Oesophagus

Gastroesophageal reflux disease (GERD)

- Consequence of the failure of the normal antireflux barrier to protect against frequent and abnormal amounts of gastroesophageal reflux

Epidmiology

- GERD is common
- The prevalence of GERD is relatively low among residents of Africa and Asia
- True prevalence of esophagitis is very difficult to define

In Asia

Possible reasons for the lower GERD prevalence include

- low dietary fat
- low body mass index (BMI)
- lower gastric acid output, possibly related to *Helicobacter pylori* infection

Associations

- Obesity and GERD
- Increasing age
- Genetics

PATHOGENESIS

Imbalance between

- Defensive factors (three-tiered)
- Aggressive factors

Protective factors

- ANTIREFLUX BARRIERS
- The first tier
- Anatomically complex region including the intrinsic lower esophageal sphincter (LES), diaphragmatic crura, the intra-abdominal location of the LES, the phrenoesophageal ligaments, and the acute angle of His

MECHANISMS OF REFLUX

- Transient Lower Esophageal Sphincter Relaxations
- Swallow-Induced Lower Esophageal Sphincter Relaxations
- Hypotensive Lower Esophageal Sphincter Pressure
- HIATAL HERNIA

ESOPHAGEAL ACID CLEARANCE

Second tier

- Volume Clearance
- Salivary and Esophageal Gland Secretions

Tissue Resistance

Third tier

- The *pre-epithelial* defense- mucous layer / buffering capacity by the surface cells to secrete bicarbonate ions into the unstirred water layer
- The *epithelial* defenses - cell membranes and intercellular junctional complexes of the esophageal mucosa

- The *postepithelial* defense is provided by the esophageal blood supply.
- Blood flow delivers oxygen, nutrients, and bicarbonate and removes H+ and CO2, thereby maintaining normal tissue acid-base balance

Aggressive factors

- GASTRIC FACTORS –
- Volume and components of the gastric refluxate

- Duodenogastric Reflux
- Delayed Gastric Emptying

CLINICAL FEATURES

- CLASSIC REFLUX SYMPTOMS - Heartburn
- Other common symptoms of GERD -are acid regurgitation and dysphagia
- Less common symptoms associated with GERD include water brash, odynophagia, burping, hiccups, nausea, and vomiting
- Some patients with GERD are asymptomatic

EXTRAESOPHAGEAL MANIFESTATIONS

- Noncardiac chest pain
- Asthma
- Posterior laryngitis,
- Chronic cough
- Recurrent pneumonitis
- Dental erosion

ASSOCIATED CONDITIONS

- The most common is pregnancy
- Scleroderma
- Zollinger-Ellison syndrome
- After Heller myotomy for achalasia
- Prolonged nasogastric intubation may cause reflux esophagitis

DIAGNOSIS

- **Tests for Reflux**

  Intraesophageal pH monitoring (catheter or catheter-free system)

  Ambulatory impedance and pH monitoring (nonacid reflux)

  Barium esophagogram

- **Tests to Assess Symptoms**

  Empirical trial of acid suppression

  Intraesophageal pH monitoring with symptom analysis

- **Tests to Assess Esophageal Damage**
  - Endoscopy
  - Wireless capsule endoscopy
  - Esophageal biopsy
  - Barium esophagogram

- **Tests to Assess Esophageal Function**
  - Esophageal manometry
  - Esophageal impedance

Endoscopic Grading Systems for Esophagitis

Los Angeles Classification

- Grade A One or more mucosal breaks confined to folds, ≤5 mm
- Grade B One or more mucosal breaks >5 mm confined to folds but not continuous between tops of mucosal folds
- Grade C Mucosal breaks continuous between tops of two or more mucosal folds but not circumferential
- Grade D Circumferential mucosal break

CLINICAL COURSE

- NONEROSIVE REFLUX DISEASE
- EROSIVE REFLUX DISEASE

COMPLICATIONS

- HEMORRHAGE, ULCERS, AND PERFORATION Clinically important hemorrhage has been reported in 7% to 18% of GERD patients
- PEPTIC ESOPHAGEAL STRICTURES
- Strictures occur in 7% to 23% of patients with untreated reflux esophagitis
- BARRETT'S ESOPHAGUS

TREATMENT OF UNCOMPLICATED DISEASE

- Lifestyle Modifications
- Elevating the head of the bed
- Avoiding tight-fitting clothes
- Losing weight if overweight
- Restricting alcohol and smoking,
- Making dietary changes
- Refraining from lying down after meals,
- Avoiding bedtime snacks.

