

ORAL CAVITY: ULCERATIVE & INFLAMMATORY LESIONS

*Mechanical **trauma & cancer** can produce ulcerations in the oral cavity & must be considered in the differential diagnosis.

Aphthous Ulcers (Canker Sores)

★ **Extremely common**; **small** (<5 mm in \emptyset), **painful, rounded, shallow ulcers**, covered with a gray-white exudate & having an erythematous rim. Appear **singly** or **in groups**, on the **nonkeratinized oral mucosa**, specially **soft palate**, **buccolabial mucosa**, **mouth floor** & **tongue lateral borders**.

★ More common in the first 2 decades of life & often **triggered** by stress, fever, ingestion of certain foods, & activation of IBD. They are **self-limited** & usually resolve within few weeks, but they may **recur** in the same or a different location in the mouth.

▷ but can occur at any age.

Herpes Simplex Virus (HSV) Infection

☹ **Herpetic stomatitis** is an extremely common infection caused by HSV type 1.

☹ The virus is transmitted by **kissing**; by middle life over 3/4 of the population has been infected.

In most adults the primary infection is asymptomatic, but the virus persists in a **dormant state within ganglia about the mouth** (e.g., **trigeminal ganglia**). ضد التنبيه

☹ With reactivation of the virus (which may be caused by fever, sun or cold exposure, RTI, or trauma), solitary or multiple small (<5 mm in \emptyset) **vesicles** containing clear fluid appear. They occur most often on the **lips** or **about the nasal orifices** & are well known as **cold sores** or **fever blisters**. (لطفة حمة)

☹ The vesicles soon rupture, leaving shallow, painful ulcers that heal within a few weeks, but recurrences are common.

☹️ The vesicles begin as an intraepithelial focus of intercellular & intracellular edema.

The infected cells become ballooned & develop intranuclear acidophilic viral inclusions.

★ Sometimes adjacent cells fuse to form giant cells known as multinucleated polykaryons. الخلايا المصابة يتحد مع بعضها.

Necrosis of the infected cells & the focal collections of edema fluid account for the intraepithelial vesicles detected clinically (F15-1). داخل الepidermis

▼ Identification of the inclusion-bearing cells or polykaryons in smears of blister fluid constitutes the diagnostic Tzanck test for HSV infection. نادر جداً ما نخله لأنه ال picture

Antiviral agents may accelerate healing of the lesions. clinical picture

☹ In 10% to 20% of those with **Herpetic stomatitis**, particularly in the **(immunocompromised)** a **more virulent disseminated eruption** develops, producing multiple vesicles throughout the oral cavity, including the gingiva & pharynx (**herpetic gingivostomatitis**) & lymphadenopathy.

التهاب اللثة والفم

☹ In very severe cases, viremia may seed the brain (causing **encephalitis**) or disseminated visceral lesions.

infl. of the brain substance.

▼ HSV type 1 may localize in many other sites, including the **conjunctivae (keratoconjunctivitis)** & the **esophagus** when a nasogastric tube is introduced through an infected oral cavity.

★ As a result of changes in sexual practices, **genital herpes** produced by HSV type 2 (the agent of **herpes genitalis**) is **increasingly seen in the oral cavity**. The infection produces vesicles in the mouth, which have the same histologic characteristics as those that develop on the genital mucous membranes & external genitalia.

Oral Candidiasis

☼ **Candida albicans** is a **normal** inhabitant of the oral cavity found in 30% to 40% of the population; it causes disease only when there is impairment of the usual protective mechanisms.

☹ **Thrush = moniliasis = pseudomembranous candidiasis** is the most common fungal infection of the oral cavity.

It is particularly common among persons rendered vulnerable by **DM, AIDS, immunodeficiency, anemia, antibiotic or glucocorticoid therapy, or disseminated cancer.**

► **GROSSLY**, typical oral candidiasis takes the form of an **adherent, white plaque, curdlike, circumscribed anywhere within the oral cavity** (F15-2). زك الجبينة.

The pseudomembrane can be scraped off to reveal an underlying granular erythematous inflammatory base.

■ H, the pseudomembrane is composed of fungal organisms superficially attached to the underlying mucosa.

☹ In milder infections there is minimal ulceration, but

☹ in severe cases the entire mucosa may be **denuded & lost**.

تخرى وكتفى و تفتت

☺ For unknown reasons, local **vagina** candidiasis may appear, not only in predisposed females, but also in apparently healthy young women, particularly during pregnancy, or in women who are using oral contraceptives or broad-spectrum antibiotics.

☹ In the particularly vulnerable host, candidiasis may

- (1) Spread into the esophagus, especially when a nasogastric tube has been introduced, or
- (2) it may produce **wide-spread** visceral lesions, when the fungus gains entry into the **bloodstream**.

☠ Disseminated candidiasis is a life-threatening infection that must be treated aggressively.

AIDS & Kaposi Sarcoma

⊖ AIDS & less advanced forms of HIV infection, are often associated with lesions in the oral cavity which may take the form of candidiasis, herpetic vesicles, gingivitis, or glossitis. → التهاب اللسان.

