Heavy metals.
- Iodine compounds
- Isoproterenol.
- Phenobarbital.
- Phenothiazine.
- Sulfisoxazole

Viral Diseases

MUMPS. (PARAMYXOVIRUS OR EPIDEMIC PAROTITIS) : acute viral infection caused by a ribonucleic acid (RNA) paramyxovirus and is transmitted by direct contact with salivary droplets.

Clinical Presentation

Mumps typically occurs in children between the ages of 4 and 6 years. The incubation period is two to three weeks.

The symptoms of mumps normally appear 2-3 weeks after the patient has been infected. However, almost 20 percent of people with the virus do not suffer any symptoms at all.

Initially, flu-like symptoms will appear, such as:

- Body aches
- Headache
- Loss of appetite and/or nausea
- General fatigue

- Fever (low-grade)

Over the next few days, the classic symptoms of mumps will develop. The main symptom is painful and swollen parotid glands, one of three sets of salivary glands; this causes the person's cheeks to puff out. The swelling normally does not occur in one go - it happens in waves.

Other associated symptoms can include:

- Pain in the sides of the face where it is swollen.
- Pain experienced when swallowing.
- Trouble swallowing.
- Fever (up to 103 degrees Fahrenheit).
- A dry mouth.
- Pain in joints.

Rarely, adults can contract mumps. In these cases, the symptoms are generally the same, but sometimes slightly worse and complications are slightly more likely.

Treatment for mumps

Drinking plenty of fluids may help to relieve the symptoms of mumps.

Because mumps is viral, antibiotics cannot be used to treat it, and at present, there are no anti-viral medications that can treat mumps.

Current treatment can only help relieve the symptoms until the infection has run its course and the body has built up an immunity, much like a cold. In most cases, people recover from mumps within 2 weeks.

Some steps can be taken to help relieve the symptoms of mumps:

- Consume plenty of fluids, ideally water - avoid fruit juices as they stimulate the production of saliva, which can be painful.
- Place something cold on the swollen area to alleviate the pain.
- Eat mushy or liquid food as chewing might be painful.
- Get sufficient rest and sleep.
- Gargle warm salt water.

- Take painkillers. Many painkillers are available to purchase over-the-counter or online, such as acetaminophen or ibuprofen.

Causes of mumps

Mumps is due to an infection by the mumps virus. It can be transmitted by respiratory secretions (e.g. saliva) from a person already affected with the condition. When contracting mumps, the virus travels from the respiratory tract to the salivary glands and reproduces, causing the glands to swell.

Examples of how mumps can be spread include:

- Sneezing or coughing.
- Using the same cutlery and plates as an infected person.
- Sharing food and drink with someone who is infected.
- Kissing.
- An infected person touching their nose or mouth and then passing it onto a surface that someone else may touch.

Individuals infected with the mumps virus are contagious for approximately 15 days (6 days before the symptoms start to show, and up to 9 days after they start). The mumps virus is part of the paramyxovirus family, a common cause of infection, especially in children.

Complications of mumps

Complications are more frequent in adults than children, the most common are:

- **Orchitis** - testicles swell and become painful, this happens to 1 in 5 adult males with mumps. The swelling normally goes down within 1 week; tenderness can last longer than that. This rarely results in infertility.
- **Oophoritis** - ovaries swell and are painful; it occurs in 1 in 20 adult females. The swelling will subside as the immune system fights off the virus. This rarely results in infertility.
- **Viral meningitis** - this is one of the rarest of the common complications. It happens when the virus spreads through the bloodstream and infects the body's central nervous system (brain and spinal cord).
- **Inflamed pancreas (pancreatitis)** - pain will be experienced in the upper abdomen; this occurs in 1 out of 20 cases and is usually mild.

If a pregnant woman contracts mumps in the first 12-16 weeks of her pregnancy, she will have a slightly increased risk of miscarriage.

Rarer complications of mumps include:

- **Encephalitis** - the brain swells causing neurological issues. In some cases, this can be fatal. This is a very rare risk factor
- **Hearing loss** - this is the rarest of all the complications.

As rare as some of these complications are, it is important to seek medical advice or help if an individual suspects they or their child, may be developing them.

Tests and diagnosis of mumps

Normally, mumps can be diagnosed by its symptoms alone, especially by examining the facial swelling. also:

- Check inside the mouth to see the position of the tonsils - when infected with mumps, a person's tonsils can get pushed to the side.
- Take the patient's temperature.
- Take a sample of blood, urine, or saliva to confirm diagnosis.
- Take a sample of CSF (cerebrospinal fluid) from the spine for testing - this is usually only in severe cases.

Prevention of mumps

- The MMR vaccine will prevent mumps, measles, and rubella.
- The mumps vaccine is the best method for preventing mumps; it can come on its own or as part of the MMR vaccine. The MMR vaccine also defends the body against rubella and measles.
- The MMR vaccine is given to an infant when they are just over 1 year old and again, as a booster, just before they start school.

Mumps usually presents with one to two days of malaise, anorexia, and low- grade pyrexia with headache followed by nonpurulent gland enlargement. Glandular swelling increases over the next few days, lasting about one week.

Twenty-five percent of cases may involve unilateral salivary gland swelling, or swelling may develop in the contralateral gland after a time delay, which can complicate diagnosis unless there is a high index of suspicion.

Ninety-five percent of symptomatic cases involve the parotid gland only, while about 10% of cases involve the bilateral submandibular and sublingual glands concomitant with the parotid swelling. A minority of cases may involve the submandibular glands alone.

Salivary gland enlargement is sudden and painful to palpation with edema affecting the overlying skin and the duct orifice. If partial duct obstruction occurs, the patient may experience pain while eating.

Bacterial Sialadenitis

Bacterial infections of the salivary glands are most commonly seen in the patients with reduced salivary gland function. An acute and sudden onset of a swollen and painful salivary gland is termed an acute bacterial sialadenitis, whereas repeated infections are termed chronic bacterial sialadenitis

Bacterial sialadenitis occurs more frequently in the parotid glands. It is theorized that the submandibular glands may be protected by the high level of mucin in the saliva, which has potent antimicrobial activity.

A purulent discharge may be expressed from the duct orifice, and samples of these exudates should be cultured for aerobes and anaerobes type of bacteria

Risk factors

Include dehydration, the use of xerogenic drugs, salivary gland diseases, nerve damage, ductal obstruction, irradiation, and chronic diseases such as diabetes mellitus and SS.Retrograde bacterial parotitis following surgery under general anesthesia is a well-recognized complication. It is due to the markedly decreased salivary flow during anesthesia, often as the result of anticholinergic drugs and relative dehydration.

Although bacterial sialadenitis occurs most frequently in the parotid glands, it can occur in any of the glands. It is thought that the antimicrobial activity of mucin, found in the saliva of the submandibular and sublingual glands, may competitively inhibit bacterial attachment to the epithelium of the salivary ducts. The serous parotid gland saliva also contains less lysosomes, IgA antibodies, and sialic acid.

Anatomy may also play a protective role; tongue movements tend to clear the floor of the mouth and protect Wharton’s duct. In contrast, the orifice of Stensen’s duct is located adjacent to the molars, where heavy bacterial colonization occurs.

Clinical Presentation

Patients usually present with a sudden onset of unilateral or bilateral salivary gland enlargement. Approximately 20% of the cases present as bilateral infections. Complaints of

fevers, chills, malaise, trismus, and dysphagia may accompany these findings. Observation of dry oral mucosa may indicate systemic dehydration.

The involved gland is enlarged, warm, painful, indurated, and tender to palpation. If Stensen's duct is involved, it may appear erythematous and edematous.in some cases there may also be erythema of the overlying skin.

Clinical examination of the involved glands involves bimanual palpation along the path of the excretory duct. In approximately 75% of cases, purulent discharge may be expressed from the orifice.

Diagnosis

Bacterial parotitis is largely a clinical diagnosis. If purulent discharge can be expressed from the duct orifice, samples should be cultured for aerobes, anaerobes, fungi, and mycobacteria. Differentiating between viral and bacterial infectious parotitis can be challenging. In general, viral infections are bilateral, affect younger patients, have prodromal symptoms, do not involve purulent drainage, and patients appear to have less toxicity. Although systemic symptoms follow the development of a symptomatic gland in suppurative parotitis, the order is usually reversed in viral parotitis.

Sialoendoscopy, US, CT, MRI sialography, or percutaneous aspiration may be helpful to rule out chronic salivary gland infections, cysts, obstructions, or neoplasms

Treatment

Treatment goals of bacterial sialadenitis include resolution of signs and symptoms of infection, elimination of the causative bacteria, rehydration, and elimination of obstruction where present. This may involve the use of antibiotics, analgesics, heat application, fluids, glandular massage, oral hygiene products, and sialogogues.

Anti-inflammatory agents including steroids may help to rapidly reduce pain and swelling. (Patients should also be instructed to massage the gland several times a day. Where possible,) medications implicated in salivary gland hypofunction should be discontinued.

according to the above management , significant improvement should be observed within 24 -48 hours

.

Appropriate antibiotic regimens should include coverage for *S. aureus* as well as oral polymicrobial aerobic and anaerobic infections. It is estimated that up to 75% of infections are caused by P-lactamase-producing bacteria, and therefore, treatment with anti-Staphylococcal

penicillin, a combination P-lactamase inhibitor, or a first-generation cephalosporin is appropriate.

Macrolides such as azithromycin with metronidazole can be an alternative for those with a penicillin allergy. Antibiotics should not be started routinely unless bacterial infection is clinically obvious. Under all circumstances, purulent discharge from the salivary gland should be cultured to confirm the diagnosis and determine antibiotic sensitivity. Antibiotic therapy may need to be modified later based on culture results.

Additional potential complications include facial nerve palsy, sepsis, mandibular osteomyelitis, internal jugular vein thrombophlebitis, and respiratory obstruction.

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Systemic Condition with Salivary Gland Involvement

1- Metabolic condition include -

• Diabetes

• Anorexia Nervosa/Bulimia

• Chronic Alcoholism

• Dehydration

2- Medication effect the salivary gland hypofunction (as we mention in the previous lecture)

There are over 400 medications that are listed as having dry mouth as an adverse event .Some drugs may not actually cause impaired salivary output but may produce alteration in saliva composition that lead to the perception of oral dryness. Common Medication Categories Associated with Salivary Hypofunction

• Anticholinergics

• Antihistamines

• Antihypertensive

• Anti-Parkinson’s disease

• Antiseizure

• Cytotoxic agents , Sedative and tranquilizers, Skeletal muscle relaxants, Tricyclic antidepressants

3- Immune conditions

A- Mikulicz's disease previously known as benign lymphoepitheliallesion, is characterized by symmetrical lacrimal, parotid, and submandibular gland enlargement with associated lymphocytic infiltrations. Histopathologically, Mikulicz's disease is associated with prominent infiltration of IgG4-positive plasmacytes in to involved exocrine glands.

Diagnosis is based on finding of salivary gland biopsy and the absence of the alterations in peripheral blood and autoimmune serologies seen in Sjogren's syndrome

B- Sjogren's syndrome (Primary and Secondary) Sjogren's syndrome is a chronic autoimmune disease characterized by symptoms of oral and ocular dryness, exocrine dysfunction and lymphocytic infiltration, and destruction of the exocrine

4.Granulomatosis diseases

A-Tuberculosis (TB) is a chronic bacterial infection, caused by Mycobacterium tuberculosis, leading to the formation of granulomas in the infected. Diagnosis depends on the identification of the bacterium. Treatment of the salivary involvement involves standard multidrug anti-TB chemotherapy.

B- Sarcoidosis is a chronic condition in which T lymphocytes, mononuclear phagocytes, and granulomas cause destruction of involved tissue. Parotid gland involvement occurs in approximately 6% of patients with sarcoidosis.

Unilateral salivary gland enlargement has been reported. Examination of a minor salivary gland biopsy specimen can confirm the diagnosis of sarcoidosis with classic noncaseating granulomata.

MANAGEMENT OF XEROSTOMIA

1- Preventing Therapy :

♣ The use of topical fluorides in a patient with salivary gland hypofunction is absolutely critical to control dental caries.

♣ avoiding cariogenic foods and beverages and brushing immediately after meals. Chronic use of alcohol and caffeine can increase oral dryness and should be minimized.

2- Symptomatic Treatment :

♣ Patients should be encouraged to sip water throughout the day; this will help moisten the oral cavity, hydrate the mucosa, and clear debris from the mouth.

♣ There are a number of oral rinses, mouthwashes, and gels available for dry mouth patients.

♣ The frequent use of products containing aloe vera or vitamin E should be encouraged. saliva replacements (‘ artificial salivas’) can be use

3- Salivary Stimulation :

Local or topical stimulation : Chewing sugar-free gums or mints. Acupuncture, with application of needles in the perioral and other regions, has been proposed as a therapy for salivary gland hypofunction and xerostomia.

Systemic stimulation pilocarpine. Aparasympathomimetic drugs Pilocarpine and Cevimeline

.

4- Therapy of Underlying Systemic Disorders:- Anti-inflammatory therapies to treat the autoimmune exocrinopathy of sjogren’s syndrome.

SIALORRHEA

Sialorrhea is defined as an excessive secretion of saliva or hypersalivation.

The cause is an increase in saliva production or a decrease in salivary clearance.

Causes

medications (pilocarpine, cevimeline, lithium, and nitrazepam), hyperhydration , infant teething, the secretory phase of menstruation, idiopathic paroxysmal hypersalivation, heavy metal poisoning (iron, lead, arsenic, mercury, thallium), organophosphorous

acetyicholinesterase poisoning, nausea, gastroesophageal reflux disease, obstructive esophagitis, neurologic changes such as in a cerebral vascular accident (CVA), neuromuscular diseases, neurologic diseases, and central neurologic infections.

Minor hypersalivation may result from local irritations, such as aphthous ulcers or an ill-fitting oral prosthesis.

• Most cases of hypersalivation are a secretion clearance issue. a blood sample should obtained and evaluated for heavy metals

• There are three types of treatments for hypersalivation according to the exact cause

• Physical therapy, medications, and surgery.

SALIVARY GLAND TUMORS

• The majority of salivary gland tumors (about 80%) arise in the parotid glands. The submandibular glands account for 10 to 15% of tumors, and the remaining tumors develop in the sublingual or minor salivary glands.

Approximetly 80% of parotid gland tumors and approximately half of submandibular gland and minor salivary gland tumors are benign. In contrast, more than 60% of tumors in the sublingual gland are malignant.

Benign Tumors.

PLEOMORPHIC ADENOMA(most common.) The majority of these tumors are found in the parotid glands. Histologically, the lesion demonstrates both epithelial and miesenchymal elements. The epithelial cells make up a trabecular pattern that is contained within a stroma. The stroma may be chondroid, myxoid, osteoid, or fibroid.

The presence of these different elements accounts for the name pleomorphic tumor or mixed tumor. One characteristic of a pleomorphic adenoma is the presence of microscopic projections of tumor outside of the capsule.

Surgical removal with adequate margins is the principal treatment.

what are the complications of the pleomorphic adenoma ?

does pleomorphic adenoma change into malignant?

MONOMORPHIC ADENOMA .

A monomorphic adenoma is a tumor that is composed predominantly of one cell type.

PAPILLARY CYSTADENOMA LYMPHOMATOSUM

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. Because this tumor contains oncocytes, it will take up technetium and will be visible on Tc 99m scintiscans

.

Larger tumors that involve a significant amount of the superficial lobe of the parotid gland are best treated by a superficial parotidectomy

ONCOCYTOMA

L ess common benign tumors that make up less than 1% of all salivary gland neoplasms. This tumor occurs almost exclusively in the parotid glands, Bilateral presentation of this tumor can occur, and it is the second most common salivary gland tumor that occurs bilaterally (after Warthin's tumor), these tumors appear noncystic and firm. The treatment for parotid

Oncocytomas is superficial parotidectomy with preservation of the facial nerve.

BASAL CELL ADENOMA CANALICULAR

ADENOMA MYOEPITHELIOMA SEBACEOUS

These lesions are derived from sebaceous glands located within salivary gland tissue. The parotid gland is the most commonly involved gland. Benign forms contain well-differentiated sebaceous cells, whereas malignant forms consist of more poorly differentiated cells. Intraoral lesions are surgically removed with a border of normal tissue.

DUCTAL PAPIL L OMA

Ductal papillomas form a subset of benign salivary gland tumors that arise from the excretory ducts, predominantly of the minor salivary glands.

Malignant Tumors

MUCOEPIDERMOID CARCENOMA

It is the most common malignant tumor of the parotid gland and the second most common malignant tumor of the submandibular , after adenoid cystic carcinoma

ADENOID CYSTIC CARCINOMA

Account for approximately 6 to 10% of all salivary gland tumors and are the most common malignant tumors of the submandibular and minor salivary glands. It is characterized by frequent late distant metastases and local recurrences, which account for low long-term survival rates.

Treatment. Because of the ability of this lesion to spread along the nerve sheaths, radical surgical excision of the lesion is the appropriate treatment. Even with aggressive surgical margins, tumor cells can remain, leading to long-term recurrence. Factors affecting the long-term prognosis are the size of the primary lesion, its anatomic location, the presence of metastases at the time of surgery, and facial nerve involvement

.

ACINIC CELL CARCINOMA

Represents about 1% of all salivary gland tumors. Between 90 and 95% of these tumors are found in the parotid gland; almost all of the remaining tumors are located in the submandibular

gland. It is the second most common malignant salivary gland tumor in children, second only to mucoepidermoid carcinoma. 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 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

CARCINOMA EX PLEOMORPHIC ADENOMA

Is a malignant tumor that arises within a preexisting pleomorphic adenoma. The malignant cells in this tumor are epithelial in origin. This tumor represents 2 to 5% of all salivary gland tumors. 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.

Treatments

For patients of any age involve surgical removal and adjuvant radiotherapy for more advanced cancers.

Efficacy of treatment of malignant tumors is dependent upon stage, location, presence of perineural invasion, treatment modality, histologic type, and presence of regional invasion.

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ADENOCARCINOMA

It is a tumor arising from salivary duct epithelium.

- The tumors may be present for weeks, months, or even several years, prior to diagnosis
- A mass or lump on the side of the face may be observed, since mostly the parotid gland is affected
- Most tumors are locally infiltrative, but some are well-defined
- Some individuals with basal cell adenocarcinomas may have other unrelated skin tumors, such as adnexal tumors of skin
- Most tumors are asymptomatic and no significant signs and symptoms are observed
- Neurological signs and symptoms, such as facial muscle weakness and pain, due to facial nerve involvement may be seen
- Pain while eating/chewing

- Persistent facial pain at the site of swelling of the tumor; this requires an immediate checkup by a healthcare provider
- Tumor infiltration into the bone
- Involvement of the lymphatic system may be seen in 25% of the cases

LYMPHOMA

Primary lymphoma of the salivary glands probably arises from lymph tissue within the glands. However, primary lymphoma of the salivary glands is rare. The major forms of lymphoma are non- Hodgkin's lymphoma (NHL) and Hodgkin's disease.Histologic examination demonstrates B-cell lymphoma tissue that originates from lymphoid tissue associated with malignant mucosa.

