Gastric and duodenal ulcer. Pancreatitis. Ileus.

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Peptid ulcer - definition

- Deep defect in the gastric and duodenal mucosa (average 3mm – several cm) extended even to muscular layer
- Peptic erosion – superficial mucosal defect (average 1-5 mm)
Symptomatology of peptid ulcer disease (PUD)

**Spontaneous**

- **Dyspepsia** persistent, recurrent (not always, e.g. NAIDs ulcers)
- **Abdominal discomfort or pain** burning or gnawing, epigastric, localised or diffuse, radiate to back or not, hunger pains slowly building up for 1-2 hours, nonspecific, benign ulcers and gastric neoplasm
- **Bloating, fullness, Mild nausea** (vomiting relieves a pain)
Symptomatology of peptid ulcer disease

Meal related
- Gastric ulcer pains is aggravated by meals (weight loss)
- Duodenal ulcer pain is relieved by meals (do not lose weight)

Emergency
- Severe gastric pain well radiating (penetration, perforation)
- Bloody vomiting and tarry stool
Peptic ulcer – location in GIT

- Common: esophagus, stomach or duodenum
- Other: at the margin of a gastroenterostomy, in the jejunum, Zollinger-Ellison syndrome, Mackel’s diverticulum with ectopic gastric mucosa
Characteristics - Gastric ulcer

- Peak 50-60y, M:F = 1(2):1
- Pain often diffuse, variable – squizing, heaviness or sharp puncuating (may absent)
- Poorly localized, may radiate to back, 1-3 h after food
- Aggravated by meals
- Severe gastric pain well radiating indicate penetration or perforation
- Seasonal occurance (autumn, spring)
Characteristics – duodenal ulcer

- M:F = 4:1, peak 30-40 y
- Pain well localized, epigastric, chronic, intermittent, relieved by alkalic food
- Often late onset 6-8h after meal or independent (night)
- Familiar occurrence
- Smokers
- Blood 0 type
- Complication – penetration into pancreas (pancreatitis)
Etiopathogenetical considerations
Gastro-duodenal physiology

- Anatomy (stomach-antrum, body, fundus)
- Components of gastric juice
  - Salts, water
  - Hydrochloric acid
  - Pepsin
  - Intrinsic factor
  - Mucus
- Components of duodenal juice
  - Enzymes (trypsin, chymotrypsin)
  - Water
  - HCO3-
  - Bile acids, bilines
Regulation of digestive activity

- Stimulates by ingestion of food
- The composition of gastric juice depends on the velocity of its production
- The gastric secretion in the morning is low and increases in the afternoon
The secretion of gastric acid

- The cephalic phase is based on sensory stimuli
- Gastric phase of stomach secretion begins as soon as the food arrives into the stomach
- The intestinal phase of gastric secretion is induced when the chyme reaches the duodenum
Hydrochlorid acid production

- Secreted by parietal cells
- Stimulated by parietal endogenous substances
  - Gastrin I, II (G) – gastrin cells
  - Acetylcholin (M1) – vagi
  - Histamine (H2)
  - Prostaglandins (E1, I2)
  - norepinephrin
- Functions
  - Converts pepsinogen into active pepsins
  - Provide low pH important for protein breakdown
  - Keeps stomach relatively free of microbes
Mucosal protection

- **Gastric mucus** – 0,1-0,5 mm soluble vs. Gel phase
  - Mucin (MUC1, MUC2, MUC5AC and MUC6 produced by columnar epithelium
  - Gel thickness prostaglandins (PG E2) COX I ↑ inhibitors ↓
- **Bicarbonate**
  - Collumnar epithelium in stomach, pancreatic juice to duodenum
  - Enters the soluble and gel mucus, buffers H+ ions
- **Mucosal (epithelial) barrier**
  - Mechanical support against H+
- **Blood supply into mucose**
  - Removal of H+ ions
  - Supply with HCO3
Break through mucosal defence

