Medical University of Graz

19ème Journée d'automne d'actualités en Gastro – entérologie

CHUV
Auditoire Yersin
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CHUV

ULCERATIVE COLITIS AND CROHN´S DISEASE

RCUH ET MALADIE DE CROHN

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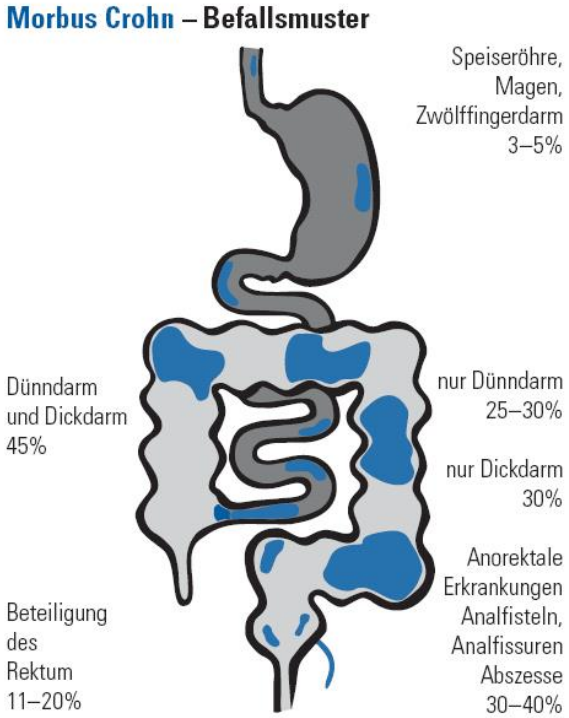
Department of Internal Medicine

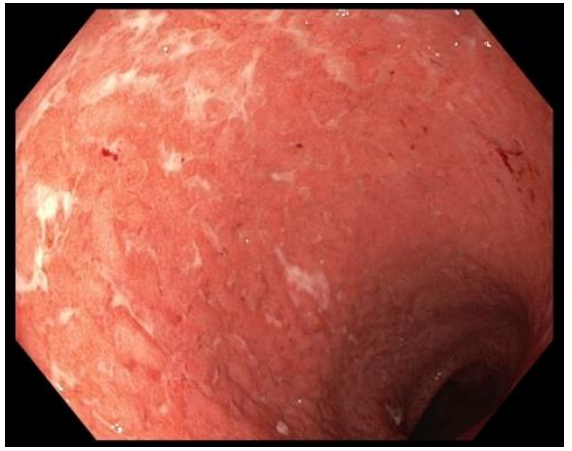
Medical University of Graz, Austria

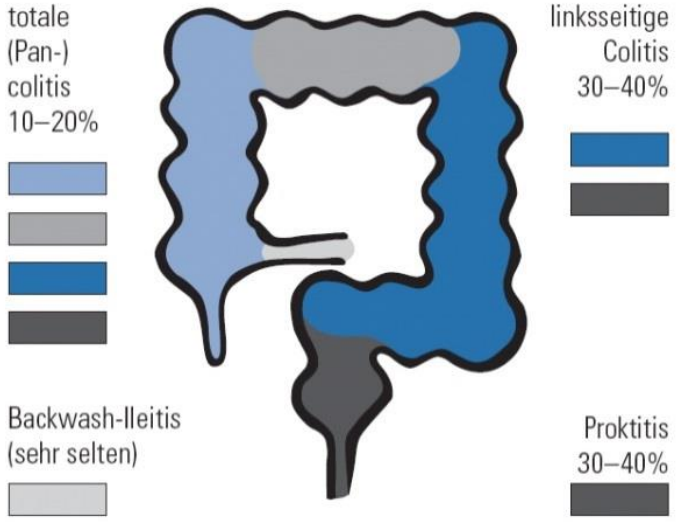
Inflammatory Bowel Diseases (IBD)

Crohn's Disease (CD)



Ulcerative Colitis (UC)





Complications of Crohn´s disease

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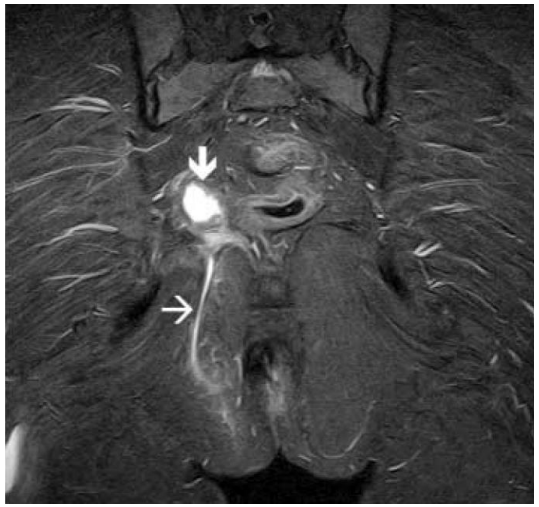
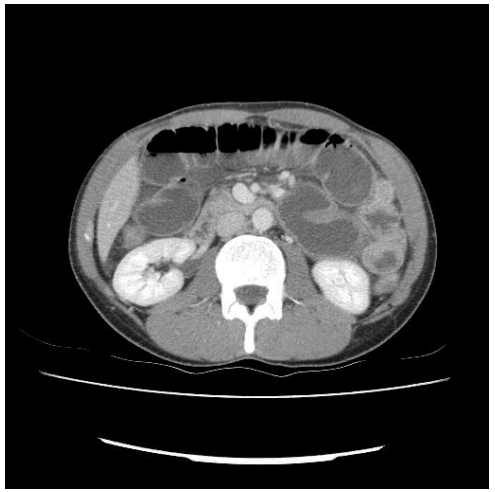
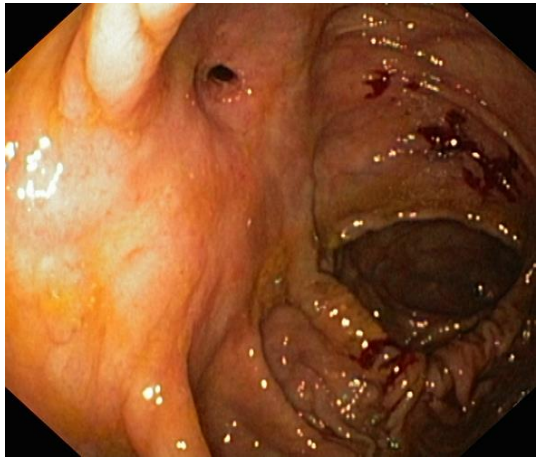
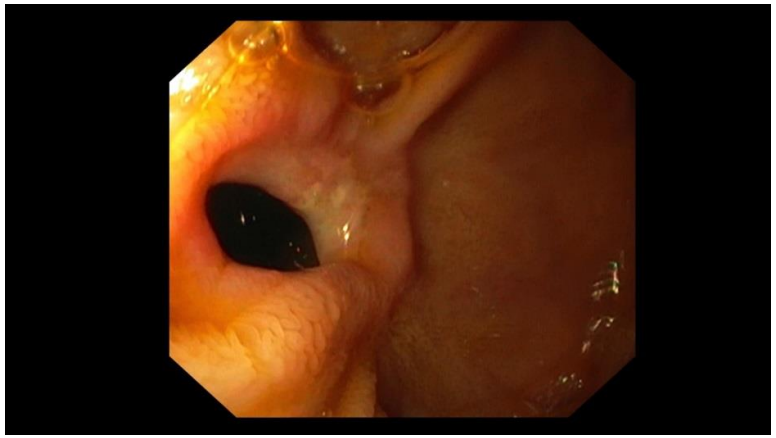
Fistula and Abscesses



