GIT PATHOLOGY

Dr. Methaq Mueen

Lec 1

Oral cavity infection:

- Herpes simplex virus infection

- -Called fever blister or cold sore

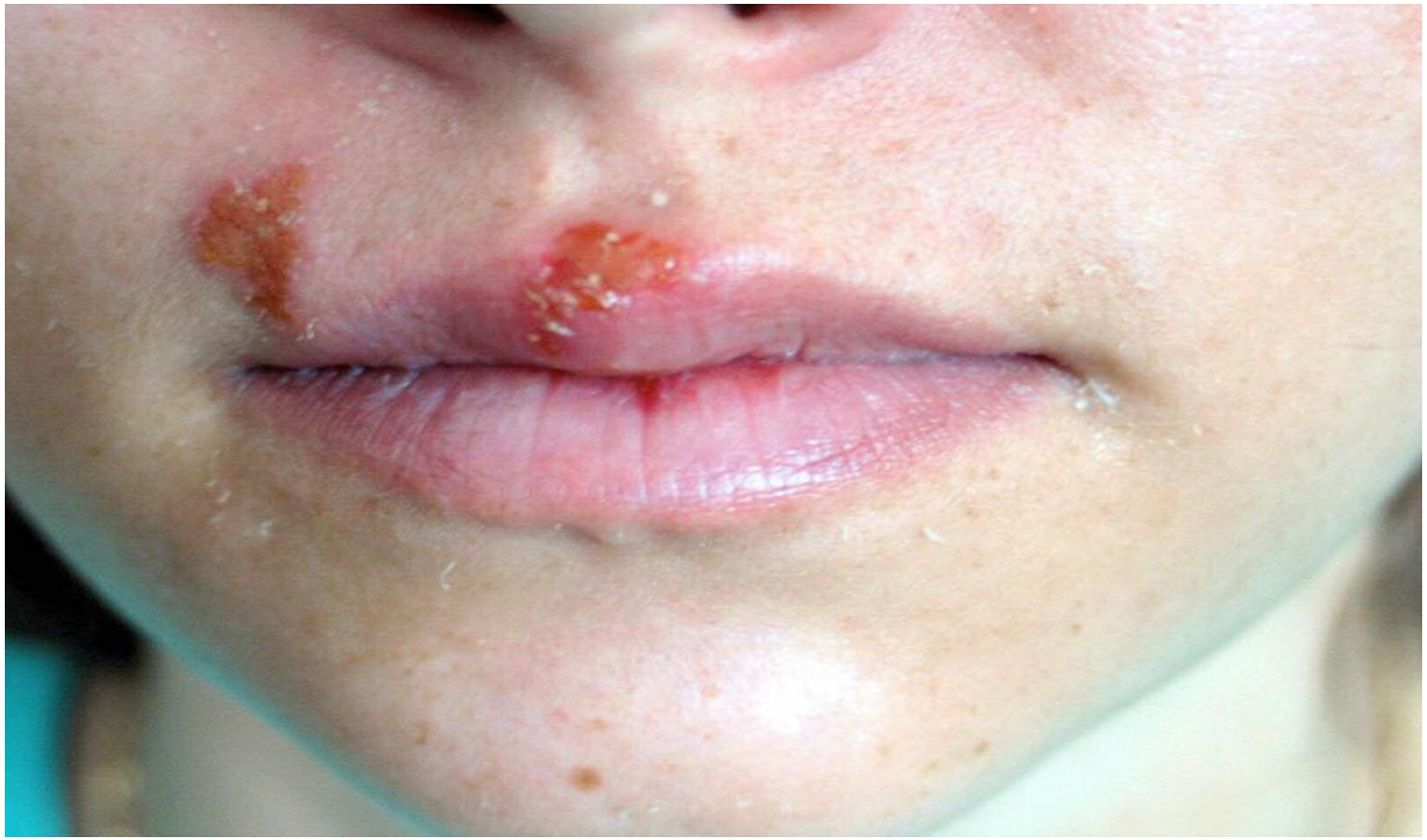
cause: HSV type I

-the primary infection is usually asymptomatic, the virus will persist in a dormant state within the ganglia about the mouth(e.g. trigeminal)and get reactivation by:

Factors that cause reactivation of HSV:

* Upper respiratory tract infection.
* fever
*ultraviolet light
- Trauma
- Pregnancy , menstruation
- Immunosuppression
- Exposure to temperature extreme (Excessive cold or heat)

Gross :This will lead to the formation of small vesicles which rupture and leave a shallow painful ulcer located around the mouth, lips &nasal orifices ■

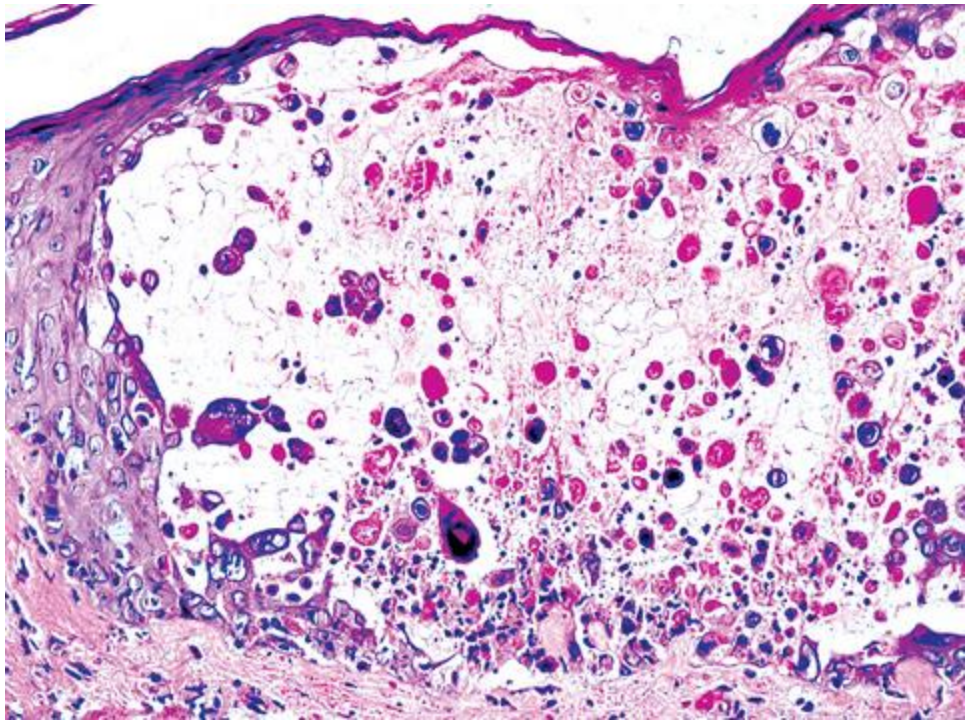


Microscopically:

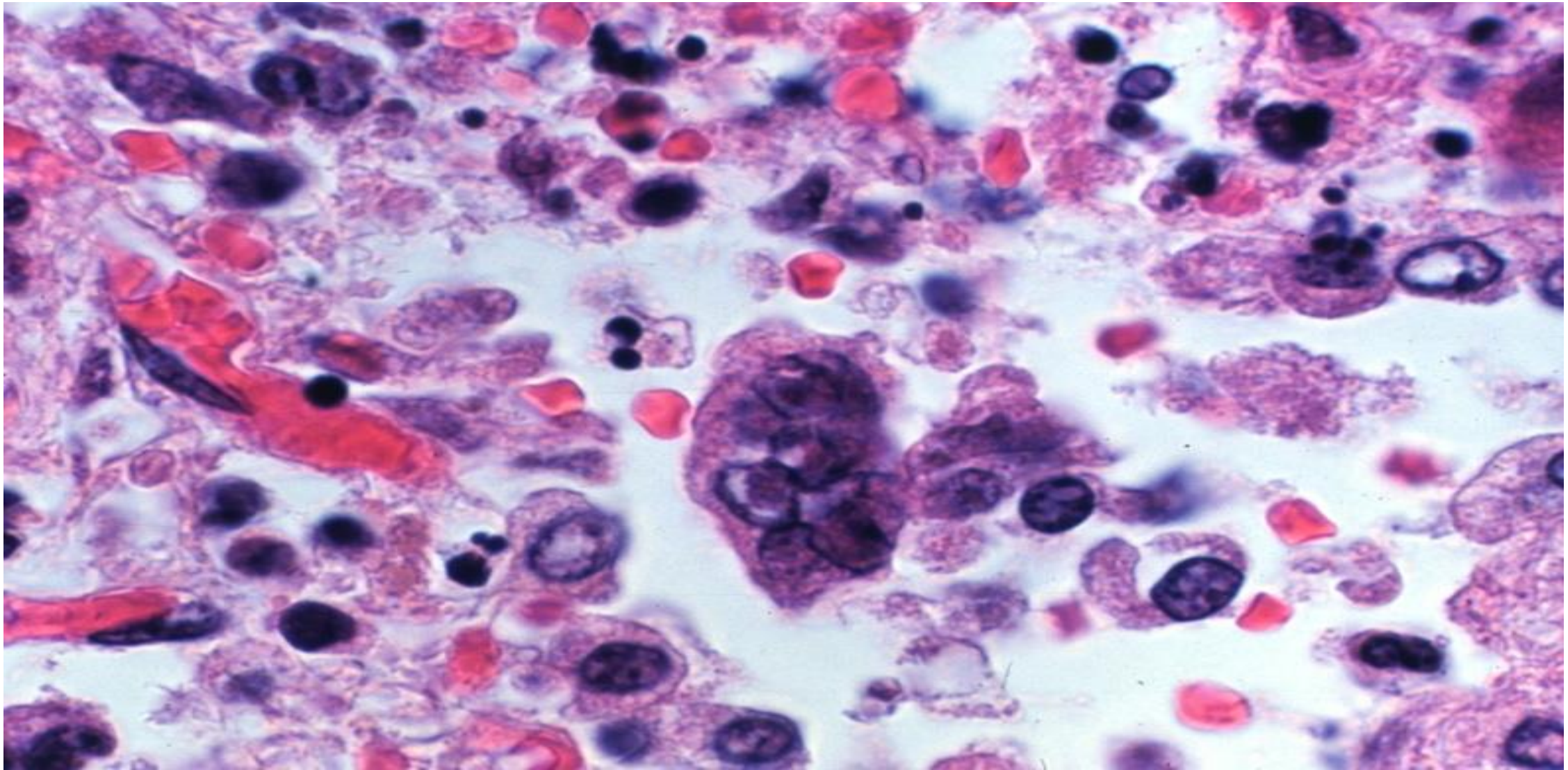
The infected cells become ballooned and have large eosinophilic intranuclear inclusions.

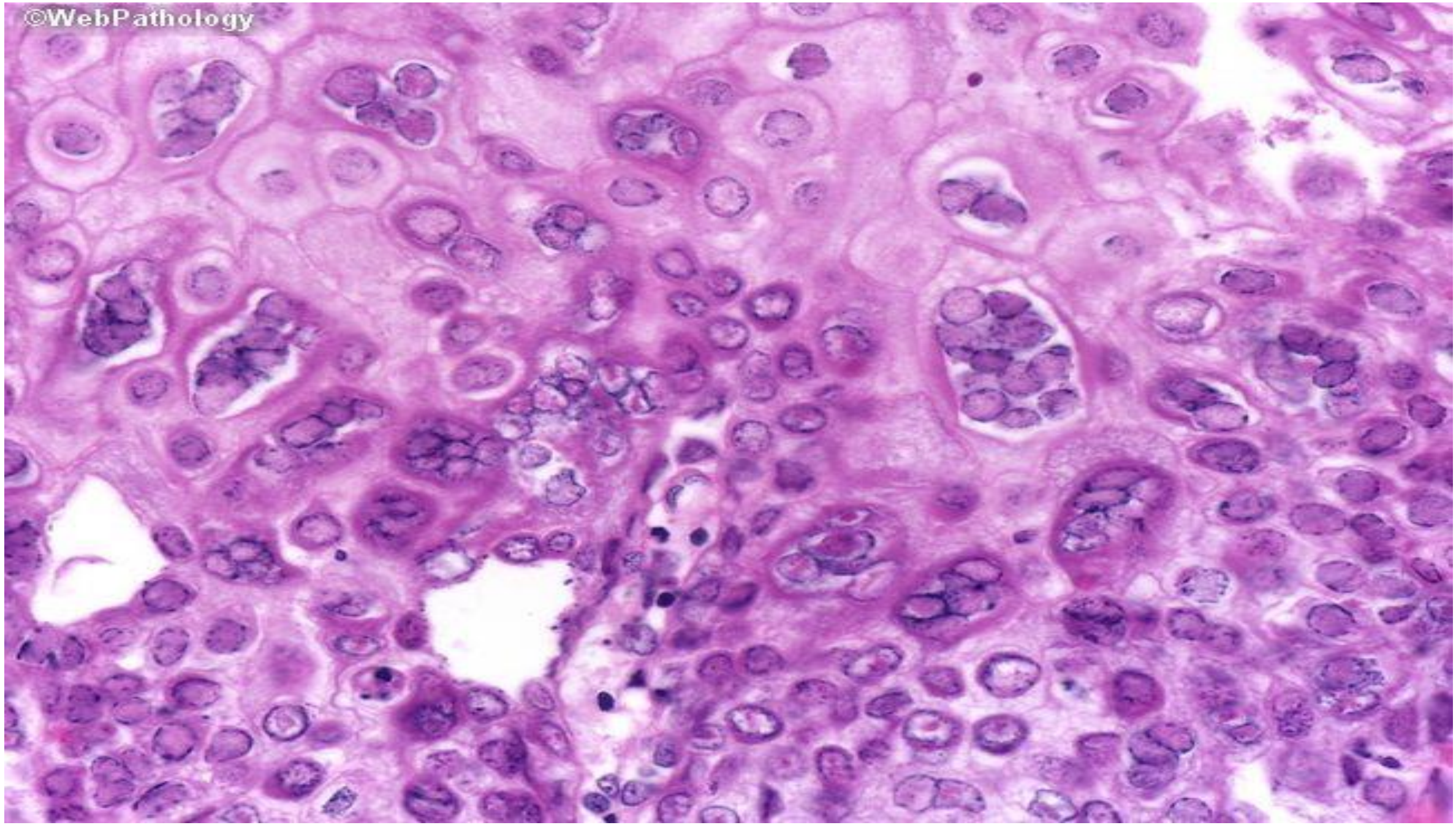
Adjacent cells commonly fuse to form large multinucleated cell.

Keratinocytes are multinucleated, acantholytic with distinct nuclear inclusions,

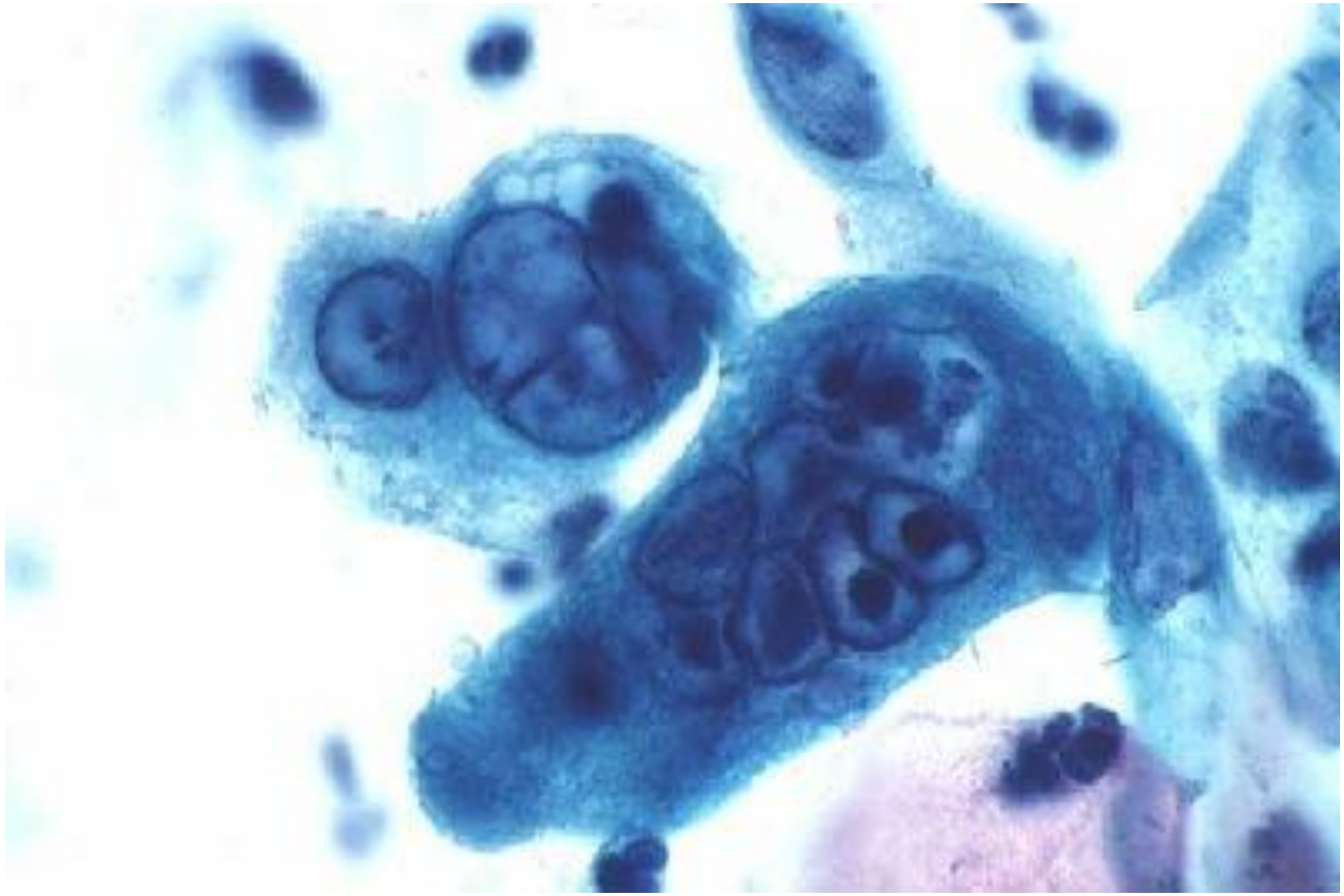


Multinucleated Giant cells with intranuclear inclusion




©WebPathology

3Ms of Herpes: Molding, Margination of chromatin and Multinucleation



2- Oral candidiasis(oral thrush)

Causative agent: Candida albicans.