- **First line defense** (mucus/bicarbonate barrier)
- **Second line defense** (epithelial cell mechanisms barrier function of apical plasma membrane)
- **Third line defense** (blood flow mediated removal of back diffused H+ and supply of energy)
  - If not working than epithelial cell injury
Break through mucosal defence

- **First line repair** - restitution
- **Second line repair** - cell replication
  - If not working than acute wound formation
- **Third line repair** – wound healing
  - If not working than ulcer formation
Etiopathogenesis

- Balance between hostile and protective factors
- „No gastric acid, no peptic ulcer“ - misconception
Etiopathogenesis

- **Aggressive factor**
  - Helicobacter pylori
  - Nonsteroidal Anti Inflammatory Drugs (NSAIDs)
  - Cushing ulcer (adrenocorticosteroids)
  - Hyperacidity (abnormalities in acid secretion)

- **Protective factors**
  - Curling ulcer (stress, gastric ischemia)
  - Abnormalities in gastric motility, duodenal-pyloric reflux,
  - GERD
  - NSAIDs (abnormality in mucus production)
Helicobacter pylori

- Barry Marshall & Robin (1982)
- Gram - curved rod, weakly virulent, likes acid environment, produces urease
- Acquired in children (10% - 80%), highest in developing countries (contaminated water ?)
- Positive in > 90% of duodenal ulcer and >80% of gastric ulcer (mainly diabetics)
- Large percentage of people infected, but not all develop peptic ulcer

**Mechanisms:**
- Role in ulcer (or cancer) controversial – gastritis
  - leaking proof hypothesis
  - gastrin link hypothesis
  - ammonia production
Nonsteroidal Anti Inflammatory Drugs

NSAIDs

- Associated with < 5% of duodenal ulcer, ~ 25% of gastric ulcer
- Inhibition of cyclooxygenase-1 (COX-1)
  - cyclo-oxygenase-1 - permanently expressed in cells
  - cyclo-oxygenase-2 - inducible inflammatory enzyme

Prostaglandins
- increase mucous and bicarbonate production,
- inhibit stomach acid secretion,
- increase blood flow within the stomach wall

Mechanisms:
  - Local injury
    - direct (weak acids, back diffusion of H+)
    - indirect (reflux of bile containing metabolites)
  - Systemic injury (predominant)
    - decreased synthesis of mucosal prostaglandins PGE2, PGI2

NSAID users: incidence of H. pylori in patients with gastric ulcers < duodenal ulcers
Mechanisms of NSAID-Related Ulcer Formation

- NSAID → Epithelial injury → Prostaglandin-mediated effects
  - ↓ Mucin
  - ↓ Surface active phospholipids
  - ↓ HCO₃ secretion
  - ↓ Mucosal proliferation

- Direct effects → Microvascular injury
  - Increased adhesion molecule expression → Neutrophil adherence → Stasis → Microvascular ischemia → Free radical formation → Ulcer

- Erosion

Hyperacidity

- **Gastrinoma** (Zollinger-Ellison sy.) peptic ulcers (0.1% of all cases) mainly in unusual locations (e.g. jejunum)
  - gastrin-producing islet cell tumor of the pancreas (gastrinoma) (50%), duodenum (20%), stomach, peripancreatic lymphnodes, liver, ovary, or small-bowel mesentery (30%)
  - in 1/4 patients part of the multiple neoplasia syndrome type I (MEN I)
  - hypertrophy of the gastric mucosa, massive gastric acid hypersecretion
  - diarrhea (steatorrhea from acid inactivation of lipase)
  - gastroesophageal reflux (episodic in 75% of patients)

- **Hypercalcaemia**
  - i.v. calcium infusion in normal volunteers induces gastric acid hypersecretion. Calcium stimulates gastrin release from gastrinomas.
  - beneficial effect of parathyreoidectomy
Other factors

Rarely, certain conditions may cause ulceration in the stomach or intestine, including:

- radiation treatments,
- bacterial or viral infections,
- physical injury
- burns (Curling ulcer)
Genetic factors

