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FACULTY OF MEDICINE
DEPARTMENT OF SURGERY DISEASES

PERFORATED PEPTIC ULCER

Methodological matherials for independent study for students

UZHHOROD

2024

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FACULTY OF MEDICINE
DEPARTMENT OF SURGERY DISEASES

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Methodical matherials are devoted to issues of etiopathogenesis, symptoms, diagnosis and treatment methods of perforated peptic ulcer (PPU). The methodical matherials are intended for senior year students of higher medical educational institutions.

Uzhhorod

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Contents

Background

Peptic ulcer disease (PUD) results from an imbalance between stomach acid-pepsin and mucosal defense barriers. It affects 4 million people worldwide annually. The incidence of PUD has been estimated at around 1.5-3%.

Perforated peptic ulcer (PPU) is a surgical emergency and is associated with short-term mortality and morbidity in up to 30 and 50% of patients, respectively. Worldwide variation in demography, socioeconomic status, *Helicobacter pylori* prevalence and prescription drugs make investigation into risk factors for PPU difficult. PPU presents as an acute abdominal condition, with localized or generalized peritonitis and a high risk for developing sepsis and death. Early diagnosis is essential but clinical signs can be obscured in the elderly, or the immunocompromised and thus delay diagnosis. Imaging has an important role in diagnosis, as does early resuscitation including administration of antibiotics. Appropriate risk-assessment and selection of therapeutic alternatives becomes important to address the risk for morbidity and mortality.

Epidemiology

The lifetime prevalence of peptic ulcer disease (PUD) is declining and is currently estimated to be between 5-10%. It tends to be less prevalent in developed countries. Just as there has been a downward trend in the overall incidence of peptic ulcer disease, so too has there been a decline in the overall rate of complications. Even though the overall incidence of complications is declining, complications including bleeding, perforation, and obstruction are responsible for nearly 150,000 hospitalizations annually in the United States. Upper GI bleeding is the most common complication of peptic ulcer disease. The next most common complication is perforation. Annual incidence of ulcer perforation is expected to be 4 to 14 cases per 100,000 individuals. Advanced age is a risk factor as 60% of patients with PUD are older than 60. Infections with *H. Pylori* and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) are each identified as risk factors for the development of bleeding ulcers and peptic ulcer perforation.

Anatomy

The **stomach** is an important organ and the most dilated portion of the digestive system. The **esophagus** precedes it, and the **small intestine** follows. It is a large, muscular, and hollow organ allowing for a capacity to hold food (fig. 1).

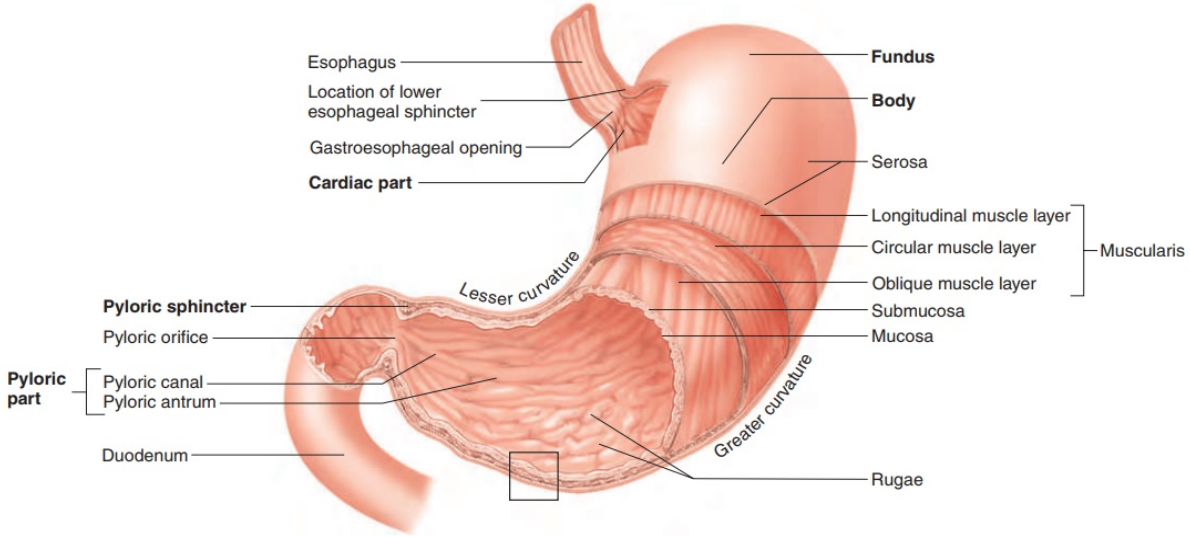

Fig. 1. Stomach anatomy.

It is comprised of **regions:** the cardia, fundus, body, antrum and pylorus. The *cardia* is connected to the esophagus and is where the food first enters the stomach. The *fundus* follows the cardia and is a bulbous, dome-shaped, superior portion of the stomach. Followed by the fundus is the *body* or the main, largest

portion of the stomach. Following the body are the *antrum* and *pylorus*, which conically funnels food into the duodenum, or upper portion of the small intestine. The stomach is located left of the midline and centrally in the upper area of the abdomen.

Structure and functions. The *primary functions* of the stomach include the temporary storage of food and the partial chemical and mechanical digestion of food.

The upper portions of the stomach relax as food enters to allow for the stomach to hold increasing quantities of food. The lower portion of the stomach contracts in a rhythmic fashion (*mechanical digestion*) to aid with the breaking down of food and mixes it with stomach juices (*chemical digestion*) which also serve to break food down and prepare the mixture, termed *chyme* at this point of digestion, for further digestion. Mixing waves in the stomach are produced, and with each wave, the pyloric sphincter allows small quantities of chyme into the duodenum. Stomach juices are secreted by the fundus of the stomach and include hydrochloric acid (HCl) and the enzyme pepsin. In addition to HCl, the stomach also produces intrinsic factor (absorption of vitamin B12, which plays a role in the production of red blood cells and neurological functions) in its parietal cells.

The stomach is capable of processing food and distributing it to the duodenum on average within 2 to 4 hours. The acidic environment of the stomach may be lethal to many types of bacteria and other microorganisms that enter the body by way of ingestion, potentially protecting the body from infection and diseases.

Blood supply and lymphatics. The celiac trunk, branching directly anteriorly from the aorta provides the main *arterial blood supply*. The trunk supplies the common hepatic artery (CHA), splenic artery, and the left gastric artery (LGA). The less curved side of the stomach is proximally supplied by a descending branch of the LGA, with its ascending branch supplying portions of the esophagus. The CHA which runs superior to the pancreas and the right branches off to the gastroduodenal artery (GDA) and continues with the branch that proceeds from the CHA being the proper hepatic artery. The right gastric artery (RGA) then branches from the proper hepatic artery. The RGA then runs from right to left across the lesser curved portion of the stomach and continues to branch into smaller vessels through the body of the stomach to join the network of smaller arteries supplying the stomach as branched off from the LGA. The posterior superior pancreaticoduodenal artery branches off of the GDA which then branches into the anterior superior pancreaticoduodenal artery and the right gastroepiploic artery, which then traverses and supplies from right to left the greater curvature of the stomach. The left gastroepiploic artery branches from the splenic artery also

supplies the greater curvature body portion of the stomach. Three to five additional smaller arteries also branch from the splenic artery to supply the stomach.

