Sri Aurobindo College of Dentistry

Indore, Madhya Pradesh

INDIA

MODULE PLAN

- TOPIC : ORAL CANCER
- SUBJECT: OMDR
- TARGET GROUP: UNDERGRADUATE DENTISTRY
- MODE: POWERPOINT – WEBINAR
- PLATFORM: INSTITUTIONAL LMS
- PRESENTER: DR.NAVDEEP JOHAR

Contents

- Cancer- is the term used for the diseases in which abnormal cells divide without control and are able to invade other tissues.

- It is a generic term for large group of diseases that can affect any part of the body.

- Other terms used are malignant tumor or Neoplasm

- Oral cancer is collective term used for the malignant tumors occurring in the oral cavity.

- Oral cancer(mouth cancer)- It is the cancer that occurs in any part of oral cavity like on tongue surface, lips, buccal mucosa, gingiva, floor of mouth, tonsils and salivary glands.

- NEOPLASM-is an abnormal mass of tissue the growth of which exceeds and is unco-ordinated with that of normal tissue and persist in the same excessive manner after cessation of stimuli which evoke the change.

All neoplasm have two basic components :

- ✓ Proliferating neoplastic cells-Parenchyma
- ✓ Fibrous connective tissue-Stroma

- Parenchyma determines the behavior and pathologic cosequences

- Stroma determines the growth and evolution of Neoplasm. It provides the frame work for parenchyma.

Epidemiology

- Malignant Neoplasm are the major causes of fear morbidity and mortality all over the world.
- Globally ‘oral cancer’ is the tenth most common causes of death
- More than 1 million new cases diagnosed annually in the U.S, cancers of the oral cavity and oropharynx accounted for 3% approx.

Gender: In males oral cancer represents more than 4 % and in female 2% of total body cancers

- Oral cancer accounts for 2% of cancer death in males and 1 % of cancer death in females.

Age: is the factor that confers the highest risk.

- 95% of oral cancers develops at the 40yrs of age and average age at the time of diagnosis occurs as the individual approaches the age of 65 yrs.

- The most common type of oral cancer is Squamous cell carcinoma.

- The overall age related incidence of OSCC suggests that time dependent factors results in the initiation and promotion of genetic events that result in malignant change.

- Sites-Tongue is the most common site of oral cancer followed by floor of mouth, buccal mucosa and gingiva.

- Lips and palate are less common sites.

Site

- The majority of oral cancers involve the tongue, oropharynx and floor of the mouth

- The lips, gingiva, dorsal tongue and palate are less common sites.

ETIOLOGY

The incidence of oral cancer is age related.

Genetic changes and duration of exposure to initiators and promoters .

These include **chemical and physical irritants, viruses, hormonal effects, cellular aging, and decreased immunologic surveillance with aging**.

Tobacco

- Tobacco contains potent carcinogens;
- **Nitrosamines,**
- **Polycyclic aromatic hydrocarbons,**
- **Nitrosodicthanolamine,**
- **Nitrosoproline, and**
- **Polonium.**

- Tobacco smoke contains
- **Carbon monoxide,**
- **Thiocyanate,**
- **Hydrogen cyanide,**
- **Nicotine, and metabolites of these constituents.**
- **Nicotine is a powerful and**

- Epidemiologic studies have shown that up to **80% of oral cancer patients were smokers.**

- In addition to the risk of primary cancers, the risk of recurrent and second primary oral cancers is related to continuing smoking after cancer treatment.

- Recurrences or a second primary oral cancer, are observed those who continued to smoke after 1 year follow up.

- The incidence of oral squamous cell cancer varies worldwide that may be due to differences in the use of tobacco products.

- **Tongue- Nonsmokers**
- **Floor of the mouth – Smokers**

- Those who use **tobacco, betel nuts, or lime to form a quid** (eg, India, Taiwan), the incidence of oral cancer is high and more commonly involves the **buccal mucosa.**

Alcohol

- All forms of alcohol, including **"hard" liquor, wine, and beer** play a role in the etiology of oral cancer.
- In some studies, **beer and wine are associated with greater risk than hard liquor.**
- The combined effects of tobacco and alcohol result in a synergistic effect on the development of oral cancer.

MECHANISM INCLUDES

- Dehydrating effects of alcohol on the mucosa,
- Increasing mucosal permeability, the effects of potential carcinogens in alcohol or tobacco.
- Secondary liver dysfunction and
- Nutritional status also may play a role

Nutritional Factors

- **Vitamin A may play a role in oral cancer.**

- This hypothesis is based on population studies in which deficiency was associated with the risk of SCC.

Other Risk Factors

- **Denture use, denture irritation, irregular teeth or restorations, and chronic cheek-biting habits** have been documented as a causative agent with no evidence.

- However, **chronic trauma in addition to other carcinogens** may cause transformation of epitelial cells causing cancer.

- **HSV-1 and HSV-2,** may modify the risk of head and neck cancer associated with exposure to tobacco, alcohol, or human papillomavirus (HPV) oncogenic subtypes.

- **High alcohol content in mouthwashes** has been implicated in oral cancer.

- In **lip cancer**, sun exposure, fair skin and a tendency to burn, pipe smoking, and alcohol are identified risk factors.

- Patients undergoing **allogenic stem cell transplantation** are at high risk of developing secondary neoplasms, particularly leukemias and lymphomas;

- OSCC has been reported up to a 14-fold increase in risk.

PATHOGENESIS

- The molecular pathogenesis of OSCC reflects an accumulation of genetic changes that occur over a period of years .

- Carcinogenesis is a genetic process that leads to a change in morphology and in cellular behaviour.

- In normal cell, regulator cells control
- Mitosis
- Cell ageing
- Terminating into cell death by apoptosis

Genetic regulators of normal and abnormal mitosis

- Regulatory genes
- Proto-oncogenes
- Antioncogenes
- Apoptosis regulatory genes
- DNA repair genes

- In cancer the transformed cells are produced by abnormal cell growth due to genetic damage to these normal controlling genes

- Activation of proto-oncogenes
- Inactivation of antioncogenes
- Abnormal apoptosis regulatory genes
- Failure of DNA repair genes

- Cells so formed are genetically and phenotypically transformed cells having phenotypic features of malignancy.

- Excessive growth
- Invasiveness
- Distant metastasis.

Excessive and growth promoting oncogenes

- Activation of oncogenes from normal proto-oncogenes occur by following mechanism:

- Point mutation or deletion
- Chromosomal translocation
- Gene amplification

- Binding of growth factor to a specific receptors (cell membrane)

Signal transducing proteins

Transmission from cytosol to nucleus via secondary messenger

Induction and activation of nuclear regulatory factor which lead to DNA transcription

Entry and progression of cell into cell cycle and leads to cell division

Growth factor receptor

- Growth factor receptor are transmembrane proteins with an external ligand binding domain and tyrosine binding domain.

- EGFR is over expressed in 80% to 100% of head and neck tumors .

- Monoclonal antibodies against EGFR have been developed and are used clinically.

Signal transducing proteins

- These proteins are located on the inner leaflet of the plasma membrane and they receive signals from outside the cell (activation of growth factors)and transmit them to nucleus.

Cyclin and cyclin dependent kinase

- The orderly progression through the various phases of the cell is controlled by cyclin and cyclin dependent kinase .

- CDKs are responsible for phosphorylation of critical target proteins that are required for progression of cell to next phase

Signal transduction pathways generate transcriptional regulators that enter the nucleus and act on DNA .

Which further lead to replication and cell division

- Over expression is seen in several tumors and this lead to sustained transcription of target genes and subsequent neoplastic transformation .

ANTI ONCOGENES

- They generally act on G1-S phase.
- They are responsible for growth inhibition but in case any mutation .
- In these cells they act like growth promoting oncogenes

- TP53 gene (p53) located on short arm (p) of chromosome 17 .
- It is normally a growth suppressor antioncogenes

- Its major functions are
  - In blocking mitotic activity
  - In promoting apoptosis

Telomerase

- Telomers are terminal tip of chromosomes .
- After each mitosis there is progressive shorting of telomers .
- Telomerase is the RNA enzyme that help in repair of such DNA and maintain the normal length in successive cell divisions.

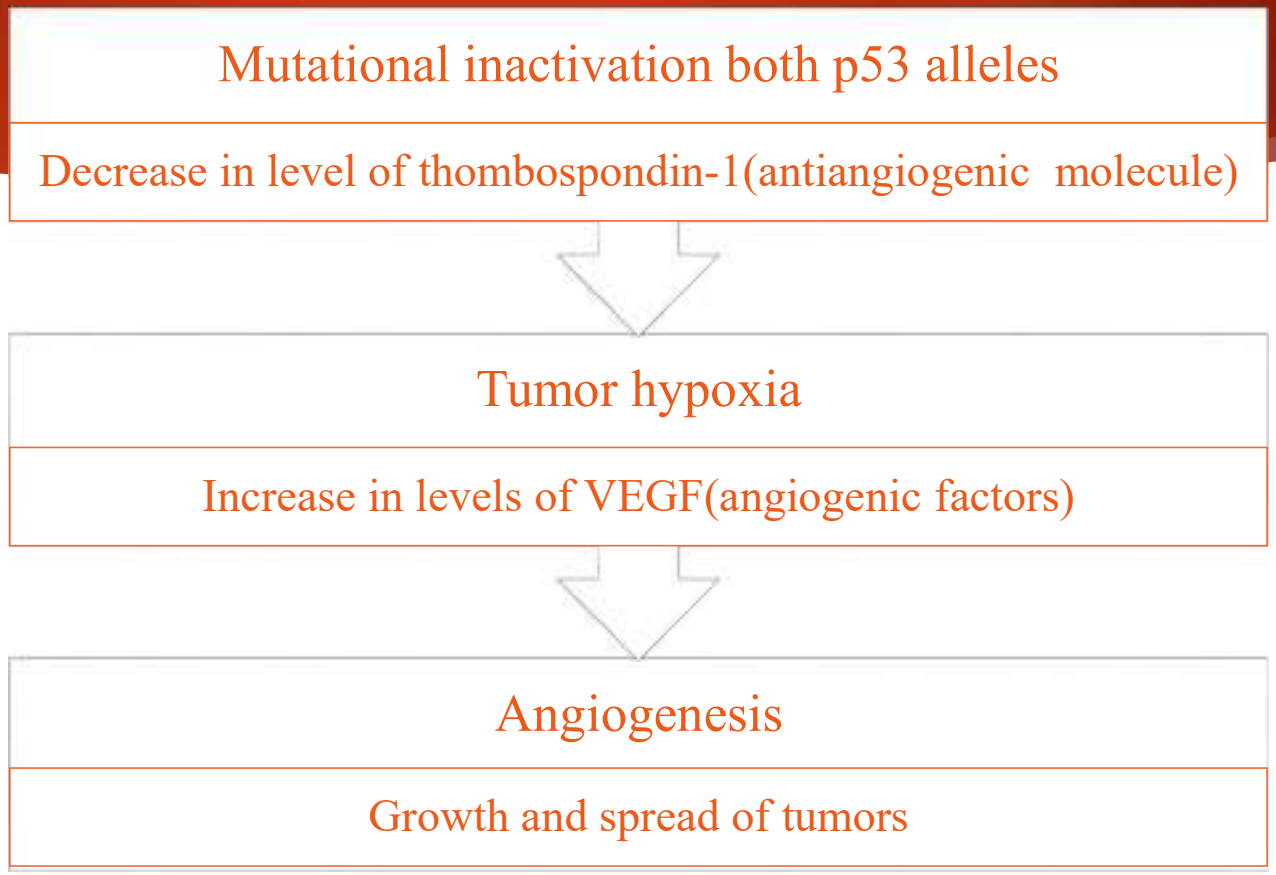
- Telomerase is active in normal stem cells but not in normal somatic cells.
- Cancer cells are markedly up regulated telomerase enzyme ,and thus telomerase length is maintained .
- Hence cancer cells avoid aging ,mitosis does not slow down or cease ,thereby immortalizing the cancer.

Tumor angiogenesis

- Neovascularisation in the cancer not only supplies the tumor with oxygen and nutrients .
- But also newly formed endothelial cells also elaborate a few growth factors for progression primary as well as metastatic carcinoma.

- Promoters of tumors angiogenesis include the most important ***vascular endothelial growth factors (VEGF) and bFGF.***

- These factors can be detected in the serum and urine in a significant fraction in cancer patients .


Mutational inactivation both p53 alleles
Decrease in level of thombospondin-1(antiangiogenic molecule)
Tumor hypoxia
Increase in levels of VEGF(angiogenic factors)
Angiogenesis
Growth and spread of tumors

- They must go through a series of step.
  - Invasion of extracellular matrix
  - Detachment of the tumor cells from each other.
  - Attachment to matrix component
  - Degradation of ECM
  - Migration of tumor cells

- Tissues are organized in compartments separated from each other by extracellular matrix (basement membrane and interstitial tissue)

- ECM is made up of collagen ,glycoprotein and proteoglycans.

- A carcinoma must first breach the underlying basement membrane and traverse connective tissue and then enter in blood circulation.