Gross: Adherent white curd like plaque (fibrino-suppurative exudate with matted micro-organisms) which is after scrapping will reveal an erythematous inflammatory base .

- **Etiological factors:**
- It is **opportunistic infection**, candida is present in the oral cavity in 50%of population , so it will appear if there is any decrease in immunity e.g.

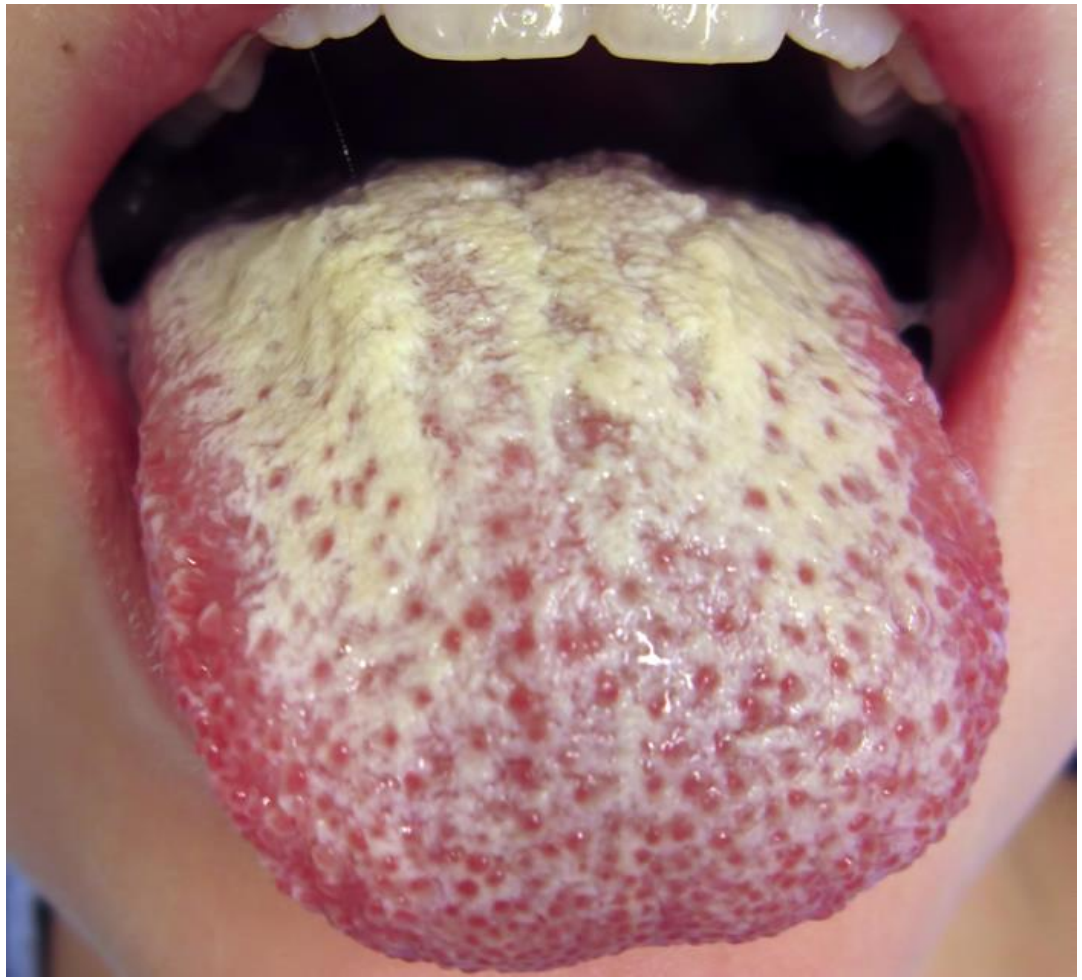
1-Diabetes mellitus,

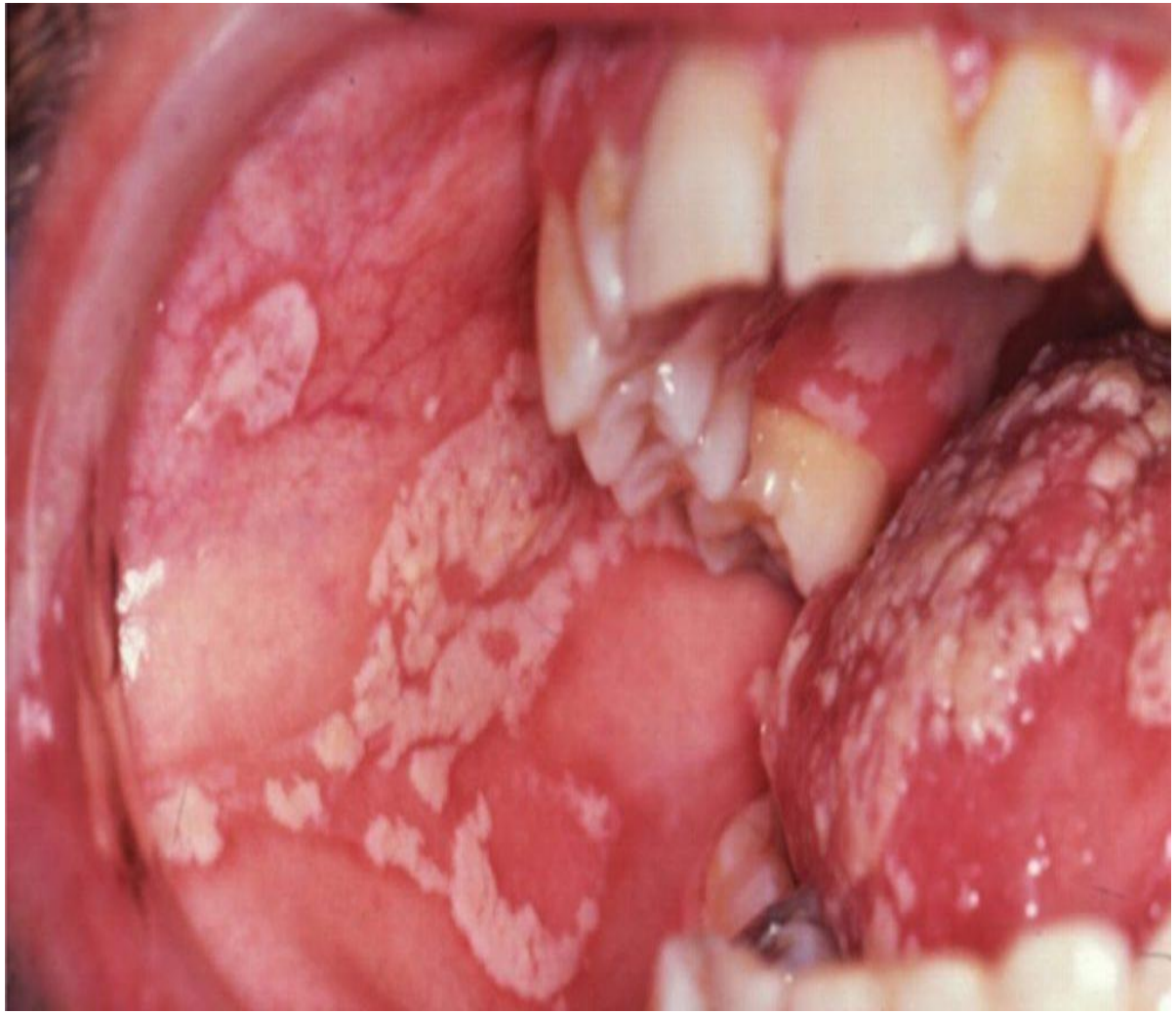
2-Immunodeficiency(congenital or acquired like AIDS),

3-some drugs like: broad spectrum antibiotic (that eliminate or alter the normal bacterial flora of the mouth) or glucocorticoid therapy, chemotherapy and Immunosuppressive treatment after organ transplant

4-debilitating diseases e.g CA.

oral candidiasis(thrush)





Oral cavity :Precancerous Lesion

- It is a benign, morphologically altered tissue that has a greater than normal risk of malignant transformation.
  - Leukoplakia
  - Erythroplakia
  - Erythroleukoplakia

Precancerous lesions:

Leukoplakia

Is a white, well defined, oral mucosal patch which can't be removed by scraping and cannot be characterized clinically or pathologically as any other disease(like thrush or lichen planus).

It is a clinical term and not a disease entity.

White color :results from thickened surface keratin layer or thickened spinous layer which masks the normal vascularity (redness) of the underlying CT.

Microscopically:

Microscopical features are highly variable:

either just

*Hyperkeratosis (thick keratin layer) +/- acanthosis(thick spinous layer due to hyperplasia) +/- variable number of chronic inflammatory cell in the underlying CT.

or

* dysplasia (mild-moderate or sever) or

*5-6% carcinoma in situ or invasive carcinoma.

Etiological factors:

The most important: Tobacco, HPV

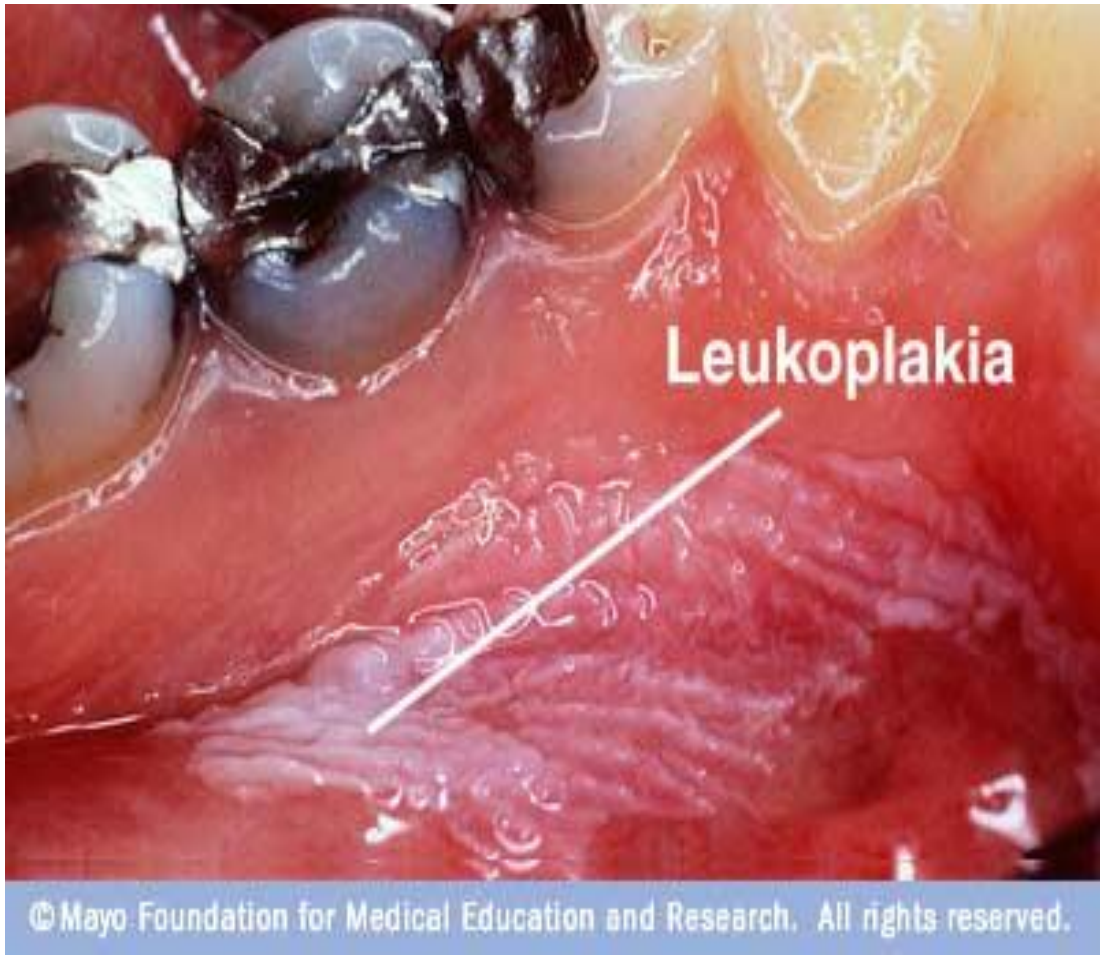
Others: alcohol, irritant food, irritation from rough teeth, or rough places of ill fitting dentures or fillings.

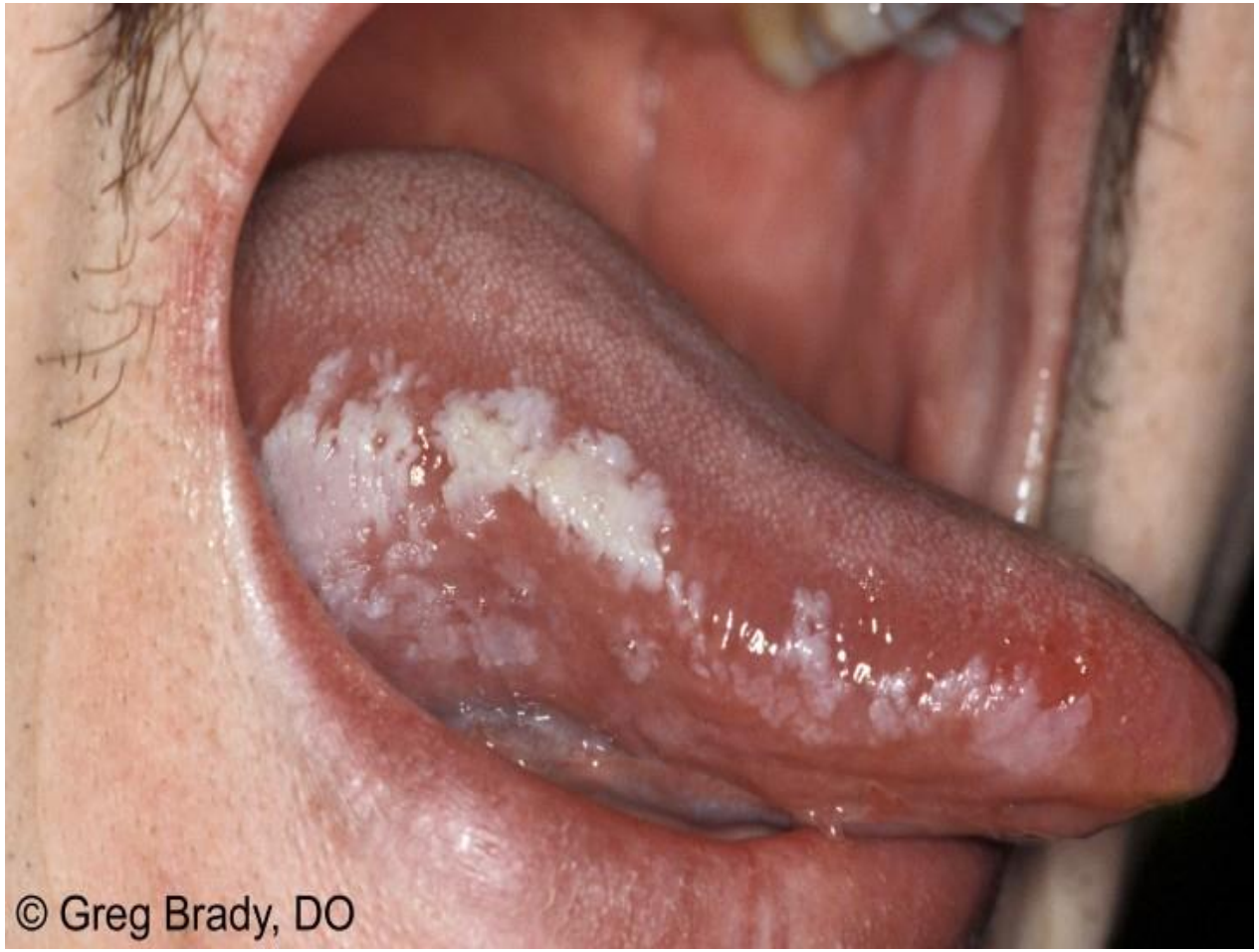
Histopathologic Alterations of Dysplastic Epithelial Cells