The left gastric (coronary) vein and the right gastric and right gastro-omental veins all achieve *venous drainage* into different segments of the *portal vein*. The short gastric veins (the vasa brevia) and the left gastroepiploic vein achieve drainage via the splenic vein.

The *lymphatic drainage* of the stomach can be understood as 4 levels. Level 1 includes the perigastric lymph nodes and follows a path of drainage of the right pericardiac, left pericardiac, along with the less curved body portion, along with the greater curved body portion, supra-pyloric, and infra-pyloric. Level 2 is comprised of drainage along the LGA, along the CHA, along with the celiac axis, at the splenic hilum, and along the splenic artery. Level 3 is characterized by drainage in the hepatoduodenal ligament, posterior to the duodenum and pancreas head, and at the source of the small bowel mesentery. Finally, the level 4 is characterized by mesocolic and paraaortic drainage.

Nerves. The autonomic nervous system provides the stomach with the innervation via parasympathetic and sympathetic nerves. The *vagus nerve* supplies *parasympathetic innervation* via the right posterior and left vagal trunks. The left vagus nerve is anterior, while the right vagus nerve is posterior. The right vagus nerve branches to the criminal nerve of Grassi for innervation of the cardia and fundus. The trunks also follow the lesser curvature region of the stomach to form the posterior and anterior gastric nerves of Latarjet innervating the body, antrum, and pylorus. *Sympathetically,* nerves are supplied, including some fibers transmitting pain, to the celiac plexus from spinal cord segments T6 through T9.

Layers. Four main *layers* constitute the stomach wall, including the mucosa, submucosa, muscularis externa, and the serosa.

The innermost layer, the *mucosa*, is covered by epithelial tissue and is mainly comprised of gastric glands that secrete gastric juices. Particularly, the fundus releases gastric juices while the cardia secretes protective mucus which coats the inner mucosal wall of the stomach via mucus (Foveolar) cells thereby protecting the stomach muscles from being digested by the gastric juices produced by the chief cells (pepsin) and parietal cells (HCl).

The *submucosa* is comprised of dense connective tissue and contains blood and lymphatic vessels along with nerves. Together, the submucosa supports the mucosal layer and has many folds analogous to that of an accordion called rugae which allows for distension of these layers when food enters the stomach.

The *muscularis externa* is the next layer and is comprised of the 3 sub-layers: running longitudinally, obliquely, and circularly as part of the stomach wall. The inner oblique layer is unique to the stomach and is primarily responsible

for the churning, mechanical digestion of food. The middle circular layer is concentric with the stomach's longitudinal axis and thickens in the region of the pylorus to form the pyloric sphincter responsible for regulating the output from the stomach into the duodenum. The next layer is the outer longitudinal layer, but between this layer and the middle circular layer, is *Auerbach's (myenteric) plexus*, which is a region of innervation for the two adjacent muscular layers. The outer longitudinal layer facilitates the movement of food in the direction of the pylorus via muscular shortening.

The final layer, the *serosa*, is made up of multiple layers of connective tissue which also connect continuously with the peritoneum.

The **duodenum** is the initial C-shaped segment of the small intestine and is a continuation of the pylorus. Distally, it is in continuation with the jejunum and ileum, with the proximal segment being the shortest and widest. Positioned inferiorly to the stomach, the duodenum is approximately 25 to 30 cm long (fig. 2).

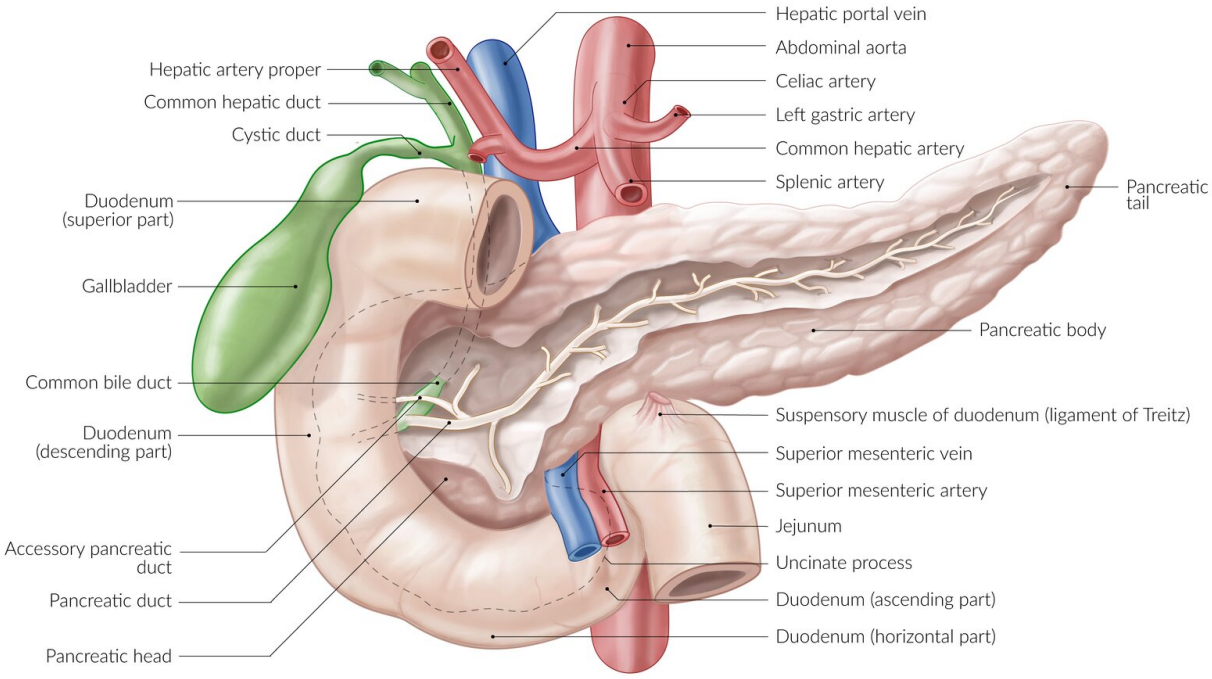

Fig. 2. Duodenum anatomy.

The 4 **segments** of the duodenum include the following: duodenal bulb, descending part, horizontal part, ascending part. The *duodenal bulb*, connects to the undersurface of the liver via the hepatoduodenal ligament, which contains the portal vein, the hepatic artery, and common bile duct. The second or *descending segment* is just above the inferior vena cava and right kidney, with the head of the pancreas lying in a C-shaped concavity. The *third (horizontal) segment* runs from right to left in front of the aorta and inferior vena cava, with the superior

mesenteric vessels in front of it.The *fourth (ascending) segment* continues as the jejunum.

The **walls** of the duodenum are made up of 4 layers of tissue that are identical to the other layers of the GI tract. From innermost to the outermost layer, these are the mucosa, submucosa, muscularis, and serosa layers. The mucosal layer lines the inner surface of the duodenum and is made of simple columnar cells with microvilli and numerous mucous glands. The submucosal layer is mostly a layer of connective tissue where blood vessels and nerves travel through. The muscularis layer contains the smooth muscle of the duodenum and allow mixing and forward peristaltic movement of chyme. The serosal layer is characterized by squamous epithelium that acts as a barrier for the duodenum from other organs.