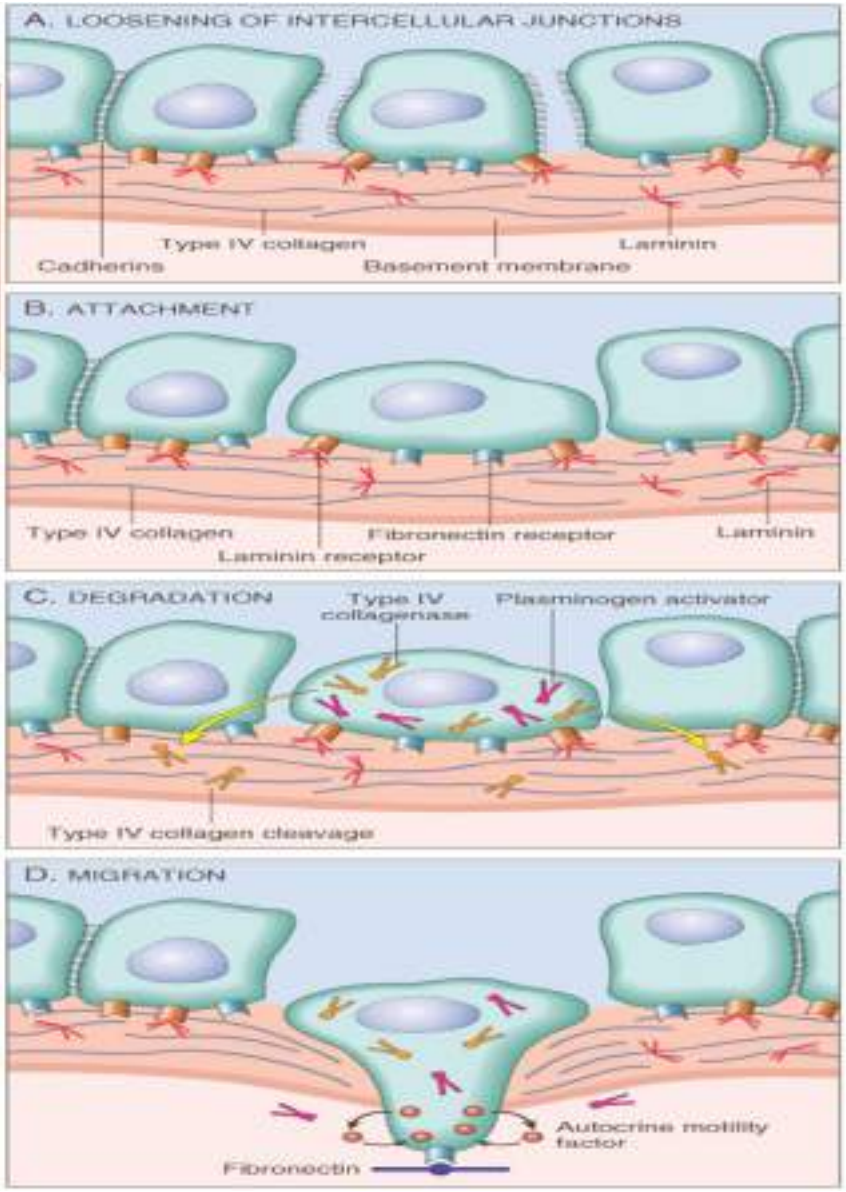
- Normally cells are glued to each other by adhesion molecules.eg is E-cadherins family homotypic adhesion in epithelial cells

- E-cadherin is linked to cytoskeleton by catenins (protein lie under plasma membrane)

- In several tumor E cadherin is normal but its expression is reduced because of mutation in catenins .

- Pressure due to growth of tumor
- Active enzymatic degradation of ECM
- These are generally proteases which are released from tumor cells
- To regulate these protease there are antiproteases

- But at invasive edges of carcinoma proteases are dominant .
- proteases include serine ,cysteine ,MMP
- MMP9 and MMP2 are collagenases that cleaves type IV collagen.
- Several invasive carcinomas show high level of collagenases.


A. LOOSENING OF INTERCELLULAR JUNCTIONS
Cadherins
Type IV collagen
Basement membrane
Laminin
B. ATTACHMENT
Type IV collagen
Laminin receptor
Fibronectin receptor
Laminin
C. DEGRADATION
Type IV collagenase
Plasminogen activator
Type IV collagen cleavage
D. MIGRATION
Autocrine motility factor
Fibronectin

Chemical carcinogenesis

- First evidence of any cause for neoplasia came from the observation of Sir Percival Pott in 1775

- There was higher incidence of carcinoma of scrotum in chimney –sweeps in London

- Factors that influence chemical carcinogenesis
- Dose
- Duration
- Mode of administration
- Individual susceptibility
- Various predisposing factor

Chemical carcinogenesis

- Initiation
- Promotion

Initiation

- Initiation results from exposure of cells to a sufficient dose of a carcinogenic agent (initiator)
- Initiation causes permanent DNA damage (mutations).
- It is therefore rapid and irreversible and has memory.

- For the change to be heritable, the damaged DNA template must be replicated.

- Thus, for initiation to occur, carcinogen-altered cells must undergo at least one cycle of proliferation so that the change in DNA becomes fixed

- ***Direct acting carcinogenes*** :they act directly without going any prior metabolic activation

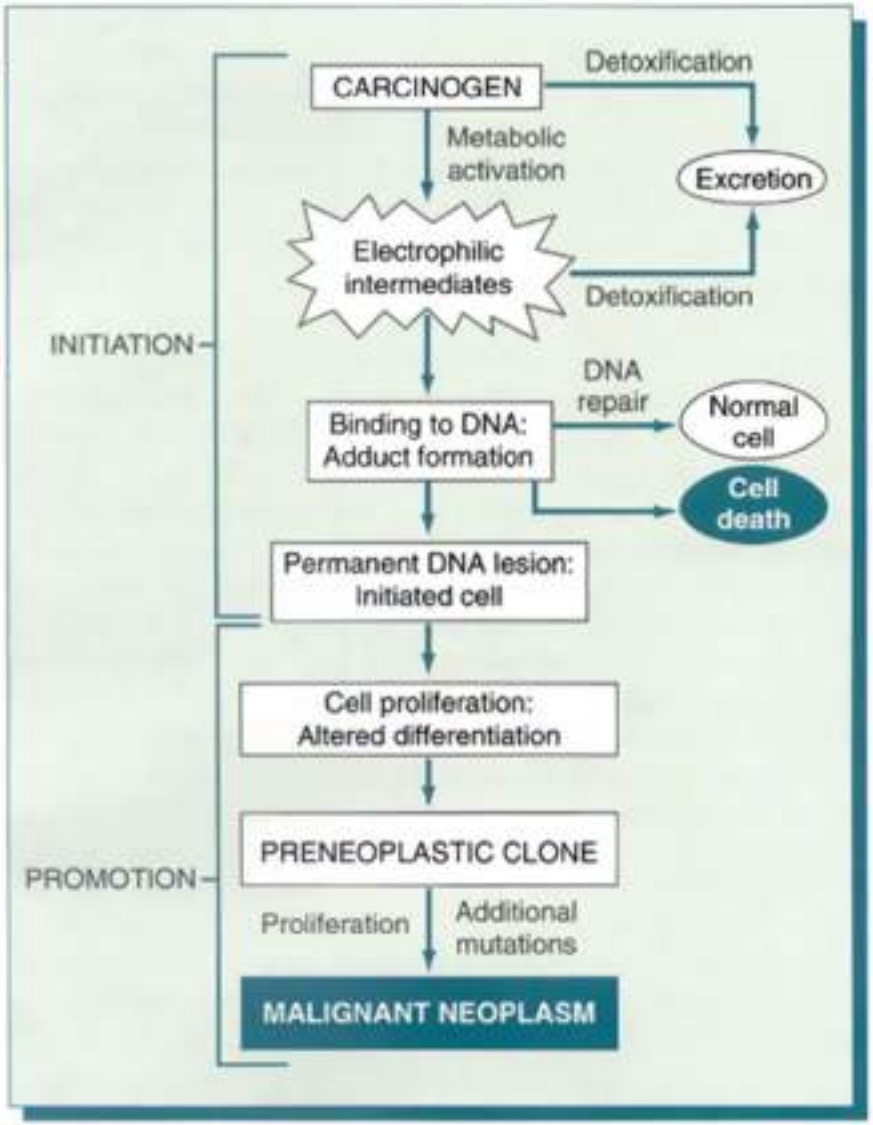
- ***Indirectly acting or procarcinogenes*:**

indirect-acting agent refers to chemicals that require metabolic conversion to an ultimate carcinogen before they become active.

Promotion of carcinogenesis

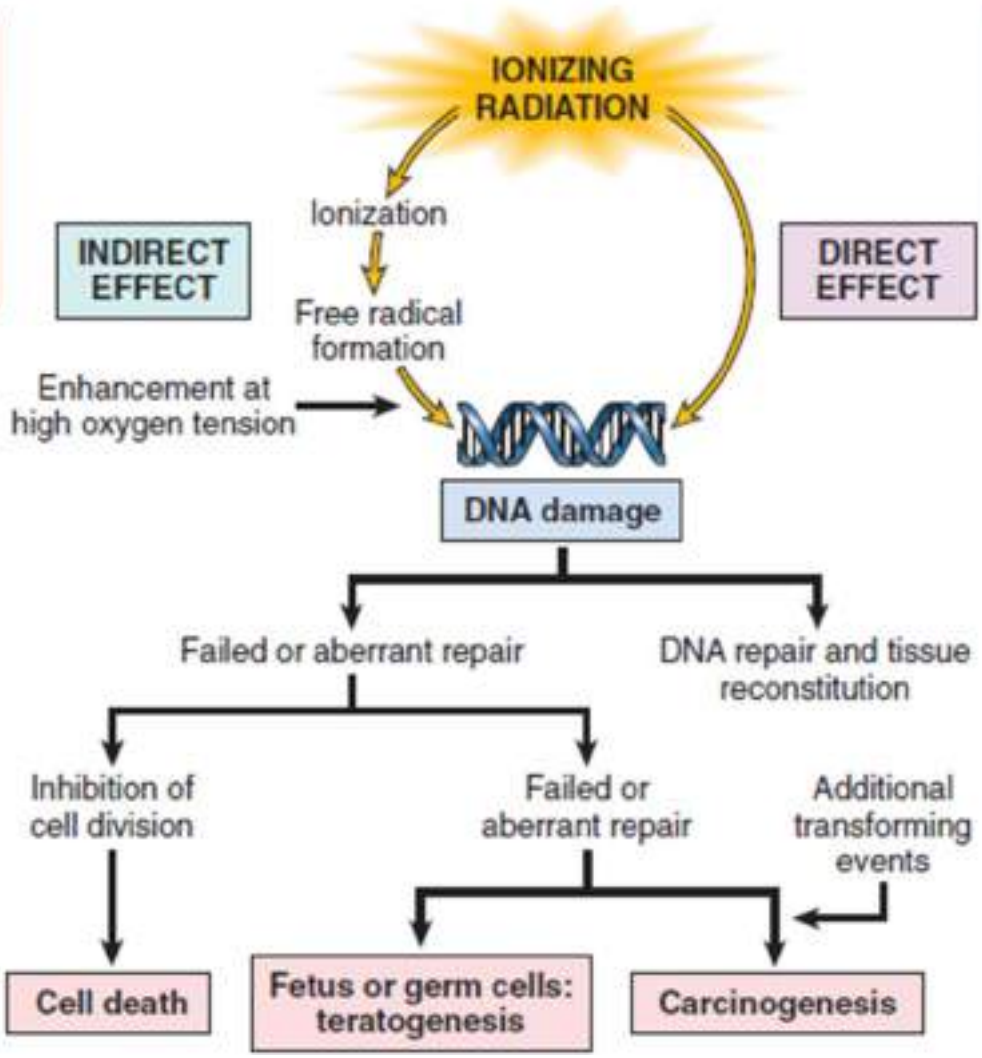
- cell proliferation may be induced by concurrent exposure to biologic agents such as viruses and parasites, dietary factors, or hormonal influences.

- Agents that do not cause mutation but instead stimulate the division of mutated cells are known as *promoters*


CARCINOGEN
Detoxification
Metabolic activation
Excretion
Electrophilic intermediates
Detoxification
INITIATION
DNA repair
Binding to DNA: Adduct formation
Normal cell
Cell death
Permanent DNA lesion: Initiated cell
Cell proliferation: Altered differentiation
PRENEOPLASTIC CLONE
PROMOTION
Proliferation
Additional mutations
MALIGNANT NEOPLASM

- Ionizing radiation is a double-edged sword. It is being used in the treatment of cancer, in diagnostic imaging, and in therapeutic or diagnostic radioisotopes, but it also produces adverse short- and long-term effects such as :

- Fibrosis
- Mutagenesis
- Carcinogenesis
- Teratogenesis


IONIZING RADIATION
Ionization
INDIRECT EFFECT
DIRECT EFFECT
Free radical formation
Enhancement at high oxygen tension
DNA damage
Failed or aberrant repair
DNA repair and tissue reconstitution
Inhibition of cell division
Failed or aberrant repair
Additional transforming events
Cell death
Fetus or germ cells: teratogenesis
Carcinogenesis

CLINICAL FEATURES

Initial symptoms

- Patient may present with awareness of a mass in the mouth and neck
- Small lesions are asymptomatic.

Late Symptoms

- Large lesions may cause some pain or paresthesia and swelling.
- Patients complain of persistent ulcer in the oral cavity.

Late Symptoms

- With advanced disease :
  - ✓ Dysphagia
  - ✓ Otalgia
  - ✓ Limited movement
  - ✓ Oral bleeding
  - ✓ Neck masses
  - ✓ Weight loss

Clinical Appearance

- Clinical presentation varies
- No two cases having a similar presentation

Clinical appearance – Early changes

- Tissue changes that may include a red, white, or mixed red-and-white lesion
- A change in the surface texture producing a smooth, granular, rough, or crusted lesion
- Presence of a non healing ulcer

Clinical appearance – Early changes

- Lesion may be flat or elevated and ulcerated or non-ulcerated and may be minimally palpable or indurated.

- Loss of function involving the tongue can affect speech, swallowing, and diet.

