INFLAMMATORY BOWEL DISEASE

Associate Professor,
PhD Svetlana Ţurcan

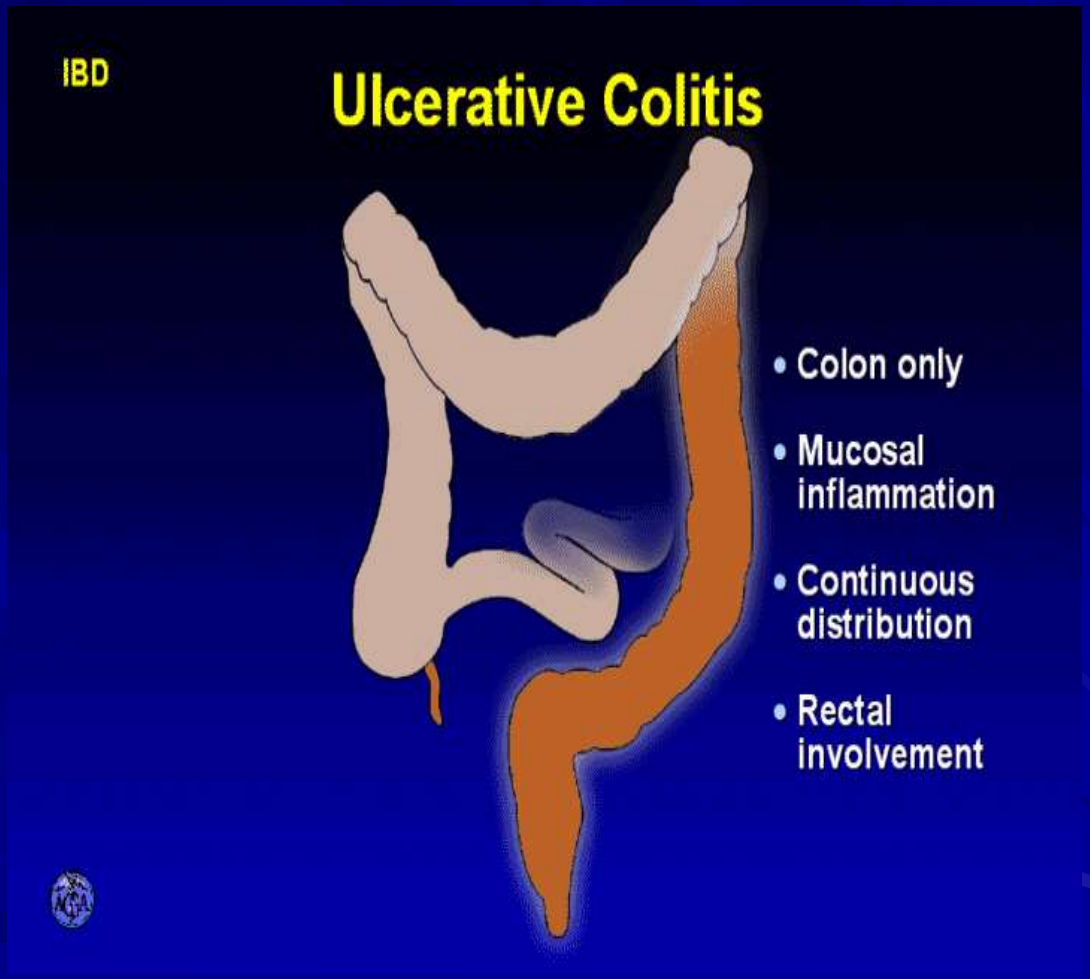
Inflammatory Bowel Disease

- IBD is a general term for a group of immune-mediated, determinate genetic chronic inflammatory disorders of unknown etiology involving the gastrointestinal tract.

- May be divided into two major groups:
  - ulcerative colitis (UC)
  - Crohn's disease (CD)
    - \+ indetminate colitis