PRESCRIPTION MEDICATIONS

- Prokinetic Drugs
- Histamine-2 Receptor Antagonists (H2RAs)
- Proton Pump Inhibitors

MAINTENANCE THERAPIES

SURGICAL THERAPY

- Laparoscopic surgery
- Nissen fundoplication, Belsey Mark IV repair, and Hill posterior gastropexy

Antireflux surgery is a reasonable option in

(1) the healthy patient with typical or atypical GERD symptoms well controlled on PPIs desiring alternative therapy because of drug expense, poor medication compliance, or fear of unknown long-term side effects;

(2) patients with volume regurgitation and aspiration symptoms not controlled on PPIs; and

(3) recurrent peptic strictures in younger patients.

ENDOSCOPIC THERAPY

- Delivery of radiofrequency energy to the gastroesophageal junction (Stretta)
- Injection of bulking agents (Enteryx)
- Implantation of a bioprosthesis (Gatekeeper) into the LES
- Suture plication of the proximal gastric folds (EndoCinch endoscopic plication system)

Barrett's esophagus

- Abnormal columnar epithelium that is predisposed to malignancy replaces the stratified squamous epithelium that normally lines the distal esophagus

DIAGNOSIS

- Barrett's esophagus is diagnosed by endoscopic examination, and
- Two criteria must be fulfilled.

  - First, the endoscopist must ascertain that columnar-appearing epithelium lines the distal esophagus.

  - Second, biopsy specimens of that columnar-appearing epithelium must show evidence of metaplasia

- Barrett's esophagus can be further categorized as long-segment (when the metaplastic epithelium extends at least 3 cm above the GEJ) or short-segment (when <3 cm of metaplastic epithelium lines the esophagus).
- The Prague C and M criteria, identifies the circumferential (C) and the maximum extent (M) of Barrett's metaplasia.

PATHOGENESIS

- GERD

DYSPLASIA (also called intraepithelial neoplasia)

- Before neoplastic Barrett's cells become malignant, some of the same genetic alterations that endow the physiologic attributes of malignancy
- Dysplasia is recognized by cytologic and architectural abnormalities in esophageal biopsy specimens

- Dysplasia is categorized as low-grade or high-grade depending on the degree of histologic abnormalities, with more pronounced abnormalities assumed to reflect more severe genetic damage and greater potential for carcinogenesis
- Patients who have non-neoplastic Barrett's esophagus develop low-grade dysplasia at the rate of 4.3% per year, and high-grade dysplasia at the rate of 0.9% per year
- The overall incidence of cancer development in patients with Barrett's esophagus is approximately 0.5% per year

MANAGEMENT

- TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE
- ENDOSCOPIC SURVEILLANCE FOR DYSPLASIA

TREATMENT OF DYSPLASIA

- For patients found to have high-grade dysplasia, there are several proposed management options, as discussed following.

- Esophagectomy
- Endoscopic Therapies

Two general types of endoscopic therapies

(1) endoscopic ablative therapy, which uses thermal energy (e.g., delivered by laser, electrocoagulation, argon plasma coagulation, the HALO360 System, B?RRX Medical, Sunnyvale, Calif., cold nitrogen gas) or photochemical energy (photodynamic therapy) to ablate the Barrett's epithelium

(2) endoscopic mucosal resection (EMR), in which a diathermic snare or endoscopic knife is used to remove a segment of Barrett's epithelium, usually down to the submucosa

Tumors of the Esophagus

EPITHELIAL TUMORS	NONEPITHELIAL TUMORS
Malignant Squamous cell carcinoma Adenocarcinoma Adenocarcinoma of the esophagogastric junction Verrucous carcinoma Carcinosarcoma Small cell carcinoma Malignant melanoma	**Malignant** Lymphoma Sarcoma, including malignant GIST Metastatic carcinoma
Benign Squamous papilloma Adenoma Inflammatory fibroid polyp	**Benign** GIST Leiomyoma Granular cell tumor Fibrovascular tumor Hemangioma Hamartoma Lipoma

CARCINOMA

- Most common types –
  - squamous cell cancer
  - adenocarcinoma
- Median age at diagnosis - 69
- Higher in men

- Squamous cell cancer - commonest type, worldwide
- More than 80% of these cancers occurring in developing countries
- Persons with low socioeconomic status - two-fold higher risk

- Squamous cell esophageal cancer - decreased in most Western countries
- Disturbing upward trend in the incidence of esophageal and gastroesophageal junctional adenocarcinoma

