Pathophysiology of the Gastrointestinal tract
Physiology

- Ingestion
- Digestion, secretion, absorption
- Motility
Gastro-oesophageal reflux (GER)

• Retrograde movement of gastric contents to oesophagus

• Connected with various disruptions of respiratory system
Gastro-oesophageal reflux (GER)

Protective mechanisms

• Antireflux barrier – lower sphincter
• Fast shift of the regurgitated material back
• Neutralization by saliva

• Disruption of the tonus of the lower sphincter
  ↓ neutralization and peristaltics
  ↓ coordination of lower oesophageal sphincter
Pyrosis

- Pain behind the sternum described as “heatburn”
- Occurs when gastric acid moves to oesophagus
- “Neutralization” drugs help
Outcomes of GER

- metaplasia
- Carcinoma in situ (Barret’s oesophagus)
- Carcinoma of oesophagus
Peptic ulcers of stomach and duodenum (PUD)

- Ulcers are chronic, often solitary lesions, that occur in any part of GIT that is exposed to aggressive factors of the gastric fluids.

- Ulceration – disruption of mucosa at least to the muscularis mucosae layer due to secretion of HCl and activation of pepsinogen.

- Erosion – superficial damage (mucosa).

- 10% of population have or will develop an ulcer.
Peptic ulcers of stomach and duodenum (PUD)

• Occur due to dysbalance of gastro-duodenal protective mechanisms and aggressive factors, while the effects are further enhanced by external or immunological factors
Peptic ulcers of stomach and duodenum (PUD)

Protective factors

- normal composition and production of mucin
- Alk. secretion of HCO$_3^-$
- intact microcirculation
- regeneration of gastric mucosa
- secretion of endogenous prostaglandins

Aggressive factors

- Helicobacter pylori
- drugs with ulcerogenous effects (NSAIDs)
- deleterious effects of duodenal fluids
- smoking, alcohol
- disruptions of microcirculation in the mucosa and submucosa
A Protective Factors
- Mucus
- Bicarbonate
- Prostaglandins
- Blood flow to mucosa
- Nitric oxide

Aggressive Factors
- Gastric acid
- H. Pylori
- Ethanol
- NSAIDs
- Oxidative stress

Healthy mucosa

B Protective Factors
- Mucus
- Bicarbonate
- Prostaglandins
- Blood flow to mucosa
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Aggressive Factors
- Gastric acid
- H. Pylori
- Ethanol
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Gastric ulcer
PUD – H. pylori infection

- colonization of gastric mucosa
- Does not enter cells, only mucosa (extracellular pathogens)
- Urease $\rightarrow$ ammonium $\rightarrow$ acid neutralization $\rightarrow$ reflexive production of acid
- Proteases $\rightarrow$ disruption of mucous layer
- Weak resistance of the mucosa
- **Digestion of the mucosa by acid and pepsin**
- Chronic ulcerations
PUD – Other factors

- Zollinger – Elisson syndrome (gastrinoma)
- Meckel’s diverticulum and ectopic gastric mucous membrane
PUD – symptomes

- Epigastric pain (heartburn)
- Pain worse at night and 1-3 hours after meal
- Nauseas, vomiting, loss of weight
- Complications: anemia, bleeding, perforation
- Cancer development is rare and connected to gastritis
PUD – animal models

- NSAIDs
- Acetic acid / acetic acid + H.pylori
- Ethanol
- Histamine
Pancreatitis

• Inflammation of the pancreas connected with edema, different degree of autodigestion, necrosis and haemorrhagia

• Acute vs chronic

• Acute:
  ➢ Edematous – self-limiting
  ➢ Necrotizing – necrosis correlates with the degree of damage
Pancreatidis

**Autodigestion**

- Proteolytic enzymes are activated in pancreas instead of duodenum
- Endotoxines, viruses, ischemia... etc.
- Activated proteolytic enzymes may activate other
- Proteolysis, edema, interstitial bleeding, vascular damage, necrosis
Pancreatitis - etiology

- Gallstones
- Alcohol
- Idiopathic
- Diseases of duodenum
- Endocrine or metabolic disease
- Immunological factors
- Hereditary factors
- Others

Other causes:
- Drugs and toxic substances
- Hypercalciemia
- Renal failure
- Viral infections
- Cystic fibrosis
- Trauma, operations
- ERCP
- Hyperlipidemia
Descending part of duodenum

Major duodenal papilla

Bile duct

Sphincter of bile duct

Hepatopancreatic ampulla

Sphincter of pancreatic duct

Pancreatic duct
Animal models of Pancreatitis

- Caerulein (↑proteolytic enzymes secretion)
- Lipopolysaccharide + ethanol
Diarrhea