- Genetic predisposition for ulcer itself
  - Familiar aggregation of ulcer disease is modest in first-degree relatives
    3x greater incidence 39% pure genetic factors; 61% individual factors
    (stress, smoking) Finnish twin cohort (13888 pairs) (Räihä et al., Arch
  - 20–50% of duodenal ulcer patients report a positive family history;
    gastric ulcer patients also report clusters of family members who are
    likewise affected

- Genetic predisposition for H. pylori

- Genetic influences for peptic ulcer are independent of genetic
  influences important for acquiring H pylori infection (Malaty et al.,
  Arch Intern Med. 160, 2000)
- increased incidence of H. Pylori caused ulcers in people with type
  Oblood
Smoking

- correlation between cigarette smoking and complications, recurrences and difficulty to heal gastric and duodenal PUD
- smokers are in about 2x risk to develop serious ulcer disease (complications) than nonsmokers
- involvement of smoking itself in ulcer etiology „de novo“ controversial (?) (? Stress associated with smoking)

Mechanisms

- smoking increases acid secretion, reduces prostaglandin and bicarbonate production and decreases mucosal blood flow
- cigarette smoking promotes action of H. pylori (co-factors) in PUD
Stress

Animal studies
- inescapable stress-related ulcer (H. Selye)

Human studies
- social and psychologic factors play a contributory role in 30% to 60% of peptic ulcer cases
- conflicting conclusions? ("ulcer-type" personality, A-type persons, choleric, occupational factors - duodenal ulcer)
- long-term adrenocorticoid treatment

Background
- stress-related acute sympathetic, catecholaminergic and adrenocortical response (GIT ischemia)
- increases in basal acid secretion (duodenal ulcers)
Other factors

COFFEE AND ACID BEVERAGES
- Coffee (both caffeinated and decaffeinated), soft drinks, and fruit juices with citric acid induce increased stomach acid production
- no studies have proven contribution to ulcers, however consuming more than three cups of coffee per day may increase susceptibility to H. Pylori infection

ALCOHOL
- mixed reports (some data have shown that alcohol may actually protect against H. Pylori)
- intensifies the risk of bleeding in those who also take NSAIDs
Causes - conclusions

**Gastric ulcer**
- ↑ mucous permeability to H⁺
- not necessary hyperacidity, even anacidity
- ↑ gastrin (in hypoacidity)
- delayed gastric emptying
- duodeno-antral regurgitation
- (bile acids)

**Duodenal ulcer**
- ↑ number of parietal cells
- ↑ gastrin only after meat
- ↓ HCO₃⁻ production
- hyperacidity
- rapid gastric emptying
- ↓ neutralisation of acid 80-90% H. pylori

Lack of protective factors predominate

Predominance of aggressive factors
Peptic ulcer disease - diagnosis

Radiological diagnosis

- In use until 70's: barium x-ray or upper GI series
- 30% false results
Peptic ulcer disease - diagnosis

Laboratory diagnosis

- refractory (to 8 weeks of therapy) or recurrent disease
- basal gastric acid output (?hypersecretion)
- gastrin calcium - (gastrinoma, MEN)
- biopsies of gastric antrum - (H. pylori)
- serologic tests - (H. pylori) IgG, IgA
- urea breath tests - (H. pylori)
Peptic ulcer disease - diagnosis

Endoscopic diagnosis – stomach

- Today‘s principal diagnostic method
- Observation
- Biopsy and histology
Duodenal Ulcer (DU)  Gastric Ulcer (GU)
Medical therapy - principles

- reduce gastric acidity by mechanisms that inhibit or neutralize acid secretion
- coat ulcer craters to prevent acid and pepsin from penetrating to the ulcer base,
- provide a prostaglandin analogs to maintain mucus
- remove environmental factors such as NSAIDs and smoking,
- reduce emotional stress (if possible)
Peptic ulcer disease - therapy