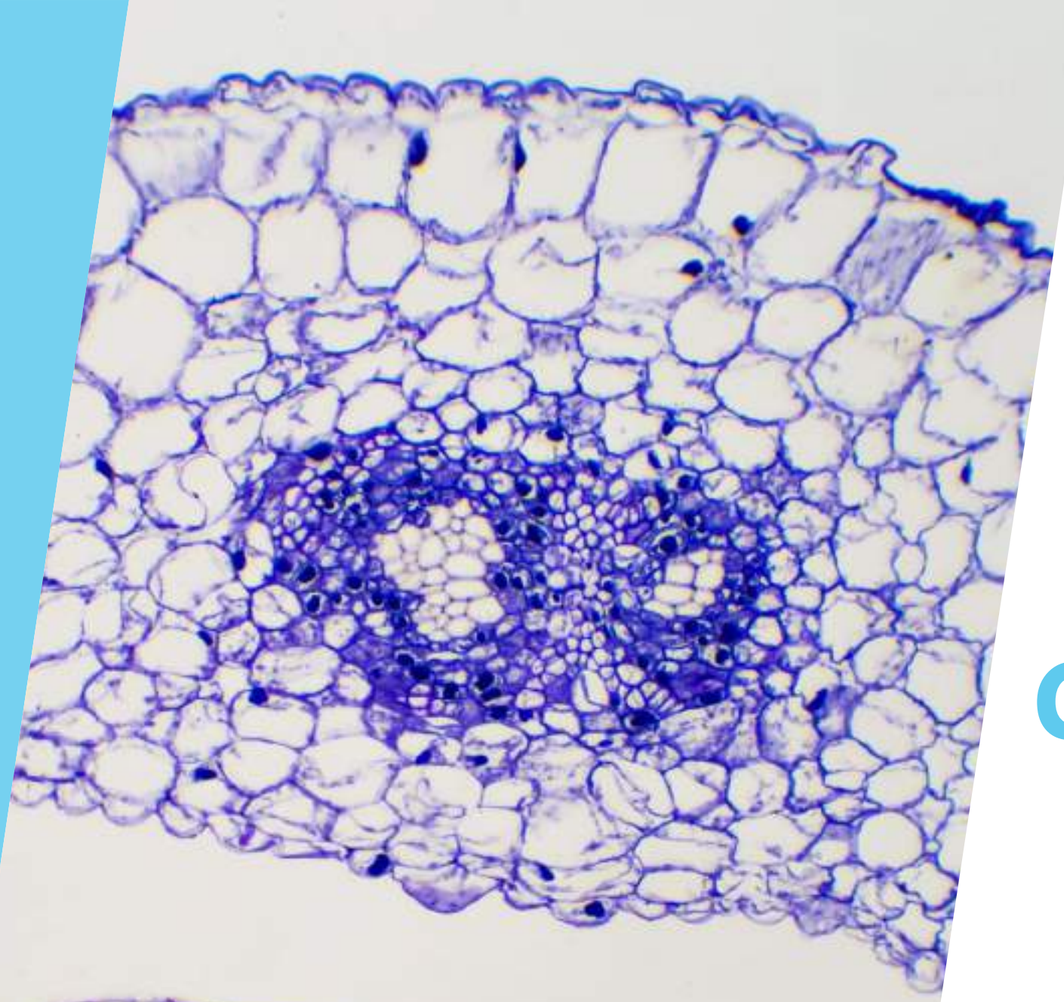
MYOEPITHELIAL CARCINOMA

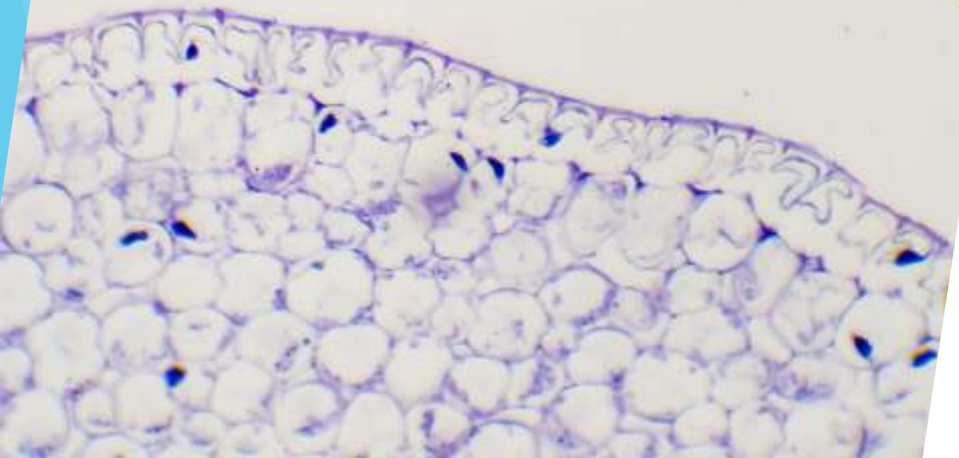
Myoepithelial carcinoma or malignant myoepithelioma is a very rare malignant salivary gland neoplasm with good short-term survival and poor long-term survival. Due to their morphologic heterogeneity, these neoplasms can be confused easily with other tumors. Early and aggressive surgical removal with close follow- up is required.

Frey's syndrome(Baillarger's syndrome ,Dupuy's syndrome ,auriculotemporal syndrome)

The frequent complication following parotidectomy is gustatory sweating or Frey syndrome. The pathogenesis of Frey syndrome is based on the aberrant regeneration of sectioned parasympathetic secretomotor fibres of the auriculotemporal nerve with inappropriate innervation of the cutaneous facial sweat glands that are normally innervated by sympathetic cholinergic fibres.

As a consequence, Frey syndrome is a disorder characterized by unilateral sweating and flushing of the facial skin in the area of the parotid gland occurring during meals that becomes evident usually 1-12 months after surgery .





Salivary Gland diseases part 2

Dr. Marwah Waleed Sh.

Necrotizing Sialometaplasia (NS)

Description and Etiology

- Benign, self-limiting, reactive inflammatory disorder of salivary tissue. NS can resemble a malignancy.
- The etiology is **unknown**, although it likely represents a local ischemic event, infectious process and an immune response to an unknown allergen. Development of NS has **been associated** with smoking, local injury, blunt force trauma, denture wear, and surgical procedures. It has been reported in pregnant patients and those with diabetes mellitus, sickle-cell disease, cocaine abuse, bulimia, and chronic vomiting.
- The incidence is higher in male ,older than 40 years

Clinical Presentation

- Painful, rapidly progressing swelling of the hard palate with central ulceration and peripheral erythema.
- The associated pain is sharp in character and may precede mucosal changes, numbness or anesthesia.
- The lesions are of rapid onset and range in size from 1 to 3 cm.
- Lesions occur predominantly on the palate; however, lesions can occur anywhere salivary gland tissue resides, including the lips, retromolar , buccal mucosa, tongue, nasal cavity, and maxillary sinus.
- Lesions are usually unilateral . Lesion affecting **the hard palate** clinically resemble salivary gland malignancies particularly carcmucoepidermoid carcinoma and adenoid cystic inoma.
- Rapid onset of NS may be a distinguishing feature. Lesions often occur shortly after an inciting event to the area such as oral surgical procedures. It is also not uncommon for lesions to develop in an individual with no history of trauma or oral habit.

Diagnosis

- Histopathologic diagnosis ,and a complete clinical history, medical history, and clinical photos.

Treatment

- A self-limiting condition typically resolving within 3-12 weeks. During this time, supportive and symptomatic treatment is usually adequate.
- Analgesics combined with use of an antiseptic mouthwash such as 0.12% chlorhexidine gluconate.
- Surgical intervention is typically not required in cases of NS; however, there are reports of resolution following debridement for particularly large lesions and those secondarily infected with bacterial species and Candida.

Cheilitis Glandularis

Description and Etiology

- Chronic inflammatory disorder affecting the minor salivary glands and their ducts in which thick saliva is secreted from dilated ductal openings.
- Superficial ulceration, painless crusting, swelling, and induration of the lip; a mucinous exudate is apparent at the ductal openings.
- **Etiology**: an autosomal dominant hereditary disease. In addition, external factors (mainly UV rays) **in fair-skinned adults and albino patients**. Additional proposed predisposing factors include **poor oral hygiene, chronic exposure to sunlight and wind, smoking, and an immunocompromised state**.
- Middle-aged and elderly men with only a few cases reported in women and children.
- it is associated with a relatively high incidence of squamous cell carcinoma of the lip (premalignant condition).

Clinical Presentation

- Thick saliva secreted from dilated ostia of swollen labial minor salivary glands. This saliva often adheres to the vermilion causing discomfort to the patient. Edema and focal ulceration may also be present.
- Lower lip, but there are reports of upper lip and even palatal involvement.
- **Differential diagnosis (DD)** of CG includes :- **multiple mucocele, chronic sialadenitis of the minor salivary glands, factitious cheilitis, orofacial granulomatosis and actinic cheilitis.**

Treatment

- Elimination of potential predisposing factors and the use of lip balms, emollients, and sunscreens for those with excessive exposure to the sun and wind are advised.
- **Topical, intralesional or systemic steroids, systemic anticholinergics, systemic antihistamines, and/or antibiotics.**
- Refractory cases require **surgical intervention** such as **cryosurgery, vermillionectomy, and/or labial mucosal stripping.**

External Beam Radiation-Induced

Pathology Description and Etiology

- Standard treatment for head and neck cancers, and the salivary glands are often within the **field of radiation**. Although therapeutic dosages for cancer are typically more than **65 Gy.**
- Permanent **salivary gland damage and symptoms of oral dryness** can develop after only **24-26 Gy.**
- Salivary gland destruction is multifactorial, including **programmed cell death (apoptosis) in conjunction with production of reactive oxygen species and other cytotoxic products.**
- **Radiation-associated impaired blood flow** may also contribute to the destruction of glandular acinar and ductal cells.

Clinical Presentation

- **Oral dryness and thick, viscous saliva** developing by the end of the second week (acute).
- **Oral mucositis(sloughing of the oral mucosa with erythema and ulceration with burning sensation)** can become **severe** enough to alter the radiation therapy regimen.
- Mucositis persists throughout radiotherapy and **continues for one to three weeks after cessation of treatment**.
- By the end of a **typical six- to seven-week** course of radiotherapy, salivary gland function is nearly absent. Hypofunction remains with only small increases to two years post-radiotherapy (post-RT).
- Permanent xerostomia and **oral complications** of salivary hypofunction impair a patient's quality of life. Signs and symptoms of **radiation-associated xerostomia** include a **burning sensation of the tongue, Assuring of the tongue and lips, new and recurrent dental caries, difficulty in wearing oral prostheses, and increased thirst. Other complications** radiation-induced salivary dysfunction include **candidiasis, microbial infections, plaque retention, Gingivitis, difficulty in speaking and tasting, dysphagia, and mucosal pain.**

Internal Radiation-Induced Pathology_ Radioactive iodine (RAI)

Astandard treatment in cases of papillary and follicular thyroid carcinomas following thyroidectomy or in cases of metastases.

- A significant portion is concentrated and secreted through the salivary gland tissue resulting in radiation exposure of the salivary parenchyma and possible damage.
- Standard doses of RAI often cause obstructive duct symptoms, while **hyposalivation from Parenchymal damage is usually observed with larger or repeated doses of RAI.**
- **Acute risks** associated with RAI include ageusia, salivary gland swelling, and pain, while long-term side effects include recurrent sialadenitis with xerostomia, stomatitis, and dental caries.
- In some circumstances, RAI treatment may lead to glandular fibrosis and permanent salivary gland hypofunction.

Clinical Presentation

- The glandular effect of RAI can be mild to severe.
- Patients may be asymptomatic or may complain of parotid gland swelling (usually bilaterally), pain, xerostomia, and decreased salivary gland function.
- RAI-induced salivary gland injury is irreversible; however, **residual functioning salivary gland tissue is often present and responsive to therapy.**
- Following administration of 131 I, patients should undergo an aggressive salivary stimulation routine that includes sugar-free lozenges, sour candies, and gums to stimulate salivary flow. This will aid in clearing the 131 I from the salivary glands and potentially decrease salivary gland damage. Stimulation of salivary flow by these means, however, should not be initiated within the first 24 hours after 131 I therapy as this has been shown to potentially increase the salivary gland side effects of the RAI.
- Pilocarpine and cevimeline used before and after RAI treatment may decrease transit time through the salivary glands, thereby diminishing exposure.

Allergic Sialadenitis

Enlargement of the salivary glands has been associated with exposures to various pharmaceutical agents and allergens .It is unclear whether all of the reported cases are true allergic reaction or whether some represent secondary infections resulting from medication that reduced salivary output.

- Compounds associated with allergic Sialadenitis
- • Ethambutol.
- • Heavy metals.
- • Iodine compounds
- • Isoproterenol.
- • Phenobarbital.
- • Phenothiazine.
- • Sulfisoxazole

Viral Diseases (MUMPS)

- (PARAMYXOVIRUS OR EPIDEMIC PAROTITIS) : acute viral infection caused by a ribonucleic acid (RNA) paramyxovirus and is transmitted by direct contact with salivary droplets.
- **Clinical Presentation**
- Mumps typically occurs in children between the ages of 4 and 6 years. The incubation period is two to three weeks. The symptoms of mumps normally appear 2-3 weeks after the patient has been infected. However, almost 20 percent of people with the virus do not suffer any symptoms at all. Initially, flu-like symptoms will appear, such as:

- Body aches
- Headache
- Loss of appetite and/or nausea
- General fatigue
- Fever (low-grade)

Over the next few days, the classic symptoms of mumps will develop. The main symptom is painful and swollen parotid glands, one of three sets of salivary glands; this causes the person's cheeks to puff out. The swelling normally does not occur in one go - it happens in waves

Other associated symptoms can include:

- • Pain in the sides of the face where it is swollen.
- • Pain experienced when swallowing.
- • Trouble swallowing.
- • Fever (up to 103 degrees Fahrenheit).
- • A dry mouth.
- • Pain in joints.
- Rarely, adults can contract mumps. In these cases, the symptoms are generally the same, but sometimes slightly worse and complications are slightly more likely.

- Treatment
- Drinking plenty of fluids may help to relieve the symptoms of mumps.
- Because mumps is viral, antibiotics cannot be used to treat it, and at present, there are no anti-viral medications that can treat mumps.
- Current treatment can only help relieve the symptoms until the infection has run its course and the body has built up an immunity, much like a cold. In most cases, people recover from mumps within 2 weeks.
- Some steps can be taken to help relieve the symptoms of mumps:
- • Consume plenty of fluids, ideally water - avoid fruit juices as they stimulate the production of saliva, which can be painful.
- • Place something cold on the swollen area to alleviate the pain.
- • Eat mushy or liquid food as chewing might be painful.
- • Get sufficient rest and sleep.
- • Gargle warm salt water.
- • Take painkillers. Many painkillers are available to purchase over-the-counter or online, such as acetaminophen or ibuprofen.

- Causes of mumps
- Mumps is due to an infection by the mumps virus. It can be transmitted by respiratory secretions (e.g. saliva) from a person already affected with the condition. When contracting mumps, the virus travels from the respiratory tract to the salivary glands and reproduces, causing the glands to swell.
- Examples of how mumps can be spread include:
- • Sneezing or coughing.
- • Using the same cutlery and plates as an infected person.
- • Sharing food and drink with someone who is infected.
- • Kissing.
- • An infected person touching their nose or mouth and then passing it onto a surface that someone else may touch.
- Individuals infected with the mumps virus are contagious for approximately 15 days (6 days before the symptoms start to show, and up to 9 days after they start). The mumps virus is part of the paramyxovirus family, a common cause of infection, especially in children.

- **Complications** are more frequent in adults than children, the most common are:
- • Orchitis - testicles swell and become painful, this happens to 1 in 5 adult males with mumps. The swelling normally goes down within 1 week; tenderness can last longer than that. This rarely results in infertility.
- • Oophoritis - ovaries swell and are painful; it occurs in 1 in 20 adult females. The swelling will subside as the immune system fights off the virus. This rarely results in infertility.
- • Viral meningitis - this is one of the rarest of the common complications. It happens when the virus spreads through the bloodstream and infects the body's central nervous system (brain and spinal cord).
- • Inflamed pancreas (pancreatitis) - pain will be experienced in the upper abdomen; this occurs in 1 out of 20 cases and is usually mild.
- If a pregnant woman contracts mumps in the first 12-16 weeks of her pregnancy, she will have a slightly increased risk of miscarriage.
- Rarer complications of mumps include:
- • Encephalitis - the brain swells causing neurological issues. In some cases, this can be fatal. This is a very rare risk factor
- • Hearing loss - this is the rarest of all the complications.
- As rare as some of these complications are, it is important to seek medical advice or help if an individual suspects they or their child, may be developing them

Tests and diagnosis of mumps

- Normally, mumps can be diagnosed by its symptoms alone, especially by examining the facial swelling. also:
- • Check inside the mouth to see the position of the tonsils - when infected with mumps, a person's tonsils can get pushed to the side.
- • Take the patient's temperature.
- • Take a sample of blood, urine, or saliva to confirm diagnosis.
- • Take a sample of CSF (cerebrospinal fluid) from the spine for testing - this is usually only in severe cases.

- Prevention of mumps • The MMR vaccine will prevent mumps, measles, and rubella.
- • The mumps vaccine is the best method for preventing mumps; it can come on its own or as part of the MMR vaccine. The MMR vaccine also defends the body against rubella and measles.
- • The MMR vaccine is given to an infant when they are just over 1 year old and again, as a booster, just before they start school.
- Mumps usually presents with one to two days of malaise, anorexia, and low- grade pyrexia with headache followed by nonpurulent gland enlargement. Glandular swelling increases over the next few days, lasting about one week.
- Twenty-five percent of cases may involve unilateral salivary gland swelling, or swelling may develop in the contralateral gland after a time delay, which can complicate diagnosis unless there is a high index of suspicion.
- Ninety-five percent of symptomatic cases involve the parotid gland only, while about
- 10% of cases involve the bilateral submandibular and sublingual glands concomitant with the parotid swelling. A minority of cases may involve the submandibular glands alone.
- Salivary gland enlargement is sudden and painful to palpation with edema affecting the overlying skin and the duct orifice. If partial duct obstruction occurs, the patient may experience pain while eating.

- Bacterial Sialadenitis
- Bacterial infections of the salivary glands are most commonly seen in the patients with reduced salivary gland function. An acute and sudden onset of a swollen and painful salivary gland is termed an acute bacterial sialadenitis, whereas repeated infections are termed chronic bacterial sialadenitis
- Bacterial sialadenitis occurs more frequently in the parotid glands. It is theorized that the submandibular glands may be protected by the high level of mucin in the saliva, which has potent antimicrobial activity.
- A purulent discharge may be expressed from the duct orifice, and samples of these exudates should be cultured for aerobes and anaerobes type of bacteria
- Risk factors
- Include dehydration, the use of xerogenic drugs, salivary gland diseases, nerve damage, ductal obstruction, irradiation, and chronic diseases such as diabetes mellitus and SS.Retrograde bacterial parotitis following surgery under general anesthesia is a well-recognized complication. It is due to the markedly decreased salivary flow during anesthesia, often as the result of anticholinergic drugs and relative dehydration.
- Although bacterial sialadenitis occurs most frequently in the parotid glands, it can occur in any of the glands. It is thought that the antimicrobial activity of mucin, found in the saliva of the submandibular and sublingual glands, may competitively inhibit bacterial attachment to the epithelium of the salivary ducts. The serous parotid gland saliva also contains less lysosomes, IgA antibodies, and sialic acid.
- Anatomy may also play a protective role; tongue movements tend to clear the floor of the mouth and protect Wharton’s duct. In contrast, the orifice of Stensen’s duct is located adjacent to the molars, where heavy bacterial colonization occurs.

