EPIDEMIOLOGICAL ANALYSIS AND MANAGEMENT OF ORAL CANCERS

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CERTIFICATE

This is to certify that this dissertation entitled **"Epidemiological Analysis and Management of Oral Cancers"** is a bonafide record done by **Dr. C. GEETHA SANKARI**, submitted as parital fulfillment for the requirements of M.S. Degree Examinations Branch I, General Surgery March 2008.

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CONTENTS

INTRODUCTION

World wide carcinoma is diagnosed annually in 10 million people.

Oral Cavity Carcinoma accounts for 2,74,000 newly diagnosed Carcinoma in World annually.

Oral cavity is the 6th most common carcinoma in the world. Lung, Stomach and prostate (In males), Breast, Cervix and colorectum (In Females) are the top three carcinomas in the world.

In well developed countries the incidence rate of oral cavity is less when compared to developing countries.

In south central Asia (India) oral cavity is the commonest in male and cervix is the commonest in Female.

According to National Cancer Registry Programme – District-wise comparison of age specific incidence – Thanjavur stands 11th place for oral cavity Carcinoma in male in India (Fig-1).

Comparison to world, developed, developing and central Asia there is a wide difference in the incidence of oral cancer. High incidence is probably due to socio economic factors habits, ignorance, late detection and lack of awareness.

Even though oral cancers are easily accessible for physical examination and Biopsy, majority reported for treatment only at the later stages. Cure rate is high if patients are treated in the early stages.

Knowing the magnitude of the problem a study is undertaken to know about the incidence in rural agro based districts from which patients attend our hospital (Fig – 2)

A Prospective epidemiological analysis of oral cavity cancer and their outcomes for the period from June 2005 to September 2007 are discussed.

AIM OF STUDY

- To analyse the incidence (Age, Sex, Occupation, Site and Histology) of oral cavity cancers in our Institution during the period 2005-2007.

- To determine the etiological factors that influences the development of oral cavity cancers in this region.

- To discuss the clinical presentation.

- Discussion of various modalities of treatment and their outcomes.

- Preventive aspects of Oral Carcinoma.

HISTORICAL REVIEW

Ebers Papyres (1500 BC)	–	Eating ulcers of the gun.
Pimpernelle – 1658	–	First Hemiglossectomy for Benign lesion
Marchetti – 1664	–	Excision of the tumor in carcinoma tongue.
F. Ruysch – 1734	–	Traumatic genesis for Carcinoma tongue was proposed
Lorenz Heister	–	To obtain a cure it was necessary to remove a margin of Normal tissue with the tumor.
In Eighteenth century	–	German surgeons accepted glossectomy as the procedure of choice in treatment of cancer tongue
Astley P.C. – 1914	–	Intratracheal insuffilation anaestheia for Excision of Entire tongue.
Theoder Fricke – 1898	–	Operation for cancer of the lip.
A.B. Johnson & Joseph D. Bryant	–	Malgagnes operation for Carcinoma lip.
Crile – 1906	–	Described the Block dissection with removal of all Nodes and Lymph bearing areolar tissue.
J.C. Stewart – 1910	–	Radical operation must include removal of the tissue adjacent to the growth and associated Lymph Nodes.
A.C. Broders – 1920	–	of Mayo Clinic reported males and smokers are at higher risk when compared to Females and non smokers.
George Brewer – 1923	–	Incidence of Lower lip is more than upper lip.

Neck dissection

Grant ward & Haynis Martin – 1940	–	Commando's operation performed in Memorial Hospital Newyork
Mccammon and Shah	–	Radical Neck dissection.
Boccas – 1960's	–	Modified Radical Neck dissection Type – 3
Medina & Byres	–	Selective neck dissection (I–III)
Khaiff	–	Selective neck dissection (II–IV)
Weber	–	Selective neck dissection (VI)

Radiotherapy

Henry Bequeral – 1897	–	Discovered Radiation
Pierre curie & Mary curie – 1898	–	Discovered Radium.
1930	–	Introduction of Brachytherapy
1950	–	Teletherapy used with Cobalt 60
1980's	–	Supplementation with Megavoltage Radiotherapy

IMRT (Intensity Modulated RT) Latest Concept.

Chemotherapy

1970's	–	Role of Adjuvant Chemotherapy
Mccomb & Felteher Moore – 1980's	–	Combined Surgical & Radio therapy techniques

Reconstruction

Karl Thiersch – 1874	–	Free skin graft
John Wolfe – 1875	–	Full thickness graft
1960'	–	Regional flaps introduced
Aryan – 1979	–	Pectoralis Major Musculocutaneous flap.

Free Flaps

In China	–	Radial Forearm flap
Heyden & Miller – 1983	–	Lateral Thigh flap

Molecular targeted therapies

Slaughter described field cancerization in the molecular Biology of oral cavity squamous cell carcinoma.

ANATOMY OF ORAL CAVITY

Oral cavity encompasses the area from the vermillion border of the lip to an Imaginary line drawn between Hard and Soft Palate, and the circumvallate Papillae Inferiorly. 7 Anatomical sites are included in the oral cavity.

1) Lip
2) Buccal mucosa
3) Upper & Lower alveolar ridge
4) Floor of Mouth
5) Anterior 2/3 of Tongue
6) Retromolar Trigone
7) Hard Palate.

Lip: Lips are composed of the orbicularis oris muscle with skin on the external surface and mucous membrane covers the internal surface.

Transition from skin to mucous membrane of the oral cavity is the lip vermillion.

Floor of Mouth

- Floor of mouth is 'U' shaped area bounded by the Lower gum and oral tongue.
- Terminates posteriorly at the insertion of anterior tonsillar pillar into the tongue.
- Paired sublingual glands lies beneath the mucous membrane.
- Whartons duct (Duct of Submandibular gland opens in the floor of mouth).

Tongue

Mobile Anterior 2/3 of tongue anterior to circumvallate papillae is considered as a part of oral cavity, posterior to circumvallate papillae is called as oropharynx.

Buccal Mucosa

Buccal mucosa is the mucous membrane covering the Inner surface of lips & cheek ending below and above with transition to the gingiva, and it ends posteriorly at the Retromolar Trigone. Parotid duct opens into the buccal mucosa at the upper second Molar tooth.

Upper and Lower Alveolar Ridge

Upper alveolar ridge extends from buccal sulcus to Hard Palate and extends up to superior end of Pterigopalatine arch posteriorly.

Lower Alveolar ridge includes the Mucosa covering the Mandible from the gingivo buccal gutter to the origin of mobile mucosa in the floor of mouth.

Both include the mucosal covering of the alveolar process of Maxilla and Mandible.

Retro molar Trigone

Behind the third molar tooth a small triangular surface is called Retromolar Trigone.

Base of the triangle - Last molar tooth.

Apex – Terminates at Maxillary tuberosity.

Hard Palate

It serves as a partition between Nasal and oral cavities.

Anterior 2/3 formed by palatine process of Maxilla.

Posterior 1/3 formed by Horizontal plate of Palatine Bone.

It drains mainly into upper deep cervical and retropharyngeal nodes.

Neck Nodes

Level I	-	I-A Sub mental
	-	I-B Submandibular
Level II	-	Extending from skull base to Carotid Bifurcation
		II_A – Anterior to Spinal accessory.
		II_B – Posterior to spinal accessory
Level III	-	Extending from Carotid Bifurcation to Omohyoid Muscle
Level IV	-	Extending from omohyoid Muscle to Clavicle
Level V	-	V_A Superior to the level of cricoid cartilage } Posterior triangle
		V_B Inferior to the level of cricoid cartilage
Level VI	-	(Pretracheal & Prelaryngeal) – Central group
Level VII	-	Superior Mediastinum.
Level VIII	-	Retropharyngeal Nodes of Rouviere – lymphnodes Posterior to Naso and oropharynx.

Oral Cavity – Lymphatic drainage

1.	Lips	Submandibular, preauricular and facial nodes
2.	Buccal mucosa	Submaxillary and submental nodes
3.	Gingiva	Submaxillary and jugulodigastric nodes
4.	Retromolar trigone	Submaxillary and jugulo-digastric nodes
5.	Hard palate	Submaxillary and upper jugular nodes
6.	Floor of mouth	Submaxillary and jugular (middle and upper) nodes
7.	Anterior two thirds of the tongue	Submaxillary and upper jugular nodes

EPIDEMIOLOGY OF ORAL CAVITY CANCERS

Incidence

- In western world it forms 2 – 4% of all newly detected cancers.

  More than 90% are primary oral malignancy (ie) Squamous cell carcinoma.

Age

- 90% of oral cavity cancer appears over the age of 40 yrs and 65 yrs is the average age at diagnosis.
- Mean age of survival is around 5 yrs from the time of diagnosis.
- Mean age of death is around 68 yrs.

Sex

- Male to female ratio is 2.2 : 1
- Men > women: 2-4 times increased risk for men than women for all racial / ethnic groups except for Filipinos, where the risk is equal for both male and female.

Race (Ethnic) Origin

- Before the age of 55 Yrs. Oral cavity – carcinoma is the 6th most common carcinoma in whites and in blacks it is the 4th most common carcinoma.
- Lip and Salivary gland tumors are more common in white Americans than Black Americans.
- When Compared to U.S.A. higher rates of oral cavity Cancers are reported in India, South East Asia, Hungary and Northern France.

SECOND PRIMARY CARCINOMA

- Second Primary carcinoma is defined as Synchronous (Different sites within 6 Months) (Or) Metachronous (different sites after 6 months) (or) same site after 3 years of Malignancy.
- Risk of second Carcinoma is more pronounced among patients younger than 60 years of age.

MOLECULAR BIOLOGY OF ORAL CAVITY SQUAMOUS CELL CARCINOMA

New exciting field which throws more light on the pathogenesis of oral cavity cancer. Dysregulation of the molecular processes that underline tumorogenesis and metastasis in oral cavity squamous cell carcinoma.

Three of these Mechanisms are

1. Field Cancerisation
2. Genetic progression
3. Cancer Controlling genes

1) Field Cancerisation

Slaughter and Colleagues had described this phenomenon.

Regions of grossly normal mucosa with chronic exposure to environmental mutagens in tobacco and Alcohol (or) Infection with HPV Contribute to the development of dysplastic mucosa.

2) Genetic Theory

Genetic alteration in histologically normal tissues and in premalignant lesion includes a) Loss of Heterozygosity

b) Activation of Telomerase

c) DNA – Hyper Methylation.

3) Cancer controlling genes

a) Oncogenes: Hyper functionality of these carcinogens directly contribute to malignant process.

In Oral Cavity Squamous Cell Carcinoma involved genes

1) EGFR (Endothelium derived Growth Factor Receptor)

2) STAT – 3 (Signal Transducer and activator of Transcription Family)

b) Tumor suppressor genes

Loss of both alleles of a tumor suppressor gene through mutation, deletion results in alteration of cellular Homeostasis (Knudson – Two hit Hypothesis)

c) Stability genes

House keeping of the cells DNA has been termed as stability genes. Mutation (or) Non-functionality results in carcinogenesis. FANCA gene has genetic predisposition for oral cavity carcinoma.

Hanahan & weinburg suggested certain alteration in physiological process such as autonomy in growth signaling, invasion of apoptosis, unresponsiveness to growth inhibitor signaling, limitless replication, angiogenesis, invasion and metastasis are the molecular changes in carcinogenesis.

GENETIC CHANGES IN ORAL CARCINOGENESIS

1) EGFR/TGF – 2α – Increased production
2) TP53 gene – Loss of P53 gene
3) TP 16 & cyclin D1 – Activation
4) BAX – proapoptic – Decreased
   BCL2 – anti apoptic – Increased
   } in poorly differentiated carcinoma

Understanding of the above molecular biology has led to therapeutic strategies that target dysregulated processes in tumor microenvironment.

RISK FACTORS

1) **Tobacco:** contains more than 300 carcinogens. Tobacco consumed in 2 ways
   a) smoking tobacco
   b) smokeless tobacco or spit tobacco

a) **Smoking tobacco:** Consumed in the form of cigarette, beedi and kreteks. Carcinogens increase the relative risk by causing mutations that disrupt the cell cycle regulation or through an effect in the immune system

b) **Spit tobacco or smokeless tobacco:**

Used in 3 forms

Chew – Leafy form of tobacco used with betel leaf & lime

Plug – That has been compressed in to brick form and consumed

Snuff – powdered form of tobacco usually sold in tins or flat cans. It causes hyperkeratosis, dysplasia and squamous cell carcinoma

Tobacco Contains Aromatic Hydrocarbons, Benzpyrene and Tobacco Specific Nitrosamines act locally on the stem cell and Interfere with DNA synthesis.

Relative Risk is 8 times (or) more.

Alcohol

Alcohol particularly hard liquor incidence is 6 times more common among drinkers than non drinkers.

- Alcohol and smoking have a synergistic effect.
- Pooling of Saliva with carcinogens results in oral cavity cancer.
- Extreme alcohol consumption of 55 drinks / week carries greater risk than tobacco alone.

U – V Radiation

- Risk of cancer of the lower lip from exposure to UV radiation, in areas close to the equator.
- Lips are at increased risk, since it lacks a pigmented layer.

Viruses

HPV (6 and 16) are at increased risk for oral cavity cancer.

HPV 16 → 5 times more common risk.

HPV 6 → 3 times more common risk.

Diet Nutrition

Iron deficiency anaemia (Plummer Wilson Syndrome) (or) Paterson Brown – Kelly Syndrome.

Vitamin A, C & E deficiency.

Dental Factors

Poor Oral Hygiene leads to higher levels of salivary acetaldehyde a Known carcinogen in oral cavity cancer.

Persistent Irritation to the oral mucosa in the form of ill fitting dentures can lead to dysplastic changes in the epithelium

Occupational exposure

Usage of certain chemicals including Formaldehyde, Nickel, Chromium and leather Tanning Products, are at increased risk.

Immune Competence

Compromised Immunity related to HIV Infection, organ transplantation, chemotherapy (or) Radiation therapy acts as contributing factors.

Genetic & Familial Syndromes

Syndromes associated with defective DNA repair including xeroderma Pigmentosa, Ataxia Telangectasia, Bloom's syndrome and Fanconis anaemia are at increased risk.

Increased risk of second primary Malignancy of oral cancer found commonly in LiFraumeni syndrome (P_{53} deficiency)

PREMALIGNANT CONDITIONS

1) Oral Leukoplakia

Defined as white keratotic Plaque (or) Patch. key pathological features include hyperkeratosis, Parakeratosis and acanthosis.

Varieties include Leukoplakia Simplex, Leukoplakia Verrucosa, and Leukoplakia erosive.

2) Erythroplakia

Red mucosal patch is more commonly found in soft palate and tonsillar fossa. 7 times higher risk than Homogenous Leukoplakia.

3) Erythroleukoplakia

5 times more risk than Homogenous Leukoplakia.

4) Proliferative verrucous Leukoplakia (PVL)

Proliferative, generally irregular white patches (or) plaques that progress slowly multifocally in the oral mucous membrane. 100% can develop Squamous / verrucous cell ca.

Most patients of PVL are non smokers; women are at increased risk than men, peak age of incidence is between 60 and 70 yrs.

5) Lichen Planus : Lymphocytic Infiltrate in epithelial layers.

6) Oral sub mucosal Fibrosis

Causative agent Areca–catecha a component of Betel-nut thought to affect collagen synthesis. It presents with thickened, White mucosa lacking elasticity.

7) Sublingual keratosis

8) Oral epithelial Dysplasia : Epithelial dysplasia characterized clinically by an alteration in oral epithelium.

Other premalignant lesions

Actinic keratosis

Discoid Lupus Erythematosis

Chronic Hyperplastic conditions

Atypia in Immunosuppression

Syphilitic Leukoplakia.

Treatment of Premalignant Conditions

- ❖ Biopsy shows no malignant transformation – observation of the patient
- ❖ Larger area shows extensive lesion – Excision of mucosa and grafting.
- ❖ Cryotherapy, CO_2 laser ablation, Low dose β carotenes, Topical steroids, Topical cyclosporine and Retinoids are used for treating premalignant conditions.

CLASSIFICATION OF TUMORS

1) Primary
2) Secondary

Primary Epithelial Origin

- Squamous Cell Carcinoma
- Adeno Carcinoma

Non Epithelial Origin

Melanoma, soft tissue sarcoma, Plasmacytomas

Squamous Cell Carcinoma and Other Variants Include

- Lymphoepithelioma,
- Spindle cell Carcinoma
- Verrucous – Papillary (exophytic)
  – Adenoid (Acantholytic)
  – Adeno Squamous
  – Baseloid

– Undifferentiated carcinoma

– Transitional cell carcinoma

– Keratinized Carcinoma

– Non Keratinized Carcinoma.

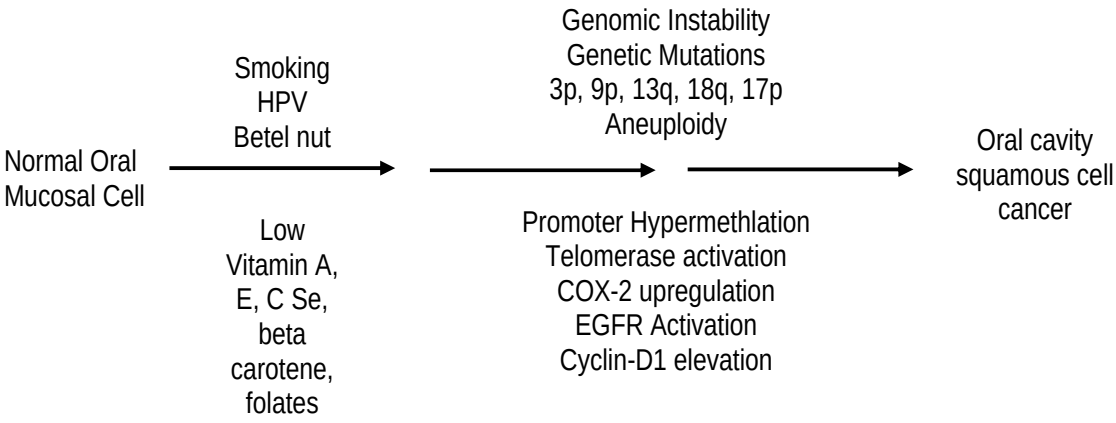
Adenocarcinoma and their variants

- Malignant Mixed Carcinoma
- Adenocystic Carcinoma
- Mucoepidermoid Carcinoma
- Acinic cell carcinoma.

PATHOLOGY

Majority of Head and Neck Cancers arise from the surface epithelium therefore squamous cell Cancer and its variants, are the most common type.

MECHANISM OF CARCINOGENESIS



Verrucous carcinoma

Verrucous is a Low grade Squamous Cell Carcinoma found most often in the oral cavity particularly in the buccal mucosa and gingiva.

Verrucous carcinoma resembles a wart with, distinct margin, Roughened, cobblestone appearance, it rarely develops Lymph node Metastasis.

HISTOLOGICAL GRADING

Broders established a histological grading for Squamous Cell Carcinoma based on Microscopic evaluation of the tumor.

Cellular differentiation based on the degree of cellular pleomorphism, frequency of mitoses and extent of Keratinisation.

It is classified as

a) Well differentiated (Grade – I)

b) Moderately differentiated (Grade II)

c) Poorly differentiated (Grade III)

d) undifferentiated (Grade IV)

Some may Include pattern of Invasion, stage of Invasion, presence of angiolymphatic tumor thickness, DNA content and their Serum Markers.

CHIEF SYMPTOMS

- ❖ Ulcer
- ❖ Swelling
- ❖ Fetor
- ❖ Excessive salivation
- ❖ Difficulty in chewing
- ❖ Lump in neck
- ❖ Pain
- ϖ Dysphonia
- ϖ Reromolar Extension
- ϖ Ankyloglossia
- ϖ Trismus
- ϖ Bony erosion
- ϖ Dysphagia

METHODS OF SPREAD OF SQUAMOUS CELL CARCINOMA

I. Local Spread

II. Lymphatic

III. Blood borne

I. LOCAL SPREAD

a) Invasion of Soft tissues

Infiltrate deeply into adjacent connective tissue, carcinoma tongue Infiltrate more posteriorly than anteriorly.

b) Invasion of Perineural spaces

Perineural spread is characteristic of adenoid cystic Carcinoma.

Centripetal Infiltration of tumor along the branches of mandibular nerve (Inferior Dental, Long Buccal, or Lingual), is common. For this reason,

whenever the mandible is resected, Inferior dental bundle should be resected as high as possible.

c) Invasion of Vessels

Invasion of arteries are rare. Main predisposing factors are irradiation of neck, necrosis of skin flap, infection and salivary fistula.

Even in patients with carotid rupture Infiltration not seen. No correlation is seen between infiltration of internal jugular vein and presence of systemic metastasis.

d) Invasion of Bones

Principle mode of access

1. Facial bones by direct extension.
2. Anatomical openings such as inferior dental canal and Incisive palatine foramen.
3. Periosteal lymphatic spread may occur.

Despite the dense cortical plate, Mandibular Invasion is more common than Maxillary Invasion.

II. LYMPHATIC SPREAD

Cancers of the oral cavity mainly Involves (Level I, II & III) (Sub mental, Sub mandibular, upper, middle cervical) and Jugulo digastric Nodes.

Important prognostic factors include multiple involved nodes, metastasis in low cervical nodes, and extra capsular invasion.

III. BLOOD BORNE SPREAD

Risk of Distant metastasis is infrequent. Poorly differentiated & younger patients are at more risk. Lungs, Liver and Bone (Vertebrae, Ribs and Skull) are involved in blood borne spread.

According to anatomical area modes of spread

1.	Lips	Skin, Commissure, Mucosa and Muscle
2.	Gingiva	Soft tissue, buccal mucosa, Periosteum, Bone, maxillary antrum and Dental nerves
3.	Buccal mucosa	Side walls of the oral cavity, Lips, Retromolar trigone and Muscles
4.	Hard palate	Soft palate, Bone, maxillary antrum and Nasal cavity
5.	Retromolar Trigone	Buccal mucosa, Anterior pillar, Gingiva and Pterygoid muscle
6.	Floor of mouth	Soft tissue, tonsils, salivary glands, Root of tongue, Base of tongue and Geniohyoid-mylohyoid muscles
7.	Tongue	Anterior two thirds of tongue, Lateral borders, Base and underside of tongue and Floor of mouth

PRETREATMENT EVALUATION

Complete History & Physical Examination

- ❖ Biopsy of the primary
- ❖ FNAC of the neck nodes.
- ❖ Incision / Excision biopsy of the nodes.

Imaging Studies

- ❖ Chest X ray – PA view.
- ❖ CT / MRI of Primary and Neck – To know the extent of primary and Cervical Nodal involvement.
- ❖ Panorex (Or) dental x ray – To Evaluate mandibular invasion.

Laboratory tests

Pre anaesthetic testing

Baseline Liver function tests

Additional laboratory tests as per the patient medical history.

Examination under anaesthesia

- Direct laryngoscopy & pharyngoscopy
- Esophagoscopy
- Bronchoscopy
- Palpation of tongue, oro and Naso Pharynx.

Neck Nodes

Histological demonstration of metastasis in a lymph node is gold standard.

Investigations for neck nodes include – computerized tomography, MRI and FDG – PET.

MRI and CT have higher sensitivity & specificity than clinical examination in detection of metastasis.

CT / MRI can detect lymph nodes larger than 1.5 cm in diameter.

FDG–PET is more sensitive & specific than CT / MRI. Current FDG–PET can detect tumors smaller than 1cm.

CT & MRI detect the metastasis, relationship of a metastatic tumor with critical structures such as internal carotid artery, cervical spine, vertebral artery and brachial plexus.

New MRI Methods

a) Volumetric Interpolated Breath Hold Examination (VIBE)

b) Functional imaging using Dynamic Contrast enhanced MRI.

c) Diffusion weighed Imaging.

d) Iron oxide enhanced MRI. (Ultra small super paramagnetic Iron oxide) USPIO.

Above techniques may have a role in future.

TNM STAGING

Primary Tumor (T)

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

T4 Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, (i.e.) chin or nose.

T4a Tumor invades adjacent structures through cortical bone, into deep muscles of tongue (genio-glossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus and skin of face.

T4b Tumor invades masticator space, pterygoid plates, skull base or encases internal carotid artery.

Regional Lymph Nodes (N)

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 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.

Distant Metastasis (M)

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

STAGING

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

TREATMENT OF ORAL CAVITY CARCINOMA

Treatment of oral cavity Carcinoma requires multimodality management.

Goals

According to the stage of tumor, the treatment protocol varies. It is roughly divided into resectable disease and unresectable disease. **"Unrescetable"** refers to tumors that cannot be removed without unacceptable morbidity and if it involves the vital structures like cervical, Brachial plexus, carotid artery it can be termed unresectable.

SURGERY

a) Surgery of the primary alone

b) Surgery of the primary with mandibulectomy

c) Surgery of the primary with neck dissection.

d) Surgery of the primary with neck dissection & mandibulectomy

I) LIP CARCINOMA

Enbloc removal of the tumor with 2cm clearance in all dimension.

Tumors less than 2 cm

i) Moh's micrographic excision

ii) Alternative forms of therapy include

Cryotherapy,

Electrocautery,

Chemotherapy (Topical application of 5FU)

Photodynamic therapy.

Alternative forms are mainly used for tumors less than 1.5 cm.

Tumors more than 2 cm

If carcinoma is advanced, bone and neural involvement should be ruled out by doing OPG (Orthopantagram) / CT / MRI of the Mandible.

If mandible is involved composite resection (Tumor removal with / Segmental Mandibulectomy and Neck dissection) is the surgery of choice.

II) TONGUE CARCINOMAS

Surgical resection of the oral tongue with tumor free margin of at least 1 cm.

T_1T_3 No	–	Partial glossectomy.
Large Cancers	–	Extensive surgery such as total glossectomy and Reconstruction.

III) ORAL CAVITY EXCLUDING TONGUE & LIP

Resection of the floor of mouth, buccal mucosa, tongue and mandible can be done by any one of the four approaches.

It includes,

a) Transoral

b) Mandible sparing (Pull through)

c) Mandibulotomy.

d) Composite resection.

a) Transoral

Tumors which are smaller anterior, superficial, well circumscribed lesions situated in the floor of mouth, anterior 2/3 of the tongue, buccal mucosa and palate are removed through this approach.

b) Pull through procedure

It is ideal for moderate sized cancers of the anterior, lateral and floor of the mouth without Involvement of the mandible. If the adequate surgical margin is not obtained it can be combined with marginal mandibulectomy.

c) Mandibulotomy

Posterior oral cavity and oropharynx are better approached by dividing the mandible lateral to midline (i.e.) Anterior to mental foramen

d) Composite resection

Tumor invades the lateral (or) anterior arch of the mandible, it needs full thickness resection of the mandible along with tumor and neck nodes. Preserving the posterior edge of ramus of mandible, coronoid and condylar processes will help in reconstruction.

RECONSTRUCTION

Lip reconstruction : Upper Lip,

Lower Lip,

Lip Commisure

Total defect is less than 30% - Primary closure.

If it is more than 30% - Partial / Full thickness Skin graft / Vicinity flap (Local)

Skin Graft

Moh's micrographic surgery, which does not involve the vernillon

Can be grafted, either by partial (or) full thickness graft.

Vicinity flap :

Labial rotation and advancement flap.