• Acute:
  - 3 loose or watery stool / 24h
  - no longer than 2 weeks
  - Infections, toxins or medications
  - Passive movement of water by gradient
Diarrhea

Types:
- secretory
- osmotic
- abnormal motility

Causes:
- abnormal absorption of solutes and water
- Secretion of electrolytes
- osmotically active solutes in the intestine
- abnormal motility
- Inflammation with exudate, pus, blood
Diarrhea from abnormal secretion

Increase in intracellular cAMP

- inhibition of NaCl absorption
- stimulation of Cl⁻ secretion
- cholera
Osmotic Diarrhea

• Accumulation of weakly absorbable solutes:
  Intake: lactulose, Mg+, SO4-, PO3

• Malabsorption

• Specific disruptions of absorption (lactose)
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Separate hard lumps</td>
<td>Very constipated</td>
</tr>
<tr>
<td>Type 2</td>
<td>Lumpy and sausage like</td>
<td>Slightly constipated</td>
</tr>
<tr>
<td>Type 3</td>
<td>A sausage shape with cracks in the surface</td>
<td>Normal</td>
</tr>
<tr>
<td>Type 4</td>
<td>Like a smooth, soft sausage or snake</td>
<td>Normal</td>
</tr>
<tr>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
<td>Lacking fibre</td>
</tr>
<tr>
<td>Type 6</td>
<td>Mushy consistency with ragged edges</td>
<td>Inflammation</td>
</tr>
<tr>
<td>Type 7</td>
<td>Liquid consistency with no solid pieces</td>
<td>Inflammation</td>
</tr>
</tbody>
</table>
Diarrhea – animal models

• E.coli O157:H7
• V. cholerae
Obstipation

Definition:
• Stool movement - irregular or with hardship

• Less than 3x per week
  ➢ increased straining at defecation
  ➢ Hard stool
  ➢ Incomplete evacuation
Obstipation

• Extraluminal lesions

• Intramural lesions

• Intraluminal causes
Extraluminal lesions

- Adhesions: 60%
- Hernias: 10%

External – Inguinal, Femoral, Umbilical, Ventral

Internal – inherited, diaphragmatic, Mesenteric causes

- Neoplasias: 20%
  Carcinomas, Extraintestinal tumors
- Abdominal abscess
Intramural lesions

- Inherited – Malrotation or duplication
- Inflammatory – Crohn’s disease – 5%
- Infectious – TB, Actinomycosis, Diverticulitis
- Trauma - hematoma

- Neoplasias – Primary/Metastatic
- Etc. - 2-3%
- Intususception, Endometriosis, radition
Intraluminal causes

- Gallstones
- Enterolites
- Bezoars
- Foreign bodies
Foreign bodies
Pathophysiology

↑ motility and contractility
• Early diarrhea
• Fluids/electrolytes/third space
• Dehydration/hypovolemia/vomiting
• Hypokaliemia/hypochloremia/met. Alkalosis
• Oliguria/hemoconcentration
• Hypotension/shock
Ileus

• intestinal distension and slower or no movement stool in the intestinal lumen *without* proved mechanical obstruction

• Laparotomy, metabolic/electrolytic hypokaliemia

• Hyponatremia, hypomagnesemia, uremia, diabetic coma, abdominal infection, retroperitoneal bleeding, intestinal ischemia, sepsa, spinal cord injuries

• Drugs – opiates, psychotropics, anticholinergics
Inflammatory bowel diseases

IBD

Crohn’s disease
- Trasmural inflammation

Ulcerative colitis
- Whole GIT
- Mucosa
- Rectum & large intestine
Morbus Crohn (Crohn’s disease)

- Chronic inflammatory process affecting whole GIT
- Mouth – anus
- Most common: terminal ileum & colon ascendend
- Prevalence 27-106 / 100 000
- M : F = 1 : 1.2
- Average age on onset: 26
Etiology

• Genetic
• Smoking
• Infectious exogenous agens
• Endogenous bacteria
• Immunopathogenesis - ↑ production of TNF
Macroscopic changes

• Small intestine
  ➢ thickened + thinned
  ➢ discontinuous injury
  ➢ ulcerations + fissures

• Large intestine
  ➢ fistulae + abscesses
  ➢ early: aftoid ulcerations
  ➢ late: large & deeper ulcers, uneven distribution
Microscopic changes

• Inflammation affects all intestinal layers (transmural)

• Chronic inflammatory response, mostly Th1 lymphocytes

• Granulomas – 50-60% patients
Crohn's disease in terminal ileum

transmural
chronic
inflammation

fissuring ulcer

granuloma
Colitis ulcerosa (Ulcerative colitis)

• mucosa of rectum and large intestine
• diffuse, continuous inflammation, anus → proximal spread
• formation of pseudopolypes
• prevalence 100-200 per 100 000