⊖ Hairy leukoplakia is an uncommon lesion seen virtually **only in persons infected with HIV.** It consists of white confluent patches, anywhere on the oral mucosa, that have a "hairy" or corrugated surface resulting from marked epithelial thickening. It is **caused by Epstein-Barr virus (EBV)** infection of epithelial cells.
HIV + not on AIDS → متخرج
على انه يصير كالتالي
موجوده في AIDS

⊖ More than 50% of individuals with Kaposi sarcoma develop intraoral purpuric discolorations or violaceous, raised, nodular masses; sometimes this involvement constitutes the presenting manifestation.

LEUKOPLAKIA & ERYTHROPLAKIA

▶ Leukoplakia refers to a (white patch or plaque) caused by epidermal thickening (hyperkeratosis) hyperplasia of stratum spongium. مهم جدا

As defined by the WHO, leukoplakia is a (white patch or plaque) that cannot be scraped off & cannot be characterized as any other disease; (thus, this term is not applied to other white lesions, such as those caused by candidiasis or lichen planus).
د. د. د.

▶ Leukoplakia plaques are ^{inner} more frequent among older men & are most often on the vermilion border of the lower lip, buccal mucosa, the hard & soft palates, & less frequently on the floor of the mouth & other intraoral sites.
يعني ما يعرف شو المرض

⊖ May appear as localized, diffuse, or multifocal smooth or roughened, leathery, white, discrete mucosal thickening. مهم جدا

■ they vary, from simple hyperkeratosis without underlying epithelial dysplasia, to mild, up to severe dysplasia bordering on carcinoma in situ (F15-3). ● Only histologic evaluation distinguishes these lesions from each other.
منها كان شكله لازم تاخذ عينه ونفحصها

- ▶ Leukoplakias are of unknown cause, except that there is a ☹️ ***strong association with the use of tobacco***, particularly pipe smoking & smokeless tobacco (pouches, snuff, chewing).
- ▶ Less strongly implicated factors are: التسخين أو مثلاً "مهنج التبغ أو الشم:
 - ☹️ ***chronic friction***, as from ill-fitting dentures or jagged teeth;
 - ☹️ ***alcohol abuse***; & ***irritant foods***.
 - ☹️ ***HPV antigen***, more recently, has been identified in some tobacco-related lesions, raising the possibility that the virus & tobacco act in concert in the induction of Leukoplakia.

☹️ Oral leukoplakia is an important because 3% to 25% (depending somewhat on location) undergo malignant transformation to **SCCa (F15-3A)**.

☹️ The transformation rate is **greatest** with **lip & tongue** Leukoplakias & lowest with those on the floor of the mouth.

■ H, the Leukoplakia that display significant dysplasia have greater probability of malignant transformation

☹️ **Remember:** It is **impossible** to distinguish the innocent lesion from the ominous one on visual inspection.

إذا سفت لخصه بفناء مستحيل تعرف انه ستونوعها الله جبار !!
هذه منبذة في سيدة

Three somewhat related lesions must be differentiated from the usual oral leukoplakia.

(1) ☺ **Hairy leukoplakia**, (see above) & seen virtually only in persons with AIDS, has a corrugated or "hairy" surface rather than the white, opaque thickening of oral leukoplakia & has not been related to the development of oral cancer.

(2) ☹ **Verrucous leukoplakia** shows a corrugated surface caused by excessive hyperkeratosis. This seemingly innocuous form of leukoplakia recurs & insidiously spreads over time, resulting in a diffuse warty-type of oral lesion that **may yet harbor squamous cell carcinoma.**

(3) ☹ **Erythroplakia** refers to red, velvety, often granular, circumscribed areas that may or may not be elevated, having poorly defined, & irregular boundaries.

■ H, erythroplakia almost invariably reveals marked epithelial dysplasia, & with malignant transformation rate of more than >50%, the recognition of this lesion becomes even more important than identification of oral leukoplakia!

CANCERS OF THE ORAL CAVITY AND TONGUE

Table 15-1 Risk Factors for Oral Cancer ☹

Leukoplakia, erythroplakia: Risk of transformation in leukoplakia 3% to 25%; More than 50% risk in erythroplakia

Tobacco use: Best-established influence, particularly pipe smoking & smokeless tobacco

Human papillomavirus (HPV) types 16 & 18: Identified by molecular probes in 30% to 50% of oral cancers.

Alcohol abuse: Weaker influence than tobacco use, but the two habits interact to greatly increase risk.

Protracted irritation: Weakly associated

كسوف السن و أدى إلى irritation

★ **The majority of oral cavity cancers are squamous cell (SCCa)**. Although they represent only **3% of all cancers in the US**, they are important clinically, as

☺ All are **readily accessible** for early identification & biopsy

☹ **BUT, unfortunately**, 50% result in death within 5 years & indeed may have already metastasized by the time the primary lesion is discovered.

لأنه المريض بهماها لذلك
بتدهور كبير قبل ما يفحصه

★ **Oral** cancers occur in elderly & is rare before the age of 40y

★ **Sites:** the 3 predominant sites of origin of oral cavity cancer in order of frequency are the:

(1) Vermilion border of the lateral margins of the lower lip,

(2) Floor of the mouth, & (3) Lateral borders of the tongue.