- **Clinical Presentation**
- Patients usually present with a sudden onset of unilateral or bilateral salivary gland enlargement. Approximately 20% of the cases present as bilateral infections. Complaints of fevers, chills, malaise, trismus, and dysphagia may accompany these findings. Observation of dry oral mucosa may indicate systemic dehydration.
- The involved gland is enlarged, warm, painful, indurated, and tender to palpation. If Stensen's duct is involved, it may appear erythematous and edematous.in some cases there may also be erythema of the overlying skin.
- Clinical examination of the involved glands involves bimanual palpation along the path of the excretory duct. In approximately 75% of cases, purulent discharge may be expressed from the orifice.

Diagnosis

- Bacterial parotitis is largely a clinical diagnosis. If purulent discharge can be expressed from the duct orifice, samples should be cultured for aerobes, anaerobes, fungi, and mycobacteria. Differentiating between viral and bacterial infectious parotitis can be challenging. In general, viral infections are bilateral, affect younger patients, have prodromal symptoms, do not involve purulent drainage, and patients appear to have less toxicity. Although systemic symptoms follow the development of a symptomatic gland in suppurative parotitis, the order is usually reversed in viral parotitis.
- Sialoendoscopy, US, CT, MRI sialography, or percutaneous aspiration may be helpful to rule out chronic salivary gland infections, cysts, obstructions, or neoplasms

Treatment

- Resolution of signs and symptoms of infection, elimination of the causative bacteria, rehydration, and elimination of obstruction where present. This may involve the use of antibiotics, analgesics, heat application, fluids, glandular massage, oral hygiene products, and sialogogues.
- Anti-inflammatory agents including steroids may help to rapidly reduce pain and swelling. (Patients should also be instructed to massage the gland several times a day. Where possible,) medications implicated in salivary gland hypofunction should be discontinued.
- according to the above management , significant improvement should be observed within 24 -48 hours.
- Appropriate antibiotic regimens should include coverage for S. aureus as well as oral polymicrobial aerobic and anaerobic infections. It is estimated that up to 75% of infections are caused by P-lactamase-producing bacteria, and therefore, treatment with anti-Staphylococcal penicillin, a combination P-lactamase inhibitor, or a first-generation cephalosporin is appropriate.
- Macrolides such as azithromycin with metronidazole can be an alternative for those with a penicillin allergy. Antibiotics should not be started routinely unless bacterial infection is clinically obvious. Under all circumstances, purulent discharge from the salivary gland should be cultured to confirm the diagnosis and determine antibiotic sensitivity. Antibiotic therapy may need to be modified later based on culture results.
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- • Antihistamines
- • Antihypertensive
- • Anti-Parkinson’s disease
- • Antiseizure
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MANAGEMENT OF XEROSTOMIA

- 1- Preventing Therapy :
- ♣The use of topical fluorides in a patient with salivary gland hypofunction is absolutely critical to control dental caries.
- ♣avoiding cariogenic foods and beverages and brushing immediately after meals. Chronic use of alcohol and caffeine can increase oral dryness and should be minimized.
- 2- Symptomatic Treatment :
- ♣Patients should be encouraged to sip water throughout the day; this will help moisten the oral cavity, hydrate the mucosa, and clear debris from the mouth.
- ♣There are a number of oral rinses, mouthwashes, and gels available for dry mouth patients.
- ♣The frequent use of products containing aloe vera or vitamin E should be encouraged. saliva replacements (‘artificial salivas’) can be use
- 3- Salivary Stimulation :
- Local or topical stimulation : Chewing sugar-free gums or mints. Acupuncture, with application of needles in the perioral and other regions, has been proposed as a therapy for salivary gland hypofunction and xerostomia.
- Systemic stimulation pilocarpine. Aparasympathomimetic drugs Pilocarpine and Cevimeline.
- 4- Therapy of Underlying Systemic Disorders:- Anti-inflammatory therapies to treat the autoimmune exocrinopathy of sjogren’s syndrome

SIALORRHEA

- Sialorrhea is defined as an excessive secretion of saliva or hypersalivation.
- The cause is an increase in saliva production or a decrease in salivary clearance.
- Causes
- medications (pilocarpine, cevimeline, lithium, and nitrazepam), hyperhydration , infant teething, the secretory phase of menstruation, idiopathic paroxysmal hypersalivation, heavy metal poisoning (iron, lead, arsenic, mercury, thallium), organophosphorous
- acetyicholinesterase poisoning, nausea, gastroesophageal reflux disease, obstructive esophagitis, neurologic changes such as in a cerebral vascular accident (CVA), neuromuscular diseases, neurologic diseases, and central neurologic infections.
- Minor hypersalivation may result from local irritations, such as aphthous ulcers or an ill-fitting oral prosthesis.
- • Most cases of hypersalivation are a secretion clearance issue. a blood sample should obtained and evaluated for heavy metals
- • There are three types of treatments for hypersalivation according to the exact cause
- • Physical therapy, medications, and surgery.

SALIVARY GLAND TUMORS

The majority of salivary gland tumors (about 80%) arise in the parotid glands. The submandibular glands account for 10 to 15% of tumors, and the remaining tumors develop in the sublingual or minor salivary glands.

- Approximetly 80% of parotid gland tumors and approximately half of submandibular gland and minor salivary gland tumors are benign. In contrast, more than 60% of tumors in the sublingual gland are malignant.
- Benign Tumors.
- PLEOMORPHIC ADENOMA(most common.) The majority of these tumors are found in the parotid glands. Histologically, the lesion demonstrates both epithelial and miesenchymal elements. The epithelial cells make up a trabecular pattern that is contained within a stroma. The stroma may be chondroid, myxoid, osteoid, or fibroid.
- The presence of these different elements accounts for the name pleomorphic tumor or mixed tumor. One characteristic of a pleomorphic adenoma is the presence of microscopic projections of tumor outside of the capsule.
- Surgical removal with adequate margins is the principal treatment.
- what are the complications of the pleomorphic adenoma ?
- does pleomorphic adenoma change into malignant?

MONOMORPHIC ADENOMA .

- A monomorphic adenoma is a tumor that is composed predominantly of one cell type.
- PAPILLARY CYSTADENOMA LYMPHOMATOSUM
- 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. Because this tumor contains oncocytes, it will take up technetium and will be visible on Tc 99m scintiscans
- Larger tumors that involve a significant amount of the superficial lobe of the parotid gland are best treated by a superficial parotidectomy

ONCOCYTOMA

- Less common benign tumors that make up less than 1% of all salivary gland neoplasms. This tumor occurs almost exclusively in the parotid glands, Bilateral presentation of this tumor can occur, and it is the second most common salivary gland tumor that occurs bilaterally (after Warthin’s tumor), these tumors appear noncystic and firm. The treatment for parotid
- oncocytomas is superficial parotidectomy with preservation of the facial nerve.

BASAL CELL ADENOMA CANALICULAR

- ADENOMA MYOEPITHELIOMA SEBACEOUS
- These lesions are derived from sebaceous glands located within salivary gland tissue. The parotid gland is the most commonly involved gland. Benign forms contain well-differentiated sebaceous cells, whereas malignant forms consist of more poorly differentiated cells. Intraoral lesions are surgically removed with a border of normal tissue.

DUCTAL PAPILLOMA

- Ductal papillomas form a subset of benign salivary gland tumors that arise from the excretory ducts, predominantly of the minor salivary glands.

Malignant Tumors

- **MUCOEPIDERMOID CARCENOMA**
- It is the most common malignant tumor of the parotid gland and the second most common malignant tumor of the submandibular , after adenoid cystic carcinoma

ADENOID CYSTIC CARCINOMA

- Account for approximately 6 to 10% of all salivary gland tumors and are the most common malignant tumors of the submandibular and minor salivary glands. It is characterized by frequent late distant metastases and local recurrences, which account for low long-term survival rates.
- Treatment. Because of the ability of this lesion to spread along the nerve sheaths, radical surgical excision of the lesion is the appropriate treatment. Even with aggressive surgical margins, tumor cells can remain, leading to long-term recurrence. Factors affecting the long-term prognosis are the size of the primary lesion, its anatomic location, the presence of metastases at the time of surgery, and facial nerve involvement.

ACINIC CELL CARCINOMA

- Represents about 1% of all salivary gland tumors. Between 90 and 95% of these tumors are found in the parotid gland; almost all of the remaining tumors are located in the submandibular gland. It is the second most common malignant salivary gland tumor in children, second only to mucoepidermoid carcinoma. 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 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

CARCINOMA EX PLEOMORPHIC ADENOMA

- Is a malignant tumor that arises within a preexisting pleomorphic adenoma. The malignant cells in this tumor are epithelial in origin. This tumor represents 2 to 5% of all salivary gland tumors. 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.
- Treatments
- For patients of any age involve surgical removal and adjuvant radiotherapy for more advanced cancers.
- Efficacy of treatment of malignant tumors is dependent upon stage, location, presence of perineural invasion, treatment modality, histologic type, and presence of regional invasion.

ADENOCARCINOMA

- It is a tumor arising from salivary duct epithelium.
- • The tumors may be present for weeks, months, or even several years, prior to diagnosis
- • A mass or lump on the side of the face may be observed, since mostly the parotid gland is affected
- • Most tumors are locally infiltrative, but some are well-defined
- • Some individuals with basal cell adenocarcinomas may have other unrelated skin tumors, such as adnexal tumors of skin
- • Most tumors are asymptomatic and no significant signs and symptoms are observed
- • Neurological signs and symptoms, such as facial muscle weakness and pain, due to facial nerve involvement may be seen
- • Pain while eating/chewing
- • Persistent facial pain at the site of swelling of the tumor; this requires an immediate checkup by a healthcare provider
- • Tumor infiltration into the bone
- • Involvement of the lymphatic system may be seen in 25% of the cases.

LYMPHOMA

- Primary lymphoma of the salivary glands probably arises from lymph tissue within the glands. However, primary lymphoma of the salivary glands is rare. The major forms of lymphoma are non-Hodgkin's lymphoma (NHL) and Hodgkin's disease. Histologic examination demonstrates B-cell lymphoma tissue that originates from lymphoid tissue associated with malignant mucosa.
- MYOEPITHELIAL CARCINOMA
- Myoepithelial carcinoma or malignant myoepithelioma is a very rare malignant salivary gland neoplasm with good short-term survival and poor long-term survival. Due to their morphologic heterogeneity, these neoplasms can be confused easily with other tumors. Early and aggressive surgical removal with close follow- up is required.

Frey's syndrome(Baillarger's syndrome ,Dupuy's syndrome ,auriculotemporal syndrome)

- The frequent complication following parotidectomy is gustatory sweating or Frey syndrome. The pathogenesis of Frey syndrome is based on the aberrant regeneration of sectioned parasympathetic secretomotor fibres of the auriculotemporal nerve with inappropriate innervation of the cutaneous facial sweat glands that are normally innervated by sympathetic cholinergic fibres.
- As a consequence, Frey syndrome is a disorder characterized by unilateral sweating and flushing of the facial skin in the area of the parotid gland occurring during meals that becomes evident usually 1-12 months after surgery

Thank you

Immunologic Diseases

Dr. Marwah Waleed Sh.

The Immune System: Protection From Pathogen Challenge

- The immune system is extremely complex, composed of both the **innate** and **adaptive** immune systems, served by **various cell types** with primary function of defending the body against infection.
- The immune system must distinguish between **self** and **non-self** and identify foreign invaders as distinct from **self.**
- The immune system can **recognize** and **clear** invading pathogens such as viruses, bacteria, or parasites, but **tolerate** antigens derived from innocent proteins, and self-antigens as well as commensal microbiota.
- The immune system is tasked with mediating responses to injury, cell death, and tumor surveillance.
- An **appropriately functioning** immune system is **vital for life** and its importance is highlighted by the fact that its **dysfunction** led to many diseases, ranging from **infection** to **cancer** and **autoimmunity**

- **In the oral cavity,** immune system dysfunction contributes to the pathology of Gingivitis, Periodontitis, Oral infections, And autoimmune manifestations of systemic or local disease.

- **The innate immune (non- specific) system** is **immediately activated.** it capable of eliminating the invading insult (injury and infection, particularly at mucosal sites).

- **When** the **innate immune** response is **unable** to control the insult, it will recruit and activate an **adaptive immune** response.

- **The adaptive immune (specific) system** is highly targeted for the type of infection **(to specific invader)**.

- It will later **provide memory** for the specific pathogen, allowing a faster and more effective immune response.

The Immune System of The Mouth

Three pillars of the oral immune system

(Successful defense)

1) Secretion of saliva.

2)An effective epithelial barrier(mucosal barrier).

3)Activation of innate and adaptive immune network cells.

1.Saliva

❖Plays a critical role in immune protection at the oral mucosal barrier.

❖Saliva contains **99% water**, but also electrolytes, enzymes for digestion (amylase, lipase), mucus, and antimicrobial components that provides effective antimicrobial defense against specific microbial pathogens.

❖**Key antimicrobial components in saliva are** :

- **Secretory immunoglobulin (Ig) A,**
- **Microbiocidal enzymes** such as lysozyme, lactoperoxidase, lactoferrin, proline-rich proteins, and antimicrobial peptides (histatins, defensins, secretory leukocyte protease inhibitor).

❖Saliva provides constant **lubrication** and ensures the health and **integrity** of the mucosal barrier.

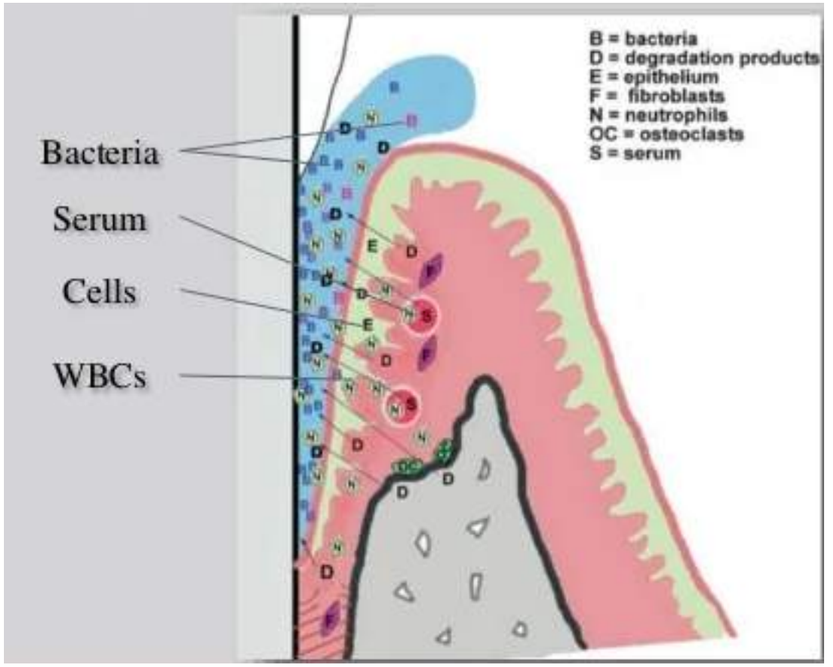
❖Patients with reduced or absent saliva (**dry mouth to hyposalivation**) suffer from mucosal inflammation and ulcerations, which lead to pain and difficulty eating.

❖Patients with **xerostomia** present predominantly with oral candidiasis as well as severe to rampant dental infections with “cariogenic” bacteria, such as Streptococcus mutans.

2. Immune Cells

❖The continual nature of local triggers (resident commensal bacterial community, continuous damage from mastication, and pathogen challenge) requires active immune surveillance within the mouth.

❖The **oral epithelial barrier** is a key interface of the human body providing **physica**l, **structural**, and **immunologic** protection to infectious challenge.



❖**The junctional epithelium**, is non-keratinized, directly attaches to the surface of the tooth, is 3-4 cells thick at its narrowest points near the teeth. It **is a weak point** in the oral mucosal barrier, It is **permeable and** serves as the **primary pathway** for the transmigration of immune cells, particularly neutrophils, and fluid into the **oral space**.

❖**Gingival crevicular fluid**, contains host-defensive **proteins**.

❖Oral epithelial cells are key sources of pro-inflammatory cytokines and chemokines and **directly** respond to pathogens.

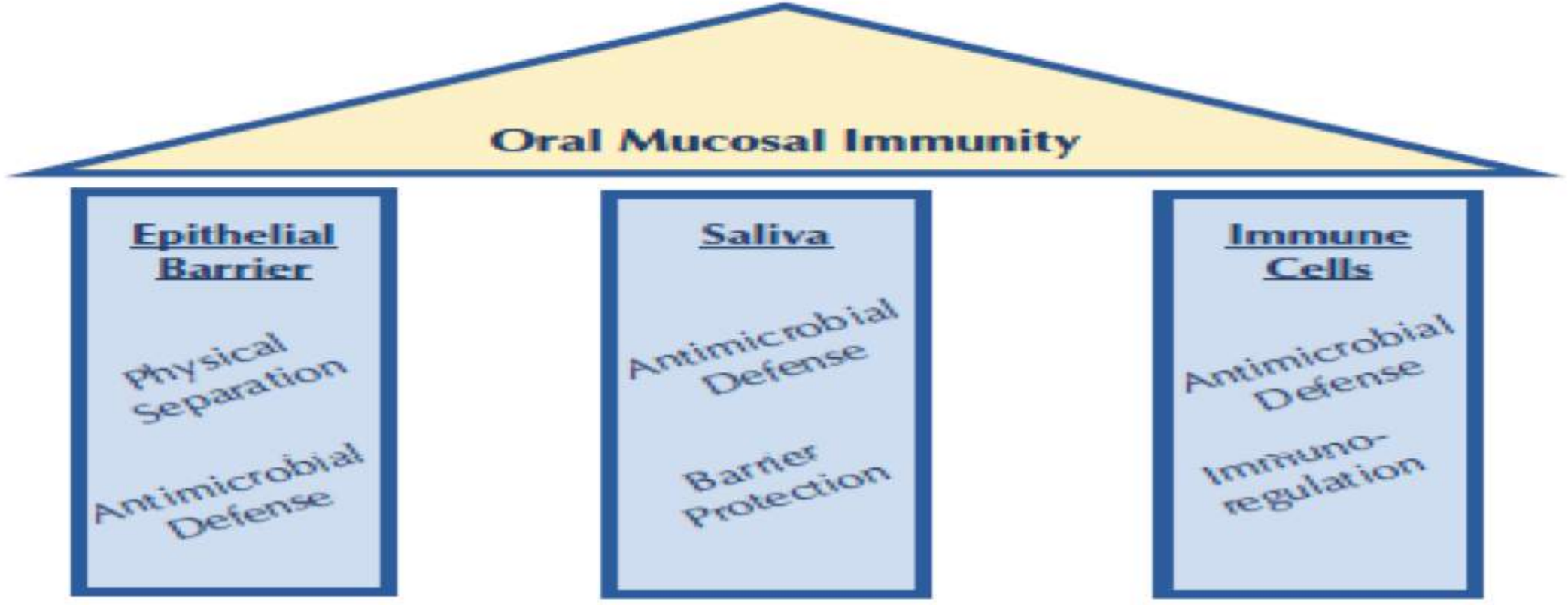


Figure 19-1 Epithelial barrier, saliva, and immune cell network are the three pillars of oral mucosal immunity, providing physical separation, antimicrobial defense, and immuno-regulation to achieve a balance between host and environment.