Stenosis and Bowel Obstruction







Medical Therapy for IBD (2020)

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Corticosteroids

- Prednisolone, methylprednisolone p.o + i.v.
- Budesonide, budesonide MMX p.o.+ topical

Salizylates

- Mesalazine p.o. + topical
- Sulfasalazine p.o.

Immunosuppressants

- Azathioprine, 6-mercaptopurine p.o.
- Methotrexate s.c.

Small Molecules

- Tofacitinib p.o. (Colitis ulzerosa)

Biologics

- TNFα antibodies
  - Infliximab i.v.
  - Adalimumab s.c.
  - Golimumab s.c. (Colitis ulzerosa)
  - Certolizumab pegol s.c.
- Integrin antibodies
  - Vedolizumab i.v.
- IL-12/IL-23 antibodies
  - Ustekinumab s.c.

Tasks for the Gastroenterologists in the Care of IBD Patients

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- Initiation, adaptation and monitoring of specific medical therapies
  - Immunosuppressants
  - Biologics
  - Steroids/Salicylates
- Management of disease complication
- Monitoring and surveillance of disease
  - Endoscopy
  - Intestinal ultrasound
  - Order of special tests (e.g. MRI enterography)

Tasks for the General Practitioner (GP) in the Care of Patients with Inflammatory Bowel Diseases (IBD)

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- Monitoring disease activity
- Surveillance and therapy of disease complications
  - Iron and vitamin deficiency
  - Long term consequences: osteoporosis, increased cancer risk
- Monitoring of IBD-treatment
  - Monitoring for side effects
  - Compliance to therapy
  - Initiate short term therapy (steroids, mesalazine)
  - Application of intravenous therapies
- Psychosocial and socioeconomic factors in IBD patients

Disease course (activity) in patients with IBD

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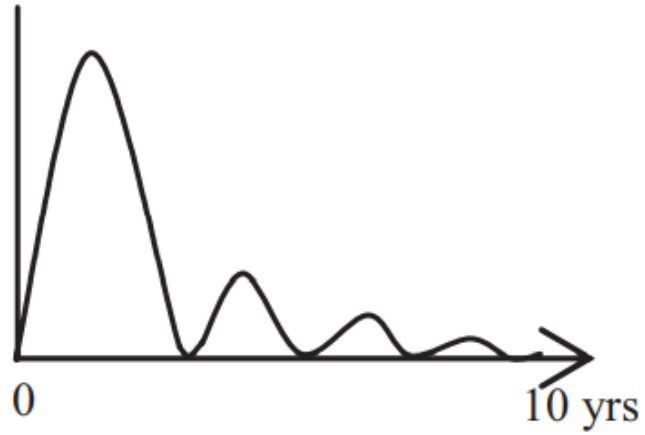
43%



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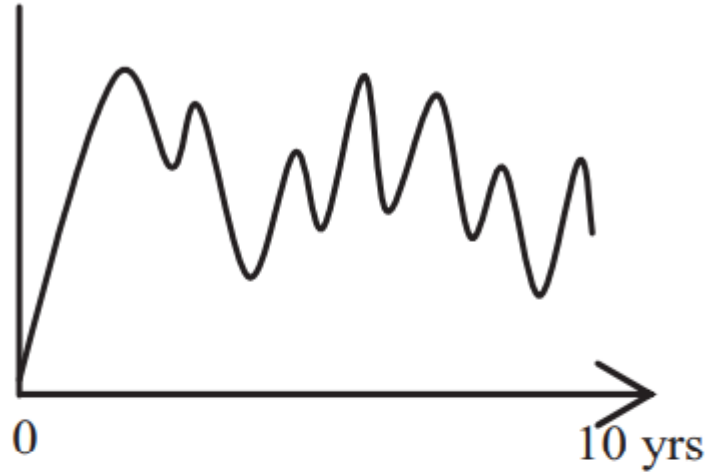

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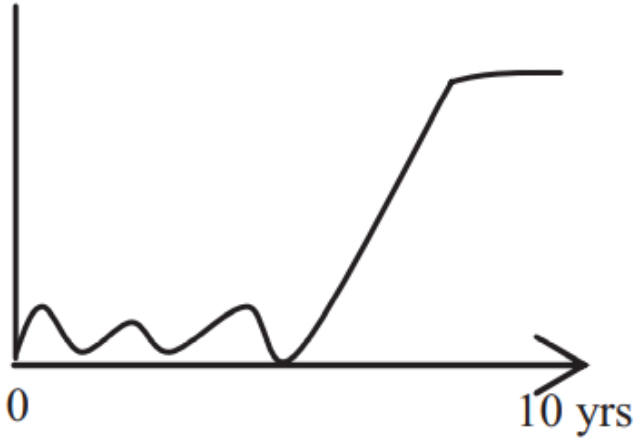