- Abbes flap (Both upper & Lower Lip defect)
- Double Abbes flap (75% central defects of lower lip)
- Eslander flap (Lower Lateral Lip)
- Gillies fan flap
- Karapandizic (Central defect more than 80%)
- Stepladder Flap / Staircase Flap. (Central & Lateral defect)

Vermillion Reconstruction

Small defect	-	Full thickness Horizontal releasing Incision.
Extreme vermillion Defect	}	Musculo–Mucosal flap eg. Fascial artery Musculo Mucosal Flap.

Tongue Reconstruction

For smaller defects	-	Primary closure (or) Skin graft either partial (or) full thickness with bolstering sutures
For Larger defects	-	Pectoralis Major Myocutaneous flap (PMMF) for total glossectomy.

Reconstruction of oral cavity excluding lip, Tongue Ca

For Cheek	-	Local flaps such as Rhomboid flap [Limberg (or) Dufourmental flap] 'V – Y' Local transposition flap.

Musculo Cutaneous flap

Sternocledomastoid flap	–	Augment mandibular coverage
Lateral & Inferior Trapezius musulocutaneous flap	–	Intra oral reconstruction.
Pectoralis Major Flap	–	Total glossectomy and Composite post mandibular defects.
Platysma flap	–	Buccal sulcus and buccal mucosa.

Free Flap

Radial Forearm flap	–	oral lining restoration.

Rectus abdominis flap (RAF)	–	Total / Subtotal glossectomy Hemimandibulectomy and complex Intra-oral defects.
Lateral thigh flap	–	Lining of oral cavity.

Recipient site complications

a) Flap necrosis

b) Infection

c) Fistula

Donor site Complications

a) Haematoma and Seroma

b) Infection and wound dehiscence

c) Partial / Total skin graft loss

d) Tendon exposure

e) Hernia and contour abnormality.

BONY INVOLVEMENT

For mandibular invasion

a) Marginal Mandibulectomy

If there is microscopic invasion of the mandible i.e. periosteum (or) cortical layers and for adequate access during the surgery marginal mandibulectomy is performed.

b) Segmental Mandibulectomy

If there is cortical Invasion of the Mandible detected clinically, radiographically, (or) intraoperatively an enbloc segmental Mandibulectomy is done.

c) Partial Mandibulectomy

Mandible and tumor are usually resected from the mental Foramen to the coronoid process generally leaving behind the condyle.

d) Hemi Mandibulectomy

Removal of the mandible-from symphysis to the condyle on one side.

RECONSTRUCTION OF MANDIBLE

Mandibular resection produces major cosmetic and functional loss and reconstruction is by Biological & Non Biological prosthesis.

Osteomyocutaneus flap

- ❖ Trapezius flap with spine of scapula
- ❖ Pectoralis Major flap with 5^{th} (or) 6^{th} rib.

Non Biological Prosthesis

a) Plastics : Acrylic, Teflon, Slapstick

b) Inert Metals : Stainless steel, Tantalum, Vitallium and Titanium.

Biological Prosthesis

Bone graft, Pedicled graft, Free Flaps.

NECK DISSECTION

Neck dissections are classified as follows

IN 1991	**IN 2001**
1. Radical Neck dissection	1. Radical Neck dissection
2. Modified Radical neck dissection	2. Modified Radical neck dissection

3. Selective Neck dissection	3. Selective Neck dissection
a. Supraomohyoid	a. SND (I-III / IV)
b. Lateral	b. SND (II-IV)
c. Posterolateral	c. SND (II-V, Post auricular, Sub occipital)
d. Anterior	d. SND (Level VI).
4. Extended Neck dissection	4. Extended Neck dissection

Various incisions are being used for neck dissection (a) Latyschevsky (b) Freund (c) Crile (d) Martin (e) Babcock and conley.

1) Radical Neck Dissection

Removal of level I-VI nodes along with removal of Internal Jugular Vein, Spinal Accessory Nerve and Sternocledomastoid Muscle.

2) Modified Neck Dissection

Removal of Level I-VI Nodes along with preservation of Internal jugular vein, Sternocledo mastoid muscle, and Spinal accessory nerve

Type – I : Preserves only Spinal Accessory Nerve.

Type – II : Preserves Internal Jugular. Vein & Spinal Accessory Nerve

Type – III : Preserves Sternocledomastoid, Internal Jugular Vein and Spinal Accessory Nerve.

3) Selective Neck Dissection

a) Supraomohyoid Neck Dissection: (SND-I-III)

Removal of Level I-III nodes.

b) Extended Supraomohyoid Neck Dissection : (SND-I-IV)

Removal of Level I-IV nodes.

c) Lateral Neck Dissection (SND II – V)

Removal of II-IV nodes along with Internal Jugular Vein

d) Posterolateral Neck Dissection : (SND II – V)

Removal of II – V group of nodes.

e) Anterior Neck Dissection: (SND VI)

Removal of Level VI nodes.

4. Extended Neck Dissection

Neck dissections can be extended to include either of the Lymph node groups that are not routinely removed i.e. Retropharyngeal, Paratracheal, Upper mediastinal (or) other structures such as skin of the neck, carotid Artery, Levator Scapula, Vagus (or) Hypoglossal nerve.

SURGERY FOR N_0 NECK

Clinical examination, imaging and pathological assessment fail to detect any evidence of regional disease it is called as N_0 Neck.

Treatment options for No Neck

a) Elective Neck Dissection
b) Elective Neck Irradiation
c) Sentinel lymph node Biopsy

Elective Neck Dissection

When the primary tumor is treated with surgery, elective neck dissection is preferred.

Elective Neck Irradiation

When primary tumor is treated with radiotherapy, elective neck irradiation is preferred.

Sentinel Lymph node Biopsy

Newer option for staging the Neck. Lymphatic drainage from a primary tumor is limited to set of regional lymph nodes, which are identified by contrast agents (or) radioactive tracers, those identified nodes are removed.

SURGERY FOR NODAL DISEASE

N_1, N_2, N_3 - Neck dissection (Modified Radical Neck dissection / Radical Neck dissection / Selective Neck Dissection) and Post Operative Radiotherapy optional if, extracapsular involvement of the nodes are present.

Surgery for Bilateral Nodal disease

Bilateral neck dissection simultaneously with preservation of one of the Internal jugular vein.

Surgery for Metastatic disease

Retropharyngeal, Internal jugular vein and Posterior triangle nodes are involved, radiotherapy is the best option. It is a bad prognostic indicator.

Complications of Block dissection

a. Infection (1.7%)
b. Air Leak
c. Bleeding
d. Chylous Fistula
e. Fascial or cerebral edema
f. Blindness
g. Apnoea
h. Jugular Vein Thrombosis

Emergency Complications

a. Carotid Artery rupture
b. Jugular Vein Blow out

Radiotherapy for Nodal Involvement

Primary Radiotherapy for the Nodes, several important factors are taken into account.

a) Nodal size

b) Nodal Number

c) Nodal fixation

d) Duration of Radiation

RADIATION THERAPY

Main stay of treatment for cancer in the head and neck region.

Choice of therapy

a) External Beam Therapy

b) Brachy Therapy

c) Intra Operative Radiation Therapy

RADIOTHERAPY FOR CANCER OF THE LIP

Definitive RT — Primary
- External beam RT $\geq$ 66 Gy (2.0 Cy / day)
- External beam RT $\geq$ 50 Gy+ brachytherapy
- Brachytherapy alone

Neck
- $\geq$ 50 Gy (2.0 Gy/day)

Adjuvant RT — Primary
- External beam RT $\geq$ 60 Gy (2.0 Gy/day)

Neck
- 50 – 60Gy (2.0 Gy/day)

RADIOTHERAPY FOR CANCER OF THE ORAL CAVITY

Definitive RT	Primary	
		External beam RT $\geq$ 70 Gy (2.0 Cy / day)
		External beam RT $\geq$ 50 Gy+ brachytherapy
		Brachytherapy alone
	Neck	
		$\geq$ 50 Gy (2.0 Gy/day)
Adjuvant RT	Primary	
		External beam RT $\geq$ 60 Gy (2.0 Gy/day)
	Neck	
		50 – 60Gy (2.0 Gy/day)

a) External Beam Radio Therapy (Teletherapy)

Dual energy linear accelerators capable of generating

i) Low energy megavoltage (4-6 mv)

ii) High energy megavoltage (15-25mv)

iii) Range of electrons (6-18 to 25 mv)

Head and neck cancers are better managed with 4-6 mv Cobalt-60 rays, with depth not more than 7-8 Cm.

Intermittent daily dose is given for 5 days in a week for a period of 7-8 weeks, neighboring normal tissues also get its share of dose and damage may occur.

Conformal Radiotherapy

High dose of radiation to the target volume and small dose to normal tissues.

IMRT (Intensity Modulated Radiotherapy)

Treatment is divided into hundreds of pencil beam each one contributing radiation to different parts of target volume. Computer controls the amount of radiation.

c) Brachy-Therapy

Selectively used in Treatment for early T1 & T2 lesions and achieves high control rates.

High doses to the target volume and simultaneous sparing of normal areas.

Implants today in use are Ir-192 (or) I_2-125, others are Radium 226, Gold-198, and Palladium-103.

Various techniques are used to place radioactive material in a desired geometric pattern. "Paris System" is most widely used.

d) Intra-operative Radiation

Either by electron beams or Orthovoltage Radiation. Mainly used for small superficial tumors (2 – 5 Cms) preferably on flat surface.

Pre-Operative Radiotherapy : It is a debate for many years.

Post Operative Radiotherapy : It is ideal in most situations.

- ❖ Surgical margins at the primary site are positive or macroscopic residual disease is present.
- ❖ Skin, Soft tissue, Cartilage and bone are involved.
- ❖ Lymph node of Neck is histologically positive.
- ❖ Advanced primary T3, T4 lesions.

Radiotherapy is usually started 4-6 weeks after surgery. Any delay after 8 Weeks is not ideal.

Advantages of Pre-Operative RT

- ❖ Inoperable lesion may be converted to operable
- ❖ Extent of surgery
- ❖ Distant metastasis may decrease.

Disadvantage of Pre-Operative RT

- ❖ Increased morbidity
- ❖ Decreased wound healing.

Advantages of Post-Operative RT

- ❖ Extent of disease is known
- ❖ Higher doses may be delivered
- ❖ Healing is superior

Disadvantages of Post-Operative RT

- ❖ Distant metastasis likely to be greater.
- ❖ Decreased vascularity at the time of radiotherapy due to surgical tampering.

Pre-Irradiation Dental Care

1) Instructions regarding the complete oro-dental hygiene, regular mouth wash, cleaning of mouth after each meal.
2) Avoid hard tooth brush.
3) Fluoride tooth paste to prevent caries.

4) Extraction has to be done, with a minimum of 2-3 weeks before starting radiotherapy.

Post Irradiation Dental Care

Extraction has to be carried out 18-24 months after radiotherapy once oral mucosa has healed.

Recommended Skin Care

- Wash the skin with lukewarm water, pat dry, and do not wash off marks.
- Use mild soaps
- Use water-based lotions or creams
- Avoid lotions with perfume and deodorants.
- Avoid direct sunlight.
- Do not use straight razors.
- Avoid tight-fitting collars
- Do not use aftershave lotions or perfumes.
- Apply only nonadherent, hydrophilic dressings to wounds.

Complications of RT

- ❖ Acute & chronic
- ❖ Dose related

Acute: Mucositis, dermatitis, hair loss, loss of taste, xerostomia, cataract.

Chronic: Soft tissue fibrosis (necrosis), Radio necrotic ulcer and Osteo radio necrosis.

Dose related

Around 20–30GY : Mucositis, ulceration, erythema, hyperpigmentation.

Around 50 GY : Dryness of mouth (Serous secretion low)

Around 65 GY : Severe ulceration.

RADIOSENSITISERS

Chemical compounds when combined with radiation should achieve greater tumor inactivation than would have been expected from the additive effect of each modality.

e.g.: Nitroimidazole compounds (Misonidazole – 2nd generation)

3rd generation (Etanidazole, Pimonidazole)

RADIOPROTECTORS

Chemical compounds that protect against radiation damage to target normal cells and not to tumor cells.

e.g.: Amifostine (WR-2721), Ethyol.

Information regarding radiosensitisers and radioprotectors will be available in near future.

- For early lesions (T1 – T3) local cure is achieved by surgery or Radio therapy alone.
- For (T3 – T4) lesions combined modality of Treatment, surgery is effective in removing large bulky lesion and irradiation for microscopic disease.

CHEMOTHERAPY

Introduction of more active chemotherapeutic agents and combinations being increasingly used in complex multimodal treatment plans along with surgery and Radiotherapy.

General Strategies

1. Induction is given before surgery or radiation (Neoadjuvant chemotherapy)

2. Concomitant chemoradiation – chemotherapy is given simultaneously with radiation.
3. Adjuvant therapy where chemotherapy is given after surgery (or) radiotherapy in an effort to reduce metastatic burden.

Induction Chemotherapy

Cisplatin (100mg/m^2) followed by 5 days infusion of 5FU(1gm/m^2/day) are given before surgery. Recently Docetaxel is added to the above regimen.

Concomitant Radiotherapy and Chemotherapy

High risk patients, disease recurrence after surgical excision, multiple nodal metastasis and extracapsular spread are present, Concomitant chemotherapy and radiotherapy showed better response.

Adjuvant Chemotherapy

After primary surgery or after primary radiotherapy cisplatin and 5FU are given.

Intra Arterial Chemotherapy

Intra Arterial infusion of 5 FU bypasses the catabolic effects of liver, thereby prolonging the therapeutic action of drugs. It is useful in maxillary sinus carcinoma.

Immunological agents & Newer Drugs

Epidermal growth factor receptor (EGFR) is over expressed in invasive squamous cell carcinoma.

- ❖ Gefitinib and erlotinib – single agent activity with advanced disease.
- ❖ Cetuximab – murine monoclonal Antibody directed against extracellular domain of EGFR. Above agents are under trial.

FOLLOWUP

American Head and Neck society guidelines for cancer surveillance.

Years Post Rx	Follow-up
1st Year	1 – 3 M
2nd Year	2 – 4 M
3rd Year	3 – 6 M
4th & 5th Year	4 – 6 M
After 5th Year	Every 12 M

CHEMOPREVENTION

Patients with oral Intraepithelial Neoplasia have an increased risk of developing squamous cell carcinoma because of combination of carcinogens and genetic predisposition.

Loss of Heterozygosity, Aneuploidy, Telomerane activation, cyclin D1 elevation, COX-2 up regulation , EGFR activation, are all incriminated in the causative factors for transformation of Oral Intraeptithelial Neoplasia to Squamous cell carcinoma.

Vitamins (A, E, C), Retinoids, Beta Carotene, Minerals, Folates and Selenium are agents, which probably prevent the transformation of Oral intraepithelial Neoplasia to oral cavity Carcinoma.

FUTURE DIRECTIONS

Nanotechnology

- Magnetic properties of hydrogen in biologic tissue is one of the most powerful diagnostic tools in medicine. It is used in Nano-technology

- ❖ Cells Irradiated with Nanoshells causes circular zones of cell death. Nanoshells mediated Infrared therapy are used for tumors under magnetic resonance.

Personalized therapy

- ❖ Microarray C-DNA library analysis allows measurement of expressions of tens of thousands of genes by cancer cells.
- ❖ In near future a treatment programme of 10 (or) even 100 monoclonal antibody based agents as determined by micro array analysis will be available.

SCREENING FOR ORAL CANCERS

Four methods are available for early cancer detection.

- Visual examination
- Application of toluidine blue
- Self screening
- Oral cytology

1. Visual examination

Sensitivity for oral visual examination 58% - 94%

Specificity rate for oral visual examination 76% - 98%

2. Application of toludine blue :

Application of toludine blue will provide demarcation between malignant and dysplastic cells. It will be useful in the early detection of oral cancers in selected subjects with precancerous lesions.

False negative and false positive rates range from 20-30%

3. Self Screening

In High risk population groups self screening is mandatory and flexibility depends on health education.

4. Oral cytology

Oral exfoliative cytology, a screening modality has major limitation. There is a high false negative rates hence biopsy is preferable than oral cytology.

MATERIALS AND METHODS

The clinical material for this study consists of 140 patients of oral cavity cancers out of 427 patients who attended Thanjavur Medical College Hospital (2005-2007).

287 were not included in the study, because of failure of follow up and irregular treatment.

The patients age, sex, Habits, socio economic status, premalignant conditions, clinical features, site of oral cavity, staging, histopathology were recorded.

Following Investigations were taken up for Diagnostic and staging purpose,

1) HPE 2) X-ray Mandible AP / Lateral

3) X-rays PNS 4) X-ray Chest-PA view

5) USG Abdomen 6) CT Fascial Bones

For Clinical assessment and for co morbid conditions

i) Urine – Albumin & Sugar

ii) Blood Hb%

iii) Renal parameters - Blood sugar, urea and serum creatinine

iv) Serum. electrolytes

v) Liver function tests

vi) Complete Haemogram

vii) Clotting Time & Bleeding Time

viii) ECG in all chest leads were taken.

Dental surgeon's opinion and help were obtained in selected cases.

Treatment protocol

Planned accordingly

1) External Beam radiotherapy
2) Surgery
    a. Primary surgery alone
    b. Primary Surgery with neck dissection
    c. Primary Surgery with Mandibulectomy
    d. Primary Surgery with neck dissection and Mandibulectomy

Primary reconstruction was done.

Immediate post operative complications were identified and treated.

In the follow up, patients were observed regarding the local recurrence nodal disease (or) recurrence in neck treated and evidence of Second primary with (or) without metastasis.

The patients were informed regarding the risk factors and advised to give up the offending Habits to have longer disease free survival.

The relatives were cautioned regarding the correlation between risk factors and oral cavity carcinoma.

OBSERVATION AND RESULTS

INCIDENCE OF ORAL CANCER IN THANJAVUR MEDICAL COLLEGE HOSPITAL

Year	Total cases of Malignancy	Total cases of oral cancer	% of oral cancers
June – Dec. 2005	709	96	13.5%
2006	1641	211	12.8%
Jan – Sep. 2007	1130	120	10.6%
	3480	**427**	**12.2%**

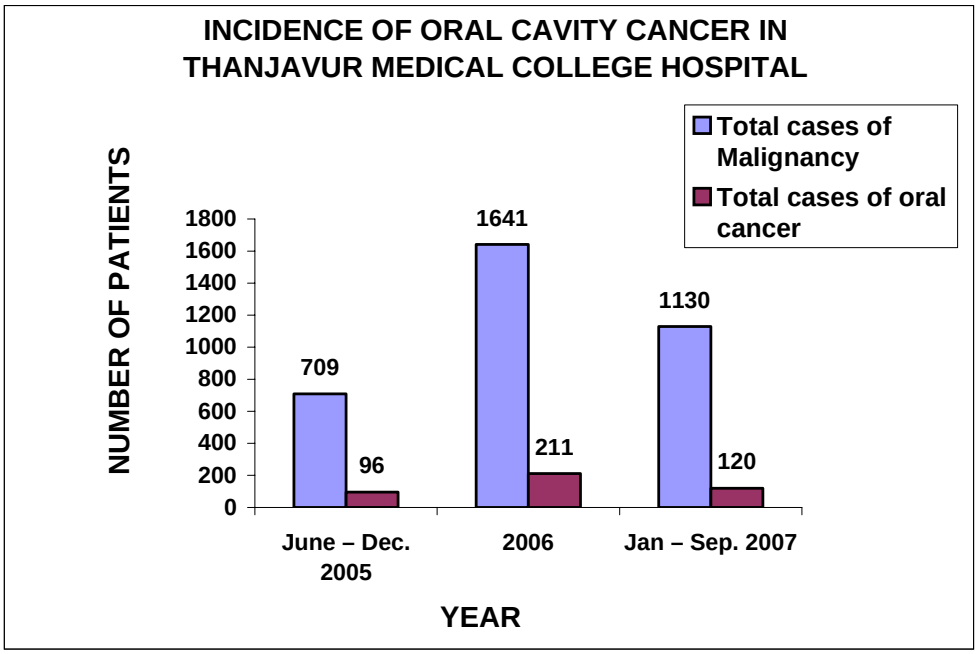


Fig – 3 - Oral Cavity Cancers constitute 12.2% of the total malignancy reported in Thanjavur Medical College Hospital.

INCIDENCE OF ORAL CANCER ACCORDING TO ANATOMICAL AREA

Sl. No.	Cancer Site	Total No of Cases	%
1.	Cheek	72	51.4
2.	Tongue	36	25.7
3.	Lips	11	7.9
4.	Alveolar Ridge	9	6.5
5.	Floor of Mouth	6	4.3
6.	Hard Palate	5	3.5
7.	Retromolar Trigone	1	0.7
	Total	**140**	

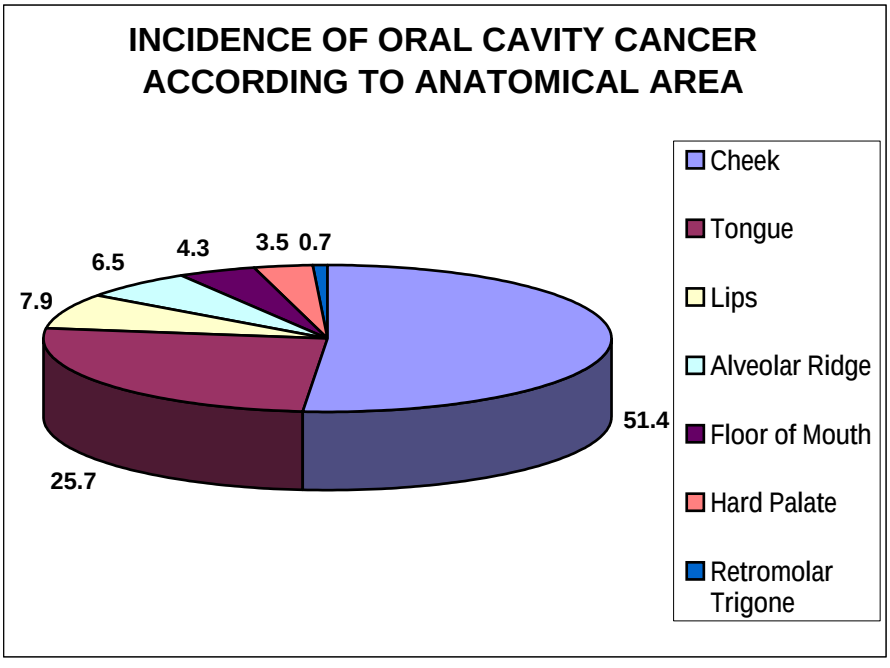


Fig – 4 - Cheek was the most common site of oral cancer reported in 51.4% and Tongue was the next common site (25.7%).

DISTRIBUTION OF PATIENTS IN VARIOUS AGE AND SEX GROUPS

Age (Year)	Male		Female		Total	
	No.	%	No.	%	No.	%
31-40	12	12.1%	6	14.6%	18	12.8%
41-50	41	41.4%	13	31.7%	54	38.6%
51-60	29	29.3%	12	29.3%	41	29.3%
61-70	10	10.1%	6	14.6%	16	11.4%
>71	7	7.1%	4	9.8%	11	7.9%
Total	**99**		**41**		**140**	

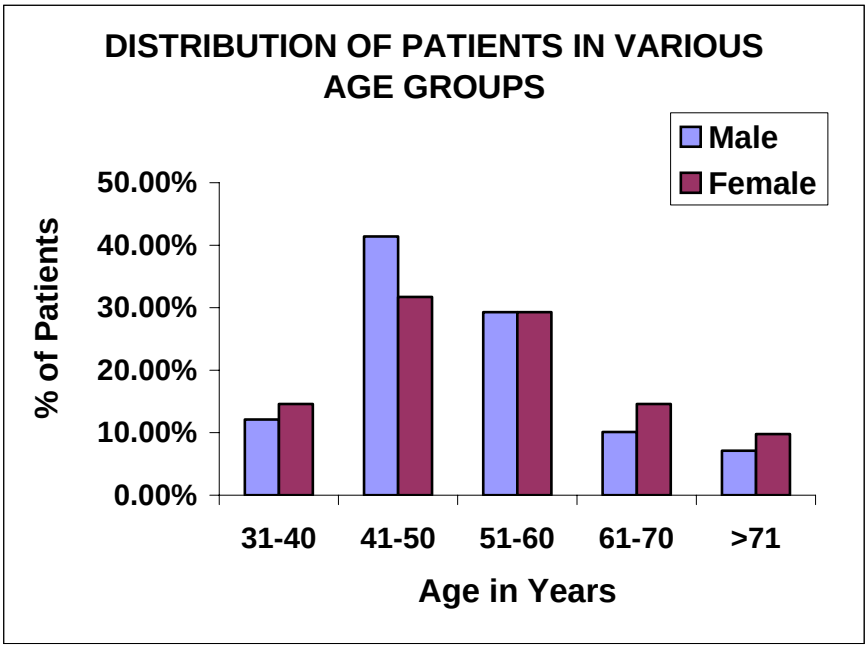


Fig – 5 - Both males and females peak age of incidence is 40 to 50 years.