Clinical appearance - Late signs

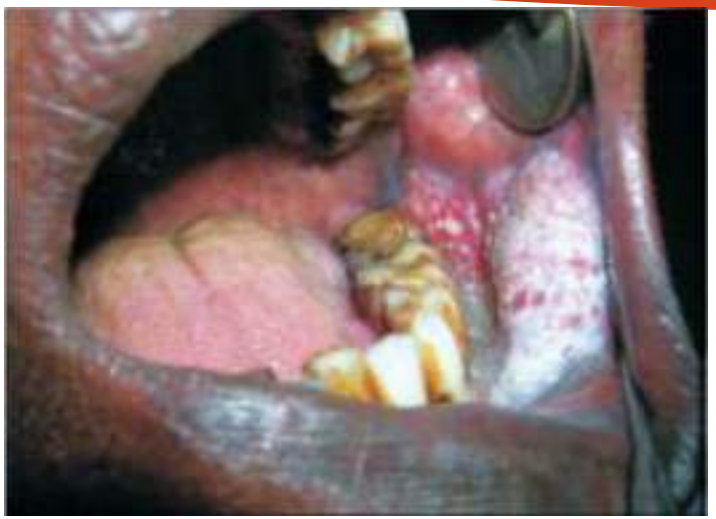
- Indurated area
- Paresthesia, dysaesthesia of tongue or the lips
- Airway obstruction
- Trismus & dysphagia
- Altered vision

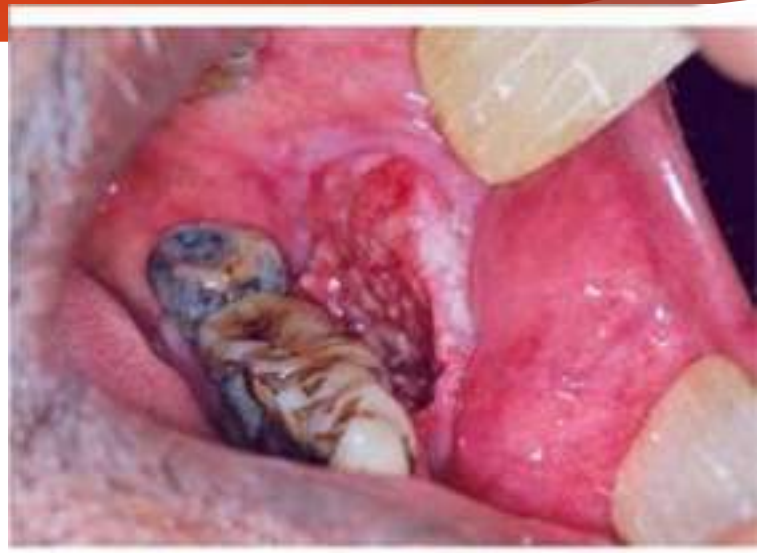
Clinical Features

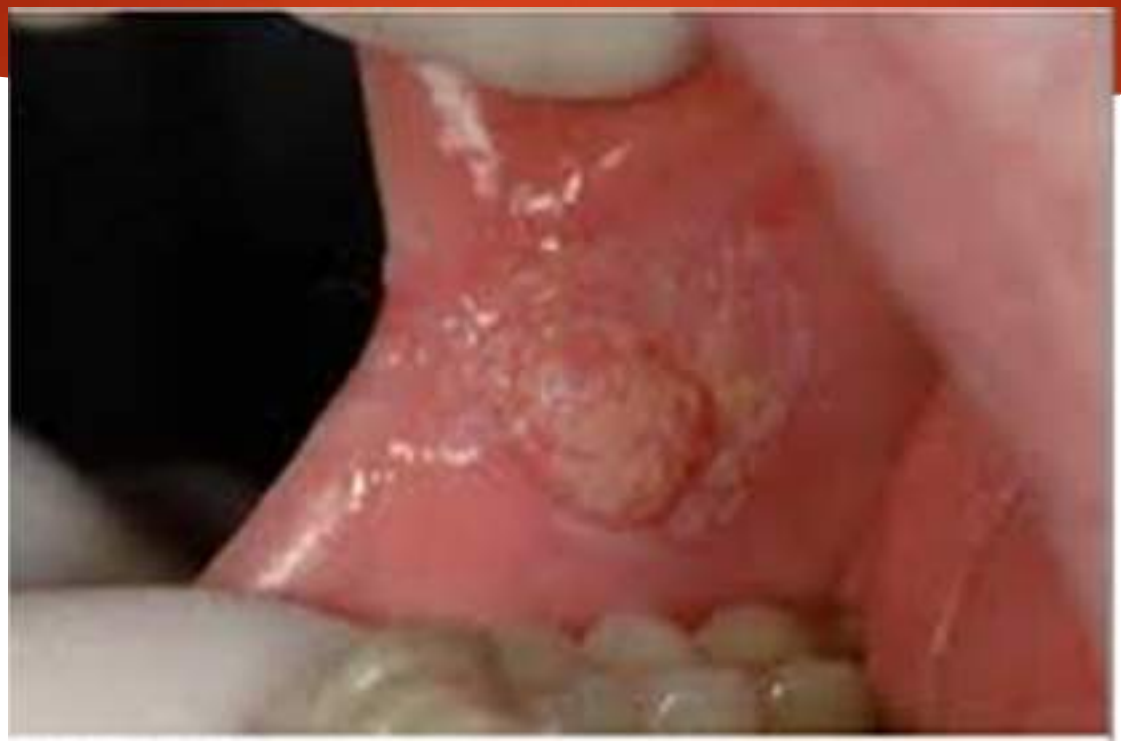
- Early red or white lesion or Mixed red & white lesion
- With time development of ulceration of irregular shape with indurated base and raised everted edges
- Later, progression to an exophytic lesion with papillary surface or endophytic lesion this is depressed irregularly shaped ulcerated central area with surrounding rolled border.

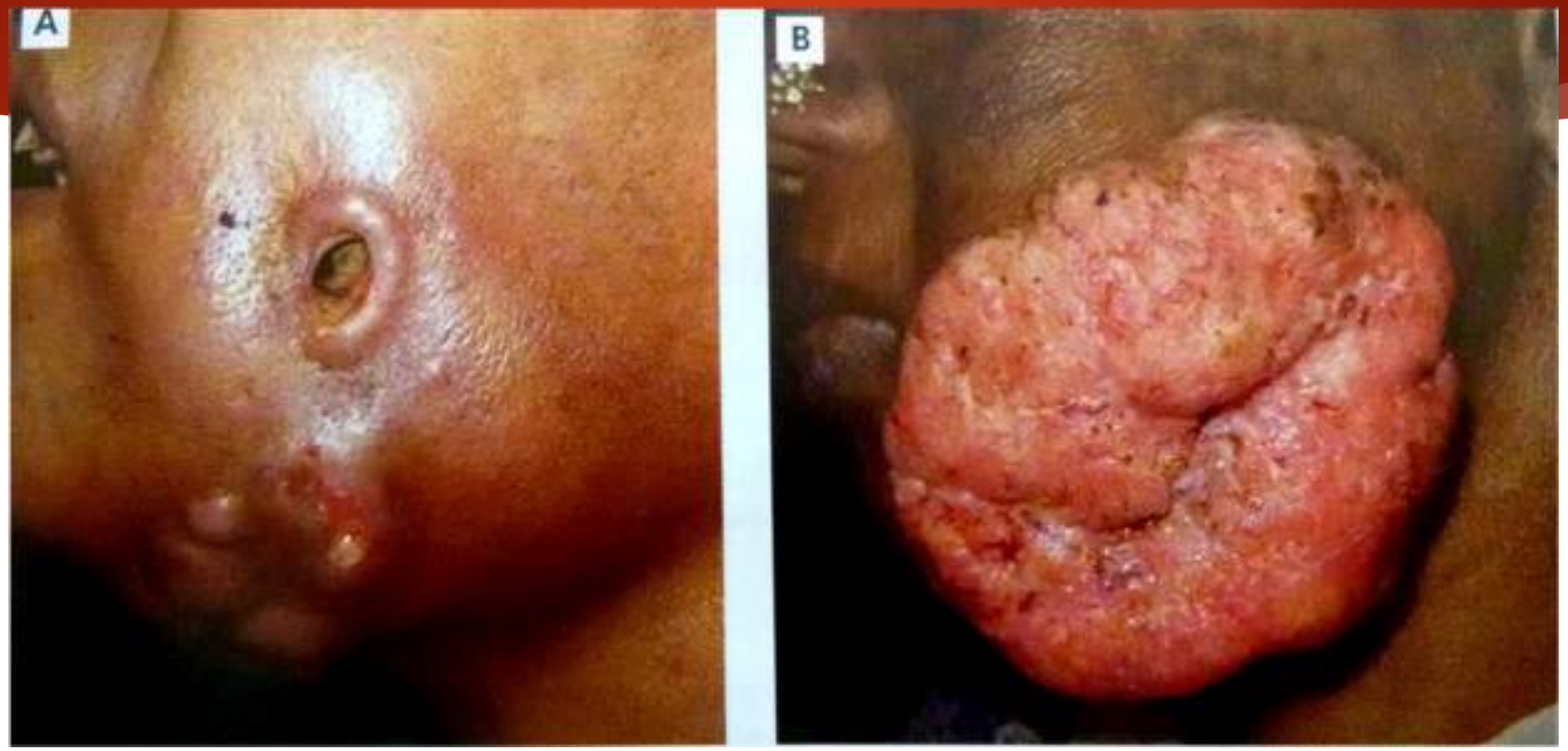
Carcinoma of Buccal Mucosa

- Lesions develop most frequently along or inferior to a line opposite the plane of occlusion.
- It usually occurs opposite to the third molar
- The tumor begins as small nodules and enlarges to form a wart-like growth which ultimately ulcerates
- Extension into the muscle of neck, alveolar mucosa and ultimately into bone may occur








A
B

Carcinoma of Floor of mouth

- Anterior portion of floor of mouth – saliva pooling
- The typical carcinoma of the floor of mouth is an indurated ulcer of varying size, on one side of the midline
- It may take form of wart-like growth, which tend to spread superficially rather than in depth.

Carcinoma of Floor of mouth

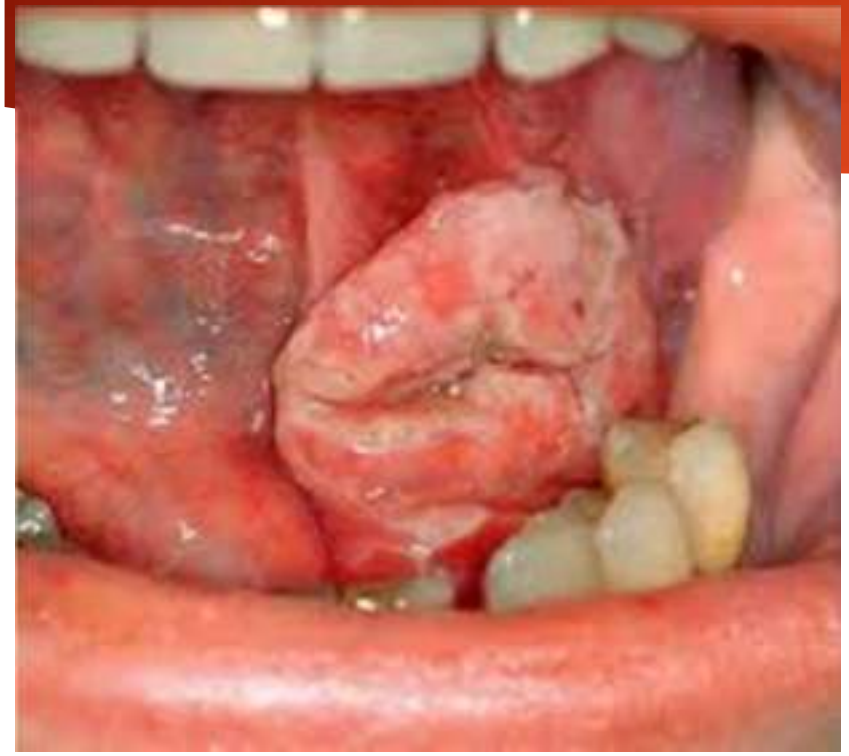
- The proximity of this tumor to the tongue produces some restricted/limited movements of tongue, often induces peculiar thickening or slurring of the speech.

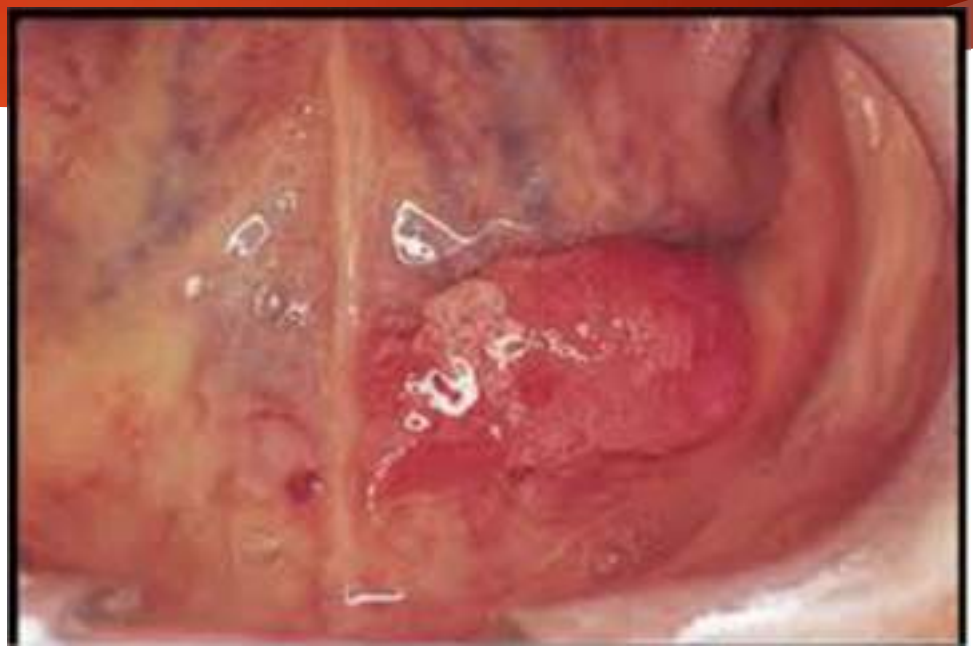
- There may be excessive salivation.