Structure and functions. The *function* of the duodenum is a continuation of the digestion process that initially began in the stomach. It receives chyme generated by the stomach through the pylorus. The digestion inside of the duodenum is facilitated by the digestive enzymes and intestinal juices secreted by the intestinal wall as well as fluids received from the gallbladder, liver, and pancreas. This is received into the duodenum by the major and minor papilla in the second part of the duodenum. The duodenal papilla is surrounded by a semicircular fold superiorly and the sphincter of Oddi which is the muscle that prevents reflux of duodenal secretions into the bile and pancreatic ducts.

The duodenum also has the unique ability to regulate its environment with hormones that are released from the duodenal epithelium. One of those hormones is secretin, which is released when the pH of the duodenum decreases to a less than desirable level. This hormone acts to neutralize the pH of the duodenum by stimulating water and bicarbonate secretion into the duodenum. This aids in the digestion process as pancreatic amylase and lipase require a certain pH to function optimally. Another hormone that is released by the duodenal epithelium is cholecystokinin. Cholecystokinin is released in the presence of fatty acids and amino acids inside of the duodenum and acts to inhibit gastric emptying and also to stimulate contraction of the gallbladder while simultaneously causing relaxation of the sphincter of Oddi to allow delivery of bile into the duodenum to aid in digestion and absorption of nutrients.

Blood supply and lymphatics. The *artetial blood supply* of the C-shaped duodenum is shared with the head of the pancreas. The proximal segment of the duodenum is supplied by the gastroduodenal artery and its branches which include the superior pancreaticoduodenal artery. The distal segment of the duodenum is supplied by the superior mesenteric artery and the inferior pancreaticoduodenal artery. The *venous drainage* follows the arteries and ultimately drains into the portal system. The duodenum also has *lymphatic vessels* which drain into the

pancreaticoduodenal lymph nodes located along the pancreaticoduodenal vessels and the superior mesenteric lymph nodes.

Nerves. The nerves of the duodenum travel throughout the submucosal layer of the duodenum. The duodenum is richly innervated by the *parasympathetic nervous system* which includes branches of the anterior and posterior vagus trunks. These parasympathetic nerves pass through the celiac plexuses and follow the celiac trunk toward the duodenum. The nerves then synapse in ganglia in the gut plexuses in the duodenum and reach their final targets through short postsynaptic fibers. The *sympathetic nerves* are branches of the celiac plexus which originate from T5 through T9. These sympathetic nerves pass through the sympathetic chain and travel through the greater splanchnic nerve and synapse in the celiac ganglia. The postsynaptic sympathetic follow the branches of the celiac trunk toward the duodenum.

Muscles. The muscles in the muscularis layer of the duodenum include the circular and longitudinal muscles. It is through the coordination of contraction of these muscles that allow for peristalsis to occur throughout the gastrointestinal tract, including the duodenum.

Etiology

Although numerous studies have indicated that seasonal variation did influence the incidence of PPU, other studies have failed to prove such a pattern. In developing world, patients tend to be young male smokers while in developed countries patients tend to be elderly with multiple co-morbidities and associated use of non-steroidal anti-inflammatory drugs (NSAIDs) or steroid. NSAIDs, *H. pylori*, physiological stress, smoking, corticosteroids and previous history of PUD are risks factors for PPU. In the presence of risk factors, recurrence of ulcer is common despite initial successful treatment.

NSAIDs are widely used for its analgesic, anti-inflammatory and anti-pyretic effects. NSAID use is known to increase the risk of PPU. About a quarter of chronic NSAID users will develop PUD and 2-4% will bleed or perforate. Drug interaction with steroids and selective serotonin reuptake inhibitors also increases the risks of PUD. Selective cyclo-oxygenase-2 inhibitors are less associated with PUD. Further, it is important to remember that PPU also may occur in children, where it is usually associated with *H. pylori* (90%).

Helicobacter pylori. *H. pylori* remains one of the commonest infections worldwide. The prevalence of *H. pylori* has decreased in developed countries due to improved hygiene and reduced transmission in early childhood. The mean prevalence of *H. pylori* in patients with PPU varies between studies due to

different diagnostic methods and geographical variations. Recent studies using histopathological methods of *H. pylori* detection have shown that *H. pylori* prevalence in patients with perforated duodenal ulcers ranges from 50% to 80%. Recurrent PUD mainly occurs in patients with *H. pylori* infection suggesting that *H. pylori* plays an important role in the development of PUD and its complications. The risk of recurrent *H. pylori* infection is significantly reduced with proton pump inhibitor therapy, but proton pump inhibitors have only a modest efficacy for reduction in ulcers with NSAID users.

Smoking. Tobacco is thought to inhibit pancreatic bicarbonate secretion, leading to increased acidity in duodenum. It also inhibits the healing of duodenal ulcers. Approximately 23% cases of PUD could be associated with smoking.

Others. Other risk factors may include excessive alcohol consumption and excessive acid production such as gastrinomas and Zollinger-Ellison syndrome (ZES). Alcohol consumption is known to damage gastric mucosa and stimulate gastrin secretion. Despite these acute effects, there is no evidence that alcohol causes PUD. ZES is caused by a gastrin secreting tumor of the pancreas that stimulates the parietal cells in stomach to increase the acidity, resulting in gastrointestinal mucosal ulceration. Over 90% of patients with ZES develop peptic ulcers and typically these ulcers are refractory to proton pump inhibitor therapy. ZES should be suspected in patients with multiple or refractory peptic ulcers, jejunal ulcers, family history of PUD and associated diarrhea. All patients with ZES should be screened for Multiple Endocrine Neoplasia 1 syndrome.

Factors specific to gastric ulcers include gastric stasis, ischemia of gastric mucosa, and duodeno-gastric reflux.

A diurnal **peak of ulcer perforations** has been observed with more perforations occurring in the morning, possibly related to circadian variation in acid-secretion. Perforation risk is increased by fasting, such as during Ramadan, which may also be due to variation in acid release and exposure. Ulcer perforation is noted to occur after bariatric surgery, after crack-cocaine or amphetamine use, and after chemotherapy with angiogenesis inhibitors such as bevacizumab. Patients with acid-hypersecretion, including those with a gastrinoma (ZES) are at risk for perforation and a gastrinoma should be ruled out in patients with multiple or recurrent ulcers.

Pathophysiology

The ulcerogenic process occurs as a result of damage to the protective mucosal lining of the stomach and duodenum. *H. pylori* infections and the use of NSAIDs and low-dose aspirin are known to damage the mucosal lining. The cost

to the mucosal lining in the setting of an *H. pylori* infection is the result of both bacterial factors and the host's inflammatory response. In the case of NSAID (and aspirin) use, mucosal damage is secondary to inhibition of cyclooxygenase 1 (COX-1) derived prostaglandins which are important in maintaining mucosal integrity. Once the mucosal layer is disrupted, the gastric epithelium is exposed to acid, and the ulcerative process ensues. If the process continues, the ulcer deepens reaching the serosal layer. A perforation occurs once the serosal layer is breached at which point the gastric contents are released into the abdominal cavity (fig. 3).

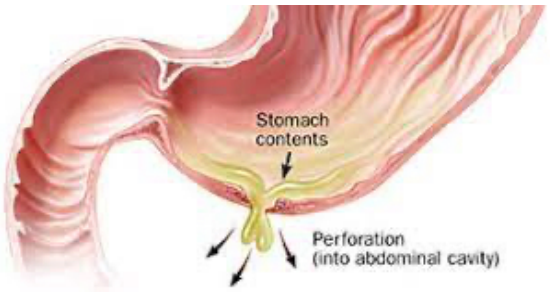

Fig. 3. Perforated peptic ulcer.