OCCUPATION WISE INCIDENCE OF ORAL CANCER

Groups	Socio-economic status	Number of Patients	%
I	Low	129	92.14%
II	Moderate	11	7.86%
III	High	-	-
		140	

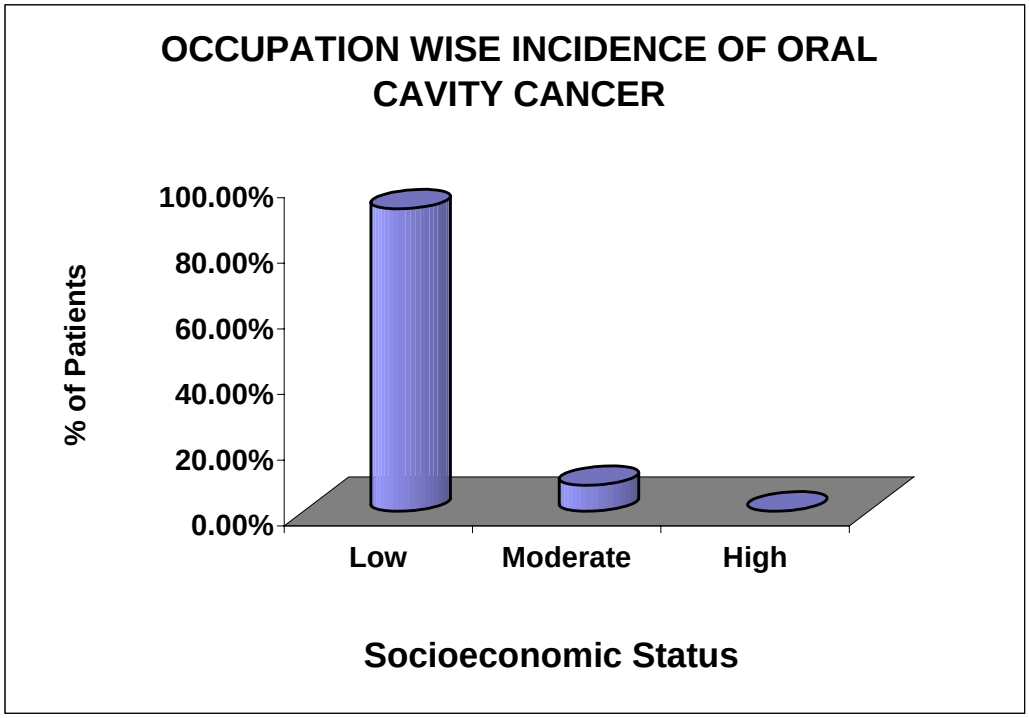


Fig – 6 – oral cancer was commonly found in low socio economic status

PREDISPOSING FACTORS FOR ORAL CANCER

Sl. No.	Factors	Total No.	%
1.	Chewing Betel nut + Tobacco	86	84.2%
	Chewing Tobacco	32	
2.	Smoking	77	55%
3.	Alcoholism	44	31.4%
4.	Dental Caries & Dental lesions	14	10.0%
5.	Nutritional deficiency	2	1.7%
6.	None	12	8.6%

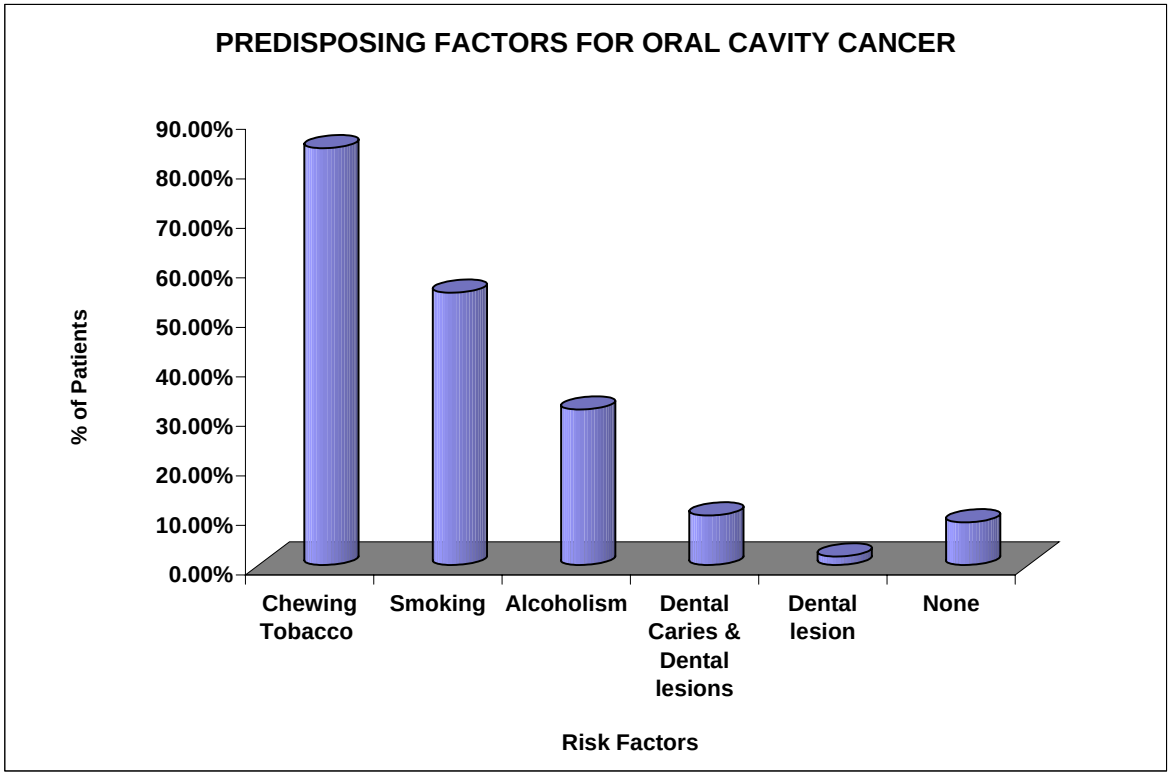


Fig – 7 - Chewing tobacco, slaked lime and betel nut was the most common risk factor.

MODES OF PRESENTATION OF ORAL CAVITY CANCER

Clinical Features	Cheek Carcinoma	Tongue Carcinoma	Lip Carcinoma	Alveolar Carcinoma	Hard Plate Carcinoma	Floor of mouth Carcinoma	Total
Ulcer	72	36	11	9	5	6	139
Swelling	31	5	8	5	2	4	55
Lump in neck	13	7	4	3	2	2	31
Pain	11	2	3	2	1	2	21
Trismus	7	-	-	-	-	-	7
Retromolar extension	5	-	-	-	-	-	5
Other Symptoms							0
Excessive Salivation	34	12	4	-	-	-	50
Difficulty in Chewing	18	-	-	-	-	-	18
Dysphagia	-	4	-	-	-	-	4
Dysphonia	-	4	2	-	-	-	6
Ankyloglossia	-	5	-	-	-	-	5

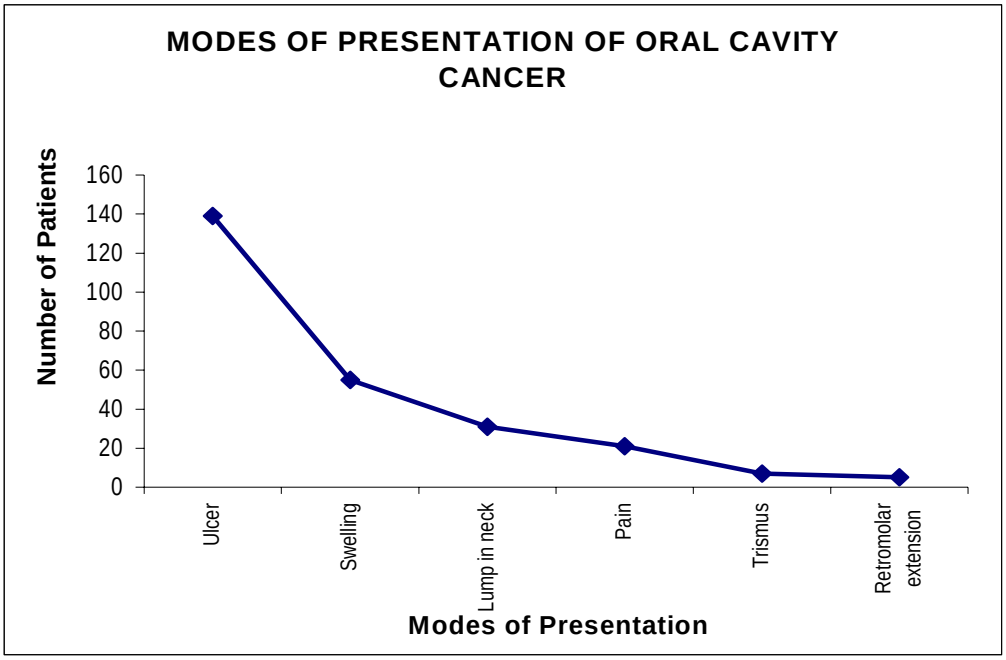


Fig – 8 - Majority of the patients reported with ulcer.

PREMALIGNANT LESIONS FOUND IN ORAL CAVITY CANCER

Sl. No.	Factors	Total No.	%
1.	Leukoplakia	51	36.4%
2.	Submucosal Fibrosis	21	15.0%
3.	Erythroplakia	17	12.2%
4.	Leukoplakia + Erythroplakia	8	5.7%
5.	Candidiasis	5	3.6%
6.	Not associated with any lesion	38	27.1%
	Total	**140**	

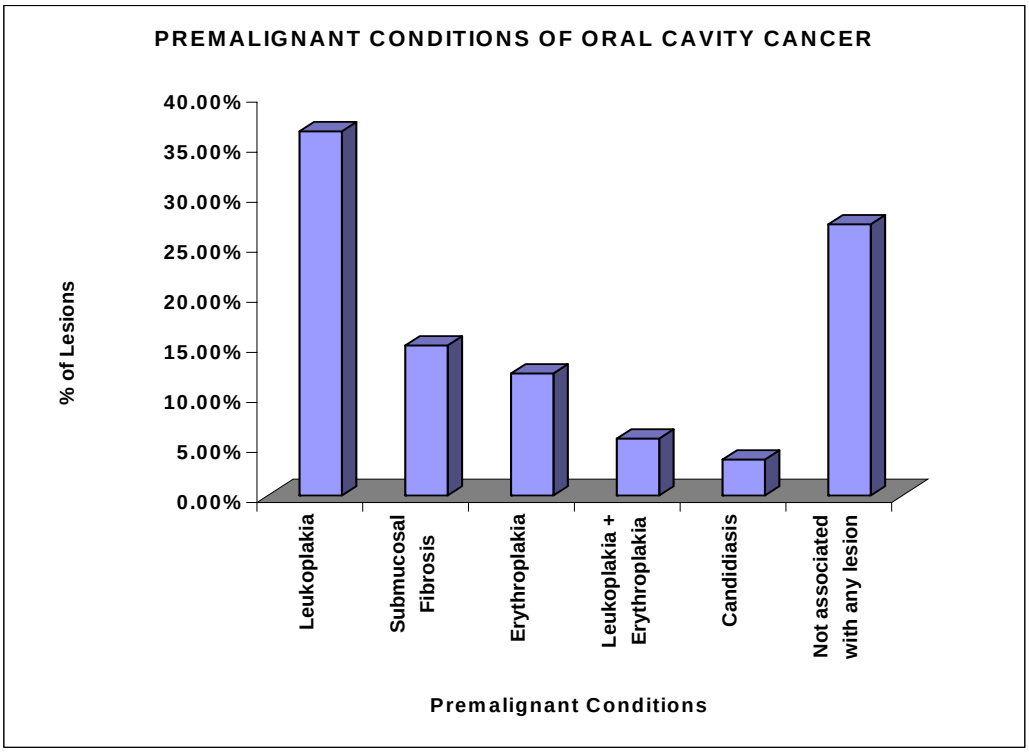


Fig – 9 - Leukoplakia was the most common premalignant condition encountered.

DISTRIBUTION OF PATIENTS ACCORDING TO THE TYPE OF GROWTH

Sl. No.	Growth Type	No. of patients	%
1.	Endophytic	83	59.3
2.	Exophytic	29	20.7
3.	Invasion of Soft tissues	19	13.6
4.	Invasion of Bone and Neurovasular bundle	9	6.4.
	Total	**140**	

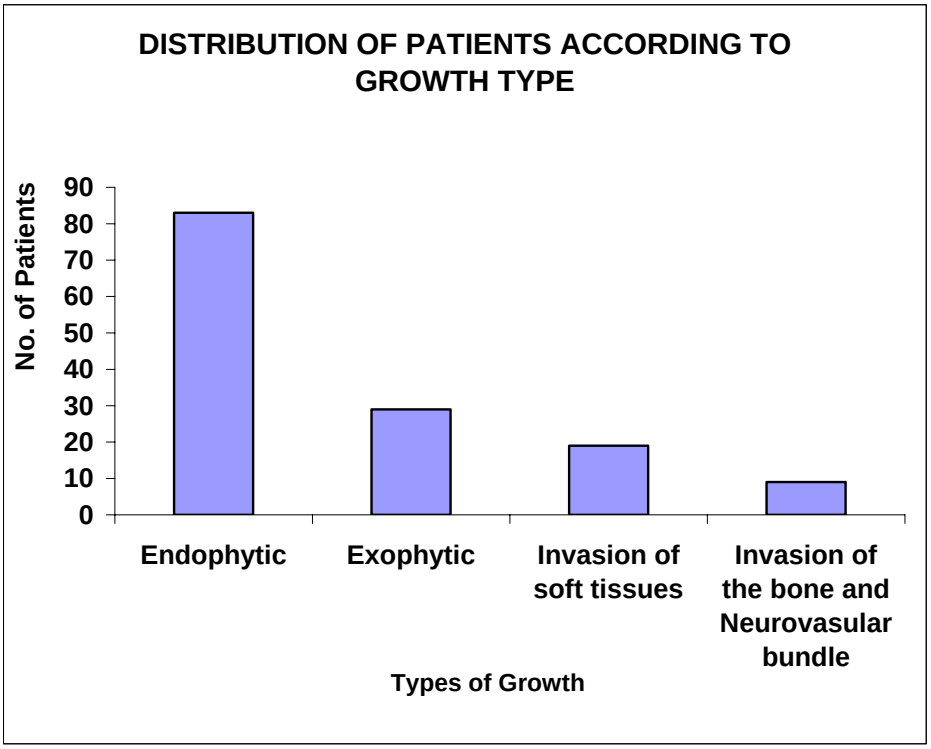


Fig – 10 - Majority of the patients presented with endophytic growth.

DISTRIBUTION OF PATIENTS ACCORDING TO HISTOLOGICAL TYPES

Sl. No.	Factors	Total No.	%	
1.	Squamous Cell Carcinoma			
	Well Differentiated	62	44.3%	
	Moderately Differentiated	49	35.0%	95.8%
	Poorly Differentiated	23	16.5%	
2.	Mucoepidermoid Carcinoma	3		2.1%
3.	Adenoid Cystic Carcinoma	2		1.4%
4.	Adeno Carcinoma	1		0.7%
	Total	**140**		

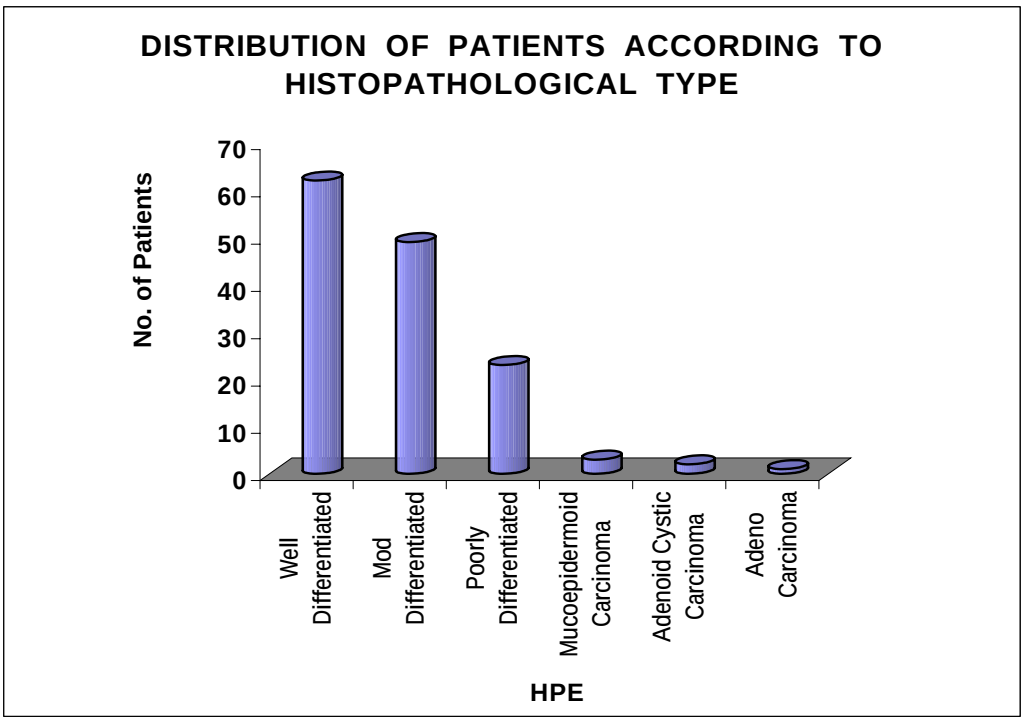


Fig – 11 - Well differentiated Squamous cell carcinoma was the major histopathological type.

DISTRIBUTION OF PATIENTS ACCORDING TO TNM STAGING

Sl. No.	No. of Patients	Percentage
I	9	6.4%
II	41	29.3%
III	62	44.3%
IV	28	20.0%
Total	**140**	

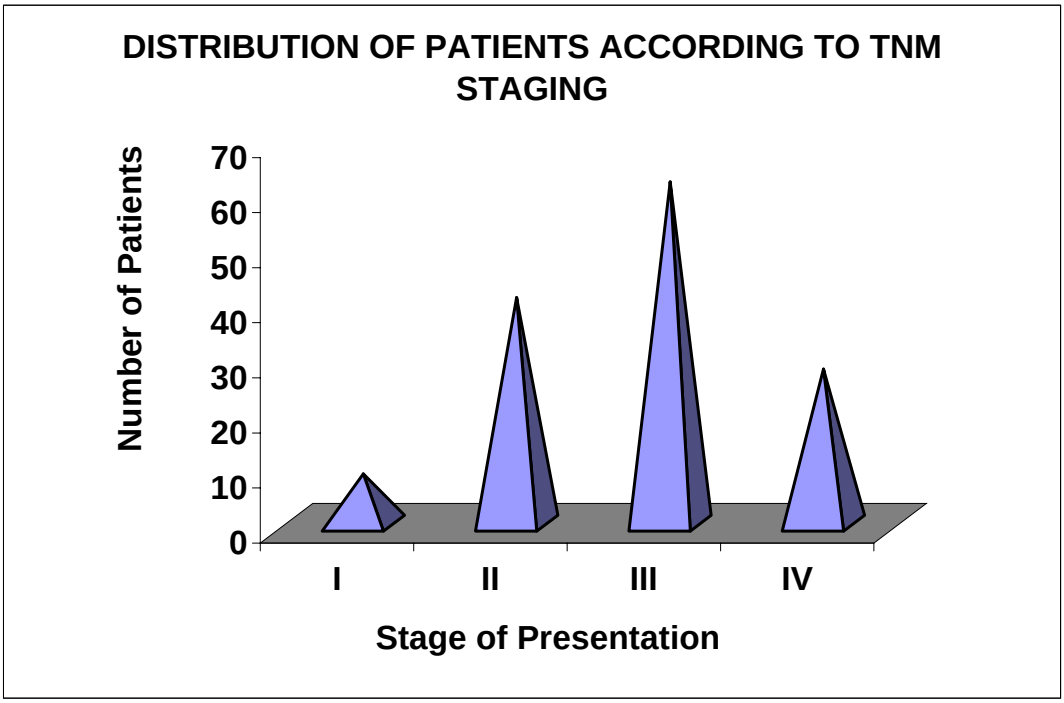


Fig – 12 - Majority of the patients reported to us were in Stage III and IV**.**

TREATMENT OUTCOMES IN ORAL CAVITY CANCER

Staying	Primary Surgery	Primary Surgery + Mandibulectomy	Primary Surgery + Neck dissection	Primary surgery + Neck dissection + Mandibulectomy	Primary Radio therapy
Stage I	8				1
Stage II	19		2		20
Stage III		8		5	49
Stage IV		3		3	22
Total	**27**	**11**	**2**	**8**	**92**

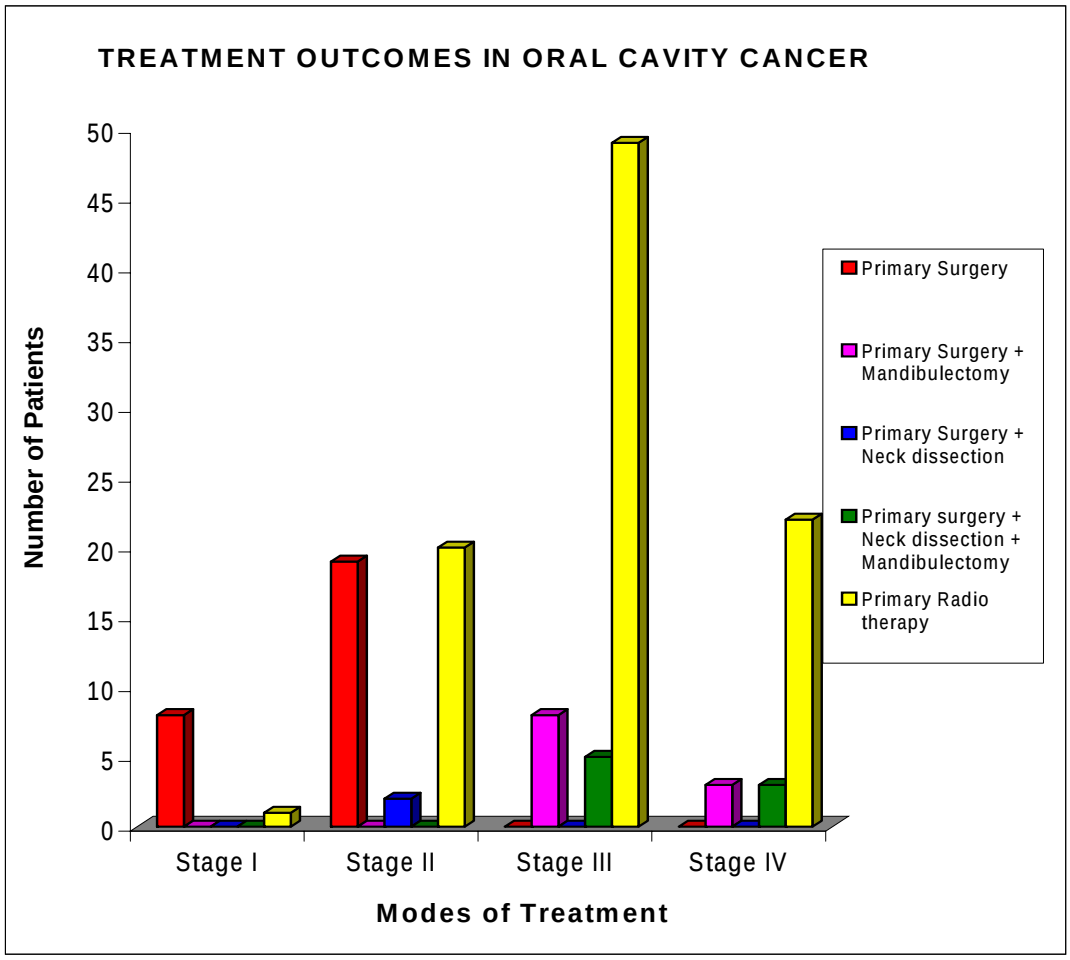


Fig – 13 - Primary Radiotherapy was given to 92 patients. Most of them were in Stage III & IV. Primary Surgery was done for majority of patients in Stage I & II.

COMPLICATIONS ENCOUNTERED IN POST-OPERATIVE PERIOD

Sl. No.	Complications	No. of cases	%
1.	Wound Infection	8	16.7%
2.	Fistula Formation	7	14.6%
3.	Flap Necrosis	5	10.4%
4.	No Specific Complaints	28	58.3%
		48	

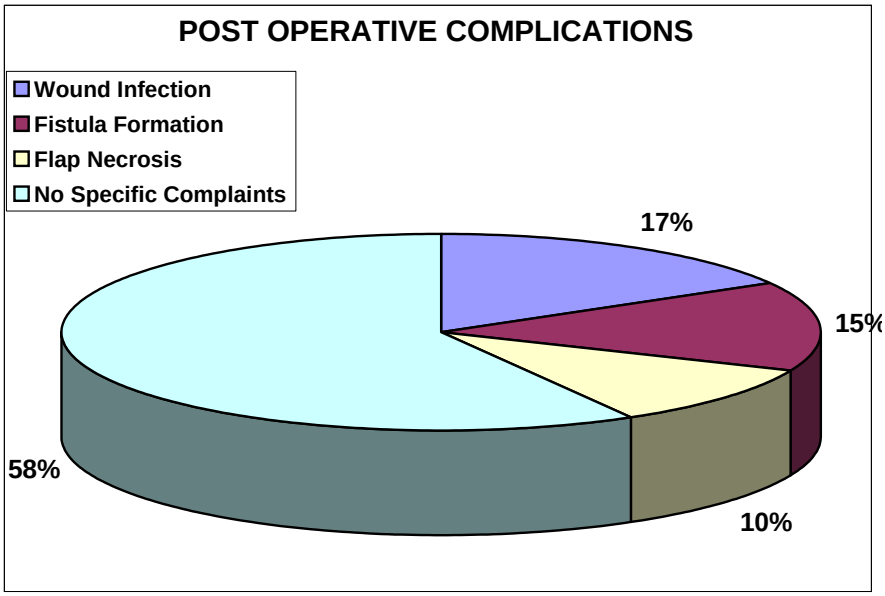


Fig – 14 - 58.3% had no specific complaints. Remaining had wound infection, Flap Necrosis and Fistula Formation.

DISCUSSION

An analysis of the incidence, predisposing factors, premalignant conditions, clinical features, type of growth, histological types, stage of presentation and treatment modalities carried out for oral cancers in our hospital for the period from June 2005 to September 2007 are discussed.

EPIDEMIOLOGICAL ANALYSIS

In our institution oral cavity cancers (12.2%) constitute the 2nd most common cancer next to breast.

According to the National Cancer Registry Programme (NCRP) - ICMR Survey shows that Oral Cavity cancer occupies the most common carcinoma in male (19.4%), is followed by hypopharynx and esophagus. In females Cervix Uterus is followed by Breast and oral cancer (38.7%).

The reference in Indian Medical Literature regarding the preponderance of oral cancer in India suggests its strong association with habit of chewing betel nut, tobacco, slacked lime and smoking habit (Nilbock *et al.*)

Cancer Institute (WIA), Chennai-statistics shows that the leading cancer site in male is oral cavity (9.9%) and in female Cervix Uterus (32.2%) among the top ten cancers (Fig – 15).

In JIPMER-oral cavity forms the most common cancer in male (16.6%) and Cervix Uterus (55.1%) forms the most common cancer in female among the top ten cancers (Fig – 16).

In our study the peak incidence of oral cavity cancer is between 40 and 50 Years.

According to the National Cancer Institute SEER Programme – USA, the mean age of diagnosis is 65 years and more than 50% occurs above the age of 60 Years.

The disparity in age incidence is mainly due to the early tobacco and betel leaf chewing habit in Indian patients reported by Shantha *et al.*

Our study reveals that chewing tobacco and betel nut present in 84.2%, and of them 80% have started it before the age of 25 Years. Young age chewing habit and the number of years of usage are the reasons for oral cancer at earlier ages.

Recently, it has been found out that increased incidence of oral cavity cancers detected at earlier ages probably due to the habit of chewing and smoking among the students evidenced by oral Cavity Cancer under the age of 35 Years (IJEY. E.M. *et al.*, 2002).

According to the centers for disease control and prevention 2002, U.S.A. - Tobacco usage was increased among middle and high school students.

MALE - FEMALE RATIO

- Male - female ratio in this study is 2 : 1.
- National Cancer Registry, U.S.A. - 2.2 : 1
- Aringnar Anna Cancer Institute, Kanchipuram – 2 : 1

It is believed that preferential sex incidence is due to the greater use of tobacco, betel nut and alcohol by men than women.

- ❖ Female cases were reported higher in Greece (Zavras A.I., *et al.* 2003).
- ❖ Snuff dripping and increased incidence of oral cancer among women in Southern United States (Win. D.M., *et al*)

SOCIO-ECONOMIC STATUS

In our study majority of patients with oral cancers (92.14%) are from low socio-economic status.

The reasons may be due to multiple factors like

a) Poor Nutritional Status.

b) Bad oral hygiene.

c) Social customs.

d) Addiction to tobacco, Betel leaf and alcohol.

e) Lack of health awareness.

ETIOLOGICAL FACTORS

Major etiological factor is chewing tobacco in more than a decade either continuously (or) intermittently.

No. of Patients			**Duration of addition in yrs.**
12	→	12.4%	> 5
39	→	39.7%	> 10
28	→	28.5%	> 15
19	→	19.4%	> 25

Information from the patients regarding the duration of addiction for chewing shows that about 87.6% of patients have been chewing tobacco for more than a decade either continuously (or) Intermittently.