Carcinoma of Floor of mouth

- Carcinoma in close relation to teeth may cause loosening or exfoliation and root resorption.

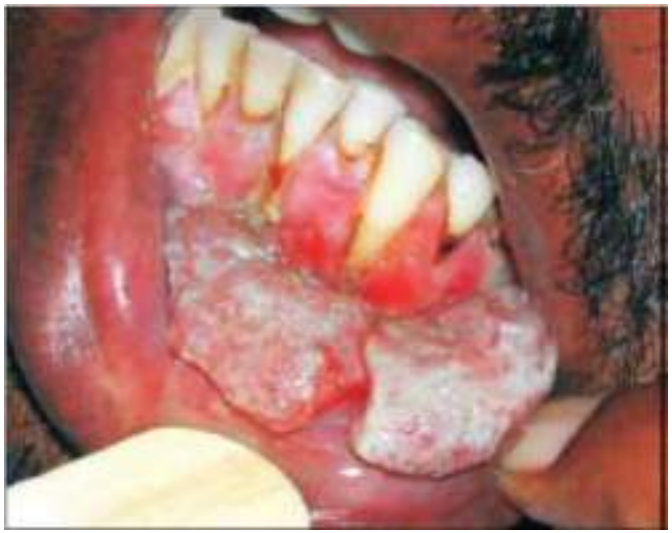
- Carcinoma of floor of mouth may invade the deeper tissues and may even extend into the submandibular and sublingual glands.

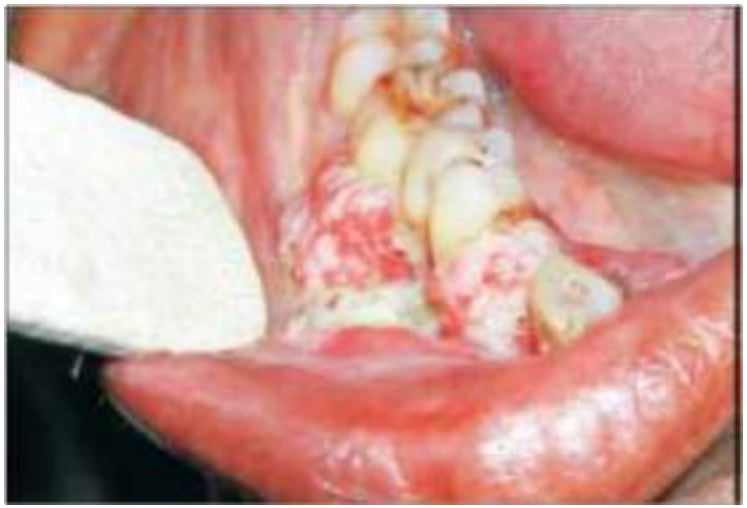


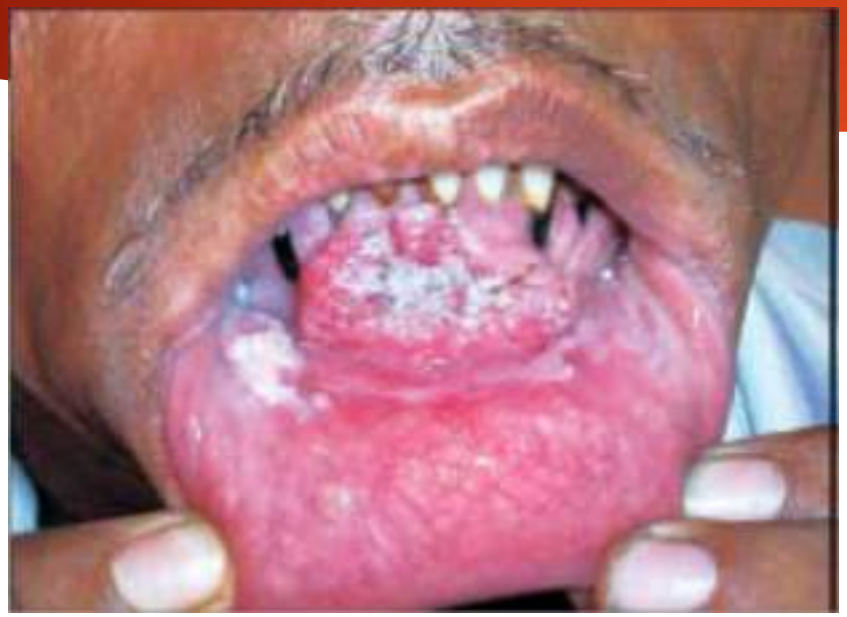


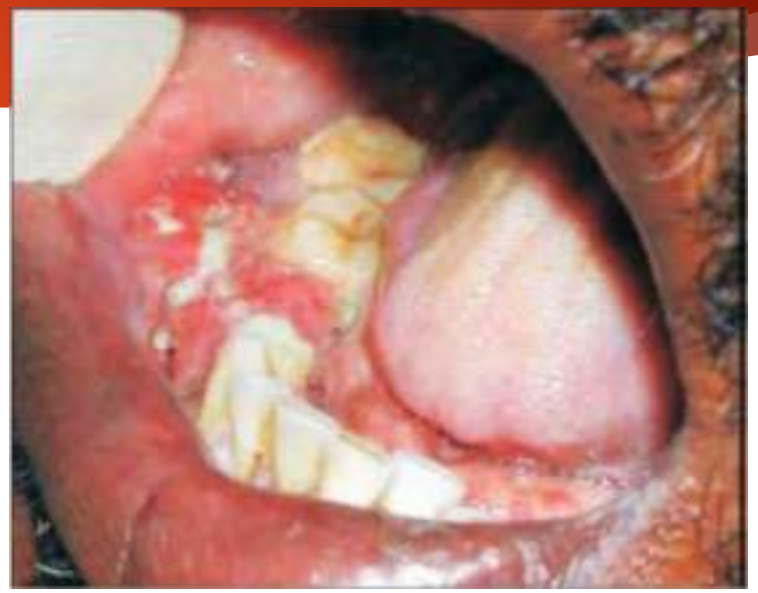
Carcinoma of Labial mucosa/ Vestibule

- Frequently encountered in people who habitually keep a mixture of tobacco lime in the labial vestibule.
- The lower labial mucosa is more commonly involved than the upper.
- The most common initial signs and symptoms are growth or swelling, soreness and ulceration that does not heal
- May spread to corners of mouth and extend extraorally



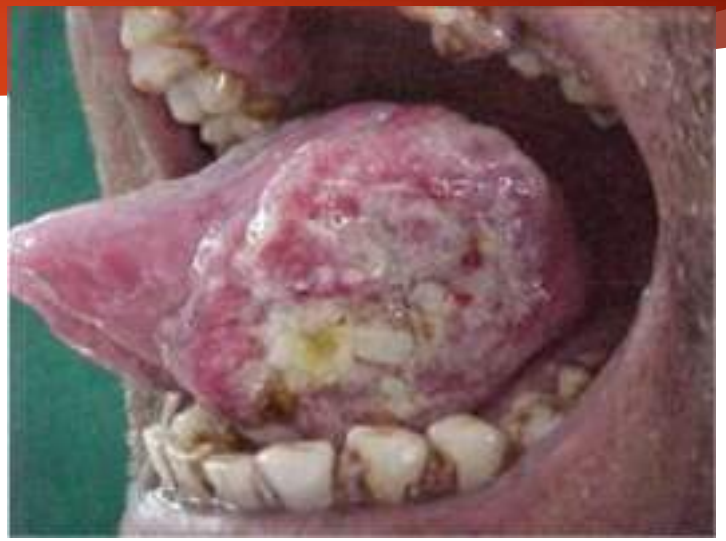






Carcinoma of Tongue

- Most commonly affected are lateral margins & ventral surface
- Appear as induration & ulceration on the tongue
- Causes interference with the tongue movements
- Swallowing & speech are affected
- Pain occurs due to involvement of lingual nerve

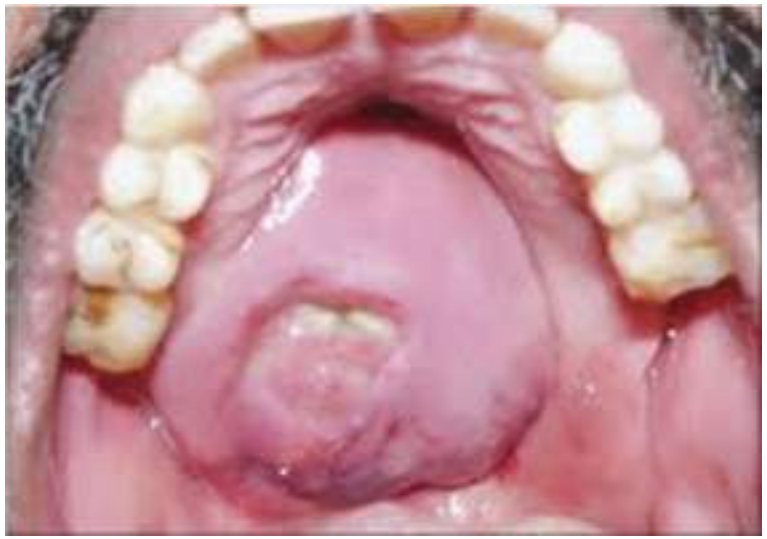


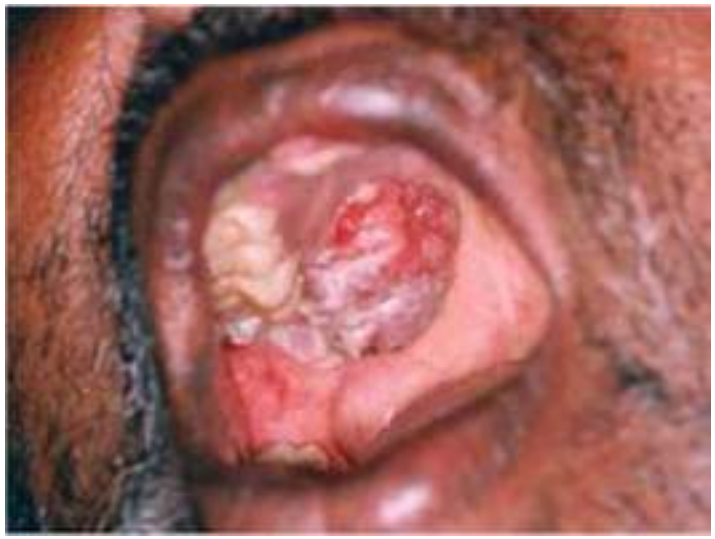
Carcinoma of Palate

- It is common in area where reverse smoking is practiced
- Usually manifests as a poorly defined ulcerated painful lesion on one side of the midline
- Most of the lesions are exophytic and with broad base and nodular surface.

Carcinoma of Palate

- Frequently crosses the midline and may extend laterally to include tonsillar pillars or even the uvula.
- The tumor of hard palate may invade the bone or occasionally the nasal cavity.
- Lesions of the soft palate may extend into the nasopharynx.





Carcinoma of maxillary sinus

- Causes facial pain, swelling & nasal obstruction
- Medial wall involvement – nasal obstruction, discharge, pain, bleeding
- Floor of sinus – expansion of alveolus, numbness of teeth, loose teeth & swelling of palate & alveolar ridge & ill fitting denture
- Roof involvement – diplopia, proptosis & pain over cheek & upper teeth

Involvement of Lymph nodes

- Lymphatic spread of oral carcinoma usually involves the submandibular, sublingual, digastric & the upper cervical nodes and, finally, the remaining nodes of the cervical chain.

- The nodes most commonly involved are those that are on the same side as the primary tumor,

Involvement of Lymph nodes

- Lymph nodes associated with cancer become ***enlarged and firm to hard in texture***.
- The nodes are not tender unless they are associated with secondary infection
- The fixation of nodes to adjacent tissue due to invasion of cells through the capsule is a late occurrence and evidence of aggressive disease.

TNM STAGING

(It is universally accepted system which is developed by UICC (Union Internationale Centre of Cancer)

- T — Primary tumor
- Tx — Primary tumor cannot be assessed
- T0 — No evidence of primary tumor
- Tis — Carcinoma in situ
- T1 — Tumor 2 cm or less in greatest dimension
- T2 — Tumor more than 2 cm but not more than 4 cm in greatest dimension
- T3 — Tumor more than 4 cm in greatest dimension

- **T4a** — (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (chin or nose).

- **T4a** — (oral cavity) Tumor invades through cortical bone, into deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, or skin of face.

- **T4b** — (lip and oral cavity) Tumor invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery.

- N — Regional lymph nodes
- NX — Regional lymph nodes cannot be assessed
- N0 — No regional lymph node metastasis

- **N1** — Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.

- **N2** — Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.

- **N2a** — Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension.
- **N2b** — Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
- **N2c** — Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
- **N3** — Metastasis in a lymph node more than 6 cm in greatest dimension.

