lecture 2[*2hrs]*

2-Diffuse Esophageal Spasm

Characterized by non-peristaltic contractions, usually of large amplitude and long duration, the lower esophageal sphincter may have normal high pressure and may not completely relax with swallowing.

Diagnosis

Barium swallow shows uncoordinated simultaneous contractions that produce the appearance of the corkscrew esophagus.

Diffuse esophageal spasm is best diagnosed by manometry, the abnormality may be episodic.

Presentation

*Chest pain usually occurs at rest but may be induced by swallowing or emotional stress. The pain may last from a few seconds to several minutes. Some cases occur in response to gastro-Esophageal reflux.

*Dysphagia for solids and liquids may occur with or without chest pain.

Treatment -PPI when gastro-Esophageal reflux is present. The agent that relaxes smooth muscle such as sublingual nitroglycerin or longer-acting agents such as isosorbide dinitrate or nifedipine before meals.

Diffuse esophageal spasm and related esophageal motor disorders must be differentiated from other causes of chest pain, particularly ischemic heart disease with atypical angina. A complete cardiac workup should be done before a non-cardiac etiology is considered seriously. The presence of dysphagia with pain should point to the esophagus as the site of disease.

Secondary causes of esophageal dysmotility

Systemic sclerosis.

The esophageal lesions in systemic sclerosis consist of atrophy of smooth muscle manifested by weakness in the lower two-thirds of the esophagus and incompetent of the LES.

Barium swallow shows dilatation and loss of peristalsis in the middle and distal portion of the esophagus with incompetent LES so GER may occur. Similar esophageal motor abnormalities are found in other collagen vascular diseases including **Raynaud's phenomenon. dermatomyositis, rheumatoid arthritis, and myasthenia gravis**.

Patients usually present with *dysphagia to solids. Liquids may cause dysphagia when the patient is recumbent*Heartburn, regurgitation, and other symptoms of gastro esophageal reflux disease (GERD). Barium swallow shows dilation and loss of peristaltic contractions in the middle and distal portions of the esophagus.

Treatment

Dietary adjustments with used soft foods, GERD, and its complications should be treated aggressively.

Causes of an esophageal stricture include *GERD *Webs and rings* Carcinoma of the esophagus*****Extrinsic compression *Corrosive ingestion *Postoperative scaring *Post radiotherapy *Following long term Naso-gastric intubations.

Esophageal Cancer

Cancer of the esophagus is more common in males than females most often after age 50. Most common are squamous cell carcinomas. Squamous cancer can arise in any part of the esophagus from the post cricoid region to the cardia.

Adenocarcinoma arises in the distal esophagus in the presence of Barrett's esophagus or from the cardia. About 15% of esophageal cancers occur in the upper third of the esophagus, 40% in the middle third, and 45% in the lower third.

Squamous cell carcinomas and adenocarcinoma of the esophagus cannot be distinguished radio graphically or endoscopically.

* **Risk factors for squamous cancer include**

1-Alcohol.

2-Smoking.

3-Celiac disease.

4-Ingestion of lye.
5-Radiation-induced strictures.
6-Achalasia.
7-Post-cricoid web.
8-Tylosis [familial hyperkeratosis of the palms and soles].

Clinical Features

*Progressive painless dysphagia for solid foods and gradually progresses to include semisolids and liquids.
*Acute dysphagia occurs because of food impaction.
*Weight loss
*Chest pain or hoarseness of voice suggest Mediastinal invasion.
*Tracheo-esophageal fistula leads to
1-Coughing after swallowing.
2-Pneumonia.
3-Plural effusion.

The disease most commonly spreads to adjacent and supraclavicular lymph nodes, liver, lungs and pleura.

Diagnosis

*Upper gastrointestinal endoscopy with biopsy is the Investigation of choice.
*Barium swallow May show ulcerating changes in the mucosa and association with deeper infiltration producing a picture like Achalasia in case of lower esophageal tumor.
*Chest X-ray shows Mediastinal lymph node and evidence of aspiration.
*Computed tomography (CT) scans of the chest and abdomen. [Assess the tumor spread to the mediastinum and Para-aortic lymph nodes].
*Endoscopic ultrasound. Shows Grade of invasion in the esophageal wall.