Tobaccos which is smoked as beedi, cigarette (or) pipe has been found in 55% of patients.

In our study alcohol usage is found in 31.4%. Alcohol has been incriminated as one of the causes for oral cancer.

Alcohol has indirect role. Almost all heavy drinkers are also heavy smokers. Alcohol in turn increases the absorption of tobacco and increases nutritional deficiency. These factors make squamous cells more susceptible for conversion into cancer cells.

Alcohol is the primary risk factor as suggested by “Mash berg *et al.* - USA.

Dental lesions such as sharp tooth and artificial denture produce constant trauma in 10.0% of the individuals has been associated with Carcinoma of Buccal mucosa.

Role of poor Nutrition in oral cancer has been thought as a significant factor. B-Complex deficiency and sideropenia have been observed in Oral Cancer patients. In our study signs of Chronic Nutritional deficiency like angular chelitis, atrophic tongue and glossitis are observed in 1.7%.

ANATOMICAL LOCATION

In our study Buccal mucosa – constitutes 51.4% of oral cavity cancer.

Increased incidence of buccal mucosa carcinoma is also found in Aringar Anna Cancer Institute, Kancheepuram.

Tongue is the most common site (25.7%), next to buccal mucosa,.

Disparity in this involvement is mainly due to the habitual tobacco and betal chewers to keep the Quid in bucco gingival sulcus.

Reverse smoking (Chutta inside the mouth) is associated with cancer of the palate found in Andhra Pradesh.

Next to tongue, Lip occupies about 7.9% in our study. Lower Lip exposure to radiation is more when compared to upper lip is the reason for higher incidence of Lower lip cancer than upper lip.

CLINICAL FEATURES

Out of 140 patients majority of them reported with ulcer or ulcero proliferative growth in the mouth.

Tumors of the oral cavity often ulcerate; this is probably due to friction of the mucous membrane during eating and partly due to Infection.

Initially the lesions are painless, but once disease advances patients reported with pain.

Other symptoms such as excessive salivation, difficulty in chewing, dysphonia, dysphagia and ankyloglossia are present. Trismus is a bad sign as it signifies extensive infiltration by an endophytic lesion. Patients with

advanced lesions reported with fungating growth, orocutaneous fistula and with extensive Jaw destruction.

PREMALIGNANT LESIONS

Premalignant lesions account for 95% of oral cancers. In our study majority of the patients had Leukoplakia (36.4%) followed by Submucosal fibrosis (15.0%), Erythroplakia, Combined Erythro Leukoplakia and Candidiasis.

Oral submucosal fibrosis is due to a component of areca-catcha in Betelnet which affects the collagen synthesis. It has been predominantly found in East India, Srilanka and South East Asia.

Pindborg and Colleagues suggested approximately 6% of all Leukoplakias become malignant.

"Sugar and Baconcyz" suggested that

31% of the lesions will disappear

30% - Improved

25% - Experienced no change

→ Exfoliative cytology of oral lesions has not proved to be helpful as majority are mostly Hyperkeratotic.

HISTOPATHOLOGICAL VARIETY

In our study, Squamous cell (95.8%) carcinoma is the most common histological variety followed by Muco epidemoid, Adenoid cystic & Adeno carcinoma.

National Cancer Data Base USA reveals

Squamous	-	86.3%
Adeno	-	5.9%
Verrucous	-	2.0%
Kaposis	-	1.5%

Out of the squamous cell carcinoma reported in our study 46.3% are well differentiated, 36.6% are moderately differentiated, and 17.1% are poorly differentiated.

In a study by Khanna et al shows that 58% are well differentiated, 32% are moderately differentiated and 10% are poorly differentiated.

Multilentric origin of oral Squamous cell carcinoma - Slaughter DP et al.
We do not encounter such cases in our study.

TYPE OF GROWTH

59.3% of the patients had Endophytic growth, 20.7% with exophytic growth and 20.0% presented with invasion of the adjoining soft tissues and bone.

STAGING

In our study about 35.7% presented with N_0 neck (Stage I & II)

64.3% presented to us with N_1, N_2, N_3 Neck (Stage III & IV)

Compared to the study of M.D. Anderson Cancer Centre

- 72% Patients presented with No neck
- 28% Patients presented with N_1, N_2, N_3 Neck

National Cancer Data Base USA

- 55% Patients presented with No neck
- 35% Patients presented with N_1, N_2, N_3 Neck

Even though oral cancers are easily accessible for physical examination and biopsy, majority presented to us in later stages.

The reasons derived from this study are,

- Majority of them are initially reviewed by general practioners and dentists and diagnosed as apthous ulcer and fungal infections, treated with antibiotics, antifungal agents and mouth washes and referred to higher centers at later stages.
- Oral Cancer ulcers are painless to start with, by the time patient presented with pain the stage of the disease advances.
- Some people are elderly and frail so there is delay in effort to visit the dentist (or) doctor.

Distant metastasis is observed in 7.5% oral cancers by merino et al.

We did not encounter a single case with distant Metastasis (IV C), probably, secondaries will start manifesting after adequate local treatment and long term follow up. The mean follow up period in our study is short.

Majority presented with submental, sub mandibular and upper deep cervical nodes (I, II).

Facial nodes are present in 2 cases.

Glandular metastasis is present probably due to active lymphatic system (pack and Ariel *et. al*). This system undergoes atrophy and degeneration with age.

Majority of patients with Nodal metastasis are between 45 and 55 Yrs. of age.

MANAGEMENT OF ORAL CAVITY CANCER

Out of 140 patients

48 patients underwent surgery.

Remaining 92 had Radiotherapy.

The main reasons for this low percentage of patients who underwent surgery are.

- Majority of our patients at the time of presentation were clinically inoperable (Late presentation).
- Some patients were not willing to accept the option of major surgical procedure.
- Poor Nutritional status / Advanced disease of the patients preclude surgical option.
- Some patients had co-morbid conditions and anaesthetically not fit for major surgical procedure and reconstruction
- In advanced lesions treated with surgery alone has got higher recurrence rate, poor outcome, hence surgery not advised.

SURGICAL PROCEDURES CLASSIFIED INTO 4 GROUPS

1. Surgery of the primary tumor
2. Surgery of the primary tumor with Mandibulectomy
3. Surgery of the primary tumor with Elective Neck dissection.
4. Surgery of the primary tumor with neck dissection with Mandibulectomy (Composite resection).

GROUP I

About 27 patients reported in stage I & Stage II, disease without Nodal Involvement / Mandibular Involvement are subjected to wide excision with tumor free Margin of 1 cm all around and depth of 0.5 cm.

3 dimensional soft tissue clearance accompanied by primary closure / partial / full thickness skin graft / Locally advanced flap – Fan flap (Gillies) Gate flap, Abbes flap are done.

GROUP II

About 11 patients in stage III & IV reported with mandibular involvement & neck nodes are treated with tumor clearance and Hemi Mandibulectomy.

Reconstruction with

1. Pectoralis major osteomyocutaneous flap with 5^{th} rib. for lining & cover with either delto pectoral flap or forehead flap
2. Free 5^{th} rib for mandible, pectoralis major myocutaneous flap for lining and cover with either delto pectoral flap or forehead flap
3. Forehead flap for both lining and cover for smaller lesions.
4. Bipaddle pectoralis major myocutaneous flap for both lining and cover.

In the above situations mandibular defect closed with wiring.

For Nodal disease primary RT are given, because of co-morbid Illness neck dissection cannot be done.

GROUP III

2 patients in stage II (No disease) had tumor clearance along with elective neck dissection.

GROUP IV

About 8 patients in stage III & IV (N_1, N_2) disease had either supraomohyoid Neck dissection (5 patients) (or) composite resection (3 patients) and reconstruction with pectoralis major myocutaneous flap for lining and cover with either delto pectoral or forehead flap.

Some cases of neck dissections had pre-operative elective tracheostomy.

RADIOTHERAPY

Radiotherapy is given in 2 forms either primary radiotherapy (or) Adjuvant radiotherapy.

In our study primary radiotherapy is given to majority of the patients in stage III & Stage IV.

In our institution external beam radiotherapy is given to the primary tumor area and to the neck in 6000 cGy for 6 weeks with 200 cGy per day for 5 days in a week.

Advancement in the radiotherapy in the form hyper fraction RT / IMRT (Intensity modulated radiotherapy) are available in Regional cancer centers.

Adjuvant RT to the primary and Neck were given to 8 patients, those who had positive margins and doubtful clearance during surgery.

COMPLICATIONS

Out of 48 patients, 8 patients had wound infection, 7 developed orocutaneous fistula and 5 patients had flap necrosis.

28 patients had no specific complaints. Wound infection treated with higher antibiotics. Necrosed area excised and skin graft applied.

FOLLOW UP

Follow up was advised at monthly intervals for 1st year and once in 3 months for the 2nd year.

During the follow up period local recurrence, Nodal recurrence and specific complaints were recorded. Out of 92 patients subjected to primary RT, 2 patients developed Nodal recurrence they were treated with Neck dissection and 1 developed local recurrence treated with surgical resection.

SUMMARY

- Oral cancer constitutes about 12.2% of total cancers reported in Thanjavur Medical College Hospital.
- Buccal mucosa was the most common site of oral cavity cancer (51.4%) with Tongue being the second most common site (25.7%).
- Peak age of incidence is 40 – 50 yrs.
- Male to Female ratio 2 : 1.
- Habit of Betel leaf, tobacco with slaked lime were the most common etiological factor.
- Low socio economic status more prone for oral cavity cancer.
- Majority had endophytic lesion (65.7%)
- Ulcer was the Chief complaint among the people who presented with oral cavity cancer.
- 95.8% of oral cancers were Squamous cell origin
- 64.3% of Patients reported in advanced stages (Stage III, IVa, IVb)
- No recorded case of distant metastasis (Stage IV-C)
- Out of 140 patients, 48 patients underwent surgery with primary reconstruction and 8 of them were given adjuvant radiotherapy.
- Post operative complications noted in 30.8%
- No post operative mortality encountered
- 92 patients were given primary radiotherapy in the form of external beam radiotherapy to tumor and neck.
- Among the above said 92 patients, 2 patients had nodal recurrence, they were treated with neck dissection, 1 patient developed local recurrence he was treated with surgical resection.

CONCLUSION

Oral Cancer is a national problem.

Oral Cancer remains a challenge as majority of the patients reported are in advanced stage.

Moh's micrographic excision and alternative forms of therapy such as Cryo, Electro, Chemo & Photo dynamic therapy for smaller lesions and wide excision along with advanced reconstructive procedure such as Free Flap – Microvascular surgery has made surgery as the anchor role in management.

With the invent of Radio sensitisers and Radio protectors, the radiotherapy as a modality of treatment has to be considered as deleterious effects are low.

Role of adjuvant chemo and concomitant role of chemo & radiotherapy are analysed by various trials.

Role of immunological agents such as Gefitinib and erlotinib and cetuximab are under trial.

Effective multimodality management has come into vogue with Radiotherapy and surgery have definitive role along with doubtful role of chemotherapy has reduced the morbidity of oral cancers.

Future developments in nanotechnology and directed therapies will alter the diagnosis and treatment of oral cancers relative to contemporary treatment modalities.

The best way to cure is by prevention. Screening of high risk group (ie) those who are in the Habit of betel nut & tobacco chewing in general population, should be done.

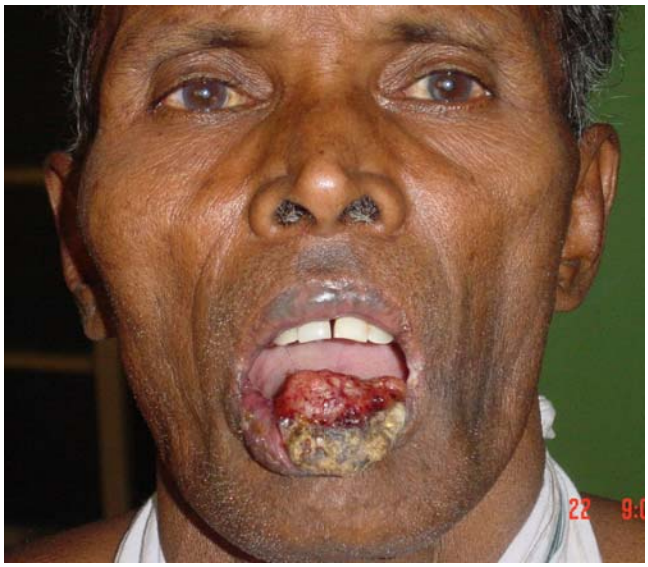
Dental surgeons and general practioners have a vital role with early detection of oral lesions and referral to higher centers for proper management.

Health education through mass media and posters in Health centers and dispensaries on the ill effects of Tobacco / Alcohol / Betel nut in a large scale by Government and Non-Government organizations will create awareness and help in prevention.

Younger population is to be educated by mass media with a ban on advertisement of Tobacco, Alcohol and screening camps will also be useful.

Case - 1

∆- carcinoma Lower Lip
Procedure –wide excision & karapandzic flap



Pre- op

Intra - op

Intra - op

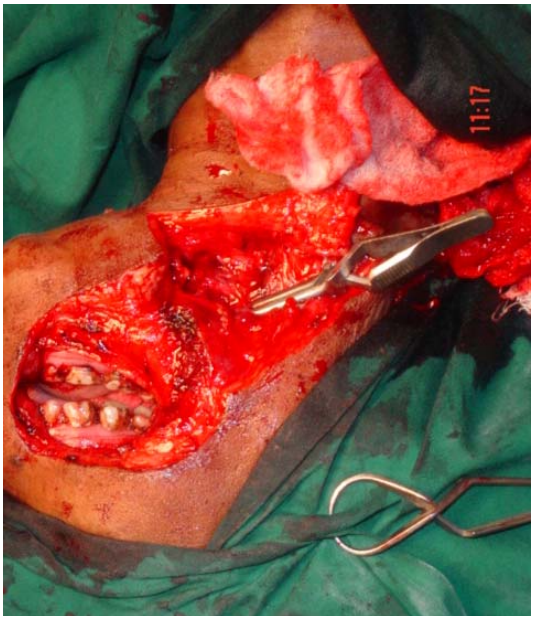
Post - op

Case - 2

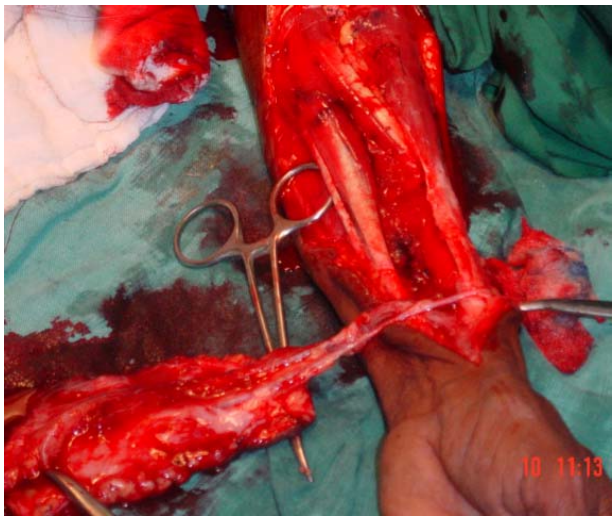
∆- Carcinoma cheek

Procedure – Wide excision & Radial artery free flap

Pre- op



Intra - op



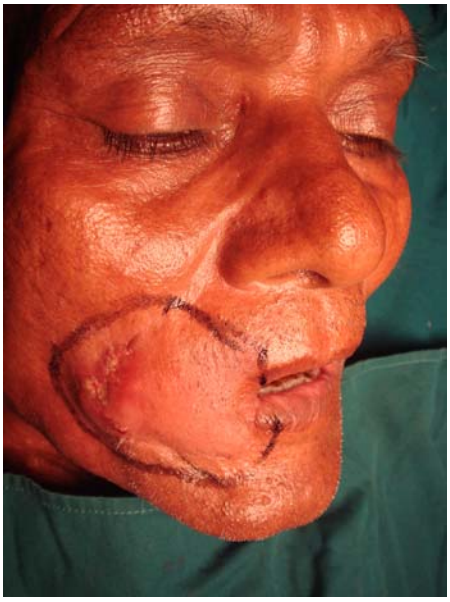
Radial artery
Free flap

Post - op

Case - 3

∆- carcinoma cheek

Procedure – wide excision & McGregor's flap



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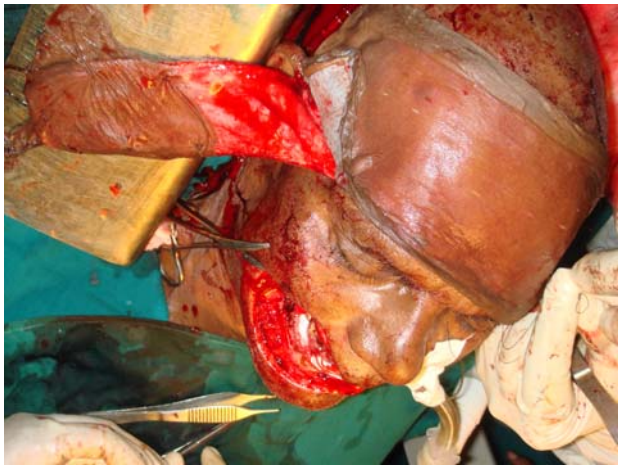
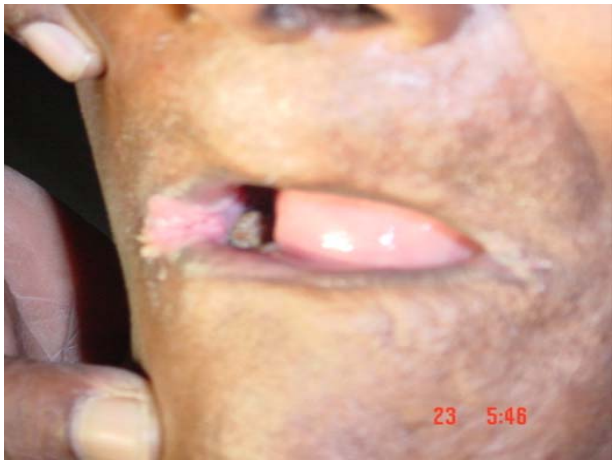


Intra - op

Post - op

Case - 4

∆- carcinoma cheek
Procedure – wide excision with Pectrolis major myocutaneous flap & deltopectoral flap for cover



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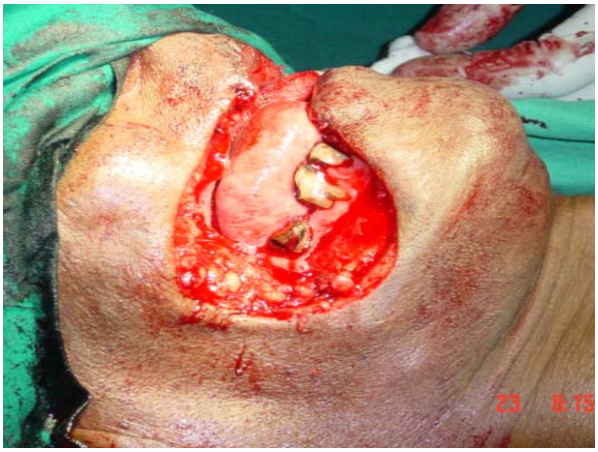
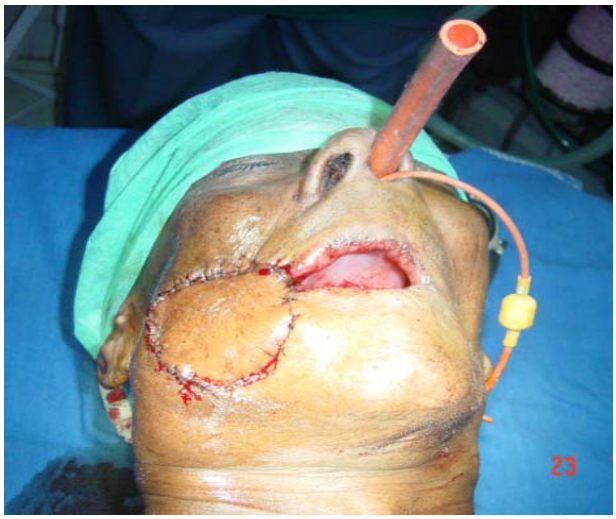


Intra - op



Post-op

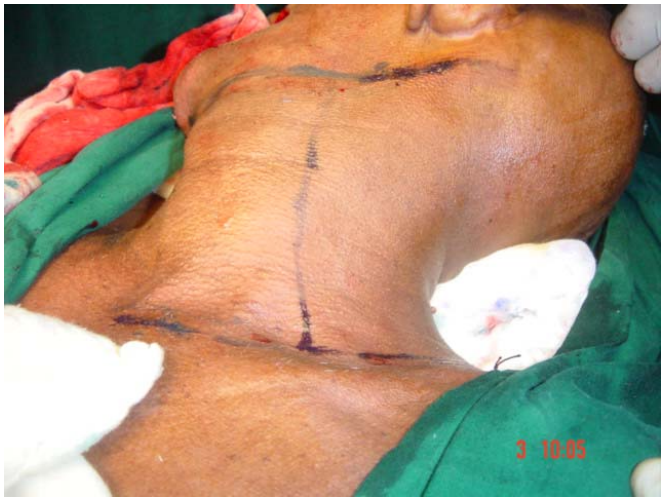
Post - op

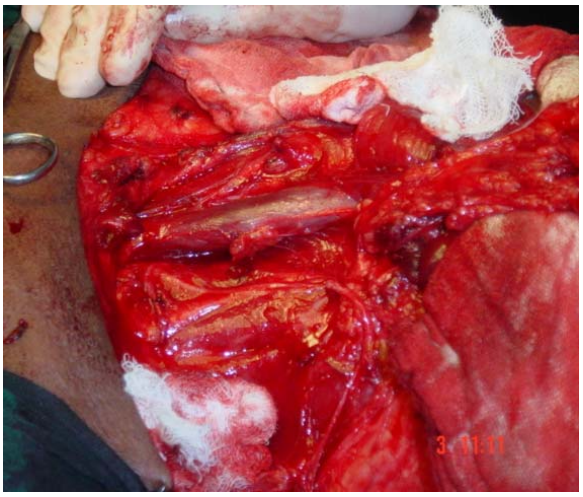
Case - 5

∆- Carcinoma cheek
Procedure – Wide excision & radical neck dissection

Pre- op

Intra - op





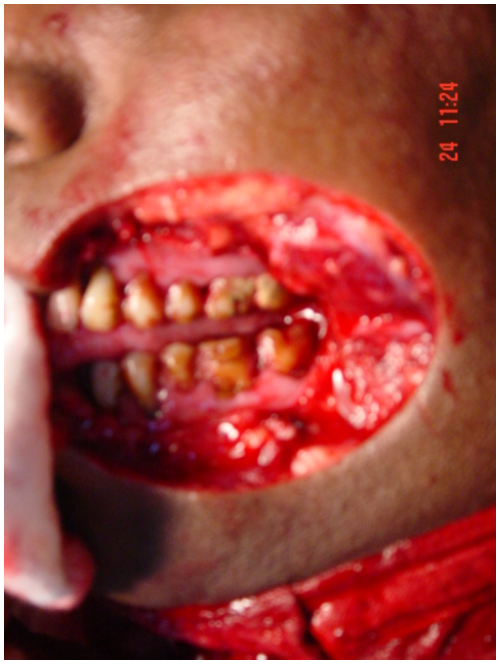
Neck dissection

Case - 6

∆- Carcinoma cheek

Procedure – wide excision & McGregor's flap

Pre- op



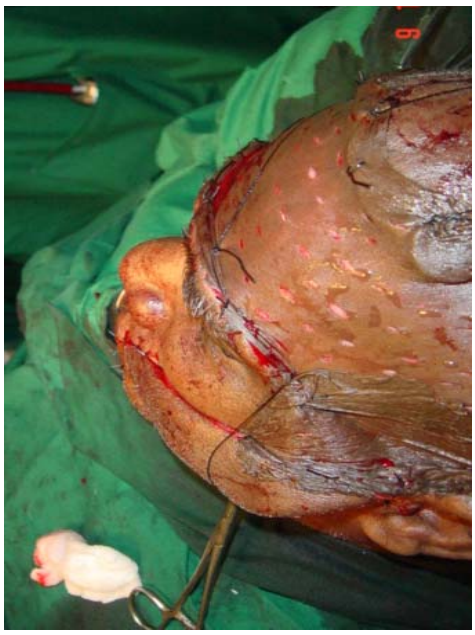
Intra - op

Post - op

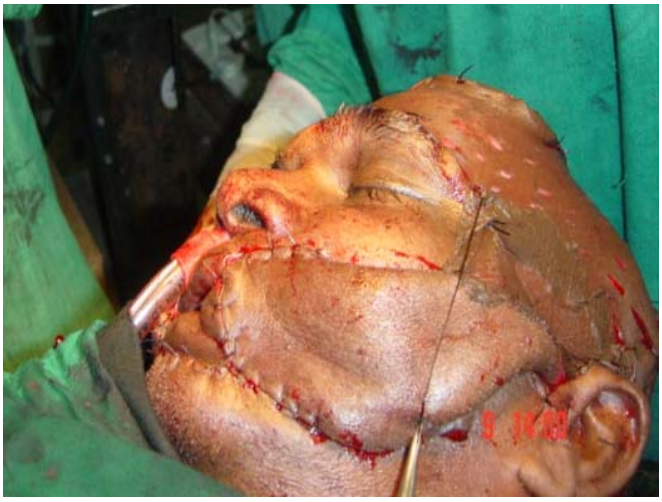
Case - 7

∆- Carcinoma cheek
Procedure – wide excision & McGregor's flap

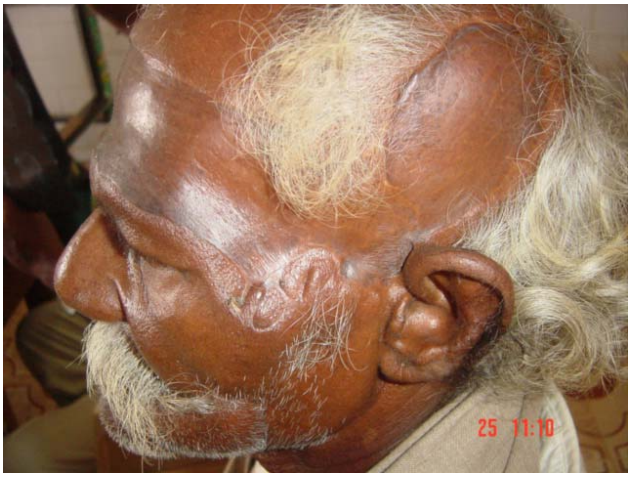
Pre- op



Intra - op

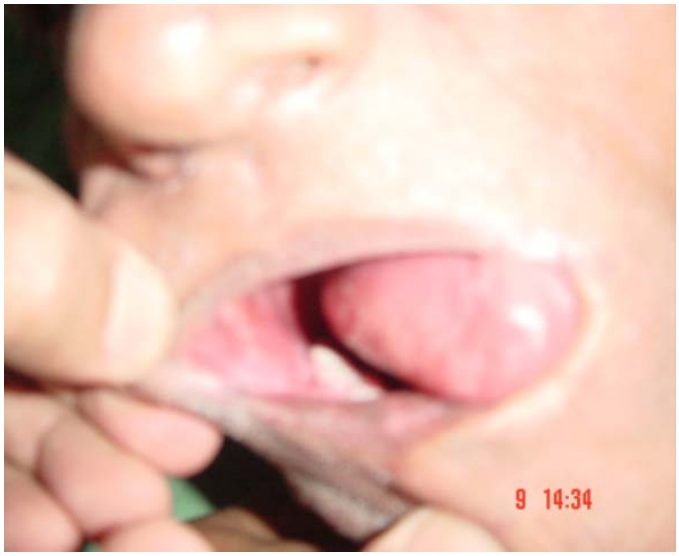


Post -op



Follow - up

Case -



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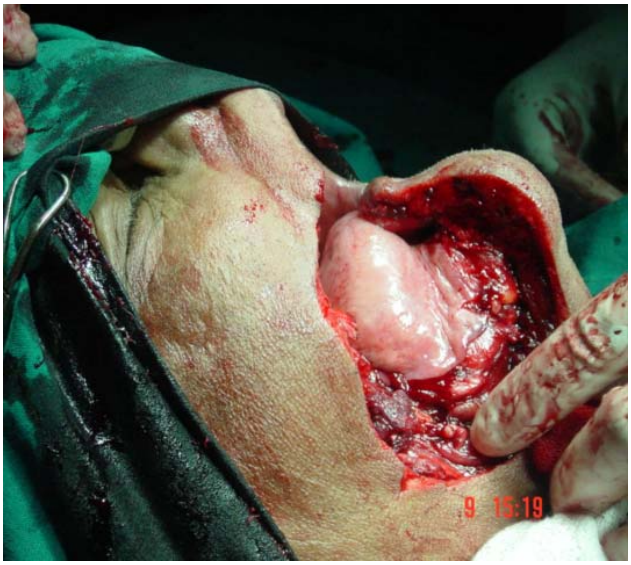

