- Small intestine
- Large intestine, rectum
- Appendix

Pathology of gastrointestinal tract II

MUDr. Helena Skálová
Enterocolitis
= intestinal inflammation

- Infectious
- Malabsorption
- Idiopathic bowel disease
- Ischemia
- Diverticulitis
Enterocolitis - symptoms

- Loss of absorptive function, ↑ secretion, ↑ osmotic pressure, destruction of mucosa with exudation and haemorrhage, disturbed motility, malabsorption

**Symptoms:**

- **Diarrhea** (↑ frequency, volume, water content)
  - normal 200g, 65-85% water → >250g, 70-95% water
  - E.g. viral enteritides, cholera

- **Dysentery** (↓ volume, pain, blood)
  - E.g. bacterial (shigellosis), amebiasis, E. coli, salmonelosis

- **Ileus** (usually paralytic)
  - E.g. ischemic

- **Adhesions in peritoneal cavity, peritonitis**
  - E.g. IBD, diverticulitis
Infectious enterocolitis

- 2nd most frequent infectious disease (/person/year)
- In developing countries 12000 † of children / day, 50% † before 5th year
- Contaminated water and food
- Acute, self-limited disease
- Different patogenes acc. to age, nutrition, immunity, environment (incl. health care, tourism)
- In 50% cases pathogene is not isolated
Viral gastroenteritis

- Rotavirus, calicivirus, adenovirus, astrovirus
- Short incubation period (1-2 days), short-term immunity
- Children, communities
- + gastritis (vomiting), colitis
- Lower vili, ↑ lymphocytes in LPM, loss of enterocyte brush border, predominance of mucinous cells, hypertrophic crypts
Bacterial enterocolitis

- **Ingestion of bacterial toxins:**
  - Rapid onset (hr), subside in 1 day
  - Intense watery diarrhea, dehydration, pain
  - *Staphylococcus aureus, Vibrio, Clostridium perfringens*

- **Infection by toxigenic microorganisms producing toxins:**
  - Onset during hr - days
  - Watery diarrhea, less commonly bloody, dehydration, pain
  - *Travelers diarrhea*

- **Infection by enteroinvasive microorganisms:**
  - Onset during hr – days
  - Destruction of epithelial cells
  - Dysentery, fever
  - *E. coli, Salmonella, Shigella, Campylobacter*
Hemorrhagic diarrhea, dysentery

**SHIGELLA DYSENTERY (SHIGELLOSIS):**
- Shigella A-D, G- anaerobic
- Shiga toxin (A)
- Antropotropic:
  - endemic in developing countries
  - dirty hands disease
  - highly infectious
- Hemorrhagic colitis:
  - blood and mucous in stools
  - spastic pain
  - fever

**ESCHERICHIA COLI:**
- Bowel comensal, causing infections in other tissues
- Bowel infection caused by enteropathogenous strains
- Verotoxin (Shiga toxin)
- Mostly children, incl. newborns
- Resamble shigella dysentery
Complications of bowel infection caused by enteroinvasive bacteria (90% enterotoxic E. coli, Shigella, Salmonella), other bacteria (Streptococcus pneumoniae), drugs ...

Mostly children

Shiga toxin injures endothelia → thrombotic microangiopathy
  - Acute renal failure
  - Hemolytic anemia (erythrocyte damage in injured vessels)
  - Thrombocytopenia (thrombocyte vasting in microthrombi)
  - Damage of other organs

Mortality 5%
Possible permanent consequences (chronic renal insufficiency, hypertension)

Check uremia in patients with infectious hemorrhagic diarrhea !!!
Salmonella diseases

**SALMONELLOSIS**
- G-
- S. enteritidis, S. typhimurium ...
- fecal contamination of chicken and beef meat
- self-limited *watery diarrhea*

**TYPHOID FEVER:**
- S. typhi
- Source: acutely and chronically ill patients, excrements
- Developing countries
- RES, macrophages

**Course:**
- 1st week: bacteriemia, fever, headache
- 2nd week: skin rash, abdominal pain, exhaustion
- 3rd week: ulceration of Payer patches, intestinal bleeding, shock
- Complications: intestinal rupture, peritonitis, cholecystitis
Other enteritides

CHOLERA

- G-, Vibrio cholerae
- Choleratoxin
- Epidemic (Ganga, Haiti)
- Source: contaminated water, food, ill people

- Watery diarrhea (paralysis of absorption)
- Water loss up to 14l/day
- Severe dehydratation, mineral disorder
- Lacks fever, abdominal pain, blood and mucous in stools

- Therapy: atb, ion and fluid substitution

PSEUDOMEMBRANÓZNÍ KOLITIDA

- Clostridium difficile
- Overgrowth after systemic atb therapy
Malabsorption

- Defective intake and transportation of nutrients by intestinal mucosa (general, selective)
- Pathologic changes due to lack of nutrients

**Symptoms:**
- diarrhea, weight loss, anemia (general malabsorption)
- intolerance of certain food components (selective - enzymatic defect)