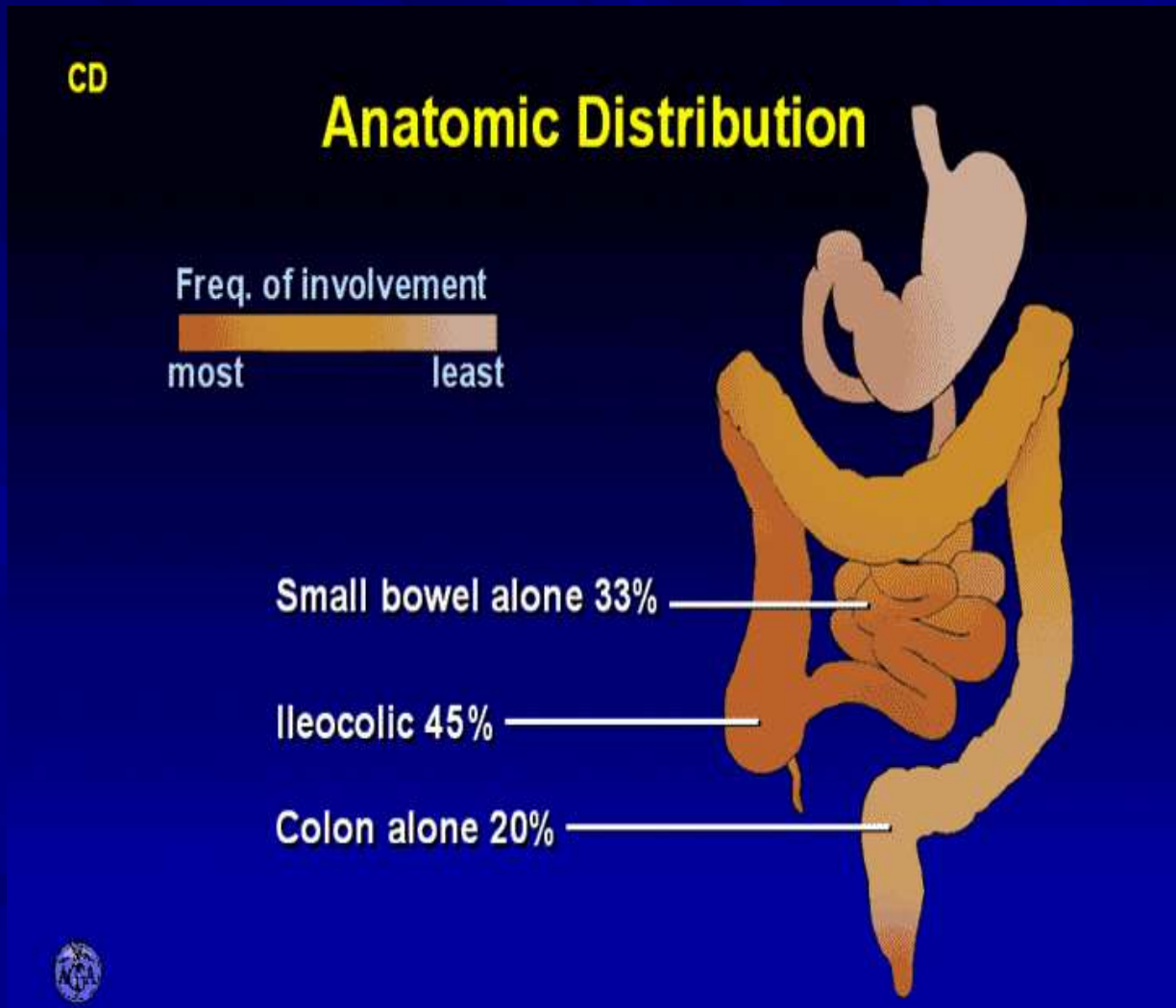
Ulcerative Colitis

- UC is characterized by inflammatory changes involving the colonic mucosa and submucosa in a continuous fashion, starting always at the rectum and extending proximally

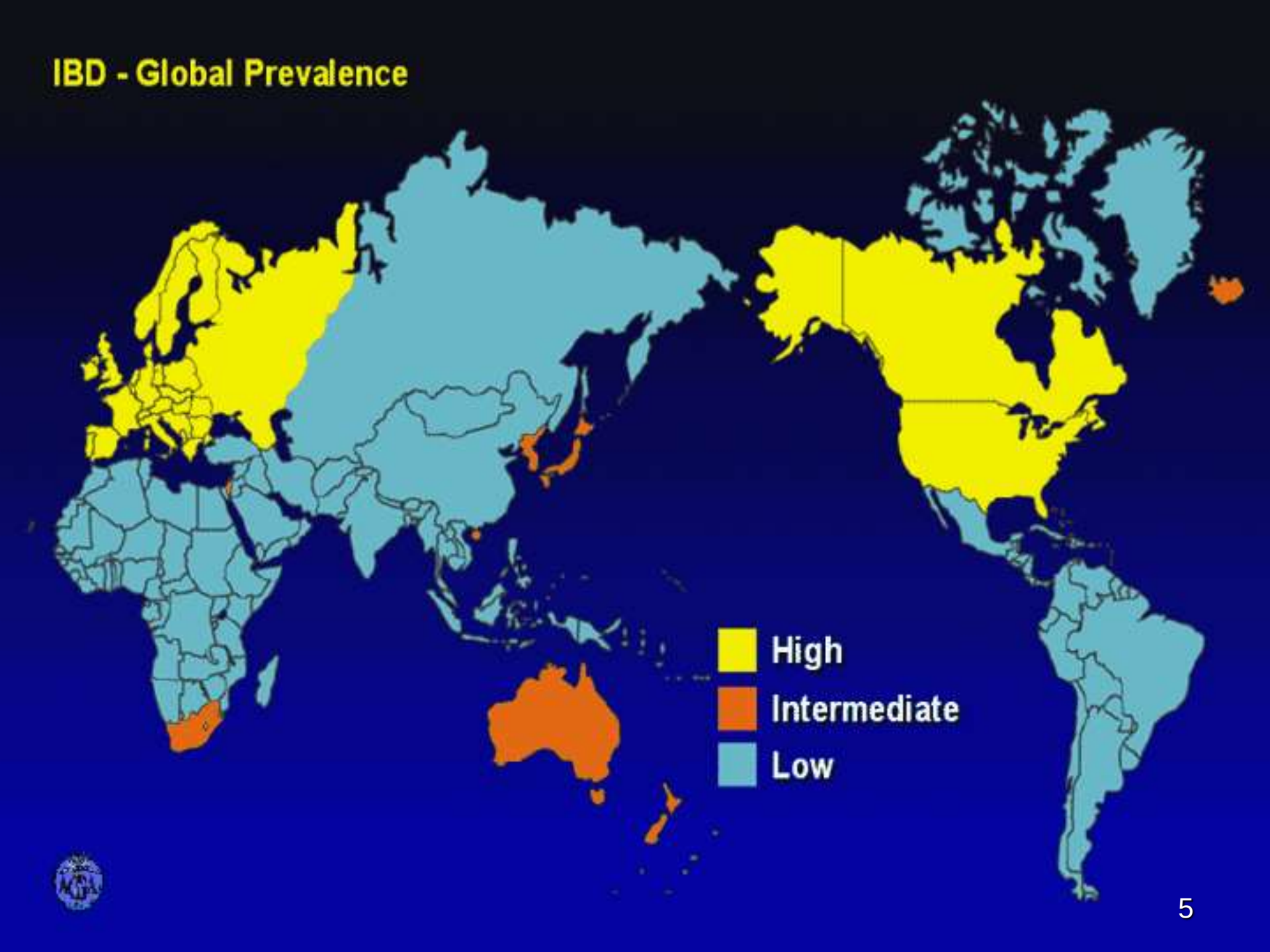


Crohn's Disease

- CD is characterized by transmural inflammation of any segment of the GIT in a discontinuous fashion (skip lesions)



IBD - Global Prevalence



Epidemiological Features of IBD

- The peak age of onset of UC and CD is between 15 and 30 years. A second peak occurs between the ages of 60 and 80.
- The male to female ratio for UC and for CD is ≈ 1 : 1.
- Urban areas have a higher prevalence of IBD than rural areas.
- High socioeconomic classes have a higher prevalence than lower socioeconomic classes.
- IBD runs in families. If a patient has IBD, the lifetime risk that a first-degree relative will be affected is ~10%.

IBD Enigma

- Why did IBD emerge in developed nations only in the middle of the 20th century?
- Why did it emerge initially as ulcerative colitis but now Crohn's disease has become the predominate form of IBD in developed nations?
- Why is IBD emerging in recent years in developing nations ang why is it that ulcerative colitis is the predominate form in these countries?
- Why does smoking cause worse course of disease in CD and is as "protector" factor in UC?
- Why incidence is more often in the medium with high income, high hygienic level ? and ???

“Hygiene” hypothesis

- Posits that the reduction in access to transmissible intestinal microorganisms (i.e. living in a cleaner environment) has reduced the ability of the immune system to become tolerant to these and other such organisms, and hence when it encounters these organism later in life it develops aberrant responses.