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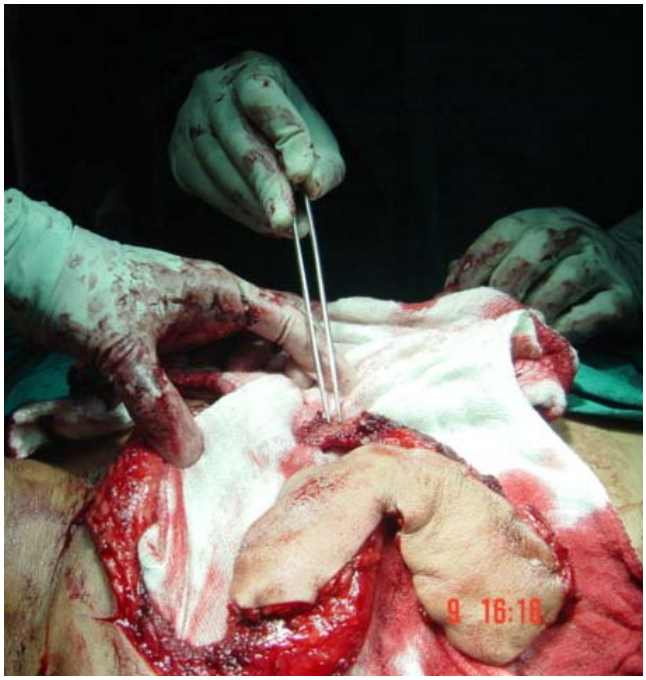
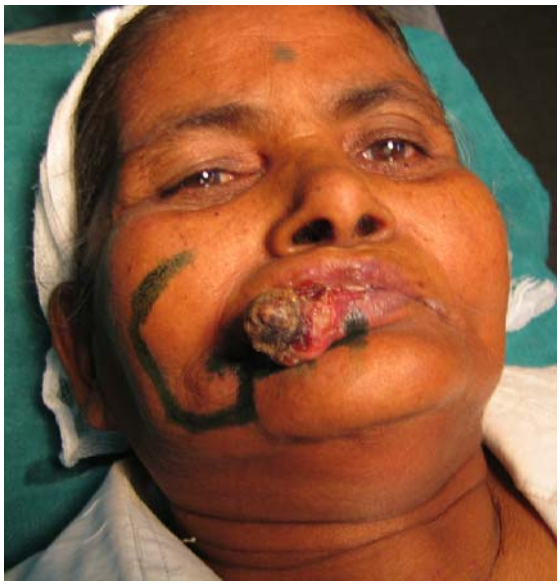


Intra - op

Post - op

Case -



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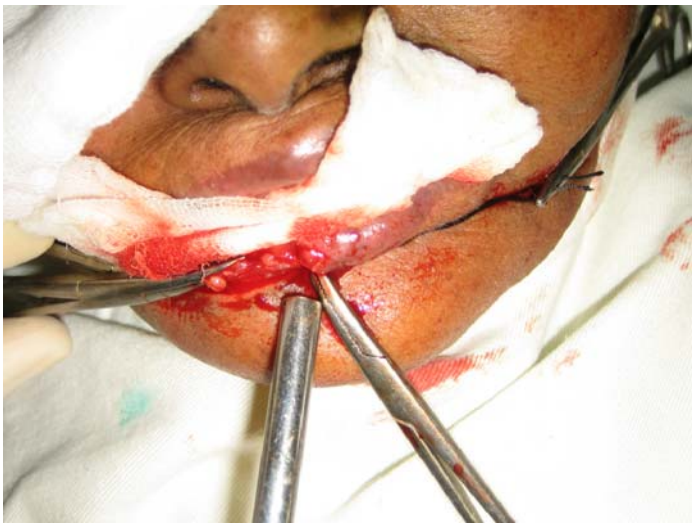

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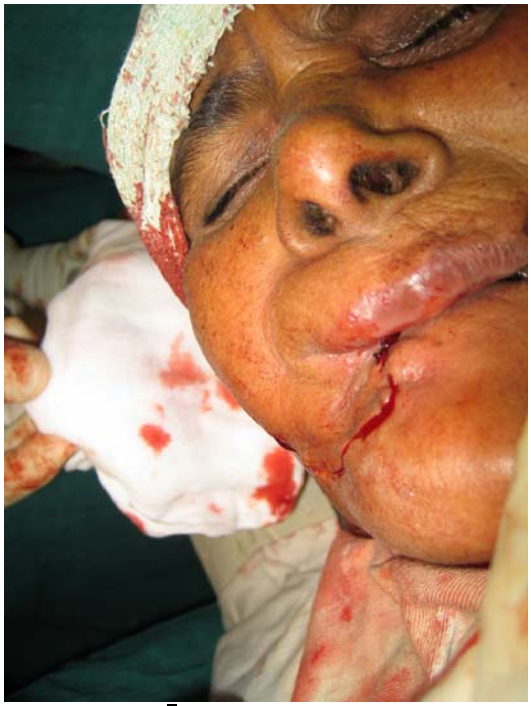

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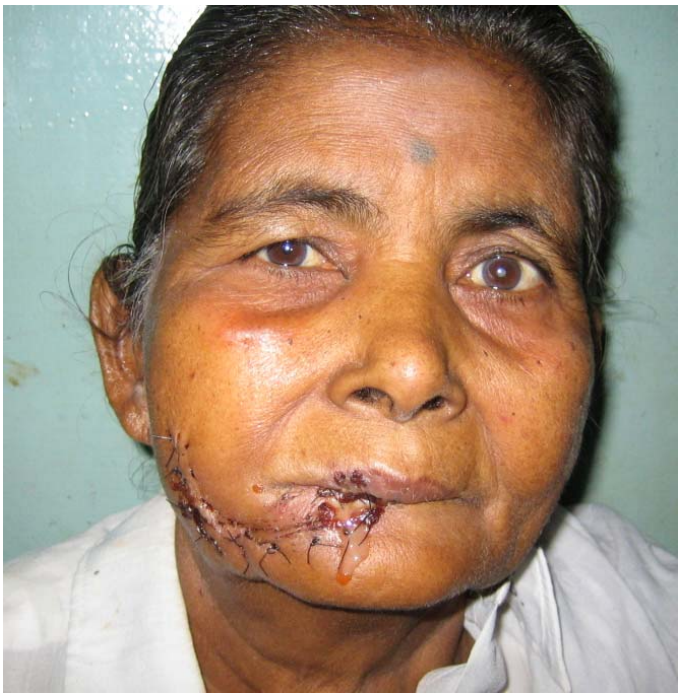
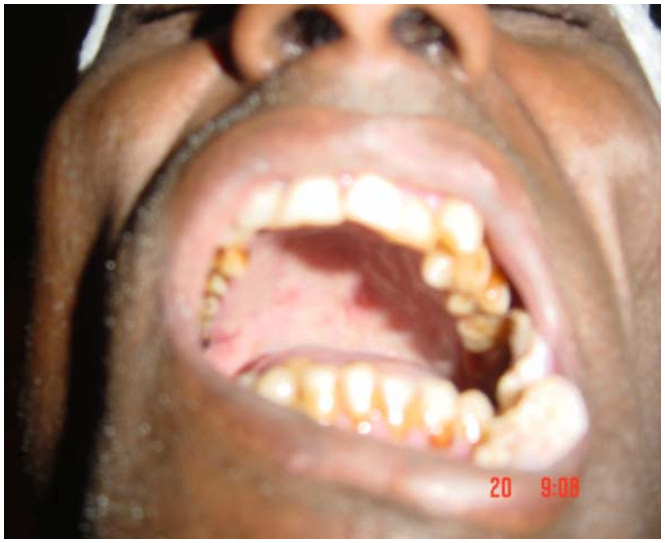


Post - op

Case -



Pre- op

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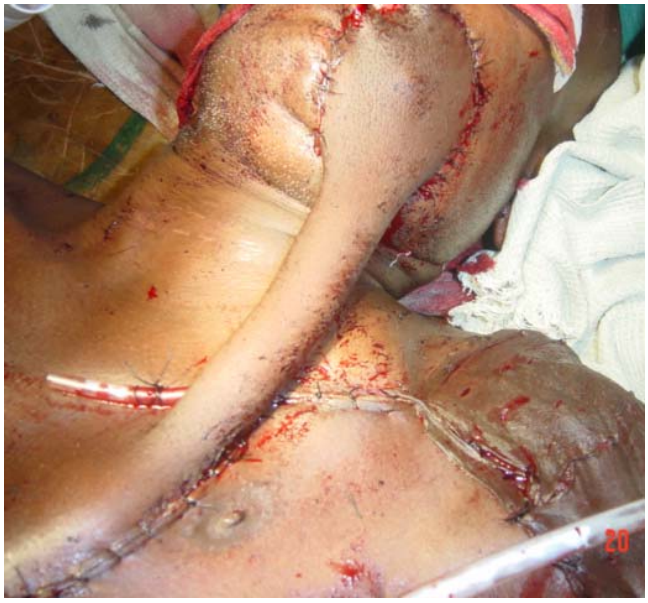

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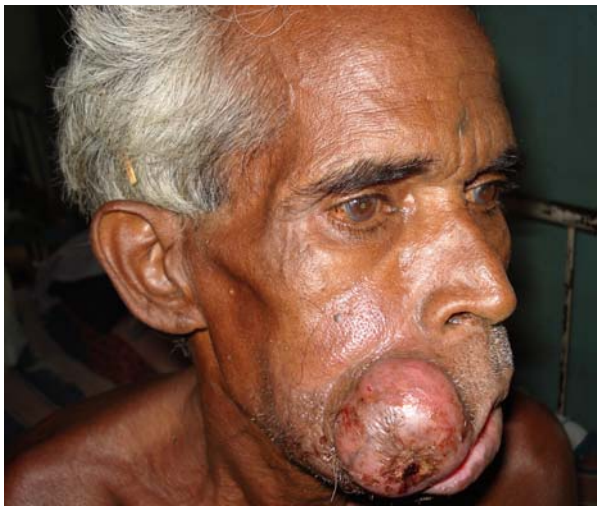

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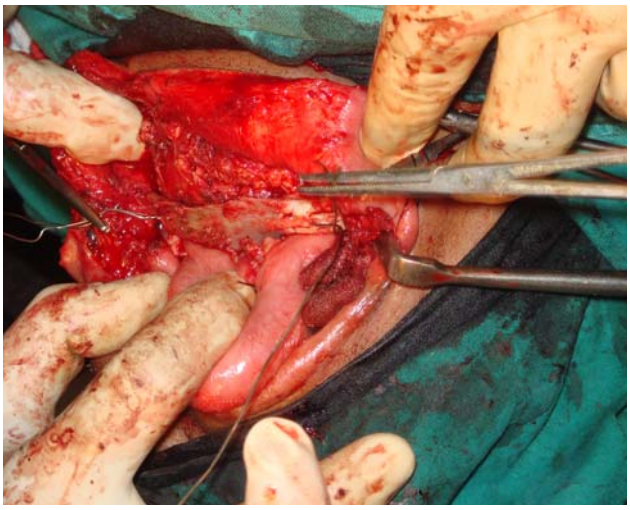

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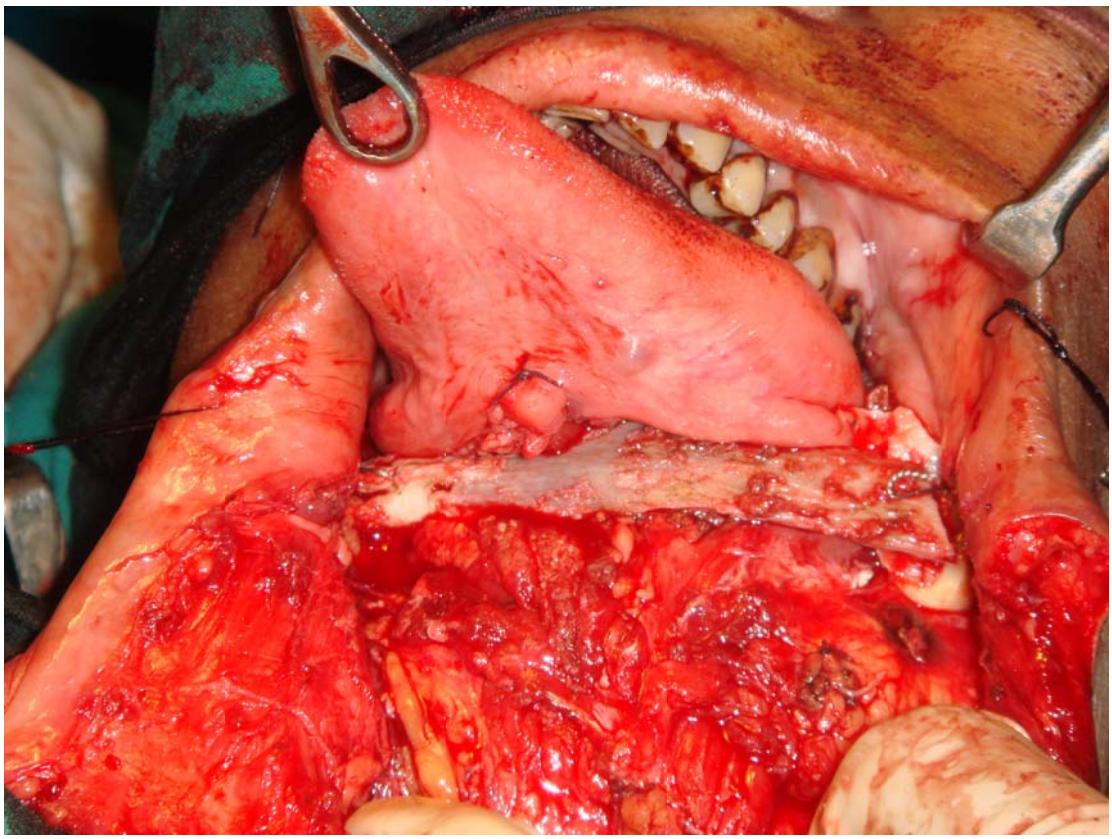
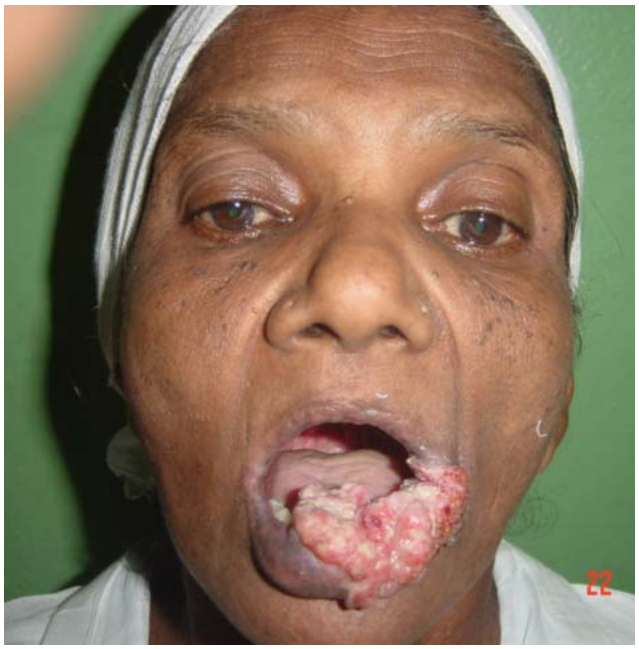
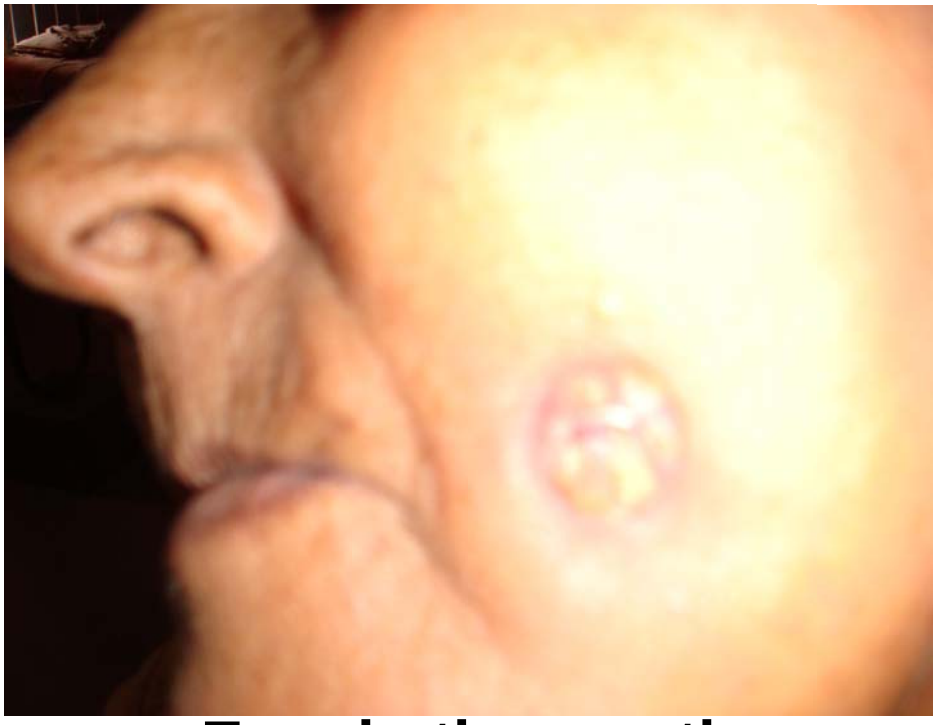