Classification

1. Modified Johnson Classification of peptic ulcers:
   - Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistentiae.
   - Type II: Ulcer in the body in combination with duodenal ulcers. Associated with acid oversecretion.
   - Type III: In the pyloric channel within 3 cm of pylorus. Associated with acid oversecretion.
   - Type IV: Proximal gastroesophageal ulcer.
   - Type V: Can occur throughout the stomach. Associated with chronic NSAID use.
2. Forms of perforation:
   - Perforation of duodenal or gastric ulcer into the free abdominal cavity.
   - Covered perforation.
   - Atypical perforation (into the lesser sac, retroperitoneal tissue).
3. Clinical stages:
   - Stage of shock (initial phase – within 2 h of onset).
   - Stage of illusion (second phase – within 2 to 12 h).
   - Stage of peritonitis (third phase – more than 12 h).

Clinical symptoms and physical examination

Peptic ulcer disease (PUD). Although approximately 70% of patients with peptic ulcer disease may initially be asymptomatic, most patients with a perforated peptic ulcer will present with symptoms. Special populations such as the extremes of age (young or elderly), immunocompromised, and those with altered level of consciousness may prove to be more challenging in obtaining a reliable history. When an honest account is obtainable, a detailed history may identify other symptoms that may have been present before ulcer perforation. The most common symptom in patients with peptic ulcer disease is dyspepsia or upper abdominal pain. This pain may be vague upper abdominal discomfort or it may be localized to either the right upper quadrant, left upper quadrant, or epigastrium. Gastric ulcers may be worsened by food whereas pain from a duodenal ulcer may be delayed 2-5 hours after eating.

Perforated peptic ulcer (PPU). When PUD worsen and eventually perforate, gastric juice and gas enters the peritoneal cavity leading to chemical peritonitis. Sudden onset of abdominal pain (*like stabbing with a dagger*) or acute deterioration of the ongoing abdominal pain is typical of PPU. Typically the pain never completely subsides despite usual premedical remedies and forces the patient to seek medical attention. The chemical peritonitis due to efflux of gastroduodenal contents and severe pain lead to tachycardia. The **classic triad** of **sudden onset of abdominal pain, tachycardia** and **abdominal rigidity** is the hallmark of PPU.

The clinical manifestation can be divided into three phases. In the *initial phase* within 2 h of onset, epigastric pain, tachycardia and cool extremities are characteristic. In the *second phase* (within 2 to 12 h), pain becomes generalized and is worse on movement. Typical signs such as abdominal rigidity and right lower quadrant tenderness (as a result of fluid tracking along the right paracolic gutter) may be seen. In the *third phase* (more than 12 h), abdominal distension, pyrexia and hypotension with acute circulatory collapse may be evident.

The **commonest presenting symptoms** are:

- sudden onset of severe epigastric pain (97%);
- abdominal distention (76%);
- vomiting (36%).

Abdominal tenderness and classical signs of peritonitis can be elicited in 88% and 66% of the patients with PPU. Other symptoms also include nausea (35%), severe dyspepsia (33%), constipation (29%) and fever (21%).

Pain may be vague upper abdominal discomfort or it may be localized to either the right upper quadrant, left upper quadrant, or epigastrium. Gastric ulcers

may be worsened by food whereas pain from a duodenal ulcer may be delayed 2-5 hours after eating. Patients who are experiencing bleeding from a peptic ulcer may complain of nausea, hematemesis, or melanotic stools. Some patients may report bright red blood per rectum or maroon-colored stool if the upper GI bleeding is brisk.

Tachycardia and **abdominal tenderness** with **rigidity** are common clinical signs. Patients with a perforated peptic ulcer are likely to have diffuse abdominal tenderness that progresses to guarding and rigidity.

Patients with peptic ulcer perforation typically will complain of sudden and severe epigastric pain. Pain while initially localized, quickly becomes more generalized in location. Patients may present with symptoms of lightheadedness or syncope secondary to hypotension from blood loss or SIRS (systemic inflammatory response syndrome)/sepsis. After several hours, abdominal pain may temporarily improve though it is still reproducible by movement.

Severe pain, systemic inflammatory response from chemical peritonitis and fluid deficit either due to poor intake or vomiting or pyrexia leads to compensatory tachycardia. In patients who delay seeking medical attention, hypotension ensues due to total body water deficit. If uninterrupted, this progresses to mental obtundation and acute kidney injury. This leads to a state where patient becomes physiologically unfit for operative intervention which is absolutely necessary. Hence it is important to establish prompt confirmatory diagnosis.

The clinical picture may be *less clear* in the obese, the immunocompromized, patients on steroids, patients with a reduced level of consciousness, in the elderly, and in children. Only two thirds of patients present with frank peritonitis, which may in part explain the diagnostic delay in some patients.

During clinical evaluation, a number of differential diagnoses must be considered, but it is particularly important to exclude a ruptured abdominal aortic aneurysm or acute pancreatitis (see Differential Diagnosis). The former, due to its high mortality if unrecognised and delayed in treatment, and; the latter, due to the primarily non-operative management.

Diagnostic imaging may have to be delayed pending resuscitation in critically ill patients. Those presenting with generalized peritonitis with or without signs of sepsis will usually be directed straight to the operating room. Notably, mortality increases with every hour surgery is delayed.

Covered perforation. In this case the perforative defect is closed by fibrin, omentum or sometimes by food particle. At the same time amount of gastric contents and air are left in the abdominal cavity. This protective mechanism leads to relief from abdominal pain, but moderate tenderness and rigidity of abdominal

wall persist in the epigastrium (*Ratner's sign*). X-ray may to reveale the presence of free gas within abdominal cavity.

The **atypical perforation** is the perforation, at which gastric or intestinal contents do not enter the abdominal cavity, but to the retroperitoneal space (ulcers of posterior wall of duodenum), large or small omentum (ulcers of greater or lesser curvature of stomach, respectively), hepatoduodenal ligament.

These patients are usually not presented with acute abdominal pain. During palpation insignificant rigidity of anterior abdominal wall muscles is revealed. On occasion, especially in the late stages of disease, can be hypodermic emphysema and crepitation.

Complications of untreated peptic ulcer perforation are severe and will eventually lead to patient demise. Short-term complications include: hypovolemia, shock, sepsis, gastrocolic fistula formation.

Diagnosis

Laboratory studies. Laboratory markers are *not diagnostic* for perforated ulcers. However, they aid in the estimation of the inflammatory response and evaluation of organ function, as well as excluding relevant differential diagnoses, such as acute pancreatitis. They also can help rule out differential diagnosis and also to understand the insult to various organ systems.

Standard labs should include complete blood count (CBC), chemistry panel, liver function tests, coagulation profile, and lipase levels (to rule out pancreatitis). Blood type and screening should be done as well.

Serum amylase should be done at index presentation to emergency unit or after a normal chest X-ray. Raised serum amylase may be associated with PPU and it's usually raised less than four times its normal level.

Tests such as *white cell count* and *C-reactive protein* may be done as part of the investigation in PPU. Leukocytosis and raised C-reactive protein may be raised as a result of inflammation or infection.