“Lifestyle Westernization” Hypothesis

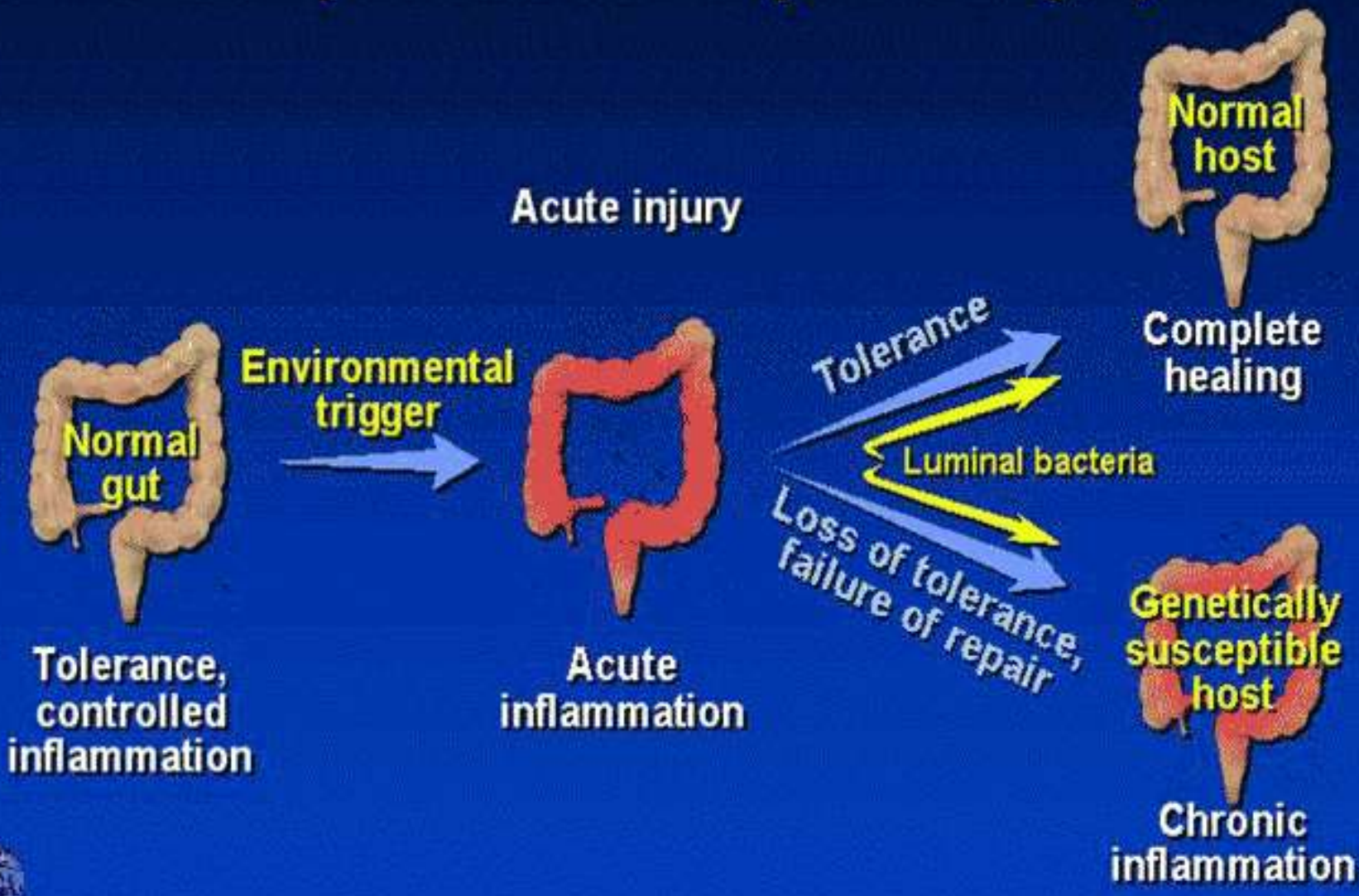
- Changes in the lifestyle in Eastern Europe and Asia during the last two decades have resulted in a more “westernized” standard way of living.
- “Westernization” of lifestyle means:
  - life rhythm acceleration;
  - increased consumption of refined sugar, fatty acids, hydrolyzed fats (fast food), cereals and bread and reduced consumption of natural products, fruit, vegetables and fibers;
  - increased stress load;
  - Increased administration of medicines.

Etiology and Pathogenesis

- The etiology of IBD is unknown
- Pathogenetic factors
  - Genetic factors: racial deferens of incidence, familial occurrence, concordance in twins (to 50% in monozygotic twins), polygenic susceptibility
  - Immune factors: extraintestinal autoimmune manifestations, immune dysregulations, therapeutic effect of immunosuppressive agents
  - Microbial factors: bacterial, fungal, viral agents as triggers of chronic inflamation
  - Environmental factors:
    - Sanitation level
    - Alimentary factors

IBD- Pathogenesis

Response to Non-specific Injury



Pattern of Disease

- **Disease onset**
  - Acute severe
  - Moderate
  - Mild
- Remission is defined as complete resolution of symptoms and endoscopic mucosal healing
- The term “relapse” is used to define a flare of symptoms in a patient with established UC who is in clinical remission, either spontaneously or after medical treatment.
- **Evolution of UC:**
  - with infrequent relapses (≤1/year),
  - with frequent relapses (≥2 relapses/year),
  - or continuous (persistent symptoms of active UC without a period of remission)

Distribution of Ulcerative Colitis

Term	Distribution	Description
E1	Proctitis	Involvement limited to the rectum (i.e. proximal extent of inflammation is distal to the rectosigmoid junction)
E2	Left-sided	Involvement limited to the proportion of the colon distal to the splenic flexure (analogous to ‘distal’ colitis)
E3	Extensive	Involvement extends proximal to the splenic flexure, including pancolitis

Disease Activity in UC (adapted from Truelove and Witts‘)

	Mild	Moderate	Severe
Bloody stools/day	< 4	4 or more *if*	≥ 6 *and*
Pulse	< 90 bpm	≤ 90 bpm	> 90 bpm *or*
Temperature	< 37.5 °C	≤ 37.8 °C	> 37.8 °C *or*
Haemoglobin	> 115 g/L	≥ 105 g/L	< 105 g/L *or*
ESR	< 20 mm/h	≤ 30 mm/h	> 30 mm/h *or*
or CRP	Normal	≤ 30 mg/L	> 30 mg/L