Treatment

*Surgery [Esophagectomy].
*Radiotherapy for [squamous carcinoma in the upper 1/3].
*Palliative for the incurable and surgically unresectable tumor of the esophagus
for [relief of pain, dysphagia, malnutrition, and Tracheo-esophageal fistulas].
Palliation include
1-Endoscopic dilatation.
2-Surgical placement of a gastrostomy or jejunostomy for hydration and feeding.
3-Endoscopic placement of an expandable metal stent to bypass the tumor.
4-Endoscopic fulguration of the obstructing tumor with lasers.

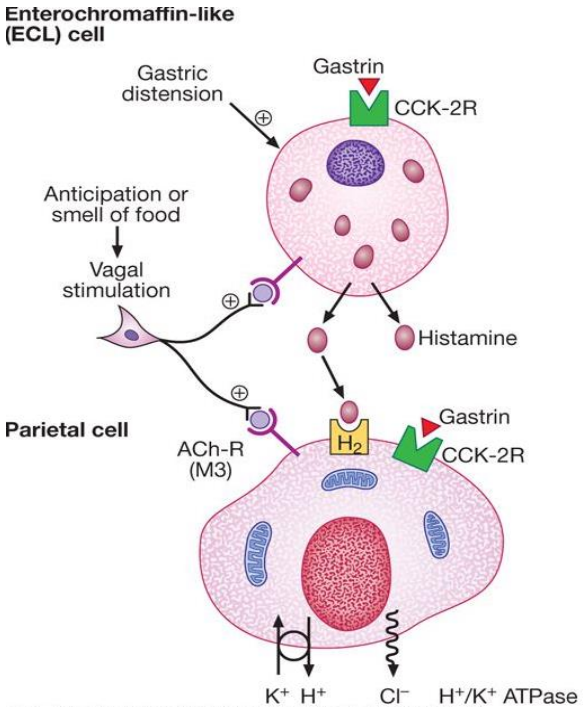
Prognosis The overall 5- years survival is 6-9 %.

Stomach and duodenum

Food is stored in the stomach for some time mixed with acid, mucus, pepsin, and gradually released into the duodenum. In addition to mucus-secreting cells that line the entire surface of the stomach.
The stomach mucosa has two important types of glands.
1-The oxyntic (acid-forming) glands are located in the body and fundus of the stomach and composed of three types of cells
A-Mucous neck cells. Which secrete mucus.
B-Chief cells. Which secrete pepsinogen.
C-Parietal cells. Which secrete hydrochloric acid and intrinsic factor.
2-The pyloric glands are located in the antral portion of the stomach which secrete mainly mucus for protection of the pyloric mucosa from the acid and Gastrin hormone.

Control of acid secretion.

Gastrin released from antral G cells in response to food binds to cholecystokinin receptors (CCK-2R) on the surface of enterochromaffin-like (ECL) cells, which in turn release histamine. The histamine binds to H_2 receptors on parietal cells and this leads to the secretion of hydrogen ions, in exchange for potassium ions at the apical membrane. Parietal cells also express CCK-2R and it is thought that activation of these receptors by gastrin is involved in the regulatory proliferation of parietal cells. Cholinergic (vagal) activity and gastric distension also stimulate acid secretion; somatostatin, vasoactive intestinal polypeptide (VIP) and gastric inhibitory polypeptide (GIP) inhibit parietal cell secretion.



Functions of HCL

1-Maintains sterility of the stomach by killing ingested bacteria.
2-Dissolves food particles and changes food into chyme.
3-Activates pepsinogen into active pepsin.
4-Provides optimum pH for the action of pepsin.
5-Helps iron and calcium absorption.

***Secretion and Activation of Pepsinogen.**

Pepsinogens are secreted by the Chief cells of the gastric gland. pepsinogen has no digestive activity. When it comes in contact with hydrochloric acid it is activated to pepsin. Pepsin functions as an active proteolytic enzyme in a highly acid medium (optimum pH 1.8 to 3.5), but above a pH of about 5 it h becomes completely inactivated.

