4th year
Systemic pathology
GIT
Dr. mohamed sabaa ch.
M.B.CH.B Ms.Pathology
THE ORAL CAVITY & OROPHARYNX

Many pathological processes can affect the constituents of the oral cavity. The more important and frequent conditions will be covered in this lecture. Diseases involving the teeth and related structures will not be discussed.

PROLIFERATIVE LESIONS

The most common proliferative lesions of the oral cavity are:

1. Irritation Fibroma and Ossifying fibroma
2. Pyogenic granuloma
3. Peripheral giant cell granuloma
Pyogenic granuloma (granuloma pyogenicum) is a highly vascular lesion that is usually seen in the gingiva of children, young adults, and pregnant women (pregnancy tumor). The lesion is typically ulcerated and bright red in color (due to rich vascularity). Microscopically there is vascular proliferation similar to that of granulation tissue. The lesion either regresses (particularly after pregnancy), or undergoes fibrous maturation and may develop into ossifying fibroma.
INFLAMMATORY CONDITIONS

Inflammatory ulcerations

The most common inflammatory ulcerations of the oral cavity are

1. Traumatic
2. Aphthous
3. Herpetic

Traumatic ulcers, usually the result of trauma (e.g. fist fighting) or licking a jagged tooth.

Aphthous ulcers are extremely common, single or multiple, painful, recurrent, superficial, ulcerations of the oral mucosa. The ulcer is covered by a thin yellow exudate and rimmed by a narrow zone of erythema.

Herpetic ulcers (see under herpes simplex infection)
INFECTIONS

1. Herpes simplex infections

Most of these are caused by herpes simplex virus (HSV) type 1 & sometimes 2. Primary HSV infection typically occurs in children aged 2 to 4 years; is often asymptomatic, but sometime presents as acute herpetic gingivostomatitis, characterized by vesicles and ulcerations throughout the oral cavity. The great majority of affected adults harbor latent HSV-1 (the virus migrates along the regional nerves and eventually becomes dormant in the local ganglia e.g., the trigeminal)
In some individuals, usually young adults, the virus becomes reactivated to produce the common but usually mild cold sore.

Factors activating the virus include

1. Trauma
2. Allergies
3. Exposure to ultraviolet light (sunlight)
4. Upper respiratory tract infections
5. Pregnancy
6. Menstruation
7. Immunosuppression

The viral infection is associated with intracellular and intercellular edema, yielding clefts that may become transformed into vesicles. The vesicles range from a few millimeters to large ones that eventually rupture to yield extremely painful, red-rimmed, shallow ulcerations.
2. Other Viral Infections

These include:

Herpes zoster -
EBV (infectious mononucleosis) -
CMV -
Enterovirus -
Measles -
3. Oral Candidiasis (thrush)
This is the most common fungal infection of the oral cavity. The thrush is a grayish white, superficial, inflammatory psudomembrane composed of the fungus enmeshed in a fibrino-suppurative exudates. This can be readily scraped off to reveal an underlying red inflammatory base.
The fungus is a normal oral flora but causes troubles only

1. In the setting of immunosuppression (e.g. diabetes mellitus, organ or bone marrow transplant recipients, neutropenia, cancer chemotherapy, or AIDS) or

2. When broad-spectrum antibiotics are taken; these eliminate or alter the normal bacterial flora of the mouth.

3. In infants, where the condition is relatively common, presumably due to immaturity of the immune system in them.
4. Deep Fungal Infections
Some fungal infections may extend deeply to involve the muscles & bones in relation to oral cavity. These include, among others, histoplasmosis, blastomycosis, and aspergillosis.

The incidence of such infections has been increasing due to increasing number of patients with AIDS, therapies for cancer, & organ transplantation.
Many systemic diseases are associated with oral lesions & it is not uncommon for oral lesions to be the first manifestation of some underlying systemic condition.