Neutrophils

- The major innate immune cells present within the oral mucosa. These are **short-lived (24–48 hours)** cells that make up about **70%** of peripheral blood WBC.
- Neutrophils are anti-microbicidal, **activated** by **bacterial products**, through ingestion of bacteria (**phagocytosis**) and release of soluble and non-soluble components that can **trap** and **kill** extracellular pathogens.
- These cells are **rapidly mobilized** to **sites of pathogen invasion,** being the first innate immune cells to extravasate from blood vessels, via a well-defined series of events, and migrate toward the infection.
- Neutrophils **release reactive oxygen species** (ROS), **granules** containing **cytotoxic compounds and antimicrobial peptides, and neutrophil extracellular traps (NETs).**

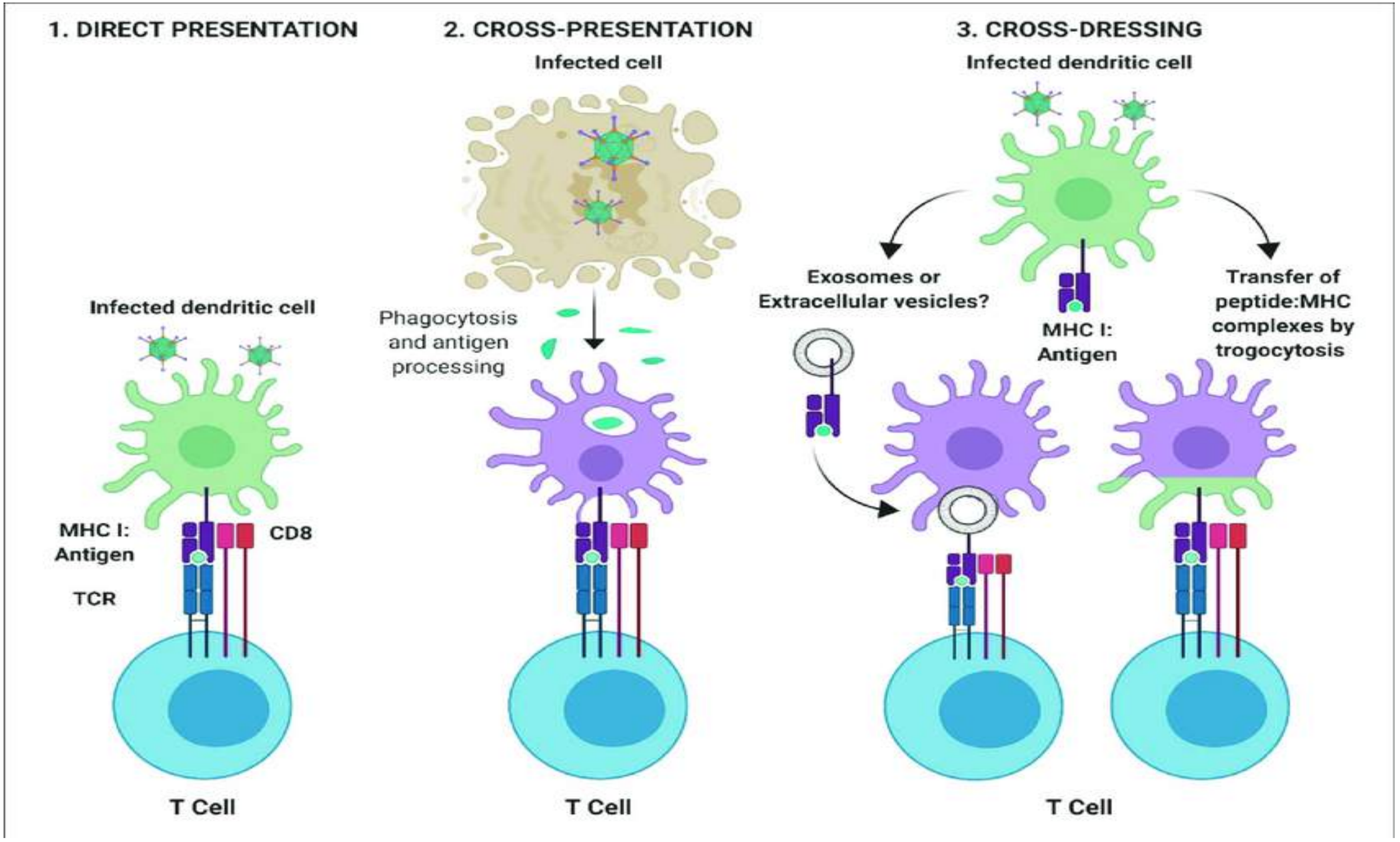
Macrophages:

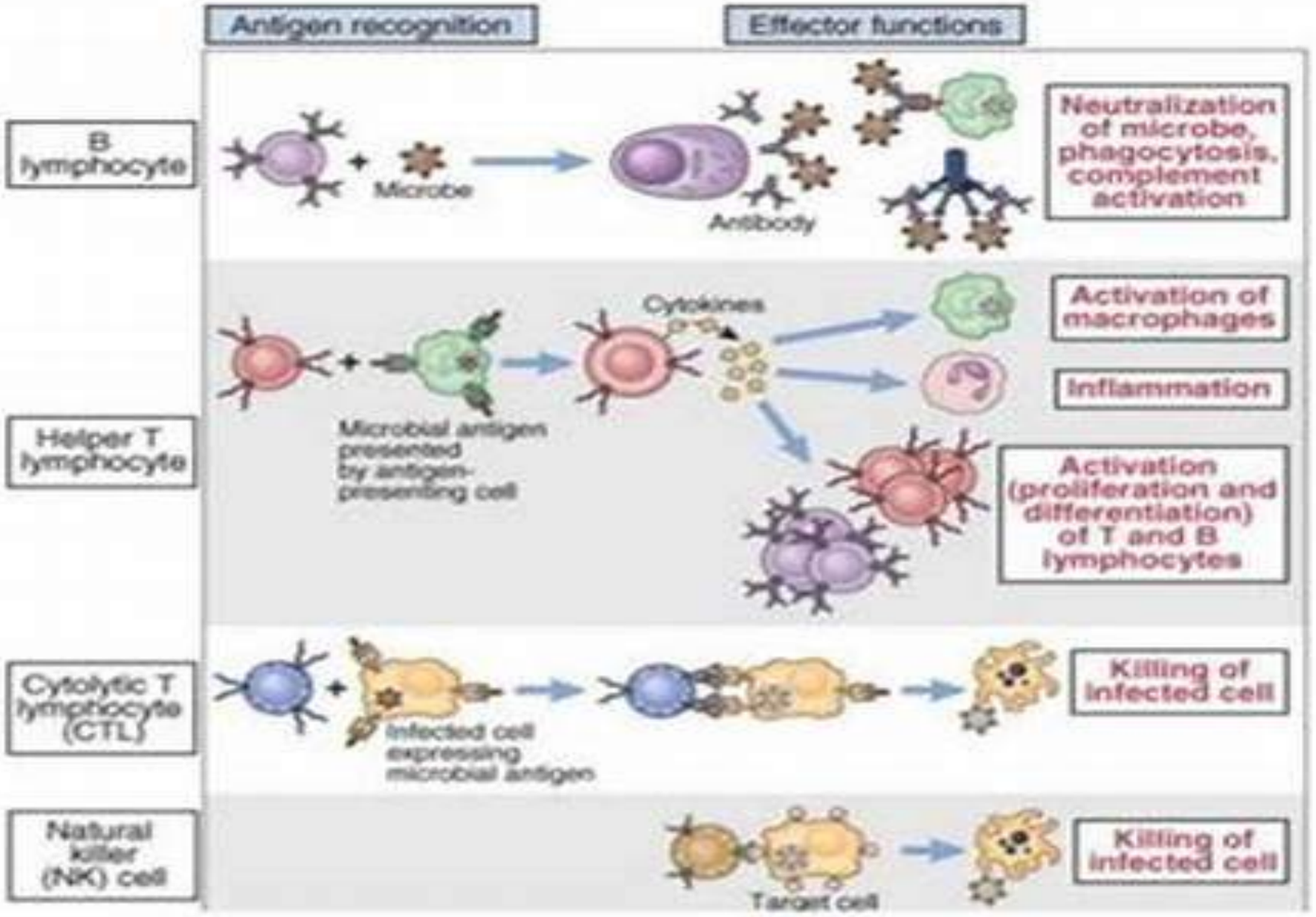
- ➤**Mononuclear phagocytes**, phagocytic cells including monocytes, macrophages, and dendritic cells.
- ➤The main function of **monocytes**, and their macrophage progeny, is to **internalize** pathogens and dead/dying cells and **degrade** them in an organelle that has a **low pH** and is filled with hydrolytic enzymes: the **phagosome**.
- ➤At other mucosal sites, **macrophages** are crucial for the maintenance of barrier homeostasis, adopting barrier-specific functions that support health.
- ➤**The main function** of **dendritic cells** is to **internalize** and **process** foreign particles to generate small peptide antigens that can be presented on their cell surface to T cells.
- ➤Therefore, these cells are considered “professional” antigen-presenting cells and are key initiators of the **adaptive immune response**

- **The complement system** is a major arm of innate immunity that enhances pathogen clearance by **promoting** pathogen phagocytosis, antigen **presentation**, and immune cell **activation**, and can also attack the cell surface of any invader.
- When the **Complement** dysregulated and has been shown to contribute to pathology in diseases such as **cancer** and **auto-inflammatory diseases**; in particular, excessive complement activation is seen in patients with periodontitis.
- **Cells of both the innate and adaptive immune systems** include innate lymphoid cells (ILCs), natural killer (NK) cells, and gamma delta (γδ)-T cells
- These cells are all at **low** frequencies in peripheral blood but are **enriched** at mucosal barrier sites.

Adaptive immunity

- **T cells to** become activated, **antigen** must be processed and bound to a class I or class II major histocompatibility complex (MHC) molecule on the surface of an antigen-presenting cells.
- **There are 2 types of T cells**: **CD4+ and CD8+ T cells**.
- **Activated CD8+ T** cells proliferate and differentiate to become **cytotoxic lymphocytes** which are highly effective killing machines capable of inducing the cell death of multiple target cells presenting their specific antigen.
- **CD4+ T cells** are activated, so they differentiate into different subsets of **T-helper**
- **Th17 cells** have been identified recently, that produce **cytokines IL-17A and IL-17F** which is **vital** for defending against **fungal infection**, and individuals with defects in the generation or function of this subset frequently present with persistent candidiasis.
- **Th17 cells** are key **mediators** of pathology in periodontitis, and that targeting these cells could provide a novel opportunity in the treatment of this disease.


1. DIRECT PRESENTATION
Infected dendritic cell
MHC I:
Antigen
CD8
TCR
T Cell
2. CROSS-PRESENTATION
Infected cell
Phagocytosis
and antigen
processing
T Cell
3. CROSS-DRESSING
Infected dendritic cell
Exosomes or
Extracellular vesicles?
MHC I:
Antigen
Transfer of
peptide:MHC
complexes by
trogocytosis
T Cell



The principal cells of the immune system are lymphocytes, antigen-presenting cells, and effector cells.

- **IgE** preferentially **bind** to antibody receptors expressed on **mast cells**, triggering the **release** of **histamine during parasitic worm infection and allergy.**
- **IgG** is the dominant antibody found **in plasma** and can be transported **across** the **placenta** to impart a degree of fetal protection.
- **The mouth** is part of the mucosal immune system, embracing all mucosal epithelium including that of the gut, lungs, respiratory and genital tracts, breast, and eyes.
- These surfaces are protected by **mucins** but adaptively by **secretory IgA**, which can be induced by immunization in the gut or nose and independently from serum IgA.
- **Antibodies** found in secretions, such as **saliva** or **bronchia**l secretions, are usually **IgA** (or sometimes IgM) produced by **plasma cells** within mucosal tissues.

Primary immunodeficiencies (PIDs)

- **(inborn errors of immunity**) include a **group** of more than 300 genetic disorders
- It caused by **single-gene mutations** and impair specific mechanisms of immune function.

➤The **clinical** presentation of PIDs is **variable** and often includes **severe** or **unusua**l infections with **a single type** of infectious agent.

➤International Union of Immunological Societies (IUIS) classification of PID diseases into **NINE categories** based upon the segment of the immune system affected, and it provides a clinically oriented strategy for disease categorization that can facilitate diagnosis and management.

➤Multiple PIDs present with significant oral manifestations, ranging from **oral infections** to **severe periodontal disease**, **craniofacial anomalies, and malignancy.**

Common oral manifestations in primary immunodeficiency

1. Recurrent herpetic infections// T-cell/NK T-cell function

2. Human papilloma viruses //B-cell
3. Odontogenic infections //Defects in **IL-17-**dependent responses
4. Chronic mucocutaneous candidiasis //Neutropenia
5. Aggressive periodontitis in children and young adults//Autoinflammatory syndromes (periodic fevers, PFAPA (periodic fever, aphthous stomatitis, pharyngitis, adenitis), and others. Neutropenia/defects in neutrophil motility/function PID with HSV susceptibility
6. Recurrent oral ulcers// Immunodeficiencies with severe HPV susceptibility

7. Head and neck squamous cell carcinoma// Immunodeficiencies with severe HPV susceptibility

Immunodeficiencies Affecting Cellular and Humoral Immunity (T Cells/B Cells)

- It affects the **development and function** of T cells and B cells (adaptive).
- They are also called **combined immunodeficiencies** (CIDs)
- **Patients** with this condition are **born** with almost **no T cells**
- Although many patients with SCID may have **B cells**, **antibody production** is **absent** because there **is no T-cell help**.
- **First few months of life** with life-threatening infections.
- Without curative therapy (hematopoietic stem-cell transplantation or gene therapy), patients typically **die from** overwhelming infection **before** 1 year of age.

Predominantly Antibody Deficiencies

- **B- cells** differentiate into **plasma cells** that produce antibodies (immunoglobulins).
- **Human antibodies are classified into five isotypes:** (IgM, IgD, IgG, IgA, and IgE) according to their **H chains**, which provide each isotype with distinct characteristics and roles.
- **IgG** is the **most** abundant antibody isotype **in the blood** (plasma), accounting for **70–75% of human immunoglobulins**.

Antibody deficiencies are categorized into the following:

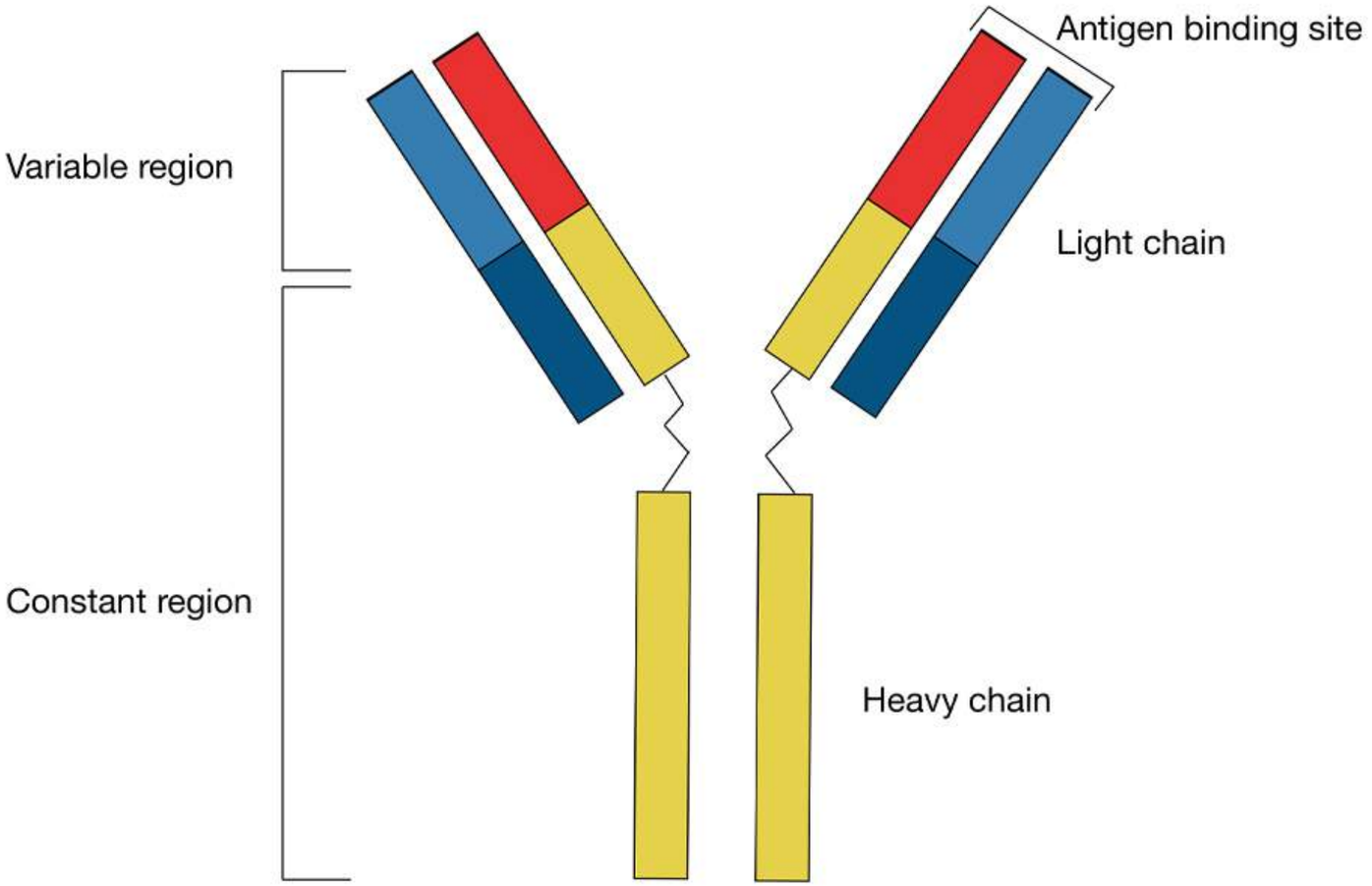
1)Severe reduction in **all serum Ig** isotypes with **absent** B cells

2)Severe reduction in **at least two serum Ig** isotypes with **normal** or **low** numbers of B cells

3)Severe reduction in **serum IgG & IgA** with increased **IgM** and **normal** numbers of B cells

4)Isotype or light-chain deficiencies with **normal** numbers of B cells

- **Patients** with **antibody deficiency** commonly present with **recurrent bacterial** infections of the upper and lower respiratory tracts (ear i, sinus i, and pneumonia,odontogenic infections) from encapsulated bacteria, such as Streptococcus pneumoniae.