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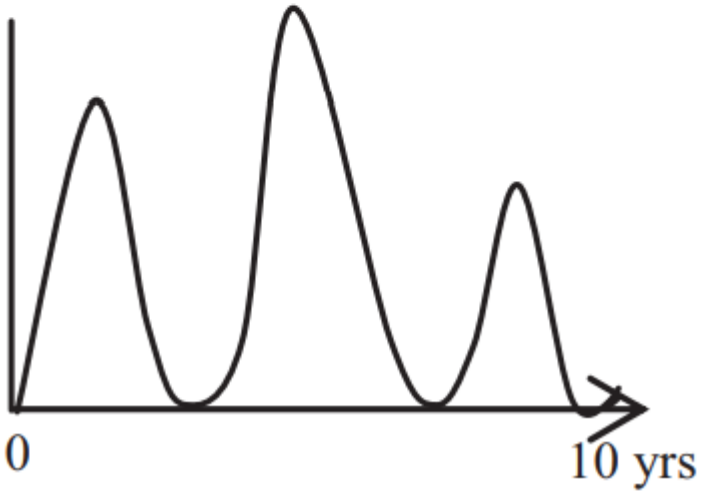
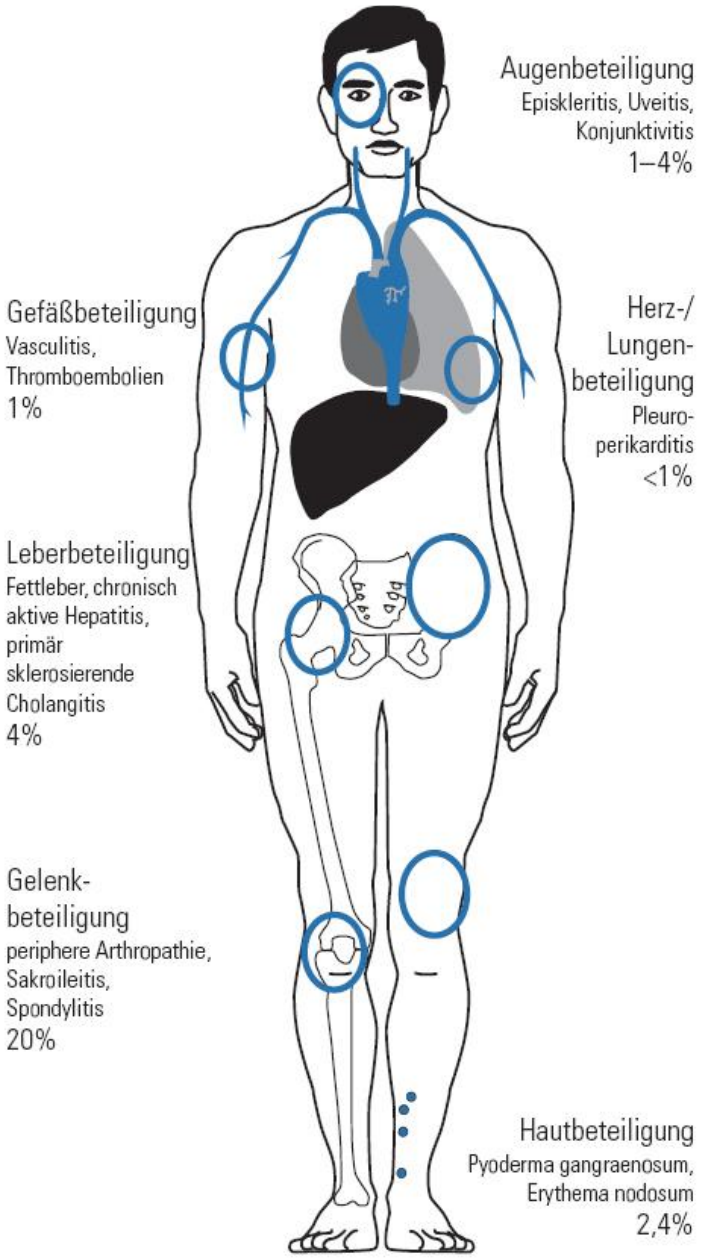


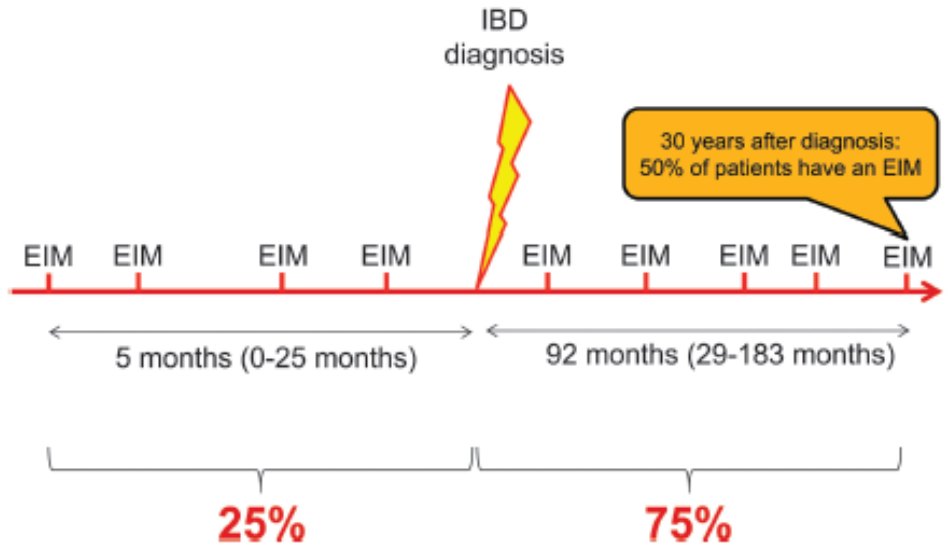
Solberg IC et al. CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2007;5:1430 –1438

Monitoring disease activity in patients with IBD

- Symptoms of disease
  - Diarrhea
    - Number of bowel movements, stool consistency, nocturnal bowel movements
  - Blood in stool
    - Most specific symptom of disease activity in ulcerative colitis
  - Abdominal pain
  - Weight loss
  - Fever
- Extraintestinal Manifestations
- Laboratory parameters