2. Scarlet fever: strawberry tongue: white coated tongue with hyperemic papillae projecting

2. Measles: Koplik spots: small whitish ulcerations (spots) on a reddened base, about Stensen duct

3. Diphtheria: dirty white, fibrinosuppurative, tough pseudomembrane over the tonsils and retropharynx

4. AIDS
   a. opportunistic oral infections: herpesvirus, Candida, other fungi
   b. Kaposi sarcoma
   c. hairy leukoplakia
5. AML (especially monocytic leukemia): enlargement of the gingivae + periodontitis

6. Melanotic pigmentation
   a. Addison disease
   b. hemochromatosis
   c. fibrous dysplasia of bone

7. Pregnancy: pyogenic granuloma ("pregnancy tumor")
TUMORS AND PRECANCEROUS LESIONS

Many of the oral cavity tumors (e.g., papillomas, hemangiomas, lymphomas) are not different from their homologous tumors elsewhere in the body. Here we will consider only oral squamous cell carcinoma and its associated precancerous lesions.

Leukoplakia and Erythroplakia are considered premalignant lesions of squamous cell carcinoma.
Leukoplakia is a white patch that cannot be scraped off and cannot be attributed clinically or microscopically to any other disease i.e. if a white lesion in the oral cavity can be given a specific diagnosis it is not a leukoplakia. As such, white patches caused by entities such as candidiasis are not leukoplakias. All leukoplakias must be considered precancerous (have the potential to progress to squamous cell carcinoma) until proved otherwise through histologic evaluation.
Erythroplakias are red velvety patches that are much less common, yet much more serious than leukoplakias. The incidence of dysplasia and thus the risk of complicating squamous cell carcinoma is much more frequent in erythroplakia compared to leukoplakias. Both leukoplakia and erythroplakia are usually found between ages of 40 and 70 years, and are much more common in males than females. The use of tobacco (cigarettes, pipes, cigars, and chewing tobacco) is the most common incriminated factor.
Squamous cell carcinoma

The vast majority (95%) of cancers of the head and neck are squamous cell carcinomas; these arise most commonly in the oral cavity. The 5-year survival rate of early-stage oral cancer is approximately 80%, but this drops to about 20% for late-stage disease. These figures highlight the importance of early diagnosis & treatment, optimally of the precancerous lesions.
The pathogenesis of squamous cell carcinoma is multifactorial.

1. Chronic smoking and alcohol consumption
2. Oncogenic variants of human papilloma virus (HPV). It is now known that at least 50% of oropharyngeal cancers, particularly those of the tonsils and the base of tongue, harbor oncogenic variants of HPV.
3. Inheritance of genomic instability; a family history of head and neck cancer is a risk factor.
4. Exposure to actinic radiation (sunlight) & pipe smoking are known predisposing factors for cancer of the lower lip.
Gross features
Squamous cell carcinoma may arise anywhere in the oral cavity, but the favored locations are
1. The tongue
2. Floor of mouth
3. Lower lip
4. Soft palate
5. Gingiva
In the early stages, cancers of the oral cavity appear as roughened areas of the mucosa. As the lesion enlarges, it typically appears as either an ulcer or a protruding mass (fungating).
Microscopic features

Early there is full-thickness dysplasia (carcinoma in situ) followed by invasion of the underlying connective tissue stroma.

The grade varies from well-differentiated keratinizing to poorly differentiated.

As a group, these tumors tend to infiltrate and extend locally before they eventually metastasize to cervical lymph nodes and more remotely. The most common sites of distant metastasis are mediastinal lymph nodes, lung, liver and bones.
SALIVARY GLANDS
There are three major salivary glands—parotid, submandibular, and sublingual. Additionally, there are numerous minor salivary glands distributed throughout the mucosa of the oral cavity.
Xerostomia refers to dry mouth due to a lack of salivary secretion; the causes include
1. Sjögren syndrome: an autoimmune disorder, that is usually also accompanied by involvement of the lacrimal glands that produces dry eyes (keratoconjunctivitis sicca).
2. Radiation therapy
Inflammation (Sialadenitis)