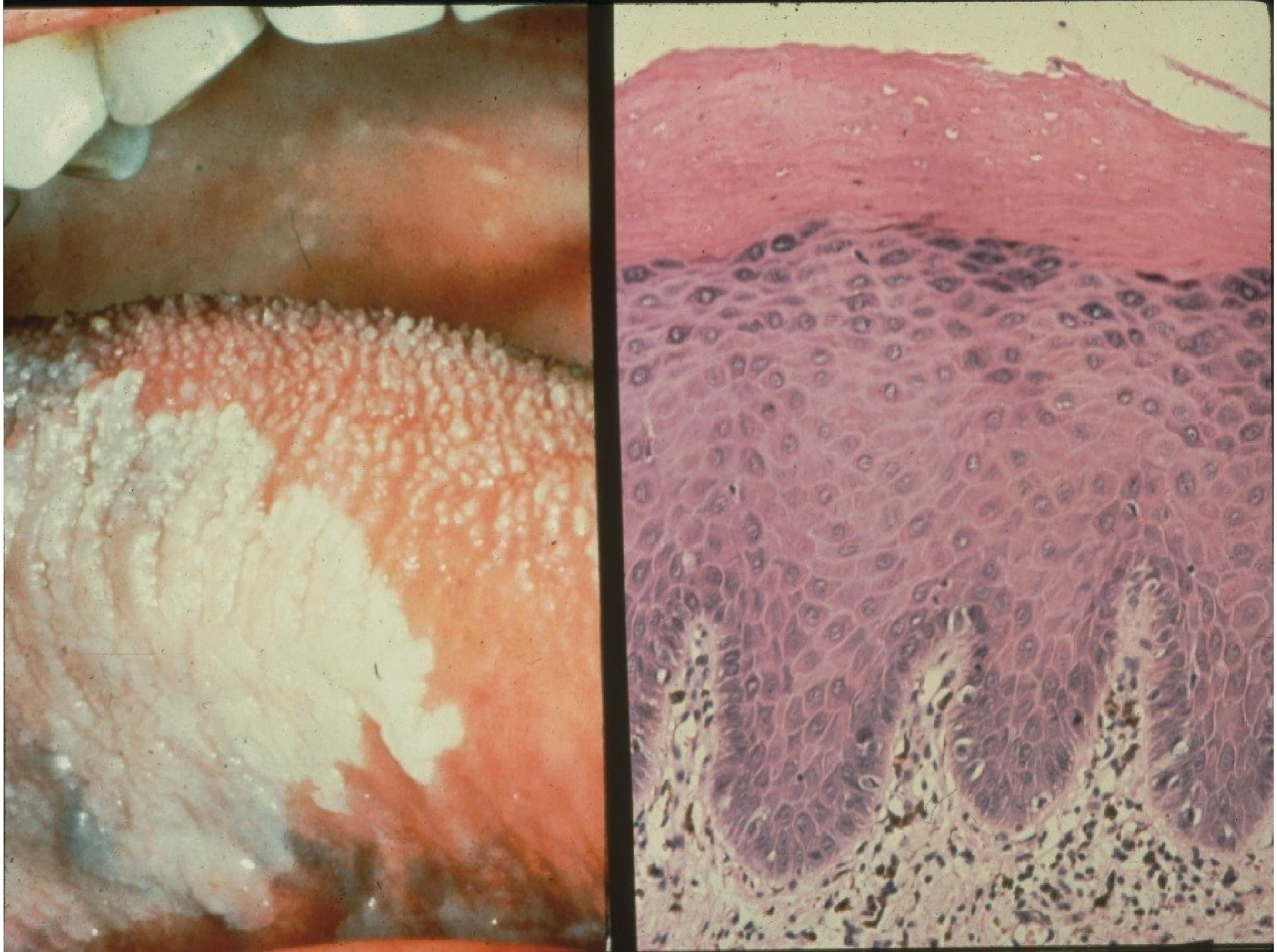
- Enlarged nuclei and cells.
- Large and prominent nucleoli.
- Increased nuclear-cytoplasmic ratio.
- Hyperchromatic (dark-staining) nuclei.
- Pleomorphic (abnormally shaped) nuclei and cells.
- Increased mitotic activity

Loss of polarity (lack of progressive maturation toward the surface).

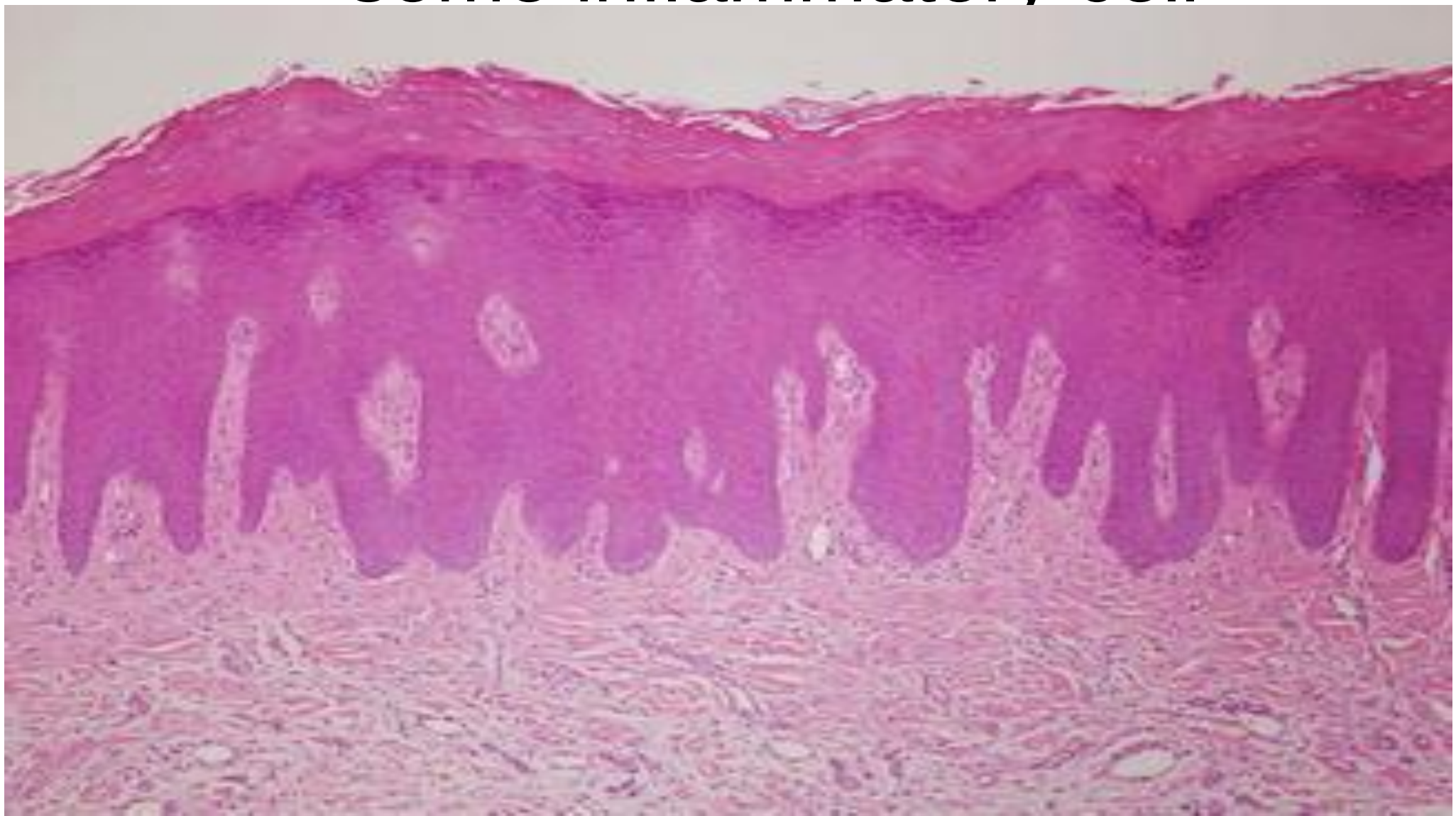
Oral leukoplakia

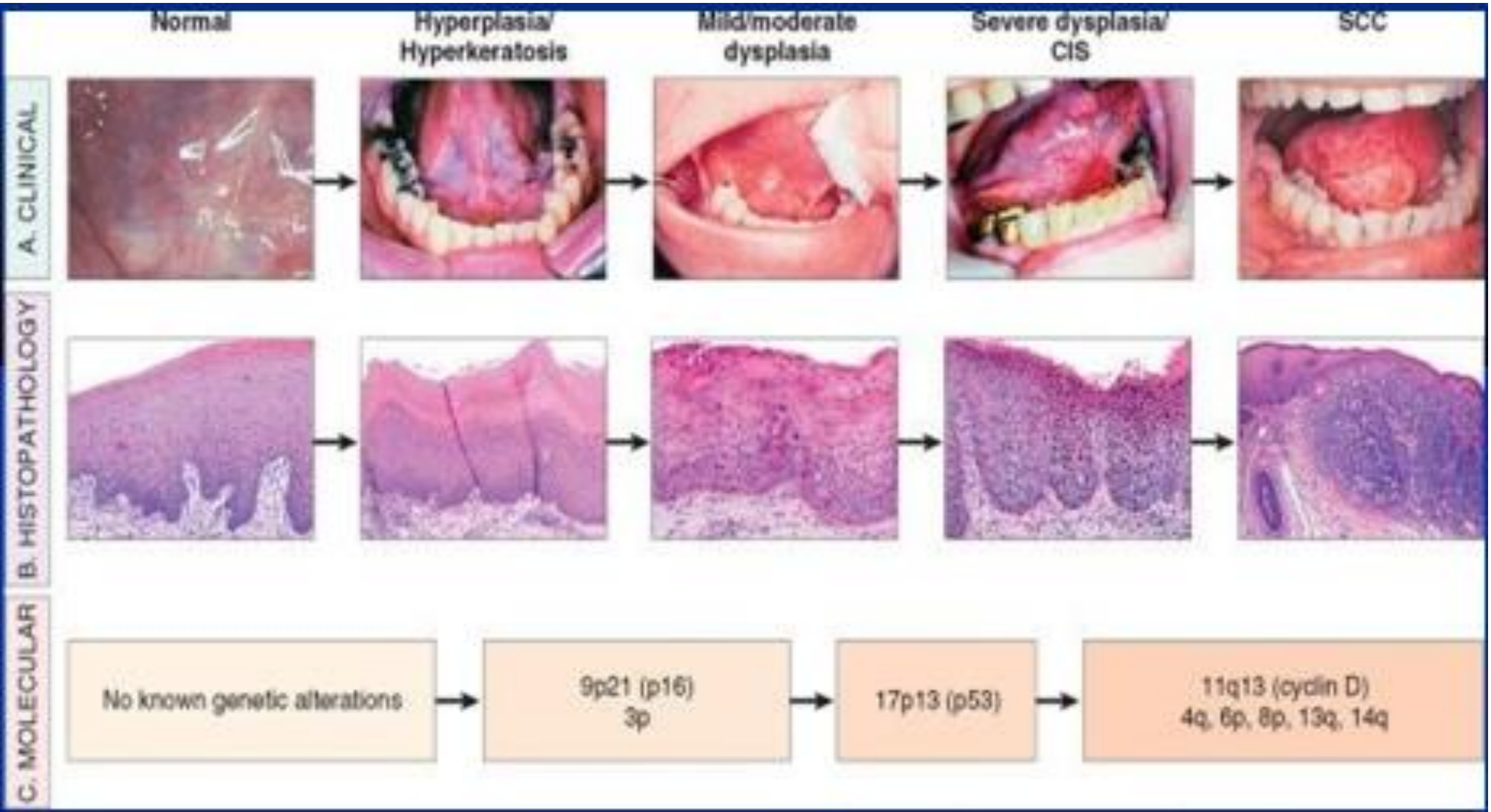






Leukoplakia : hyperkeratosis, hyperplasia some inflammatory cell




Normal
Hyperplasia/
Hyperkeratosis
Mild/moderate
dysplasia
Severe dysplasia/
CIS
SCC
A. CLINICAL
B. HISTOPATHOLOGY
C. MOLECULAR
No known genetic alterations
9p21 (p16)
3p
17p13 (p53)
11q13 (cyclin D)
4q, 6p, 8p, 13q, 14q

Approximately 3% of the world's population has leukoplakic lesions,

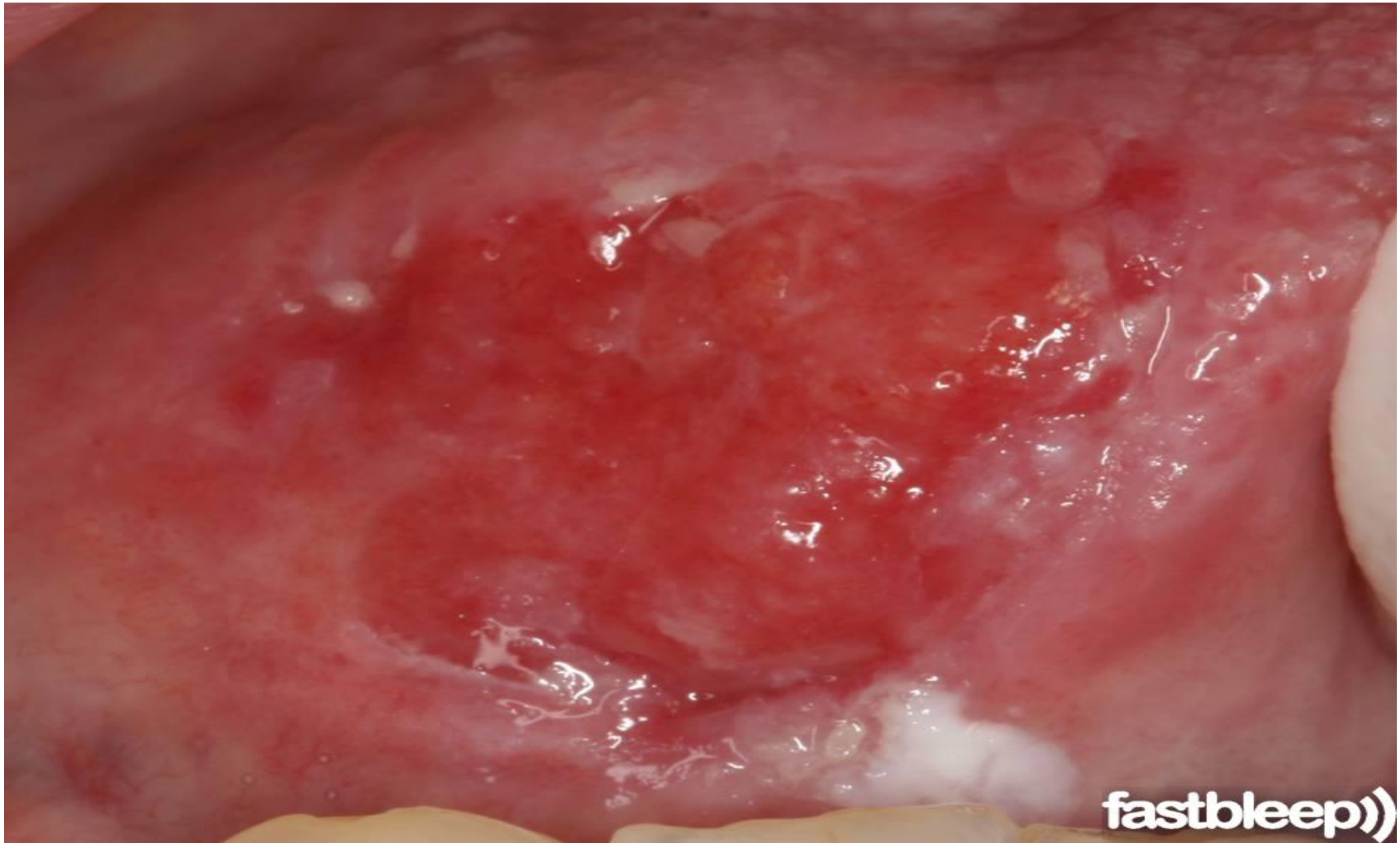
of which 5% to 25% are **premalignant** and may progress to squamous cell carcinoma.

Thus, all leukoplakias must be considered **precancerous**, until proved otherwise by means of histologic evaluation.