Clinical Features of UC

Intestinal

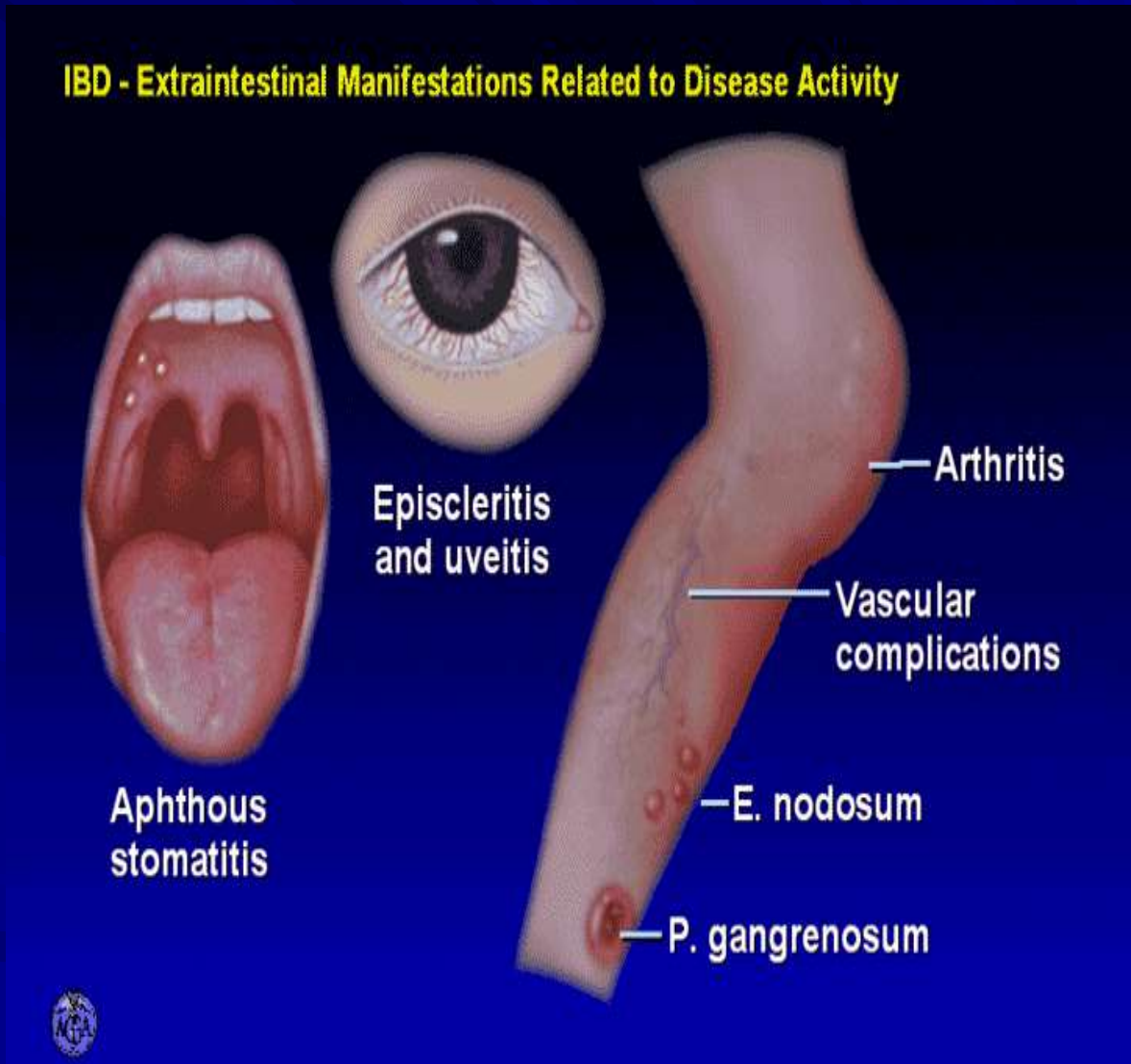
- Bloody diarrhea (often nocturnal and/or postprandial)
- Rectal bleeding
- Urgency and frequent trips to the toilet
- Predefecational cramps

Systemic

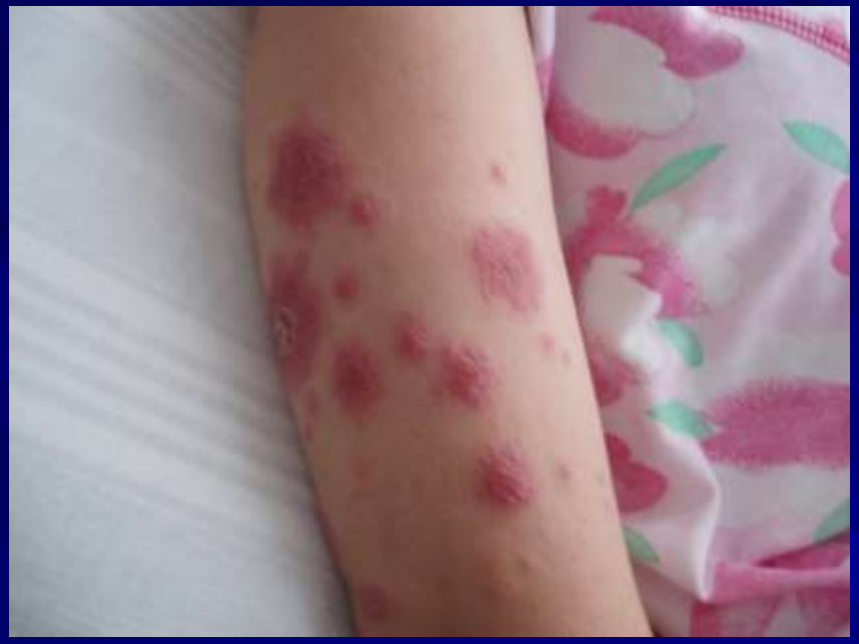
- Malaise
- Anorexia
- Weight Loss
- Fever
- Anemia
- Symptoms of dehydration

