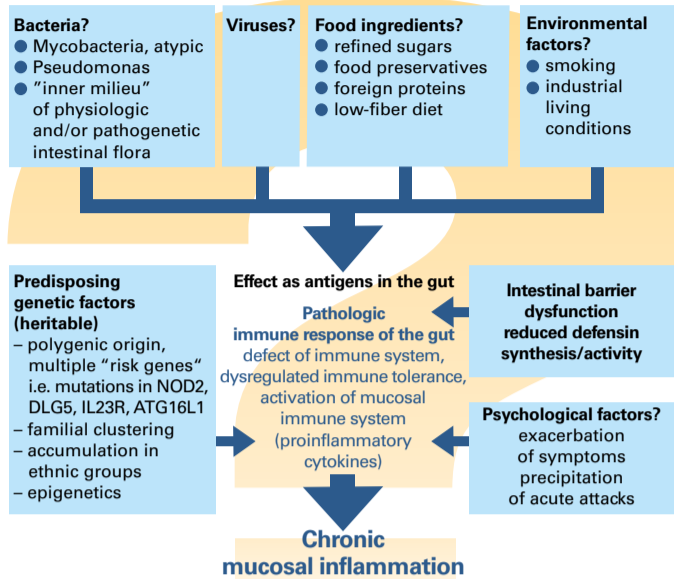


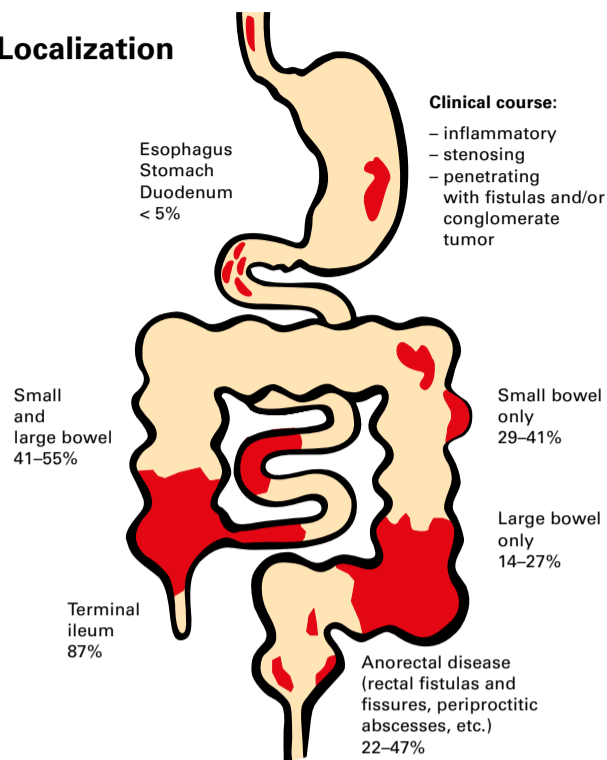
Crohn's Disease

Epidemiology – Etiopathology – Clinical features – Diagnosis – Therapy

Aspects of etiopathology



Localization



Epidemiology (Europe)

Incidence (new cases):
up to 12 cases/100,000 inhabitants per year

Prevalence (patients):
up to 320 cases/100,000 inhabitants

Clinical features and findings

Acute attacks alternate with asymptomatic or low-symptomatic intervals

Intestinal symptoms:

abdominal pain, especially postprandial
diarrhea (in 20% constipation)
blood in stool (rare)
symptoms of malabsorption
anal lesions

extraintestinal symptoms:

anemia, fever
general feeling of illness
weight loss
arthritis, sacroiliitis
erythema nodosum
pyoderma gangraenosum (rare)
secondary amenorrhea
stomatitis aphthosa
eye symptoms

Clinical findings:

tenderness, abdominal pain caused by palpation
palpable resistance
conglomerate tumor
anal fistulas, periproctitic abscesses
gallstones (involvement of the small bowel), nephrolithiasis
osteoporosis