Elevated *creatinine, urea* and *metabolic acidosis* reflects systemic inflammatory response syndrome (SIRS) and prerenal injury.

Serum gastrin levels are indicated in patients with history of recurrent ulcers or recalcitrant PUD and can help establish diagnosis of Zollinger Ellison syndrome. In patients with suspected parathyroid disorders, *serum calcium* levels are indicated.

Blood cultures should be taken early, prior to starting broad-spectrum antibiotics, although it is important that antibiotic treatment is not be delayed. An arterial blood gas may serve as an adjunct to clinical evaluation of vital functions

(e.g. pH, lactate, base excess, oxygen saturation) and measure the degree of metabolic compromise in septic patients.

Imaging studies.

Radiography. An urgent erect chest X-ray and serum amylase/lipase is basic essential test in a patient with acute upper abdominal pain. In modern era it is not prudent to perform an exploratory laparotomy and establish a diagnosis of perforated ulcer or acute pancreatitis. Approximately 75% of PPU have free air under diaphragm on erect chest X-ray. In a patient with upper abdominal symptoms, free air on an erect chest X-ray establishes a diagnosis of PPU. In some patients, an abdominal X-ray may have been performed by emergency physician or primary medical team. It can show signs such as appearance of gas on both sides of the bowel wall (*Rigler's sign*), a large volume of free gas resulting in a large round black area (*Football sign*) and gas outlining soft tissue structures such as liver edge or falciform ligament. Thus, demonstration of *"free air" (pneumoperitoneum)* on radiological examination is highly indicative of a perforated viscus organ (fig. 4). An erect chest x-ray or an upright abdominal X-ray is easy, cheap and quick to perform and may be diagnostic.

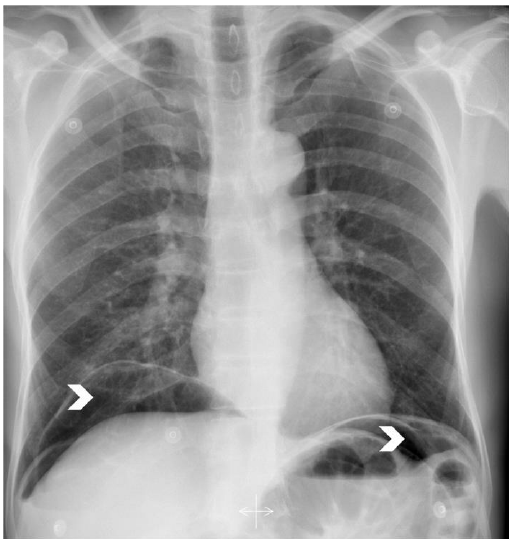

Fig. 4. Chest radiography. *Perforated duodenal ulcer: lucent areas of free intraperitoneal gas (white arrowheads).*

Computed tomography. CT scan is recommended as it has a diagnostic accuracy as high as 98%. Besides, CT scan can exclude acute pancreatitis that would not need surgical intervention. CT scan is performed in supine position and free air is usually seen anteriorly just below the anterior abdominal wall (fig. 5). The falciform ligament can sometimes be visible when air is present on both sides.

In resource poor healthcare facilities, oral gastrografin can be used to diagnose PPU. Water-soluble contrast leaking into the peritoneal cavity can confirm the diagnosis of PPU. Absence of a leak does not exclude PPU as the

perforation may have sealed off spontaneously. Barium study is contraindicated in gastrointestinal perforation and should be avoided as a tool to diagnose PPU.

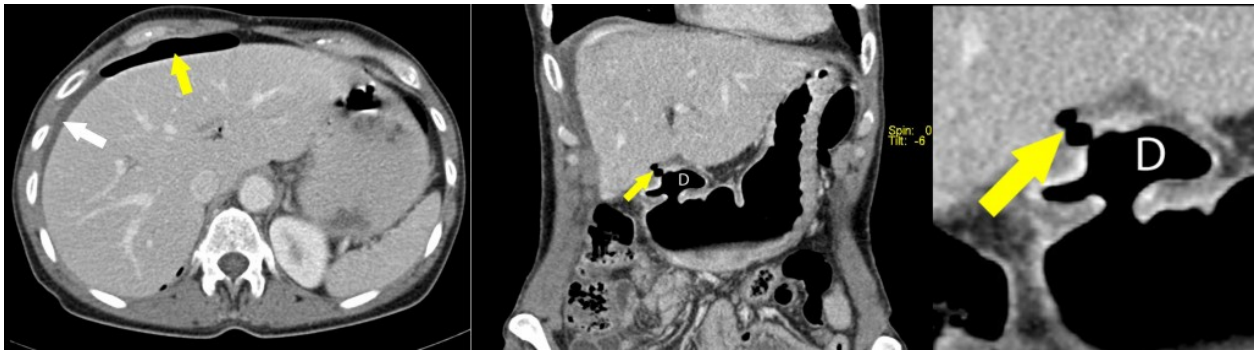

Fig. 5. Abdominal CT scan. *Perforated duodenal ulcer. Transverse CT image on the left shows the free gas anterior to the liver (yellow arrow), as well some free fluid (white arrow). On the coronal image (middle and, magnified, right): defect (arrow) in the wall of the duodenum (D), due to a perforated peptic ulcer.*

The traditional practice of instilling air via the nasogastric tube and repeating the erect chest X-ray after few minutes is not recommended except in resource poor facilities. It takes time and a repeat negative chest X-ray does not rule out the diagnosis of PPU and still a CT scan would be warranted.

Rarely a CT scan is performed even when an erect chest X-ray reveals free air under diaphragm. The utility of this CT scan is justified when clinical presentation is not specific to upper gastrointestinal pathology or a malignancy is suspected and patients' hemodynamics is not deranged. In patients with acute kidney injury, a non-contrast CT scan is adequate to see free air. Oral contrast with CT scan is a useful tool and if free leak is seen, diagnosis is certain.

Endoscopy allows you to detect an ulcer, and sometimes a perforated hole in it. After endoscopy, the abdominal radiography always reveals free gas in the abdominal cavity (due to air entering the abdominal cavity during endoscopy). Endoscopy allows to perform a **biopsy** and rule out gastric outlet obstruction in case of large perforations. Gastric ulcers are premalignant and hence biopsy of the ulcer or perforation margins are indicated in such patients. If found positive for neoplasia, thorough staging using endoscopy and imaging is used to stage and grade the disease, followed by resection or a combination of chemotherapy and surgery is recommended.

Exploratory (diagnostic) laparotomy or laparoscopy can help to reveal a perforated peptic ulcer (fig. 6).

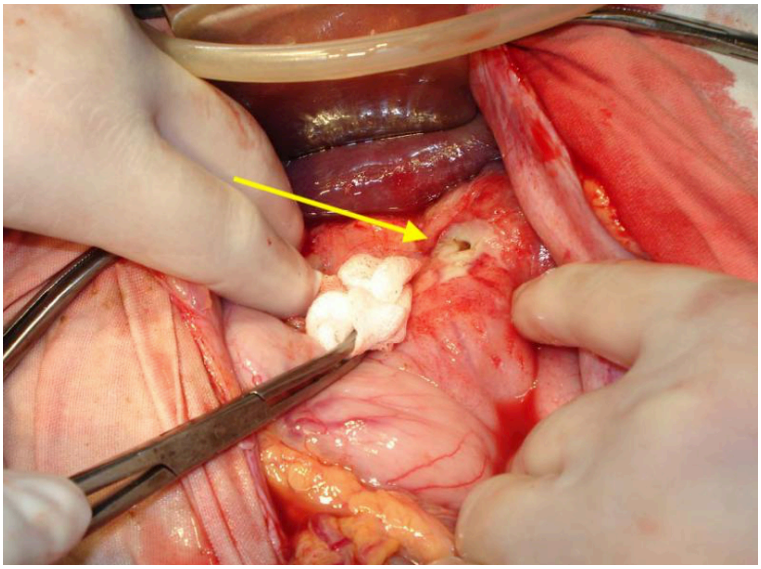

Fig. 6. Perforated peptic ulcer (arrow).