- Celiac disease
- Tropical sprue
- Enzymatic defect – lactasis, defective transportation of glucose, galactose, fructose, cystinuria ...
- Whipple disease
- Postradiation enteritis and colitis
- Amyloidosis
- Pancreatic enzymes defficiency (chronic pancreatitis)
- Idiopatic bowel disease
Celiac disease  
(celiac sprue, gluten enteropathy)

- Allergy to wheat proteins (gluten)
- Chronic inflammation, T-lymfocytes
- **Antibodies** against tissue transglutaminase, endomysium, gliadin, reticulin → serology
- **Symptoms:** diarrhea, flatulence, weight loss, fatigue
- Children: slow growth (small, thin figure), neurological defects
- Accompanying autoimmune diseases: e.g. dermatitis herpetiformis
- Complications: Refractery celiac disease, lymphoma
- **Therapy:** gluten-free diet
- Whites, familiar (HLA-DQ2)
- Dg. In any age, mainly children and young adults
Whipple disease

- **Tropheryma whippelii** (G+)
- Men, white, 40-50 y.o.
- **Intestine, CNS, joints**
- **Symptoms:** diarrhea, weight loss, polyarthritis, psychiatric changes, cardiac abnormalities
- Duration: years
- **Therapy:** atb
Idiopathic bowel disease: Crohn disease, Ulcerative colitis

- Chronic relapsing inflammatory diseases
- Inadequate immune reaction to common intestinal flora in genetically predisposed individuals (T-lymphocytes)
- Highest incidence: Europe, USA
- **Symptoms:** repeated diarrhea with some blood (days - weeks), abdominal pain, weight loss, fatigue, subfebrile temperature
- **Dg.:** symptoms, X-rays, lab, biopsy
- **Associated diseases:** primary sclerosing cholangitis (PSC), polyarthritis, iriditis, carcinoma (UC)
Crohn disease

- **Segmental** damage in whole GIT, esp. small and large intestine, starting usually in terminal ileum

- **Transmural inflammation, aphtous and fissural ulcers, fistulas, strictures, adhesions, abscesses, stenosis**

- Micro: nonnecrotizing **microgranulomas**

- **Complications:** stenosis, failure of passage, perforation, peritonitis, fistulas between intestinal loops, to other organs, on skin surface (perianal), bleeding, malabsorption, AA amyloidosis, carcinoma

- Any age, mainly 20-30 y.o., whites
Ulcerative colitis

- Large intestine (proctitis), in pancolitis also terminal ileum
- Flat, large ulcerations in mucosa, pseudopolyps (mucosal regeneration and hyperplasia)
- Micro: no microgranulomas
- **Complications:** toxic megacolon, bleeding, perforation, peritonitis, carcinoma
- Therapy: 20% colectomy
Causes of acute ischemic enterocolitis:
- Occlusion of tr. coeliacus, a. mesenterica superior et anterior (thrombosis, embolia) → transmural necrosis
- Hypoperfusion (cardiac failure, shock) – necrosis of mucosa and other parts of intestinal wall
- Other: volvulus, stricture, herniation, amyloidosis, vasculitides (polyartetriitis nodosa, Henoch-Schönlein, Wegener)

Causes of chronic ischemic enterocolitis:
- Atherosclerosis
- Amyloidosis

Symptoms:
- Transmural necrosis: strong pain, bloody stool, signs of peritoneal irritation
- Absence of peristalsis (paralytic ileus), nausea, vomiting, shock

RF: higher age, cardiac disease, adhesions in peritoneal cavity
Obstruction of intestine
Ileus (= intestinal blockage)

- **Mechanic:**
  - Occlusion (tumor, foreign body, bile stone, parazites)
  - Stenosis
  - Compression
  - Strangulation

- **Paralytic:**
  - Hamorrhagic necrosis
  - Suppurative peritonitis
  - Postsurgical
  - Spastic (lead poisoning)

- **Complications:**
  - peritonitis
  - necrosis and perforation above stenosis
  - mineral disbalance
Acquired focal dilation of intestinal wall (0.5-1cm)

Colon, mostly sigmoideum
Oesophagus, stomach, duodenum, appendix

Thin or absent muscularis propria

50\% patients over 60 y.o. (Europe, USA)

Complications: diverticulitis, obstruction, perforation, stenosis
Most common inborn defect in GIT (3%)

- Rest of ductus omphaloentericus (10 cm above IC valve)
- Usually 1-10 cm in length

- Often contains ectopic tissue:
  - gastric mucosa (colonisation by H. pylori, inflammation)
  - pancreatic tissue

- **Complication:** inflammation, ulceration, bleeding, bowel obstruction, tumor
Colonic polyps

- Polyp = mucosal bulge
- On stalk, sessile
- Hyperplastic
- Inflammatory
- Mezenchymal tumor
- Adenoma
- Carcinoma from adenoma
Colonic adenoma