rare: amyloidosis, association with ankylosing spondylitis

Laboratory findings

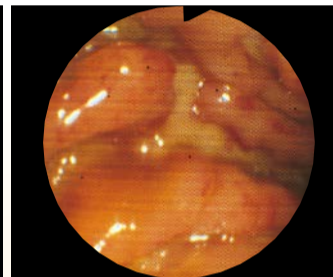
- Disease activity:** ESR after Westergren ↑
leukocytes ↑
thrombocytosis
hemoglobin ↓
total protein ↓, electrophoresis
acute-phase proteins ↑
C-reactive protein ↑
calprotectin in stool ↑
- Deficiencies:** albumin ↓
iron ↓, ferritin ↓, (transferrin ↑)
vitamin B₁₂ ↓, folate ↓, zinc ↓, magnesium ↓
electrolytes, vitamin D ↓
- Exclusion of infectious causes:** serologic detection of infectious agents (antibody titers)
direct detection of infectious agents in stool culture, mucosal smear, and mucosa biopsies
procalcitonin in serum
- Special investigations:** ¹⁴C-glycocholic acid breath test, cholestyramine test (bile acid absorption), glucose-H₂ breath test (bacterial overgrowth), lactose-H₂ breath test (lactose intolerance) and fecal α₁-antitrypsin excretion (protein loss)

Diagnosis



Endoscopy

- aphthous lesions and ulcers in normal or inflamed mucosa
- fissural ulcers
- cobblestone relief
- narrowing of the lumen, stenosing
- segmental, discontinuous spread within the bowel, rectum spared (80%)

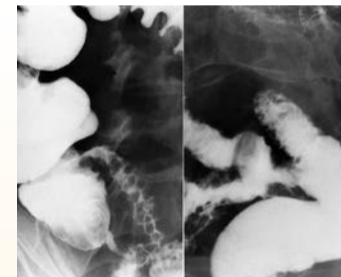


Small bowel diagnosis

- capsule endoscopy (cave: stenosis) or (double)-balloon endoscopy (PE-sampling)

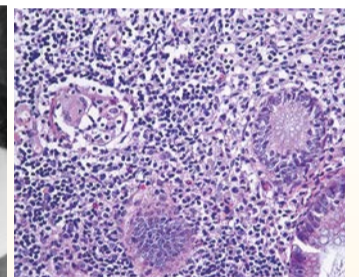
(Radio)diagnostic treatment

In case of complications (fistulas, abscess):
CT, MRI, MRI-Sellink for small bowel diagnosis



Radiology

- ulcers (aphthous lesions)
- cobblestone relief
- reduced distension of the gut
- distance phenomenon (thickening of the wall) with asymmetry
- shrinkage of the mesenteric root
- fistulas
- narrowing of the lumen, stenosis (filiform)
- segmental, discontinuous spread within the bowel



Histology

- lymphocytic infiltration, transmural, discontinuous extension
- focal lymphoid hyperplasia
- fibrosis of all layers of the wall
- fissures
- epithelioid cell granulomas (30–60%) in the submucosa
- crypt abscesses (rare)
- goblet cells unchanged (colon)

Differential diagnosis

- enterocolitis caused by infectious agents
Campylobacter jejuni/coli, Yersinia enterocolitica, Salmonella, Shigella, Amoeba, Chlamydia
- pseudomembranous colitis (Clostridium difficile)
- ischemic colitis
- radiation colitis
- ulcerative colitis
- collagenous colitis
- drug-induced colitis
- acute appendicitis
- malignancy of the gut
- celiac disease, food allergy
- diverticulitis

Severity of the attack

- Severity of acute attack according to clinical criteria CDAI (Crohn's disease activity index), Best (1976):**
< 150 points inactive disease, remission
150–220 points mild attack
220–450 points moderate attack
> 450 points severe attack
- Course of disease corresponding to Vienna classification (1998)/Montreal classification (2006):**
Considering age at diagnosis, location and behavior
• inflammatory, non-penetrating, non-stricturing phenotype
• stricturing phenotype
• penetrating, fistulizing phenotype



Ultrasound

Thickening of the wall, stenoses, conglomerate tumor, abscesses in the abdomen, fistulas



OP findings

Resected ileocecal specimen with stenosed terminal ileum

Medical therapy for induction of remission

- Mild to moderate attack: ileocecal involvement:** mesalazine (5-ASA) 3–4.5 g/day orally (in mild attack: if possible monotherapy) and/or budesonide 9 mg/day orally (without extraintestinal manifestations)
- Solely colonic involvement:** systemically acting glucocorticoids or sulfasalazine 3–6 g/day orally (indicated if joints are affected, but increased number of side effects)
- Involvement of rectum and distal colon:** topical treatment with mesalazine (5-ASA) suppositories, foam or enemas, corticosteroid foam or enemas or budesonide foam or enemas