Exploratory laparotomy or laparoscopy are carried out only in cases, when other imaging and diagnostic methods are non-informative.

Differential Diagnosis

The evaluation of a patient in whom perforated peptic ulcer is suspected should be done quickly as the morbidity and mortality increase significantly with time.

Differential diagnosis includes but is not limited to the following:

- Abdominal aortic aneurysm (AAA).
- Acute coronary syndrome.
- Aortic dissection.
- Appendicitis.
- Boerhaave syndrome.
- Cholecystitis.
- Cholelithiasis.
- Choledocholithiasis.
- Diverticulitis.
- Duodenitis.
- Esophagitis.
- Foreign body ingestion.
- Gastritis.
- Hepatitis.
- Hernia.

- Mesenteric ischemia.
- Neoplasm.
- Nephrolithiasis.
- Pyelonephritis.
- Small bowel obstruction.
- Ureterolithiasis.
- Volvulus.

Treatment

Perforated peptic ulcers are life-threatening conditions with a mortality rate that approaches 30%. Early surgery and aggressive management of sepsis are the mainstays of therapy.

Non-operative management. An initial emergent surgery consultation is required in all patients with peritonitis even before definitive diagnosis. Patients should be resuscitated with crystalloids, antibiotics, and analgesics. All conservative management ("**Taylor method**") consists of nasogastric suction, intravenous drip, antibiotics and repeated clinical assessment.

Administration of early intravenous *antibiotics* should be considered, especially for patients presenting with SIRS criteria. Once the diagnosis of peptic ulcer perforation is made, a *nasogastric tube* should be placed, and *IV proton pump inhibitor (PPI)* should be administered, IV antibiotics should be given, and a surgical evaluation must be done. Then the decision can be made regarding whether the patient will require surgery.

Sepsis accounts for approximately half of all mortalities in the setting of perforated peptic ulcers. Given the high prevalence of sepsis and its associated mortality, antibiotics should be administered to all patients with a perforated peptic ulcer. Antibiotics should be broad-spectrum and cover gram-negative rods and anaerobes. A combination of a third-generation cephalosporin and metronidazole is a reasonable choice as is monotherapy with a combination beta-lactam/beta-lactamase inhibitor (i.e., ampicillin-sulbactam, piperacillin-tazobactam).

Intravenous PPI help bleeding cessation and facilitate healing, but efficacy in perforated ulcers has not been established. That said, intravenous PPI administration should be given to creating a neutral pH environment that aids in maintaining platelet aggregation and hence should promote rapid sealing of perforated ulcers.

A gastrograffin dye study is essential to confirm absence of leakage in patients selected for non-operative management. If patients are clinically stable and

improving, especially with a sealed perforation, surgery may not be warranted. However, if they deteriorate, regardless of the presence and size of the leak, urgent operation is indicated.

Different studies suggest that PPU with a sealed perforation can be managed conservatively. The advantages of conservative management include avoidance of surgery, risks of general anaesthesia and post-operative complications. On the other hand, disadvantages include misdiagnosis and higher mortality rate if conservative management fails. In clinical practice, non-operative management strategy is resource intensive and it requires a commitment of active regular clinical examination along with round the clock availability of a surgeon and if there is clinical deterioration, emergency surgery is warranted. The essential components of non-operative management of PPU can be grouped as "R"s: (1) Radiologically undetected leak; (2) Repeated clinical examination; (3) Repeated blood investigations; (4) Respiratory and renal support; (5) Resources for monitoring; and (6) Readiness to operate.

Surgical treatment. Management of PPU is primarily surgical and different suture techniques for closure of the perforation are described.

There are many operative methods that could be used to treat PPU. Primary closure by interrupted sutures, closure by interrupted sutures covered with a pedicled omentum on top of the repair (Cellan-Jones repair) and plugging the perforation with a free omental plug (Graham patch) are the most common techniques.

Closure of a perforated peptic ulcer (fig. 7).

Ulcer excision. Perforated duodenal ulcers and small prepyloric ulcers without pathological findings can be oversewn without excision.

Gastric ulcers or ulcers suspected of malignancy should be excised completely. If there is doubt, a wedge excision will also suffice. The excision serves to establish the histological diagnosis and possibly to prepare for a pyloroplasty when the location is intrapyloric. Excision is performed using the scalpel or diathermy and should take the possibility of repair into consideration (fig. 7-1). Intrapyloric ulcers should undergo a partial pyloroplasty, comprising a longitudinal incision and transverse closure (fig. 8).

Ulcer closure is accomplished with deep interrupted stitches (2-0 PGA) between two stay sutures. The suture distances are 0.6 to 0.8 cm from the ulcer margin and from the adjacent stitches. Usually, three or four interrupted sutures are sufficient (fig. 7-2, 7-3).