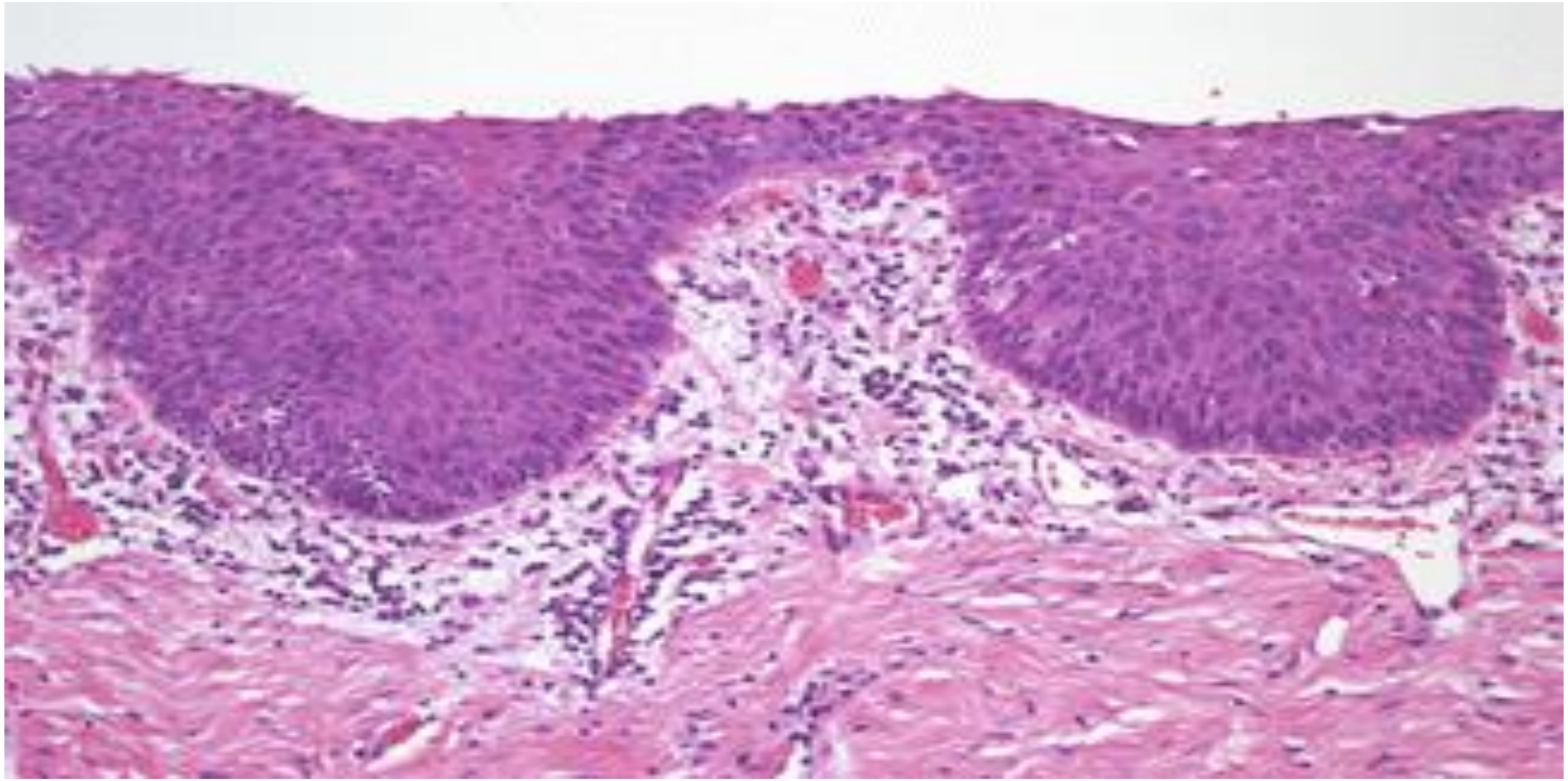
Erythroplakia: is a red, velvety, possibly eroded area that is flat or slightly depressed relative to the surrounding mucosa.

Histologically: 90% shows sever dysplasia, carcinoma in situ, or minimally invasive carcinoma. Often, an intense subepithelial inflammatory reaction with **vascular dilation** is seen that likely contributes to the reddish clinical appearance.

Erythroplakia is associated with a much greater risk of malignant transformation than leukoplakia(around 50%).


fastbleep

Erythroplakia



Age : typically affect persons between the ages of 40 and 70 years (it may be seen in adults at any age)

male :female ratio is 2 : 1

Although the etiology is multifactorial,

tobacco use (cigarettes and chewing tobacco) is the most common risk factor for leukoplakia and erythroplakia.

Carcinoma of the oral cavity

95% are squamous cell carcinoma.

Predisposing factors:

- leukoplakia (the risk of transformation is 3-25%),
- Erythroplakia (the risk of transformation is 50%)
- tobacco
- human papilloma virus 16 &18
- alcohol

Pathogenesis:

1-Mutations frequently involve P53 or p63

2-Infection with oncogenic variants of human papillomavirus (HPV), particularly HPV-16

Oral squamous cell carcinomas are classically linked to tobacco and alcohol use, but the incidence of HPV associated lesions is rising.

Grossly:

In early stages, these cancers can appear as:

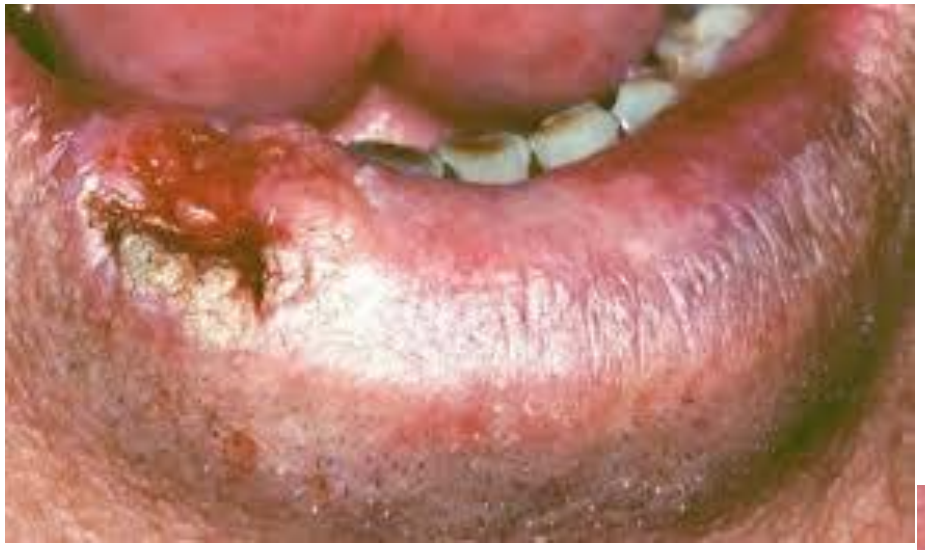
1- raised, firm, pearly plaques

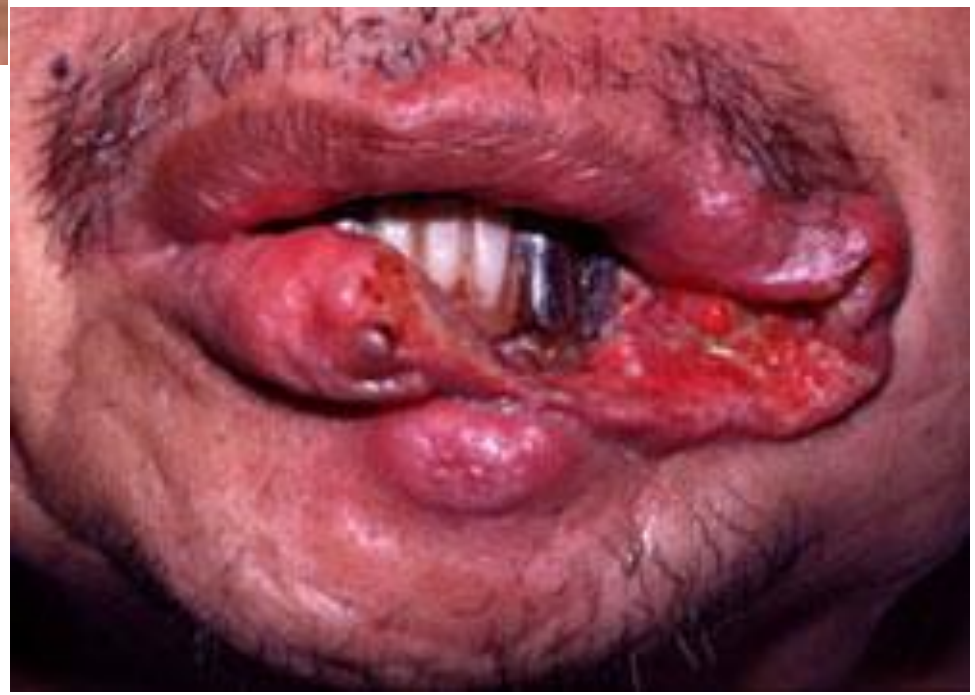
2- or as irregular, roughened mucosal thickenings.

Either pattern may be superimposed on a background of a leukoplakia or erythroplakia.

As these lesions enlarge, they typically form ulcerated and protruding masses that have irregular and indurated or rolled borders

Squmous cell carcinoma (lip) gross

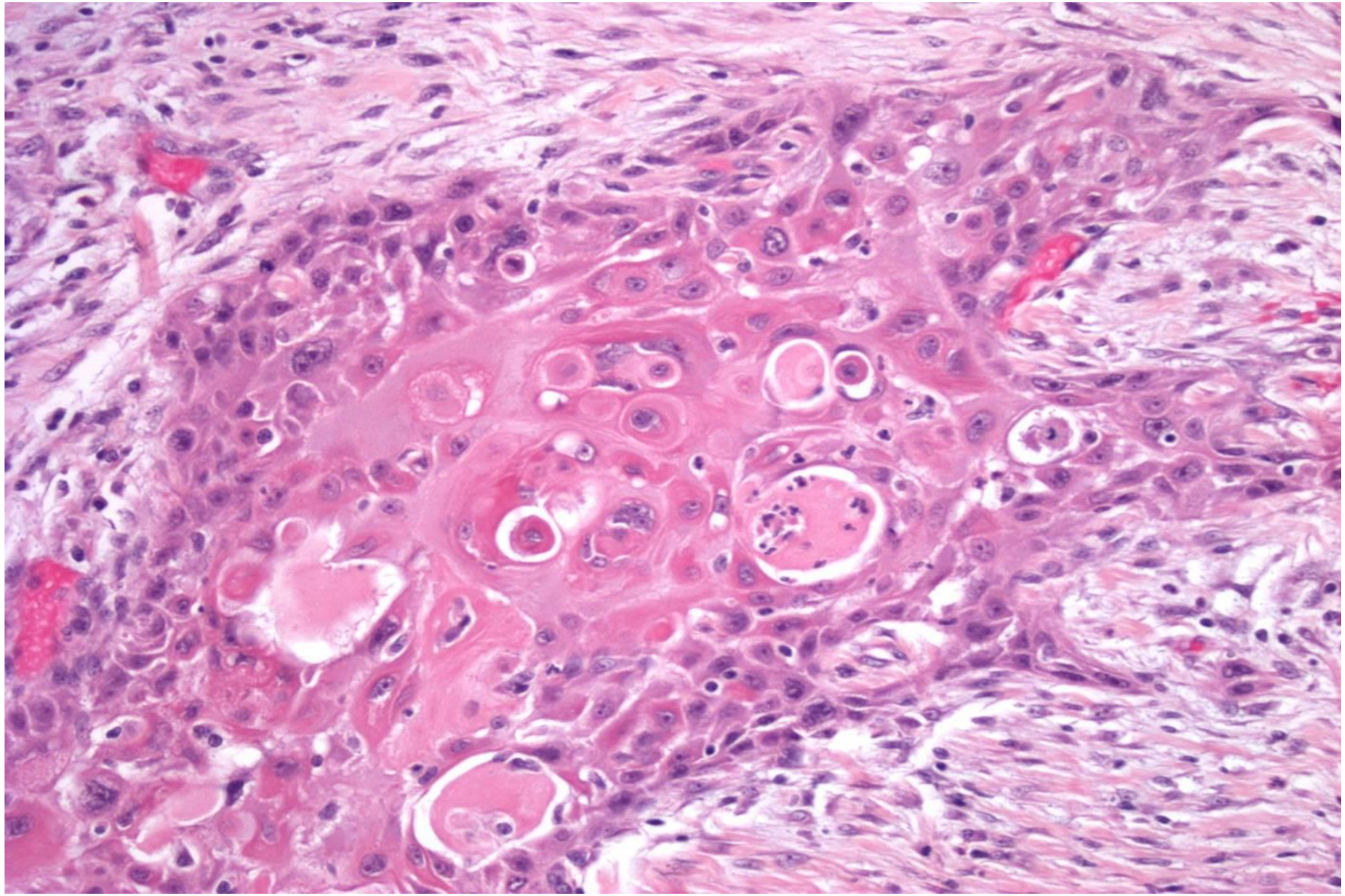




Microscopically

A majority of oral cavity cancers are squamous cell carcinomas with different grades(well, moderate or poorly differentiated).

Oral squamous cell carcinoma :Mic. Histologic appearance demonstrating nests and islands of malignant keratinocytes invading the underlying connective tissue stroma with keratin pearls



- **Site:**

Lower lip, floor of the mouth, tongue, hard palate, base of the tongue .

DX: biopsy from the lesion

Treatment: eliminate the cause

Surgical removal

- **Prognosis:**

Best, in lips lesion

Poor, in floor of the mouth & tongue

The Salivary glands

Parotid gland, submandibular ,sublingual and many minor salivary glands distributed in upper aerodigestive tract.

Common diseases : inflammation and neoplasia

Sialadenitis (inflammation of salivary gland)

Causes: Either: Viral, bacterial, or autoimmune.

1- Viral: the most common virus is mumps virus. which affect mainly the parotid gland.

In children it is self limiting disease.

In adult it may be accompanied by pancreatitis or orchitis causing sterility.

2- Bacterial: Which is mainly unilateral involvement, painful enlargement.

Occur following an obstruction of major excretory duct by e.g stone (sialolithiasis).

Following major surgical procedure in old dehydrated patients.

Most common causative bacteria are staph. aureus &strep. Viridans.

3- Autoimmune

usually bilateral

seen in Sjogren syndrome : in which there is wide spread involvement of salivary glands, mucous secreting and lacrimal glands causing :

a- Dry mouth (xerostomia)

b- Dry eye (xeroconjunctivitis sicca)

c- Small % may evolve to malignant lymphoma

- **Tumors of salivary glands**

About 80% of the salivary gland tumors occur in the parotid gland.

the likelihood of a salivary gland tumor being malignant is inversely proportional to the size of the gland. i.e.the **larger** the gland, the **less** likelihood to be malignant .