Extraintestinal Manifestations

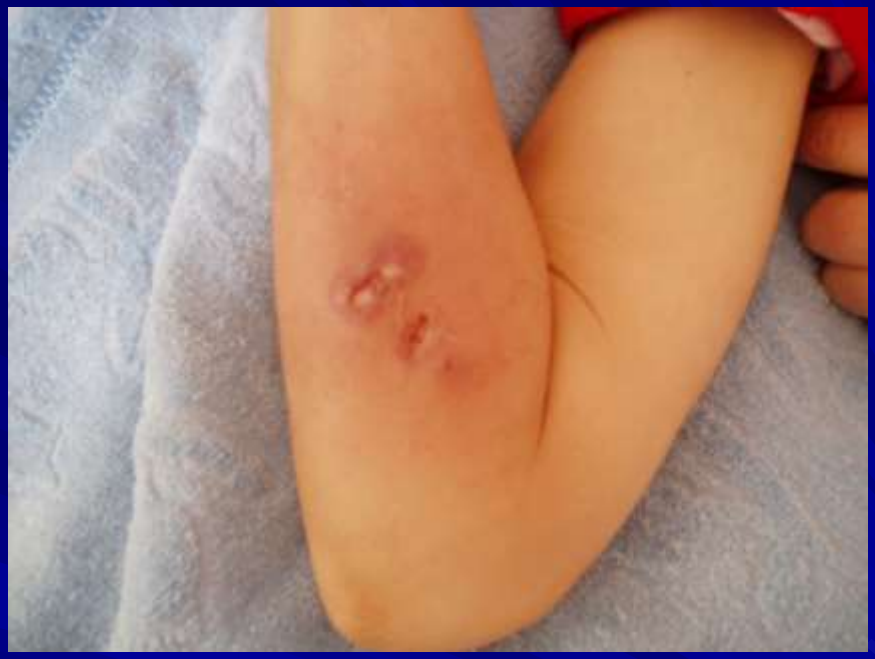
- Musculoskeletal
  - Arthritis
  - Sacroiliitis
  - Ankylosing spondylitis
- Skin
  - Aphthous ulcerative stomatitis
  - Erythema nodosum
  - Pyoderma gangrenosum
- Ocular
  - Episcleritis
  - Uveitis



Extraintestinal Manifestations



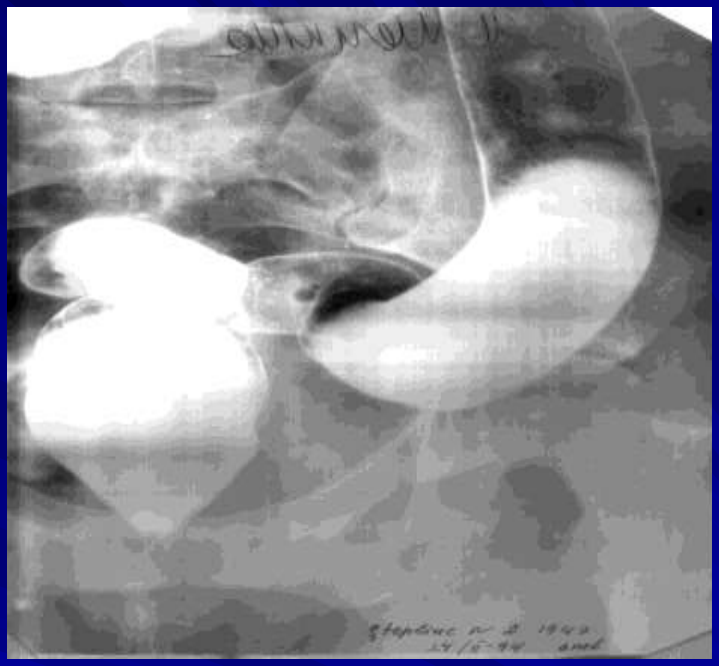
Erythema nodosum



Pyoderma gangrenosum

Common Complications of UC

- Massive bleeding
- Perforation with peritonitis
- Toxic dilatation of the colon (toxic megacolon)
- Malignization
- Severe anemia
- Sepsis



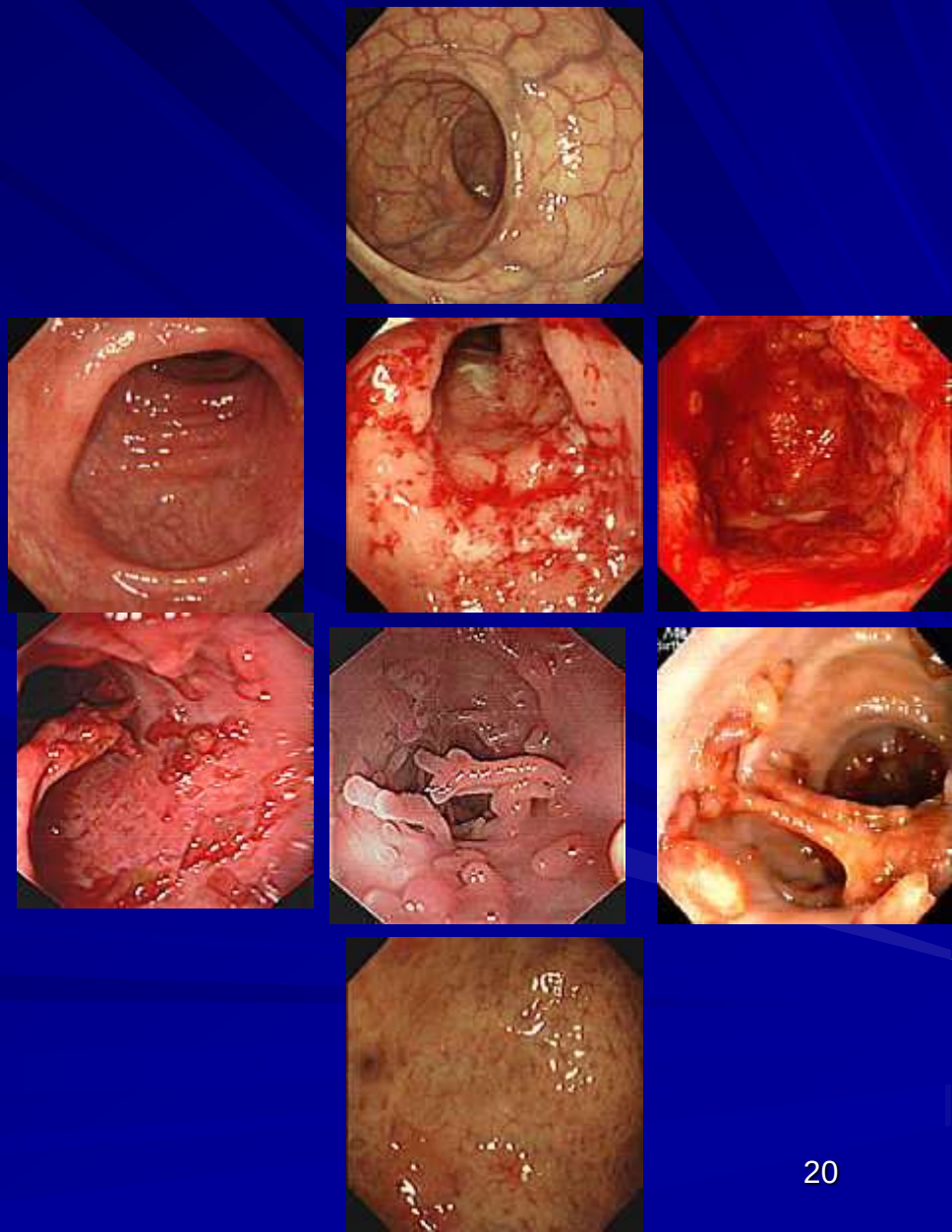
Toxic megacolon

Diagnosis: Physical Examination

- In patients with UC physical examination should include:
  - general well-being,
  - pulse rate, blood pressure,
  - body temperature,
  - body weight and height,
  - abdominal examination for distention and tenderness,
  - perineal inspection, digital rectal examination,
  - oral inspection, and check for eye, skin and/or joint involvement.
- Physical examination may be unremarkable in patients with mild or even moderate disease