★ **Grossly,**

• **Early** lesions appear as **pearly white to gray**, circumscribed **thickenings** of the mucosa, resembling leukoplakic patches.

• **Later**, they may grow in an **exophytic**, visible & palpable nodular mass & eventually **fungating** tumor, ^{to the outside.}

or they may assume an **endophytic invasive pattern, with central necrosis to create malignant ulcer.**

ulcer ^{دخول} ^{invasive} ^{ويعمل} ^{ورم كبير} ^{exophytic} ^{تكون} ^{الورم} ^{لما ينم} ^{هريا} ^{تكون} ^{surface} ^{في} ^{مكان} ^{كذلك}

■ SCCa are usually moderately to well-differentiated keratinizing tumors (F15-4).

Before the lesions become advanced it may be possible to identify epithelial atypia, dysplasia, or ca in situ in the margins, suggesting origin from leukoplakia or erythroplakia.

carcinoma → with lymph. sarcoma → with blood.

⊗ Regional LN spread is present at the time of initial diagnosis:

- only rarely with lip cancer
- in 50% of cases of tongue cancer, &
- in > 60% of with cancer of the floor of the mouth.

Distance metastases is less common than regional spread.

▶ **Clinically**, (1) many lesions are **asymptomatic** & therefore they are ignored by the patient &

(2) Some may cause **local pain or difficulty in chewing**.

⊗ When these cancers are discovered at an **early stage**, 5-year survival can **exceed 90%**.

وإذا ما في LN involve. وكان سببانه فقط هون منيح بكون

⊗ However, the overall 5-year survival rates (5ySR) after surgery & adjuvant radiation & chemotherapy are only **40%** for ca of the base of the tongue, pharynx, & floor of the mouth

without LN metastasis,

5years بعدوا لدة

▼ compared with less than **20%** for those with LN metastasis.

لذلك الشغلة المهمة هوالتحصين المبكر.

SALIVARY GLAND DISEASES

Sialadenitis التهاب الغدد اللعابية

★ **Mucocele**, the most common lesion of the salivary glands results from blockage or rupture of a salivary gland duct, with consequent leakage of saliva into the surrounding tissues, most often found in the **lower lip**, as a consequence of trauma.

▶ **Sialadenitis** is inflammation of the major salivary glands, may be of **traumatic, viral, bacterial, or autoimmune origin**.

النكاف
★ **Mumps**: is a common cause of sialadenitis. It is an infectious viral disease, caused by paramyxovirus, which may produce enlargement of all the major salivary glands, but predominantly the parotids.

■ H, there is diffuse, interstitial inflammation marked by edema & a mononuclear cell infiltration & sometimes, by focal necrosis.

⊗ Although childhood mumps is self-limiting disease, **mumps in adults may be accompanied by orchitis** (which, if bilateral, may causes permanent sterility), or **pancreatitis**.

التهاب بال testis

★ Bacterial sialadenitis mostly occur secondary to:

(1) Ductal obstruction by stone (sialolithiasis, F3.9),

تكوّن الحصى
الغدة اللعابية وقنواتها.

(2) Retrograde entry of oral cavity bacteria (most commonly *Staphylococcus aureus* & *Streptococcus viridans*), under conditions of severe systemic dehydration such as the postoperative state. In addition, persons with chronic, debilitating medical conditions, or compromised immune function are at ↑ risk for acute bacterial sialadenitis.

★ The sialadenitis may be largely interstitial, may cause focal areas of suppurative necrosis, or even abscess formation.

العقوى الشحصية الى ما يقدر يبلغ ماء او اي اخرى لازم يفضل نفسه ففحة حيث يفضل لهما
منع دخول
المرضى
القريبة

• Sjögren syndrome is a clinico-pathological entity, characterized by dry mouth (xerostomia) & dry eyes (keratoconjunctivitis sicca), resulting from immune-mediated destruction of all the major & minor salivary glands; as well as the lacrimal glands, and causes ↓ production of saliva & tears.

dry.

لا بدوت تفحشات في هذه الغدد (اللعاب أو الدمعية) بدون ألم وهكذا .

★ The combination of salivary & lacrimal gland inflammatory enlargement, which is usually painless, & xerostomia, whatever the cause, is sometimes referred to as Mikulicz syndrome.
The causes include sarcoidosis, leukemia, lymphoma, & idiopathic lymphoepithelial hyperplasia.

Salivary Gland Tumors (T)

- The salivary gland give rise to **30 types** of tumors!
- About 80% of T occur within the parotid glands, 10% in the submandibular, 10% in sublingual and minor salivary glands
- ☺ In the parotids, 70% of these T are benign, mucosa
- ☹ whereas 40% of submandibular glands & 50% of minor glands, & 80% of sublingual glands are cancerous
- ☹ Thus, the likelihood that a salivary gland tumor is **malignant** is **inversely** proportional, roughly, **to the size of the gland!**
- M/F ratio is 1:1, & T usually occur in 6th or 7th decade.

▶ The most common *malignant T of the salivary gland* is mucoepidermoid carcinoma, 65% of which occurs in the parotids. ● When primary or recurrent benign T are present for many (10-20) years, malignant transformation may occur, referred to then as a malignant mixed salivary gland tumor.

