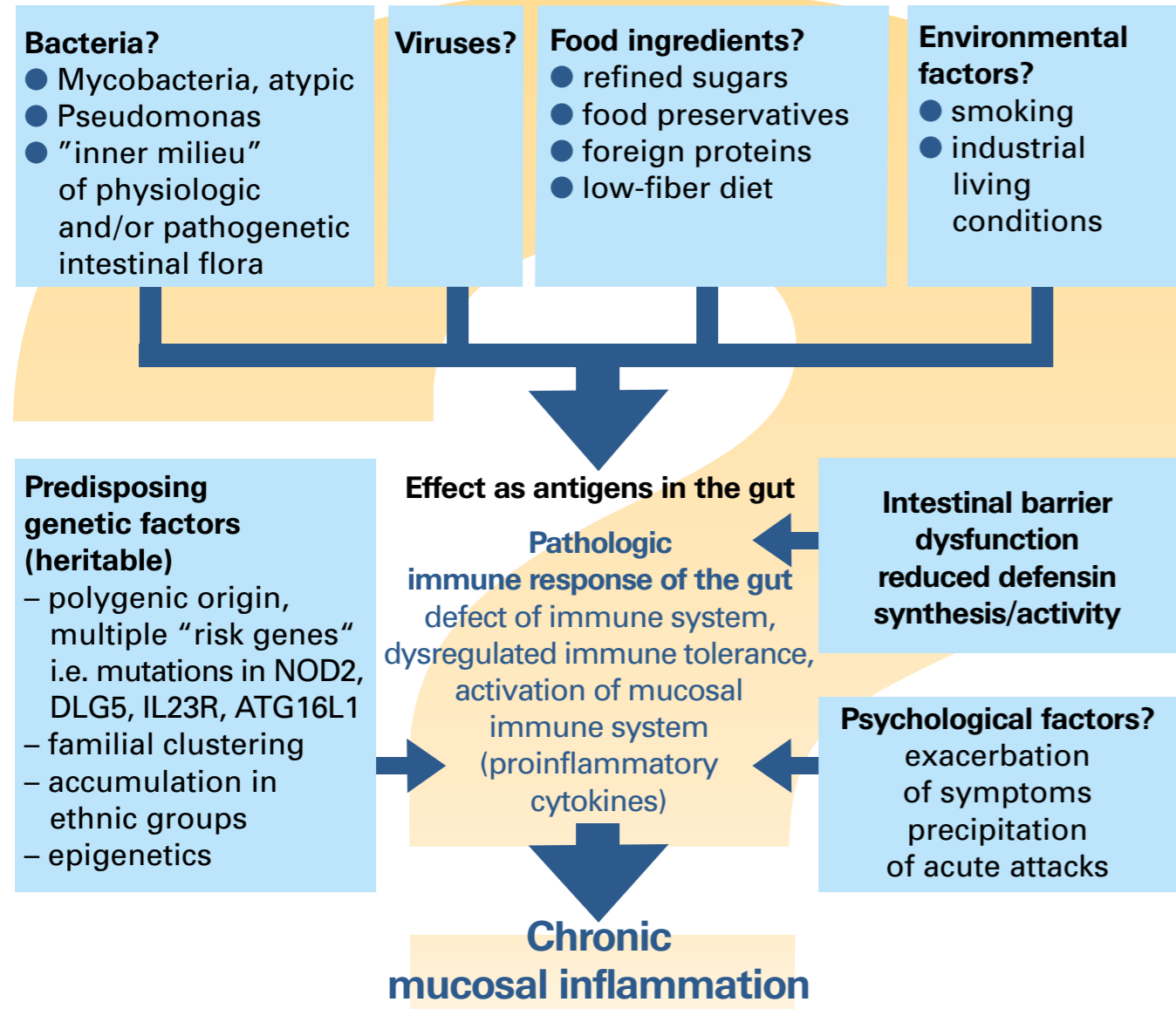


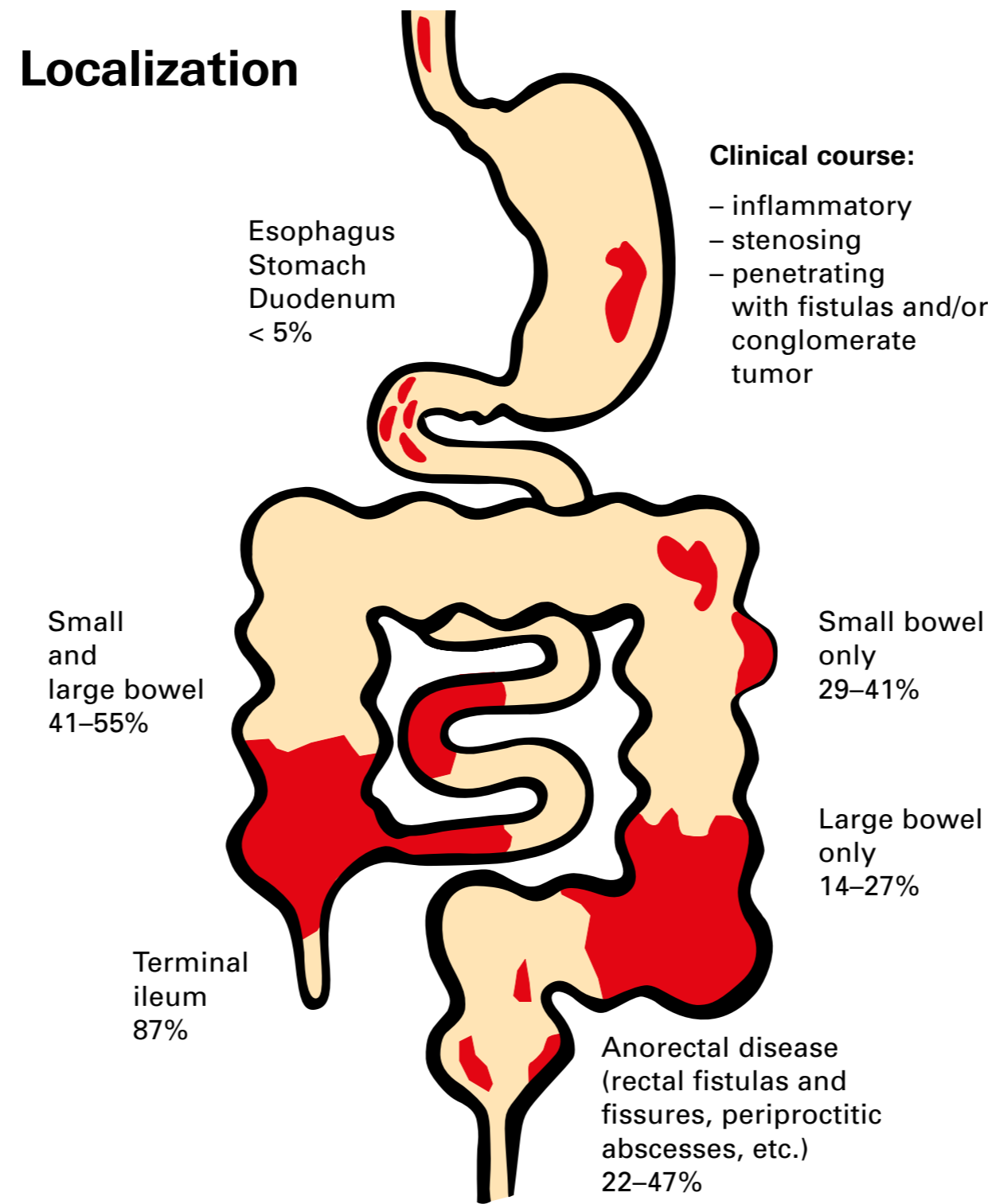
# Crohn's Disease

## 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

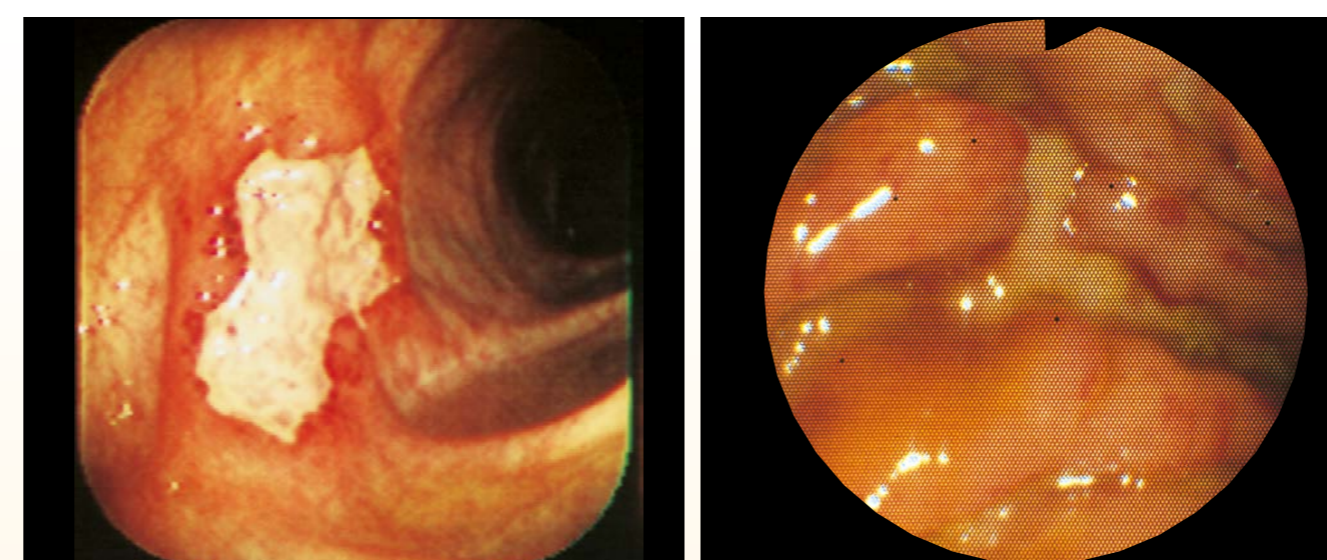
**Clinical findings:**  
 tenderness, abdominal pain caused by palpation  
 palpable resistance  
 conglomerate tumor  
 anal fistulas, periproctitic abscesses  
 gallstones (involvement of the small bowel), nephrolithiasis  
 osteoporosis

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 B<sub>12</sub> ↓, 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:** <sup>14</sup>C-glycocholic acid breath test, cholestyramine test (bile acid absorption), glucose-H<sub>2</sub> breath test (bacterial overgrowth), lactose-H<sub>2</sub> breath test (lactose intolerance) and fecal α<sub>1</sub>-antitrypsin excretion (protein loss)