Immunoglobulin structure

Diseases of Immune Dysregulation

- Numerous Primary immunodeficiencies present with features of **dysregulated inflammatory responses** that often lead to autoimmune phenomena, including cytopenias and solid organ autoimmunity, in addition to lymphoproliferation and malignancy. **Subcategories of PID with immune dysregulation include the following:**
- 1)Regulatory T-cell defects
- 2)Autoimmune lymphoproliferative syndrome
- 3)Immune dysregulation with colitis
- 4)Familial hemophagocytic lymphohistiocytosis syndromes
- 5)Autoimmunity with/without lymphoproliferation.
- The treatment of immune disorders with coexisting immune deficiency and immune dysregulation is challenging, as it requires careful balancing of immunosuppression and control of infection.

genital Defects of Phagocyte Number and/or on

- **P es** protect the body from harmful **bacteria and fungi** and initiat ement with adaptive immune responses.
- Throu gocytosis and release of immune mediators, these cells also play l roles in wound healing as well as in the resolution of inflamma **Main subcategories in this section include the following**

1)Congeni ropenia (due to defective neutrophil development).

2)Defects i phil **motility.**

3)Defects i id respiratory burst.

4)Non-lyn defects (which include defects in the development of monocyt phages)

- **Co neutrophil** defects and defects in neutrophil motility and fun e been linked to severe aggressive periodontitis at a young as recurrent oral ulcerations.

Congenital Neutropenia

➤Congenital neutropenia is caused by mutations in genes affecting granulopoiesis (development of neutrophils in the bone marrow).

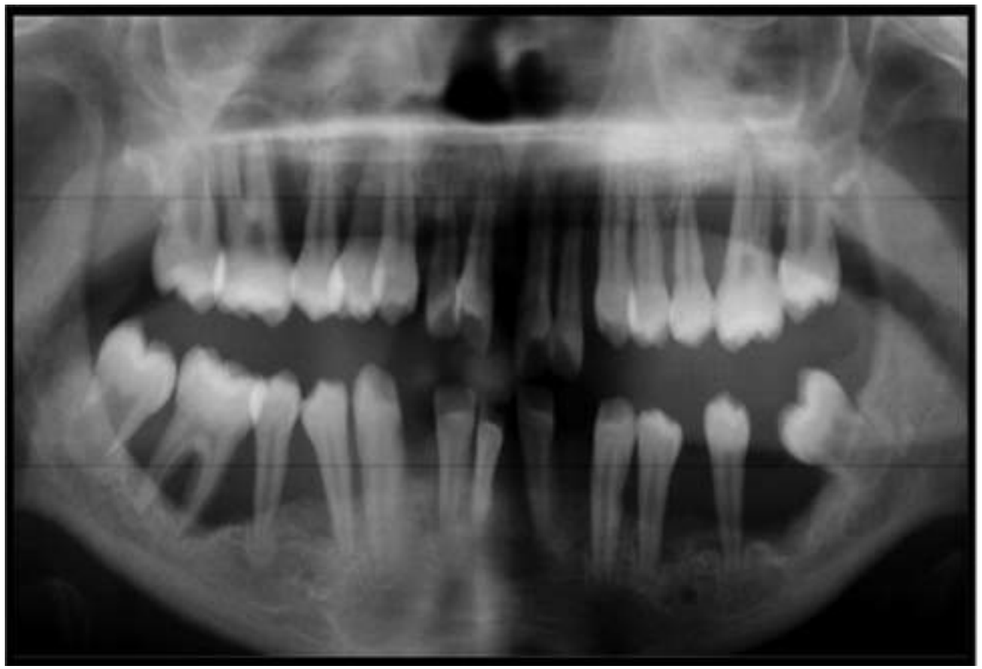
➤Patients with such mutations have peripheral neutrophil counts below 0.5 × 109/L (1.5– 1.8 × 109/L in health) and frequent bacterial/fungal infections, as well as severe periodontitis that begins in childhood.

❑Granulocyte colony-stimulating factor (G-CSF) **treatment** leads to improvement of infection susceptibility with varying results in the resolution of periodontitis.

❑Hematopoietic Stem-cell transplant has been shown to reverse the phenotype of periodontitis in these patients.

Leukocyte Adhesion Deficiency I

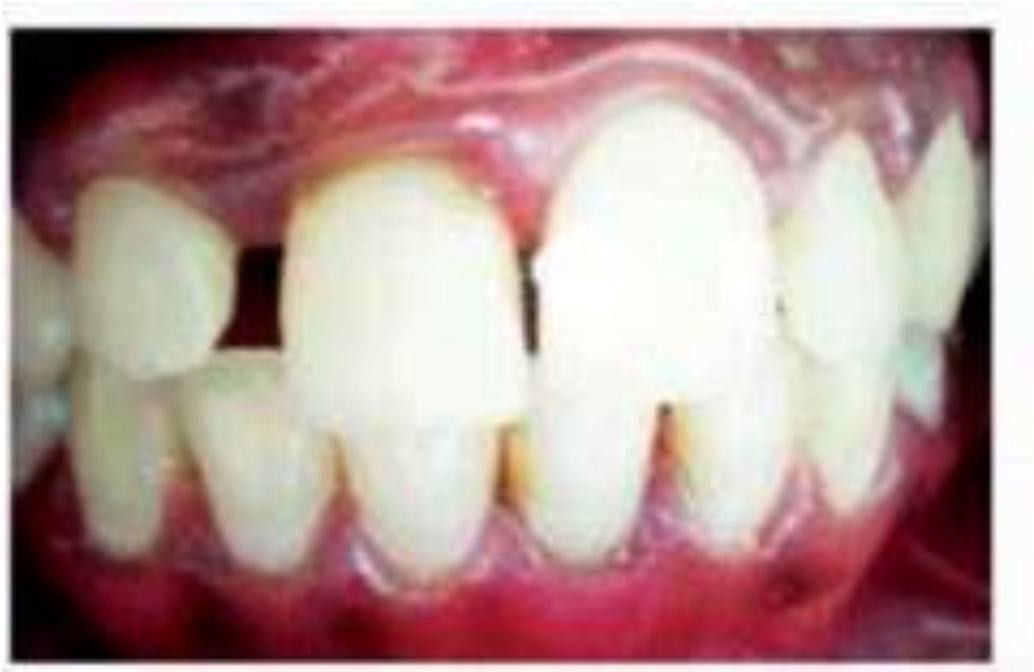
- **Is a rare** disorder **of leukocyte adhesion** and **transmigration**, which results from mutations in the ITGB2 gene.
- **Deficiency in CD18 prevents** neutrophil adhesion to endothelial surfaces and extravasation into tissues, results in **severe tissue neutropenia**.
- Patients with disorder suffer from recurrent infections, defective wound healing, and in the oral cavity present with severe to aggressive periodontitis and recurrent oral ulcers.
- **Periodontitis** in these patients has been shown to be recalcitrant to standard-of-care treatment with **loss of dentition in the teenage years.**



Severe periodontitis in leukocyte adhesion deficiency-1. Panoramic radiograph of a 13-year-old male with leukocyte adhesion deficiency-1. Severe (almost complete) bone loss is evident through the entire dentition.

Localized Juvenile Periodontitis (LIP)

- Is a **genetic defect** impairing for mylpeptide-induced chemotaxis of neutrophils, which presents with specific predisposition to a **severe but localized form of periodontitis** in the **teenage** years.



Defects of Intrinsic and Innate Immunity

The **innate immune system** typically provides initial nonspecific immunity to pathogens, including initial recognition and responses, and is mediated primarily through **phagocytes**, Antigen-presenting cells(**APCs)**, and **innate lymphocytes.**

➤Susceptibly to **viral infection** is **most** often related to **defects in NK cells** and **innate lymphocytes** that protect the body from HSV, VZV, Epstein–Barr virus (EBV), and cytomegalovirus (CMV) infections and play a role in tumor surveillance.

Three subcategories in this section are related to viral susceptibility:

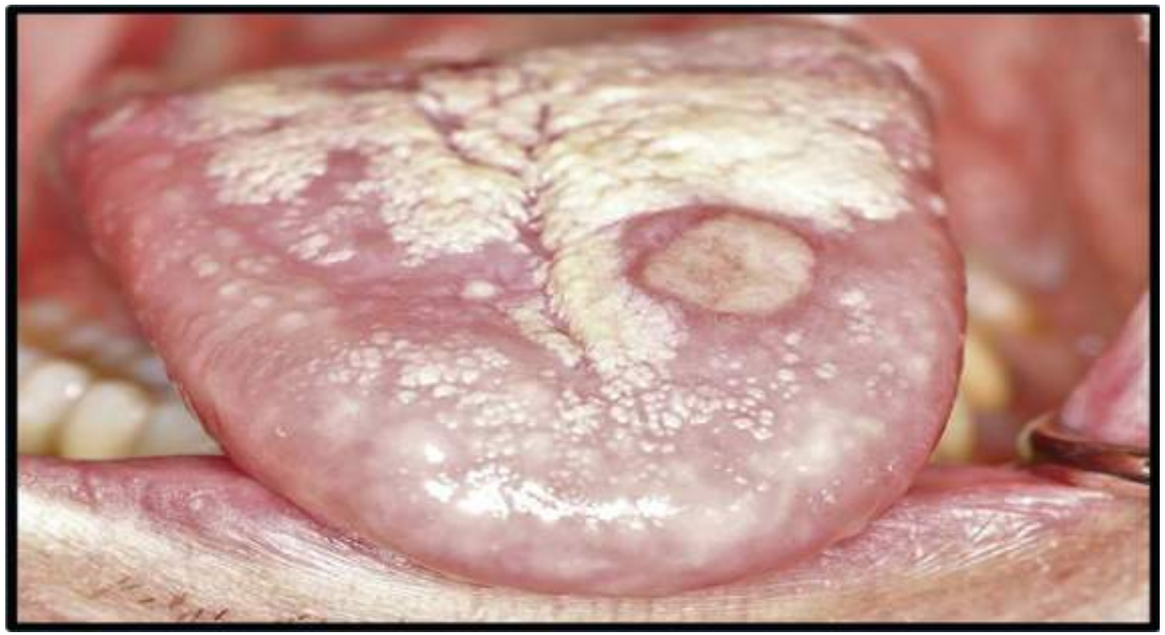
1.Epidermodysplasia verruciformis (HPV susceptibility).

2.Predisposition to severe viral infection (NK/T cell deficiencies).

3.Herpes simplex encephalitis due to defects in signaling in resident central nervous system (CNS) innate cells.

Predisposition to fungal disease Is associated with **defective recognition of fungi**, leading to invasive fungal disease) or defective IL-17 responses (leading to mucocutaneous candidiasis).

- **Warts**, **hypogammaglobulinemia, recurrent infections**, and **myelokathexis (WHIM)** It is caused by gain-of-function mutations in the chemokine receptor CXCR4. (impaired egress of mature neutrophils from bone marrow). **Mucocutaneus (oral) candidiasis;** Defective responses to the **IL-17 cytokine.**



Severe oral candidiasis in a patient with IL-17 deficiency.

Auto-inflammatory Disorders

Overactivation of innate inflammatory pathways occurs in **a nonspecific**, antigen independent manner and most commonly will cause recurrent fevers, skin rashes, and tissue damage. **Genetic testing** is necessary to confirm the diagnosis.

- **Subcategories in this group include the following:**
- **1)Type I** interferonopathies. Defective regulation of type I interferon response is associated with severe inflammatory phenotypes and autoimmunity, presenting as **atypical, severe, early-onset rheumatic diseases.**
- **2)**Defects affecting the inflammasome. The **inflammasome** is a multiprotein intracellular complex that detects microorganisms and cell damage–related mediators and acts to activate pro-inflammatory cytokines such as IL-1β and IL-18.
- **3)** Non-inflammatory-related conditions, including (pyogenic sterile arthritis, pyoderma gangrenosum, acne). **Typical oral manifestation** for many of the auto-inflammatory syndromes is recurrent oral ulcers during periods of disease activity and inflammation (most prominent in periodic fever, aphthous stomatitis, pharyngitis, and adenitis).

Complement Deficiencies

- The complement arm of the immune system **protects** the body from **bacterial** pathogens by opsonizing (more susceptible) bacteria and leading to their phagocytosis and destruction.
- Additionally, complement proteins also **play a role** in **clearance** of apoptotic cell debris, which is necessary for the resolution of inflammation.
- Defective clearance of apoptotic cell debris is linked to **persistent** inflammation and autoimmunity.
- **Complement defects** have not been clearly linked to **oral phenotypes** to date.

Autoimmune diseases

- An **immune-mediated** response **against self**.
- Organ-specific autoimmunity (such as primary biliary cirrhosis) to organ-specific with systemic manifestations (such as Sjögren syndrome) to multiorgan systemic disease (such as SLE).
- **Common pathogenetic mechanism is the breakdown of immune tolerance**
- Genetic susceptibility and environmental triggering is thought to underlie the pathogenesis of **all** autoimmune disorders.
- **The orofacial area, oral mucosa and the salivary glands**, is affected either **directly** as a manifestation of their clinical phenotype, or **indirectly** due to possible comorbidities or adverse effects of the **medications** used for treatment.

Sjögren Syndrome

- ➤Is an autoimmune disorder in which **immunocytes** damage the salivary, lacrimal, and other exocrine glands and is thus termed an **autoimmune exocrinopathy**.
- ➤**Dry mouth** and **dry eyes** are seen with **lymphoid infiltrates** in these and other exocrine glands and serum autoantibodies.

- **Sjögren syndrome has two major clinical forms:**

- ➤**Primary Sjögren syndrome (SS-1),** in which dry eyes and dry mouth are seen in the **absence** of a connective tissue disease.
- ➤**Secondary Sjögren syndrome (SS-2)**, **which is more common**, in which eyes and dry mouth are seen together with other autoimmune diseases, usually of connective tissue—most usually **rheumatoid arthritis**, SLE, polymyositis, scleroderma, or mixed connective tissue disease.
- ➤**Sjögren syndrome** shows a wide spectrum of clinical manifestations and new diagnostic criteria tend **not** to distinguish between the two clinical forms.

Systemic Lupus Erythematosus(SLE)

- **SLE** is **chronic inflammatory autoimmune disorder** that is characterized by insufficient immune tolerance **to** nuclear antigens and pathologic production **antinuclear antibodies (ANA)** such as those **against double-stranded (ds) DNA**, are a hallmark of lupus.
- The role of **genetic susceptibility** in **SLE** is evident from the high heritability (43.9%) and the **relative risk** (5.87%) in **first degree** relatives of patients with SLE.
- **Environmental factors: viral** and other **microbiome** triggering has been extensively hypothesized. **Hormonal deregulations** and other **environmental** triggers, such as ultraviolet radiation, tobacco consumption, and physiologic factors, have been investigated.
- **Clinical Features** ➤(females are affected 1.2–15 times more than male. **SLE** may be difficult to diagnose, especially in the **early stages** (constitutional symptoms), such as fatigue, headache, arthralgias, lymph node enlargement, fever, and significant weight loss, occur, causing diagnostic **dilemmas** with other autoimmune connective tissue diseases as well as neoplastic processes or infections.

SLE may be characterized by the involvement of various specific organs.

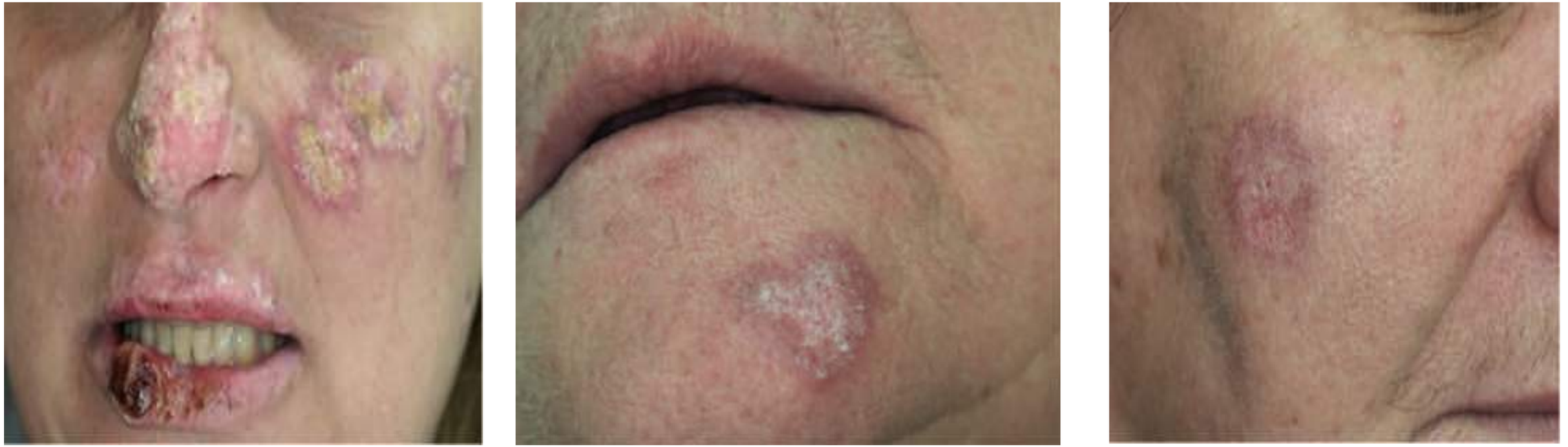
- **1.Renal disease**, The term lupus nephritis, which has been used to describe kidney involvement in lupus patients.
- 2.The **musculoskeletal system** is also commonly affected
- **3.Arthritis and arthralgias** are a dominant feature of SLE.
- **4.Cardiovascular** manifestations are also common in SLE and typically include vasculitis and pericardial effusions
- 5.Involvement of the **central or peripheral nervous system** in SLE may be associated with poor prognosis.
- 6.Anxiety, mood disorders, psychosis, seizures, headaches, and myelin defects are examples of CNS manifestations in SLE, while various types of peripheral neuropathies have also been described.
- 7.Pulmonary involvement, gastrointestinal disease, genitourinary disorders, ocular manifestations.
- **Mucocutaneous Manifestations**

➤**Most** lupus patients will develop cutaneous and mucosal lesions during their disease.

➤The most common lesion is a facial eruption that characterizes acute cutaneous lupus erythema (also known as the “butterfly rash”), presenting as erythema in a malar distribution over the **cheeks and nose** (but sparing the nasolabial folds) that appears after **sun exposure**.