- M — Distant metastasis
- MX — Distant metastasis cannot be assessed
- M0 — No distant metastasis
- M1 — Distant metastasis

Stage grouping

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

Stage IVA	T1, T2, T3	N2	M0
	T4a	N0, N1, N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

DIAGNOSIS OF ORAL CANCER

1. Habit history & clinical examination
2. Imaging
3. Diagnostic procedures
4. Laboratory test

Habit history & clinical examination

- Early detection of malignant lesions is a continuing goal.
- Thorough head and neck and intraoral examination is a prerequisite.
- Cervical lymph nodes
- Most commonly on same side
  - Submental
  - Submandibular
  - Digastric
  - Upper cervical nodes

Aids to oral examination

- Imaging And Light Technologies
- Vital Tissue Staining Using Toluidine Blue
- Computer-assisted cytology of oral brush biopsy specimens

Imaging

- Routine radiographs : IOPA, OPG, Occlusal, PA View, occipitomental
- CT scan
- Bone scans
- PET
- USG

Diagnostic procedures

- Exfoliative cytology
- Toluidine blue staining
- FNAC
- Biopsy
- Molecular markers

Laboratory test

- CBC
- Liver function test

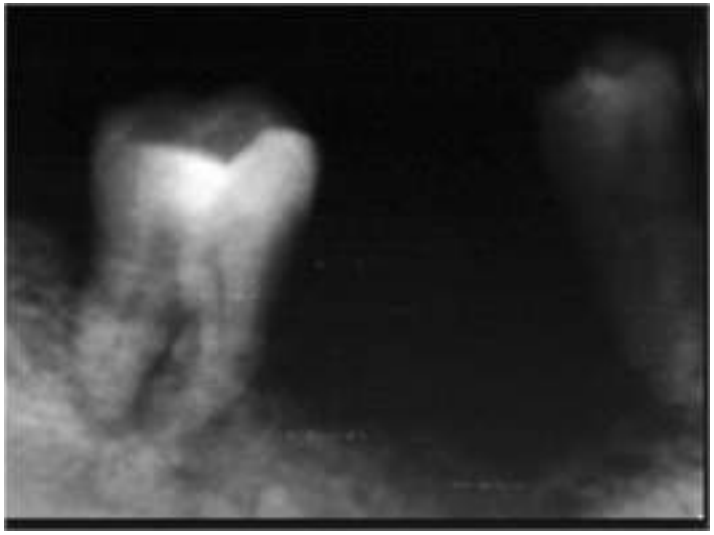
Imaging

- Routine radiology
- Computed tomography (CT)
- Nuclear scinti-scanning
- Magnetic resonance imaging (MRI)
- Ultrasonography (USG)
- Positron emission therapy (PET)

Routine Radiography

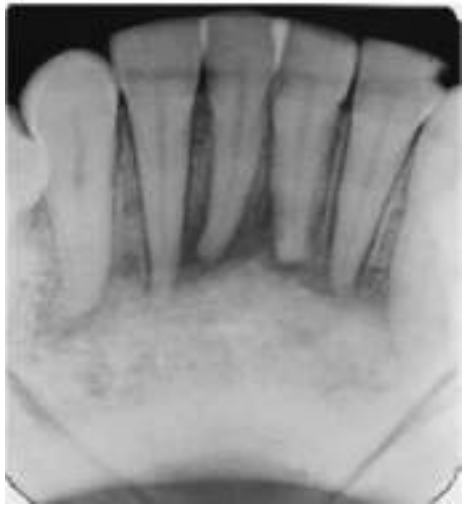
Radiographic features of malignancy

- Ill-defined invasive borders followed by bone destruction.

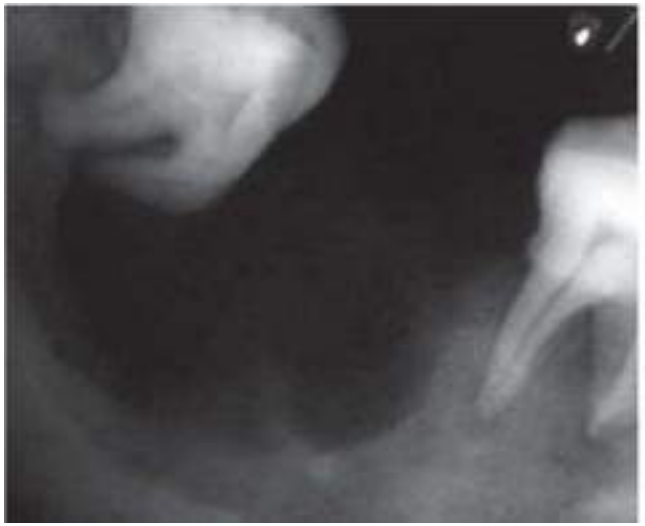


- Destruction of the cortical boundary (floor of maxillary antrum) with an adjacent soft tissue mass

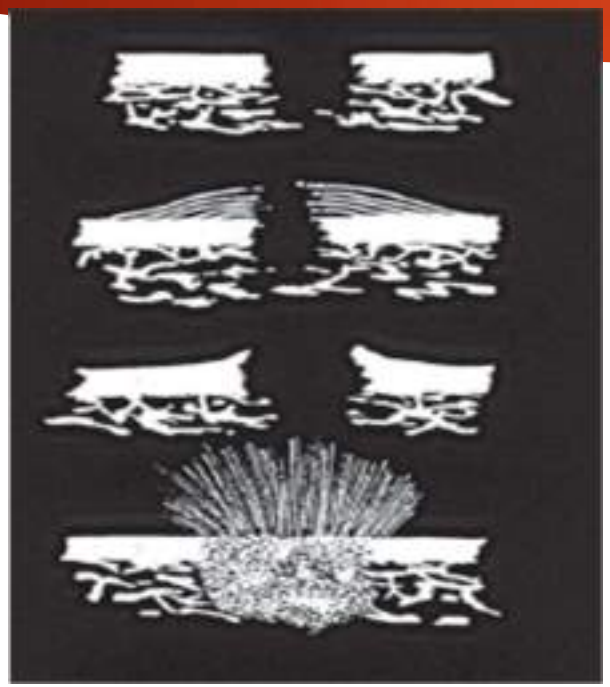
Tumor invasion along the periodontal membrane space causing irregular thickening of this space.

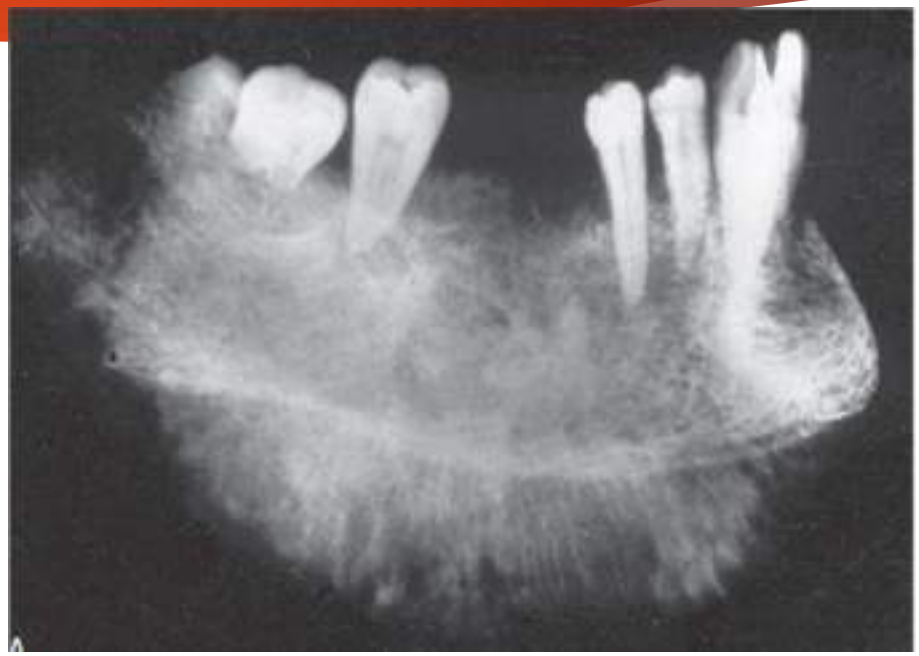


- Multifocal lesions destroying and displacing the teeth

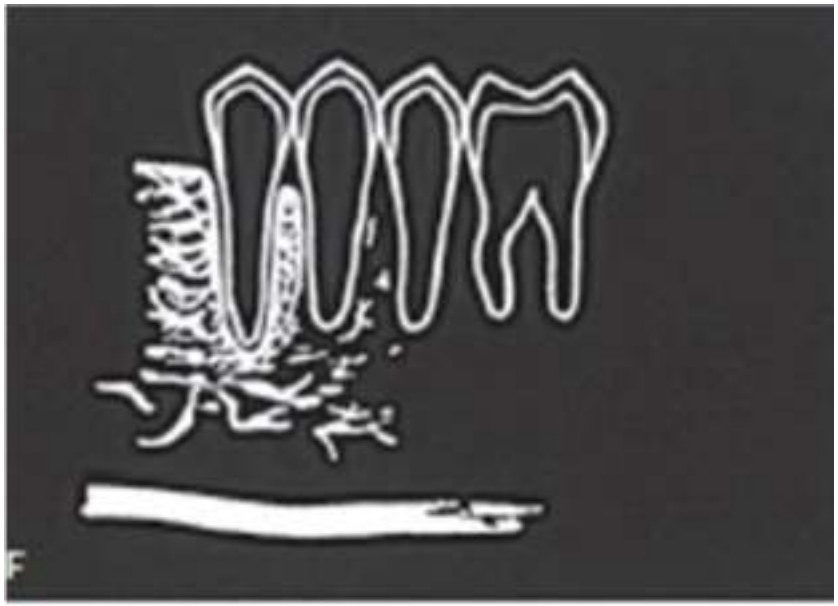


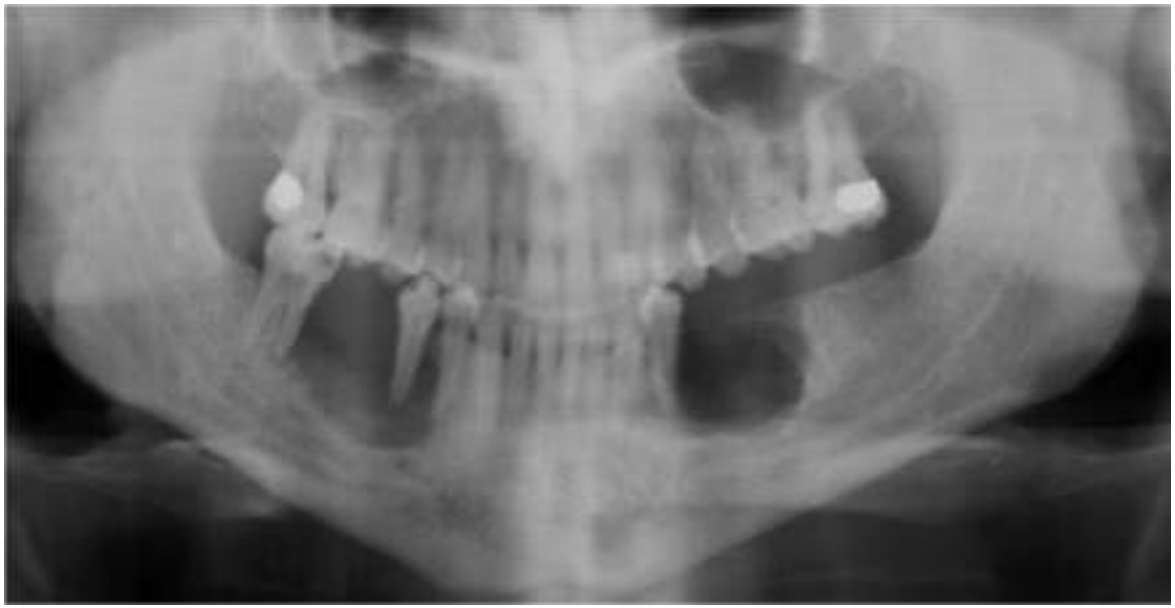
- Cortical Bone Destruction Without Periosteal Reaction
- Laminated Periosteal Reaction With Destruction Of The Cortical Bone And The New Periosteal Bone
- Destruction Of Cortical Bone With Periosteal Reaction At The Periphery Forming Codman ' S Triangles
- A Spiculated Or Sunray Type Of Periosteal Reaction.





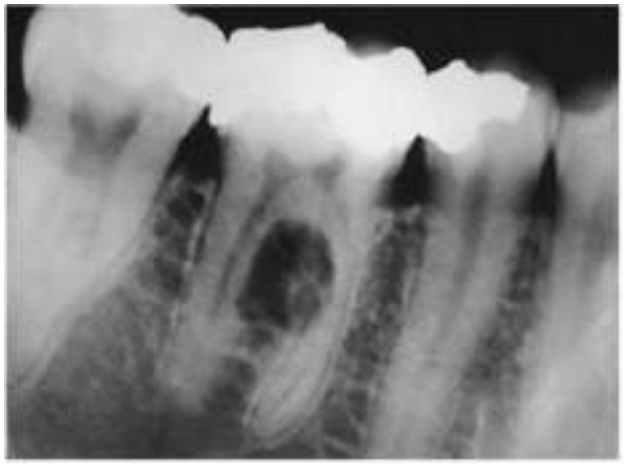
- Bone destruction around existing teeth, producing an appearance of teeth floating in space.