Pleomorphic Adenoma (Mixed Tumor) of Salivary Glands benign tumor

- ★ accounts for more than **90% of BT** of the salivary glands.
- ★ a slowly-growing T, rarely exceeding 6 cm in Ø.
- ★ mostly arise in the superficial parotid, causing painless discrete mass & swelling at the angle of the jaw.

★ Although the T is well-demarcated, & apparently encapsulated, histologic examination often reveals multiple sites where the T penetrates the capsule, therefore, adequate margins of resection are thus necessary to prevent recurrences. This may require sacrifice of the facial nerve, which pass through the parotid gland.

- ★ 10% of T excisions are followed by recurrence.

■ Characteristically, T is histologically **heterogeneous** with: 2 elements
(I) **epithelial T cells** forming ducts, acini, tubules, strands, or sheets. The cells are small, dark, & range from cuboidal to spindle forms, these epithelial cells are...

مداخله

(II) These epithelial elements are intermingled with a loose, often **myxoid connective tissue** stroma sometimes containing islands of apparent cartilage or, rarely, bone (F15-5 & 6-2).

★ Immunohistochemical evidence suggests that all of the diverse cell types in the T are of **myoepithelial derivation.**

النوعيت من الخلايا ناسئة من هنا

Warthin Tumor (Papillary Cystadenoma Lymphomatosum)

- **Infrequent BT** occurs only in the parotid gland.
- It is thought to arise from heterotopic salivary tissue trapped within a regional LN during embryogenesis.
- Usually, small, well-encapsulated round mass, cut section (C/S) reveals mucin-containing cystic spaces (F3-13) within a soft gray background.

ان حبة في مكان غير الاعتيادي
الطبقة المبطنة لها هي اذ كادت عبارة عن طبقة جذا

■ H, it shows: (1) a two-tiered epithelial layer lining the branching, cystic, or cleftlike spaces; & (2) an immediately subjacent, well-developed **lymphoid tissue** + germinal centers.

A recurrence rate of about 10% is attributed to incomplete excision, multicentricity, or a 2nd primary tumor.

Malignant transformation is rare; about half of reported cases have had prior radiation exposure.

بقية ال gland
مابين كتوك عن دم آخر
غير الي كتته

المريء ESOPHAGUS

عسر و صعوبة بالبلع

Symptoms: ★ All esophageal lesions produce Dysphagia (difficulty in swallowing), mostly due to narrowing or obstruction of lumen, or deranged esophageal motor function.

Usually ★ Heartburn (retrosternal burning pain) reflects regurgitation of gastric contents into the lower esophagus.

Less commonly, ★ Hematemesis (vomiting of fresh blood) & Melena (black, sticky & shiny stool) due to the presence of altered blood) are evidence of severe inflammation, ulceration, or laceration of the esophageal mucosa. Massive hematemesis may be due to rupture of esophageal varices.

نزول
من ال
esophagus
من المعدة
وتغير لونها
وبنفس أسود

من الحالات بعبوت
دوالي المريء
30%

ANATOMIC & MOTOR DISORDERS

Table 15-2: Infrequent Anatomic Disorders of the Esophagus:

التصنيف Disorder = Clinical Presentation & Pathology

• **Stenosis** - Adult with progressive dysphagia to solids & eventually, to all solid and liquid foods; usually due to lower esophageal narrowing resulting from ⇒ chronic inflammatory disease, including gastroesophageal reflux.

المريء عما شكرا حبال ليس له تجويف
الانكل أو الكليب رج يروح إلى ال lung
اختناق

• **Atresia (absence of a lumen) & fistula** - Newborn with aspiration, paroxysmal suffocation, pneumonia; esophageal atresia + tracheoesophageal fistula may occur together.

• **Webs, rings** - Episodic dysphagia to solid foods; an acquired mucosal web or mucosal & submucosal concentric ring partially occluding the esophagus.

• **Diverticula** - An acquired outpouching of the esophageal wall resulting in episodic food regurgitation, especially nocturnal; sometimes pain is present;

حلقات Achalasia عندي tube لازم يرتخى حتى يموت

• **Achalasia** means "failure to relax", or incomplete relaxation of the lower esophageal sphincter (LES) due to ↑ LES tone in response to swallowing, producing functional obstruction, with consequent dilation of the more proximal esophagus (F15-6). Achalasia characteristic triad are incomplete LES relaxation + ↑LES tone + esophageal aperistalsis.

الانكل

ما يتحرك بـ sphincter
★ **Achalasia** occurs most commonly as (I) a primary disorder of uncertain etiology, with loss of intrinsic inhibitory innervation of the LES, resulting in:

التي يعمل على التقلص والارتخاء

carcinoma: oesophagus

مشهم جدا جدا

⊖ (1) Progressive **dilation** of the esophagus, above the level of the LES. The wall of the esophagus may be of normal, thicker than normal {because of hypertrophy of the muscularis}, or markedly thinned by dilation.

هي بتحفر الأكلانه بسفح من ضلال قشمن
oesophagus

The **myenteric ganglia** are usually absent from the body of the esophagus (causes esophageal aperistalsis), but may/may not be reduced in number in the region of the lower esophageal sphincter.