➤**Photosensitivity** is also a common theme for skin lesions associated with SLE

SLE

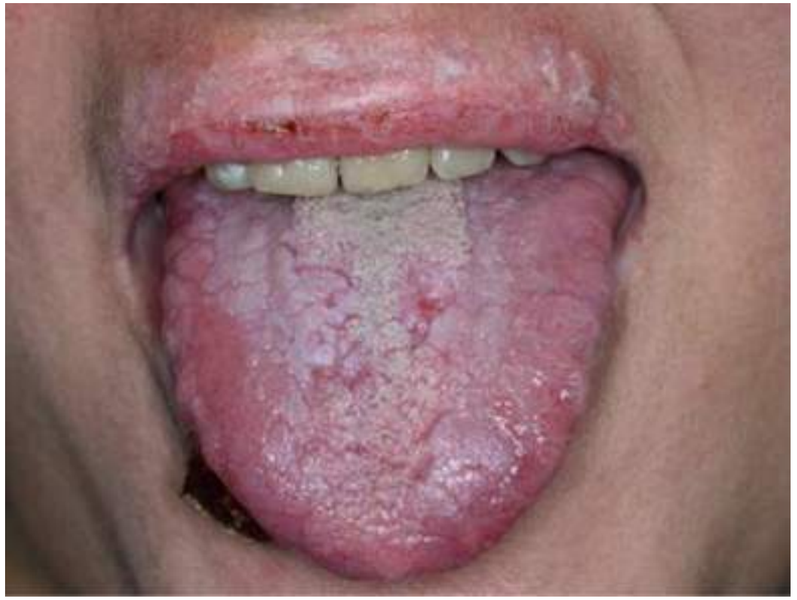


Extraoral cutaneous lesions in systemic lupus erythematosus (SLE). (A) Diffuse discoid lesions on the skin of a patient with SLE with development of squamous cell carcinomas on the vermillion border of the lower lip. Right lower lip presents with exophytic mass and ulcerations. (B–C) Discoid lesions on the facial skin of another patient with SLE.

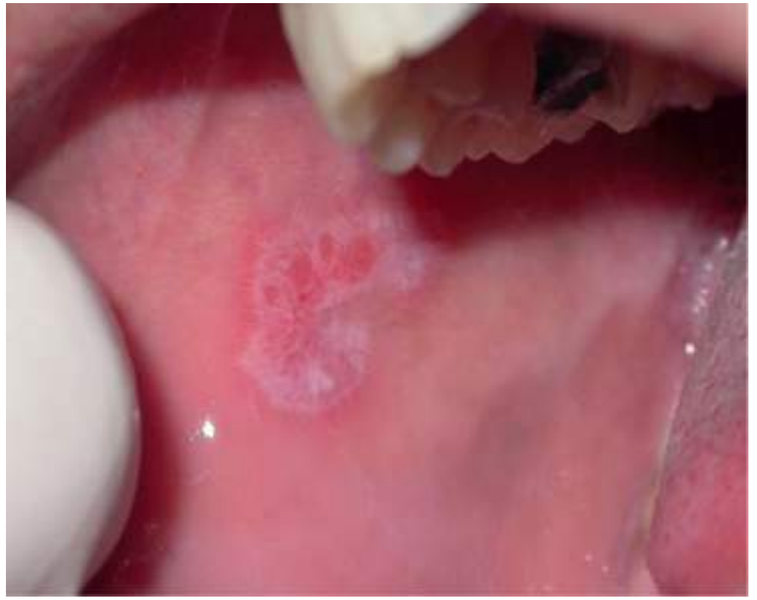
Oral Manifestations

- Typically, oral lesions in SLE occur in approximately 5–40% of patients, include **nonspecific ulcerations** and **erythematous or discoid lesions**, and predominantly affect the **palatal mucosa**, **buccal mucosa**, and **gingiva**
- **Oral ulcerations** are common and included among the classification criteria of SLE.
- The vermillion border of the lower lip can be **characteristically** involved (lupus cheilitis).
- The temporomandibular joint (TMJ) can also be affected.
- The oral manifestations of the cutaneous forms of lupus erythematosus (CLE) closely mimic those of oral lichen planus. The most common sites of involvement are the **lips** (vermillion border and labial mucosa) and the buccal mucosa.
- Oral lesions (such as discoid plaques, cobblestone, or macules) are correlated to the **disease activity.**
- On **rare occasions**, squamous cell carcinoma may arise in discoid lesions affecting the lips or even intraoral sites. So, it is considered an oral, potentially malignant disorder based on the World Health Organization (WHO) classification.

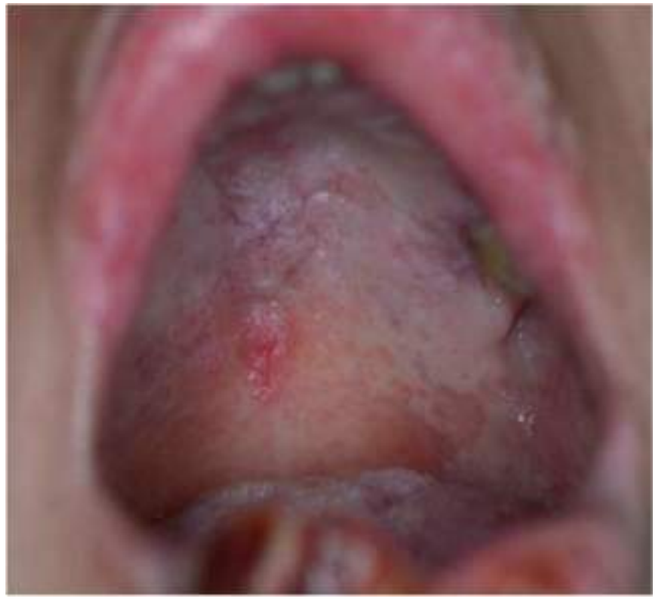
Systemic Lupus Erythematosus(SLE)



Nondescript widespread white coating on dorsal surface of tongue



Central erythematous area surrounded by radiating white striations



Nondescript white and red lesions on hard palate

Laboratory Findings

- Anemia (mainly related to chronic disease, iron deficiency, or hemolysis).
- **Leukopenia** (lymphopenia and/or neutropenia),
- Thrombocytopenia (autoimmune or related to hypersplenism or hemolysis) and their extent correlates with disease activity.
- Erythrocyte sedimentation rate (ESR) is usually elevated along with **normal** C-reactive protein (CRP), which is a characteristic feature of SLE.
- ANAs **are positive** in more than 95% of SLE patients and, despite their lack of specificity (being detected in several other autoimmune diseases and in healthy subjects), can be used as a reliable screening test.
- **Anti-double-stranded DNA (anti-dsDNA)** and anti-Smith antigen (anti-Sm) antibodies **are positive** in approximately 50–70% and 30–40% of SLE patients, respectively.
- Decrease in complement markers (hypocomplementemia), especially CH50, C3, and C4.

Management

➤**Treating SLE** is challenging and depends on the extent of manifestations, the type of target organ(s), and the severity of disease as well as possible morbidities

➤**Corticosteroids** remain the main choice during management of SLE, due to their effectiveness in limiting disease and flares. However, because of common complications after their long-term use (such as diabetes, infections, osteoporosis, hypertension, and avascular necrosis of bone).

- Other I**mmunosuppressants** include cyclophosphamide, mycophenolate mofetil, and azathioprine, which should also be used with caution due to their toxic effects.
- **Biologic agents** affecting the B-cell component of the immune system, including belimumab, rituximab, ofatumumab, and atacicept, that present efficacy in limiting disease activity.

For the management of oral complications of lupus erythematosus, Topical or intralesional administration of corticosteroids seems to be the **first treatment option.**

Systemic Sclerosis (Scleroderma)

➤The word “scleroderma,” meaning hard skin; characterizing a diverse group of disorders that exhibit **excessive cutaneous fibrosis** .

➤Major disease subsets include **localized scleroderma** (LSc), which is **limited to skin** involvement, and **systemic sclerosis** (SSc), a heterogenous disease, which affects a **wide range of organs in addition to the skin,** leading to significant morbidity. **SSc is subclassified into multiple subsets of disease:**

- **1.Limited cutaneous** SSc; refers to skin lesions in distal areas.
- **2.Diffuse cutaneous** SSc involves the proximal limbs or trunk, with a short history of Raynaud’s phenomenon and frequent renal or cardiac involvement as well as lung fibrosis.
- **3.Sine scleroderma** with clinical and serologic evidence of SSc without skin sclerosis.
- **4.SSc overlap syndrome** refers to one of the subsets in addition to manifestations from other autoimmune diseases. **Both LSc and SSc are considered rare entities**; **women** are more commonly involved than men and a racial predisposition for Caucasian.

Pathogenesis

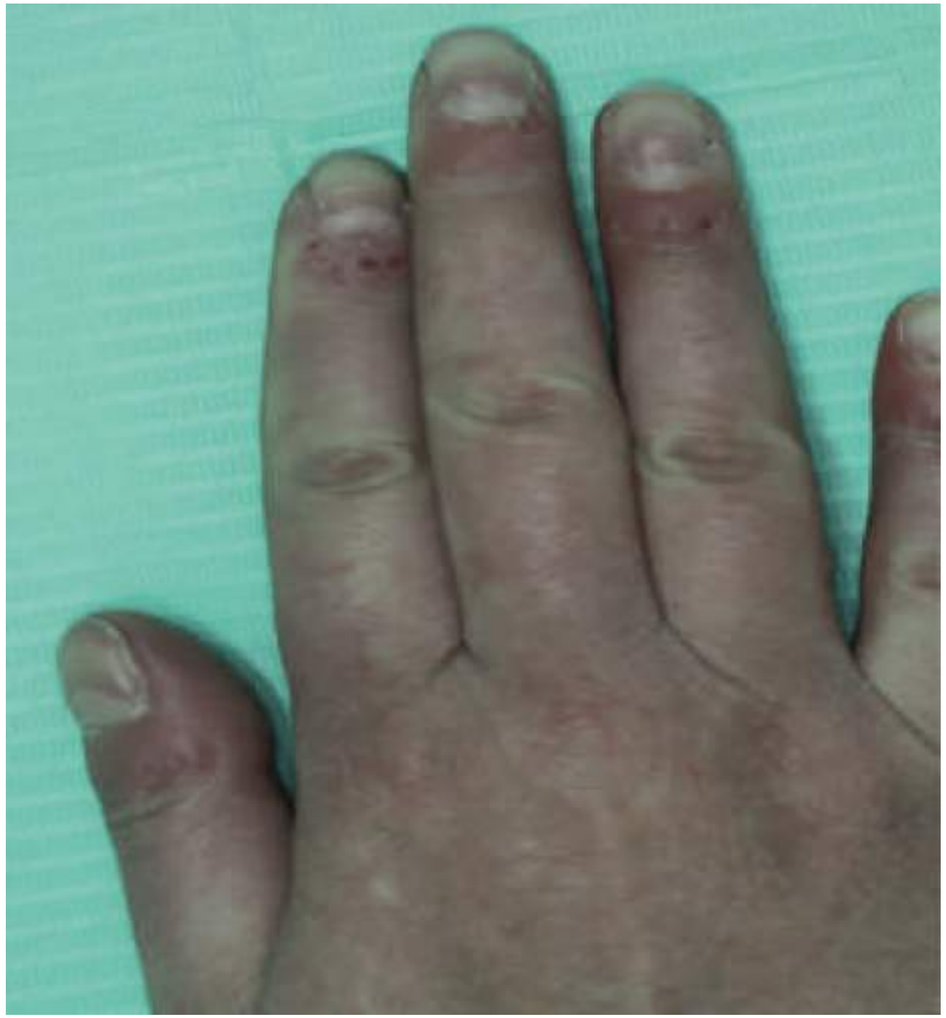
➤Immune activation, vascular damage, and excessive synthesis of extracellular matrix.

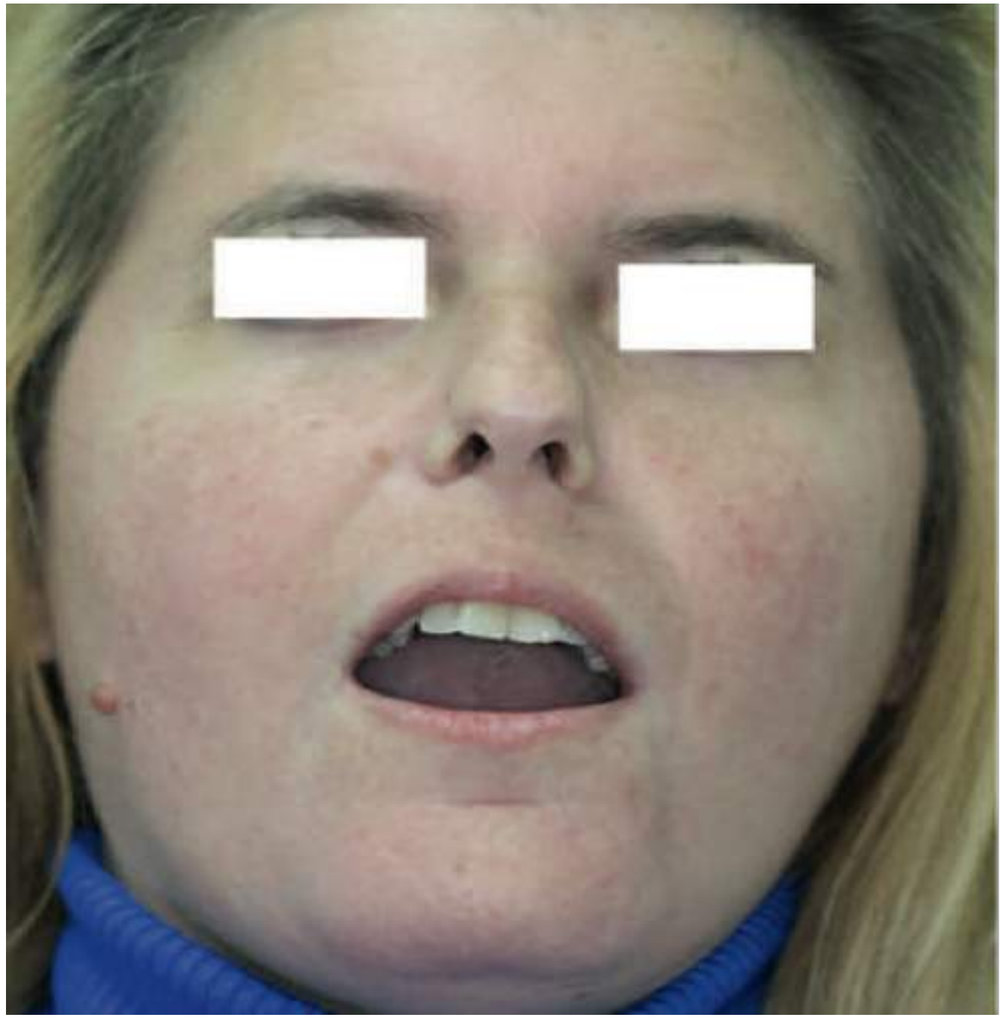
➤Interplay between **early** immunologic events and **vascular changes**, which result in the generation of a population of activated **fibroblasts** which is the effector cell in the disease.

Clinical Features

Cutaneous Manifestations

- **Skin thickening** is the hallmark of cutaneous involvement in SSc.
- Skin involvement may be of acute onset in diffuse SSc or **more slowly** growing in limited SSc.
- The extremities and especially the **fingers** may be affected, causing a “puffy” appearance; progressively, the thin overlying skin becomes prone to ulceration, and, in advanced stages, deformities may occur.
- C**alcifications** of the skin may occur with the clinical presentation of multiple **subcutaneous nodules**.
- Hypo- or hyperpigmented areas as well as telangiectasias may be observed.





Extraoral manifestations in systemic sclerosis (SSc). (A) Finger involvement in SSc with thin, tense skin prone to ulceration. (B) Mask-like appearance of the face in a patient with SSc.

- **Raynaud’s phenomenon** is the most common initial sign, developing simultaneously or prior to cutaneous involvement.
- Musculoskeletal involvement takes the form of generalized arthralgias and morning stiffness resembling RA.
- Myopathy is also common and is accompanied by **elevated** serum muscle enzymes.
- During late stages, **fibrosis** of the gastrointestinal tract may result in malabsorption
- Pulmonary complications including interstitial lung disease and pulmonary hypertension
- Inflammatory processes may involve the heart, causing arrhythmias, hypertension, pericardial effusions,
- **Renal involvement** is common and, before the initiation of angiotensin-converting enzyme inhibitors, was the **most common cause of death in SSc patients**
- **Renal crisis** is most encountered in patients with early onset of diffuse scleroderma.

Oral Manifestations

- The lips become rigid, which, in addition to the generalized skin sclerosis, results in a **mask-like appearance of the face.**
- Mouth opening is significantly **decreased** (microstomia) and the tongue becomes hard, leading to difficulties in speech and swallowing.
- Telangiectasias are also frequently present.
- Mandibular movement may be limited secondary to muscular fibrosis
- Myofascial pain, especially involving **the masseter and posterior belly of the digastric muscle**, feeling of locked jaw, and arthralgia are common symptoms in SSc patients
- Mandibular resorption, either at the **angle** of the mandible**, condyles**, **coronoid** processes, or **digastric region**
- Periodontal disease, xerostomia, and susceptibility to local infections.
- **Xerostomia**, related to fibrosis of the salivary glands, secondary Sjögren syndrome, or medications, may predispose to dental and periodontal disease as well as candidiasis.

Laboratory Findings: The following **routine laboratory tests** are recommended in patients with **suspected SSc**:

- CBC and differential, which may reveal anemia due to malabsorption of iron or gastrointestinal blood loss.
- Serum creatinine level, which may indicate renal dysfunction.
- Creatine kinase (CK), which may be **elevated** in patients with myopathy or myositis.
- Urinalysis. The following **serologic tests** may **support** the diagnosis if **positive**:
- Antinuclear antibody (ANA).
- Anti-topoisomerase I (anti-Scl-70) antibody.
- Anticentromere antibody (ACA).
- Anti-RNA polymerase III antibody.

Diagnosis is made **upon exclusion** of **similar entities** that could justify the clinical manifestations, **including generalized morphea (painless, discolored patches on skin)**. **Skin sclerosis of the fingers of both hands** extending proximal to the metacarpophalangeal joints is by itself sufficient for classification as SSc, while other clinical or serologic features are helpful classification criteria.

Management

➤The selected treatment is also based on the stage of disease and possible morbidities

➤Treatment of SSc aims at **limiting the inflammatory process** that characterizes its clinical phenotype as well as managing the distinct clinical manifestations involving separate organs.

➤Patients with limited mouth opening should undergo several **stretching exercises** that have been reported to be effective.

➤A poorer prognosis (black race or male gender).

➤**Early treatment** is considered essential to **reduce mortality**, since the progression of disease during the **first three years** is **fast.**

Rheumatoid Arthritis (RA)

➤RA is a **chronic inflammatory autoimmune disease** that is characterized by symmetric involvement of joints in a progressively destructive manner, which can cause significant disability if not properly treated

➤RA is considered among the **most common** autoimmune diseases, presenting a reported incidence of 0.5–1%.