Rib graft

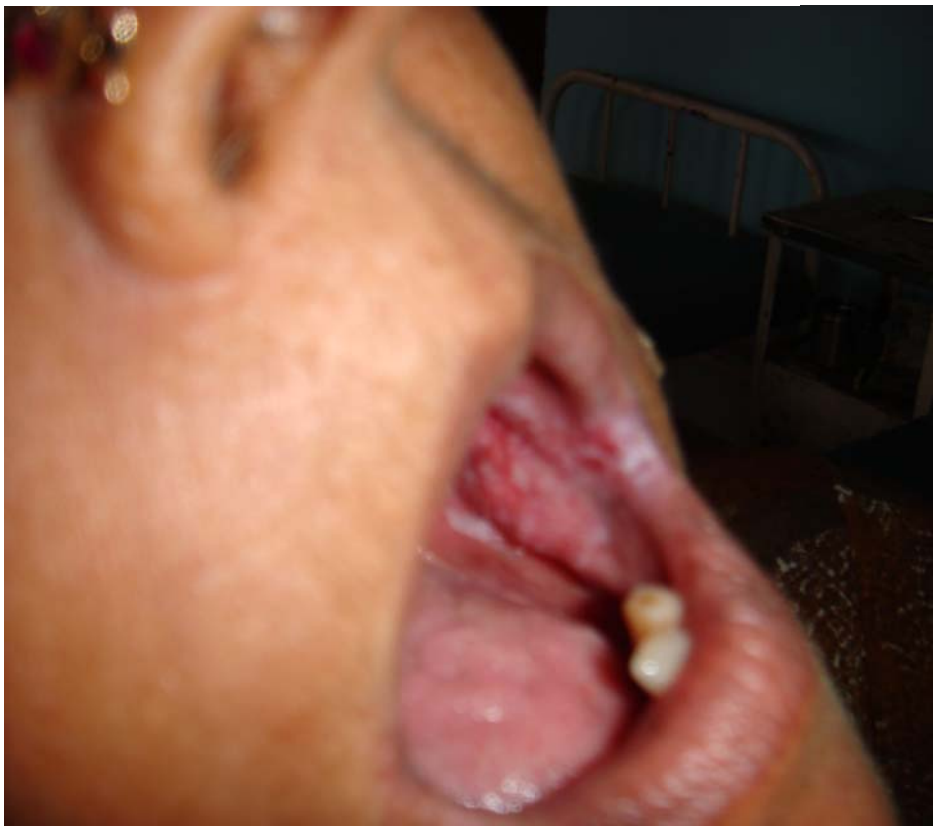
Advanced lesions



Carcinoma cheek

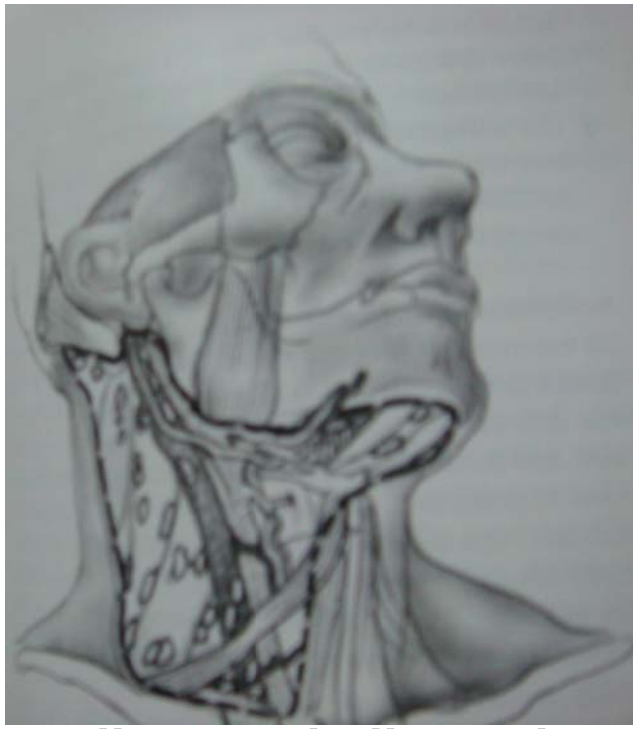


Exophytic growth

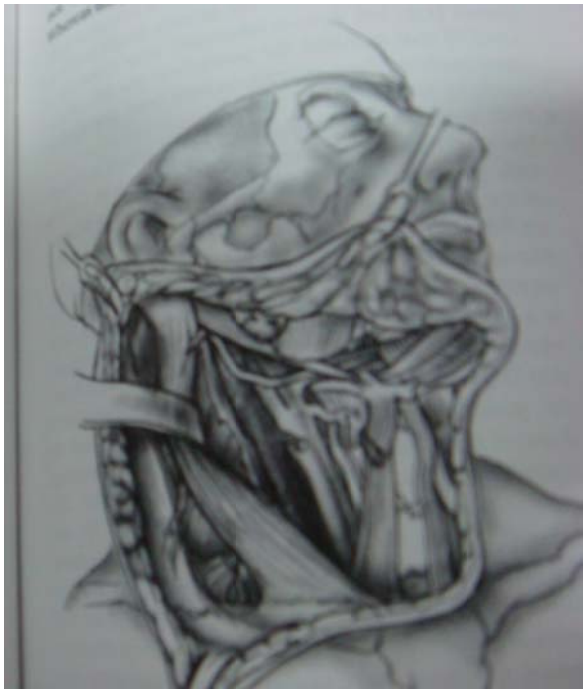


Endophytic growth

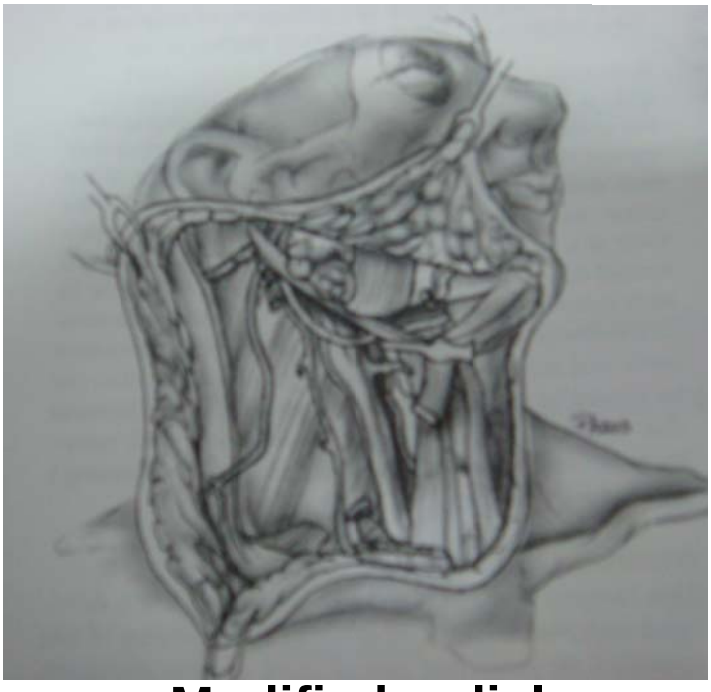
Types of neck dissection



Radical neck dissection

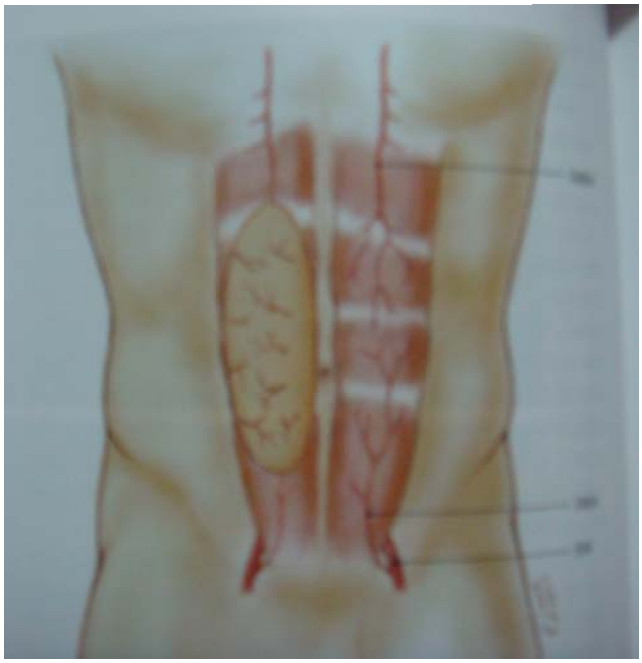


Modified radical neck dissection type - I

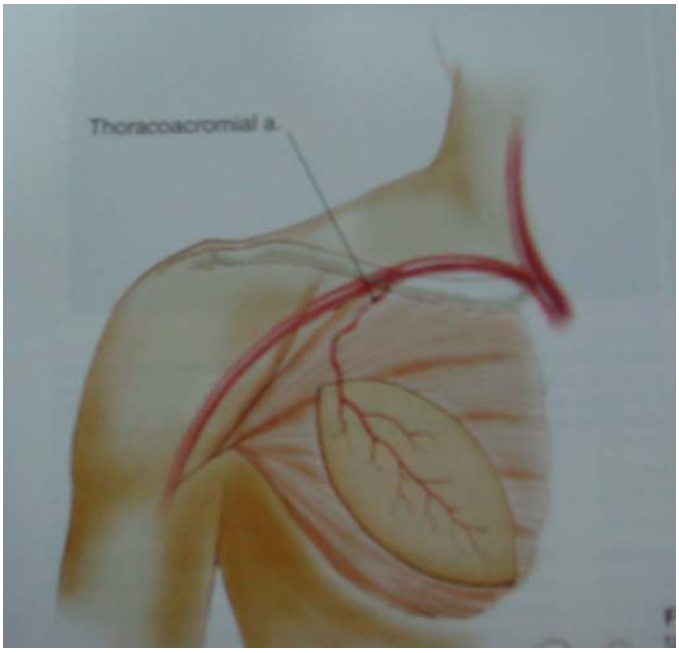


Modified radial neck dissection type - III

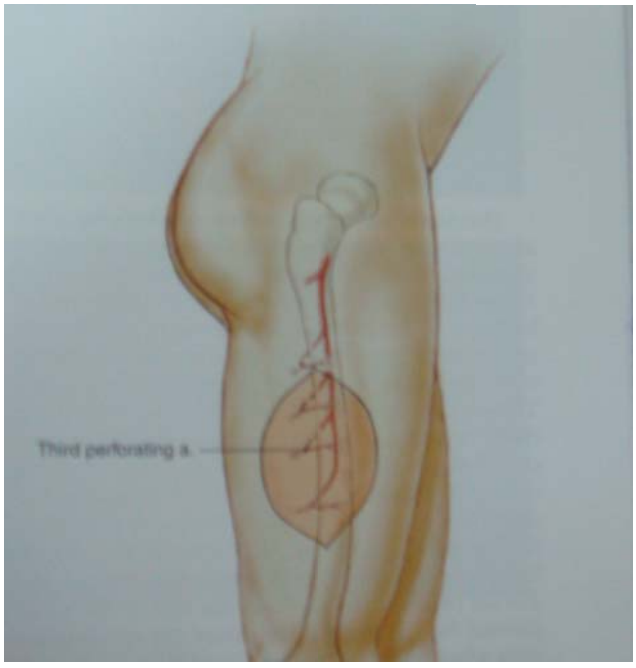
Types of flap



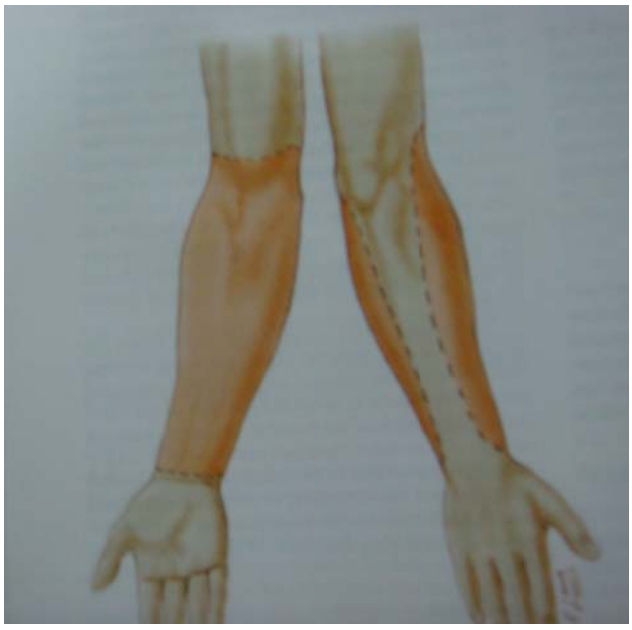
Rectus abdominus musculocutaneous flap



Pectoralis major musculocutaneous flap

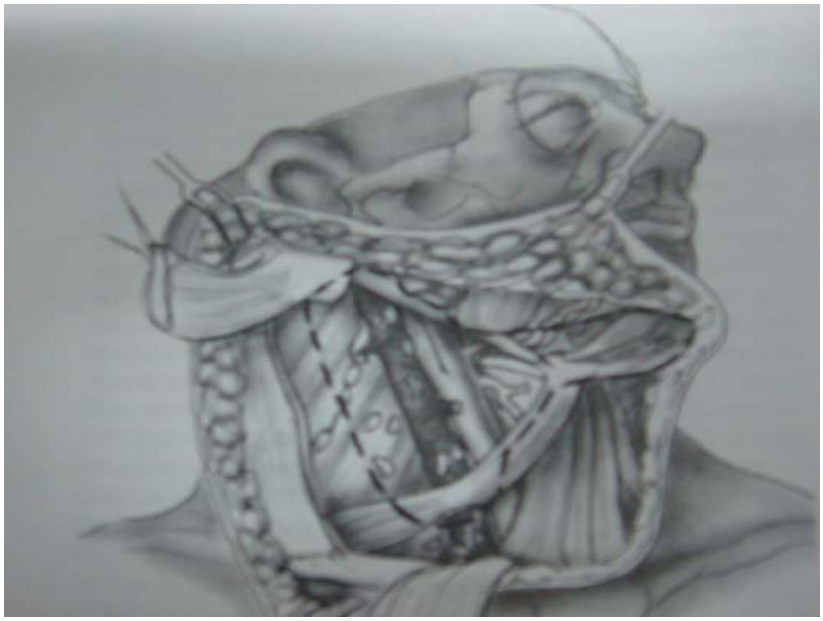


Lateral thigh flap

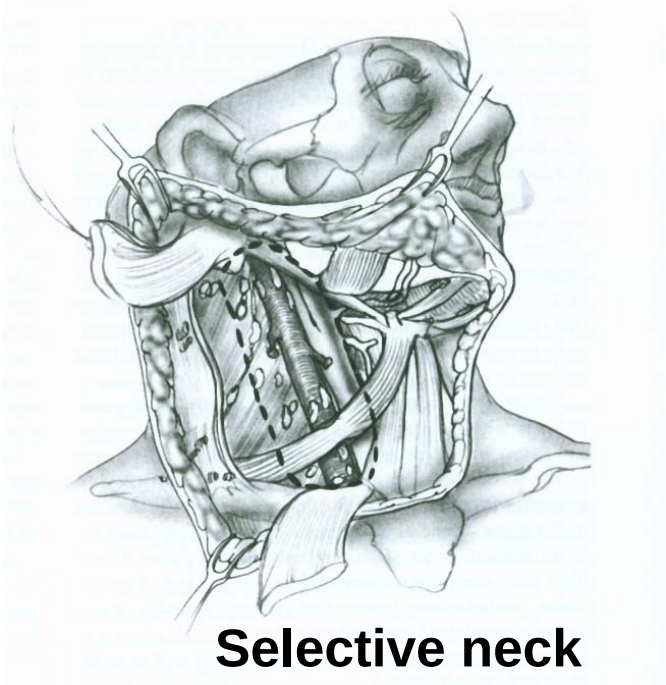


Radial forearm flap

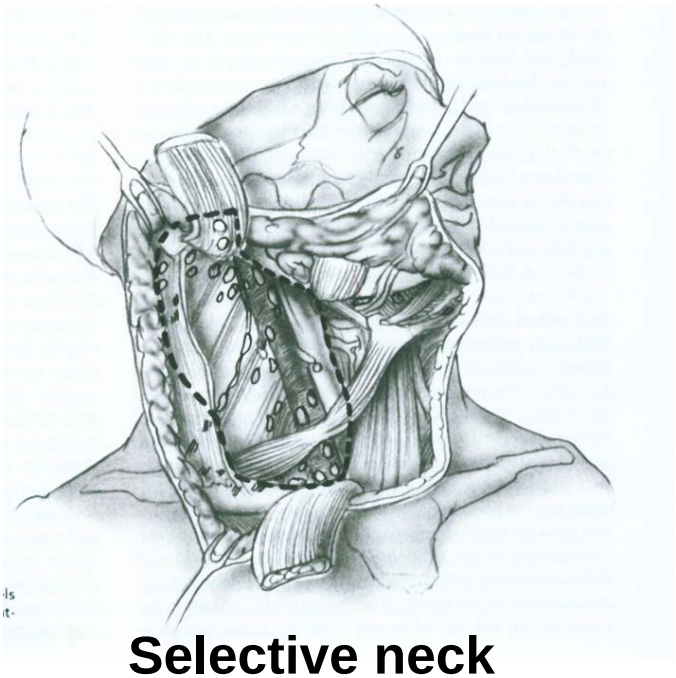
Types of neck dissection



Selective neck dissection I-III (Supra omohyoid neck dissection)

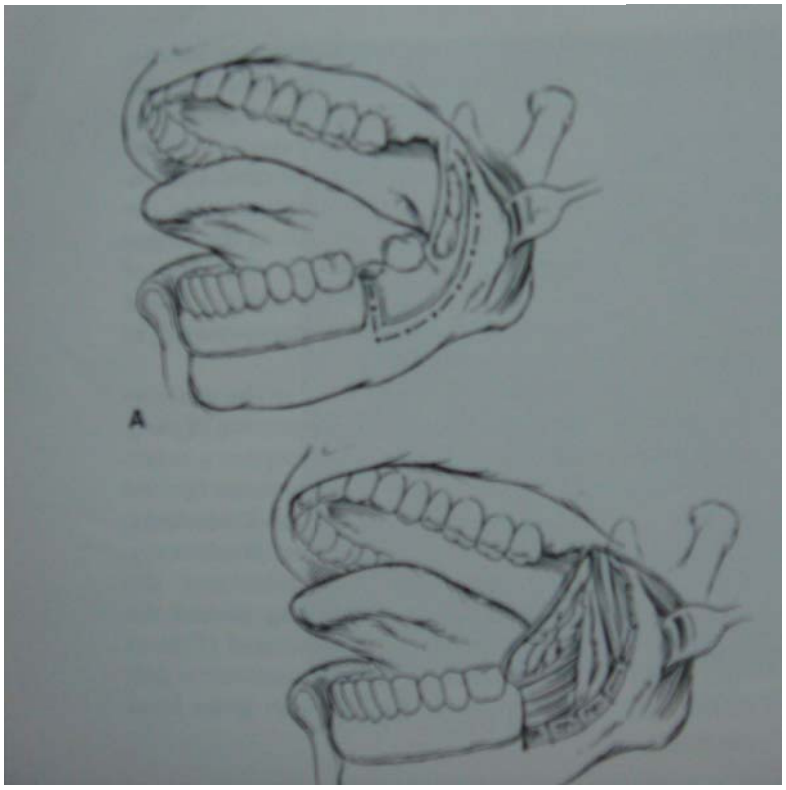


Selective neck dissection II-IV (Lateral neck dissection)

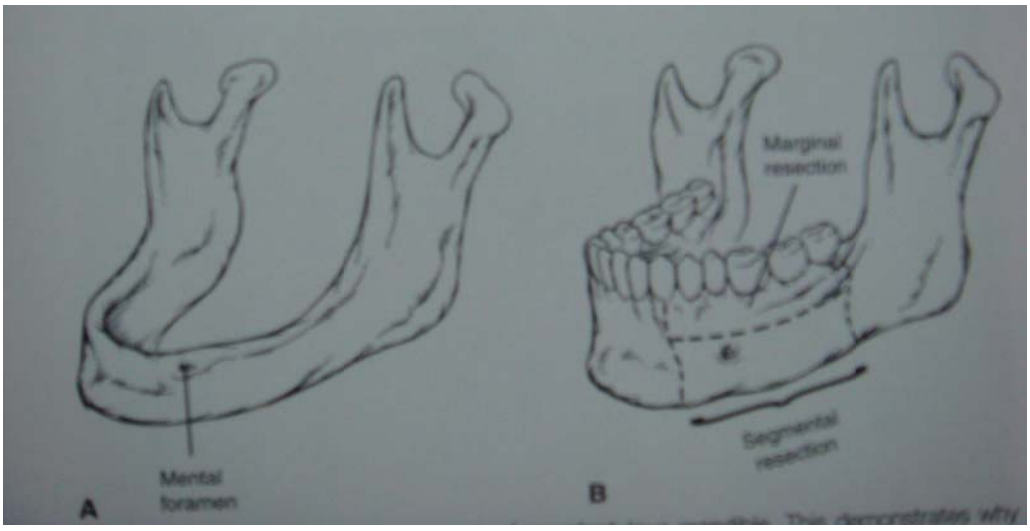


Selective neck dissection II-V (Posterolateral neck dissection)