Sialadenitis refers to inflammation of a salivary gland; it may be

1. Traumatic
2. Infectious: viral, bacterial
3. Autoimmune

The most common form of viral sialadenitis is mumps, which usually affects the parotids. The pancreas and testes may also be involved.
Bacterial sialadenitis is seen as a complication of
1. Stones obstructing ducts of a major salivary gland (Sialolithiasis), particularly the submandibular.
2. Dehydration with decreased secretory function as is sometimes occurs in
   a. patients on long-term phenothiazines that suppress salivary secretion.
   b. elderly patients with a recent major thoracic or abdominal surgery.
Unilateral involvement of a single gland is the rule and the inflammation may be suppurative.

The inflammatory involvement causes painful enlargement and sometimes a purulent ductal discharge.

Sjögren syndrome causes an immunologically mediated sialadenitis i.e. inflammatory damage of the salivary tissues.
NEOPLASMS OF SALIVARY GLANDS

Neoplasms of the salivary glands (benign and malignant) are generally uncommon, constituting less than 2% of human tumors. We will restrict our discussion on the more common examples.

The relative frequency distributions of these tumors in relation to various salivary glands are as follows:

- Parotid gland 80%
- Submandibular gland 10%
- Minor salivary and sublingual glands 10%
The incidence of malignant tumors within the glands is, however, different from the above:

- Sublingual tumors 80%
- Minor salivary glands 50%
- Submandibular glands 40%
- Parotid glands 25%
These tumors usually occur in adults, with a slight female predominance. Excluded from this rule is Warthin tumor, which occurs much more frequently in males than in females. The benign tumors occur most often around the age of 50 to 60 years; the malignant ones tend to appear in older age groups. Neoplasms of the parotid produce distinctive swellings in front of, or below the ear. Clinically, there are no reliable criteria to differentiate benign from the malignant tumors; therefore, pathological evaluation is necessary.
Pleomorphic Adenomas (Mixed Salivary Gland Tumors)

These benign tumors commonly occur within the parotid gland (constitute 60% of all parotid tumors).

Gross features

★ Most tumors are rounded, encapsulated masses.
★ The cut surface is gray-white with myxoid and light blue translucent areas of chondroid.

Microscopic features

★ The main constituents are a mixture of ductal epithelial and myoepithelial cells, and it is believed that all the other elements, including mesenchymal, are derived from the above cells (hence the name adenoma).
The epithelial/myoepithelial components of the neoplasm are arranged as glands, strands, or sheets. These various epithelial/myoepithelial elements are dispersed within a background of loose myxoid tissue that may contain islands of cartilage-like islands and, rarely bone.

- Sometimes, squamous differentiation is present.
- In some instances, the tumor capsule is focally deficient allowing the tumor to extend as tongue-like protrusions into the surrounding normal tissue. Enucleation of the tumor is, therefore, not advisable because residual foci (the protrusions) may be left behind and act as a potential source of multifocal recurrences.

The incidence of malignant transformation increases with the duration of the tumor.
Warthin Tumor is the second most common salivary gland neoplasm. It is benign, arises usually in the parotid gland and occurs more commonly in males than in females. About 10% are multifocal and 10% bilateral. Smokers have a higher risk than nonsmokers for developing these tumors. Grossly, it is round to oval, encapsulated mass & on section display gray tissue with narrow cystic or cleft-like spaces filled with secretion. Microscopically, these spaces are lined by a double layer of neoplastic epithelial cells resting on a dense lymphoid stroma, sometimes with germinal centers. This lympho-epithelial lining frequently project into the spaces. The epithelial cells are oncoytes as evidenced by their eosinophilic granular cytoplasm (stuffed with mitochondria).
ESOPHAGUS
The main functions of the esophagus are to 1. Conduct food and fluids from the pharynx to the stomach 2. Prevent reflux of gastric contents into the esophagus. These functions require motor activity coordinated with swallowing, i.e. wave of peristalsis, associated with relaxation of the LES in anticipation of the peristaltic wave. This is followed by closure of the LES after the swallowing reflex. Maintenance of sphincter tone (positive pressure relative to the rest of esophagus) is necessary to prevent reflux of gastric contents.
CONGENITAL ANOMALIES