Diagnosis: Endoscopy

- Continuous lesions from rectum (always) to proximal parts of colon (only)
- Diffuse erythema
- Loss of mucosal vascularity
- Friability of the mucosa
- Superficial ulcerations
- Exudate consisting of mucus, blood, pus
- Pseudopolyps



Diagnosis: Laboratory Tests

- Initial laboratory investigations should include a full blood count, serum urea, creatinine, electrolytes, liver enzymes, iron studies, and C-reactive protein (CRP).
- CRP and erythrocyte sedimentation rate (ESR) are useful markers to monitor the response to treatment in severe colitis.
- Microbiological testing for infectious diarrhea including Clostridium difficile toxin is recommended.
- Although faecal inflammatory markers are generally not considered sufficient to be included routinely in the diagnostic work up of UC, calprotectin, a neutrophil-derived protein, merits further consideration.

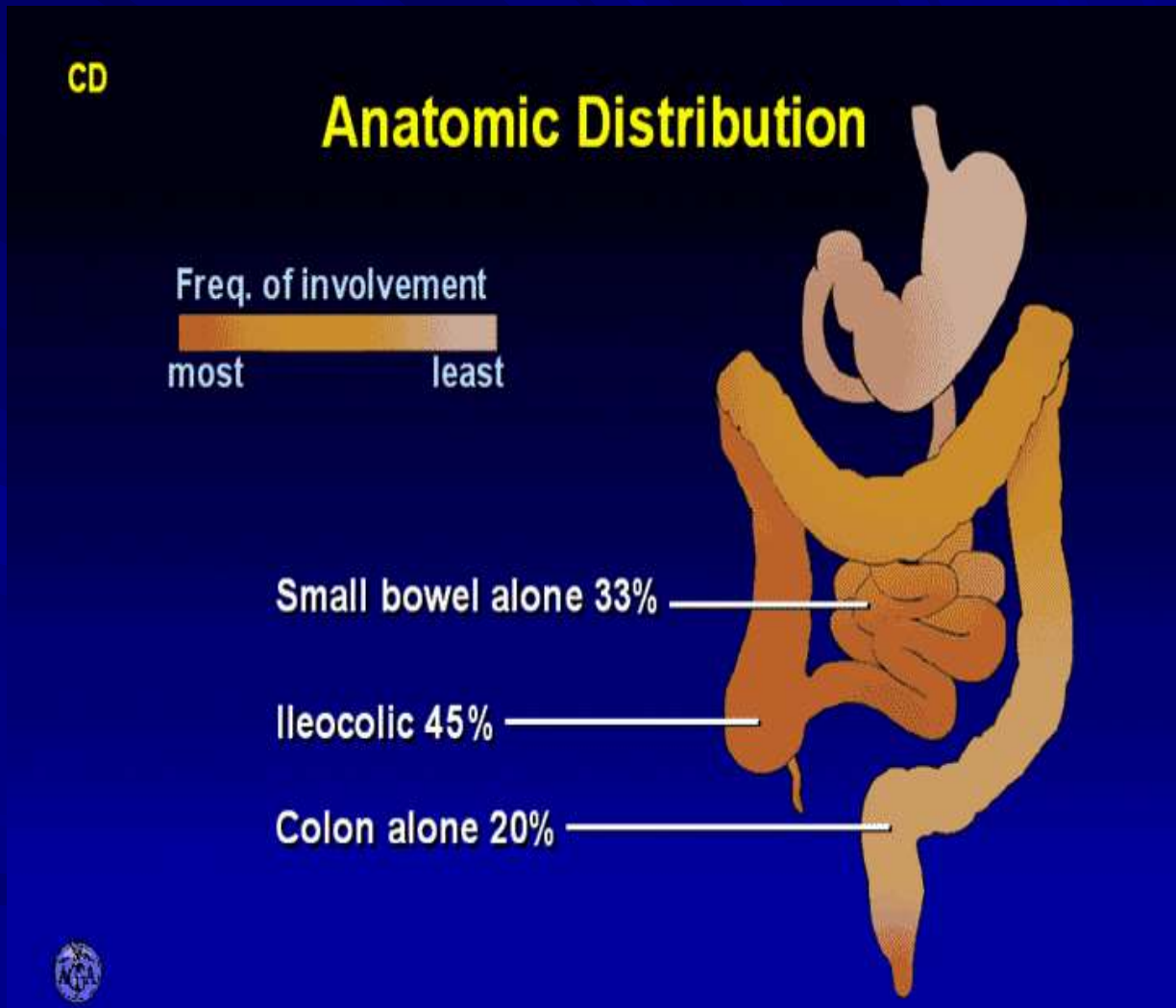
- Perinuclear antineutrophil cytoplasmic antibody (pANCA)

Differential Diagnosis

- Infectious colitis (Salmonella, Şigella, Campilobacter jejuni, Yersinia enterocolitica, Clostridium dificile, Chlamydia)
- Tuberculosis
- Ischemic colitis
- Radiation enteritis
- Drug induced enterocolitis
- Diverticulitis
- Appendicitis
- Colon cancer
- Lymphoma

Crohn's Disease

- CD is characterized by transmural inflammation of any segment of the GIT in a discontinuous fashion (skip lesions)



Montreal Classification of CD

Age at disease onset:

A1 – < 17

A2 – 17-40

A3 – > 40

Localization:

L1 – ileum;
L2 – colon;
L3 – ileocolon;
L4 – upper segment of GIT.

