Primary Care of the Patient with IBD

Essentials for Residents of Internal medicine

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Ulcerative Colitis

- an increase in IBD in southern and central Europe, Asia, Latin America, and Africa
- The prevalence = 37 to 246 cases per 100,000
- slightly more prevalent in males.
- Incidence = bimodal with a peak onset
  - 20- 40 years of age
  - a lesser peak after 60 years of age
- Men >women to be diagnosed with ulcerative colitis in the later decades of life.
- There is a higher incidence in urban areas

Crohn Disease

- incidence rate = 3.1 to 14.6 cases per 100,000 person-years.
- prevalence rate = 26 to 201 cases per 100,000
- slightly more prevalent in females.
- traditionally bimodal disease onset that tends to be 5 to 10 years earlier than for ulcerative colitis

Localisation of IBD

CD

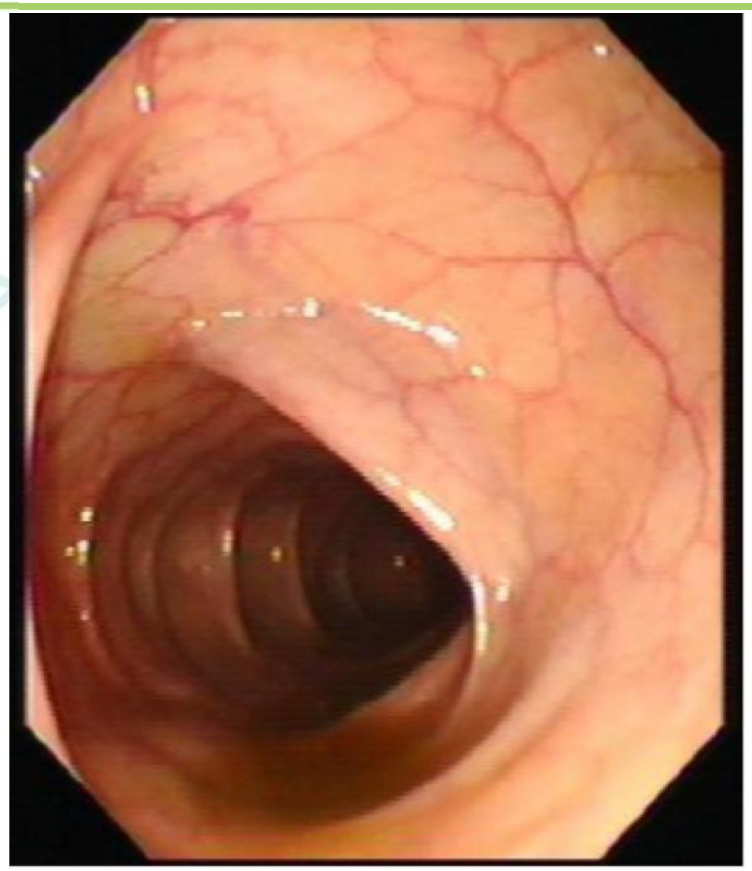
Small bowel:	30-40%
Ileocecal region:	30-45%
Colon:	20-30%

UC

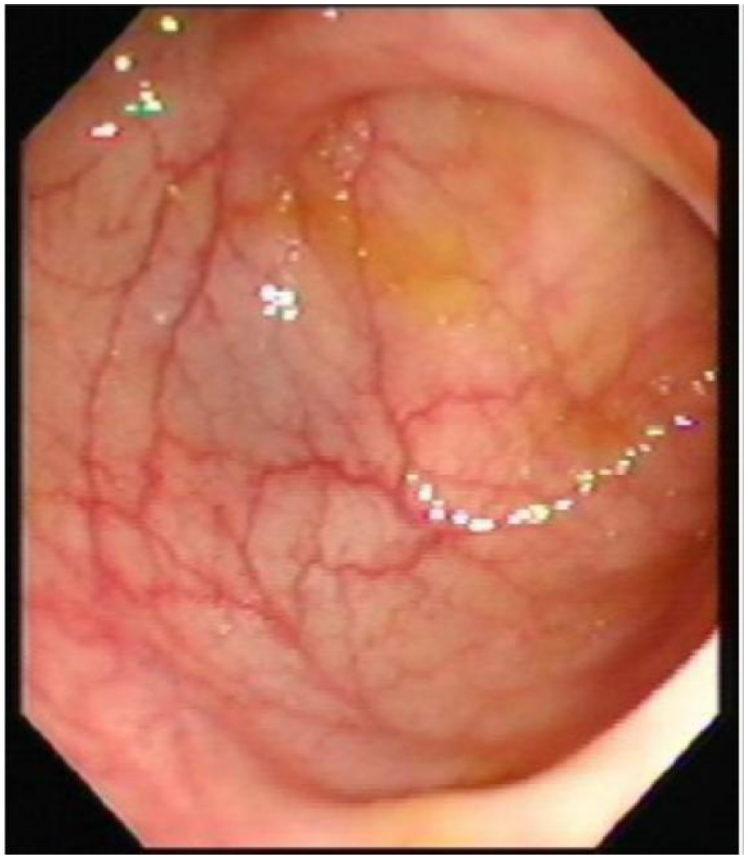
Rectum:	95%
Leftsided-colitis:	75%
Pancolitis:	15-25%