Several congenital anomalies affect the esophagus including the presence of ectopic gastric mucosa & pancreatic tissues within the esophageal wall, congenital cysts & congenital herniation of the esophageal wall into the thorax. The latter is due to impaired formation of the diaphragm. Atresia and fistulas are uncommon but must be recognized & corrected early because they cause immediate regurgitation, suffocation & aspiration pneumonitis when feeding is attempted. In atresia, a segment of the esophagus is represented by only a noncanalized cord, with the upper pouch connected to the bronchus or the trachea and a lower pouch leading to the stomach.
Webs, rings, and stenosis

Mucosal webs are shelf-like, eccentric protrusions of the mucosa into the esophageal lumen. These are most common in the upper esophagus. The triad of upper esophageal web, iron-deficiency anemia, and glossitis is referred to as Plummer-Vinson syndrome. This condition is associated with an increased risk for postcricoid esophageal carcinoma.

Esophageal rings unlike webs are concentric plates of tissue protruding into the lumen of the distal esophagus. Esophageal webs and rings are encountered most frequently in women over age 40. Episodic dysphagia is the main symptom.

Stenosis consists of fibrous thickening of the esophageal wall. 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, scleroderma and caustic injury. Stenosis usually manifests as progressive dysphagia, at first to solid foods but eventually to fluids as well.
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
Achalasia

Achalasia means "failure to relax." It is characterized by three major abnormalities:

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

In most instances, achalasia is an idiopathic disorder. In this condition there is progressive dilation of the esophagus above the persistently contracted LES. 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. Young adults are usually affected and present with progressive dysphagia.
Complications of achalasia are
1. Aspiration pneumononitis of undigested food
2. Monilial esophagitis
3. Esophageal squamous cell carcinoma (about 5% of patients)
4. Lower esophagoeal diverticula
Hiatal Hernia

Hiatal hernia is characterized by separation of the diaphragmatic crura leading to widening of the space around the esophageal wall. Two types of hiatal hernia are recognized:

1. The sliding type (95%)
2. The paraesophageal type

In the sliding hernia the stomach skates up through the patent hiatus above the diaphragm creating a bell-shaped dilation. In paraesophageal hernias, a separate portion of the stomach, usually along the greater curvature, enters the thorax through the widened foramen. The cause of hiatal hernia is unknown. It is not clear whether it is a congenital malformation or is acquired during life. Only about 10% of adults with a sliding hernia suffer from heartburn or regurgitation of gastric juices into the mouth. These are due to incompetence of the LES and are accentuated by positions favoring reflux (bending forward, lying supine) and obesity.
Complications of hiatal hernias include
1. Ulceration, bleeding and perforation (both types)
2. Reflux esophagitis (frequent with sliding hernias)
3. Strangulation of paraesophageal hernias
Diverticula
By definition a diverticulum is a "focal out pouching of the alimentary tract wall that contains all or some of its constituents"; they are divided into
1. False diverticulum is an out pouching of the mucosa and submucosa through weak points in the muscular wall.
2. True diverticulum consists of all the layers of the wall and is thought to be due to motor dysfunction of the esophagus. They may develop in three regions of the esophagus
   a. Zenker diverticulum, located immediately above the UES
   b. Traction diverticulum near the midpoint of the esophagus
   c. Epiphrenic diverticulum immediately above the LES.
Lacerations (Mallory-Weiss Syndrome)
These refer to longitudinal tears at the GEJ or gastric cardia and are the consequence of severe retching or vomiting. They are encountered most commonly in alcoholics, since they are susceptible to episodes of excessive vomiting, but have been reported in persons with no history of vomiting or alcoholism. During episodes of prolonged vomiting, reflex relaxation of LES fails to occur. The refluxing gastric contents suddenly overcome the contracted musculature leading to forced, massive dilation of the lower esophagus with tearing of the stretched wall.
Pathological features