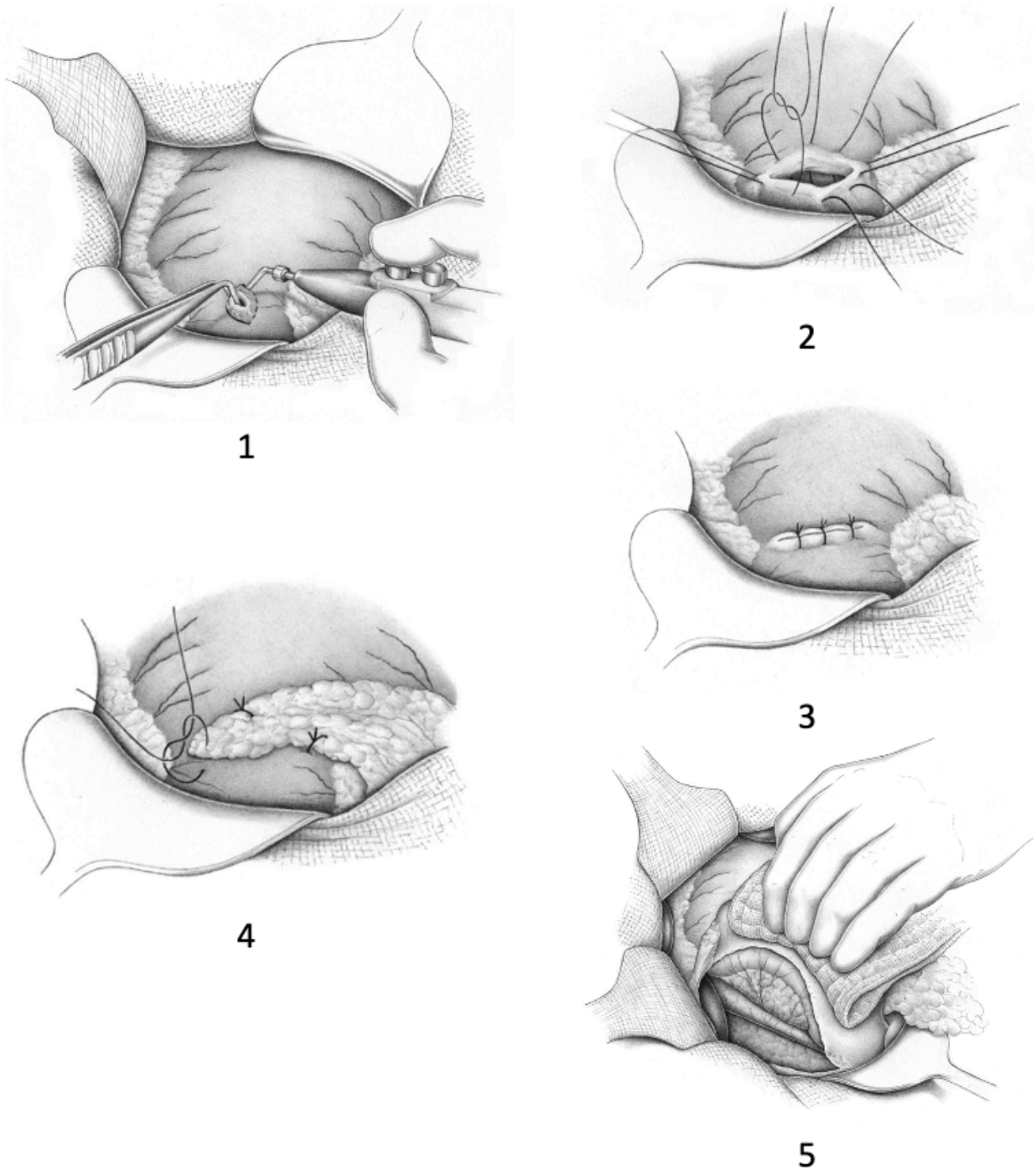

Fig. 7. Closure of a perforated peptic ulcer.

Omental onlay patch. If the tissue bearing the sutures does not provide enough support, if the sutures are under tension, and with friable tissue, it is recommended to cover the suture line with an omental patch, which is secured to the anterior gastric wall with interrupted sutures – 2-0 PGA (fig. 7-4).

Mobilization of the duodenum (Kocher maneuver). It is recommended to Kocherize (mobilize) the duodenum in cases with large anterior wall defects and significant suture tension in order to place the sutures without tension (fig. 7-5). If the perforated ulcer extends to more than half of the circumference (i.e. if there is

an “amputating ulcer”), then a Billroth I gastroduodenostomy is recommended, with resection of the antrum and pylorus together with restoration of continuity using a Billroth I anastomosis (fig. 10).

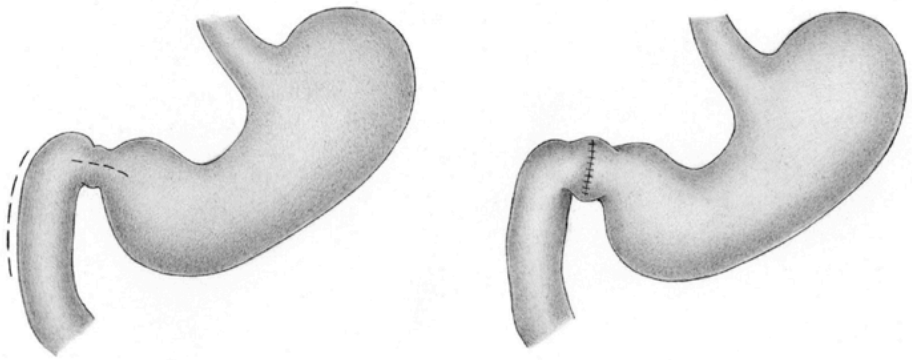

Fig. 8. Pyloroplasty. *After longitudinal incision of the pylorus and mobilization of the duodenum by a Kocher maneuver, the pylorus can be widened without tension using a transverse suture.*

Sometimes a perforation may be too large (i.e. >2 cm) or the inflamed tissues too friable to allow for a safe primary suture. Also, if a leak follows an attempt at primary repair, a second repair may not be feasible. In these instances, resection may be a safer option. Notably, large gastric ulcers or persistent leaks should raise the suspicion of malignancy, which may be encountered in up to 30% in this situation.

Gastrectomy. Nowadays, emergency gastrectomy (fig. 9) is reserved for a giant ulcer or a suspicion of malignancy when it is not safe to perform omental patch repair.

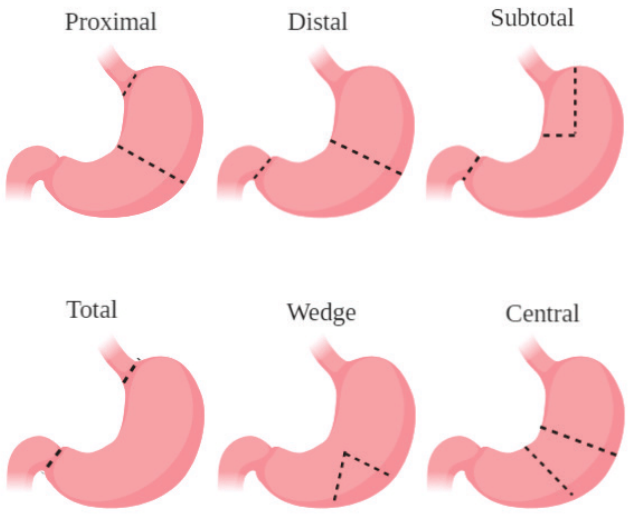

Fig. 9. Gastrectomy types.

A study comparing outcomes after gastrectomy and simple closure repair showed that there were no significant differences in patient recoveries. Longer operating times, ventilation and postoperative blood transfusion are associated with increased mortality. The larger size of perforation is associated with higher mortality and post-operative anastomotic leak. Gastric resections for acid reduction have become less favorable after proton pump inhibitors era.

There are several different techniques for restoring the digestive tract after gastrectomy but the goal in all of them is to obtain effective food intake with a low postoperative morbidity. Three reconstruction techniques are commonly performed after gastric resection: gastro-duodenostomy (*Billroth I or Péan reconstruction*), gastro-jejunostomy between the remnant stomach and the first jejunal loop (*Billroth II*), and gastro-jejunostomy with *Roux-en-Y reconstruction* (fig. 10). A Roux-en-Y reconstruction is the preferred technique after distal gastrectomy because the functional and endoscopic results are better than those achieved with Billroth I or II, while there are no differences in mortality and morbidity.

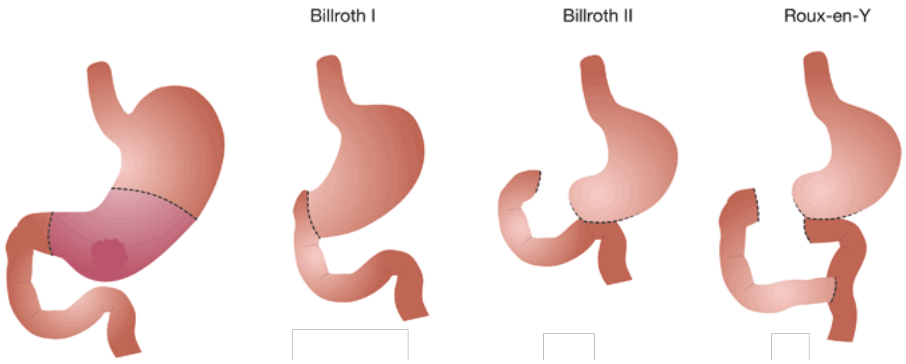

Fig. 10. Reconstruction types after gastrectomy.