Inflammation in the location of the esophageal myenteric plexus is Ⓡ pathognomonic of the disease.

⊖ (2) Food stasis produces **secondary** mucosal inflammation & ulceration proximal to the lower esophageal sphincter.

*endoscopy is very imp. to investigate and Dx.

(II) **Secondary achalasia**, less common than the primary may arise from diverse pathologic processes that impair esophageal function, classic example is:

⊖ **Chagas disease**, caused by *Trypanosoma cruzi*, which causes destruction of the myenteric plexus of the esophagus, duodenum, colon, & ureter.

في أمريكا الجنوبية

الأشني
عشر

Disorders of the dorsal motor nuclei such as polio, & autonomic neuropathy in DM can cause secondary achalasia.

► Clinically, achalasia is characterized by progressive dysphagia. Nocturnal regurgitation & aspiration of undigested food may occur. ^{ويحدث عدوى (pneumonia) في الرئة المملوثة بالكثير مما يرجع إلى الرئة رجوع}

⊖ Achalasia most serious complication is the hazard of developing esophageal SCCa reported to occur in about 5% of patients & typically at an earlier age than in those without it. ^{أصغر من العمر المزمورض إلى بصرفه}

Hiatal Hernia (HH)

► Cause of HH is separation of the diaphragmatic crura & widening of the space between the muscular crura & the esophageal wall which → permits a dilated segment of the stomach to protrude above the diaphragm.

⊖ Two anatomic patterns of HH are recognized (F15-6):

(1) Sliding or axial HH, constituting (95%) of cases; protrusion of the stomach above the diaphragm creates a bell-shaped dilation, bounded below by the diaphragmatic narrowing, &

(2) Paraesophageal (rolling) or nonaxial HH (5%), in which a separate portion of the stomach (usually along the greater curvature), enters the thorax through the widened foramen.

^{جزء من المعدة يعبر من خلال الفتحة مما لها أعرض زيادة (1)}

⊖ The cause of this deranged anatomy, whether congenital or acquired, is unknown!

► HH, on the basis of radiographic studies, are reported in → 1% to 20% of adults, & ↑ in incidence with age. BUT only about 9% of these adults, suffer from heartburn or regurgitation of gastric juices into the mouth!

^{بغف ما بيت تكوا من الحلاصات}

★ Therefore, symptoms of HH are more likely result from → incompetence of the LES rather than from the HH per se & are accentuated by → positions favoring reflux (bending forward, lying supine) & → obesity.

★ Although most individuals with sliding HH do not have reflux esophagitis, those with severe reflux esophagitis are likely to have a sliding HH.

^{وخاصة الsliding}

⊖ Other complications of both types of HH include: mucosal peptic ulceration (F 4-6), bleeding, & perforation. Paraesophageal HH rarely induce reflux, but they can become strangulated or obstructed.

^{تختلف أو تستأوسنف}

Lacerations (Mallory-Weiss Syndrome)

☹️ **Mallory-Weiss tears** are longitudinal tears in the lower esophagus, at the esophagogastric junction (F15-7).

☹️ They may occur during severe vomiting for any reason, especially in chronic alcoholics after a bout (attack) of severe retching (the try for vomiting) or vomiting.

كثير يد تفق 5
من مش قادر

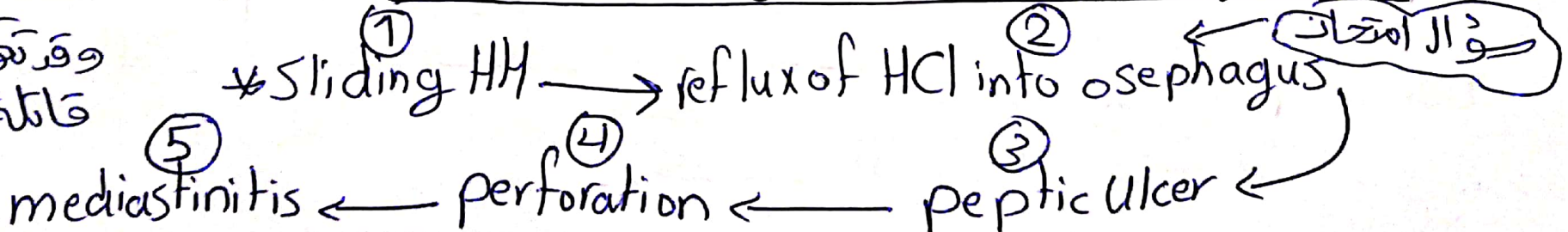
► **Cause:** is → inadequate relaxation of the musculature of the lower esophageal sphincter (LES) during vomiting, with stretching & tearing of the esophagogastric junction at the moment of expulsion of gastric contents.

لازم يرتخي عنان يطالع هذا القيء

المنطق كثير يزيد في المعدة وهذا يمزق البطانة تحت ال esophagus

• It **account for 5% to 10% of upper GIT bleeding episodes**. Mostly, the bleeding is not profuse & ceases without surgical intervention, **But** ☠️ life-threatening hematemesis may occur.