• Early phase: accumulation of neutrophiles in crypts of Lieberkuhn – formation of abscesses
• Later phase: mucosal ulcerations and pseudopolyps
• Late phase: dysplastic changes of mucous membrane - ↑ risk of carcinoma
## MC vs UC

<table>
<thead>
<tr>
<th>Morbus Crohn</th>
<th>Colitis ulcerosa</th>
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<tr>
<td>• Transmural inflammation</td>
<td>• Pseudopolypyes</td>
</tr>
<tr>
<td>• Granulomas</td>
<td>• Diffuse infl.</td>
</tr>
<tr>
<td>• Discontinuos infl.</td>
<td>• Toxic megacolon</td>
</tr>
<tr>
<td>• Fat deposition</td>
<td>• Tumors</td>
</tr>
<tr>
<td>• Fissueres and fistules</td>
<td>• Rectum &amp; large intestine</td>
</tr>
<tr>
<td>• Tumors</td>
<td></td>
</tr>
<tr>
<td>• Anywhere in GIT</td>
<td></td>
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Liver

Function

• Metabolism – fat, sacharides and proteins
• Secretory – bile, bile acids, salts and pigments
• Excretory – bilirubin, drugs, toxins
• Syntetic – albumin, coagulation factors
• Depository – vitamines, sacharides, etc.
• Detoxification – toxins, ammonia, etc.
Icterus

• **yellow** colloration of skin, mucous membranes & sclera due to increase in serum bilirubin > 40-50 umol/L, 3mg/dL
  - Conjugated vs Non-conjugated
  - Obstructive vs Non-obstructive
  - Pre-hepatal, hepatal & post-hepatal
  - Ikterus ≠ liver damage
Ikterus

Metabolism of bilirubin

• Blood
  Bond to proteins and free

• Urine
  Urobilinogen

• Stool
  Sterkobilin
Ikterus - causes

• **Pre hepatal** (acholuric) – hemolytic
  - non-conjugated/indirect BIL/ pale urine

• **Hepatal** – viruses, alcohol, toxins, drugs
  - Hepatic damage – non-conjugated
  - Obstruction of tubules - conjugated

• **Post hepatal** (obstructive) – stone, tumor
  - conjugated/ direct BIL, dark yellow urine
Cirrhosis

**Diffuse** hepatic damage characterized by:

1. Total loss of normal architecture
2. Replacement of functional tissue by fibrous tissue
3. Nodules with parenchymal regeneration
Healthy liver
Cirrhosis
Etiology

• Alcohol 60-70%
• Virus hepatitis 10%
• Gall bladder disease 5-10%
• Cryptogenous cirrhosis – 10-15%
• Metabolic disruptions
  ➢ Primary hemochromatosis – 5%
  ➢ Wilson’s disease
• Drug induced liver damage
• Malnutrition
Complications

• Bleeding varices
• Hepatocellular failure
  ➢ Malnutrition, low levels of albumin and coagulation factors
• Hepatal encephalopathy
• Portal hypertension
  ➢ Ascites, portosystemous anastomoses, varices, splenomegaly
• Hepatocellular carcinoma
Portal Hypertension
Ascites in cirrhosis

- ascites = "beer belly"
Cholelithiasis

- Gall stones = crystalized bile
  - 80% cholesterol stones
  - 20% bilirubin stones (pigment stones)
Cholelithiasis - pathogenesis

• Bile – elimination of cholesterol
• Concentration of cholesterol trespass dilution capacity of the bile
• Formation of crystals
• Crystals → stones
• Pigment stones: non-conjugated bilirubin
• Bilirubin precipitates and forms crystals
Risk factors

- Age and sex (elderly, women)
- Race and demographics (native Americans, developed countries)
- Decreased motility of gallbladder (pregnancy, spinal cord injuries)
- Inherited (familial anamnesis, metabolic disruptions)
- Environment (estrogens, obesity, treatment by klofibrates)

- As much as 80% of patients are without risk factors (apart from age and sex)!
Acute cholecystitis

• **Calculus:** acute inflammation due to presence of a stone
  ➢ the most common complication of cholelithiasis

• **Acalculous:** without stones, the pathogenesis is less clear
  ➢ enlarged gall bladder, tense
  ➢ acute inflammation
  ➢ the wall is edematous and thickened
  ➢ complications: gangrene, perforation
Chronic cholecystitis

- Usually without the anamnesis of acute diseases
- Usually linked to presence of gall stones
- Symptoms resemble those of acute form
- Pathogens only in 1/3 of cases
- Patogenesis – various and often minimal
  - Normal or enlarged
  - The wall is thickened
  - Chronic inflammation
Ďakujem za pozornosť.