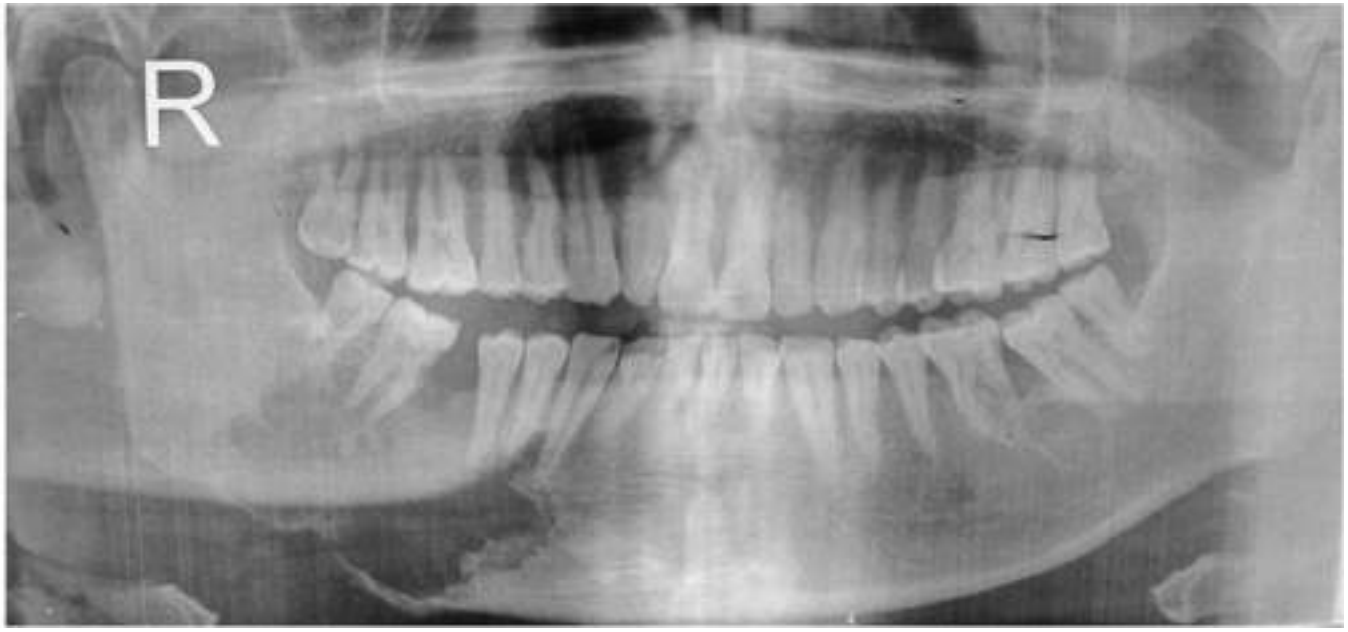


Routine radiography

- IOPA: subtle bone changes bony trabecular architecture

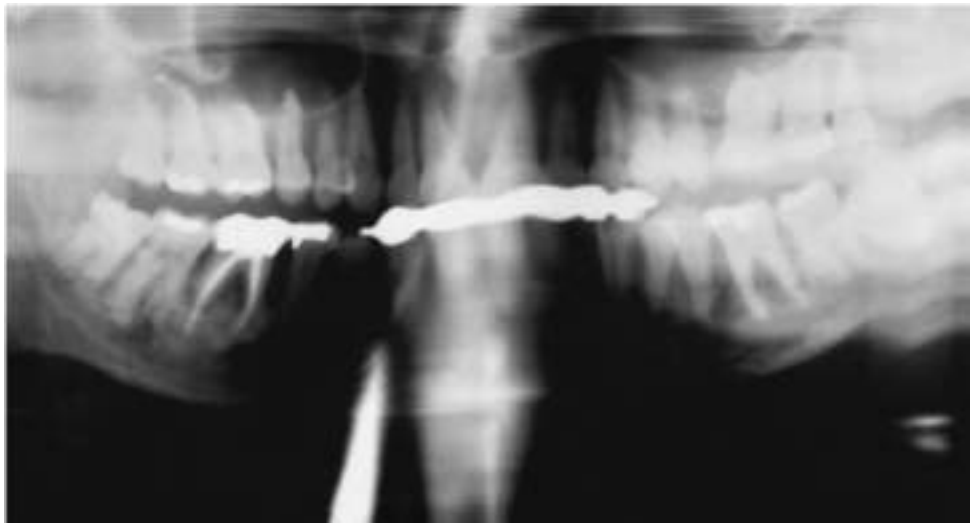


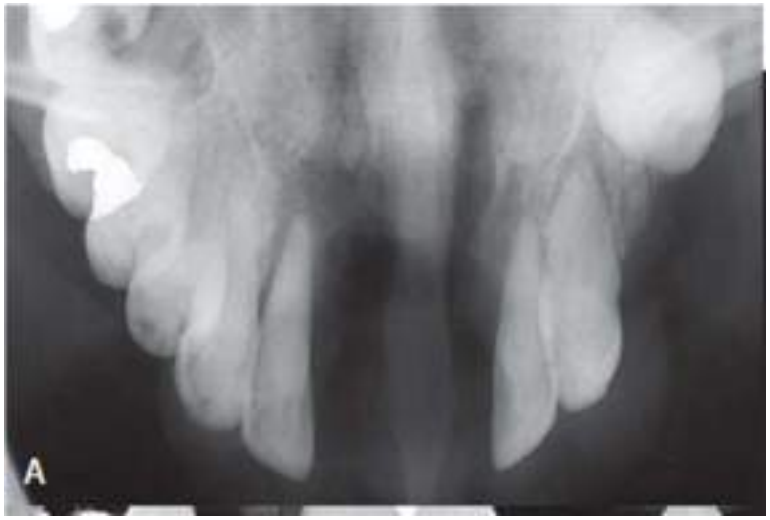
OPG



Occlusal

- Bony changes in anterior aspect of jaw not visible on OPG

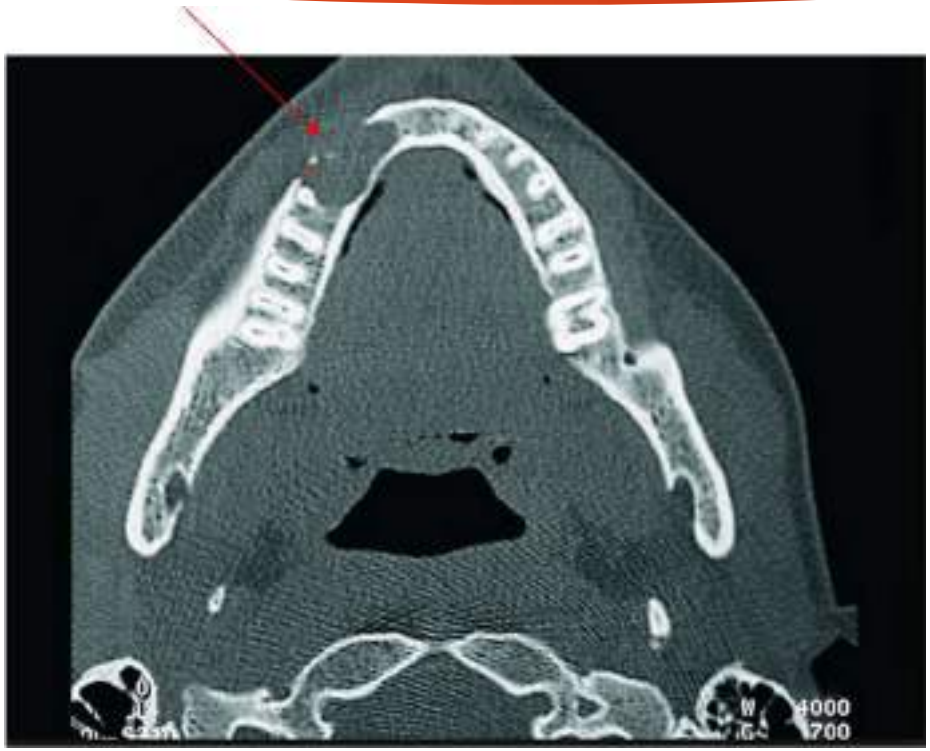




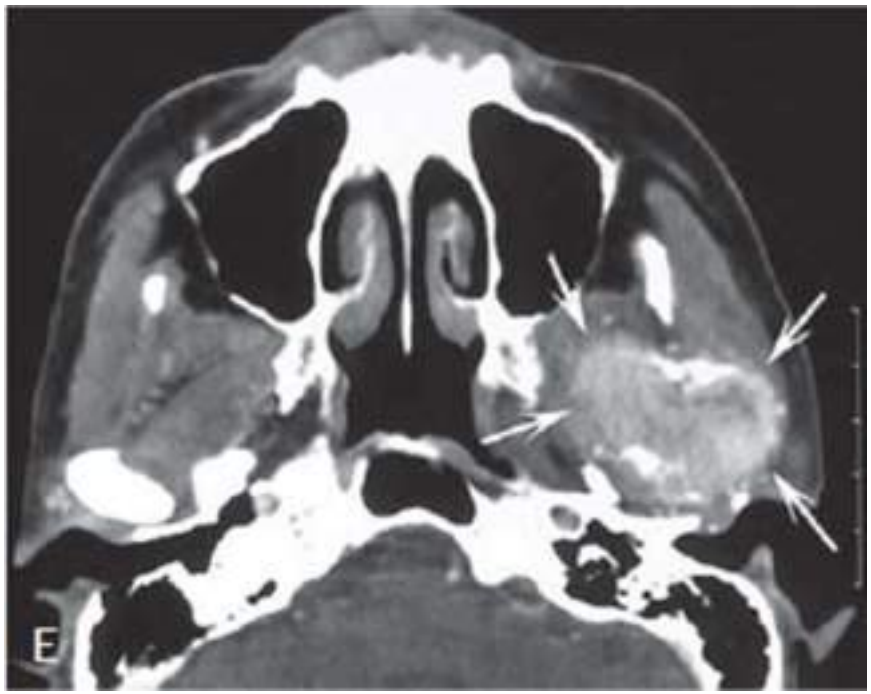
CT SCAN & MRI

- Help assess size & extent of tumor in 3 dimension
- CT and MRI aid in determining the status of the cervical lymph nodes.
- CT allows bony assessment
- MRI sensitive to evaluate intracranial invasion
- Extensive metastasis may be assessed using CT with contrast or MRI with Gadolinium contrast
- Lymph nodes not assessable for clinical examination or FNAC may be assessed with CT MRI

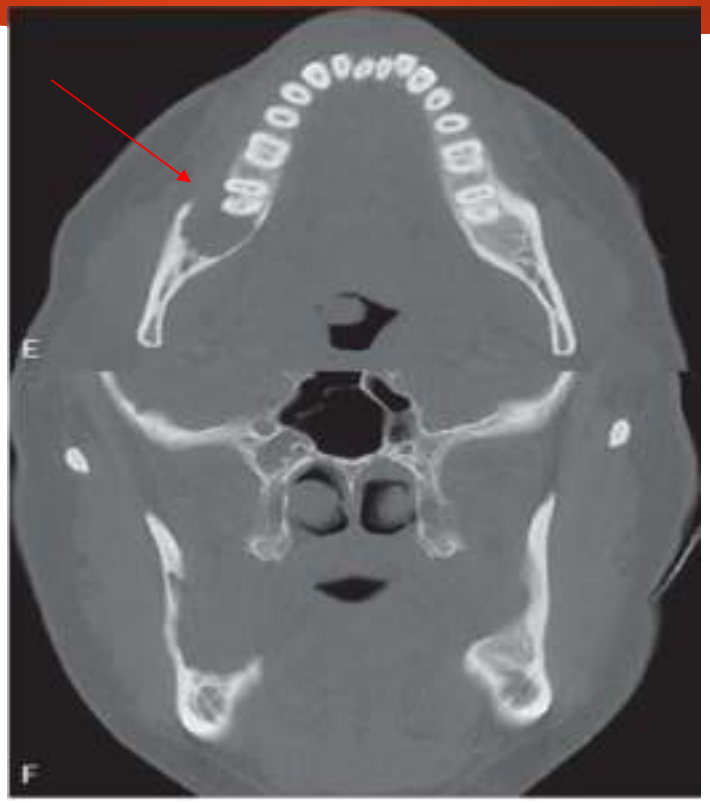
Ct scan



CT SCAN



CT SCAN



MRI

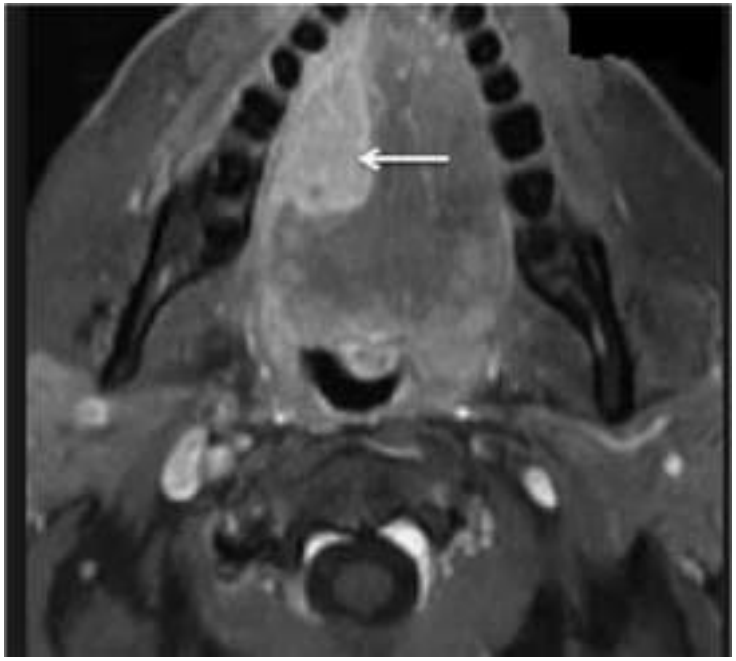
- Soft tissue involvement of the antrum and nasopharynx can be assessed with CT and MRI
- MRI is rapidly replacing CT as the imaging technique of choice for the head and neck.
- Each MRI image should include T1-weighted images, which demonstrate normal anatomy with detail and soft tissue definition

MRI

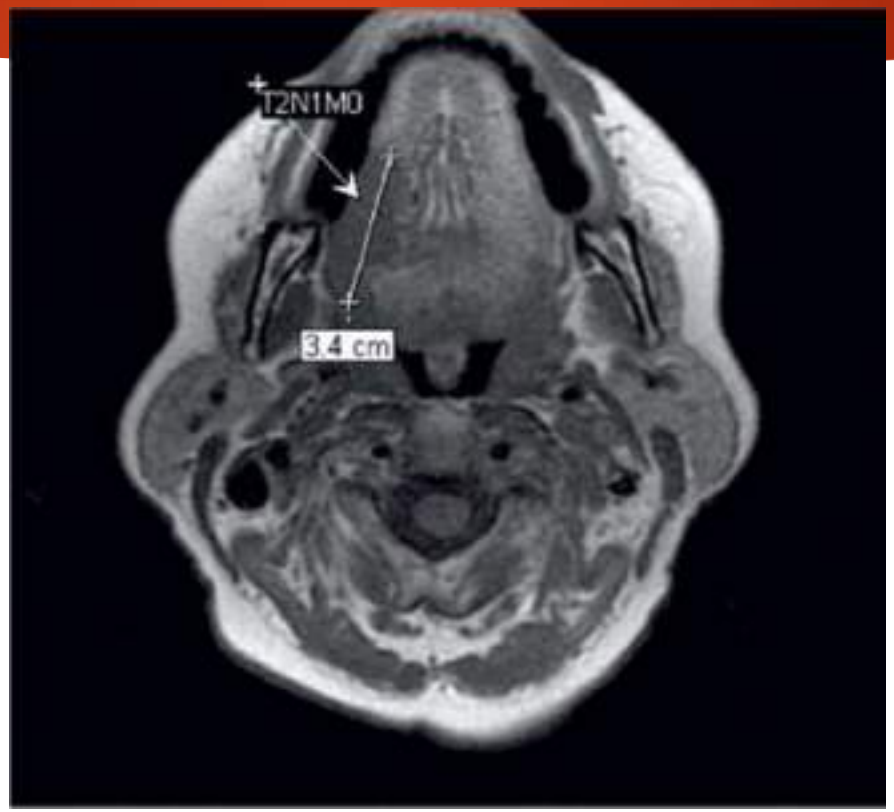
- T2-weighted images, which demonstrate the tumor in comparison with adjacent muscle and other soft tissues.