وقد تكون قاتلة



الدوالي **VARICES** elongation, dilatation, tortuous vessels

► When portal venous blood flow into the liver is impeded or obstructed (most common example is cirrhosis or fibrosis)...

⇒ The resultant portal hypertension induces the formation of collateral bypass channels wherever the portal & systemic systems communicate

⇒ Portal blood flow is thereby diverted through the stomach veins into the plexus of esophageal submucosal veins, thence into the azygos veins & the superior vena cava.

⇒ The ↑ pressure in the esophageal plexus produces dilated tortuous vessels called varices.

☹ Endoscopically, when the varices are unruptured they appear as tortuous dilated veins lying primarily within the submucosa of the distal esophagus & proximal stomach.

★ The covering mucosa may be normal with irregular protrusion into the lumen, or eroded & inflamed because of its exposed position, resulting in further weakening of the tissue support of the dilated veins (F15-8 & F4.3)

NB. {varices are collapsed in surgical or PM specimens}.

لما نعمل نالغور بقدر أشوفه
مهمة جدا
تكون collapsed وليس tortuous
biopsy مع يكون

السلاية مهم جداً

★ Varices are **asymptomatic** until they rupture.

☹️ **Variceal rupture produces massive hemorrhage (H) into the lumen, & into the esophageal wall.**

★ **Varices are present in 2/3 of all cirrhotic patients.**

★ In the US, esophageal varices are most often associated with alcoholic cirrhosis.

☠️ **50% of deaths in cirrhotic patients result from rupture of a varix, either as a direct result of the H or from the hepatic coma triggered by the H (How?)**

فقد الدم الشديد ← hypovolemic shock
النزف hemorrhage
hepatic failure
interesting
من الـ Amonia

☹️ However, **even** when varices are present, they account for less than 50% of all episodes of **hematemesis**, with bleeding from **concomitant** → **gastritis**, → **PU**, or → **esophageal laceration** accounts for the rest.

☹️ Once begun, variceal H subsides spontaneously in 50% of cases. Treatment is by endoscopic injection of thrombotic agents (**sclerotherapy**) or **balloon tamponade**.

المنطقة الي

☠️ When varices bleed, **20% to 30% of patients die during the 1st episode**. Among survivors, rebleeding occurs in 70% within 1 year, with a similar rate of mortality for each episode.

ESOPHAGITIS

• Injury to the esophageal mucosa with subsequent inflammation (esophagitis) is a common condition worldwide.

مواد حارقة

► **Esophagitis** may be caused by ingestion of corrosive or irritant substances, prolonged naso-gastric (NG) intubation, uremia, & radiation or chemotherapy, among other causes.

☹️ **Esophagitis** prevalence in northern Iran is more than **80%**; it is also extremely high in regions of China. The basis of this prevalence is **unknown!**

The majority of cases in Western countries is attributable to
☹️ **reflux of gastric contents (reflux esophagitis, or gastroesophageal reflux GER disease).** extremely common.

☀️ It affects about 0.5% of the US adult population (375Millions), (i.e., 1 Million); & its dominant symptom is **recurrent heartburn.**

↓ **Efficacy of esophageal antireflux mechanisms**, CNS depressants, **alcohol or tobacco** exposure may be the contributing causes;

☹️ But most often **no obvious etiology is identifiable!**

مافي ← من معروف الي غير معروف contributing

☹ **Grossly**, mild esophagitis may appear as simple hyperemia. In severe esophagitis, there may be confluent epithelial erosions or total ulceration into the submucosa.

↳ Very superficial injury to mucosa.

■ Three histologic features are characteristic of uncomplicated **reflux esophagitis**, although only one or two may be present:

- (1) Intraepithelial eosinophils with/without neutrophils (Intraepithelial neutrophils are markers of severe injury);
- (2) **Basal zone hyperplasia (F15-9); &**
- (3) **Elongation of lamina propria papillae.**

► Clinically, there is heartburn [the severity of which is not closely related to the presence & degree of anatomic esophagitis], sometimes accompanied by regurgitation of a sour brash:
(عسوية و مرارة (عنف) وصل إلى الفم cavity)

☹ **Complications** of severe reflux esophagitis are:

Bleeding, Ulceration, Stricture, & Barrett esophagus, with its predisposition to malignancy. (تصبب) predisposing to Adenocarcinoma.

مفهوم جوا جوا

BARRETT ESOPHAGUS

▼ **(D)** Is replacement of the normal distal esophageal stratified squamous mucosa by metaplastic columnar epithelium containing goblet cells. (F15-11).

▼ **Barrett e. is a complication** of long-standing gastroesophageal reflux, occurring in 5%-15% of persons with persistent symptomatic reflux disease.

▼ **Barrett e. however** has been detected in about the same proportions in asymptomatic populations!

▼ **Barrett e.** affects males more than females (4:1) & is much more common in whites than in other races.