Extraintestinal manifestations in patients with IBD





Vavricka SR et al. Inflamm Bowel Dis 2015;21:1982–1992

Initial tests by the GP if IBD flare is suspected

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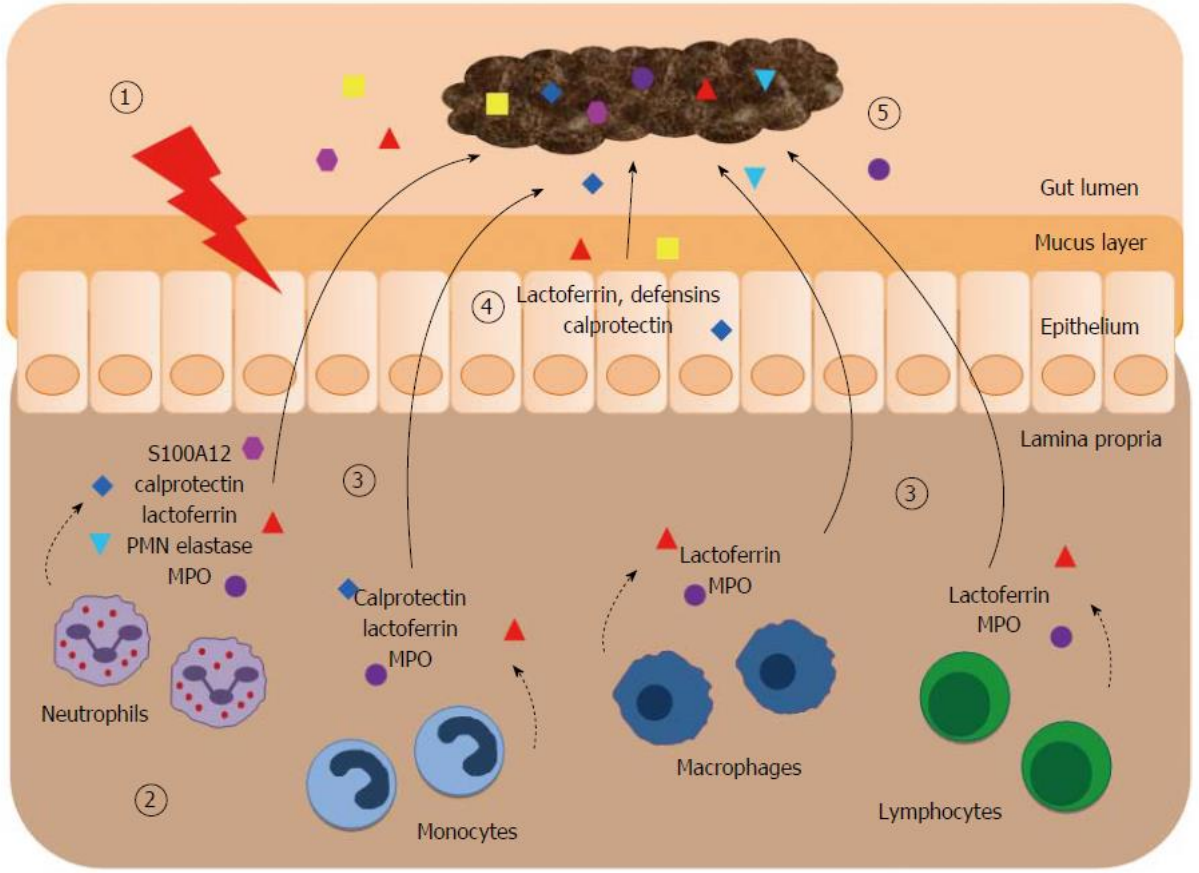
- Fecal calprotectin
- Stool tests for bacterial infections
  - Stool culture (or multiplex PCR): *Campylobacter* spp., *Salmonella* spp., *Shigella* spp., *Yersinia* spp.
  - GDH-EIA and Toxin-EIA for *C. difficile*
- Blood count
- CRP

Fecal Calprotectin – Biomarker for intestinal inflammation

- Measurement with EIA in stool
- Test for the presence of intestinal inflammation
  - > 100 (50) µg/g stool suggest intestinal inflammation
  - Not possible to differentiate between causes of inflammation
- Parameter for monitoring disease activity in IBD patients
  - Difficult to differentiate between no or mild inflammation
  - Repeated measurements necessary



Däbritz J et al. World J Gastroenterol 2014 20: 363-375

Fecal Calprotectin – Monitoring of IBD

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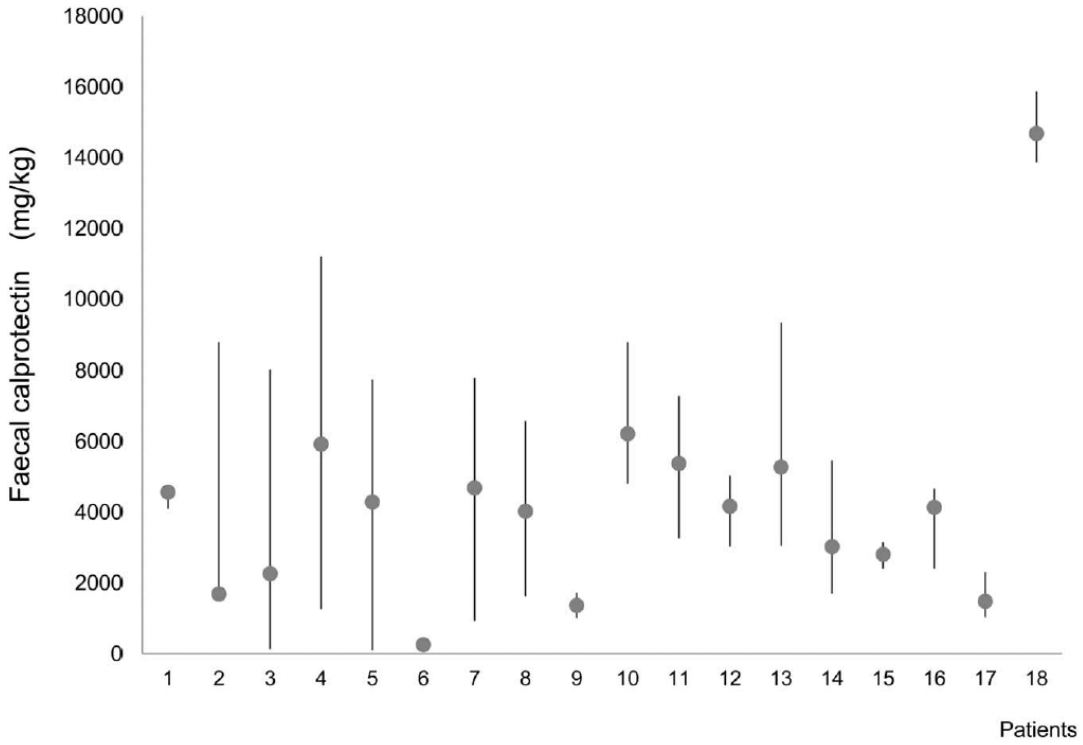
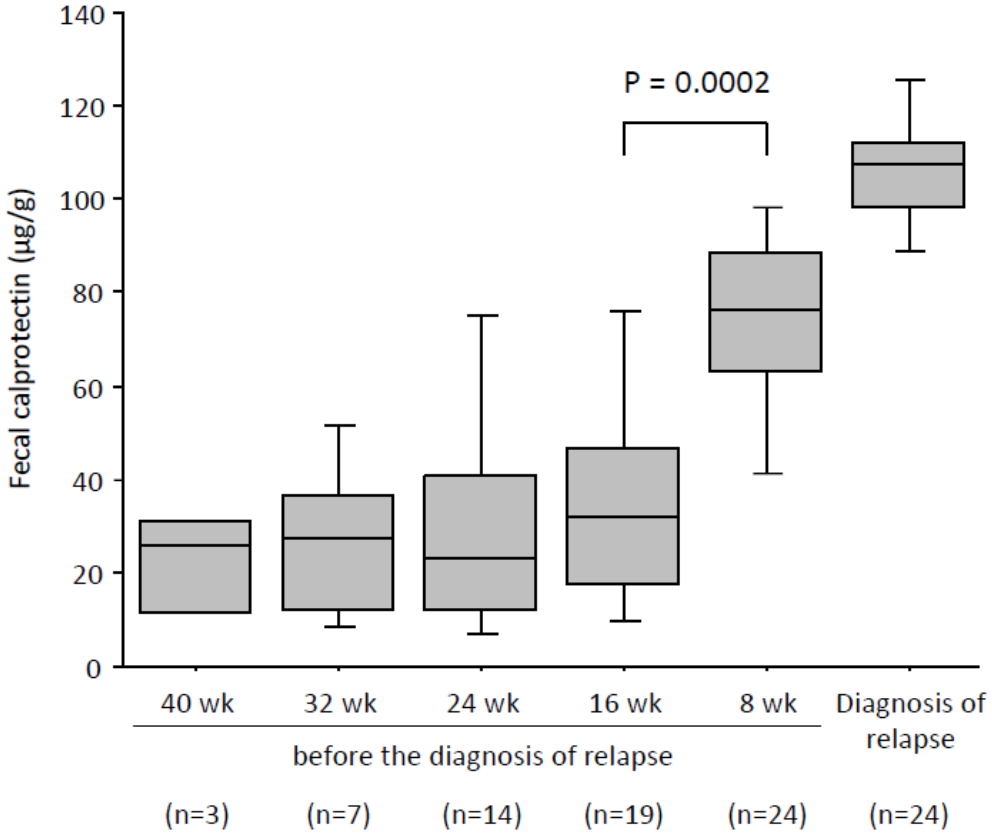
Large variations of measurements on the same day in the same patients