The linear irregular lacerations, which are usually found astride the GEJ or in the gastric cardia, are oriented along the axis of the esophageal lumen. The tears may involve only the mucosa or may penetrate deeply to perforate the wall. Infection of the mucosal defect may lead to inflammatory ulcer or to mediastinitis. Usually the bleeding is not profuse and stops without surgical intervention. Healing is the usual outcome. Rarely esophageal rupture occurs.
Esophageal Varices

Portal hypertension when sufficiently prolonged or severe induces the formation of collateral bypass veins wherever the portal and caval venous systems communicate. Esophageal varices refer to the prominent plexus of deep mucosal and submucosal venous collaterals of the lower esophagus subsequent to the diversion of portal blood through them through the coronary veins of the stomach. From the varices the blood is diverted into the azygos veins, and eventually into the systemic veins. Varices develop in 90% of cirrhotic patients. Worldwide, after alcoholic cirrhosis, hepatic schistosomiasis is the second most common cause of variceal bleeding.
Pathological features

The increased pressure in the esophageal plexus produces dilated tortuous vessels that are liable to rupture. Varices appear as tortuous dilated veins lying primarily within the submucosa of the distal esophagus and proximal stomach.

The net effect is irregular protrusion of the overlying mucosa into the lumen. The mucosa is often eroded because of its exposed position.

Variceal rupture produces massive hemorrhage into the lumen. In this instance, the overlying mucosa appears ulcerated and necrotic.

Rupture of esophageal varices usually produces massive hematemesis. Among patients with advanced liver cirrhosis, such a rupture is responsible for 50% of the deaths. Some patients die as a direct consequence of the hemorrhage (hypovolemic shock); others of hepatic coma triggered by the hemorrhage.
Esophagitis
This term refers to inflammation of the esophageal mucosa. It may be caused by a variety of physical, chemical, or biologic agents. Reflux Esophagitis (Gastroesophageal Reflux Disease or GERD) is the most important cause of esophagitis and signifies esophagitis associated with reflux of gastric contents into the lower esophagus. Many causative factors are involved, the most important is decreased efficacy of esophageal antireflux mechanisms, particularly LES tone. In most instances, no cause is identified. However, the following may be contributatory
a. Central nervous system depressants including alcohol
b. Smoking
c. Pregnancy
d. Nasogastric tube
e. Sliding hiatal hernia
f. Hypothyroidism
g. Systemic sclerosis

Any one of the above mechanism may be the primary cause in an individual case, but more than one is likely to be involved in most instances. The action of gastric juices is vital to the development of esophageal mucosal injury.
Gross (endoscopic) features

- These depend on the causative agent and on the duration and severity of the exposure.
- Mild esophagitis may appear grossly as simple hyperemia. In contrast, the mucosa in severe esophagitis shows confluent erosions or total ulceration into the submucosa.

Microscopic features

Three histologic features are characteristic:

1. Inflammatory cells including eosinophils within the squamous mucosa.
2. Basal cells hyperplasia
3. Extension of lamina propria papillae into the upper third of the mucosa.
The disease mostly affects those over the age of 40 years. The clinical manifestations consist of dysphagia, heartburn, regurgitation of a sour fluid into the mouth, hematemesis, or melena. Rarely, there are episodes of severe chest pain that may be mistaken for a "heart attack."