ETIOLOGY AND RISK FACTORS (SQUAMOUS CELL CANCER)

- Dietary and Nutritional Factors

  - Drinking from non–tap water
  - Exposure to polycyclic aromatic hydrocarbons commonly present in soot extract of coal-burning stoves
  - Dietary intake of N-nitroso compounds
  - Low levels of selenium
  - zinc deficiency
  - low dietary folate intake

- Alcohol and Tobacco
- *Tylosis*
- *Plummer-Vinson syndrome*
- *Radiation therapy*
- Patients with history of *squamous cell cancer of the upper aero-digestive tract*
- *Achalasia*
- Ingestion of *lye*, a caustic corrosive agent

ETIOLOGY AND RISK FACTORS (ADENOCARCINOMA)

- Dietary and Nutritional Factors
- Diets high in fiber, *beta-carotene*, folate, and vitamins C, E, and B6 may be protective
- Diets high in cholesterol, animal protein, and *vitamin B12* may be associated an with increased risk of esophageal adenocarcinoma

- Alcohol and Tobacco
- Association between alcohol and tobacco use is less consistent
- **Obesity**
- **Barrett's Esophagus**

- Squamous cell esophageal cancers
  - 50% to 60% middle third
  - 33% distal esophagus
  - 10% proximal esophagus
- Almost all esophageal adenocarcinomas arise in the setting of Barrett's esophagus and typically occur in the distal third of the esophagus, including the esophagogastric junction

CLINICAL FEATURES

- Progressive dysphagia
- Disproportionate weight loss.
- Chest pain or pain radiating to the back
- Hoarseness can result from recurrent laryngeal nerve involvement by the tumor per se or metastatic lymph nodes.
- Esophago -respiratory fistula develops in approximately 5% to 15% of all patients with advanced esophageal cancer
- Fistula usually manifests with intractable cough and recurrent pneumonia.
- Uncommon sites of fistulae from esophageal carcinoma include extension to the aorta, pleura, pericardium, and mediastinum.

DIAGNOSIS

- Contrast Esophagography
- Computed Tomography
- Endoscopy and Biopsy
  - Conventional Chromoendoscopy
  - Electronic Chromoendoscopy
  - Spectroscopic Imaging
- Endoscopic Ultrasonography
- PET

TREATMENT

- Early Esophageal Cancers
- Early esophageal cancers include carcinoma in situ (Tis) or cancers that invades the mucosa (T1a or T1m) or submucosa (T1b or T1sm) but without nodal disease (i.e., T1, N0, M0)

Endoscopic Therapy

- Early esophageal cancers with m1 or m2 depth of invasion have little or no risk of nodal disease.
- In such patients, endoscopic resection may be an attractive alternative to surgery.