***Secretion of Intrinsic Factor.** The intrinsic factor is secreted by the parietal cells along with the secretion of hydrochloric acid.

Pernicious anemia Autoimmune destruction of parietal cells results in the deficient secretion of intrinsic factor

*Gastrin hormone secreted by G cells in the antrum it acts either directly on oxyntic glands or indirectly through stimulation of the secretion of histamine from enterochromaffin-like cells.

Secretion of mucous in the stomach,

There are 2 types of mucous

1-Soluble mucous--It is secreted by mucous neck cells of the gastric glands in response to vagal stimulation.

2-Insoluble mucous--It is secreted by the surface epithelium of the gastric body, fundus and pyloric region it forma a layer 1.5 mm in thickness to protect the gastric mucous against the mechanical friction with food and to neutralize the corrosive effect of the acid.

3-Phases of Gastric Secretion-Gastric secretion occurs in 3 phases

1-The Cephalic Phase.
The cephalic phase results from the sight, smell, thought, or taste of food. The Neurogenic signals causing the cephalic phase originate in the cerebral cortex and the appetite centers. These signals are transmitted through the vagus nerves to the stomach. Vagal stimulation increases gastric secretion by acetylcholine and by Gastrin releasing peptide that stimulates Gastrin secretion. This phase of secretion normally accounts for about 20 percent of the gastric secretion associated with eating a meal.
2-Gastric Phase. Once food enters the stomach it excites gastric secretion by
3 mechanisms
(1) Long vago-vagal reflexes from the stomach to the brain and back to the stomach.
(2) Local enteric reflexes.
(3) The gastrin mechanism.
3-Intestinal Phase. The presence of food in the duodenum will continue to cause the secretion of small amounts of gastric juice.
inhibition of Gastric Secretion
inhibition of gastric secretion results from two mechanisms.
1-Neural mechanism
***** Entero-gastric reflex. This reflex can be initiated by
*Distention of the small bowel.
*The presence of acid in the upper intestine.
*The presence of protein breakdown products.
*Irritation of the mucosa.
this reflex is transmitted through the myenteric nervous system, extrinsic sympathetic and vagus nerves.
2-Hormonal mechanism The presence of acid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids or any irritating factor in the upper small intestine causes the release of several intestinal hormones which include
[***secretin, gastric inhibitory peptide, vasoactive intestinal polypeptide, and Somatostatin***] all these hormones inhibit gastric secretion.
Gastric Secretion during the Interdigestive Period.
The stomach secretes a few milliliters of gastric juice composed mainly of mucus, pepsin, and no acid each hour during the Interdigestive period. Emotional stimuli increase Interdigestive gastric secretion. This increase of secretion can be one of the causative factors in the development of peptic ulcers**.**

Peptic Ulcer Disease[PUD]

Ulcers are defined as a break in the mucosal surface >5 mm in size in an area exposed to HCL which include [lower esophagus, stomach, duodenum and in the jejunum after surgical anastomosis to the stomach or in the ileum adjacent to Meckel's diverticulum].
*Ulcers may be acute or chronic both penetrate the muscularis mucosa.
*Acute ulcer shows no evidence of fibrosis.
The male to female ratio for duodenal ulcer varies from 5:1--2:1 whilst that for gastric ulcer is 2:1 or less.
*Duodenal Ulcers Occur mostly in the first part of the duodenum. They are usually less than 1 cm in diameter but can occasionally reach 3 to 6 cm (giant ulcer).
Factors involved in the development of PUD.
1-H. Pylori infection. ,
H. pylori is a major pathogen in humans. Is a gram-negative micro-aerophilic rod microorganism, It is S-shaped and contains multiple flagella. Lives in the mucus layer of the

stomach. Initially, H. pylori localized in the antrum but over time migrate towards the body and fundus of the stomach. More than 50% of world populations are infected with the bacterium.
H. pylori transmission occurs from person to person, following an oral-oral or fecal-oral route or through inadequately sterilized endoscopes and nasogastric tube.

Pathophysiology

H.pylori infection is usually causing chronic active gastritis but only 10 - 15% of infected individuals develop peptic ulceration.