- زائده
- ▶ **Pathogenesis:** ① prolonged & recurrent gastroesophageal
- ② ⇒ **Reflux** produce inflammation & eventually
- ③ ⇒ **Ulceration** of the squamous epithelial lining.
- ④ ⇒ **Healing** occurs by ingrowth of progenitor cells & re-epithelialization. In the microenvironment of an abnormally acidic low pH in the distal esophagus caused by acid reflux, the cells differentiate into columnar epithelium.
- ⑤ ⇒ **Metaplastic columnar epithelium** is thought to be more resistant to injury from refluxing gastric contents

⊖ **Complications of Barrett e.:** ^① Ulcer & stricture ^② may develop, but, the chief complication of Barrett e. is the risk of the development of adenocarcinoma. most important one.

in lower part of esophagus mucin secreting mucosa

⊖ **Barrett e.** patients have a 30 to 100 fold greater risk of developing esophageal adenoca than do normal populations.

The greatest risk being associated with high-grade dysplasia.

☺ Hence, **periodic screening** for high-grade **dysplasia** with esophageal biopsy is recommended for sufferers whom require therapeutic interventions.

► **GROSSLY**, (F15-10) **Barrett e.** appears as a salmon-pink, velvety mucosa between the smooth, **pale-pink** esophageal squamous mucosa & the lusher light brown gastric mucosa.

It may exist as (1) ^{لسان} **"tongues"** extending up from the gastroesophageal junction, as (2) an irregular circumferential band displacing the squamocolumnar junction cephalad (upwards), or as (3) isolated patches (islands) in the distal esophagus.

جزء امري كله غير منتظم
بال esophagus

جزر متفرقة وممتدة بالجزء الاخير من
esophagus

موضوع مهم جداً.

ESOPHAGEAL CARCINOMA

• **Worldwide**, SCCa constitutes 90% of esophageal cancers, however, in **US**, there has been a very **large** ↑ (**3 to 5 fold in the last 40 years**) in the incidence of **adenocarcinoma** associated with Barrett esophagus, which has **surpassed** **SCCa incidence in the US!** تجاوز

☺ Adenoca arising in Barrett e. is more common in whites than in blacks. By contrast, SCCa is more common in blacks worldwide. There are striking & puzzling differences in the geographic incidence of esophageal ca.

☺ In the **US**, there are **60 new cases**/Million population/year, accounting for 1% to 2% of all cancer deaths; while

☺ In regions of **Asia** extending from the northern China to Iran, the prevalence is well over **1000 new cases**/Million/year & 20% of cancer deaths are caused by esophageal ca, mainly SCCa!

فوق هائل بين ار كا ← يعني 16 ضعف من الموجود في ار كا

Table 15-3 Risk Factors for esophageal **SCCa**

Esophageal Disorders - Long-standing *esophagitis* - *Achalasia* - *Plummer-Vinson syndrome* (esophageal webs, microcytic hypochromic anemia, atrophic glossitis) more in females.

Life-style - *Alcohol* consumption - *Tobacco* abuse

Dietary = Deficiency of vitamins (A, C, riboflavin, thiamine, pyridoxine) - Deficiency of trace metals (zinc, molybdenum) - Fungal contamination of foodstuffs - High content of nitrites/nitrosamines

Genetic Predisposition: Tylosis (hyperkeratosis of palms & soles)

Squamous Cell Carcinoma (SCCa)

▶ An important **contributing variable** is retarded passage of food through the esophagus, & prolonging mucosal exposure to potential carcinogens such as those contained in tobacco & alcohol (Table 15-3). These **(two)** agents are associated with the majority of SCCa in Europe & US.

▶ However, other influences, perhaps in the **diet**, must underlie the very high incidence of this cancer among the orthodox Moslems of Iran, whom neither drink nor smoke!

▶ The high levels of **nitrosamines & fungi contained** in some foods probably account for the very high incidence of this tumor in some regions of China. A strong association with **Human Papilloma Virus (HPV)** occurs only in high-incidence areas.

صبار في أكثر من سبب بعينه .

▶ Abnormalities affecting the p16/INK4 tumor suppressor gene & the **EGFR** are frequently present in SCCa of the esophagus. Mutations in p53 are detected in as many as 50% of these T & are generally correlate with the use of tobacco & alcohol. Unlike ca colon, mutations in the KRAS & APC genes are uncommon.

rate in osepagus.

Morphology: SCCa are usually preceded by a long period of mucosal **epithelial dysplasia**, ⇒ followed by **ca in situ** &, ⇒ finally, after invading the basement membrane, the emergence of **invasive ca**.

▶ **GROSSLY**, early lesions appear as small gray-white, plaquelike thickenings or elevations of the mucosa.

تبخن لظهي In months to years, these lesions enlarged, taking 1 of 3 forms:

- لبنو ويرتفع إلى التجويف
- (1) **Polypoid exophytic** masses, that protrude into the lumen
 - (2) **Diffuse infiltrative T** that cause thickening & rigidity of the wall & narrowing of the lumen. بجهيف اللumen.
 - (3) **Ulcerating T** that invade deeply & may erode the respiratory tree, aorta, or elsewhere (F15-12 & 4.7) &

▼ Whichever the pattern of esophageal SCC; about

20% arise in upper 1/3 & the cervical esophagus,

50% in the middle 1/3, &

30% in the lower 1/3.

most common site.

Adenocarcinoma (Adenoca)

☹️ Barrett e. is the only recognized precursor of esophageal adenocarcinoma.