The potential consequences of severe reflux esophagitis are

1. Bleeding
2. Ulceration
3. Stricture formation
4. Tendency to develop Barrett esophagus
Barrett Esophagus (BE)
10% of patients with long-standing GERD develop this complication. BE is the single most important risk factor for esophageal adenocarcinoma. BE refers to columnar metaplasia of the distal squamous mucosa; this occurs in response to prolonged injury induced by refluxing gastric contents. Two criteria are required for the diagnosis of Barrett esophagus:
1. Endoscopic evidence of columnar lining above the GEJ
2. Histologic confirmation of the above in biopsy specimens.

The pathogenesis of Barrett esophagus appears to be due to a change in the differentiation program of stem cells of the esophageal mucosa. Since the most frequent metaplastic change is the presence of columnar cells admixed with goblet cells, the term "intestinal metaplasia" is used to describe the histological alteration.
Gross features

Barrett esophagus is recognized as a red, velvety mucosa located between the smooth, pale pink esophageal squamous mucosa and the light brown gastric mucosa.

It is displayed as tongues, patches or broad circumferential bands replacing the squamocolumnar junction several centimeters.
Microscopic features

- The esophageal squamous epithelium is replaced by metaplastic columnar epithelium, including interspersed goblet cells, & may show a villous pattern (as that of the small intestine hence the term intestinal metaplasia).

- Critical to the pathologic evaluation of patients with Barrett mucosa is the search for dysplasia within the metaplastic epithelium. This dysplastic change is the presumed precursor of malignancy (adenocarcinoma). Dysplasia is recognized by the presence of cytologic and architectural abnormalities in the columnar epithelium, consisting of enlarged, crowded, and stratified hyperchromatic nuclei with loss of intervening stroma between adjacent glandular structures. Depending on the severity of the changes, dysplasia is classified as low-grade or high-grade.
Approximately 50% of patients with high-grade dysplasia may already have adjacent adenocarcinoma.

Most patients with the first diagnosis of Barrett esophagus are between 40 and 60 years. Barrett esophagus is clinically significant due to

1. The secondary complications of local peptic ulceration with bleeding and stricture.

2. The development of adenocarcinoma, which in patients with long segment disease (over 3 cm of Barrett mucosa), occurs at a frequency that is 30- to 40 times greater than that of the general population.
Other causes of esophagitis

In addition to GERD (which is, in fact, a chemical injury), esophageal inflammation may have many origins. Examples include ingestion of mucosal irritants (such as alcohol, corrosive acids or alkalis as in suicide attempts), cytotoxic anticancer therapy, bacteremia or viremia (in immunosuppressed patients), fungal infection (in debilitated or immunosuppressed patients or during broad-spectrum antimicrobial therapy; candidiasis by far the most common), and uremia.
TUMORS

Benign Tumors
Leiomyomas are the most common benign tumors of the esophagus.

Malignant Tumors
Carcinomas of the esophagus (5% of all cancers of the GIT) have, generally, a poor prognosis because they are often discovered too late. Worldwide, squamous cell carcinomas constitute 90% of esophageal cancers, followed by adenocarcinoma. Other tumors are rare.
Squamous Cell Carcinoma (SCC)
Most SCCs occur in adults over the age of 50. The disease is more common in males than females. The regions with high incidence include Iran & China. Blacks throughout the world are at higher risk than are whites.

Etiology and Pathogenesis
Factors Associated with the Development of Squamous Cell Carcinoma of the Esophagus are classified as
1. Dietary
Deficiency of vitamins (A, C, riboflavin, thiamine, and pyridoxine) & trace elements (zinc)
Fungal contamination of foodstuffs
High content of nitrites/nitrosamines
Betel chewing (betel: the leaf of a climbing evergreen shrub, of the pepper family, which is chewed in the East with a little lime.)
2. Lifestyle
   Burning-hot food
   Alcohol consumption
   Tobacco abuse

3. Esophageal Disorders
   Long-standing esophagitis
   Achalasia
   Plummer-Vinson syndrome

4. Genetic Predisposition
   Long-standing celiac disease
   Racial disposition
The marked geographical variations in the incidence of the disease strongly implicate dietary and environmental factors, with a contribution from genetic predisposition. The majority of cancers in Europe and the United States are attributable to alcohol and tobacco. Some alcoholic drinks contain significant amounts of such carcinogens as polycyclic hydrocarbons, nitrosamines, and other mutagenic compounds. Nutritional deficiencies associated with alcoholism may contribute to the process of carcinogenesis.