Calafat M et al. Inflamm Bowel Dis 2015;21:1072–1076

Can predict relapse in some asymptomatic IBD patients



Yamamoto T et al. Alimentary Pharmacology & Therapeutic 2015 42(5):549-58

Monitoring disease and therapy with blood tests

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- **Blood count**
  - **Anemia** (disease activity, iron deficiency)
  - **Thrombocytosis** (disease activity, iron deficiency)
  - **Leukocytosis** (steroids, severe disease activity, abscess)
  - Regular measurement in patients (every 8-12 weeks) due to risk for leukopenia in patients treated with
    - Azathioprine, 6-mercaptopurine, methotrexate, tofacitinib
- **Liver enzymes** (AST, ALT, GGT, AP), **kidney function** (Crea, BUN)
  - Azathioprine, methotrexate
- **C-reactive protein (CRP)**
  - Normal values do not rule out active disease
  - Very high values suggestive for complications (abscess)
- **Vitamin B12** (in patients with ileal disease or ileal resections), **folate**

Anemia in IBD patients

Most common complication of IBD: 30% adults; 70% children

- Significant impact on quality of life
- **Common cause:**
  - **Iron delicacy**
    - Blood loss
    - Iron-malabsorption (inflammation)
  - **Anemia of chronic disease (ACD)**
    - Dysregulation of iron homeostasis
- **Other causes:**
  - Vitamin B12 and/or folate-deficiency
  - Drug induced (sulfasalazine, 5-ASA, azathioprin, MTX)

Dignass AU et al. *Journal of Crohn's and Colitis*, 2015, 211–222

Iron and vitamin B12 therapy

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- **Oral iron therapy**
  - Mild Anemia (Hb > 10 g/dL) or iron deficiency without anemia
  - No or mild IBD activity
- **Intravenous iron therapy**
  - Severe Anemia (Hb < 10 g/dL)
  - Moderate-severe IBD activity
  - Intolerance of oral iron therapy
- **Vitamin B12 supplementation**
  - In patients with documented vitamin B12 deficiency and ileal disease or resections
  - Life-long parenteral vitamin B12 therapy (1mg every 3 months i.m.)

Dignass AU et al. *Journal of Crohn's and Colitis*, 2015, 211–222

Osteoporosis and IBD

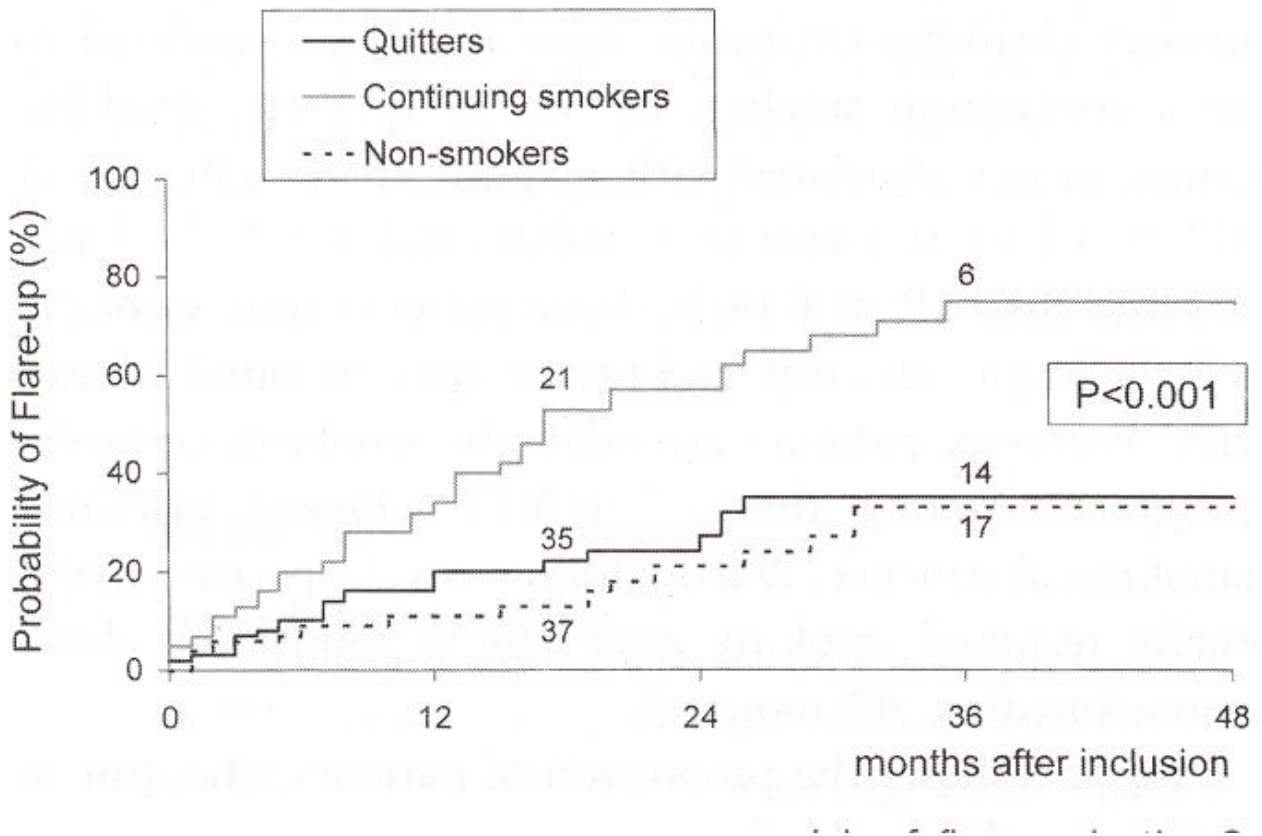
- Risk factors
  - Chronic inflammation
  - Corticosteroid treatment
  - Extensive small-bowel disease or resection
  - Nutritional and Vitamin D deficiency
  - Age, smoking, Low physical activity
- Prevention
  - Stop smoking
  - Adequate dietary calcium [1g/day]
  - Use of calcium and vitamin D during steroid therapy
- Therapy
  - Calcium and vitamin D (Ca 500–1000mg/day and vitamin D [800–1000 IU/day])
  - Management of underlying inflammation
  - Bisphosphonates (in postmenopausal women or those with previous spontaneous fractures)