Parotid :15-30% of the tumors are malignant

Submandibular gland: 40% are malignant

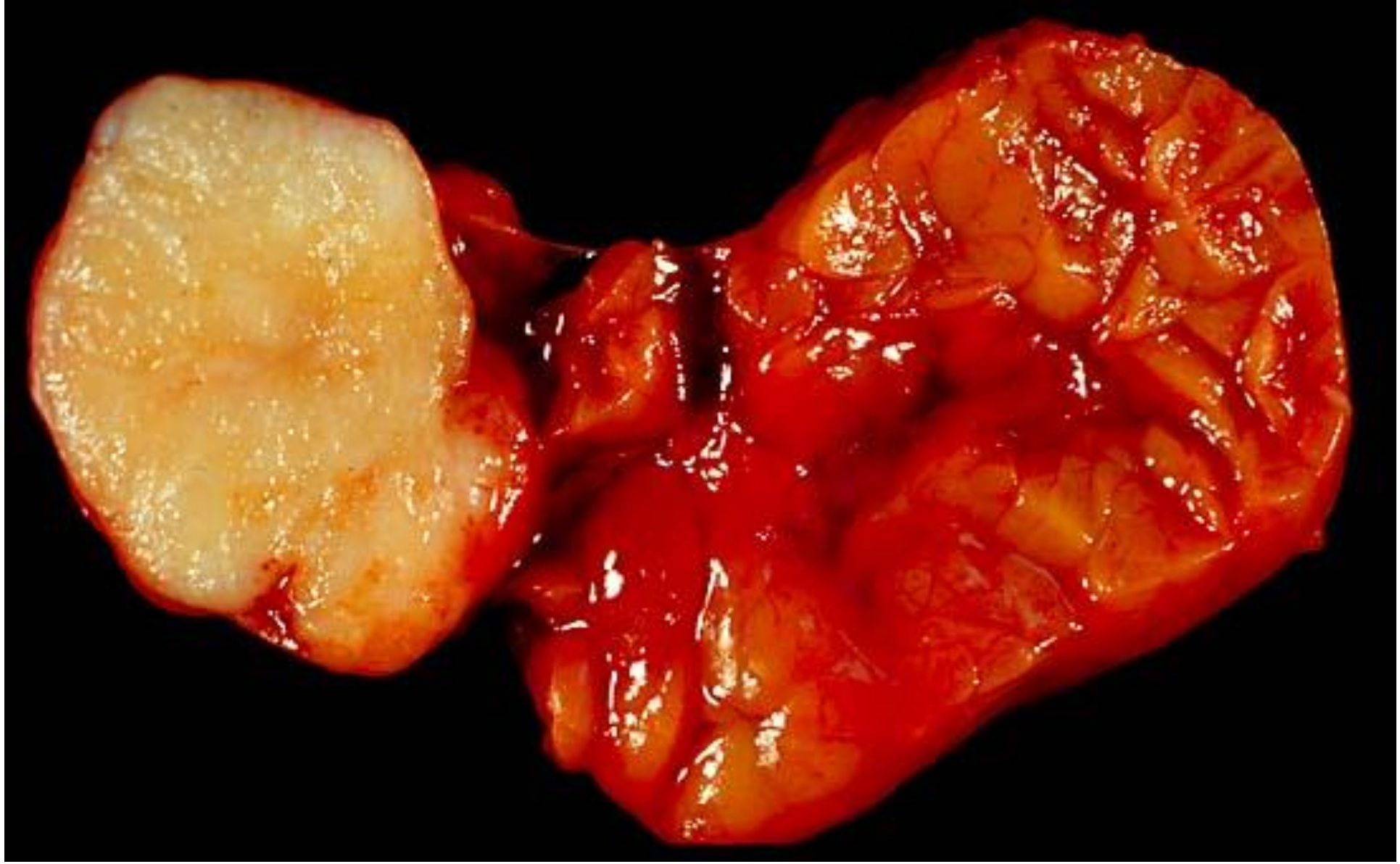
Sublingual : 70-90 % of the tumors are malignant

- **Benign tumors**: e.g
- pleomorphic adenoma (mixed tumor)
- Warthin tumor
- **Malignant tumors**: e.g
- mucoepidermoid carcinoma.
- adenoid cystic carcinoma.

- *Pleomorphic adenoma (benign mixed tumor of salivary gland):*
- Account for 90% of benign tumors of salivary glands
- Causes painless swelling at the angle of the jaw (in front of and below the ear (palpable discrete mass)
- **Grossly** encapsulated but histological examination reveals capsular penetration which necessities adequate resection margins to prevent recurrence which occur in 10%.

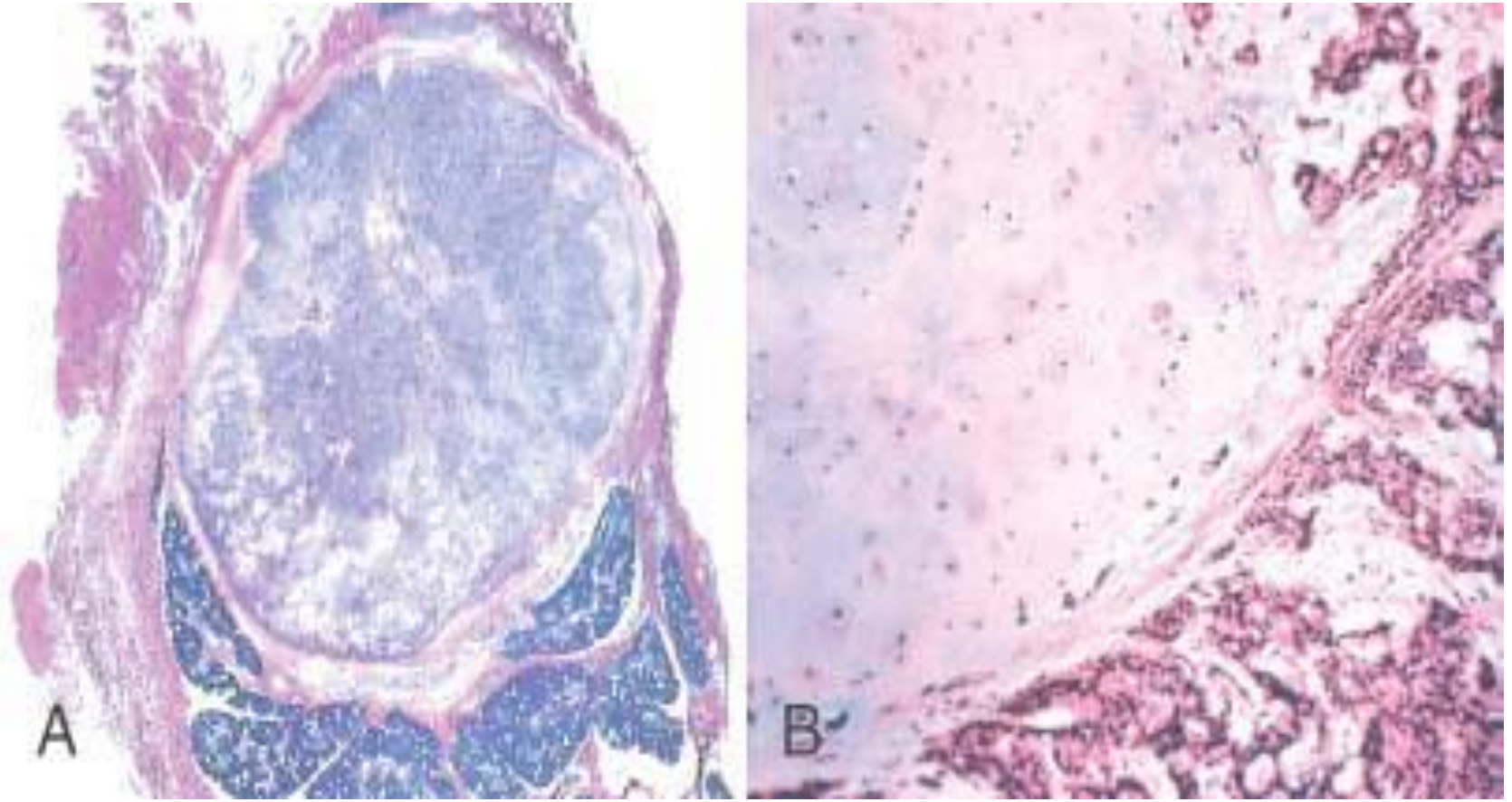
- Microscopically: The characteristic feature is heterogeneity, tumor cells are small &dark &form ducts, acini, tubules, strands or sheets &these cells intermingled with loose myxoid connective tissue stoma containing cartilage &rarely bone.

Pleomorphic adenoma (parotid gland)

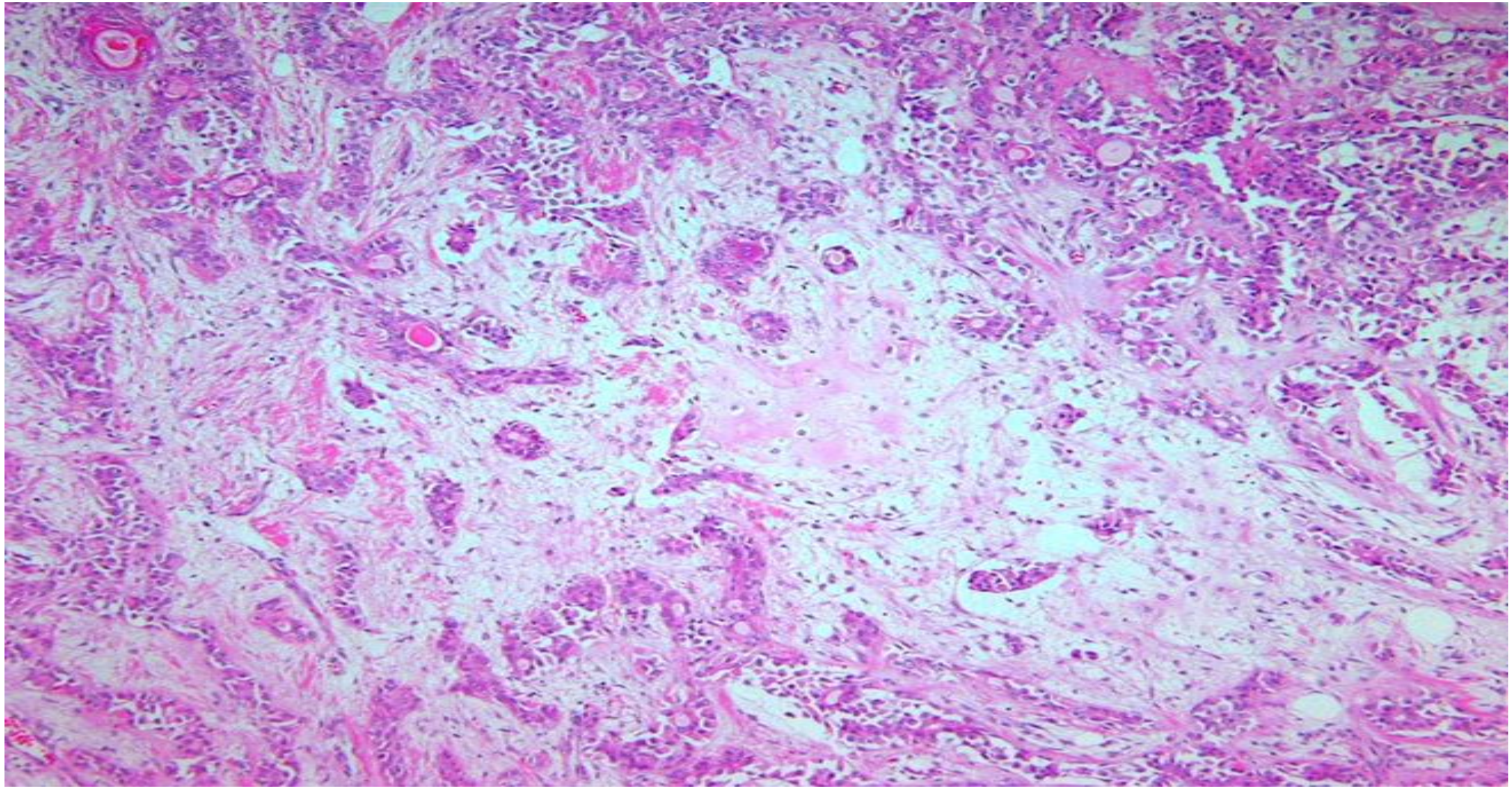


Parotid gland mass: Pleomorphic adenoma, the tumor at the left side is white gray well circumscribed, encapsulated lobulated mass without hemorrhage or necrosis &,(the normal lobulated gland)at the right

Pleomorphic adenoma. *A,* Low-power view showing a well-demarcated tumor with adjacent normal salivary gland parenchyma. *B,* High-power view showing epithelial cells as well as myoepithelial cells found within a chondroid matrix material.



mixed proliferation of both proliferated ducts (composed of epithelial cells and myoepithelial cells) found within myxoid stroma and sometimes chondroid matrix material.
These lesions are usually slow-growing, but can recur following incomplete resection.
Infrequently, a carcinoma can arise in a pleomorphic adenoma



Warthin Tumor

second most common benign salivary gland neoplasm.

It arises almost exclusively in the parotid gland

Male >female

5th to 7th decades of life.

About 10% are multifocal, and 10% bilateral.

Smokers have eight times the risk of nonsmokers for developing these tumors.

It is small, well encapsulated, round to ovoid mass that on section reveal mucin containing cystic spaces within soft gray background.

Microscopically:

Spaces or clefts are lined by a double layer of neoplastic epithelial cells resting on a dense lymphoid stroma sometimes with germinal centers.

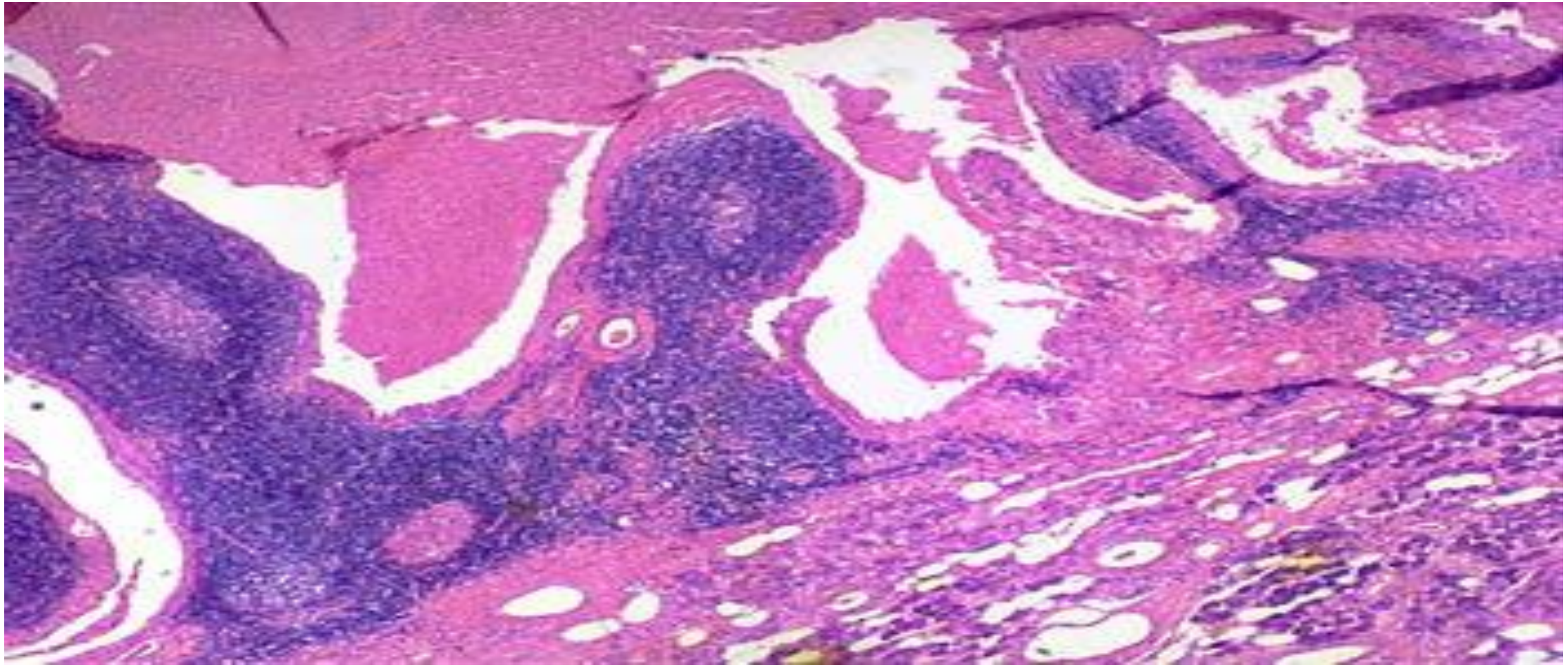
The double layer of lining cells is distinctive;

the upper layer consists of palisading columnar cells with abundant, finely granular, eosinophilic cytoplasm,

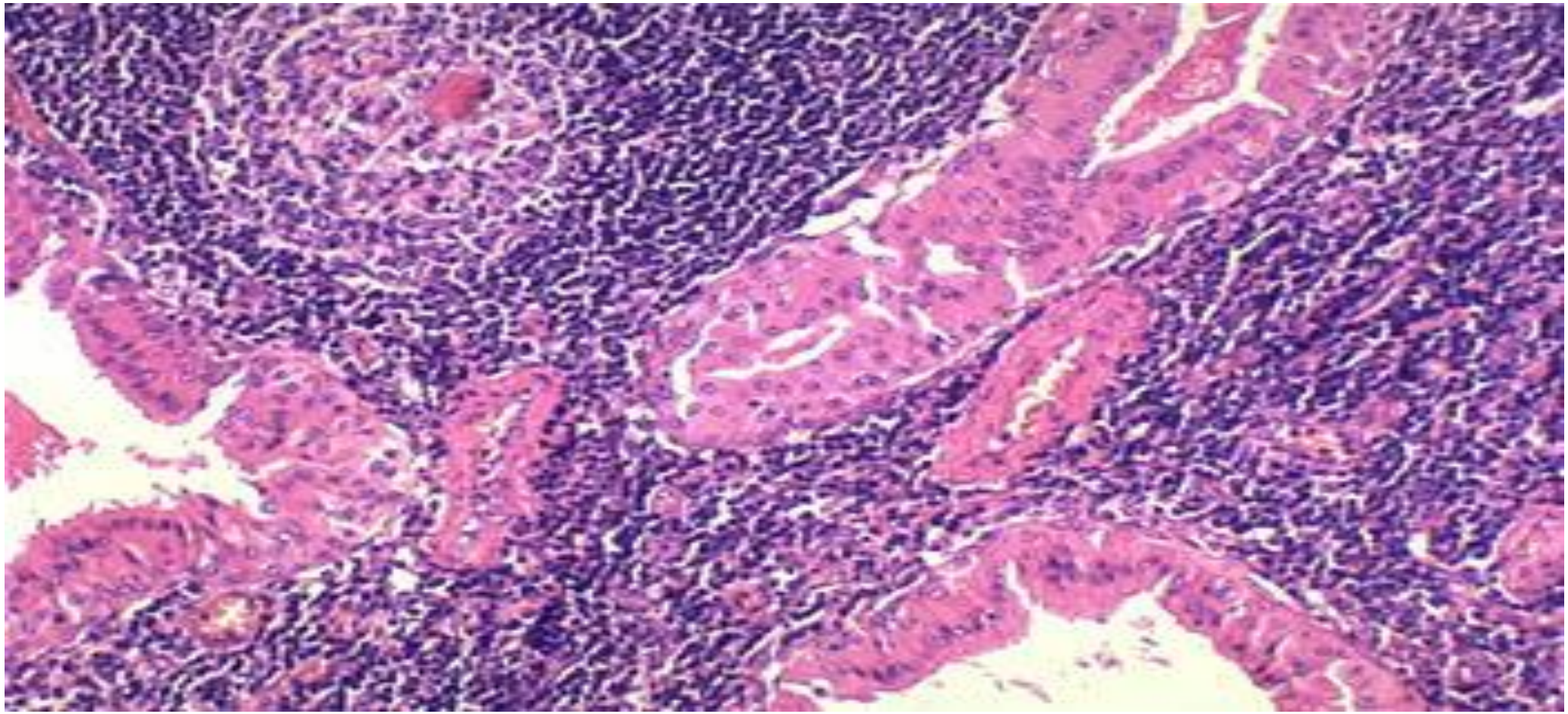
while the lower layer is comprised of cuboidal to polygonal cells.