Medical therapy

- Antacids - large doses required 1 and 3 hours after meals, magnesium hydroxide - diarrhoea
- Histamine H2-receptor antagonists - cimetidine, ranitidine, famotidine and nizatidine
- Proton pump inhibitors – resistant to other therapies, prevent NSAID gastroduodenal ulcers, omeprazole, lansoprazole
- Prostaglabin stimulators - Sucralfate, Misoprostol
Peptic ulcer disease - therapy

Surgery

- Vagotony
- Bilroth I (antrectomy) + vagotomy
- Pyloroplasty + truncal vagotomy
Complications

- **Hemorrhage**
  - Most common, 5–20% of patients, duodenal > gastric ulcers,
  - men > women, 75% stops spontaneously, 25% need surgery
  - Vomiting of blood
  - Melena

- **Perforation**
  - 5–10% ulcers, in 15% die
  - Peritonitis
  - gastric > duodenal ulcers

- **Penetration**
  - 5-10% of perforating ulcers
  - pancreas, bile ducts, liver,
  - small or large intestine

- **Gastric outlet obstruction**
  - 5% ulcers, pyloric stenosis
  - inflammation, scarring
  - duodenal > gastric ulcer
  - endoscopic ditation
  - surgery
Pancreatitits
Acute pancreatitis

- 1–2 % of patients hospitalised in surgical wards with the diagnosis of acute abdomen
- The incidence of the disease in men equals with that in women
- The disease occurs especially in the fifth decade of life
Etiologic factors of acute pancreatitis

- Disease of gallbladder and bile ducts
- Alcoholism
- Obstruction of draining ducts and Vater’s papilla
- Duodenal diseases (ulcer, diverticulum, obstruction)
- Injuries, surgeries
- Infections (viral, bacterial and parasitic)
- Endocrine metabolic impairments (diabetes mellitus, hyperlipaemia, hypercalcaemia)
- Toxic substances (alcohol, drugs – thiazides, glucocorticoids, etc.)
- Immunologic factors
- Hereditary factors
- Idiopathic pancreatitis
Acute pancreatitis - definition

- Inflammatory impairment of pancreas
- Associated with oedema, various stages of autodigestion, necrosis and haemorrhage in its parts
- Cause - the intrapancreatic activation of proteases (it is not exactly known why)
- High morbidity and mortality
- The mortality rate in severe haemorrhagic necrotic pancreatitis currently reaches even 70 %
Acute pancreatitis - etiopathogenesis

- at the beginning, the cell impairment of the ducts and acini is either evident or hidden
- which brings about the release of digestive pancreatic enzymes
- hydrolases trigger the activation of proteolytic, lipolytic and other pancreatic enzymes
Acute pancreatitis - etiopathogenesis

- The activation of these enzymes causes an impairment of blood vessels and lymphatic pathways.
- The impairment of capillaries and lymphatic ducts ends up by their obstruction or overall destruction.
- Consequently, an impairment or even autodigestion of the acinar cells release and activate enzymes and cellular proteins.
- The pancreatic kallikrein system is activated.
Acute pancreatitis - etiopathogenesis

- Further progression brings about an overall vasodilatation, increased capillary permeability, shock with acute renal failure.
- The subsequent change resides in the occurrence of ARDS (adult respiratory distress syndrome).
- Finally, the chain of events leads to irreversible shock.
Acute pancreatitis - symptomatology

- Pain - projects from the epigastric area into the back
- Nausea and vomiting with intestinal hypermotility, paralytic ileus
- Ascites
- Obstructive jaundice
- Hypovolaemia, hypotension, circulatory shock
- Disseminated intravascular coagulation
- Pulmonary oedema, renal failure
- Hyperglycaemia
- Development of tetany
- Pancreatic encephalopathy
Acute pancreatitis - therapy

- The basic therapeutic rule is to discontinue autodigestion and avoid the systemic impairments developing in consequence of the release of enzymes into circulation.