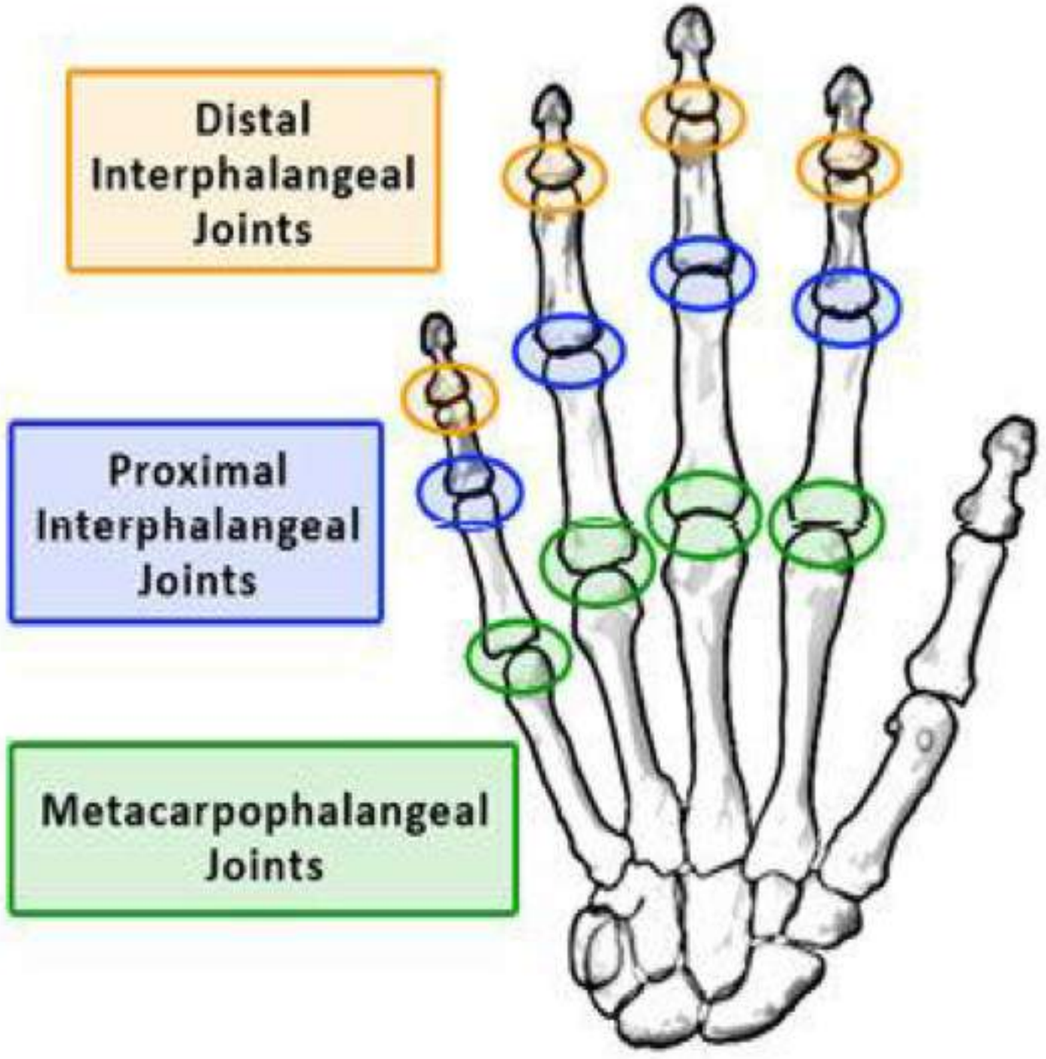
➤RA involves patients in their **middle age** with a **female predominance.**

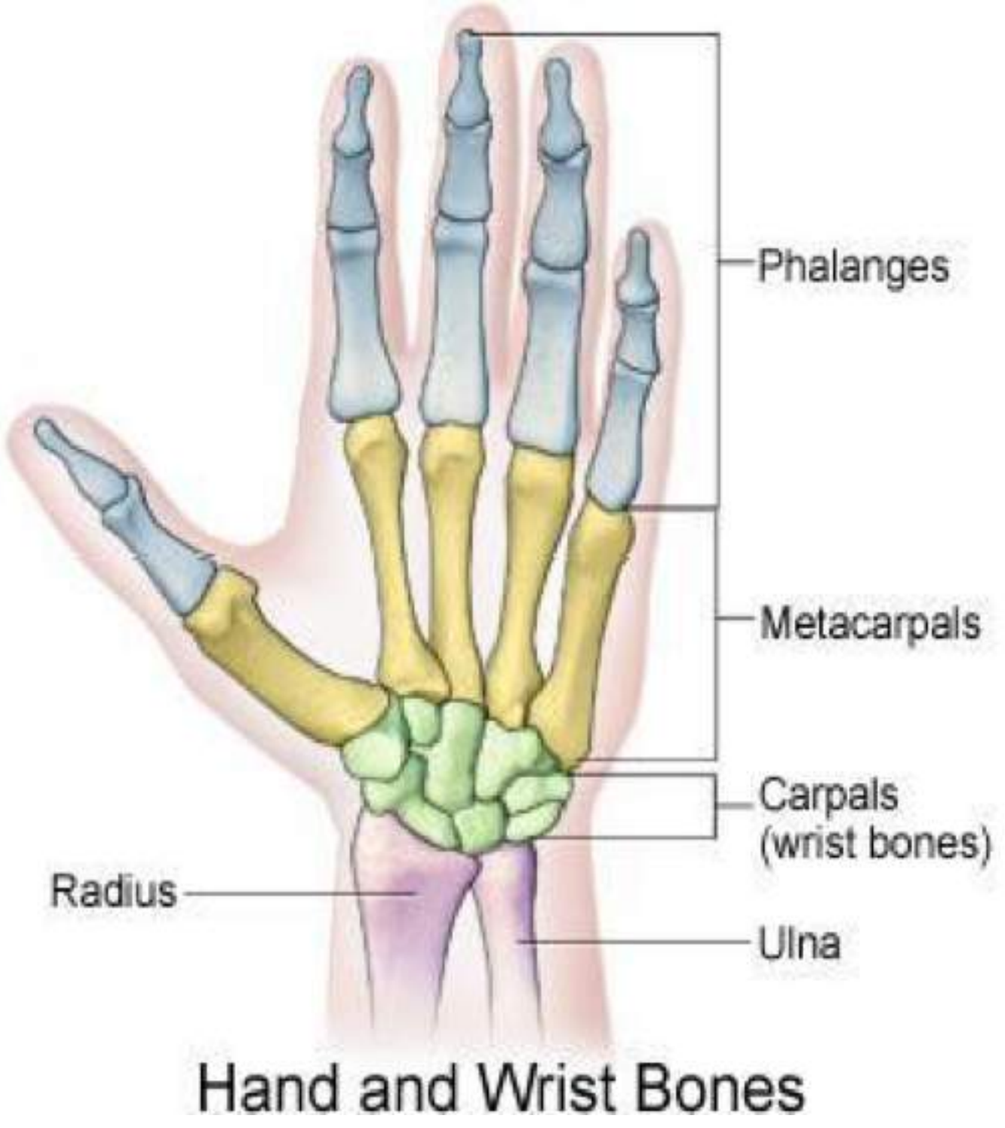
Pathogenesis (Genetics and Environment)

➤A combination of host genetic and environmental factors is thought to underlie disease triggering.

➤RA immune cell infiltration of the synovial membranes of joints with T cells, B cells, monocytes, and neutrophils leads to inflammation of synovial membranes, “pannus” (Pannus is an abnormal layer of fibrovascular tissue or granulation tissue formation) and subsequent bone and cartilage erosion.

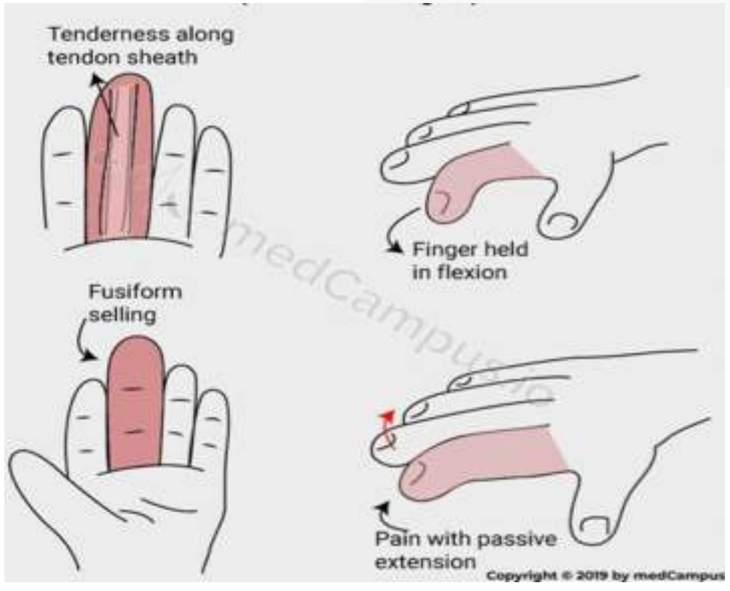
- Inflammatory mediators such as tumor necrosis factor (TNF) and IL-6 are clearly involved in disease activity.
- **One interesting aspect of the disease is that autoantibodies often develop 1–10 years prior to disease onset**.
- Specifically, antibodies to citrullinated proteins (ACPA) develop 5–10 years before disease onset
- A genetic predisposition has clearly been defined in RA, most significantly associated with **HLA class II antigens**.
- In addition to genetic susceptibility, epigenetic modifications may be observed including modified DNA methylations (methylations : is a biological process by which methyl groups are added to the DNA molecule).
- Environmental triggers including smoking, alcohol consumption, socioeconomic level, and infectious agents, such as **periodontal pathogens**, have been associated with the development of RA.





Hand and Wrist Bones


Dactylitis
HEALTHY HAND
DACTYLITIS
MEDICALNEWSTODAY


Tenderness along tendon sheath
Finger held in flexion
Fusiform selling
Pain with passive extension
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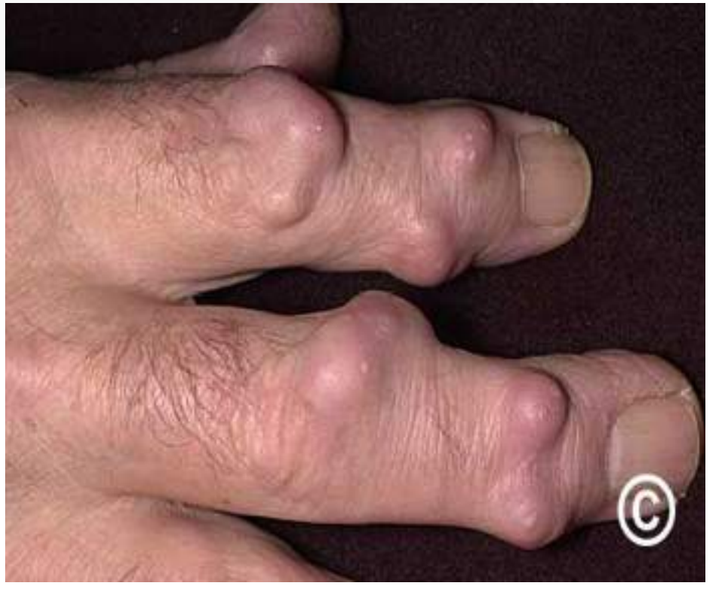


Clinical Presentation

- The inflammatory process primarily involves the wrists and metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal articulations.
- Accompanying morning stiffness lasting from 30 minutes to several hours is also common.
- The **fingers** are affected in a fusiform pattern, mainly around the joints, in contrast to **psoriatic arthritis** where the whole digit is swollen (“sausage digit”).
- ➤If RA is insufficiently treated, extraskeletal manifestations may develop.

- The occurrence of **firm masses** called rheumatoid nodules, especially in subcutaneous areas in proximity to bony prominences, is the most frequent finding.
- **Severe complications** is the **necrotizing vasculitis** of the small and medium-sized arteries, interstitial lung disease, or cardiovascular disease, with the latter being the most common cause of **mortality** among RA patients.

Intra- and Extra-oral Manifestations

- The **TMJ** is involved in almost every patient with RA according to the Helkimo index. clinical signs or symptoms of TMJ involvement, such as pain, crepitation, reduced mouth opening, and impaired movement, have been described in RA patients.
- **In advanced stages**, progressive condylar destruction may cause malocclusion and anterior open bite, joint ankylosis, and facial asymmetry **RA** may show several other manifestations in the orofacial area; secondary Sjögren syndrome, dental and periodontal disease, oral side effects of systemic medications used to treat RA have been reported.

Diagnosis is primarily made by evaluation of the clinical and immunologic findings

Laboratory Findings

♣The main laboratory findings in patients with RA include **acute-phase** reactants and autoantibodies.

♣**CRP and ESR** are the most significant markers used to detect inflammatory responses, with the **forme**r being **more specific** in measuring disease activity due to its association with inflammatory cytokines expressed in RA.

♣The main autoantibodies used for diagnosis of RA are cyclic citrullinated peptides (anti-CCP) and rheumatoid factor.

♣Both are specific markers, even though they are occasionally expressed in other diseases.

Management

- Due to significant progress in understanding of the disease, irreversible joint damage can be prevented today in 90% of patients.
- Initial-phase treatment for RA typically involves methotrexate (used as monotherapy or in combination with corticosteroids), which is considered an efficient treatment for RA and is associated with few and easily controllable adverse effects.
- Symptomatology may also be improved by non-steroidal anti-inflammatory drugs (NSAIDs), which however **do not** inhibit disease development and should be used as supplementary therapy before a definite diagnosis of RA is established.
- Subsequent treatment typically involves disease-modifying anti rheumatic drugs such as **TNF inhibitors**, **IL-6 inhibitors**, and **small-molecule inhibitors**.

Mixed Connective Tissue Disease(MCTD)

- Highlights the overlapping character between autoimmune inflammatory disorders.
- Presenting clinical manifestations in the spectrum of SLE, Sjögren syndrome, as well as inflammatory myopathies.
- **Females** seem to be more frequently involved compared to males and the disease could show an early onset.

Pathogenesis The cornerstone in the pathogenesis is the presence of the **anti-ribonucleoprotein** (RNP) antibodies. A genetic predisposition and especially the presence of distinct subsets of **HLAs** may play a key role.

Clinical Features

- ➤Clinical manifestations identical to various connective tissue diseases are present, including Raynaud's phenomenon and "puffy" or swollen hands, myositis, arthritis, interstitial lung disease, pulmonary hypertension, cutaneous lesions and alopecia, esophageal dysmotility, neurologic symptoms, as well as renal disease
- ➤**Orofacial** involvements of MCTD have **rarely** **been reported**

Diagnosis

- Is typically **difficult**. To date, various diagnostic (and/or classification) criteria have been proposed for MCTD, which, as **in every other connective tissue disease**, includes immunologic (anti-U1-RNP detection) as well as clinical parameters.

Management

- ➤Management mainly includes i**mmunosuppressants**, especially corticosteroids, as well as **steroid-sparing medications**, such as methotrexate, cyclosporine, and azathioprine.
- ➤Specific manifestations including Raynaud's phenomenon should be treated accordingly with calcium-channel blockers.

Dermatomyositis and other Inflammatory Myopathies

- ➤Inflammatory Myopathies (IM)are a complex group of diseases falling under the term “**myositis,**” .
- ➤Generally characterized by **inflammatory processes** involving the **muscles** in addition to **extramuscular** manifestations.
- ➤**Myositis** may involve adults or juveniles.
- ➤Dermatomyositis (DM) is one of the main disease subsets characterized by skin involvement accompanying the progressive muscle weakness
- ➤DM is also the **most prevalent** myopathy in **young** patients (juvenile DM).
- ➤**Myositis** may be associated with **malignant neoplasms** (cancer related myositis)
- ➤IMs are considered **rare**, males more commonly than females.
- **Laboratory and Other Findings** The main laboratory feature in IMs is the **presence of elevated muscle enzymes**, especially **Creatine kinase** (CK), which also helps determine disease activity in individual patients. **Diagnosis** Diagnosis of IMs is made upon correlation of clinical, laboratory, and histopathologic manifestations.

Pathogenesis

- IMs are generally characterized by immune and non-immune events initiated in a context of genetic predisposition as well as environmental triggers
- **Inflammatory cells** of the immune system accumulating in lesions of IMs include T cells , B cells secreting autoantibodies, and cells of the macrophage-dendritic lineage.
- **Non-immune system**, including hypoxia, endoplasmic reticulum (ER) stress, and autophagy.
- **Muscle involvement** in dermatomyositis is believed to be a result of autoimmune attack against endomysial capillaries, leading to ischemia and **atrophy of the muscle fibers .**

Clinical Features

- Dermatomyositis is characterized by varying amounts of **proximal muscle weakness** with symmetric distribution and cutaneous involvement.
- Muscle involvement may range from mild to severe causing serious disabilities
- Regarding the oral manifestations of patients with Ims, a **decrease** in masticatory forces and **increased** incidence of temporomandibular disorders (TMDs) has been reported.

Management **Treating IMs may be a challenge;**

- First-line treatment of these patients mainly includes corticosteroids in addition to reinforcement of physical exercise, followed by steroid-sparing immunosuppressive agents (including azathioprine and methotrexate).
- Intravenous immunoglobulins and biologic agents may be used in severe cases.
- While in patients exhibiting **dysphagia invasive** management or injection of botulinum toxin is proposed.
- **Plasmapheresis** (plasma exchange) may also be performed in patients with interstitial lung disease. (Plasmapheresis is often done to remove extra antibodies, abnormal proteins, or other harmful substances from the blood).
- **Oral manifestations** of DM should also be managed accordingly.
- **Follow-up** of these patients is essential to control dental and periodontal health as well as to identify early signs of cancer.
- IMs exhibit **variable prognosis** that depends on the onset of treatment and severity of organ involvement.

Granulomatosis with Polyangiitis (GPA)

?➤Also known as **Wegener's granulomatosis** is an autoimmune disease classified under ANCA-associated vasculitis (**antineutrophil cytoplasmic antibodies**)

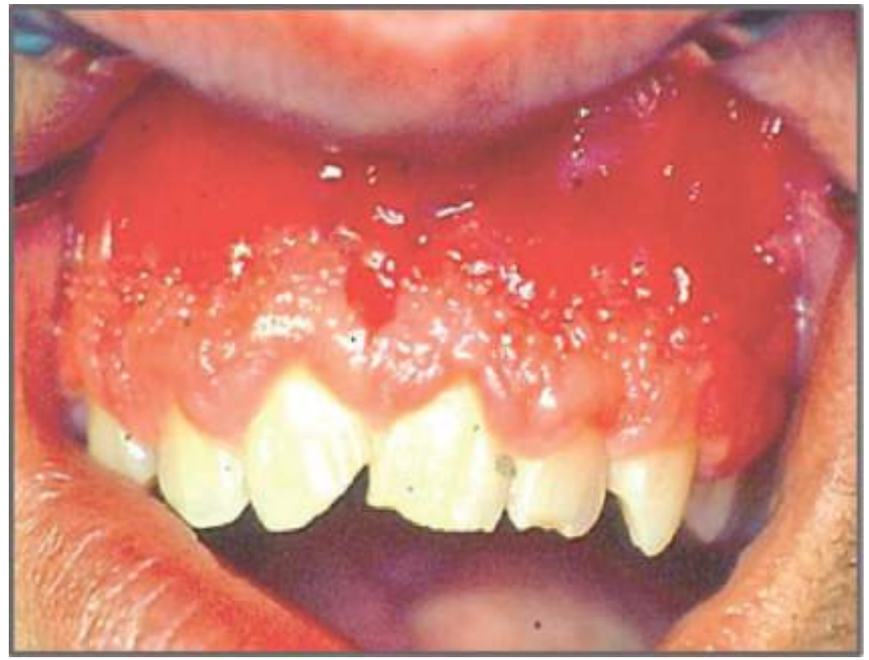
?➤**Small-vessel necrotizing vasculitis with granulomatous features**, resulting in multisystemic manifestations with significant morbidity and mortality**.**

?➤**Rare disease**, with **older** age, more than **60 years**.