The granular appearance of the cytoplasm of the upper layer of cells is due to the presence of numerous mitochondria, a feature referred to as "oncocytic".

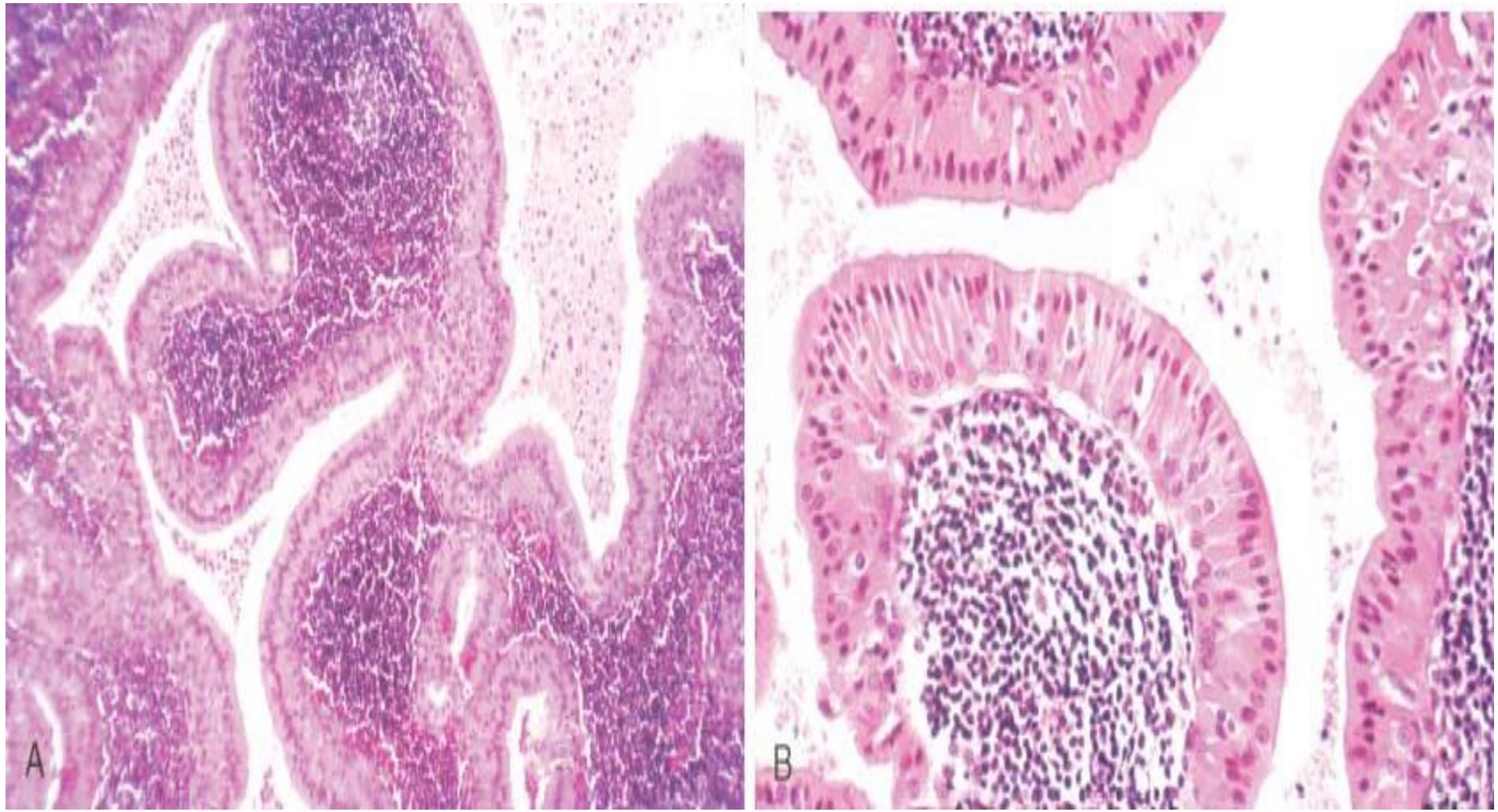
Warthin tumor



Warthin tumor



Warthin tumor. A, Low-power view showing epithelial and lymphoid elements. Note the follicular germinal center beneath the epithelium. B, Cystic spaces separate lobules of neoplastic epithelium consisting of a double layer of eosinophilic epithelial cells based on a reactive lymphoid stroma.



Esophagus

Congenital disorders:

Agenesis, atresia, fistula and stenosis

Acquired disorders

Stenosis, webs and rings, hiatus hernia, achalasia

Inflammation

reflux esophahitus

tumors

The Esophagus

It is a muscular tube of 23-25 cm, **its function** is to

1-conduct food and fluid from the pharynx to the stomach

2- Prevent reflux of gastric content by the presence of two physiological sphincters:

* Upper esophageal sphincter (UES) at the cricopharyngeal muscle
* Lower esophageal sphincter (LES) proximal to the esophageo-gastric junction.

- **Microscopically:**

1- Mucosa: lined by non keratinizing squamous epithelium.

2- Lamina propria

3- Submucosa: containing glands

4- Muscularis propria:

5- No serosal coat

Lined by stratified squamous epithelium

Muscle coat:

- Inner circular (Thinner)
- Outer longitudinal (Thicker)

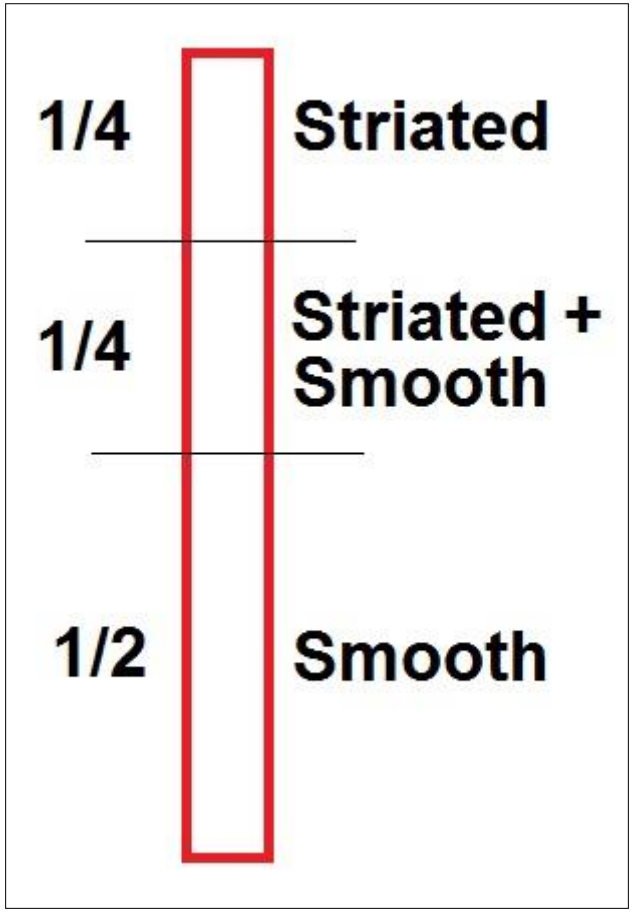
Upper portion – voluntary

Lower portion – involuntary

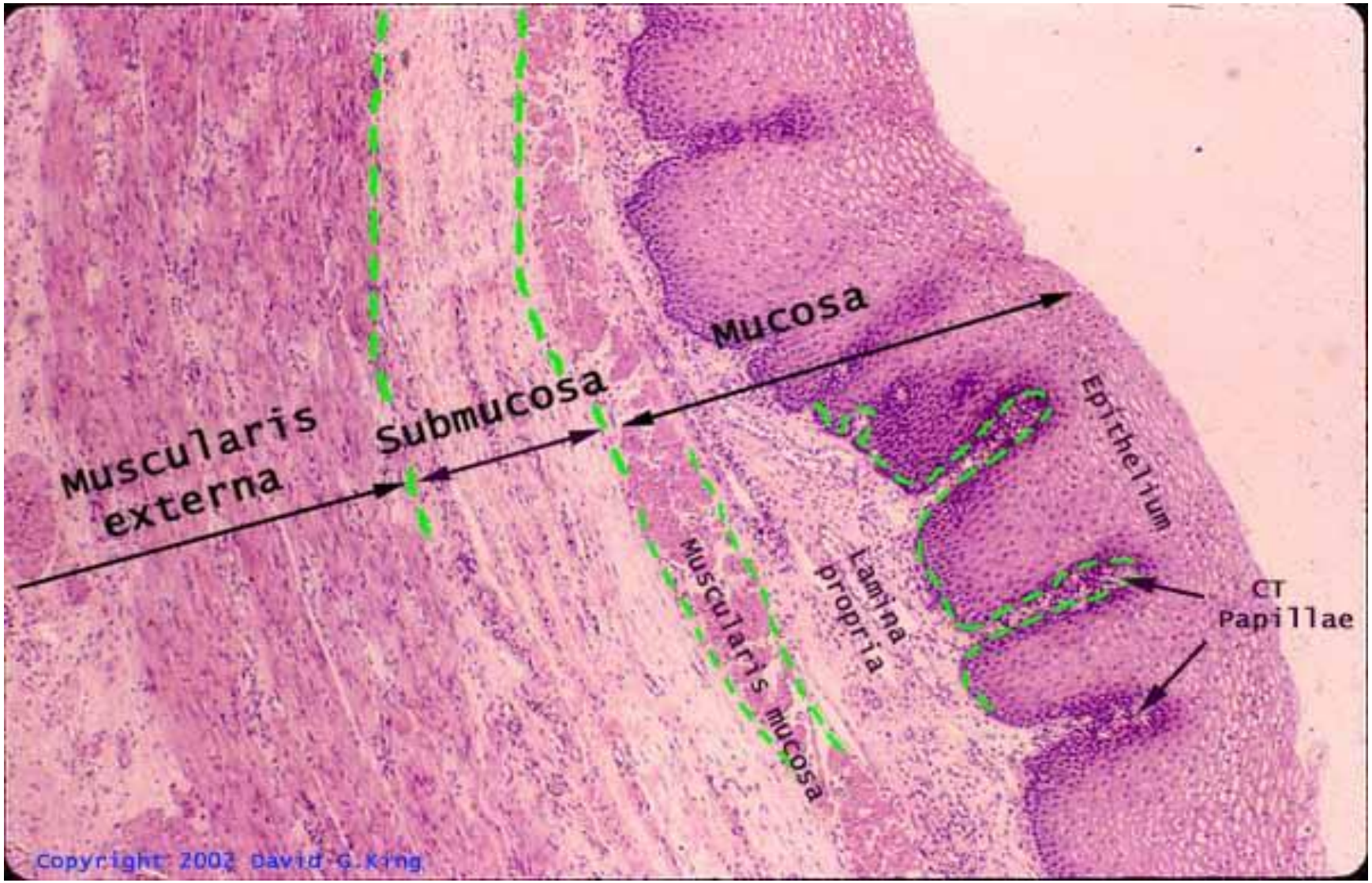
No serosa

Spincters:

- UES (at the level of the sixth cervical vertebra)
- LES (1 to 2 cm above the hiatus)



Esophageal histology



- **Symptoms of esophageal disorder:**

1-dysphagia: is difficulty in swallowing is encountered both with :

A-deranged esophageal motor function and

b- with diseases that narrow or obstruct the lumen.

2-Heart burn: is a retrosternal burning pain due to regurgitation of gastric contents into the lower esophagus

3- odynophagia: pain on swallowing, usually due to esophagitis.

4- hematemesis:(vomiting of blood) are sometimes evoked by esophageal disease, particularly by those lesions associated with inflammation or ulceration of the esophageal mucosa, esophageal varices.

5-Melena: black tarry stool due to upper GIT bleeding(esophagus and stomach) with digested iron appear ad black.while lower GIT bleedind ususally appear fresh blood(not subjected to digestion by gastric acid and pepsin)

6-respiratory symptoms: cough and dyspnea due to:

aspiration of esophageal content due to congenital fistula or

acid regurgitation.

- **Congenital anomalies:**
- Present at birth with vomiting gastric distension or aspiration pneumonia asphyxia
- **Agenesis:** complete absence of esophagus , rare condition.
- The most important and common is :
- **Stenosis**: partial obstruction or narrowing of esophageal lumen
- esophageal atresia and tracheoesophageal fistula.
- ***Atresia:***
- a thin, noncanalized cord replaces a segment of esophagus, causing a mechanical obstruction(i.e. congenital absence of the normal canal (blind end of the canal).

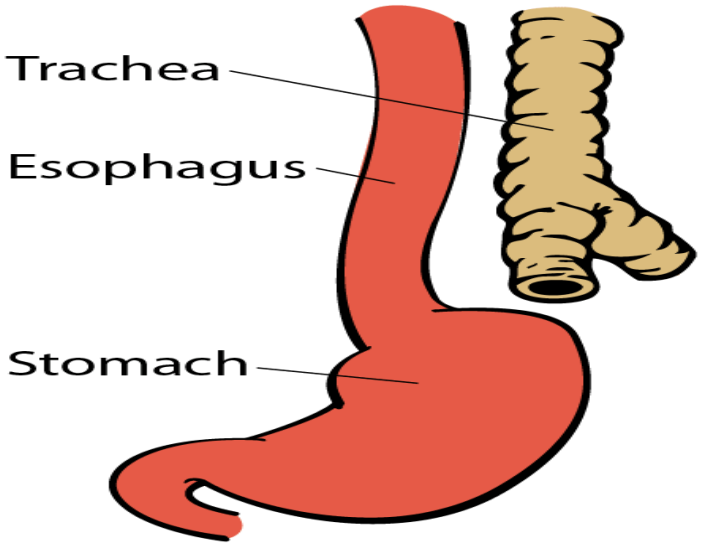
Usually atresia is associated with fistula (tracheoesophageal)

- ***Tracheo-esophageal fistula:***

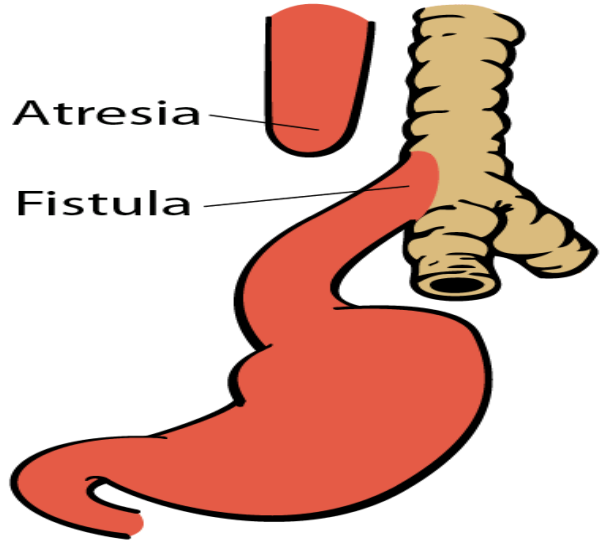
Fistula :Latin word (tube): abnormal connection between two epithelial surfaces (between two tubular organs or tubular organs with body surface or skin)

Atresia occurs most commonly at or near the tracheal bifurcation and is usually associated with a fistula connecting the upper or lower esophageal pouches to a bronchus or the trachea .