>90% of all DUs were associated with H. pylori and 70% of patients with GU.

Virulence factors of H pylori include

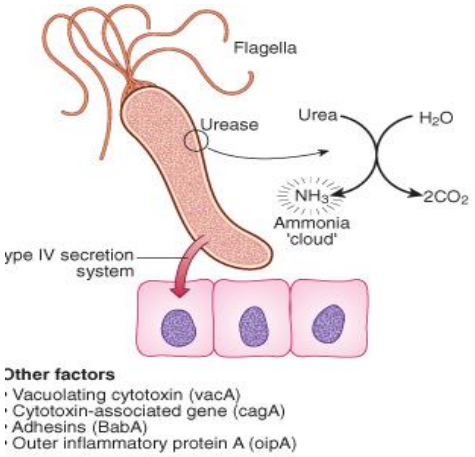
A-Motility helps bacteria to move from gastric lumen with low ph. to the mucosal surface where pH is neutral.

B-Adhesions [BebA] helps HP to bind to the gastric epithelium.

C-Urease –HP produces urease an enzyme that breaks down urea to carbon dioxide and alkaline ammonia. ammonia protects the bacterium from the gastric acid environment.

D-Toxins

*Vacuolating Cytotoxin[vagA] that cause a local inflammatory response and tissue injury of gastric mucosa.*Cytotoxin –associated gene. cagA allows the bacterial macromolecule to translocate into the host cell.*Phospholipase A which help H. Pylori to penetrate gastric mucus.

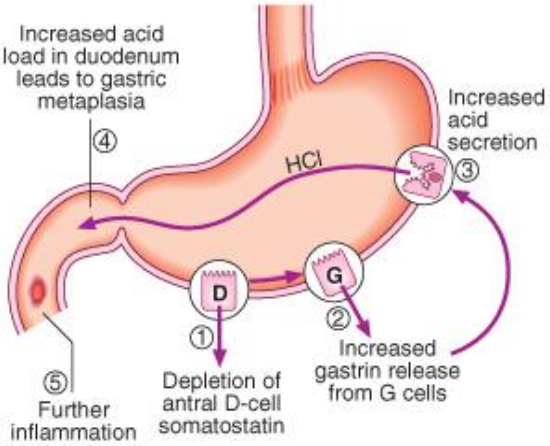


in response to H. pylori infection, several cytokines are released including, tumor necrosis factor (TNF), interleukins [IL-1, IL-6], and interferon and granulocyte-macrophage colony-stimulating factor causing an inflammatory response.

Pathogenesis of DU in HP infection.

Once infection in the antrum is established there is

*Depletion of antral Somatostatin and increase gastrin release from G cells. Gastrin hormone stimulates acid secretion through gastrin receptors on parietal cells and by inducing histamine release from ECL cells .histamine stimulate H2 receptor on parietal cells both stimuli to increase HCL secretion .increase acid secretion leading to duodenal mucosal damage, Continuing damage at duodenal mucosa stimulates the development of patches of gastric metaplasia in the duodenum, which in turn are colonized by H.pylori thereby allowing further damage and eventual ulceration.



The role of H.pylori in the pathogenesis of gastric ulcer is less clear but H.pylori probably reduces gastric mucosal resistance to attack from pepsin and acid.
Approximately 1% of infected persons H.pylori causes pangastritis leading to gastric atrophy and hypochlorhydria this allows bacteria to proliferate within the stomach these may produce nitrites from dietary nitrates predisposing to the development of gastric cancer. The results of H. pylori infection are Gastritis, gastric and duodenal ulcers, multifocal atrophic gastritis, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer.

2-NSAID -

Prostaglandins stimulate the secretion of both mucus and bicarbonate and to maintain mucosal blood flow. The mechanisms of injury due to NSAID are multiple and include both direct mucosal injury and by inhibition of prostaglandins that are protective of the mucosa.