Vagotomy. Vagus nerve plays an important role in the regulation of gastrin release and gastric acid secretion. Vagotomy is a procedure that transects the vagal trunks (*truncal vagotomy*) or distal nerve fibers (*highly selective vagotomy*). Truncal vagotomy aims to reduce the gastric acid secretion, thus reducing the risks of recurrent PUD. Selective vagotomy, which spares the hepatic and celiac divisions of the vagal trunks, are associated with higher long-term recurrence rates. Therefore, selective vagotomy is no longer performed. Few prospective randomized studies also reported substantially less ulcer recurrence in patients who underwent vagotomy in addition to omental patch repair. Nonetheless, vagotomy is now seldom performed for PPU due to the availability of medications such as histamine receptor antagonists, proton pump inhibitors and *H. pylori* eradication.

Laparoscopic approach. Laparoscopic repair techniques mirror techniques of open surgery and in particular sutureless techniques are more prominently

described. This may in part due to training in intra-corporeal knotting skills. Sutureless techniques involve gelatin sponge plug with fibrin glue sealing or endoscopic clipping.

"Dilution with solution is the solution to pollution". Towards the end of surgery, some surgeons like to irrigate the peritoneal cavity with 6-10 litres and even up to 30 litres of warm saline although no evidence has been found in literature to support that irrigation can lower the risk of sepsis. On the other hand, pneumoperitonuem induced during laparoscopic surgery may increase the risk of bacterial dissemination. It also seems to be a surgeon's preference whether or not to leave a drain at the end of surgery. There is no evidence to support that leaving a drain in can reduce the incidence of intra-abdominal collections. On the contrary, it may lead to infection of drain site and increased risk of intestinal obstruction.

Marginal ulcer perforation. Any form of gastroenteric reconstruction can lead to the development of ulcer at the margins of the gastrojejunal anastomosis, known as marginal ulcer. The incidence of marginal ulcer is around 1% to 16%. The ulcer tends to develop on the jejunal side of the stoma since it is directly exposed to the gastric acid. Local ischemia, NSAIDS, anastomotic tension, chronic irritation due to the suture material and duodenal reflux are implicated in the etiopathogenesis of marginal ulcer. Marginal ulcer can rarely lead to perforation. The presentation of patients with marginal ulcer perforation should be similar to PPU, however it may not be so. The small bowel contents has increased bacterial load and will also neutralize the gastric acid.

Operative management for marginal ulcer perforation includes anastomotic revision such as converting Billroth II gastro-jejunostomy reconstruction into a Roux-en-Y. It can also be treated with simple omental patch repair.

Surgical complications include the following:

- Pneumonia (30%).
- Wound infection.
- Abdominal abscess (15%).
- Cardiac problems.
- Diarrhea (30% after vagotomy).
- Dumping syndromes (10% after vagotomy and drainage procedures).

Postoperative care. Younger patients with no or limited systemic insult may have a faster recovery than elderly patient with several co-morbidities. Also, patients developing severe sepsis and associated organ failure have increased need for supportive care, a longer length of stay and higher risk for mortality.

Postoperative care should follow the recommended bundles by the Surviving sepsis campaign in order to reduce mortality. In a non-randomised study, PPU

patients were managed according to a protocol from hospital admission to 3 days postoperatively. The protocol aimed at preventing, detecting and treating sepsis, including risk stratification, sepsis screening, minimization of surgical delay, fluid resuscitation, broad-spectrum antibiotics, adequate monitoring, and administration of nutrition and fluids postoperatively.

Early administration of broad-spectrum intravenous antiobiotics is important, but the effect of additional antifungal therapy is not clear. More intra-abdominal infections, longer stay and higher mortality are associated with positive fungal cultures in PPU patients, but data to support routine antifungal therapy is scarce and has not demonstrated an effect on mortality.

Eradication of *H. pylori* significantly reduces the incidence of ulcer recurrence at 8 weeks after surgery.

Endoscopic follow-up after surgery. After surgery for gastric ulcers, routine post-operative endoscopy is often performed to rule out malignancy as the primary cause for perforation, as up to 13% of gastric perforations may be due to a gastric cancer. This is usually scheduled some 6 weeks after recovery from the procedure and after completion of *H. pylori* eradication. Endoscopic follow-up is usually not recommended in duodenal ulcers, as the risk for malignancy is very low. However, distinction between duodenal and gastric location can be difficult in the juxtapyloric region and in very inflamed and contaminated settings. Endoscopy should be considered if exact location is uncertain and no perioperative biopsy done.

Multiple choice questions

1. Anatomical parts of the duodenum are:
   A. Fundus, body, neck.
   B. Head, neck, body, tail.
   C. Left lobe, right lobe.
   D. Cardia, fundus, body, antrum, pylorus.
   E. Bulb, descending part, horizontal part, ascending part.

2. Abdominal pain in the moment of perforation is described:
   A. Like stabbing with a dagger.
   B. Moderate pain.
   C. Colicky pain.
   D. Dull pain.
   E. Intermittent pain.

3. Specific finding on abdominal radiography in cases of ulcer perforation:
   A. Air-fluid levels.
   B. Pneumoperitoneum (free gas in abdominal cavity).
   C. Distended bowel loops.
   D. Displacement of stomach into the mediastinum.
   E. None of the answers.

4. Complications of surgical treatment of perforated ulcers include:
   A. Pneumonia.
   B. Wound infection.
   C. Abdominal abscess.
   D. Dumping syndrome.
   E. All answers are correct.

5. Reconstruction methods after partial gastrectomy include:
   A. Billroth I.
   B. Billroth II.
   C. Roux-en-Y.
   D. Answers A and B.
   E. Answers A, B and C.

Clinical cases

1. A 62-year-old male patient complains of severe abdominal pain that started suddenly 2 hours ago. He has a history of gastric ulcer for 10 years without proper treatment. Physical examination: abdominal rigidity and tenderness, vomiting, tachycardia. Abdominal radiography: free gas in the abdominal cavity. What is the most likely diagnosis?

A. Perforated peptic ulcer.
B. Acute cholecystitis.
C. Acute bowel obstruction.
D. Acute gastritis.
E. Acute pancreatitis.

2. You examine a 45 y.o. female patient with clinical picture of perforated hollow organ. Which initial diagnostic method is indicated to confirm the perforation?

A. ECG.
B. CBC.
C. Abdominal radiography.
D. CT scan of chest and abdomen.
E. Ultrasonography of abdomen.

3. Female patient, 52 y.o. is presented with clinical signs of perforated peptic ulcer. History: gastric ulcer for 15 years. Physical examination: abdominal rigidity and tenderness. Abdomianl radiography and CT scan of abdomen confirm the presence of air in the abdominal cavity. What is the best method of treatment?

A. Antibiotics.
B. Infusion therapy.
C. Proton-pomp inhibitors.
D. Nasogastric tube.
E. Urgent surgical treatment.

MCQ answers						**Clinical cases answers**			
Question	1	2	3	4	5	Case	1	2	3
Answer	E	A	B	E	E	Answer	A	C	E

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