Types of mandibulectomies

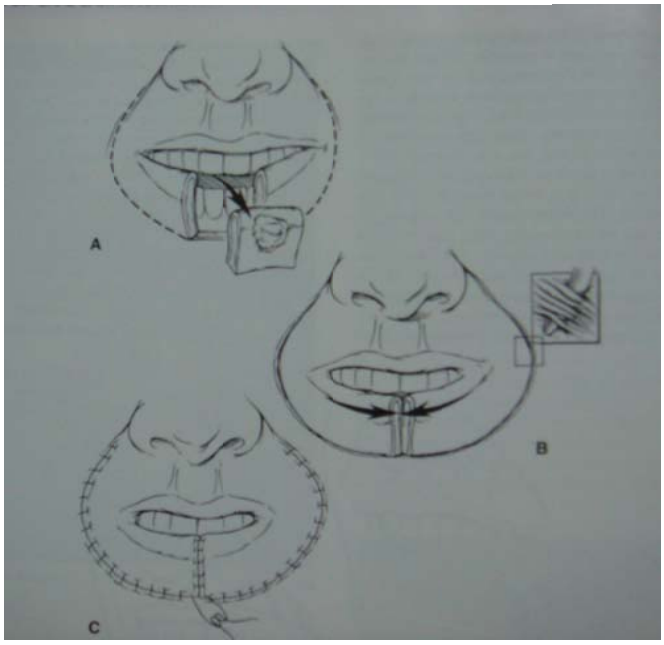


L shaped Marginal mandibulectomy

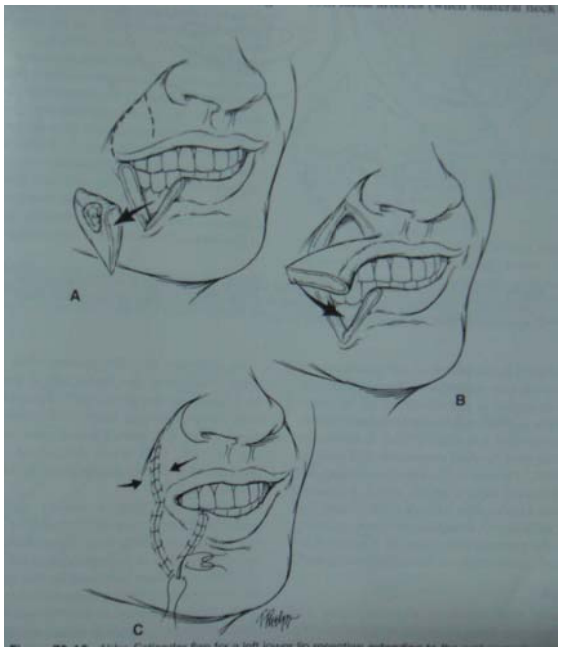


Segmental & Marginal mandibulectomy

Types of flap

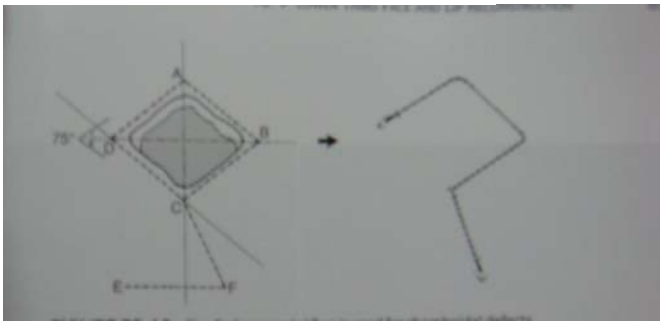


Karapandzic flap
Central lower lip defect

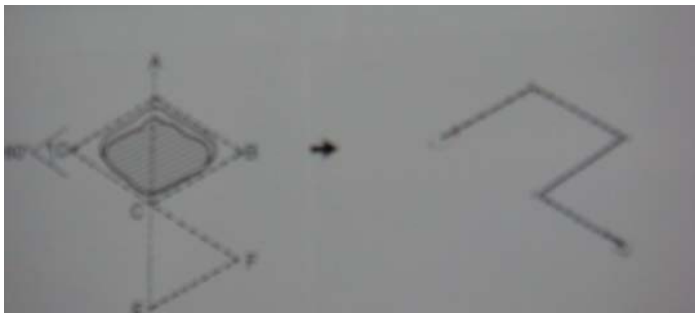


Abbe – Eslander flap

Rhomboid flap



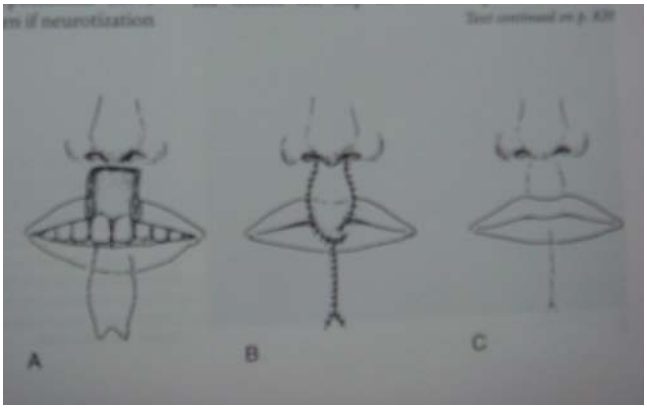
Limberg flap



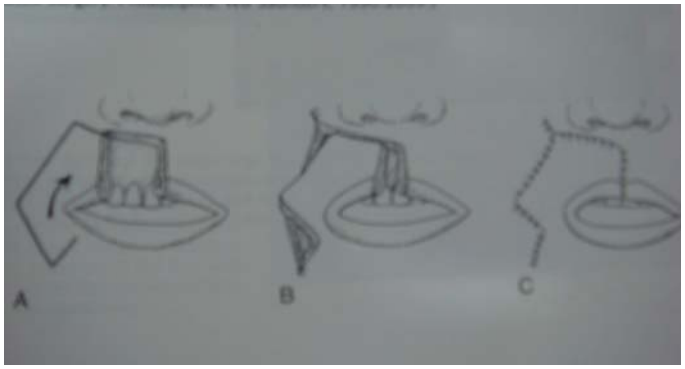
Dufourmental flap

Types of flap

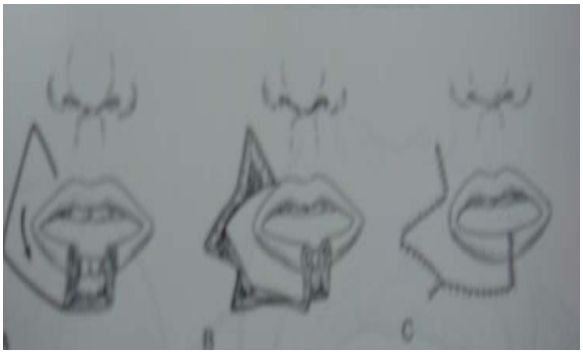
Eslander flap
Lower lip defect



Abbes flap
Central upper lip defect

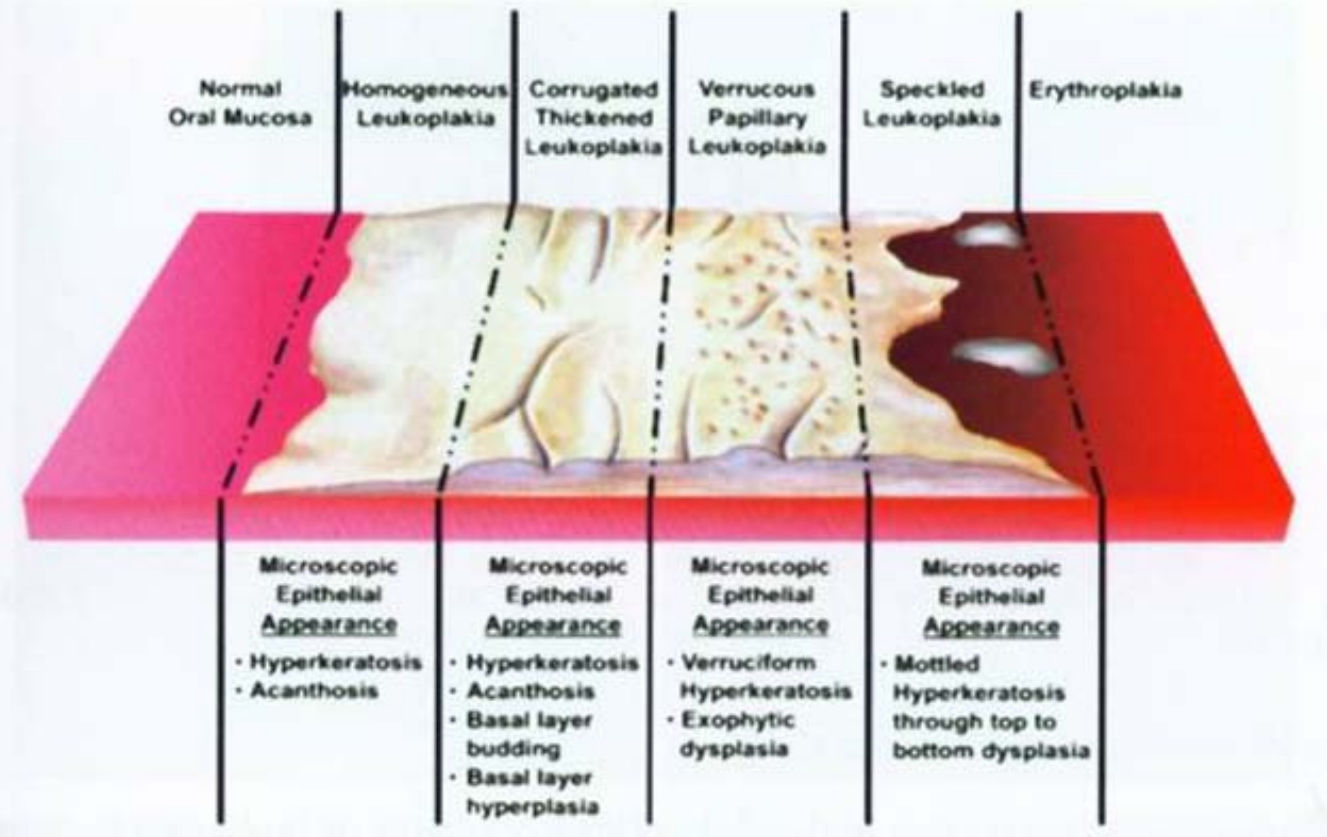


A to C fan flap
Upper lip defect

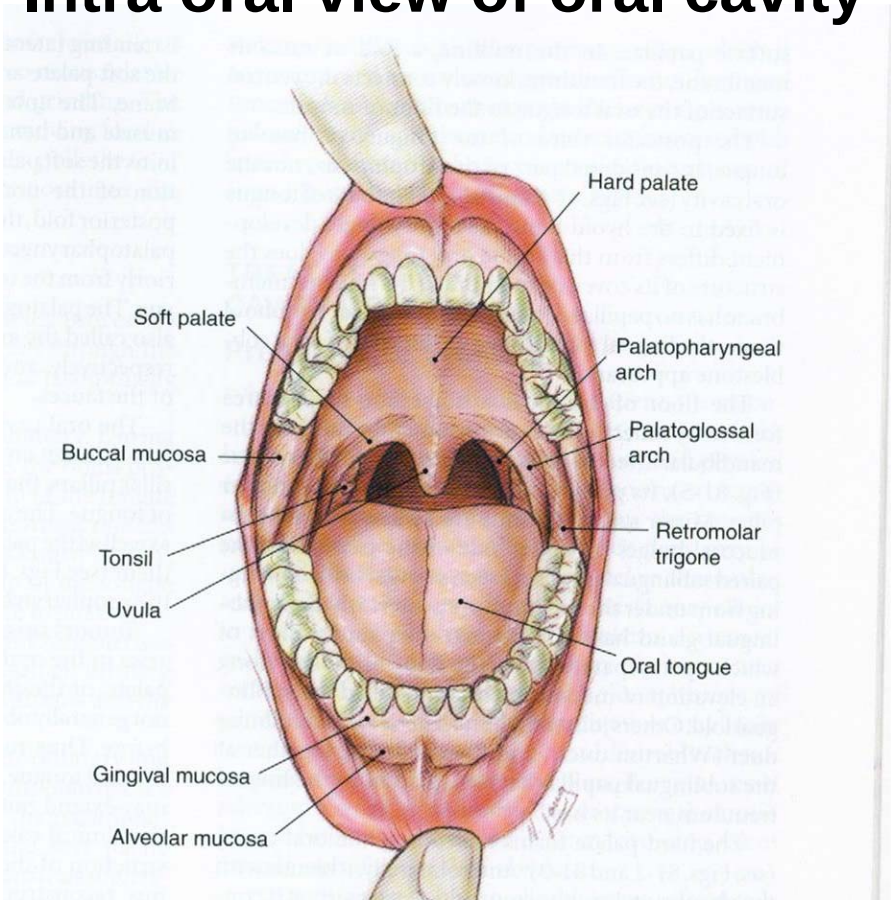


A to C fan flap
Lower lip defect

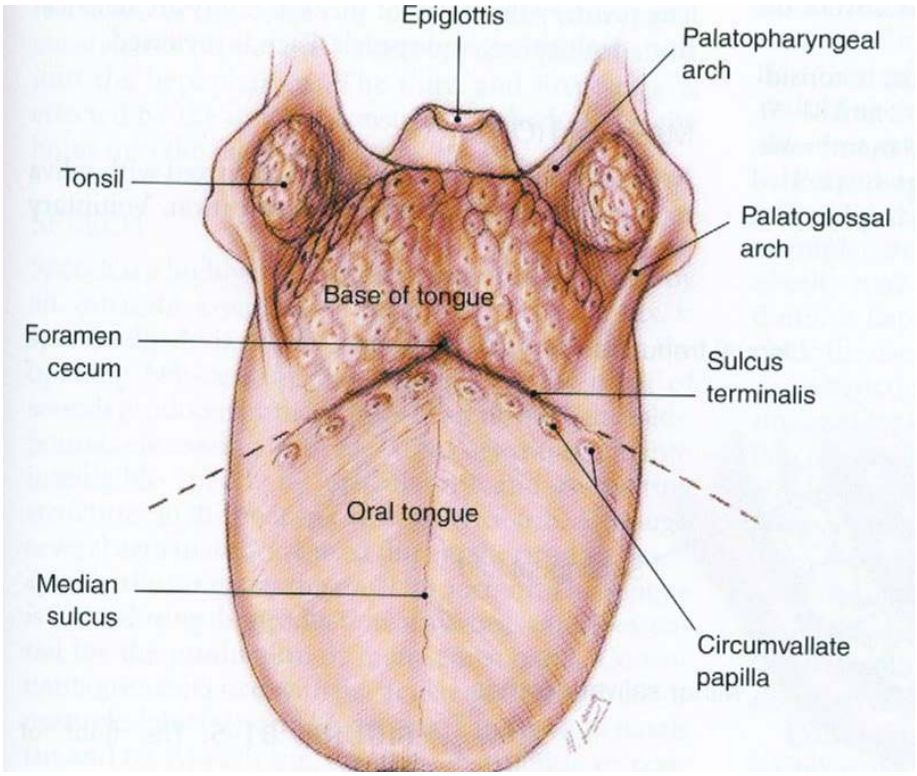
Pathology of oral epithelial lesions



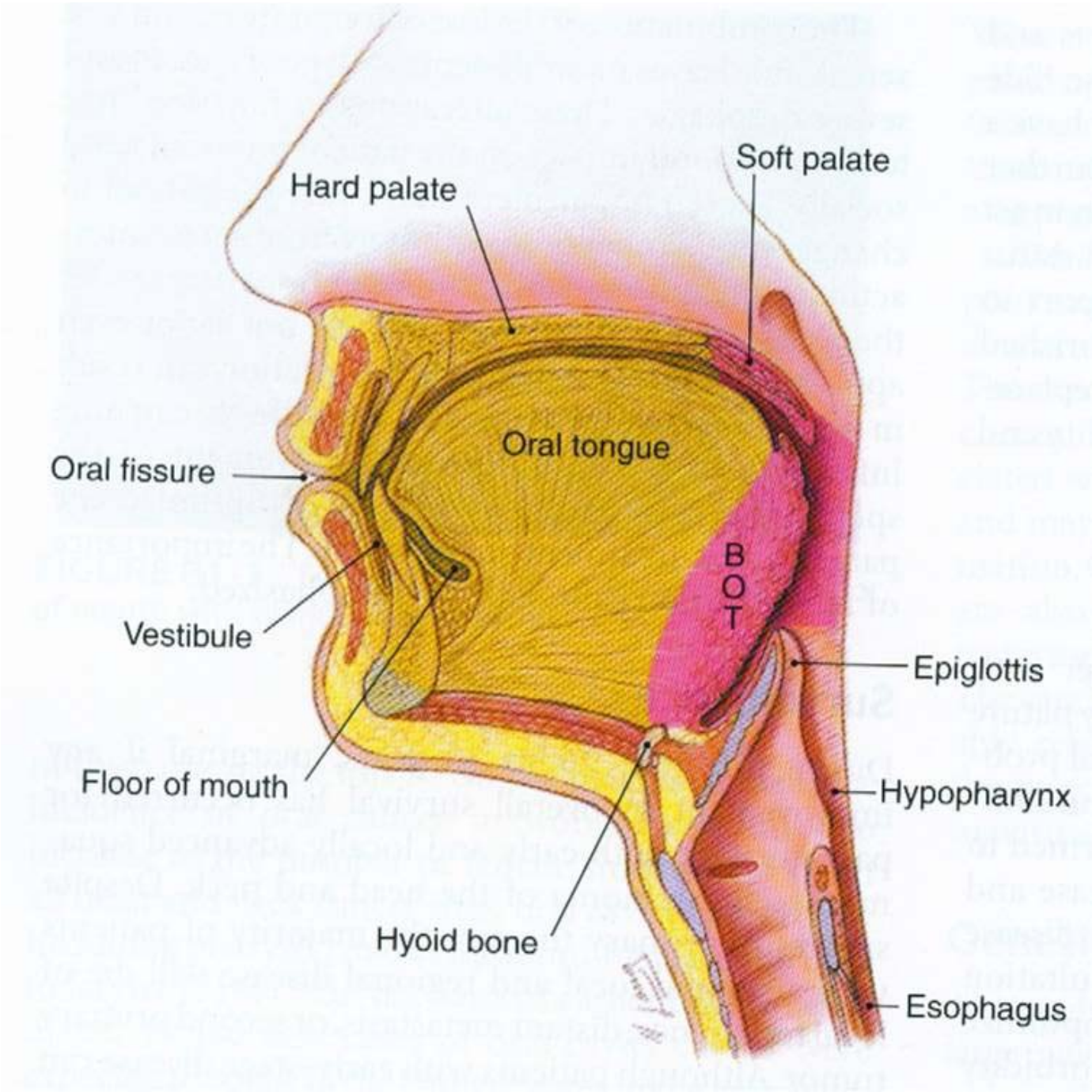
Intra oral view of oral cavity



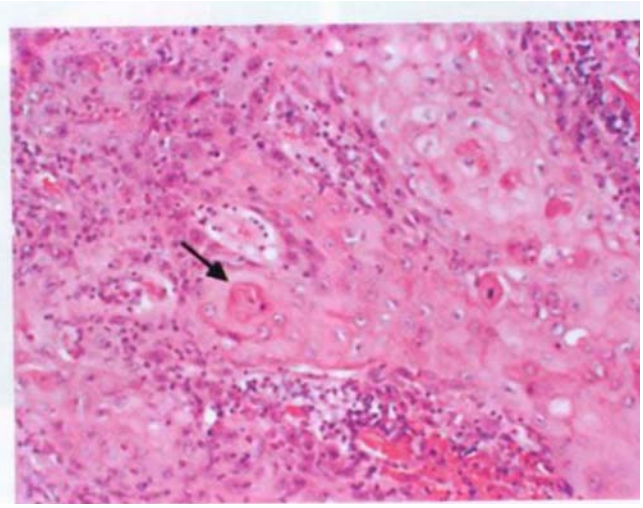
The Tongue



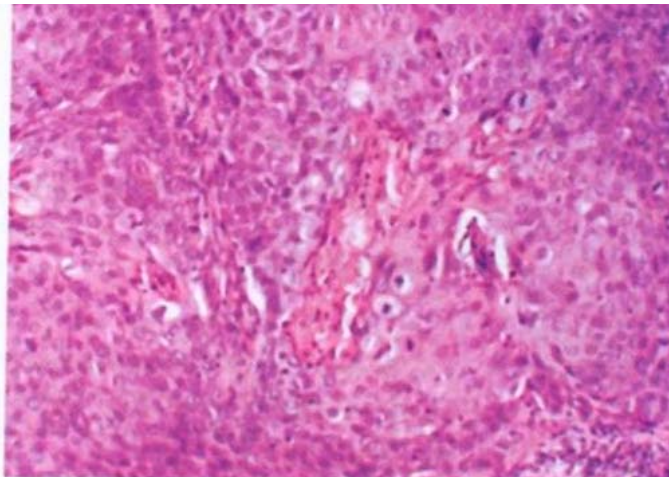
Anatomy of oral cavity



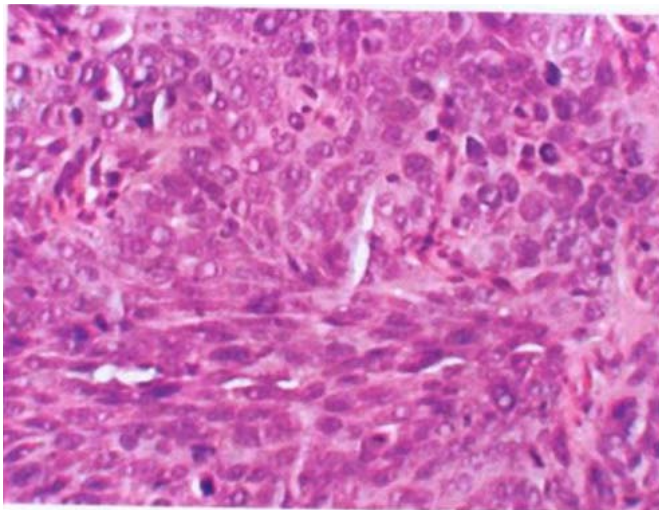
Histology of Squamous cell carcinoma



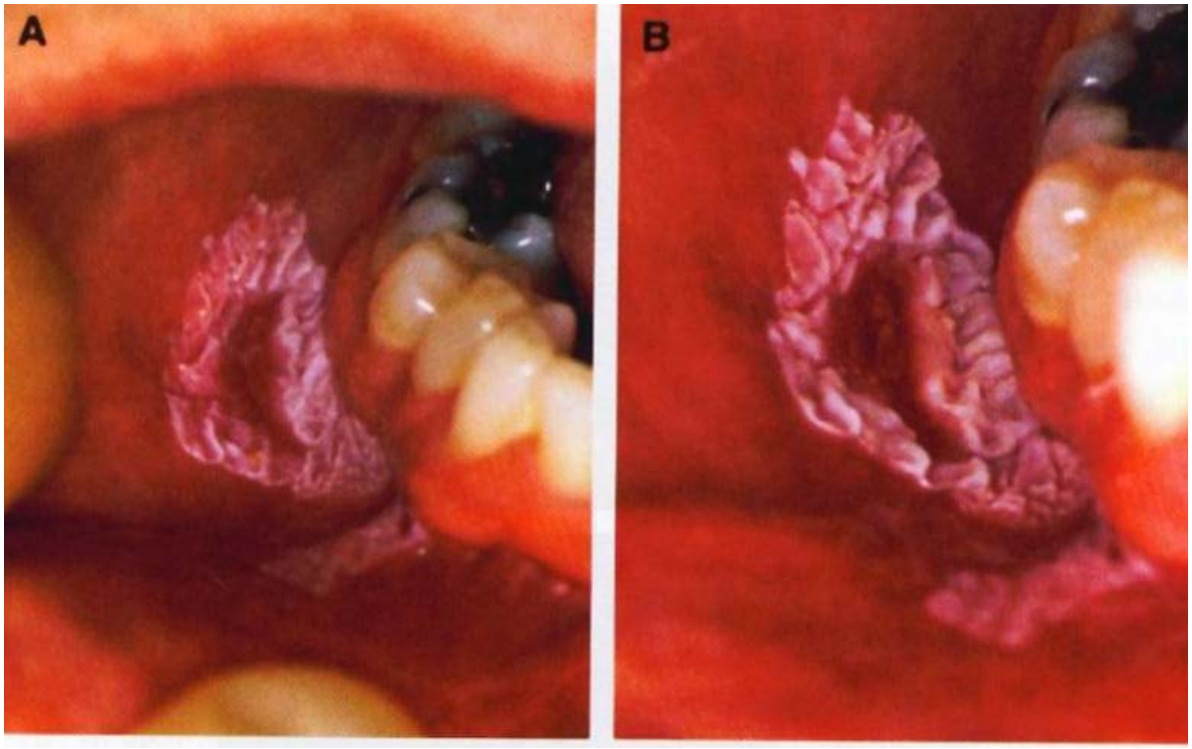
Well differentiated



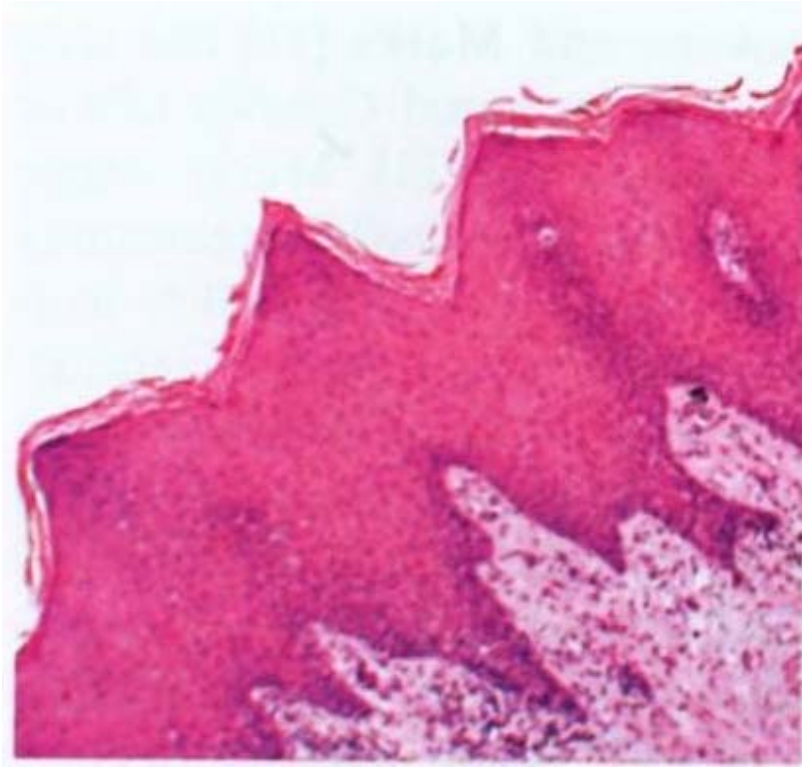
Moderately differentiated



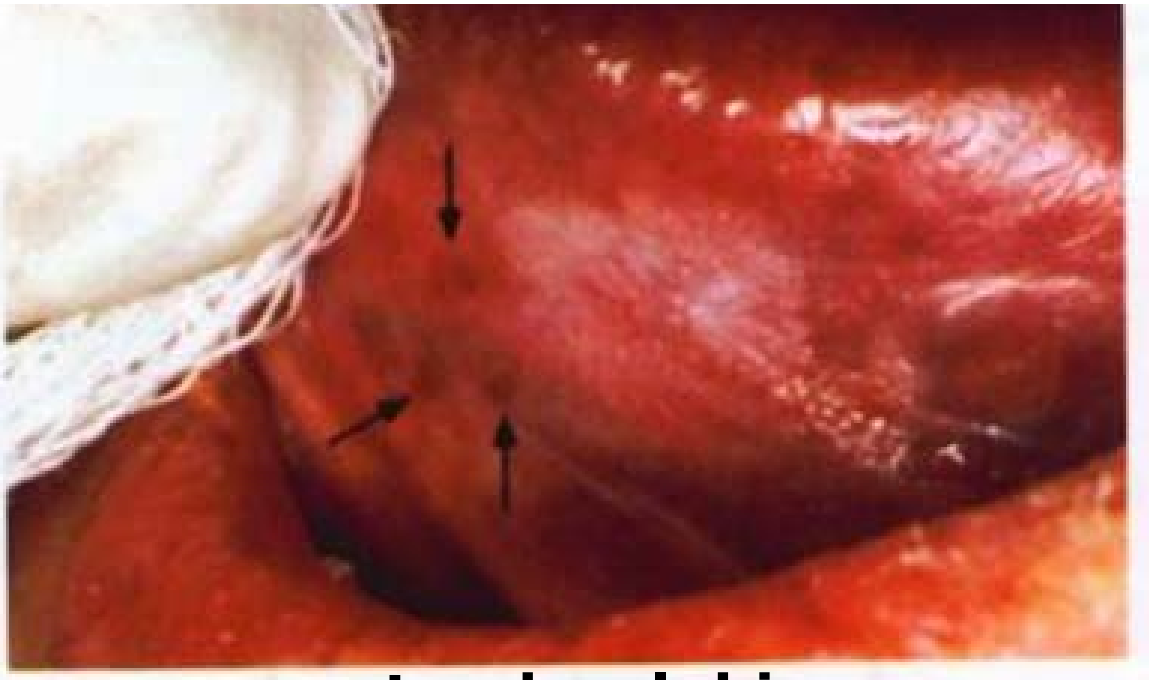
Poorly differentiated



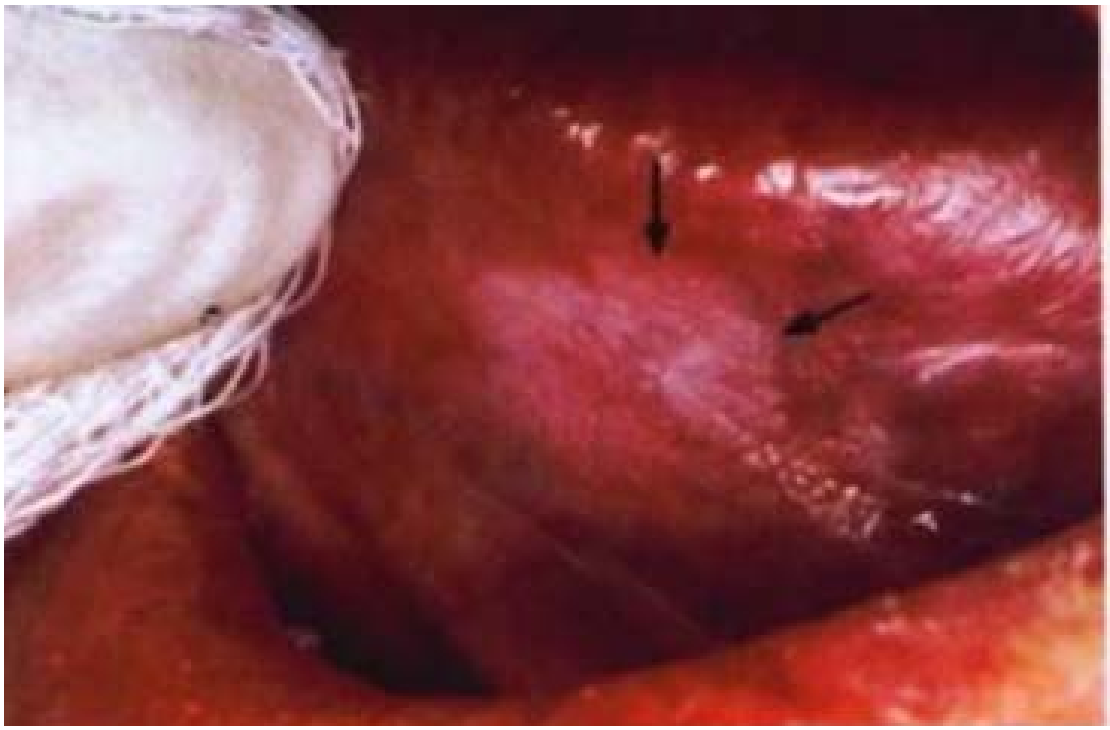
Proliferative verucous leukolakia



Histology of proliferative verrucous leukoplakia

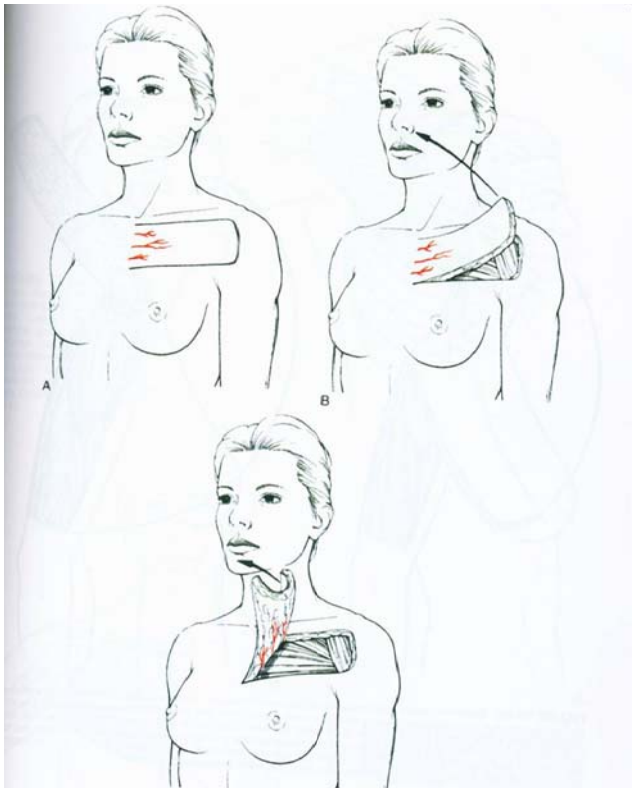


Leukoplakia

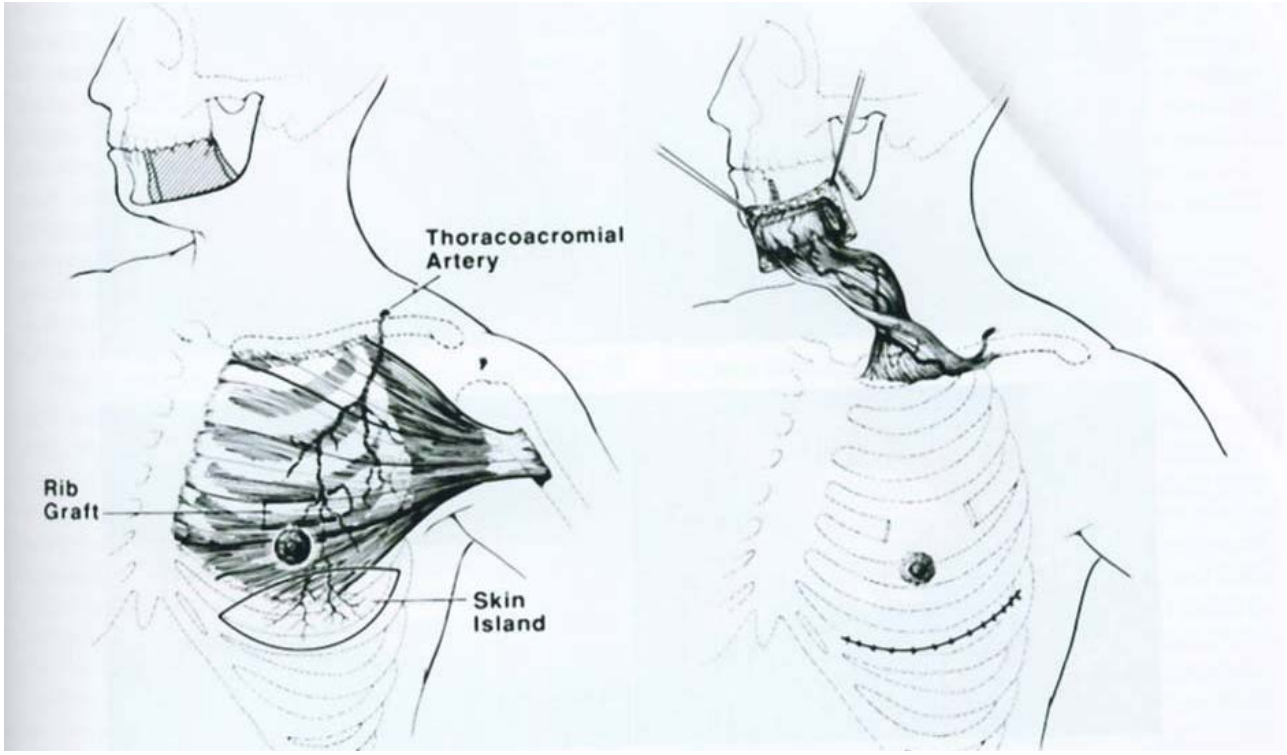


Erythroplakia

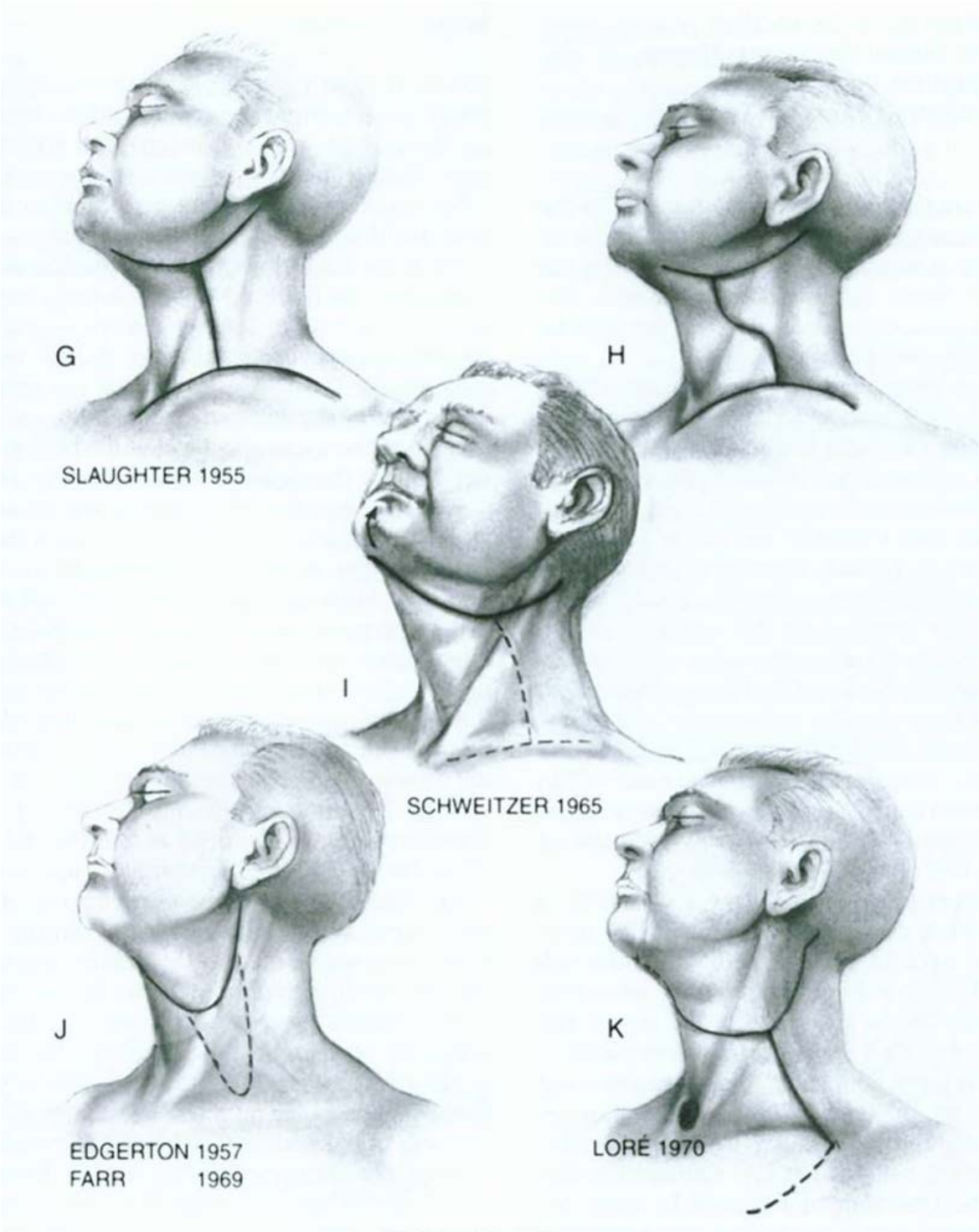
Deltopectoral flap



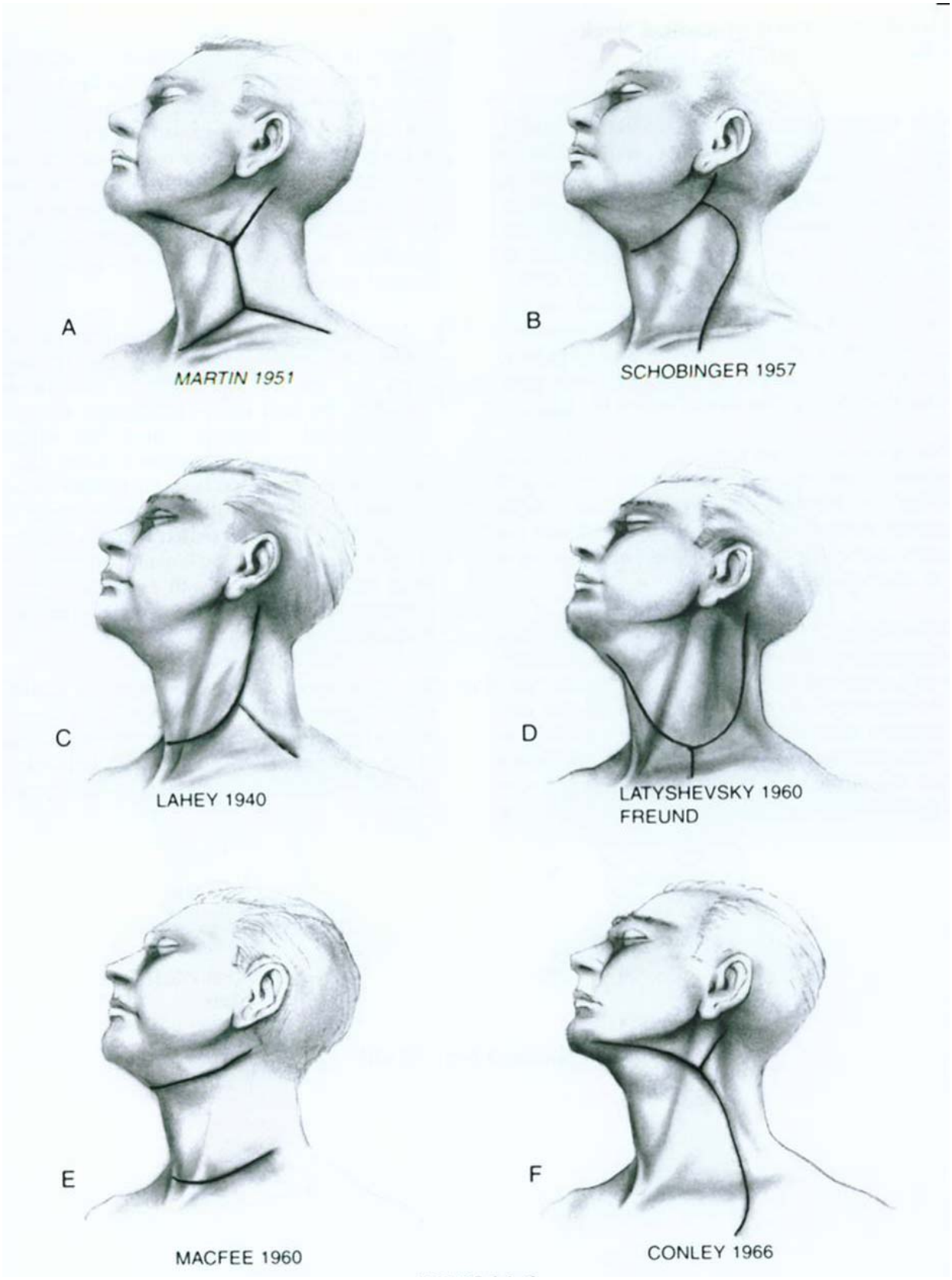
Pectoralis major osteomyo cutaneous flap