- Surgical intervention may reside in resection of necrotic part of pancreas and removal of ascitic fluid
Chronic pancreatitis

- Progressive destruction of glandular parenchyma with gradual extinguishment of acinar cells, fibrosis and tissue atrophy
- Impairments of the pancreatic exocrine function
- Impairment of endocrine function occurs later
Ileus – Intestinal obstruction
Ileus – Intestinal obstruction

- Intestinal contents cannot be forced further in aboral direction
- Transit of intestinal content depends:
  - on an intact state of intestinal lumen
  - on peristalsis
Intestinal motility

Depends on the

- functional state of intestinal musculature
- supply by oxygen
- inervous and humoral regulation
Intestinal obstruction - etiopathogenesis

- Mechanical obstruction of the intestinal lumen (occlusion, obturation)
  - Compression
  - Obturation
  - Strangulation

- Paralysis of the intestinal musculature (intestinal pseudoobstruction)
  - Spasm
  - Paralysis
Ileus

- Severe state is developing which is even now incurable – the ileus
- Intestinal inactivity, autodigestion of the intestinal mucosa and breakdown of the internal environment
Ileus - causes

- postobstructional (mechanical obstruction)
- pseudoobstructional (cessation of intestinal peristalsis)
Ileus

- Irreversible, incurable clinical syndrome
- Early diagnosis and treatment
- Acute abdominal pain, often immediately followed by surgical intervention
- 20% of all urgent surgical intervention
- 95% of cases yield an affliction of the small intestine (abdominal adhesions)
- Abdominal adhesions (spontaneously, or in consequence of intraperitoneal inflammation.)
The majority of adhesions causing intestinal obstruction is however caused by preceding operations.

5% of abdominal operations are complicated by intestinal obstruction.

Internal and external hernias, and tumours (Most frequent causes of the small intestine obstruction)
Mechanical obstruction - Etiology

- more frequently in the elderly population
- caused by tumours, inflammatory processes and volvulus
Mechanical obstruction - Etiology

- In the intestinal lumen (polypoid tumours, intussusception, bezoars, meconium, bile stones, etc.)
- Intramural (congenital anomalies – e.g. atresia, stenosis, Meckel’s diverticulum, tumours, etc.)
- In the intestinal surroundings (congenital, but especially post-operative adhesions, hernias, volvulus, compression of intestine by abscess, tumour, etc.)
Acute pseudoobstruction

- Can accompany the conditions
  - after laparotomy and orthopedic operations
  - diseases of abdominal organs (intestinal ischaemia, pancreatitis, pyelonephritis, peritonitis, intraperitoneal abscess)
  - diseases of thoracic organs (pneumonia, acute myocardial infarction)
  - overall diseases (sepsis, shock, polytrauma, decreased level of plasma potassium).
Chronic pseudoobstruction

- primary (familial visceral myopathies)
- secondary (collagenoses, muscular dystrophies, amyloidoses, radiation impairment)
- diseases of the smooth intestinal muscles
- diseases of the myenteric plexus (familial visceral neuropathy, paraneoplastic degeneration, Chagas’ disease, intestinal agangliosis, neuronal intestinal dysplasia, myotonic dystrophy),
Chronic pseudoobstruction

- diverticulosis of the small intestine
- coeliac sprue
- jejunoileal bypass
- some neurologic diseases (Parkinson’s disease, tumours in the brain stem)
- Endocrine and metabolic disorders (myxoedema, feochromocytoma, hypoparathyreoidism...)
- drugs (opiates, phenothiazines, clonidine, tricyclic antidepressive drugs, vincristine)
Ileus - Pathogenesis

Clinical manifestation of intestinal obstruction vary as they are determined by:

- Mechanism
- Localisation
- Stage of obstruction,
- actual state of the gastrointestinal system
- organism per se
Intestinal obstruction

- Impairs the intestinal transport, secretion, digestion, absorption and immunity functions
- Leads to hypoxia - primary mechanism in the pathogenesis of ileus
- Hypoxia decreases the resistance of intestinal mucosa and thereby enables autodigestion
Intestinal obstruction

- The correct function of intestinal mucosa is determined by a continuous supply of oxygen
  - by blood
  - by aerophagia (alimentary respiration)
- Hypoxia of intestinal mucosa can be formally caused
  - by intestinal hypoperfusion,
  - hypoxaemia
  - hypoventilation of the intestinal lumen
Luminal hypoventilation