- MRI allows more accurate distinctions between tumor and benign inflammatory disease than CT.

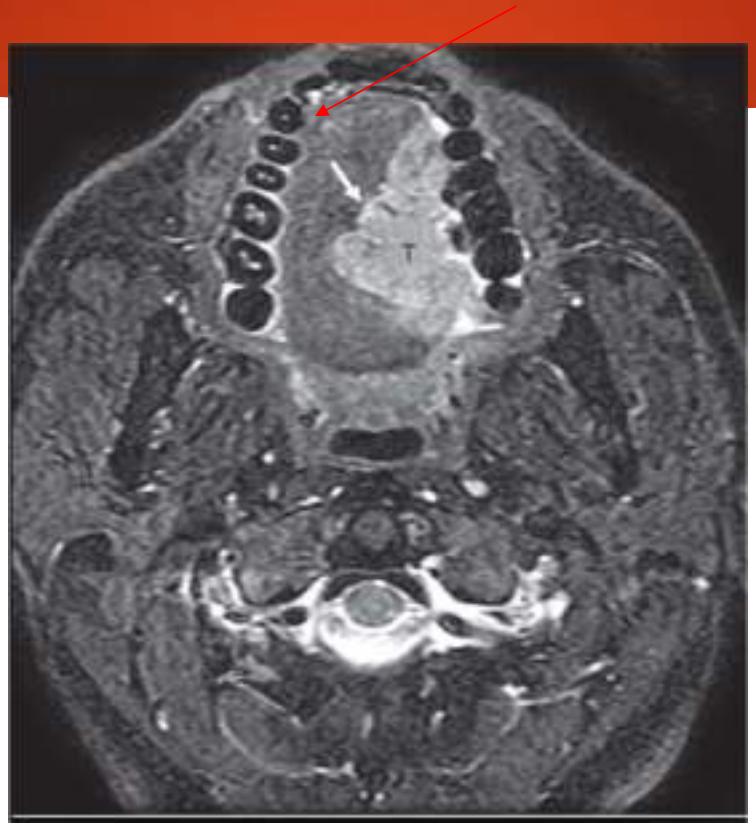
MRI



MRI

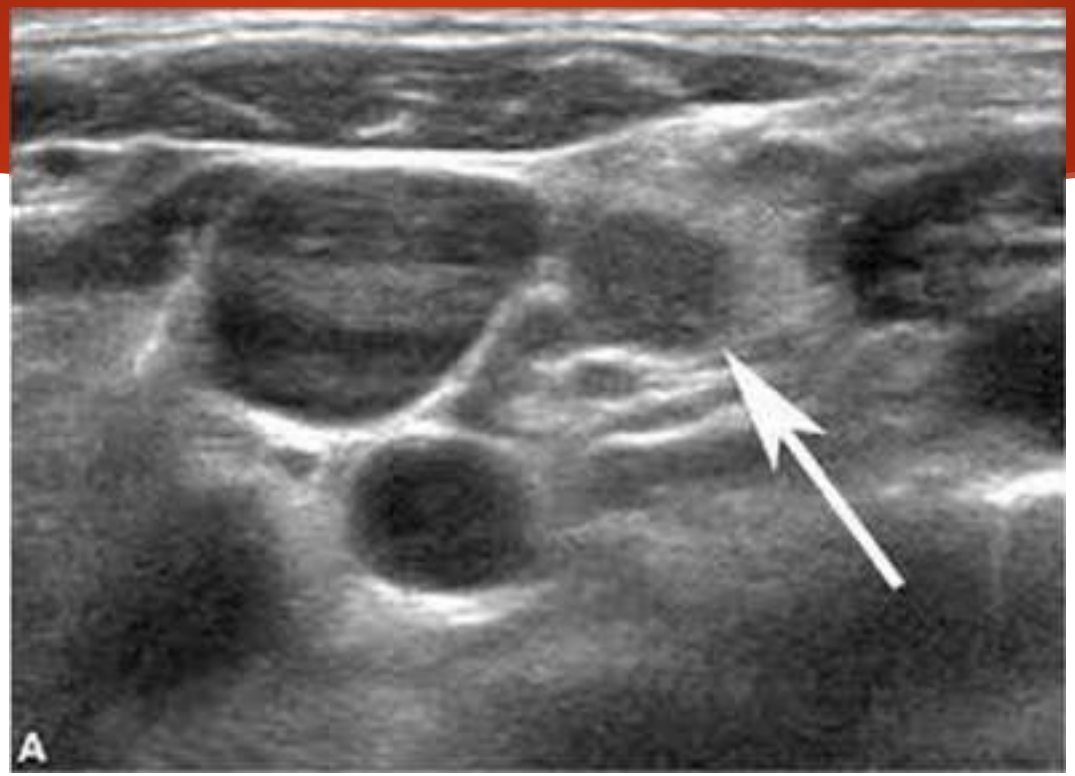


MRI

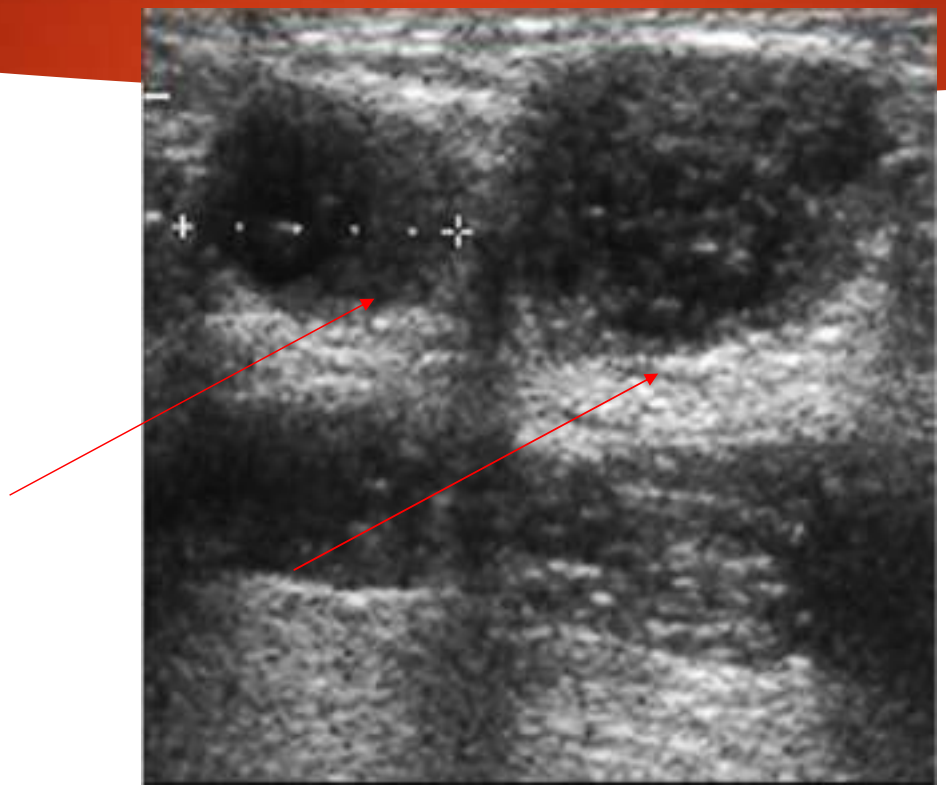


Ultrasonography (USG)

- Can provide evidence of bone involvement and can indicate the extent of some soft tissue lesions.
- May also be of value for imaging salivary gland masses and for the assessment of lymph nodes
- Differentiation between benign and malignant nodes may not be possible.
- The ultrasonographically guided needle biopsy technique may be useful in the assessment of head and neck masses



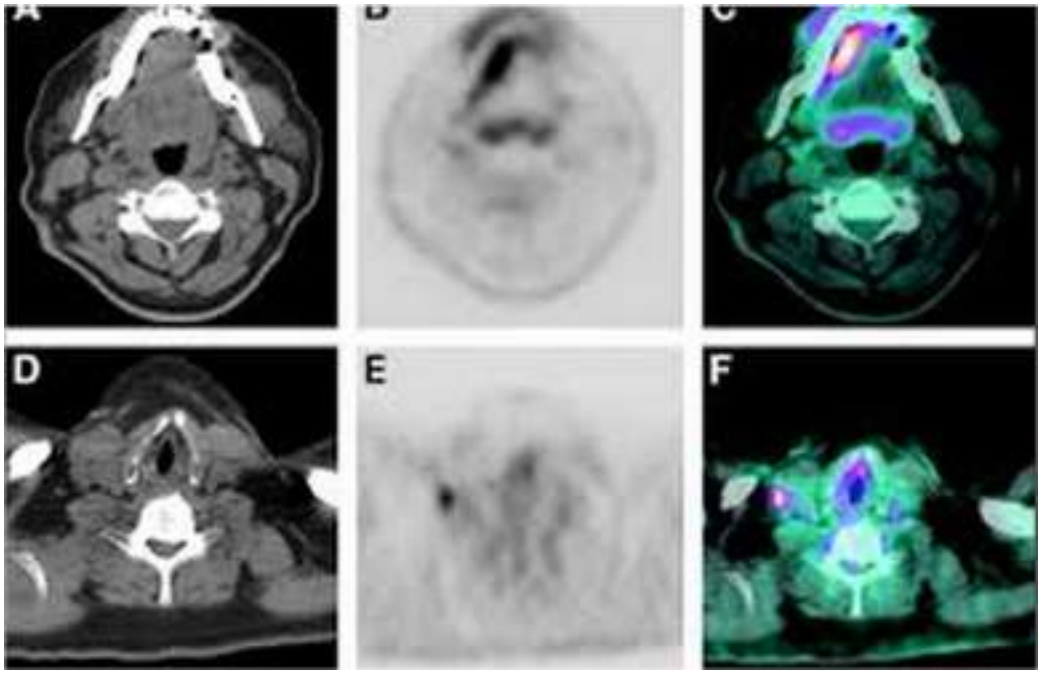
USG cervical lymph nodes



PET Scan

- :

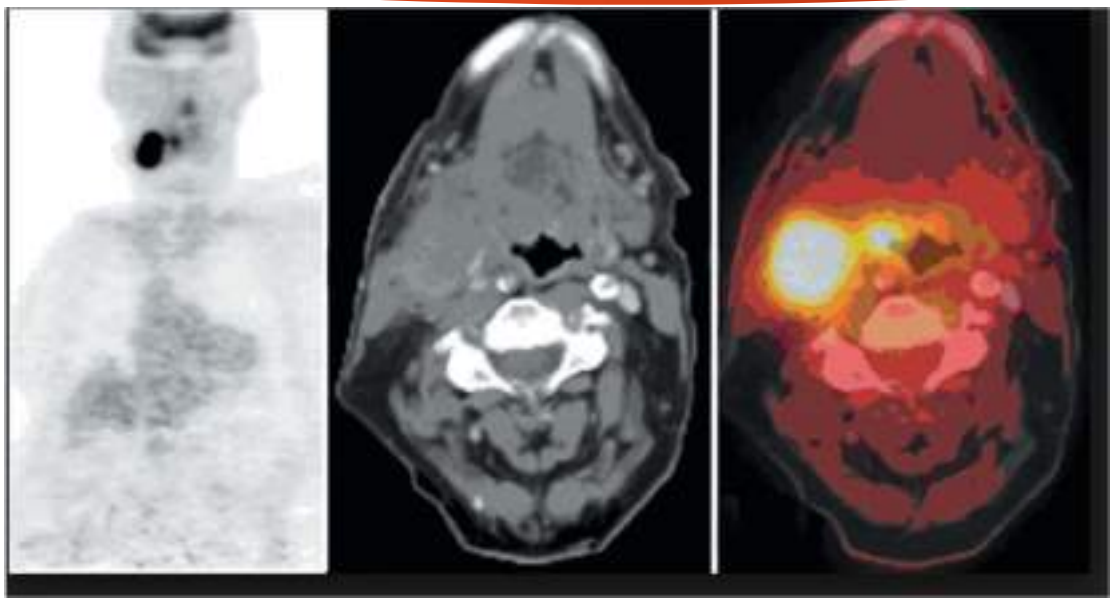
- Using the radiolabeled glucose analog 18-fluorodeoxyglucose (18FDG) offers a functional imaging approach for the entire body.