3-Acid pepsin versus mucosal resistance

An ulcer form when there is an imbalance between aggressive factors[acids, pepsin, bile acids], and defensive factors[mucus, bicarbonate, prostaglandins, mucosal blood flow].An ulcer occurs only in the presence of acid and pepsin. Most DU patients have exaggerated acid secretion in response to hypergastrinemia produced by H pylori. factors involved in the development of GU include * impaired mucosal defense mechanism resulting from a combination of H pylori infection, NSAID, and smoking.

4-Genetic Predisposition First-degree relatives of DU patients are three times as likely to develop an ulcer.

5-Smoking.

Smokers have ulcers more frequently than nonsmokers. Smoking decreases healing rates, impair response to therapy, and increases ulcer complications such as perforation.

PATHOLOGY

*Chronic gastric ulcer usually single. 90% is situated on the lesser curve within the antrum or at the junction between the body and antral mucosa.
*Chronic DU usually occurs in the first part of the duodenum.
50% are on the anterior wall. * PU may be single or multiple
*GU and DU coexist in 10%.

Clinical features

PU is a chronic condition with relapse and remission lasting for a long time.
DU and GU share common symptoms. Including

A*Recurrent abdominal pain which has 3 characteristics

1-Localization to the epigastrium. The patient indicates epigastric pain site with 2 or 3 fingers
2-Relationship to food. The typical pain in DU occurs 90 min to 3 h after a meal.
The pain in GU is precipitated by the food. *Pain is frequently relieved by antacids or food
*****Pain that awakens the patient from sleep (between midnight and 3 A.M.) mostly in DU
3-Episodic pain [periodicity] pain is episodic and may last for several weeks between episodes there is no pain.
The mechanism for the development of abdominal pain in ulcer patients include
-Acid-induced activation of chemical receptors.
-Enhanced sensitivity to bile acids and pepsin.
-Altered gastro-duodenal motility.

B*Anorexia, Nausea, and Vomiting

C*Hematemesis and or Melena

Physical Examination

*May be normal .some patients have Epigastric tenderness .

*A tender board like the abdomen and absent bowel sounds suggests perforation

*Tachycardia and postural hypotension suggest dehydration secondary to vomiting or active gastrointestinal blood loss.

*Presence of a succussion splash [suggesting gastric outlet obstruction].

*Wasting and dehydration

Differential diagnosis of PUD.

1-Functional dyspepsia[NUD]. refers to a group of heterogeneous disorders characterized by upper abdominal pain without the presence of an ulcer.

2- Gastric tumors.3- GERD

4- Pancreatico-biliary disease. (Biliary colic, chronic pancreatitis].

5- Gastro-duodenal Crohn's disease

Investigations

***CBC and serum electrolyte are indicated in the evaluation of patients with vomiting or bleeding

*Serum amylase helps evaluate patients with persistent pain that radiates to the back.

*Serum gastrin level in the fasting state

Documentation of an ulcer requires either an Endoscopic procedure or a radiographic (barium study).

1-Endoscopy [OGD]the most sensitive and specific approach for examining the upper gastrointestinal tract. In addition to permitting direct visualization of the mucosa also facilitates tissue biopsy to rule out malignancy (GU) or H. pylori. *Multiple biopsies of a GU should be taken to roll out malignancy *Repeat endoscopy to document healing of GU at 8 to 12 weeks and biopsy should be taken from the ulcer if is still present

2-Barium studies. The sensitivity of single-contrast barium meals for detecting a DU is about 80%, with a double-contrast study providing detection rates as high as 90%. Sensitivity for detection is decreased in* small ulcers (<0.5 cm), *presence of previous scarring, *or in postoperative patients. Ulcers >3 cm in size or those associated with a mass are more malignant. Radiographic studies that show a GU must be followed by endoscopy and biopsy.

3-Test for H. Pylori infection include

1-non-invasive test [do not require endoscopy] include

*Serological HP antibody can persist after the previous infection and after eradication of HP [at least 18 m]

For those reasons cannot be used for the diagnosis of active HP infection.

***The Urea Breath Test (UBT)** is a simple, non-invasive test to demonstrate Helicobacter pylori (H. pylori) infection. The test is simple. The orally given urea, isotopically labeled with 14C or 13C, is hydrolyzed by the enzyme urease of H. pylori, and *CO2 is expired in a breath at 20 min**.t**o avoid false-negative results, testing should be performed 4 to 6 weeks after the end of treatment and 5 days after the end of acid-suppressive drugs**.** Sensitivity ranges from 85-95%.