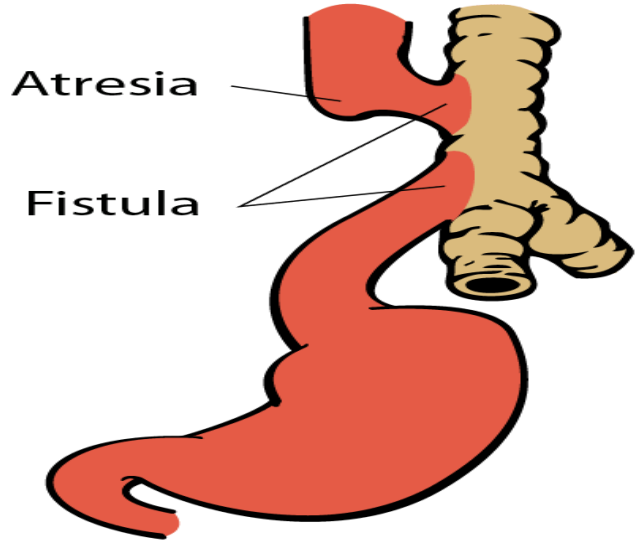
In other cases, a fistula can be present without atresia



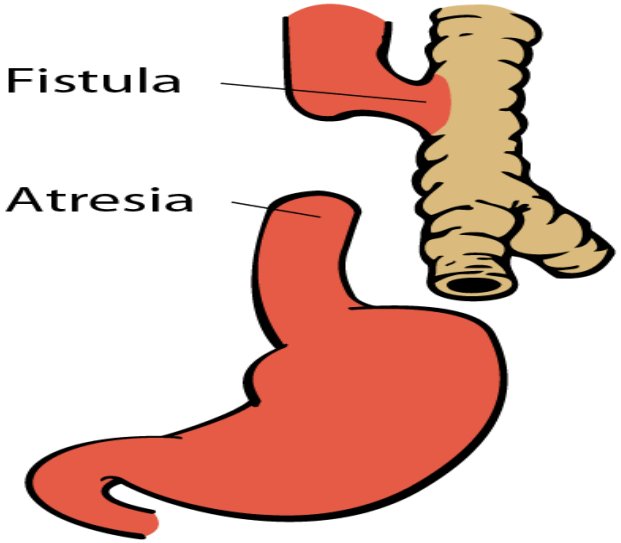
Normal Anatomy



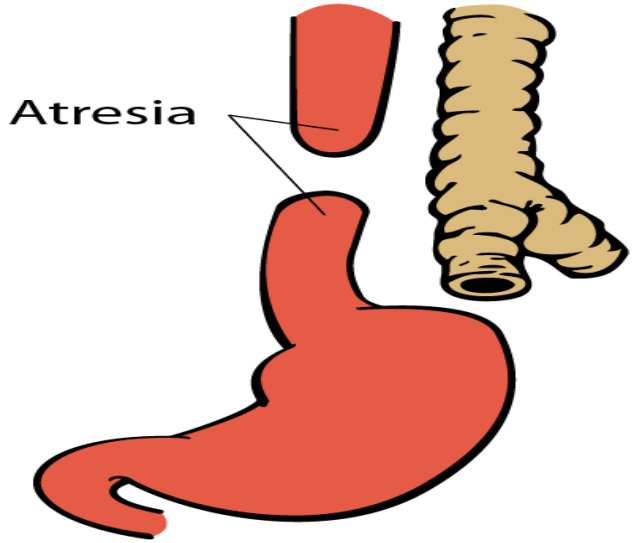
Atresia with distal Fistula



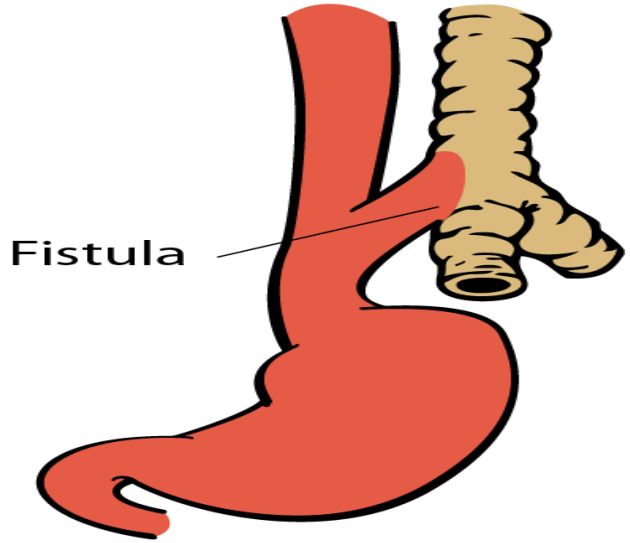
Atresia with double Fistula



Atresia with proximal Fistula

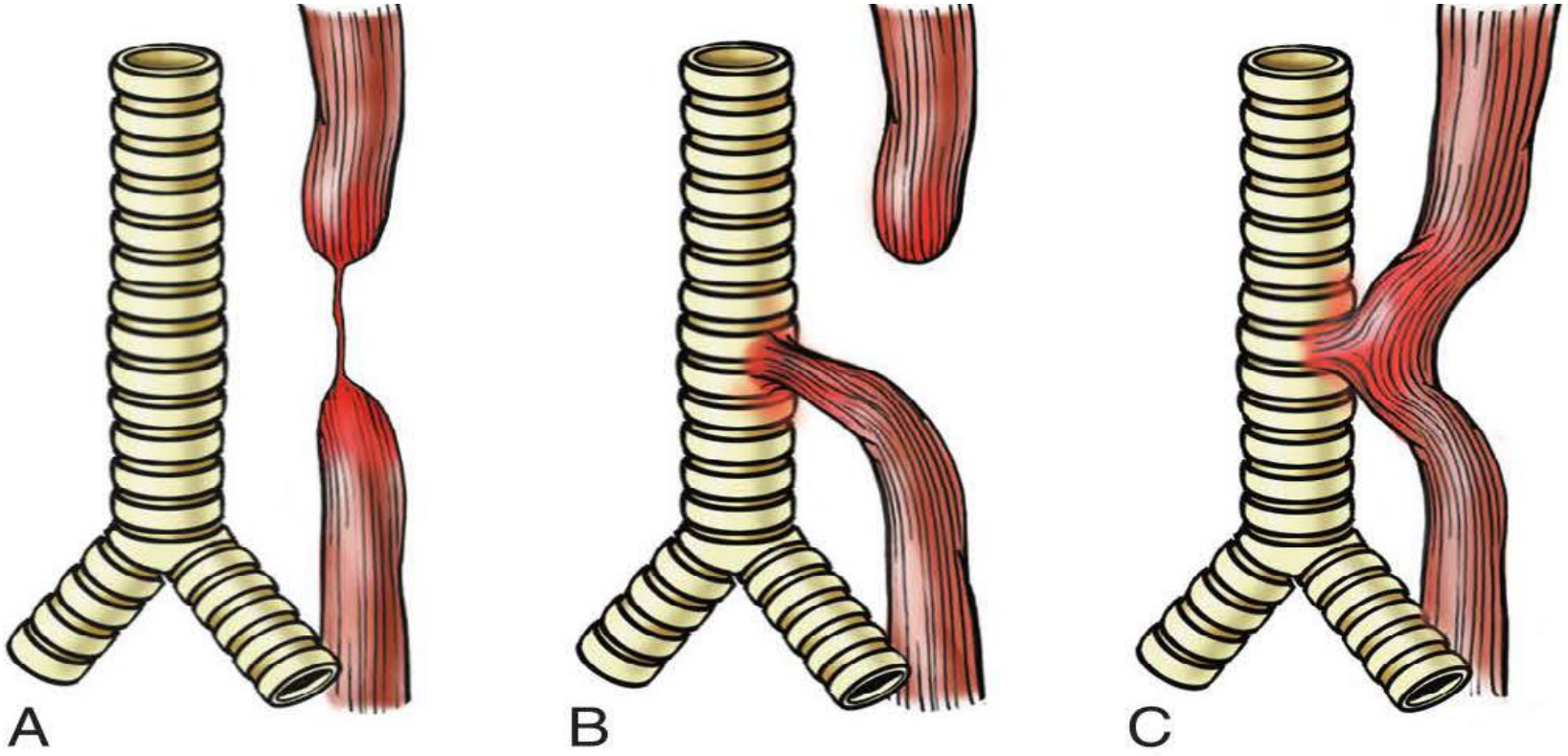


Atresia



Fistula

Most common 82%



Esophageal atresia and Tracheoesophageal fistula.

A, Blind upper and lower esophageal segments with thin cord of connective tissue linking the two segment.

B, Blind upper segment with fistula between lower segment and trachea.

C, Fistula between patent esophagus and trachea.

Type B is the most common.

What is the dangerous type ?why?

A/esophageal atresia with proximal fistula because It will lead to the passage of food from the esophagus to the trachea leading to aspiration pneumonia which leads to suffocation from food.

Acquired lesions: Webs, rings, and stenosis

1-Stenosis: causes: inflammation, tumors, postsurgical, autoimmune disease(scleroderma)

2-Mucosal webs are small, thin, eccentric lesion composed of a fibrovascular connective tissue and overlying epithelium mucosal membrane projects into the esophageal lumen. These are most common in the upper esophagus.

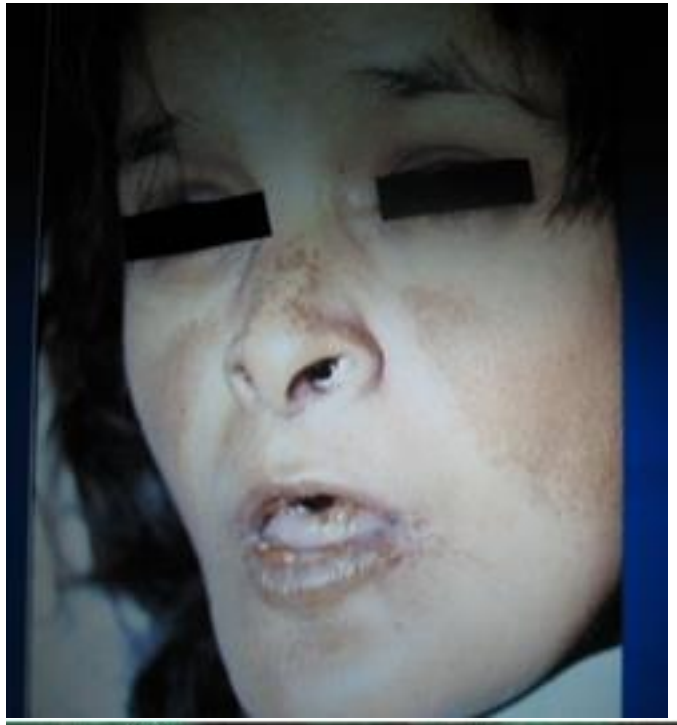
The main symptom : nonprogressive dysphagia associated with incompletely chewed food.

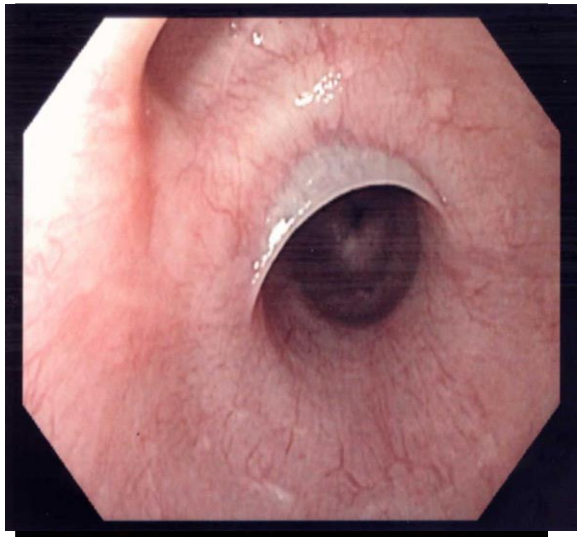
There is syndrome associated with syndrome

Upper esophageal web + iron deficiency anemia + atrophic glossitis(beef like tongue) + angular stomatitis are called **plummer Vinson syndrome.** This carry a risk of esophageal squamous cell carcinoma .

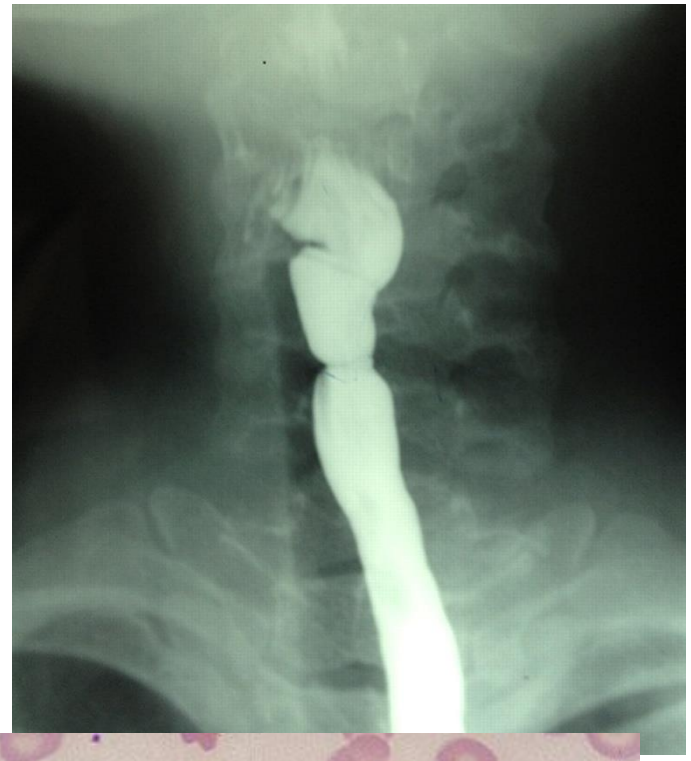
Case - 45yo female with weakness and difficulty in swallowing

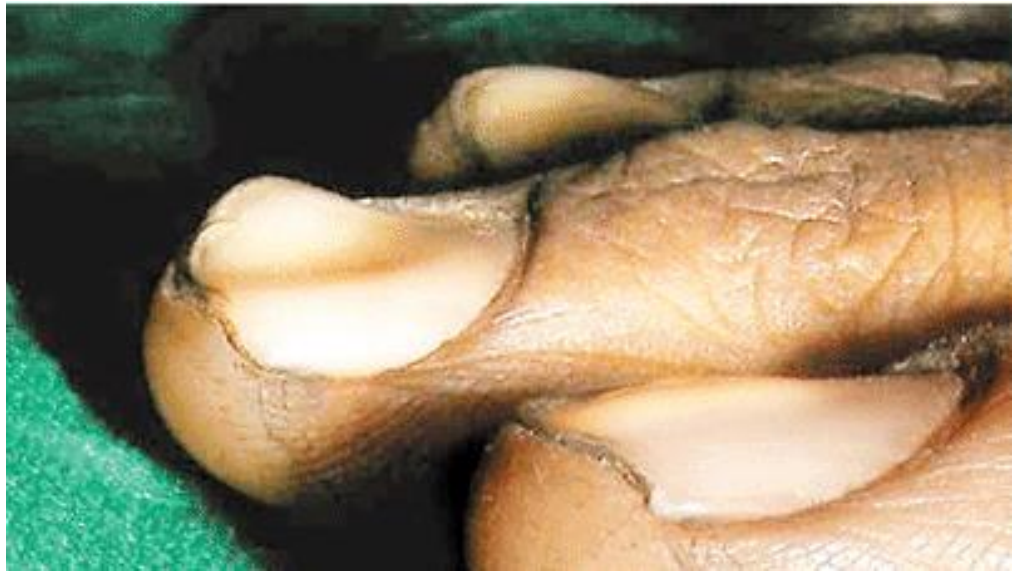
What are your findings? Diagnosis?

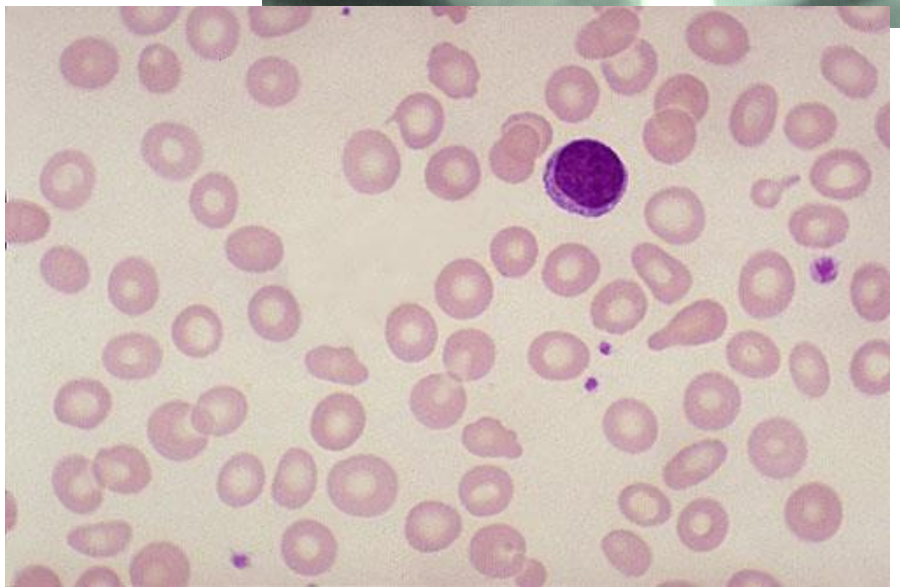




Endoscopic view of esophagus







Findings

Angular stomatitis

Atrophic glositis

Esophageal web (Endoscopy, Barium swallow)

Koilonychia (spoon shape nail

Microcytic hypochromic anemia

What is your diagnosis?