☹️ The degree of dysplasia is the strongest predictor of the progression to cancer. Individuals with low-grade dysplasia have very low rates of progression to adenoca....

But, the progression to adenoca may be 10% or more per year in individuals with high-grade dysplasia. 10% كل سنة رج يتحولوا الى cancer أواكثر

● Overall, the risk for developing adenoca varies from (30 to more than 100-fold above normal)

☺️ There are **no specific markers** that precisely identify the transition from high-grade dysplasia to cancer.

▶ **Grossly**, adenoca seem to arise from dysplastic mucosa in the setting of Barrett e. لأنه reflux بهيس في ال distal

☀️ Unlike SCCa, they are usually in the **distal one-third** of the esophagus & may invade the subjacent gastric cardia. لجبرع (ال history)

Initially appearing as **flat or raised patches** on intact mucosa, they may develop into **large nodular masses** or **diffusely infiltrative**, or show deeply **ulceration**. هل كانت في stomach ومطلع أم العكس؟ (تعمد على ال history)

■ H, in keeping with the morphology of the preexisting metaplastic mucosa, the **tumors are mucin-producing adenocarcinoma** showing intestinal-type features. ال انكل ال صلب بعين (gradual) السائل بعين الشنت

☹️ Clinically, all esophageal cancers, adenocarcinomas & SCCa are slow & insidious in onset, producing dysphagia with gradual & late obstruction, followed by anorexia, weight loss, fatigue, weakness & pain on swallowing.

▼ **Diagnosis** is usually made by **imaging, endoscopy & biopsy techniques**. اناستوموز (تبرغ stomach إلى ال thorax) مع ال pharynx

☹️ **Surgical excision is rarely curative**, because esophageal cancers extensively invade the rich lymphatic network & adjacent structures relatively early in their development, thus,

much emphasis is placed on the... barben لذلك يخلص tube أو tube في ال abdomen هتتا ربتا برصه

☺️ **surveillance procedures** for individuals with persistent manifestations of chronic esophagitis or known Barrett e.

STOMACH

T15- 4 Congenital Gastric Anomalies: Condition & Comment:

★ **Pyloric stenosis** - 1 in 300-900 live births, M/Female ratio 3:1, = muscular hypertrophy of pyloric smooth muscle wall,
⇒ persistent, nonbilious projectile vomiting in young infant.

★ **Diaphragmatic hernia** - Rare, = herniation of stomach & other abdominal contents into thorax through a diaphragmatic defect, Symptoms: acute respiratory distress in newborn,

★ **Gastric heterotopia** = a nidus of gastric mucosa in the esophagus or small intestine ("ectopic rest"), Uncommon,
⇒ asymptomatic, or an anomalous (atypical) **PU** in adult.

► **Clinically**, gastric disorders give rise to symptoms similar to esophageal disorders: primarily heartburn & vague epigastric pain. With breach of the gastric mucosa & bleeding, either as a hematemesis or melena may ensue,

★ **BUT** unlike esophageal bleeding which is red & liquid, the blood quickly thrombose or solidify & turns brown in the acid environment of the stomach lumen; & therefore vomited blood has the appearance of (coffee grounds) with black granules.

fresh → vomiting from stomach.
black → vomiting from **GASTRITIS**

Gastritis is simply defined as inflammation of the gastric mucosa. By far the majority of cases are chronic gastritis, but occasionally, distinct forms of acute gastritis are encountered.

Chronic Gastritis

★ (D) the presence of chronic inflammatory changes in the mucosa, leading eventually to mucosal (atrophy & intestinal metaplasia).

☺ In the West, the prevalence of histologic changes of chronic gastritis is higher than 50% in the later decades of life.

Pathogenesis

(A) The important & the most common (90%) etiology for chronic gastritis is chronic infection {H. pylori associated chronic gastritis}.

This organism is a worldwide pathogen, & **American** adults older than age 50 show prevalence rates approaching 50%.

☺ In endemically infected areas, the infection seems to be acquired in childhood & persists for decades, with **most infected individuals having the associated gastritis, but are asymptomatic**.

☺ ☺ (Robin Warren, a pathologist, & Barry Marshall, a medical student at the time of the discovery, received the **2005 Nobel prize** in Medicine for their identification in **1982 of *H. pylori*, originally called *Campylobacter*, in 1875 !**).

لنا ▶ *H. pylori* is a noninvasive, non-spore-forming, S-shaped gram-negative rod measuring $3.5 \mu\text{m} \times 0.5 \mu\text{m}$.

▶ The gastritis develops as a result of the combined influence of bacterial enzymes & toxins; & release of noxious chemicals by recruited neutrophils (see PU).

⇒ *H. pylori* associated gastritis may develop in two patterns:

gastritis (1) Antral-type with high acid production & ↑ risk
antrum. for the development of DU, &

كل (2) Pangastritis with multifocal mucosal atrophy, with
المحرة low acid secretion & ↑ risk for gastric adenocarcinoma.

ص ← ▶ Most individuals with PU, whether DU or GU, have *H. pylori* infection.
مريض

☺ Persons with *H. pylori* associated chronic gastritis usually improve symptomatically when treated with antibiotics & proton pump inhibitors.

لكن في مرات عديدة
يرجع المرض.