***Fecal H pylori antigen test.** An antibody test is available to test for HP antigen in stool samples. Has similar sensitivity and specificity as UBT.

2- Invasive require an endoscopy to take biopsies from the antrum and body of the stomach.

*Histology gives information on the presence or absence of gastritis, gastric atrophy, intestinal metaplasia, MALT lymphoma, and cancer

*Rapid urease tests [this is done on a mucosal biopsy specimen from the antrum, body, or incisura angular of the stomach.

* Microbiological culture

indications to test for H. pylori include:

Active PUD (gastric or duodenal ulcer)

History of PUD, without prior treatment for Hp

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma

Following endoscopic resection of early gastric cancer

Uninvestigated dyspepsia (depending upon H. pylori prevalence).

Treatment of PUD

1- General measures include

* Patients should avoid smoking, aspirin, and NSAID.

*No special dietary advice is required

Antisecretory agents: administered orally (8 weeks for duodenal ulcer and 8–12 weeks for gastric ulcer).

The drugs used to treat PUD are the following

Group	**Examples**
Antacids and	Aluminum hydroxide, magnesium trisilicate, [neutralize gastric acid]
H_2-antagonists	Ranitidine, cimetidine famotidine, nizatidine,
Proton pump inhibitors (PPIs)	[omeprazole 20 mg, lansoprazole 30 mg pantoprazole 40 mg, rabeprazole20 mg, esomeprazole 40 mg, or Lansoprazole 30 mg].
Complex salts	Sucralfate viscous, paste-like material that coats the ulcer bed
Prostaglandin analogs	Misoprostol [stimulates gastric mucus and bicarbonate secretion after oral ingestion];

2-H. pylori eradication

First-line therapy

Triple therapy:

The combination of two antibiotics [clarithromycin 500 mg and amoxicillin 1 gr or metronidazole500 mg] taken simultaneously with PPI twice daily for 10-14 days eradication rate 70-85%.

Quadruple therapy consists of a PPI, amoxicillin, clarithromycin, and a nitroimidazole (metronidazole or tinidazole 500 mg) or

bismuth-based quadruple therapy with a PPI, bismuth, metronidazole, and tetracycline 500mg. These regimens are associated with H. pylori eradication rates of >90%.

For prior treatment failures, bismuth quadruple therapy or levofloxacin-containing therapy (PPI, amoxicillin 1gr twice daily and levofloxacin500mg once daily) or Rifabutin-containing therapy (PPI, amoxicillin, and rifabutin300mg) is indicated after at least three recommended options have failed.

High-dose H2RAs may be substituted for PPIs in the event of allergy or adverse effects, although PPIs are generally recommended

Eradication of H Pylori should be confirmed after treatment 4-6 W by UBT or fecal antigen test

Surgical therapy.

*Elective for medically refractory disease.

*Urgent for an ulcer-related complication like [Bleeding, perforation and gastric outlet obstructions].

Surgical treatment is designed to decrease gastric acid secretion.

Complications of PUD.

***Gastrointestinal Bleeding** is the most common complication of PUD. It occurs in 15% of patients and more common in individuals >60 years old. The higher incidence in the elderly is likely due to the increased use of NSAIDs in this group. About 20% of patients with ulcer-related hemorrhage bleed without any preceding warning signs or symptoms.

***Perforation**

Characterized by sudden onset of severe, generalized abdominal pain.

***Penetration** is a form of perforation in which the ulcer bed tunnels into an adjacent organ. DU tends to penetrate posteriorly into the pancreas leading to pancreatitis, whereas GU tends to penetrate the left hepatic lobe. Gastro-colic fistulas may occur with GU.

***Gastric Outlet Obstruction**

Signs and symptoms of obstruction include *[early satiety, nausea, vomiting, abdominal pain after food and weight loss] *large quantities of gastric content are often vomited and vomiting of food

eaten 24 h or more.
*Nasogastric aspiration of at least 200ml of fluid from the stomach after an overnight fast.
*Evidence of wasting and dehydration*A succession splash and Visible gastric peristalsis.