Synonyms:

Plummer-Vinson Syndrome(USA)

Patterson-Kelly Syndrome(UK)

Sideropenic dysphagia

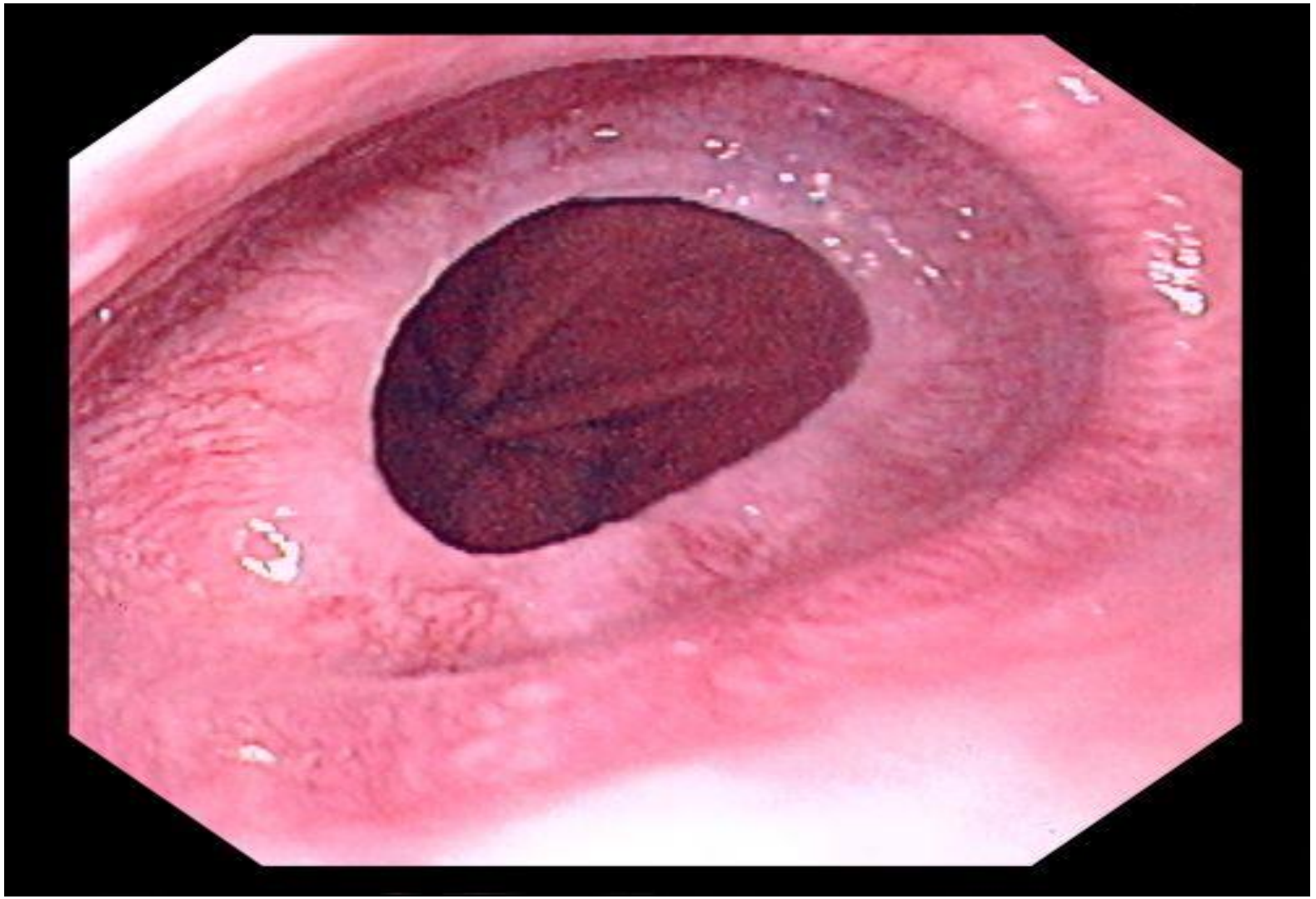
3-Esophageal rings unlike webs are circumferential, concentric plates of tissue protruding into the lumen, thicker and include mucosa, submucosa, and, occasionally, hypertrophic muscularis propria . It usually found in the distal esophagus

.

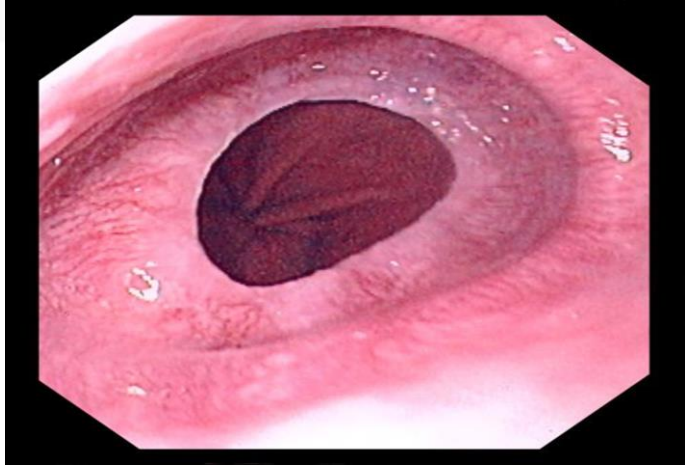
Episodic dysphagia is the main symptom.

Esophageal webs and rings are encountered most frequently in women over age 40

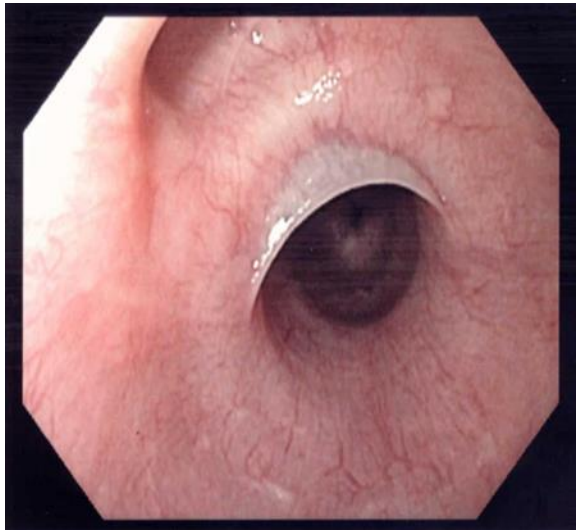
Esophageal ring



Rings or Webs



- Ring
  - Circumferential, muscle or mucosa, at distal esophagus
  - Schatzki's ring
  - Eosinophilic Esophagitis (>15 eosinophils/hpf in mucosa)
- Web
  - Part of lumen, mucosal, proximal esophagus
  - Plummer Vinson



Stenosis : consists of fibrous thickening of the esophageal wall.

Causes:

Although it may be congenital,

it is more frequently the result of severe esophageal injury with inflammatory scarring, as from gastroesophageal reflux disease (GERD),

radiation,

Stenosis usually manifests as progressive dysphagia,at first to solid foods but eventually to fluids as well.

Lesions associated with motor dysfunction:

Coordinated motor activity is important for proper function of the esophagus. The major entities that are caused by motor dysfunction of the esophagus are

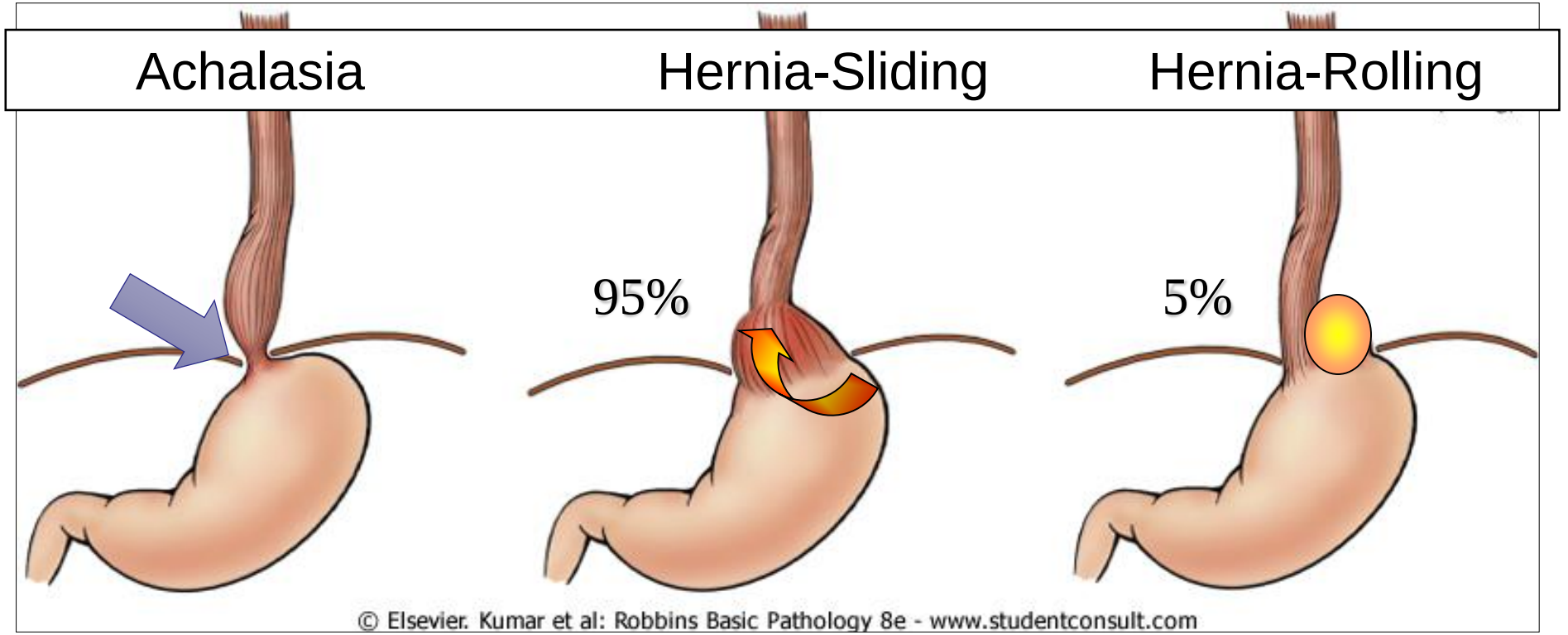
1. Achalasia

2. Hiatal hernia

3. Diverticula

4. Mallory-Weiss tear

Oesophagus motility Disorders:



Hernia: 30% incidence over 50years. (mostly asymptomatic)
Achalasia: Lack of relaxation of lower sphincter.

Lesions with motor dysfunction:

- ***1-Achalasia***
- ***(Greek: does not relax):***
- Failure of the lower esophageal sphincter to relax in response to swallowing producing functional obstruction leading to accumulation of food in the more proximal esophagus causing its dilatation & inflammation (esophagitis)

It is characterized by three major abnormalities:

1. Aperistalsis (failure of peristalsis)
2. Increased resting tone of the LES
3. Icomplete relaxation of the LES in response to swallowing

The wall of the esophagus :

may be of normal thickness,

thicker than normal owing to hypertrophy of the muscular wall,

or markedly thinned by dilation (when dilatation overruns hypertrophy).

The mucosa just above the LES may show inflammation and ulceration.

- **Signs and symptoms:**

The symptoms become manifested in young adulthood

a- progressive dysphagia for solid and then to fluid.

b- Nocturnal regurgitation of undigested food s.t aspiration pneumonea

- **Etiology:**
- 1- Primary: Uncertain causes possibly due to degenerative process involving the distal esophageal inhibitory neural(ganglion cells) innervation of the esophagus.

This leads to increased tone, an inability to relax of the lower esophageal sphincter, and esophageal aperistalsis.

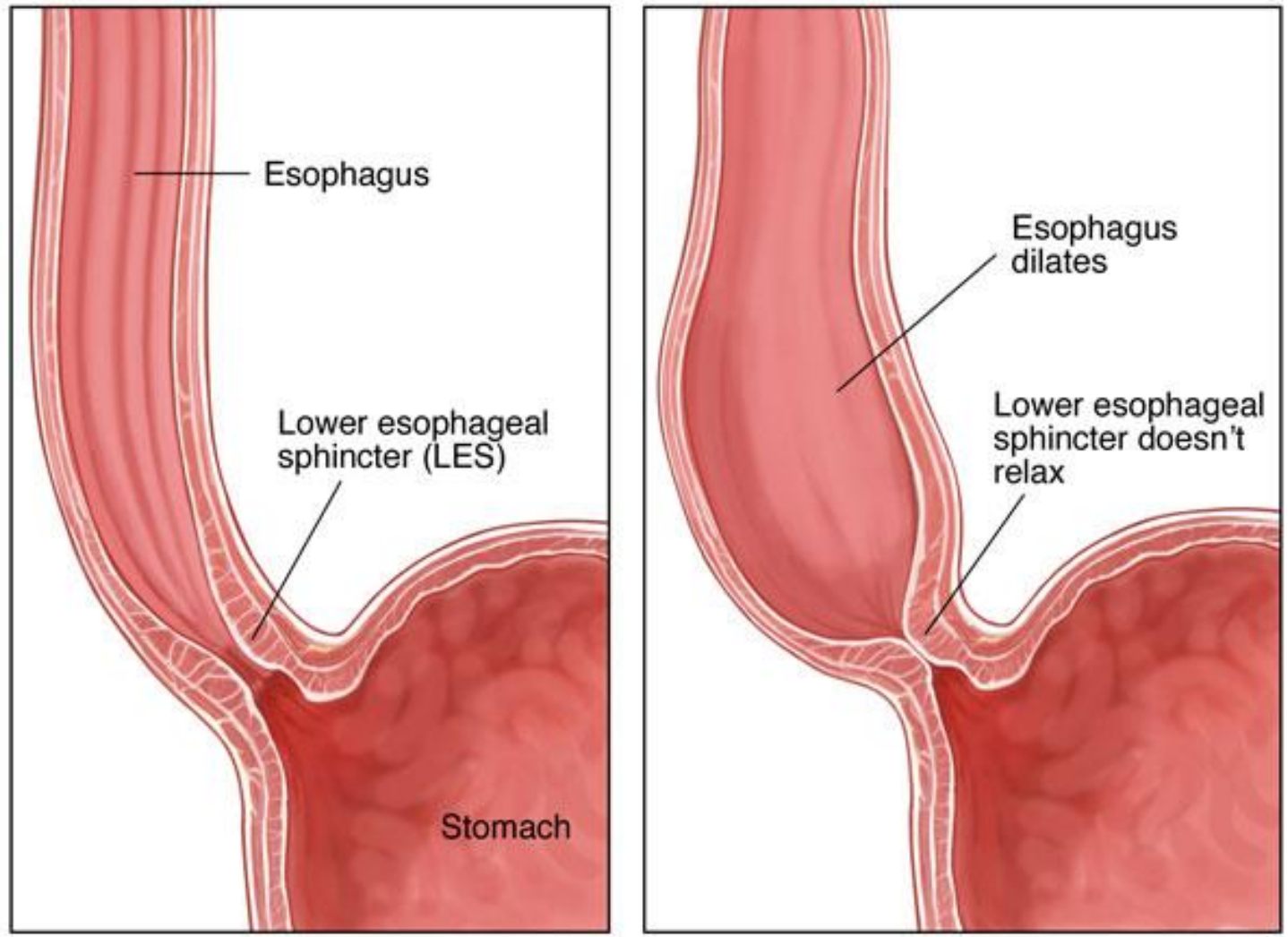
2- Secondary: A-Chagas disease caused by Trypanosoma cruzi parasitic infection lead to destruction of the myenteric plexus, failure of peristalsis, and esophageal dilatation. Duodenal, colonic, and ureteric myenteric plexuses can also be affected in Chagas disease.

B-DM injury to vagal nerve.

3-occasional coexistence of achalasia with other autoimmune diseases suggest immune-mediated destruction of inhibitory esophageal neurons.

Complications:

* Aspiration of undigested food which may cause pneumonia
* Candida esophagitis
- Lower esophageal diverticuli(pleural of diverticulum)
* Squamous cell carcinoma develops in 5% of cases.



Esophageal Achalasia

Achalasia: gross

Narrowing of LES and proximal dilatation of esophagus