- Conventional radiography will detect advanced involvement (>1 cm)
- Detection of smaller masses or lymph nodes with PET CT

- PET-CT provides information for:

- staging and in the evaluation of patients with suspected recurrent squamous cell carcinoma
- in whom anatomic imaging is inconclusive due to the locoregional distortions rendered by surgery and radiotherapy



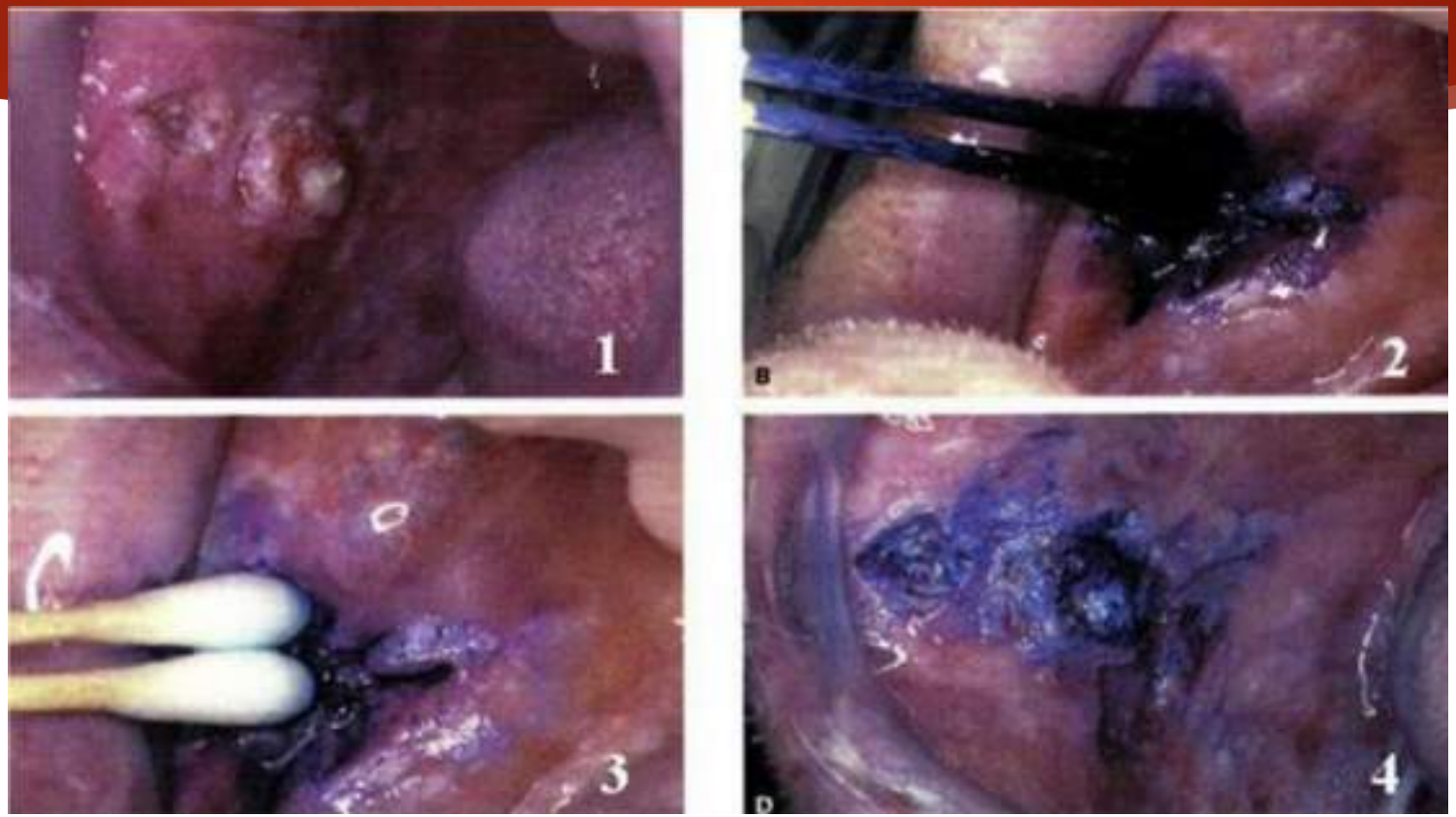
Acquisition of a Tissue Specimen

- Exfoliative Cytology
- Fine-needle Aspiration (FNA)
- Standard biopsy

Vital staining

- Aids in early detection of oral precancerous & malignant lesion
- Toluidine blue can be applied directly to suspicious lesions or used as an oral rinse.
- Basic metachromatic dye stains acidic tissues
- Stains mitochondrial DNA & altered DNA in premalignant & malignant lesions with increased DNA in cells

- The assessment of dye uptake depends on clinical judgment and experience
- Positive retention of toluidine blue (particularly in areas of leukoplakia, erythroplakia, and uptake in a peripheral pattern of an ulcer) may indicate the need for biopsy.
- False-positive dye retention may occur in inflammatory and ulcerative lesions
- A return appointment in 14 days, providing time for inflammatory lesions to improve, may lead to a decrease in false-positive results.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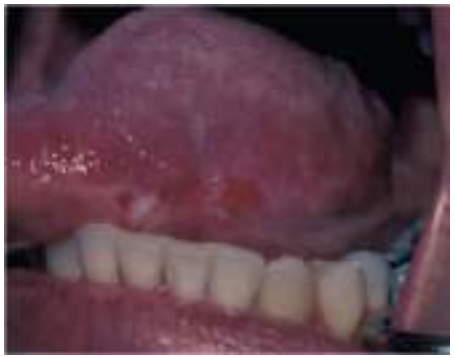
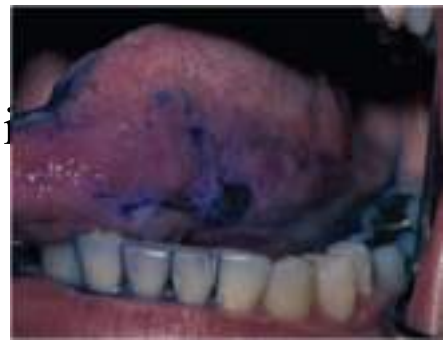
- Toluidine blue predicts oral premalignant lesions at risk of progressing to squamous cell cancer



- provides guidance for the selection for the biopsy site

- accelerates the decision to biopsy

- In postradiotherapy follow-up, the retention of toluidine blue may assist i distinguishing nonhealing ulcers and persistent or recurrent disease.



Exfoliation cytology

- Dysplastic cells have fewer & weaker connections
- Tend to slough off
- Collected & studied

- Sample can be collected with
  - Tongue blade
  - Cement spatula
  - Brush

- Cytology reported as
- Class I: normal cells
- Class II : (atypical) presence if minor atypia
- Class III: (intermediate) cells display wider atypia more suggestive of cancer precancer, ca in situ
- Class IV: suggestive of cancer a few cells with malignant characteristic or with borderline characteristics. Biopsy mandatory

Brush biopsy

- Uses brush to obtain complete trans-epitheleial biopsy specimen
- Provides cellular representation of basal, intermediate & superficial layer
- Does not require topical anaesthesia minimal bleeding & pain

Results

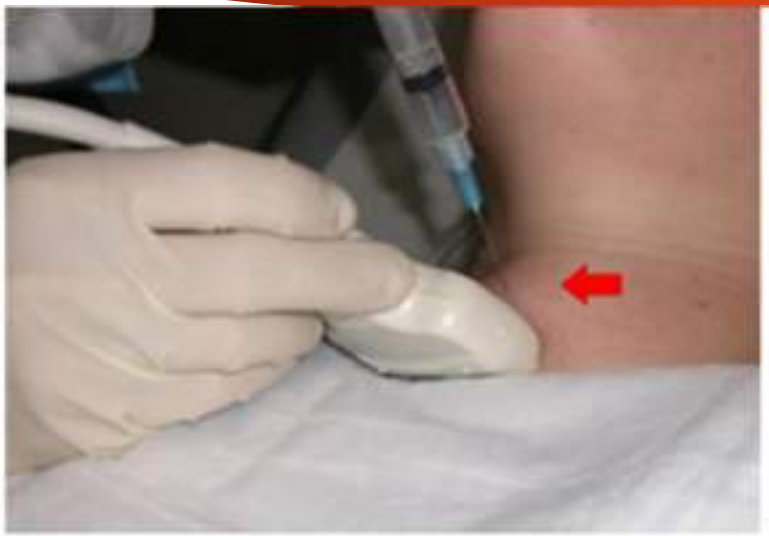
- Inadequate : incomplete trans epithelial specimen
- Negative : no abnormality
- Atypical : abnormal changes of uncertain diagnosis
- Positive : evidence of cellular atypia & carcinoma

- Computer-assisted analysis of oral brush cytology is completed on Pap-stained exfoliated cells, scanned by computer for abnormal cell morphology and keratinization

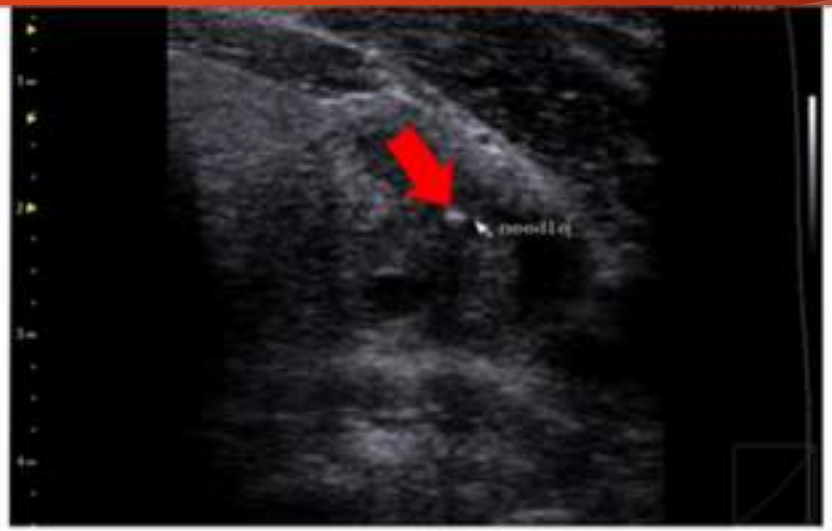
- Final diagnosis is made by an examining pathologist on the basis of standard histomorphologic criteria

- Open biopsy of enlarged lymph nodes is not recommended; in such cases,
- FNA biopsy should be considered.

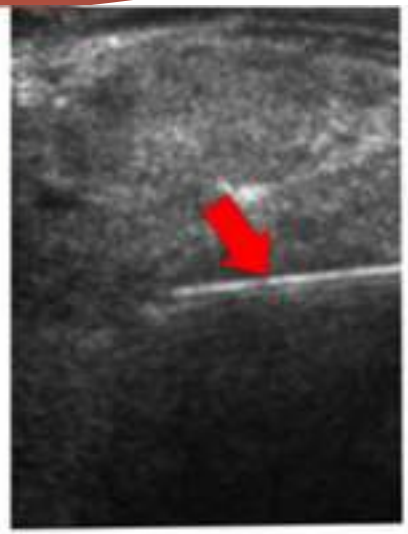
- FNA also may aid the evaluation of suspicious masses in other areas of the head and neck, including masses that involve the salivary glands, tongue, and palate



Ultrasound-guided Fine-needle aspiration cytology (FNAC) of a thyroid gland mass (red arrow)



Ultrasound-guidance showing the tip of the needle (red arrow) in the mass in question confirming accurate targeting



Ultrasound-guidance showing the shaft of the needle (red arrow) in the mass in question confirming accurate targeting

Histopathology

- Microscopic examination is required for diagnosis.
- Dysplasia or atypia describes a range of cellular abnormalities that includes changes in
  - cell size and morphology
  - increased mitotic figures
  - hyperchromatism
  - alteration in normal cellular orientation
  - maturation

- The descriptions of mild, moderate and severe dysplasia refer to epithelial abnormality of varying severity.

- When the abnormality involves the full thickness of the epithelium, the diagnosis is carcinoma in situ.

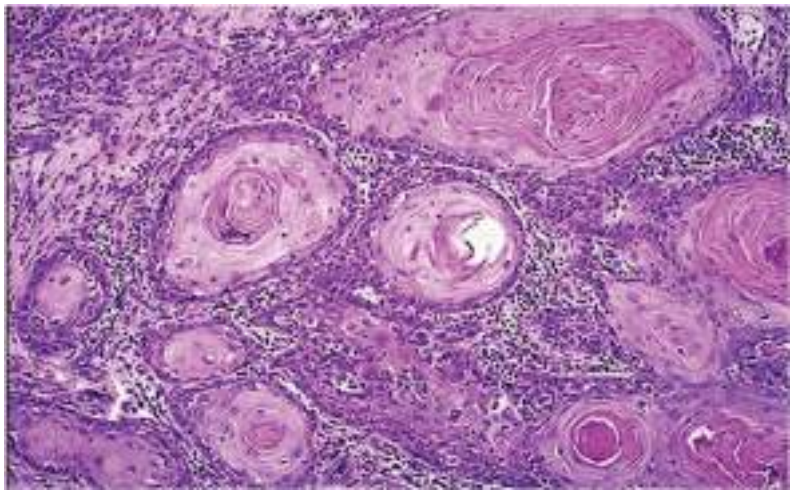
- When the basement membrane is violated, carcinoma is diagnosed.

- Squamous cell carcinoma graded as

- Well differentiated
- Moderately differentiated
- Poorly differentiated

Well differentiated

- Cells arranged in sheets or nests characteristic of squamous origin
- Cells are large & show distinct cell membrane
- Nuclei are distinctly dark stating
- Increased number of mitotic figure
- Individual cell keratinization
- Keratin pearl



Moderately differentiated

- Less resemblance to squamous epithelium
- Altered cell to cell contact
- Greater number of mitotic cells
- Varied shape & size
- Keratin pearl may not present

Poorly differentiated

- Proliferation of anaplastic cells
- Highly invasive
- Poor prognosis
- Bear little resemblance to cell of origin
- Cells show lack of cohesiveness
- Very high mitotic figure

MANAGEMENT