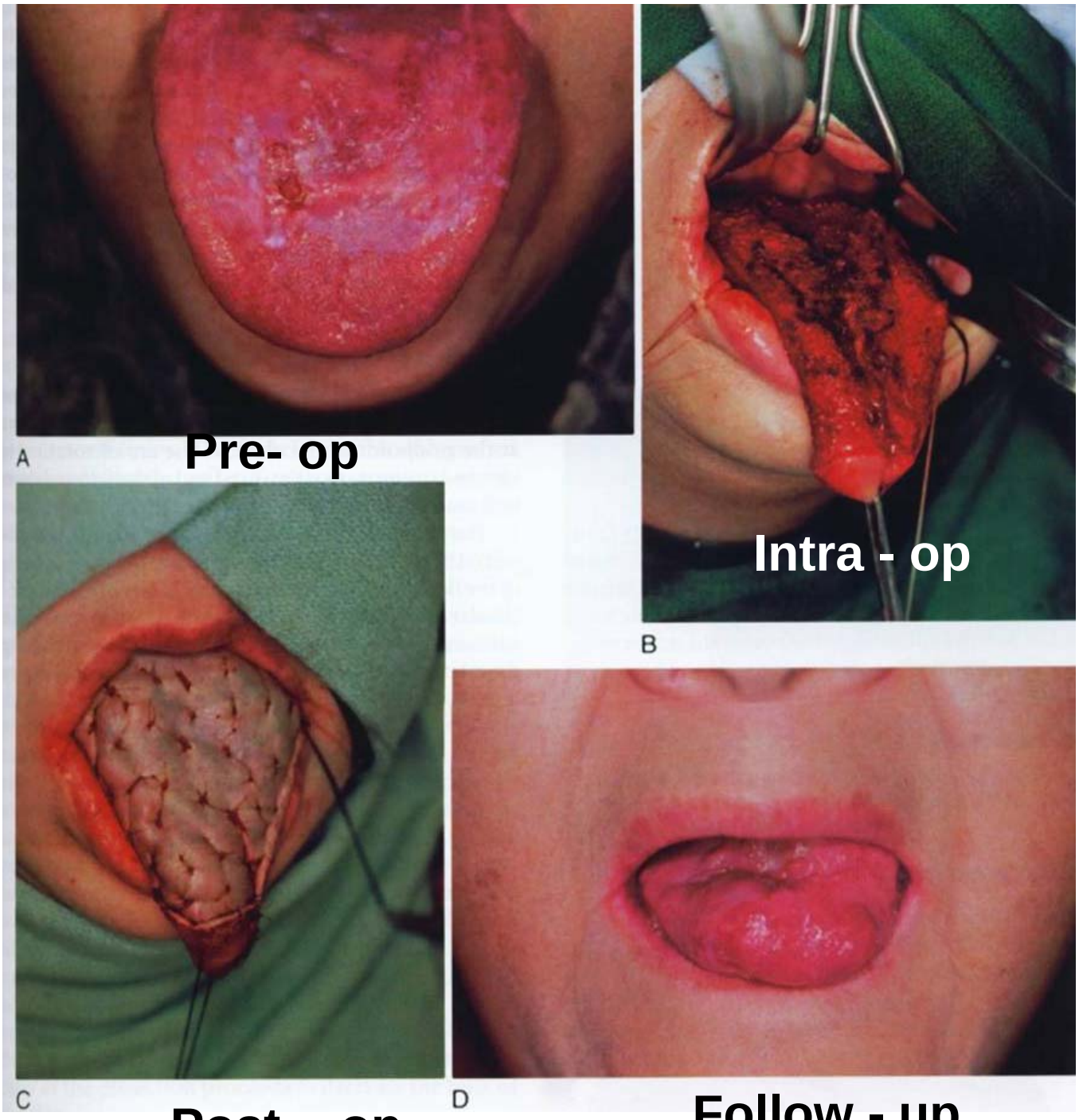
Various incisions for neck dissection

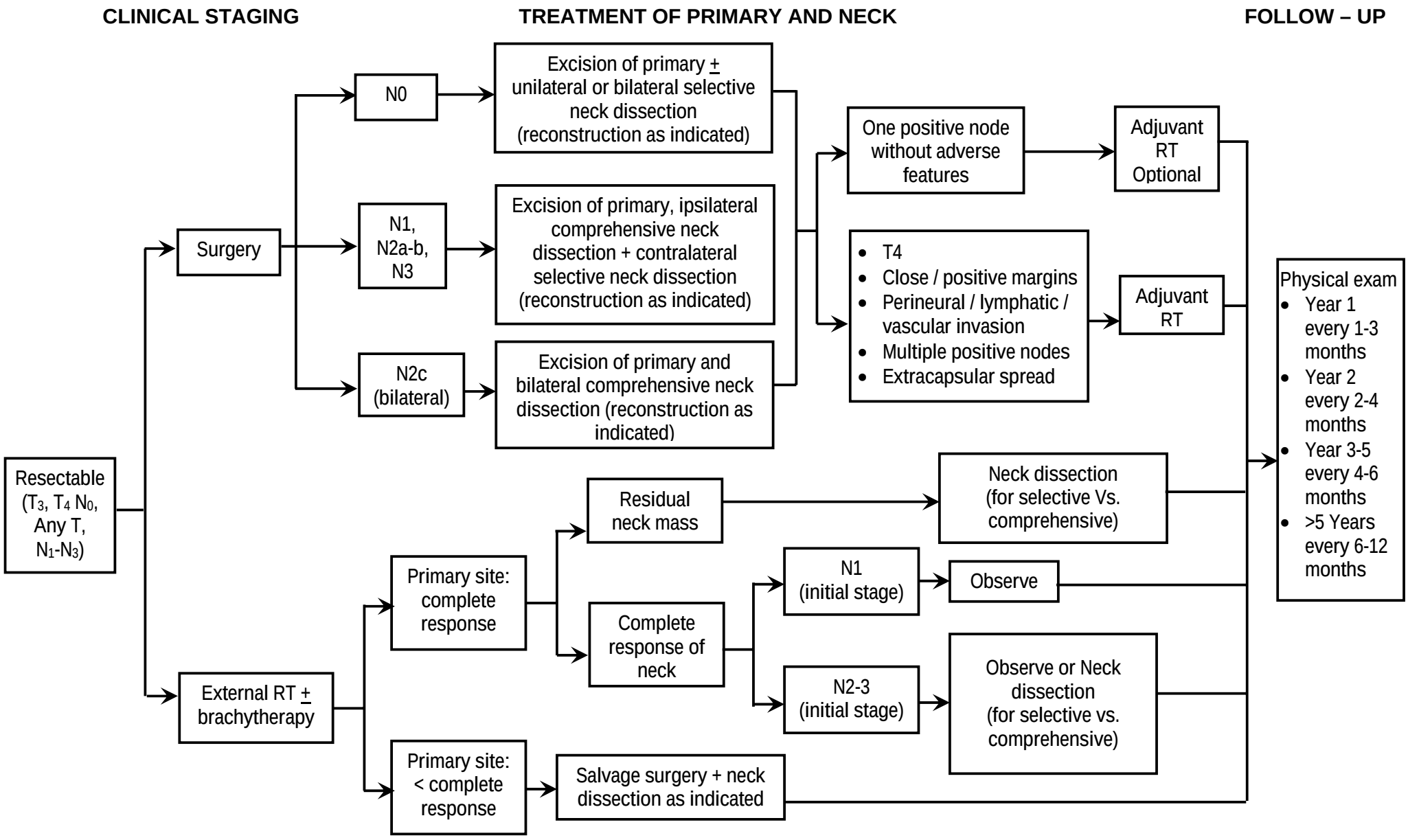


Various incisions for neck dissection

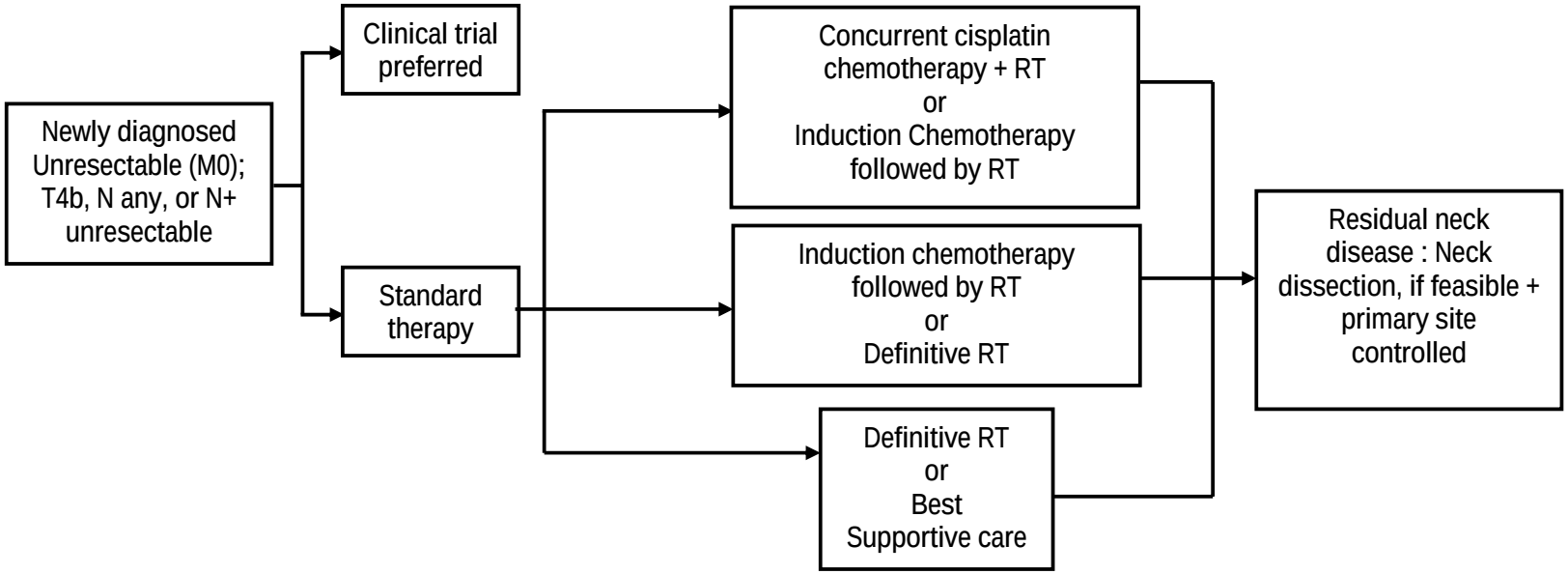


Leukoplakia



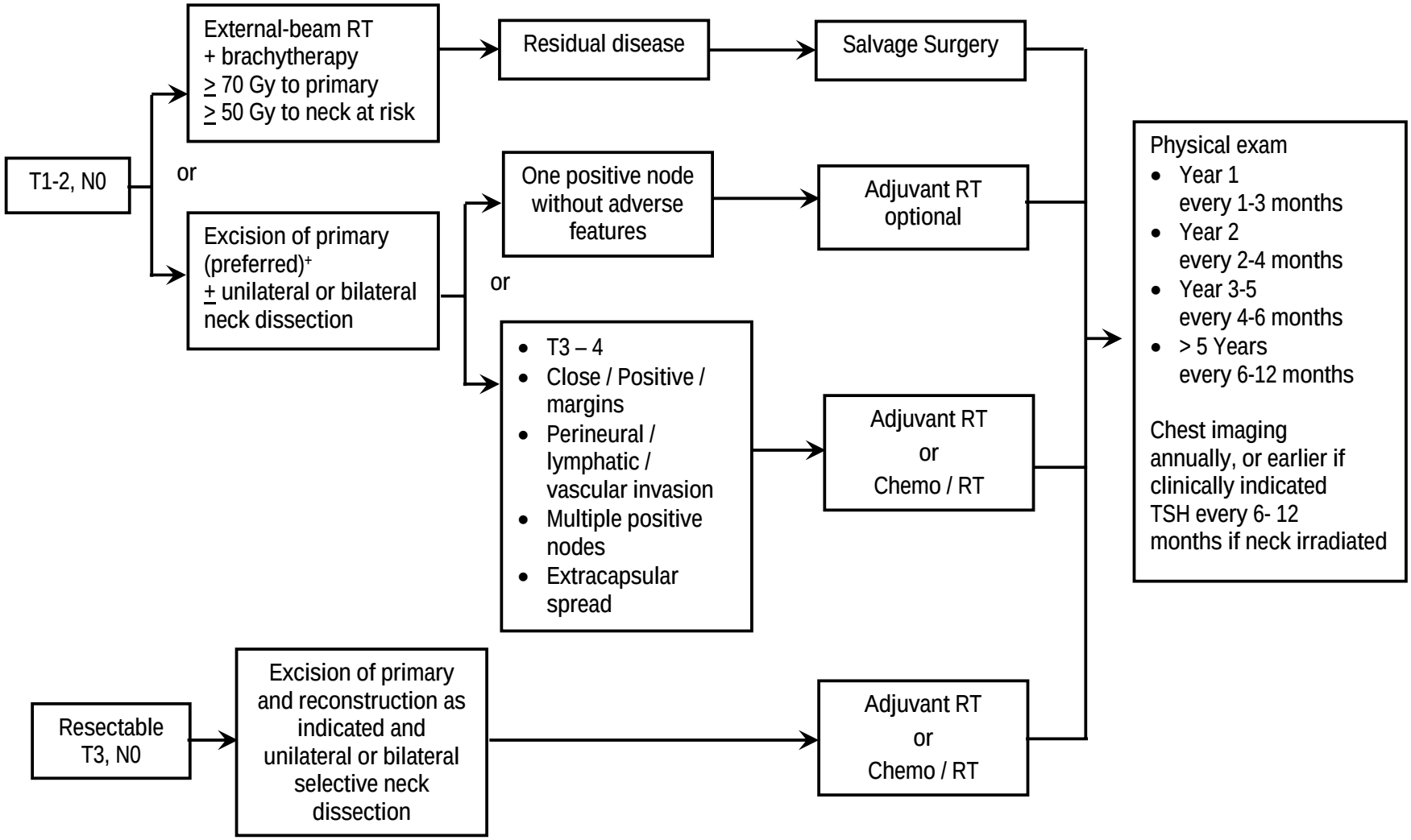

CLINICAL STAGING
TREATMENT OF PRIMARY AND NECK
FOLLOW – UP
Resectable (T_3, T_4 N_0, Any T, N_1-N_3)
Surgery
External RT ± brachytherapy
N0
N1, N2a-b, N3
N2c (bilateral)
Excision of primary ± unilateral or bilateral selective neck dissection (reconstruction as indicated)
Excision of primary, ipsilateral comprehensive neck dissection + contralateral selective neck dissection (reconstruction as indicated)
Excision of primary and bilateral comprehensive neck dissection (reconstruction as indicated)
One positive node without adverse features
T4
Close / positive margins
Perineural / lymphatic / vascular invasion
Multiple positive nodes
Extracapsular spread
Adjuvant RT Optional
Adjuvant RT
Primary site: complete response
Primary site: < complete response
Residual neck mass
Complete response of neck
Salvage surgery + neck dissection as indicated
N1 (initial stage)
N2-3 (initial stage)
Observe
Observe or Neck dissection (for selective vs. comprehensive)
Neck dissection (for selective Vs. comprehensive)
Physical exam
Year 1 every 1-3 months
Year 2 every 2-4 months
Year 3-5 every 4-6 months
>5 Years every 6-12 months

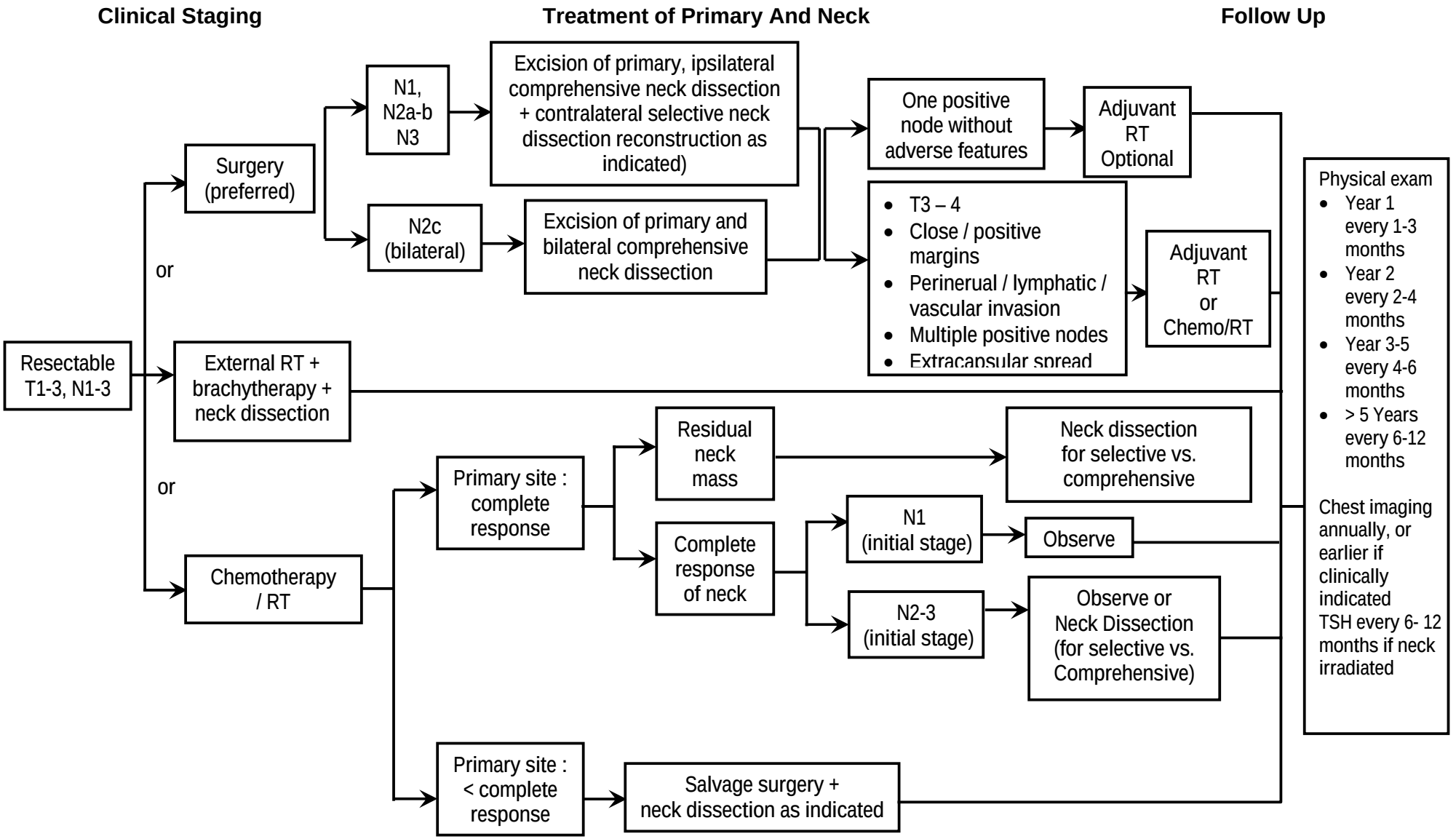
CLINICAL STAGING **TREATMENT OF PRIMARY & NECK**



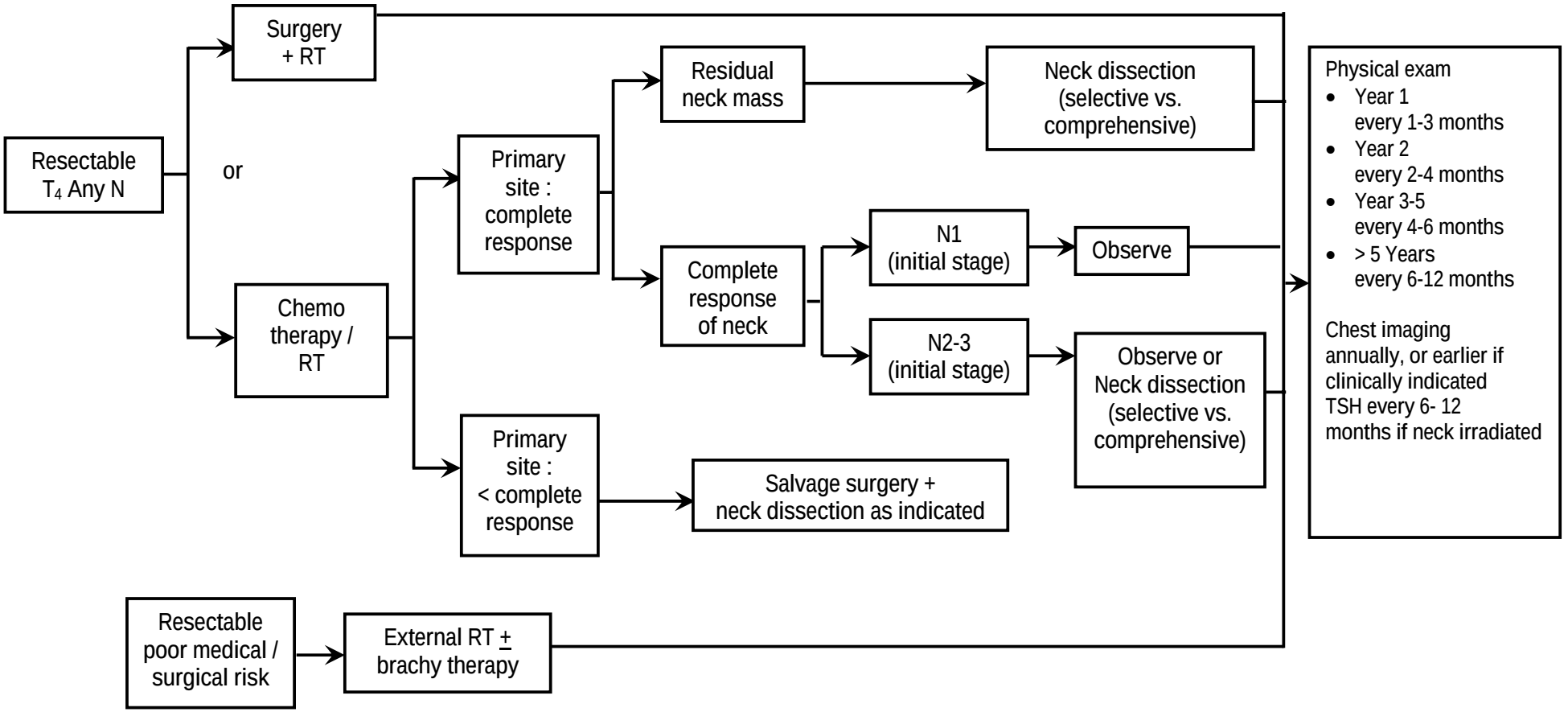
TREATMENT ALGORITHM FOR CANCER OF THE ORAL CAVITY

Clinical Staging | **Treatment of Primary And Neck** | **Follow Up**




Clinical Staging
Treatment of Primary And Neck
Follow Up
Resectable T1-3, N1-3
Surgery (preferred)
or
External RT + brachytherapy + neck dissection
or
Chemotherapy / RT
N1, N2a-b N3
N2c (bilateral)
Excision of primary, ipsilateral comprehensive neck dissection + contralateral selective neck dissection reconstruction as indicated)
Excision of primary and bilateral comprehensive neck dissection
One positive node without adverse features
Adjuvant RT Optional
T3 – 4
Close / positive margins
Perinerual / lymphatic / vascular invasion
Multiple positive nodes
Extracapsular spread
Adjuvant RT or Chemo/RT
Primary site : complete response
Residual neck mass
Neck dissection for selective vs. comprehensive
Complete response of neck
N1 (initial stage)
Observe
N2-3 (initial stage)
Observe or Neck Dissection (for selective vs. Comprehensive)
Primary site : < complete response
Salvage surgery + neck dissection as indicated
Physical exam
Year 1 every 1-3 months
Year 2 every 2-4 months
Year 3-5 every 4-6 months
> 5 Years every 6-12 months
Chest imaging annually, or earlier if clinically indicated
TSH every 6- 12 months if neck irradiated

Clinical Staging **Treatment of Primary And Neck** **Follow Up**



TREATMENT ALGORITHM FOR CANCER OF THE LIP