Harbord M et al. Journal of Crohn's and Colitis 2016 Volume 10:239–254

Smoking and Crohn´s disease

- Patients who smoke have a more severe disease course of Crohn´s disease

- Offer help to patients for quitting smoking



Cosnes J et al. *Gastroenterology* 2001;**120**:1093

Salizylates: Mesalazine

(Asacol®, Asazine®, Mezavant®, Pentasa®, Salofalk®)

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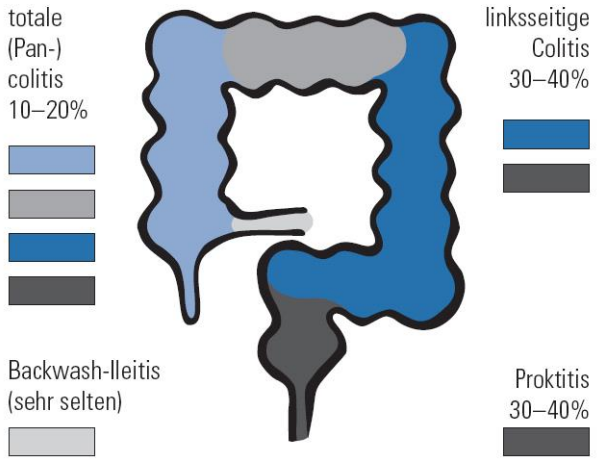
- **Therapy of first choice in mild to moderate ulcerative colitis**
  - Acute UC: 3-4 g/d p.o.
  - Maintaining remission: 1.5-2g /d
  - Once daily dosing is more effective
  - Topical therapy (suppository or enema) in UC located to the rectum or left colon
  - Combination of topical and oral mesalazine is more in pancolitis than only oral therapy

- **Use in Crohn´s disease less established – should be only used in mild forms**

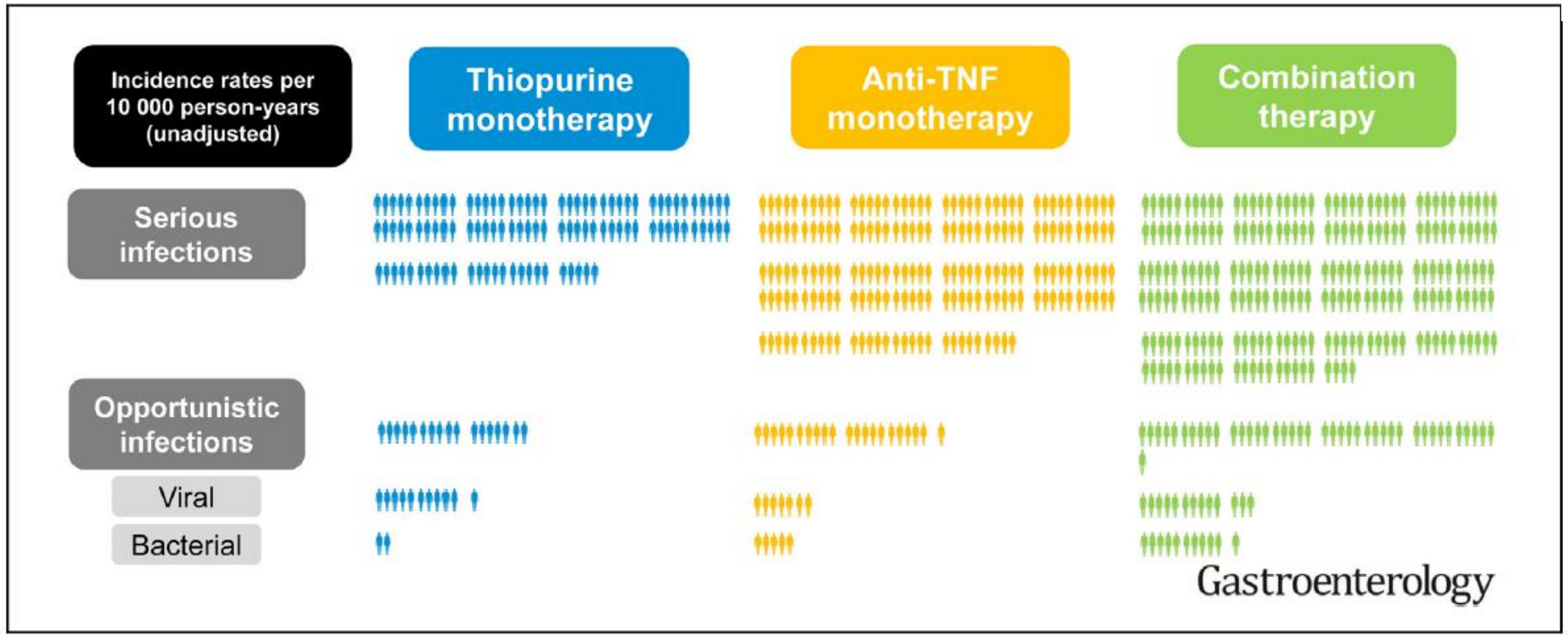


Corticosteroids

- **Prednisolone 0.5-1 mg/kg**
  Methylprednisolone 0.4-0.8 mg/kg
  - Therapy of acute flare of ulcerative colitis or Crohn´s disease
  - Taper of steroid dose over 8-12 weeks
  - Avoid long term and repeated therapy!!!
  - Increases rates of infections