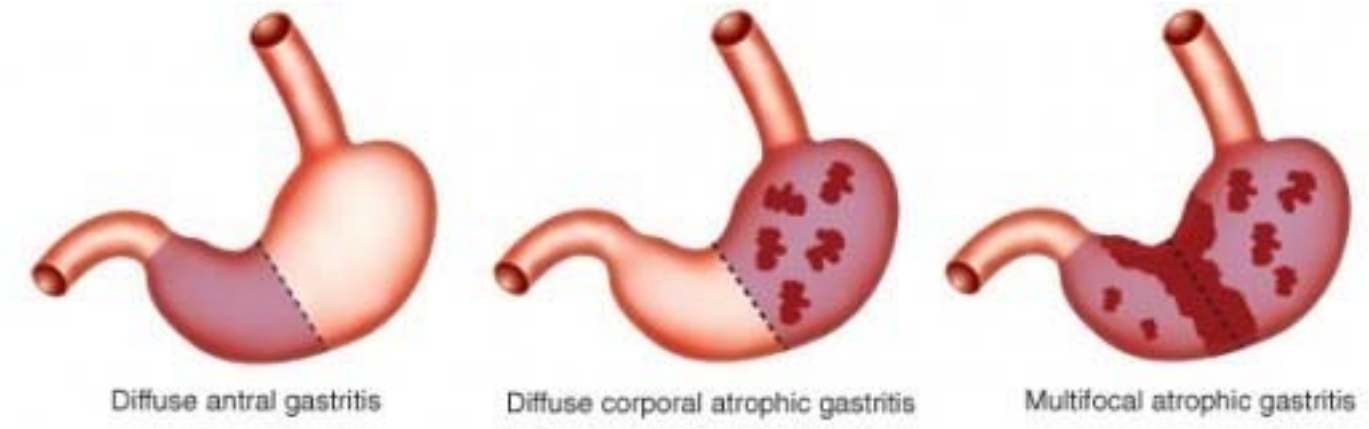
Surgical Therapy

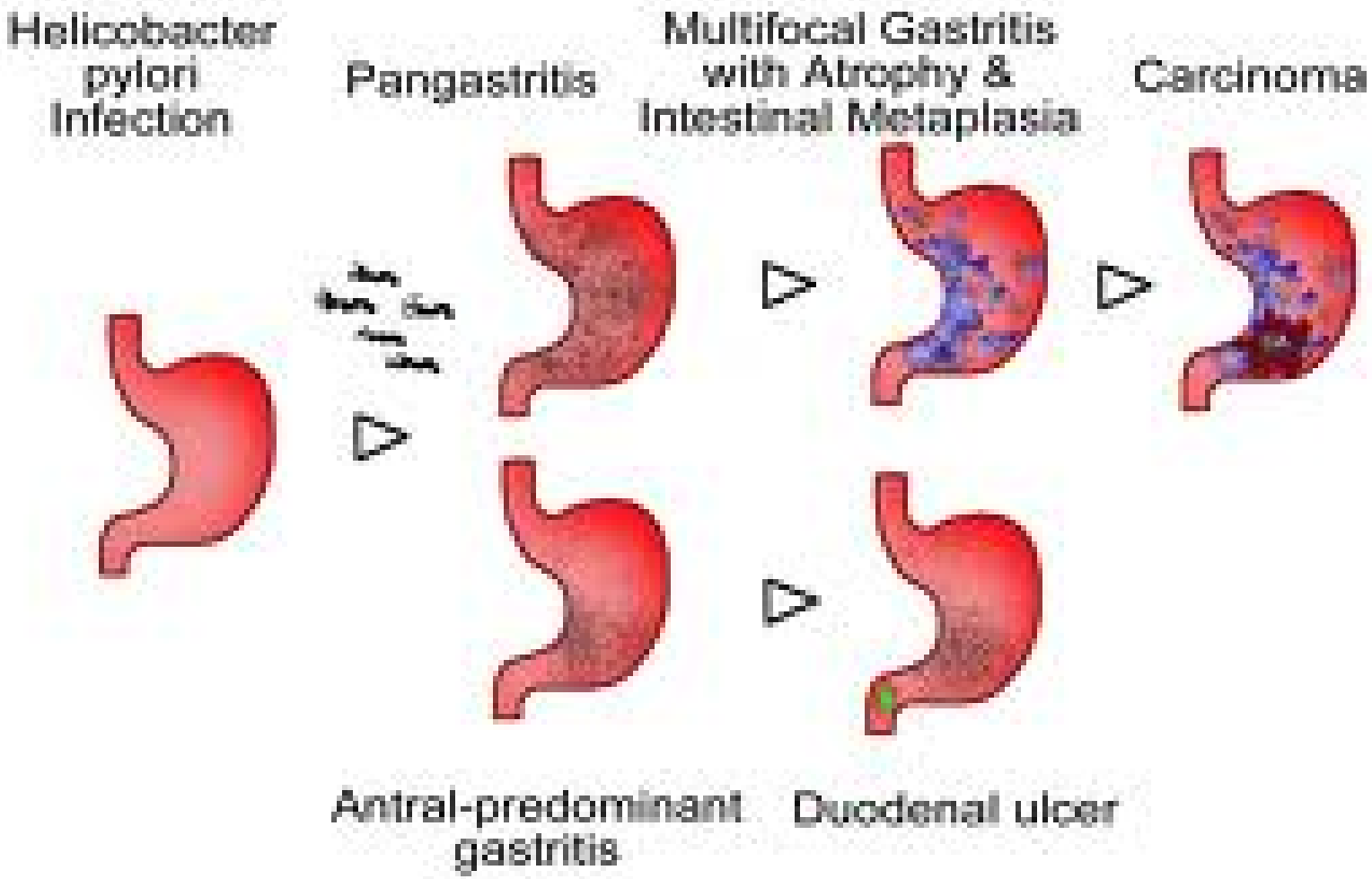
- Radiation Therapy and Chemotherapy

Esophageal Stent Placement

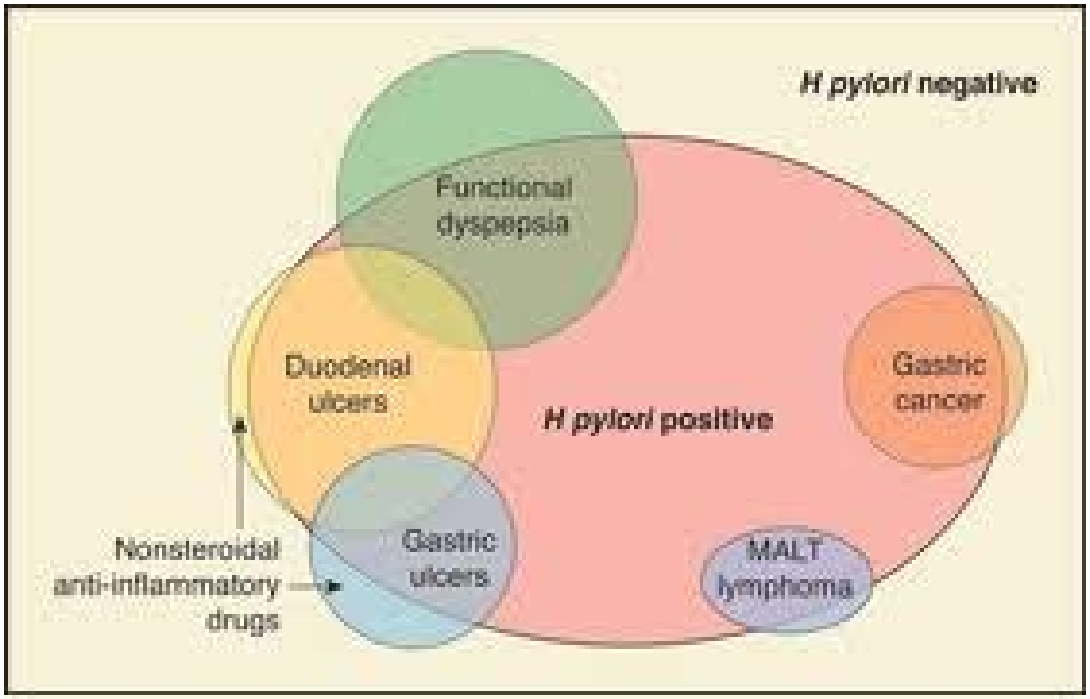
CHRONIC GASTRITIS

Three types




Helicobacter pylori Infection
Pangastritis
Multifocal Gastritis with Atrophy & Intestinal Metaplasia
Carcinoma
Antral-predominant gastritis
Duodenal ulcer

Peptic Ulcer Disease



HELICOBACTER PYLORI INFECTION

- *H. pylori* infection was the cause of 90% or more of duodenal ulcers, and 60% or more of all gastric ulcers
- ASPIRIN AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS
- Smoking
- The role of alcohol remains uncertain
- An association between the ingestion of spicy foods and peptic ulcer disease is weak, at best
- Emotional stress was proposed as a major cause of ulcer disease or as a precipitant of ulcer complications

CLINICAL FEATURES

- The “classic” symptoms attributed to peptic ulcer disease included a burning pain the epigastrium relieved by antacids

DIAGNOSIS