Refractory ulcer

Include GU that fails to heal after 12 weeks and a DU that doesn't heal after 8 weeks of therapy.

Causes of Refractory Ulcer include * Poor compliance* Persistent H. pylori infection* NSAID use*Cigarette smoking*For a GU, malignancy must be excluded * Gastric hyper secretory state like ZES.
*Ischemia, Crohn's disease, amyloidosis, Sarcoidosis, lymphoma, eosinophilic gastroenteritis, or infection [cytomegalovirus (CMV), tuberculosis, or syphilis].

ZOLLINGER-ELLISON SYNDROME [ZES]

This is a rare disorder characterized by
1-Severe peptic ulceration.
2-Gastric acid hyper secretion[Due to unregulated gastrin release].
3-Gastrinoma[a non B cell endocrine tumor that secret gastrin hormone].
The incidence of ZES varies from 0.1 to 1% of individuals presenting with PUD. Males are more commonly affected than females and the majority of patients are diagnosed between ages 30 and 50y.

Pathophysiology of ZES

Hypersecretion of gastrin by gastrinoma. Gastrin hormone stimulates acid secretion through gastrin receptors on parietal cells and by inducing histamine release from ECL cells .histamine stimulates the H2 receptor on parietal cells both stimuli increases HCL secretion. Gastrin also has a trophic action on gastric epithelial cells leading to increase Parietal cell mass.
*90% of gastrinoma is found in the pancreatic head or proximal duodenal wall may be multiple, Size range from 1 mm to 20 cm. About ½ to 2/3 are malignant. 20-60% of these patients also have adenomas of the parathyroid and pituitary glands [multiple endocrine neoplasias, MEN type 1].

Clinical Manifestations

Gastric acid hypersecretion is responsible for the signs and symptoms observed in-patients with ZES.

1- Peptic ulcer is the most common clinical manifestation, occurring in >90% of patients. Initial presentation and ulcer location may be indistinguishable from common PUD.

Clinical situations that should create suspicion of gastrinoma are
1-Ulcers in unusual locations (the second part of the duodenum and beyond).
2-Ulcers refractory to standard medical therapy.
3-Ulcer recurrence after acid-reducing surgery.
4-Ulcers presenting with frank complications (bleeding, obstruction, and perforation).

2-Diarrhea

Occur in up to 50% of patients. Mechanism of diarrhea include*volume overload to the small bowel due to hyper secretion. *Pancreatic enzyme inactivation by acids these leads to diarrhea and Steatorrhea*damage of intestinal epithelium by acids.
*Diarrhea may have a secretory component due to the direct effect of gastrin on enterocytes or co secretion of additional hormones by the tumor-like vasoactive intestinal peptide.

Diagnosis

1- Fasting Gastrin level >150 -- 200 pg/mL.
2- Hypersecretion of acid under basal conditions with little increase after pentagastrin maybe confirmed by gastric aspiration.
3- increase in gastrin level > 120 pg after 20 mint of secretin hormone injection.
Other conditions associated with an elevated serum gastrin level include gastric hypochlorhydria with or without pernicious anemia, G cell hyperplasia, gastric outlet obstruction, renal failure, H. pylori infection.
4-Tumor localization by

*CT scan, MRI and US, EUS, and selective arteriography with sampling from portal vein tributaries.
*Localization of gastrinoma by measuring the uptake of somatostatin analog.

Treatment

1-Directed at ameliorating the signs and symptoms related to hormone overproduction.
2-Curative resection of the neoplasm.
3-Control tumor growth in metastatic disease.

Approximately 30% of tumors are small and single and can be localized and resected but sometimes tumor is multifocal and some with metastatic disease and surgery is inappropriate.
*PPIs are the treatment of choice and have decreased the need for total gastrectomy.
*Somatostatin analog has inhibitory effects on gastrin release from receptor-bearing tumors and
inhibits gastric acid secretion.

Prognosis. Overall 5year survival is 60-70% and patients should be monitored for the developmental MEN type1.