- **Budesonide**
  - 9mg/d for 3 months
  - Less side effects than systemic corticosteroids
  - Effective in Crohn´s disease located to the small bowel or ileocecal region
  - Special galenic formulation (Cortiment MMX) for the use in ulcerative colitis

Risk for severe and opportunistic infections due to IBD therapy



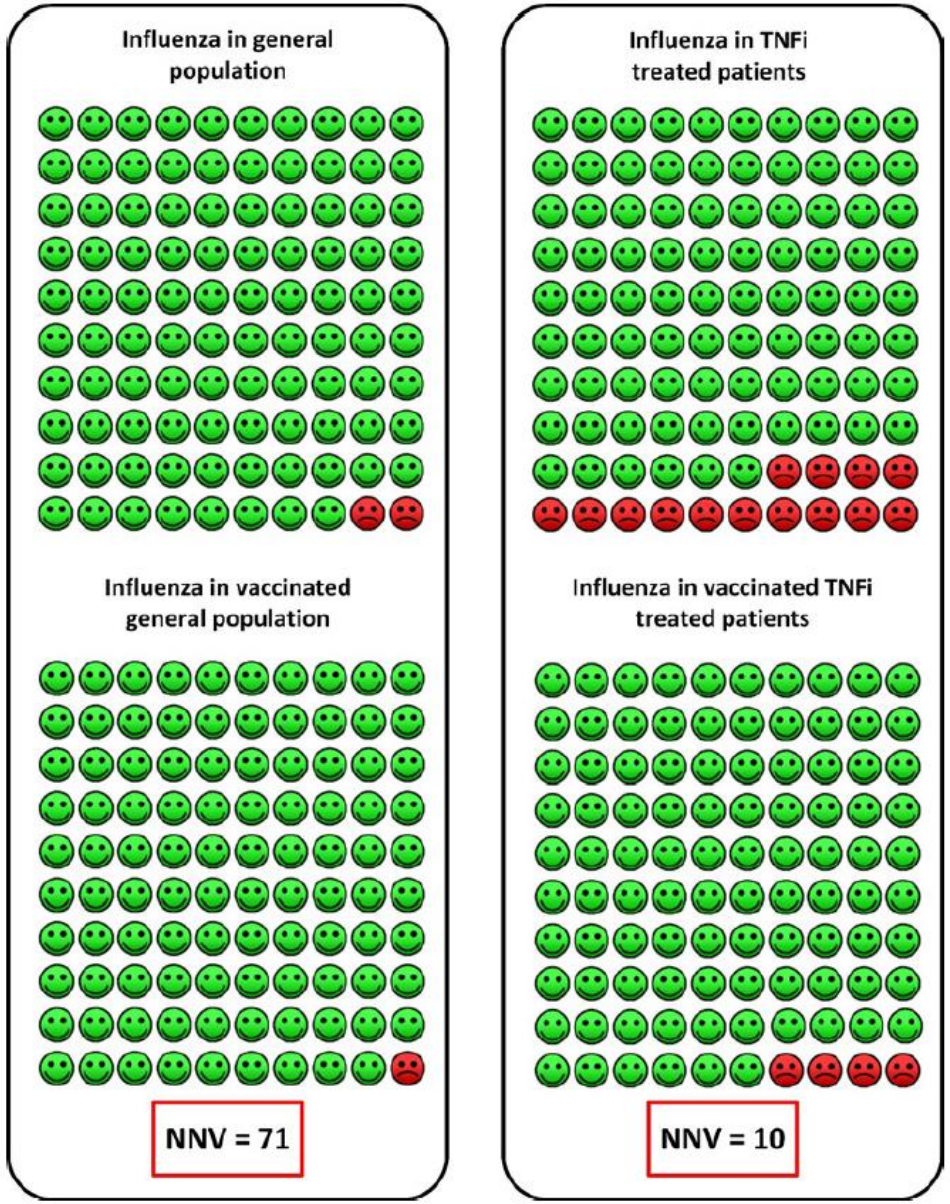
Risk for severe and bacterial infections is increased by anti-TNF agents

Risk for opportunistic viral infections is increased by thiopurines (azathioprine)

Combination therapy has highest risk for infections

Kirchgesner et al. Gastroenterology. 2018

Influenza vaccination in patients with immunosuppression



- **<u>Live vaccines are contraindicated in patients treated with anti-TNF</u>**
- **Other vaccines are recommended in patients with immunosuppression**
- **Number needed to vaccinate (NNV) against influenza is lower in patients treated immunosuppression**
- **$200 to $400 for preventing one case of influenza**
- Healthy individuals
  - 2.3% (71 in 221) in individuals without vaccination to 0.9% in vaccinated individuals
- Patients treated with Adalimumab
  - 14% (55 of 382) in not-vaccinated patients and 4% (8 of 179) in vaccinated patients

Adami G et al. Ann Rheumat Dis 2019; 78:192-193

IBD therapy and COVID 19 infection

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- **Biologics used for IBD therapy do not increase the risk for severe or lethal COVID 19 infections**
- **For other IBD therapies some data suggest a higher risk for severe COVID 19 infections however these data are preliminary**
  - Immunosuppressants (azathioprine)
    - Combination with Anti-TNF
  - Corticosteroids
  - Mesalazine (5-ASA) ??
- **Active IBD also predispose to more severe COVID 19 infections**
- **It is not recommended to delay initiation or stop immunomodulatory IBD therapies due to the COVID 19 pandemic**