- pathogenetic mechanism of mechanical intestinal obstruction and pseudoobstruction
- caused by
  - every mechanical obstacle disabling the transport of intestinal contents
  - by all changes leading to the cessation of peristalsis.
Intestinal pseudoobstruction - etiology

- Heterogenous character
- All impairments of the contractile apparatus of the intestinal smooth musculature
- Excitation-contraction coupling
- Local impairments of intestinal circulation
- All situations associated with activation of the sympathetic system and centralisation of circulation
- As all hypoxaemic states
Intestinal obstruction

- vomitus, diarrhoea (organism strives to get rid of the deoxygenated intestinal contents)
- aerophagia (to compensate the physiological level of oxygen in the intestinal lumen by)
- absorption ceases
- the mucosa afflicted by autodigestion develops inflammation with a pronounced exudation
- finally the mucosa succumbs to necrosis
- impair the immunity functions of the intestinal wall, the state of which enables the development of migrating peritonitis
Intestinal obstruction

- Reduced absorption, increased secretion, exudation (lead to the accumulation of fluid in the intestinal lumen)
- Vomiting, reduced oral intake of food, the oedema of the intestinal wall and splanchnic vasodilatation (hypovolaemia)
- Can deduct as much as 6 l of fluid from the circulation system
- Centralisation of circulation
Intestinal obstruction

- Hypoperfusion of respiratory muscles
- Reduce the ventilation of the lungs (pneumonia)
- Hypovolaemia and hypoxaemia (shock)
- The possibility of autodigestion and the tendency to limitate intestinal
Intestinal obstruction

- Hypoxia of intestinal mucosa stimulates aerophagia
- Intestinal distention
- Hypoxia becomes more profound as the epithelial cells occur in anoxic environment of pure nitrogen
- The intestinal distention limitates the movement abilities of the diaphragm
- Comprime the mesenterium, thus deteriorating the intestinal perfusion, and increasing the congestion of the intestinal wall
Intestinal obstruction

- Bacteria proliferate out of control
- Bacteria can enter the mesenteric lymph and portal circuit
- Endotoxins directly incur damage to intestinal mucosa, but can also transgress the walls of the obstructed bowel
- Impaired of myoelectrical and motor activities
Pathophysiological principles of ileus prevention

- Intestinal obstruction is curable until ileus develops
- Measures disabling ileus to develop
- Luminal ventilation, removal of digestive juices from the intestinal lumen, the procurement of sufficient intestinal perfusion by oxygenated blood
- Surgical therapy (assessment of the localisation and cause of obstruction, resection of the necrotic intestine)
Pathophysiological principles of ileus prevention

- Intestinal transport can be renewed solely by means of conservative therapy.
- Intestinal pseudoobstruction often requires a long-term conservative therapy.
- An exclusively conservative therapy increases the risk of the development of intestinal strangulation.
- Intussusception, volvulus or incarcerated hernia, it will be necessary to operate immediately.
Pathophysiological principles of Ileus prevention

- It is necessary to monitor continuously the serum electrolytes, acid-base balance and haemogram.
- Metabolic acidosis and leukocytosis are frequently present in coincidence with intestinal strangulation and advanced ileus.
OVERVIEW OF THE ILEUS PREVENTION

- Procurement of luminal ventilation
  - Gastrointestinal aspiration
  - Intraluminal insufflation of oxygen

- Removal of digestive juices
  - Gastrointestinal aspiration
  - Fasting prior to operation
  - Parenteral nutrition
  - Fasting after operation until the reappearance of intestinal motility

- Procurement of intestinal perfusion by oxygenated blood
  - Infusion therapy – maintenance of the volume and capacity of blood to transport oxygen. Correction of the deficit in fluids and electrolytes
  - Optimalisation of the cardiopulmonal and renal systems
  - Anaesthesia without hypoxaemia
  - Spinal anaesthesia
Thanks for your attention