- **Pathogenesis**
- The exact etiology of GPA development has not yet been fully elucidated.
- **Exposure** to external triggers, such as dust or silica, is included among the most frequent **exogenous** factors associated with GPA.
- Infectious agents, such as Staphylococcus aureus of the upper aerodigestive tract.

Clinical Features

- Upper aerodigestive tract is the predominant site.
- **Generalized forms** with major organ dysfunction and deteriorating general health.
- The ear, nose, and throat (ENT) region is considered the most involved.
- **Oral mucosal involvement** also exhibits heterogeneous manifestations.
- **Acute and rapidly** progressing lesions are observed in widespread disease, including oral ulcerations with occasional necrosis.
- **Perforation of the palate** may be observed.
- Characteristic vegetating or granular appearance of gingiva, called "**strawberry gingivitis,**" the first manifestation of GPA.



Diffuse gingival involvement in granulomatosis with polyangiitis (GPA), assuming a characteristic "strawberry gingivitis" appearance.

Diagnosis

- **Clinical** and **histopathologic** features with biopsy are essential.
- Anemia, leukocytosis, and eosinophilia may be observed.
- ESR and CRP may also be elevated, especially in **active disease**.
- Other laboratory findings (e.g., urine proteinuria in kidney involvement).
- **The most important serologic marker for GPA is ANCA (Antineutrophil cytoplasmic antibodies).**

Management

- The major **aim** of treatment for patients with GPA is to **achieve remission** and survival by minimizing recurrences and fatal outcomes.
- The **first phase** of treatment, consisting of immunosuppressive therapy (including cyclophosphamide and rituximab) in addition to glucocorticoids, and the **second phase** (remission maintenance).
- **The most common causes of death are infections and kidney failure**.

General Considerations for Dental Management of Patients With Immune-mediated Diseases

1.Susceptibility to Infections

- Dental and oral mucosal infections has been considered a risk factor for distal infections, particularly during invasive dental procedures.
- Odontogenic infections have been associated with infectious endocarditis, but also with infections in the **CNS** and less commonly with distal skeletal infections.
- Septicemia from oral infections with the organism **Leptotricia buccalis.**
- There are no specific guidelines for dental management and/or for use of antibiotic prophylaxis in patients with **primary immunodeficiencies**.

- **Common recommendations** include **aggressive prevention** to avoid and treat early oral and dental infections in such patients, close monitoring, and coordination of treatment with the medical team.
- Due to the **severity of immunodeficiency** in such patients, often dental treatment will be **advised** to be performed within the hospital setting.
- Patients with autoimmune diseases are also often considered immunocompromised, either because of the disease itself or **secondary** to the use of immunosuppressive medications.
- **Leukopenia** is also a possible manifestation of autoimmune diseases, or the medications used to treat them and is associated with susceptibility to infections.
- Patients with different levels of neutropenia concluded that **extractions** are **safe** and with few associated complications.

- There is also **no consensus** regarding the use of antibiotics in patients under corticosteroid treatment.
- **As a result, the main consideration is the potential modification of the dose of corticosteroids to prevent an adrenal crisis**.
- **Herpes zoster or HPV infection** is considered common in patients with **SLE** and could manifest in the oral cavity.
- **Oral candidiasis** may also be frequently encountered in **autoimmune disease** patients as a side effect of corticosteroid or other **immunosuppressive treatment** or a consequence of **reduced salivary flow.**
- **SLE and other autoimmune disorders lead to valvular disease**, requiring prosthesis and increasing the risk for bacterial endocarditis following surgical procedures.
- Such patients will require antibiotic prophylaxis prior to surgical procedures, based on the most recent guidelines about patients with valvular disease from the American Heart Association and the American College of Cardiology.
- Patients with **prosthetic joints do not require** antibiotic prophylaxis prior to dental procedures to avoid infection of the prosthetic joints.

2. Risk of Bleeding

➤**Coagulation** is commonly impaired in autoimmune diseases for **multiple reasons**, including:

- Thrombocytopenia associated with the disease (e.g., in SLE).
- Use of certain myelotoxic medications.
- Treatment with anticoagulants or antiplatelet regimens (in patients with risk for thrombosis).

➤Such patients may be at increased risk of bleeding after surgical interventions.

➤Recent studies suggest that **extractions** in patients with thrombocytopenia are usually **safe** and complications are **easily** managed with local measures.

➤However, patients exhibiting **a platelet count under 50,000/µL** require **platelet transfusion**, so cases with severe thrombocytopenia should be managed in a **hospital** environment.

➤With anticoagulant therapy, **INR** (PT test/PT normal)should be measured and if its value is **between 2.0 and 3.5**, **minor interventions are allowed**, while for more invasive procedures, replacement of the regimen with low molecular weight **heparin** should be considered.

➤**Discontinuation of antiplatelet therapy** should be considered prior to intervention.

➤Communication between the patient’s dental and medical practitioners is necessary.

3. Adrenal Suppression

- **Corticosteroids** are used to treat autoimmune connective tissue diseases due to their significant efficacy in **limiting** disease activity. However, their side effects, including adrenal suppression, should be taken into consideration during dental treatment. Due to absence of specific guidelines, every case should be individualized, and treatment planned with the caring physician.

4. Cardiovascular Disease

➤The general condition should be assessed before starting any minor or invasive procedure and establish a communication with the patient's physician.

➤Antianxiety techniques and pain control play a key role in the prevention of medical emergencies

5. Liver and/or Kidney Disease

- **Renal involvement** is common in patients with autoimmune diseases (lupus nephritis)
- **Renal and liver** function should be monitored, as the **doses** of common medications prescribed by the dentist may be **modified**.
- Dental procedures should be performed under appropriate conditions in patients under hemodialysis (treatment should be **performed the day after dialysis**).

6. Hyposalivation and Xerostomia

- The salivary glands are a common site of involvement by several autoimmune diseases as a part of their phenotypic characteristics, or an adverse effect of certain medications.

7. Dental and Periodontal Disease

- Periodontal disease is more **prevalen**t in patients with various autoimmune diseases.
- Appropriate periodontal treatment with frequent follow-up visits.
- **Toothbrushes** with customized handles and of special size are useful for patients displaying impaired manual dexterity (e.g., in patients with Systemic sclerosis (SSc), scleroderma or RA) or in cases of reduced mouth opening (in patients with SSc).

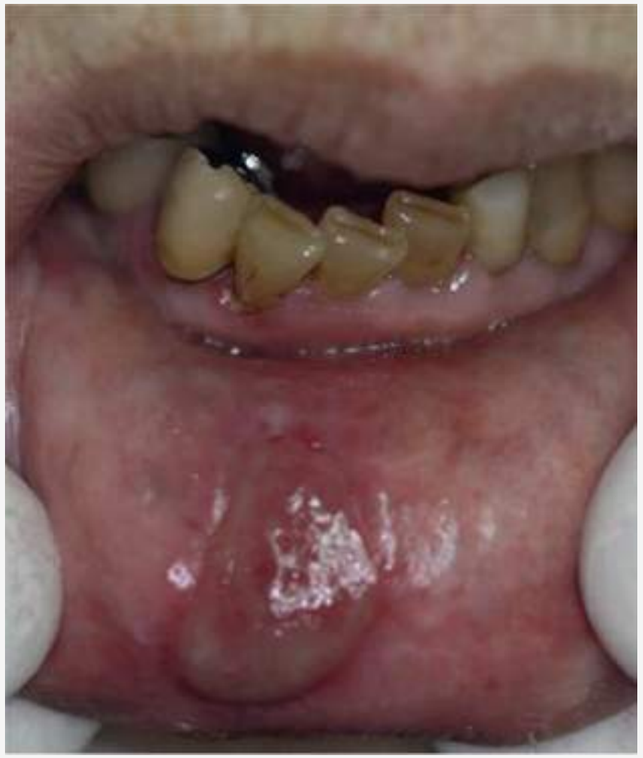
Oral Mucosal Involvement as an Adverse Effect of Immunosuppressive Therapy

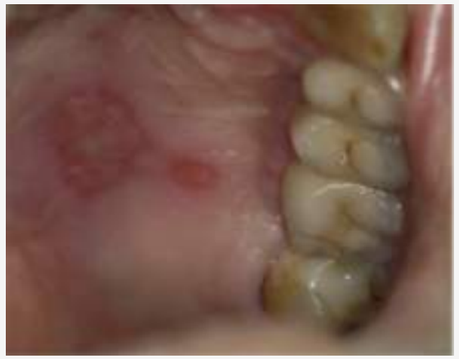
- The clinician should be aware and suspicious of these conditions, especially if their **…logi…** off…

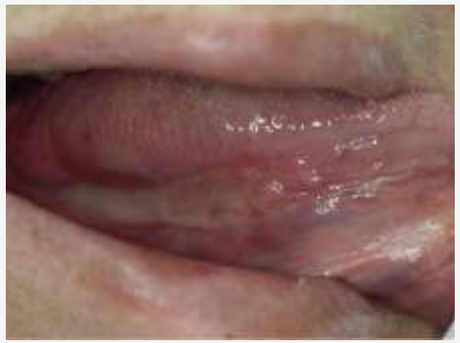
Systemic drug administration (methotrexate) may also cause occasional adverse mucosal reactions, which may vary from **mucosal ulcers** or **erythema** to **lichenoid lesions**.

Anemia, neutropenia, and thrombocytopenia induced by certain myelotoxic medications (or by certain diseases, including SLE) may cause corresponding oral mucosal lesions in the oral cavity (Anemia= **atrophy**, neutropenia= **neutropenic ulcers**, and thrombocytopenia= **petechiae**).

Medications for rheumatic diseases induce pigmentation (e.g., related to hydroxychloroquine) or **diffuse gingival enlargement** (e.g., due to cyclosporine).





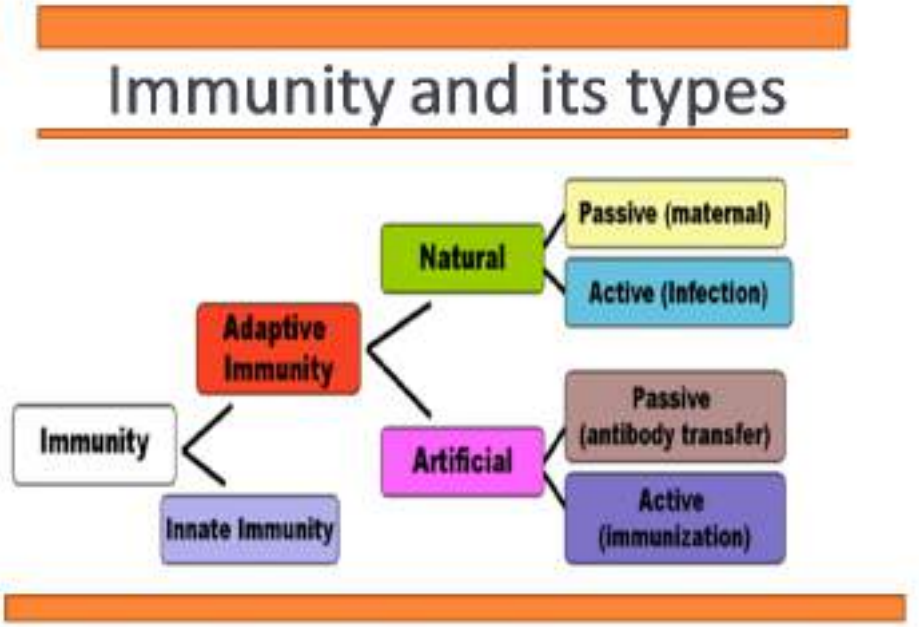


- **Oral aphthous-like lesions associated with methotrexate treatment in a patient with rheumatoid arthritis: (A) tongue; (B) lip; (C) palate**

THANK YOU

Oral Manifestations of the Allergic Conditions

Immunity: Is the ability of an organism to resist infections.
It is divided into
A - Species (innate) immunity e.g. rat is immune to syphilis
B - Adaptive (acquired) immunity Ab development to destroy Ag



Bacteria and virus (Ag) are soluble proteins introduced into the host cell and stimulate reticuloendothelial system (spleen, lymph nodes, bone marrow) to produce Ab.
Anti-bodies (Ab) , are altered serum globulin molecules when brought in contact with protein or microbes (i.e. Antigen) their production would be excited.

The Ag may be destroyed by:

- Agglutination
- Precipitation
- Lyses
- Neutralization
- Production of phagocytosis

Allergy:

Immunologic reactions are detrimental to the tissue or physiology of the host .
Antibodies are immunoglobulins produced by plasma cells and of 5 types :
IgA, IgD, IgE, IgG , IgM
The Ab are located either in :
1- Circulation (in blood stream).
2- Fixed (to cells).

Immunoglobulins

- IgA can be found in areas containing mucus (e.g. in the saliva, gut, respiratory tract and in the urogenital tract) and prevents the colonization of mucosal areas by pathogens.
- IgD functions mainly as an antigen receptor on B cells.
- IgE binds to allergens and triggers histamine release from mast cells (the underlying mechanism of allergy) and also provides protection against helminths (worms).
- IgG (in its four forms) provides the majority of antibody-based immunity against invading pathogens.
- IgM is expressed on the surface of B cells and also in a secreted form with very high affinity for eliminating pathogens in the early stages of B cell mediated immunity (i.e. before there is sufficient IgG to do the job).

When the individual exposed to the same Ag two things happen :
1- Ag may be neutralized or destroyed in the blood stream, by circulating Ab (person is immune).
2- The circulating Ab are not enough to destroy Ag, later reach the tissue cells where it reacts with fixed Ab.
The reaction leads either to:

- Destroy the cell
- Release of histamine (as Angioedema, Skin rash, Hay fever, Urticaria).
- Spasm of smooth muscles (Asthma)

Allergens

are substances that stimulate the immune reactions and divided into:-

A- Soluble proteins (e.g. those in bacteria and viruses).The condition is called bacterial allergy as in tuberculin test.

B- Nonbacterial substances (fresh fruits & vegetables, fish, feather, hair, pollen, milk, drugs...etc) This condition is called atopy (hereditary).

Depending on the speed, allergy may be classified into :

1- Immediate (or anaphylactic) reactions. Occur in seconds up to 30 minutes.

2- Accelerated reactions Occur in 1 hr to 72 hrs.

3- Delayed reactions Occur in days or weeks

Anaphylaxis typically presents many different symptoms over minutes or hours with an average onset of 5 to 30 minutes. The most common areas affected include:

- Skin Symptoms typically include generalized hives, itchiness, flushing, or swelling.
- Respiratory symptoms and signs that may be present include shortness of breath, wheezes, or stridor. The wheezing is typically caused by spasms of the bronchial muscles while stridor is related to upper airway obstruction secondary to swelling. Hoarseness, pain with swallowing, or a cough may also occur.
- Gastrointestinal, symptoms may include crampy abdominal pain, diarrhea, and vomiting. There may be confusion, a loss of bladder control or pelvic pain similar to that of uterine cramps.
- Dilation of blood vessels around the brain may cause headaches. A feeling of anxiety
- Heart and vasculature Coronary artery spasm may occur with subsequent myocardial infarction, dysrhythmia, or cardiac arrest. Those with underlying coronary disease are at greater risk of cardiac effects from anaphylaxis. The coronary spasm is related to the presence of histamine-releasing cells in the heart. While a fast heart rate caused by low blood pressure is more common, a Bezold-Jarisch reflex has been described in 10%of cases where a slow heart rate is associated with low blood pressure A drop in blood pressure or shock (either distributive or cardiogenic) may cause the feeling of lightheadedness or loss of consciousness. Rarely very low blood pressure may be the only sign of anaphylaxis

In sensitized person; allergic reaction of the oral tissues could be due to:

- Systemic intake (drug eruption, stomatitis medicamentosa)
- Direct contact (contact stomatitis, stomatitis venenata)
- Materials used in dental practice that may stimulate allergic reactions are;
- Rubber or latex (gloves, rubber cups, rubber dams)
- Formalin (in endodontic therapy, tooth pastes)
- Fillings (isopaste, light cure, free mercury of amalgam)
- Impression materials (rubber base, silicon)
- Lining materials
- Dentures (acrylics, chrome-cobalt, gold alloys)
- Other chemicals and materials (heptane, phenol, procaine, lip sticks, cinnamon, and flavors in mouth washes...etc)

Clinical Findings of the oral tissue reactions to the allergens:

1- Swellings (e.g. Angioedema)
2- Ulcerative Lesions (e.g. Allergic mucositis, Erythema Multiforme)
3-White lesions (e.g. Lichenoid eruptions)
4-Red lesions (e.g. Plasma cell gingivitis)

A. Angioedema (Angioneurotic Oedema)

* Well demarcated localized bilateral painless swelling (edema) which makes it different from periapical abscess of the anterior teeth.
* It involves the deeper layers of the skin including the subcutaneous tissue.
* The lips are the common site but may occur anywhere on skin or mucous membrane.
* Recurrent episodes of urticaria and/or oedema
* if less than 6 weeks duration are considered acute attacks existed beyond this period are designated chronic.

Causes of the reaction:

a- A significant cases are idiopathic.
b- Ingestion of food drug or contact with allergen.
c- A recurrent form is inherited as an autosomal dominant trait.

Management

Avoidance of the allergen (food, pollen, drug) and use of antihistamines, cortisone and adrenalin in sever form.

Hereditary type does not respond to antihistamines, corticosteroids, or epinephrine and in an emergency, fresh frozen blood plasma should be given i.v.

B. Allergic stomatitis

* Localized area of erythema
* Edematous tissue
* Vesiculation or bullous eruption
* Ulccratives lesions (cracking, assuring of lips, and angular cheilitis) may be associating oral findings.

3- Lichenoid drug eruptions

The incidence of oral lesions without skin eruptions is common.

The etiology is mostly due to drug intake (e.g. antibiotics, antihypertensives, antiarrhythmics, antimalarials, dental materials..etc)

The clinical and the pathogenesis are identical to lichen planus.

4- Plasma cell gingivitis

It is a rare condition; the cause of which is still not fully understood and is characterized by massive infiltration of plasma cells into the subepithelial tissue.

Clinical complication due to contact allergy characterized by generalized erythematous, edematous attached gingiva usually accompanied by inflammation of the lip and tongue.

The disease should be distinguished from neoplastic plasma cell disease such as plasma cytoma, and multiple myeloma.