- Polypous lesion, pedunculated or sessile
- Tubular, vilous, tubulovilous, serrated
- Low grade – high grade dysplazia
- Risk of carcinoma ↑ in sessile vilous adenoma > 4 cm
- 50% after 60. y.o.
- Sporadic, familiar, FAP
- Biopsy:
  - Nontumorous polyp x adenoma x carcinoma
  - Degree of dysplazia
  - Resection margins
Colorectal carcinoma

- 98% adenocarcinoma, 55% rectosigmoidoideum
- Malignant transformation of adenoma
- Carcinogenesis: APC, K-RAS, p53 ...
- RF: diet, obesity, lack of movement
- Symptoms: fatigue, weakness, anemia, occult bleeding, dyscomfort
- Metastases: LN, liver, lungs, bones
- Prognosis depends on stage (local invasion, absence/presence of lymphnodal and distant metastases)
- 60-80 y.o., before 50 y.o. in patients with UC, FAP, Lynch syndrome
- ↑ USA, Australia, New Zealand, Middle and Eastern Europe
- ↓ Mexico, South America, Africa, Japan
Familiar adenomatous polyposis (FAP)

- AD, germ line mutation of APC
- Hundreds to thousands adenomas all over colon
- Adenocarcinoma in the age around 20 years
- Adenomas, adenocarcinoma of duodenum (major papilla)
- Fundic gland polyps in stomach

- Gardner syndrome:
  - atheromas, osteomas, desmoids
- Turcot syndrome:
  - brain tumors
Lynch syndrome
(Hereditary nonpolyposis colorectal carcinoma, HNPCC)

- AD, defective systém of DNA repair (mutation of mismatch repair genes)
- Flat adenomas, dysplasia, no polyps
- Colorectal (CRC), endometroid, urotelial carcinomas, carcinoma of stomach, small intestine ...
- CRC- before 50. years, in left colon, may be multiple
- Proof of MSI (microsatellite instability) by IHC or molecular methods

- Turcot syndrome:
  - brain tumors
Acute appendicitis

- Any age, mostly adolescents, young adults (7% population)

- Koprostasis, bile stone, parazites (oxyuriasis) → pressure on the wall → ischemia

- Serous → ulcerophlegmonous → gangrenous

- Symptoms: pain, peritoneal irritation, nausea, vomiting, ↑temperature, leucocytosis

- Complications: 2% perforation, pyelophlebitis, portal thrombosis, liver abscesses, bacteriemia

- Dif. dq.: lymphadenitis mesenterialis, acute salpingitis, extrauterine gravidity ...

- Chronic appendicitis: questionable diagnosis, except Crohn disease!
Neuroendocrine tumor (NET) = carcinoid

- **Neuroendocrine tumor (NET)**
- Neuroendocrine carcinoma (NEC)
- From DNES (diffuse neuroendocrine system)

- Often incidental finding in resected appendix
- Appendical appex, 1-3 cm
- **Symptoms:**
  - acute appendicitis
  - **carcinoid syndrome** (serotonin production, metastases in liver):
    - intermittent flush
    - astmatic attacks
    - attacks of diarrhea
    - thickening of tricuspid a pulmon. valve

- Most frequent tumor of appendixu and small intestine
- Other locations: stomach, pancreas, bronchi ...
**Most frequent GIT tumors - summary**

- **Esophagus:**
  Adenocarcinoma, squamous carcinoma

- **Stomach:**
  Intestinal and diffuse adenocarcinoma

- **Small intestine and appendix:**
  NET

- **Large intestine and rectum:**
  Adenoma, adenocarcinoma
Incidence of GIT malignant tumors

WORLDWIDE INCIDENCE OF CARCINOMAS

1. Colorectal
2. Stomach
3. Liver
4. Esophagus
5. Pancreas
6. Oral cavity
7. Gall bladder

CZECH REPUBLIC – INCIDENCE, MORTALITY

<table>
<thead>
<tr>
<th>Carcinoma</th>
<th>Incidence (new cases / year)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>8100</td>
<td>50%</td>
</tr>
<tr>
<td>Stomach</td>
<td>1600</td>
<td>80%</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>1000</td>
<td>60%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>450</td>
<td>90%</td>
</tr>
</tbody>
</table>
Incidence of malignant tumors

WORLDWIDE

• Men:
  1. Lung cancer
  2. Prostate cancer
  3. Colorectal cancer

• Women:
  1. Breast cancer
  2. Cancer of uterine cervix
  3. Colorectal cancer
  4. Lung cancer

CZECH REPUBLIC

• Men:
  1. Prostate cancer
  2. Colorectal cancer
  3. Lung cancer ↓

• Women:
  1. Breast cancer
  2. Colorectal cancer
  3. Cancer of uterus
  4. Lung cancer ↑

↑ cancer of pancreas, ovarium, stomach

Mortality:
  1. Cardiovascular diseases (50%)
  2. Tumors (30%)

Highest mortality: lung and breast cancer
Lowest mortality: prostate cancer