Evolution forms:

B1 – without stenosis or penetration (inflammatory form);

B2 – with stenosis;

B3 – with penetration;

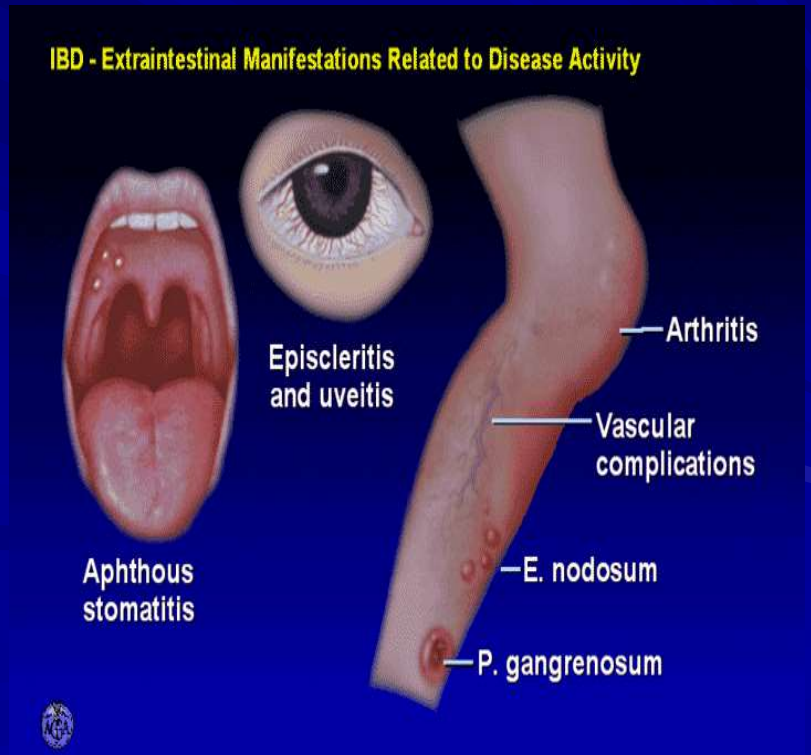
B1(or 2 or 3) p – with perianal affectation s (fistulae, perirectal abscesses etc.).

Clinical Features CD

Intestinal and systemic manifestation

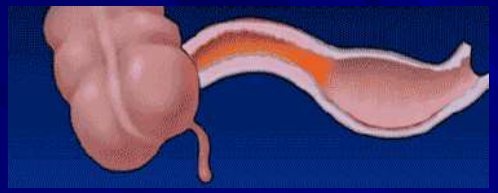
- Abdominal pain
- Fever
- Weight loss
- Palpable inflammatory mass in abdomen
- Perianal disease: anal fissures, abscess, fistula
- Nonbloody diarrhea

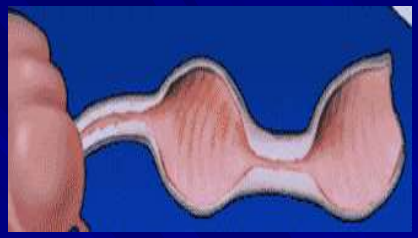
Extraintestinal Manifestations

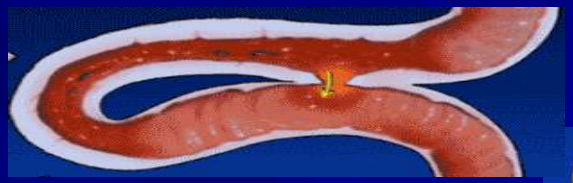


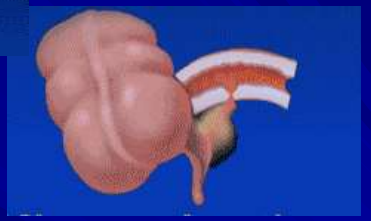
Common Complications of IBD

- Intestinal strictures and obstruction
- Fistulization
- Abdominal abscess
- Cancer