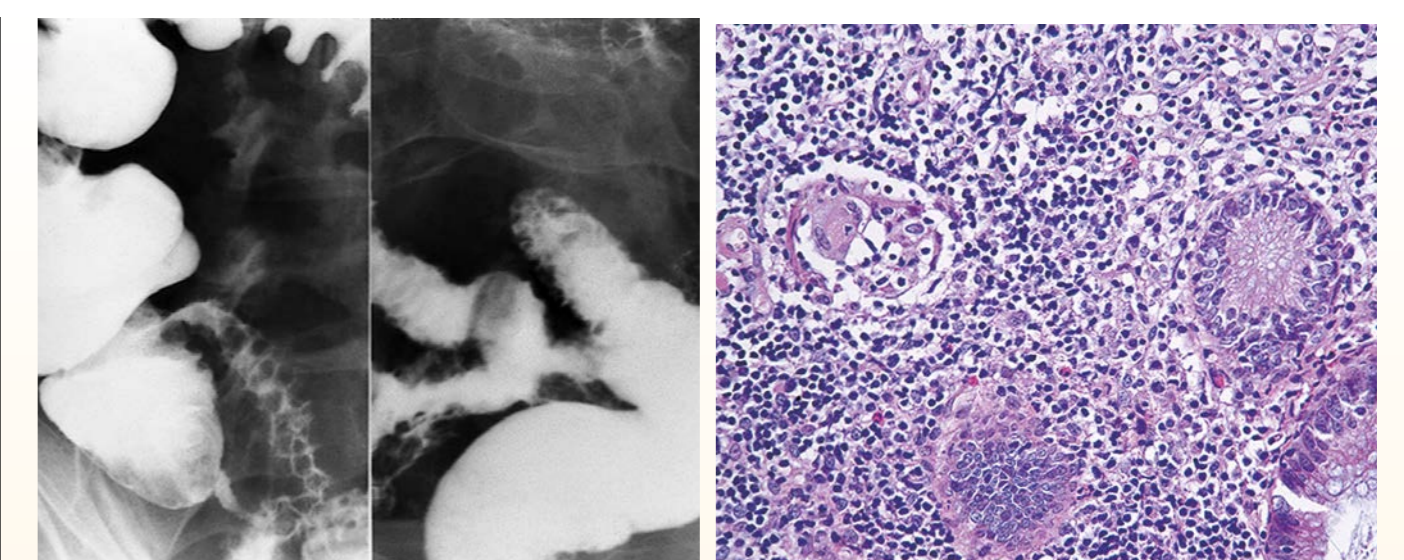
### Diagnosis



**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)  
 • shrinkage of the mesenteric root with asymmetry  
 • fistulas  
 • narrowing of the lumen, stenosis (filiform)  
 • segmental, discontinuous spread within the bowel

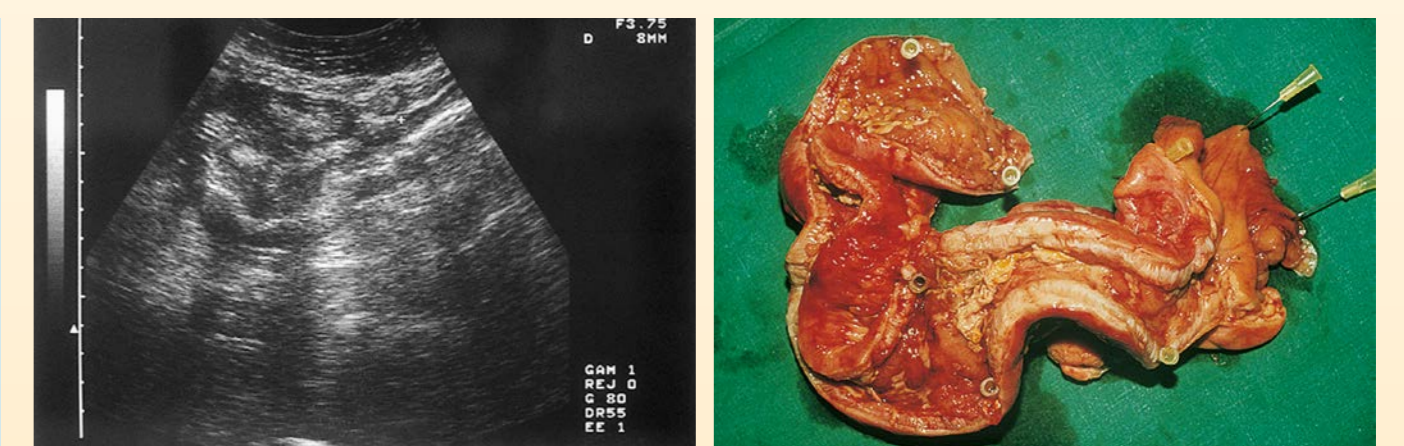
**Histology**  
 • lymphocytic infiltration, transmural, discontinuous extension  
 • focal lymphoid hyperplasia  
 • fibrosis of all layers of the wall  
 • fissures  
 • epithelioid cell granulomas (30–60%) in the submucosa  
 • crypt abscesses (rare)  
 • goblet cells unchanged (colon)

### 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)

**α<sub>4</sub>β<sub>7</sub>-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 B<sub>12</sub>, 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: viscerocutaneous  
 viscerovisceral  
 viscerovesical (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%)