Human papillomavirus DNA is found frequently in esophageal squamous cell carcinomas from high-incidence regions.
Gross features

Like squamous cell carcinomas arising in other locations, those of the esophagus begin as in situ lesions.

When they become overt, about 20% of these tumors are located in the upper third, 50% in the middle third, and 30% in the lower third of the esophagus.

Early lesions appear as small, gray-white, plaque-like thickenings of the mucosa but with progression, three gross patterns are encountered:

1. Fungating (polypoid) (60%) that protrudes into the lumen
2. Flat (diffusely infiltrative) (15%) that tends to spread within the wall of the esophagus, causing thickening, rigidity, and narrowing of the lumen
3. Excavated (ulcerated) (25%) that digs deeply into surrounding structures and may erode into the respiratory tree (with resultant fistula and pneumonia) or aorta (with catastrophic bleeding) or may permeate the mediastinum and pericardium.
Local extension into adjacent mediastinal structures occurs early, possibly due to the absence of serosa for most of the esophagus. Tumors located in the upper third of the esophagus also metastasize to cervical lymph nodes; those in the middle third to the mediastinal, paratracheal, and tracheobronchial lymph nodes; and those in the lower third most often spread to the gastric and celiac groups of nodes.
Microscopic features

- Most squamous cell carcinomas are moderately to well-differentiated,
- They are invasive tumors that have infiltrated through the wall or beyond.

The rich lymphatic network in the submucosa promotes extensive circumferential and longitudinal spread.

Esophageal carcinomas are usually quite large by the time of diagnosis, produces dysphagia and obstruction gradually. Cachexia is frequent. Hemorrhage and sepsis may accompany ulceration of the tumor.

The five-year survival rate in patients with superficial esophageal carcinoma is about 75%, compared to 25% in patients who undergo "curative" surgery for more advanced disease. Local recurrence and distant metastasis following surgery are common. The presence of lymph node metastases at the time of resection significantly reduces survival.
Adenocarcinoma
With increasing recognition of Barrett mucosa, most adenocarcinomas in the lower third of the esophagus arise from the Barrett mucosa.

Etiology and Pathogenesis
These focus on Barrett esophagus. The lifetime risk for cancer development from Barrett esophagus is approximately 10%. Tobacco exposure and obesity are risk factors. Helicobacter pylori infection may be a contributing factor.
Gross features:

- adenocarcinomas arising in the setting of Barrett esophagus are usually located in the distal esophagus and may invade the adjacent gastric cardia.
- As is the case with squamous cell carcinomas, adenocarcinomas initially appear as flat raised patches that may develop into large nodular fungating masses or may exhibit diffusely infiltrative or deeply ulcerative features.
Microscopic features

- Most tumors are mucin-producing glandular tumors exhibiting intestinal-type features.
- Multiple foci of dysplastic mucosa are frequently present adjacent to the tumor.

Adenocarcinomas arising in Barrett esophagus chiefly occur in patients over the age of 40 years and similar to Barrett esophagus, it is more common in men than in women, and in whites more than blacks (in contrast to squamous cell carcinomas).
As in other forms of esophageal carcinoma, patients usually present because of difficulty swallowing, progressive weight loss, bleeding, and chest pain. The prognosis is as poor as that for other forms of esophageal cancer, with under 20% overall five-year survival. Identification and resection of early cancers with invasion limited to the mucosa or submucosa improves five-year survival to over 80%. Regression or surgical removal of Barrett esophagus has not yet been shown to eliminate the risk for adenocarcinoma.