- Moderate to severe attack:** Prednisone orally (rarely i.v. necessary, but higher doses may be used)
- | | | | | | | | |
|--------|-----------|--------|-----------|--------|-----------|-------------------|------------------------------------|
| Week 1 | 60 mg/day | Week 3 | 30 mg/day | Week 5 | 20 mg/day | Week 7 – Week 12: | 10 mg/5 mg/day, tapering of dosage |
| Week 2 | 40 mg/day | Week 4 | 25 mg/day | Week 6 | 15 mg/day | | |

Dosage reduction according to clinical improvement (possibly more slowly), for specific situations to avoid early recurrence, prolong 10-mg-dosage period, if necessary additionally topical treatment

For esophageal and gastroduodenal location early treatment with systemically acting corticosteroids and/or immunosuppressives combined with proton pump inhibitors

Moderate to severe attack with steroid-dependent or steroid-refractory course:

- Frequent acute attacks (chronically active/persistent course)
Chronic fistula disease
- Azathioprine** 2–2.5 mg/kg body weight/day (effective after 3–6 months), possibly increasing dosage, check EBV serostatus before starting treatment
- 6-mercaptopurine** 1–1.5 mg/kg body weight/day (alternatively in case of gastrointestinal intolerance to azathioprine)
- Methotrexate** 25 mg/week i.m. or s.c., if effective continuation with 10–15 mg/week s.c.
- Strong inflammatory activity, severe clinical course, if rapid therapy success is necessary and if surgery is not possible:
- TNF-α-antibodies:** infliximab 5 mg/kg body weight i.v. at weeks 0, 2, and 6, thereafter every 8 weeks (infliximab biosimilars accordingly) or adalimumab 80 mg s.c. at week 0, thereafter 40 mg s.c. every 2 weeks (if rapid therapy success is necessary: adalimumab 160 mg s.c. at week 0, 80 mg s.c. at week 2, thereafter 40 mg s.c. every 2 weeks)
- α₁β₂-integrin-antibodies:** vedolizumab 300 mg i.v. at weeks 0, 2 and 6, thereafter every 8 weeks
- IL-12/IL-23-antibodies:** ustekinumab i.v. at week 0 (≤55 kg: 260 mg; >55 kg until ≤85 kg: 390 mg; >85 kg: 520 mg), 90 mg s.c. at week 8, thereafter 90 mg s.c. every 12 weeks

Cave: Possible long-term risks not yet completely known! Before initiation of therapy with biologics: exclusion of TBC / latent TBC (chest x-ray, Interferon-gamma release assay); Hepatitis B, C; HIV, EBV; severe infections, abscesses, severe heart failure, neurological disorders

- Alternative drugs:**
- elemental diet ("astronaut's diet") for 4–12 weeks (only small bowel involvement) by a naso-duodenal feeding tube
 - metronidazole 500–1000 mg/day (no longer than 4 weeks) (for symptomatic fistula treatment)
 - antibiotics, i.e. ciprofloxacin 2 x 250 mg to 2 x 500 mg

Therapy during remission/ Long-term treatment for maintenance of remission

- cessation of smoking (start withdrawal of nicotine)
- mesalazine (5-ASA) 3–4 g/day, moderately active only for patients after surgery
- continuation of a primary effective treatment with azathioprine, 6-mercaptopurine or methotrexate (10–15 mg/week) without steroids (at least for 4 years) or after remission induction with TNF-α-antibodies
- biologics: see induction therapy
- fiber-rich, wholesome diet (cave: stenosis)
- replacement of deficiencies (nutrition therapy, vitamin B₁₂, folic acid, iron, zinc, fat-soluble vitamins, calcium, possibly bisphosphonates)
- cholestyramine in cholegous diarrhea
- antidiarrheal agents (codeine, lomotil, loperamide)
- lactose-free diet in case of lactose intolerance
- reconsider surgical options in an interdisciplinary consultation

Complications in the course of Crohn's disease:

- frequently: stenoses with following acute complete ileus or chronic (sub-)ileus perforation and peritonitis
abscess formation in the abdomen, loop abscess
septic-toxic situation
resistance to drug treatment
- rarely: severe bleeding
toxic megacolon
ureteral obstruction
severe extraintestinal symptoms and accompanying diseases, e.g. PSC, colon carcinoma (small bowel?)
- fistulas: viscerovisceral
viscerocutaneous
viscero-vesical (urinary tract infections)
rectovaginal

Surgical therapy (interdisciplinary cooperation)

- macroscopic resection of involved small or large bowel; resection should be performed "gut-sparing" in the healthy
- end-to-end anastomoses
- extirpation of fistulas
- stricturoplasty
- alternatively endoscopic balloon dilatation for defined stenosis instead of surgery (long-term response 25–50%)