- **Alarm Features in Patients with Suspected Peptic Ulcer Disease***
- Age older than 55 years with new-onset dyspepsia
  Family history of upper gastrointestinal cancer
  Gastrointestinal bleeding, acute or chronic, including unexplained iron deficiency
  Jaundice
  Left supraclavicular lymphadenopathy (Virchow's node)
  Palpable abdominal mass
  Persistent vomiting
  Progressive dysphagia
  Unintended weight loss

- EGD

COMPLICATIONS

- HEMORRHAGE
- PENETRATION AND PERFORATION
- OBSTRUCTION

Treatment of Peptic Ulcer Disease

Antacids

- Proton Pump Inhibitors
- H2#

MUCOSA-PROTECTIVE AGENTS
Sucralfate

Bismuth

prostaglandin E2 (PGE2)analogues

ULCERS ASSOCIATED WITH *HELICOBACTER PYLORI* INFECTION

TREATMENT OF COMPLICATIONS OF PEPTIC ULCER DISEASE

- HEMORRHAGE

Forrest classification

- Clean base (type III)
- Flat pigmentation (type IIc)
- Adherent clot (type IIb)
- Nonbleeding visible vessel (type IIa)
- Active bleeding (type I)

- Pharmacological
- Endoscopic
- Surgical

PERFORATION

OBSTRUCTION

- Endoscpic
- Surgical