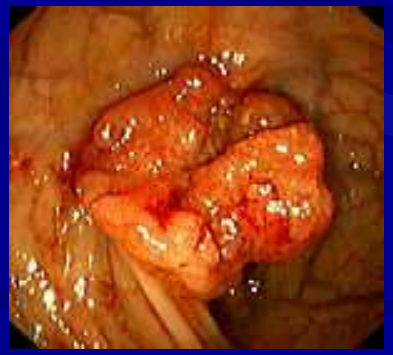






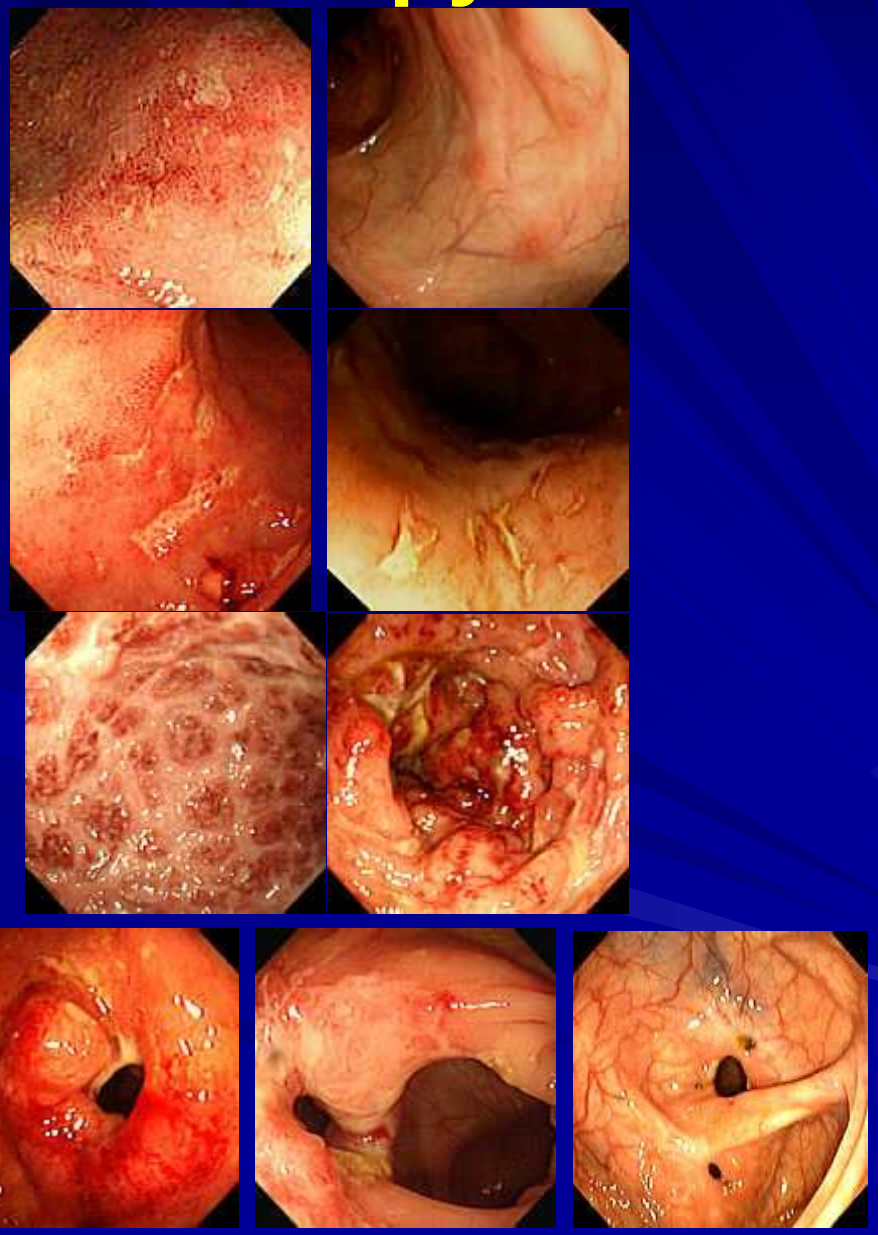


- Severe extraintestinal manifestation
- Osteoporosis
- Malignization



Diagnosis: Endoscopy

- Skip lesions of any segment of the GIT
- Aphthoid ulcerations
- Deep linear ulcers
  which with segments of edematous or uninvolved mucosa lead to the characteristic pattern called
- “Cobblestone”
- Strictures
- Fistulas



UC and CD treatment

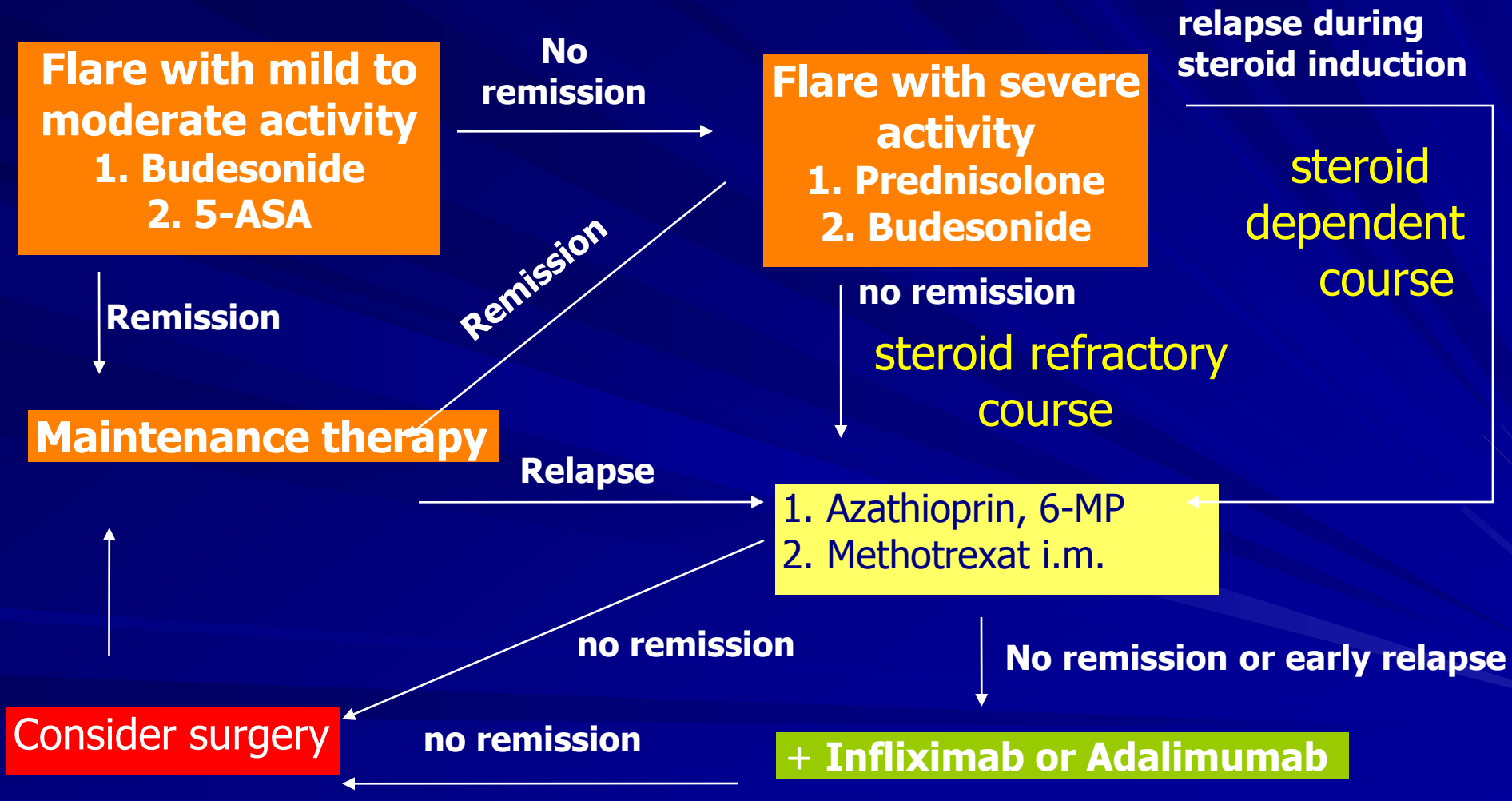
Remission Induction

1. **Aminosalicylates – 5-ASA** (oral, rectal):
   - Sulfasalazine
   - Mesalamine (Salofalk, Asacol, Pentasa etc.)
2. **Corticosteroids :**
   - Local (budesonide) (rectal, oral)
   - Sistemic (rectal, oral, IV)
3. **Immunosuppressive agents** (azathioprine etc.)
4. **Biotherapy** (infliximab, adalimumab etc,)

Remission Maintenance

1. **Aminosalicylates** (oral, rectal):
   - Sulfasalazine
   - Mesalamine (Salofalk, Asacol, Pentasa etc.)
3. **Immunosuppressive agents** (azathioprine) etc.)
2. **Biotherapy** (infliximab, adalimumab)

Algorithm for induction of remission in Crohn's disease



Prognosis

- The risk of neoplasia in chronic UC increases with duration and extent of disease. The risk of cancer rises 0.5–1% per year after 8–10 years of disease in patients with pancolitis. Annual or biennial colonoscopy with multiple biopsies is recommended for patients with > 10 years of pancolitis or left-sided colitis.
- Risk factors for developing cancer in Crohn's colitis are long-duration and extensive disease, bypassed colon segments, colon strictures, PSC, and family history of colon cancer.
- When compared to the general population, IBD patients have an impaired quality of life, but practically similar surveillance (in case of adequate treatment)