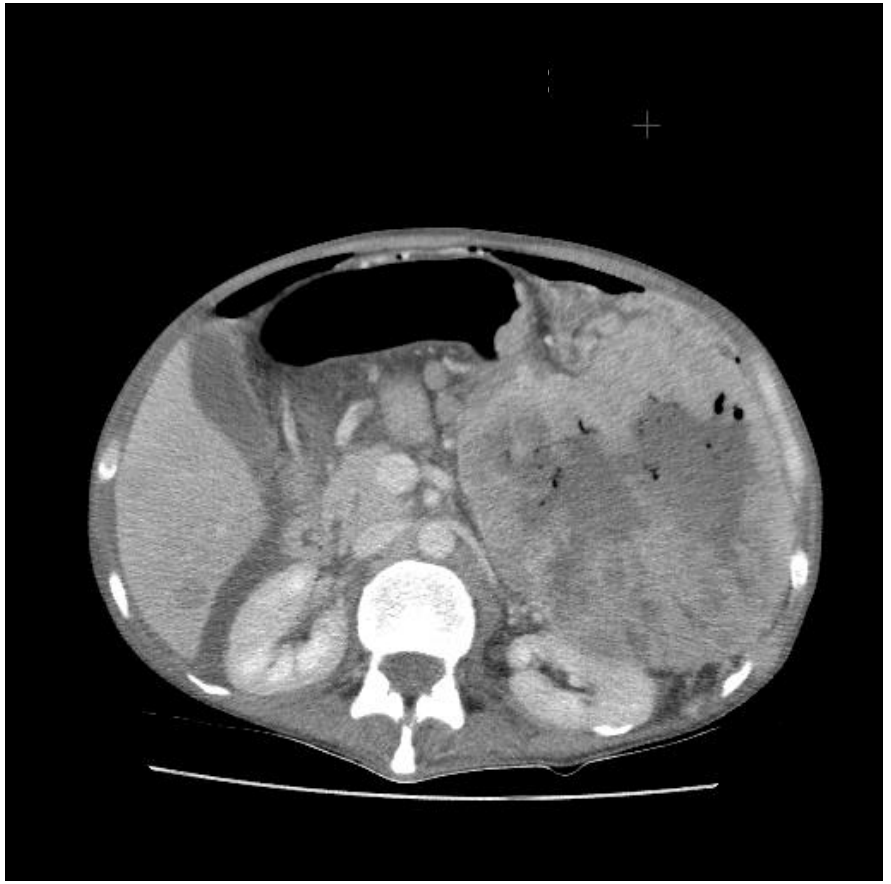
Ungaro RC et al. Gut 2020 Oct 20;gutjnl-2020-322539. doi: 10.1136/gutjnl-2020-322539
Brenner EJ et al. Gastroenterology 2020 Aug;159(2):481-491.

Other side effects of IBD therapy

- **Anti-TNF**
  - Psoriasis/psoriasiform skin reaction (common)
  - Allergic infusion reactions (infliximab)
  - Arthritis
- **Azathioprine**
  - Pancreatitis
  - Intolerance (flue like symptoms)
  - Elevated liver enzymes
  - Hematologic abnormalities
  - Increased rate for non-melanoma skin cancer, lymphoma and cervical cancer

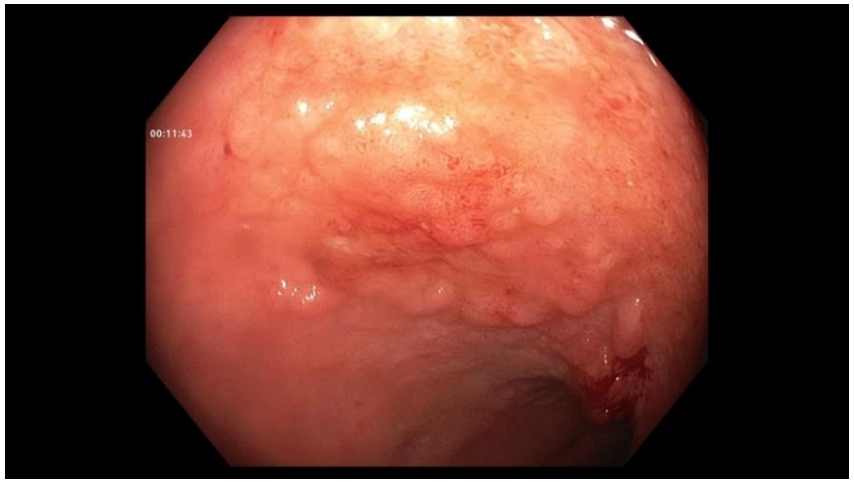
Long term complication of colitis: Increased rate of colon cancer

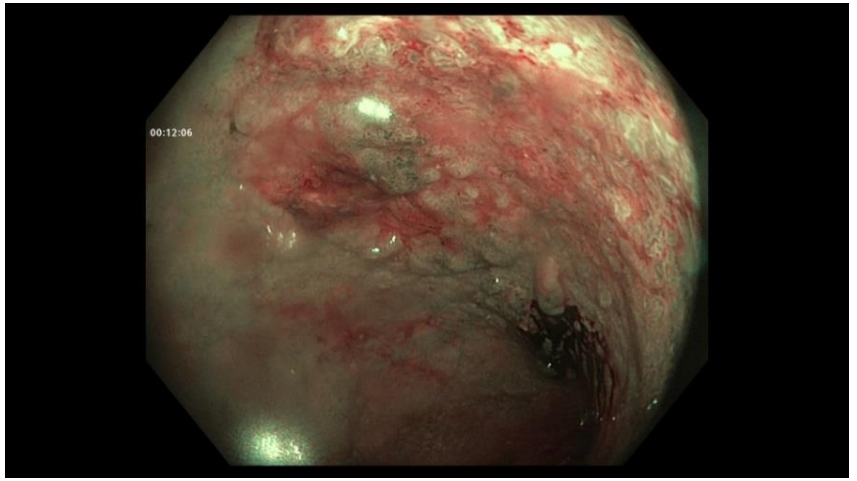
- 44 year old patient with ulcerative colitis
- After diagnosis of ulcerative colitis 15 years ago the patient never went to a control examination – only consulted alternative medicine
- Presented to the ER with perforated Colon-cancer



Colorectal cancer in IBD patients

- Increased risk for colorectal cancer in patients with ulcerative colitis and Crohn´s disease involving the colon
- Risk increases with > 8 years disease duration
- Risk factors:
  - Extensive colitis
  - High inflammatory activity
  - Family history for colorectal cancer
  - Primary sclerosing cholangitis (PSC)
- Patients should start surveillance colonoscopy
  - After 8 years disease duration
  - Every 1-3 years according to the individual risk profile





Psychosocial and socioeconomic factors in IBD patients

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- Risk for work disability is twice as high in IBD patients compared to a control population after a follow up of 10 years
  - Young patients
  - Some patients fail to finish school, professional education, or university
- IBD patients have an 3 fold increased rate of depression and a high rate of anxiety disorders
- Approximately 50% of patients need at least once a short term psychotherapy
- Physicians treating IBD patients should be aware of these problems and offer help and refer patients to according therapies

Conclusions

- The General Practitioner has an pivotal role in the treatment and management of IBD patients
  - Monitoring of disease activity
  - Monitoring of treatment (side effects e.g. infections)
    - Vaccination of patients with IS
  - Monitoring for disease complications
  - Initiation of certain therapies
- A good cooperation with the Gastroenterologist is an important factor for the successful long term treatment of these patients