Endoscopy of a normal colon

descending colon



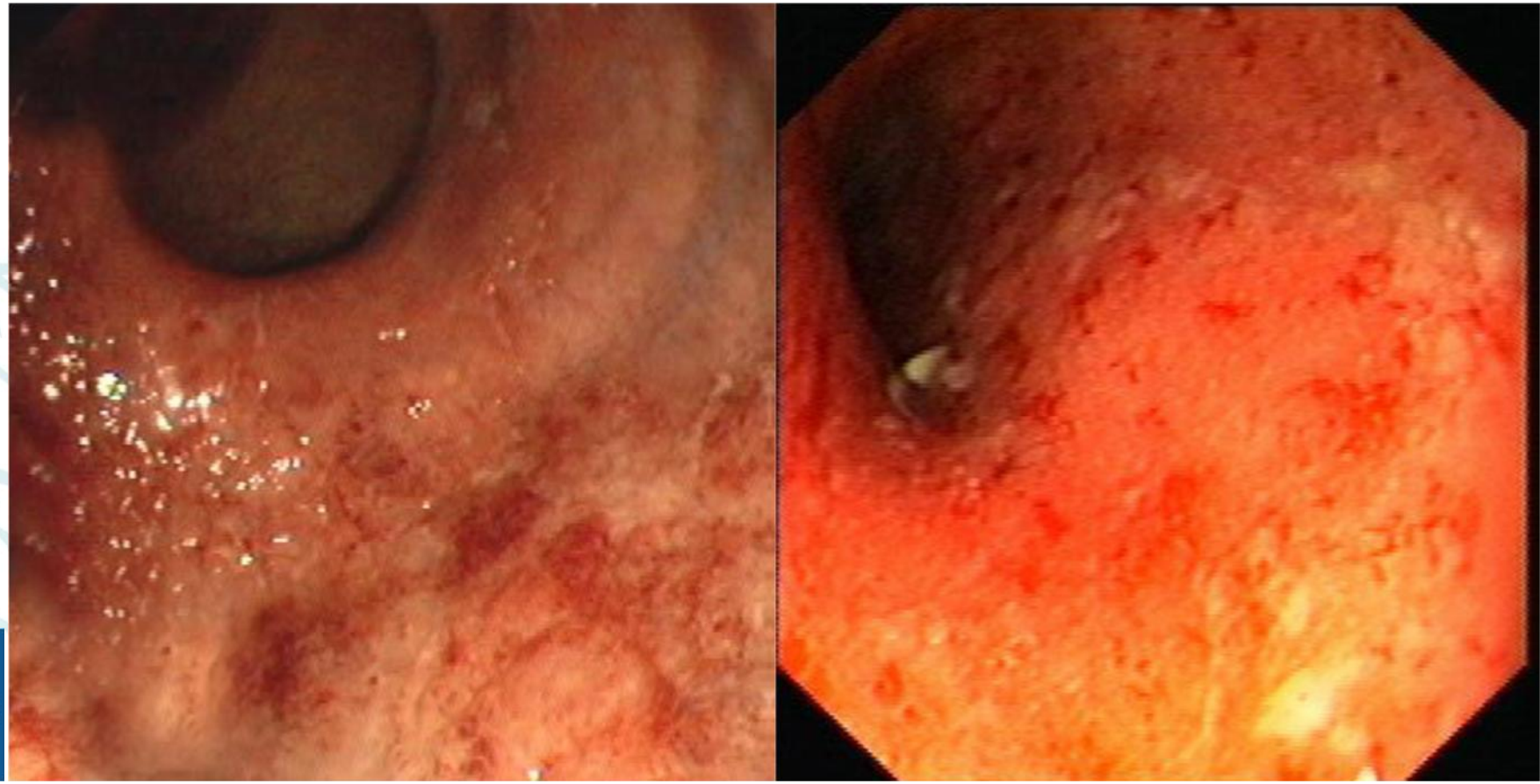
rectum



European Crohn's and Colitis Organisation

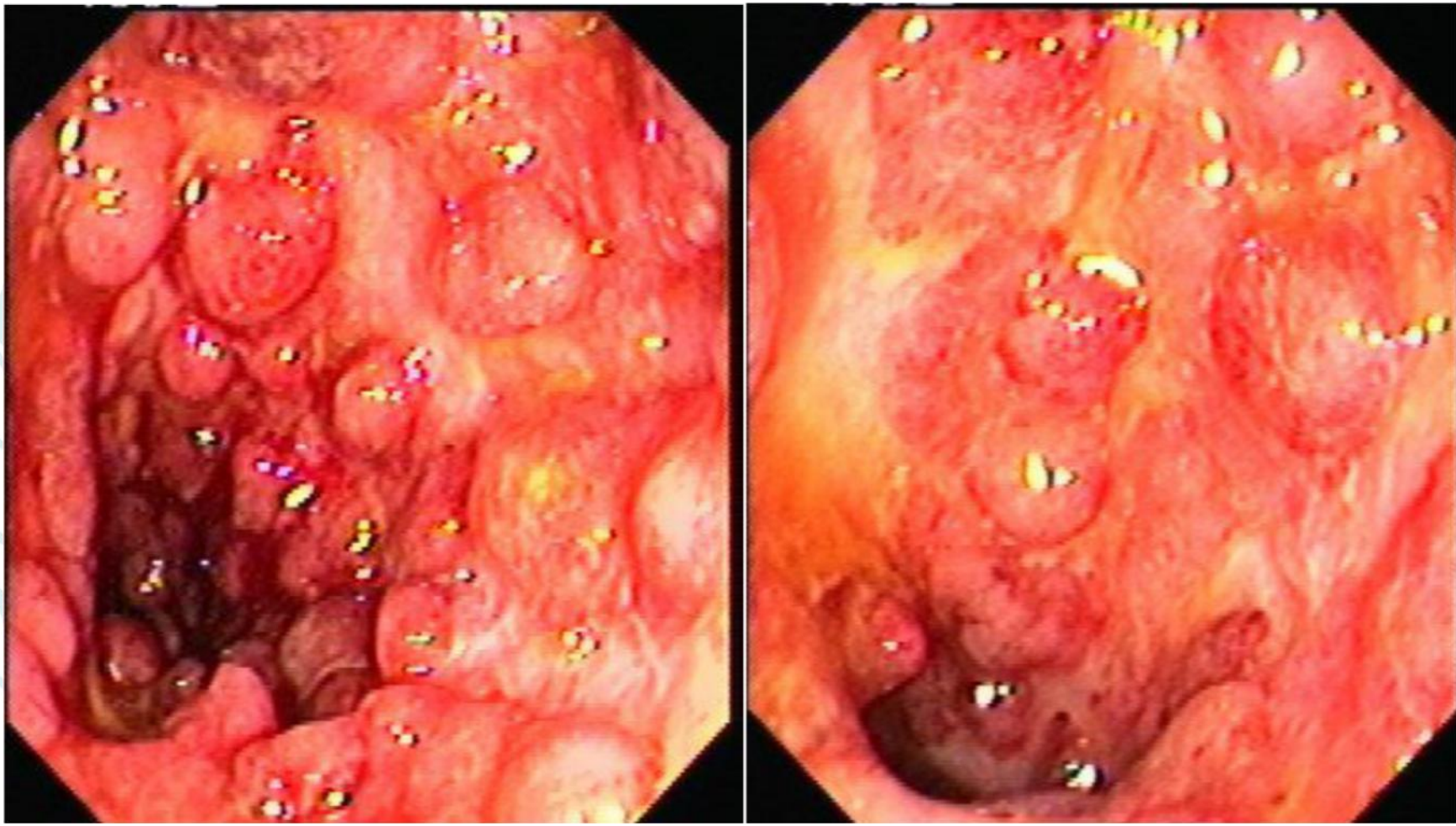
U.C

rectum



European Crohn's and Colitis Organisation

Chronic active UC



European Crohn's and Colitis Organisation

Common extraintestinal manifestations in inflammatory bowel disease

Cutaneous	Erythema nodosum Pyoderma gangrenosum
Hematologic	Venous thromboembolism
Hepatobiliary	Primary sclerosing cholangitis
Ocular	Episcleritis Scleritis Uveitis
Musculoskeletal	Sacroiliitis Ankylosing spondylitis Type 1 peripheral arthritis (pauciarticular) Type 2 peripheral arthritis (polyarticular) Osteoporosis

Initial diagnostic evaluation of suspected flare or complication of inflammatory bowel disease

Clinical Evaluation	
History	Fever, abdominal pain, diarrhea, number of stools per 24 h, nocturnal stools, bloody stool, tenesmus, fecal urgency, or obstructive symptoms Extraintestinal manifestations including eye, skin, or joint symptoms Precipitating factors, such as antibiotic exposure or travel Perianal complaints in Crohn patients
Vital Signs	Fever, tachycardia, or hypotension
Physical examination	Dehydration, malnutrition, or pallor Abdominal tenderness, rebound, signs of obstruction, or a palpable right lower quadrant mass Extraintestinal manifestations of eye, joint, or skin Perianal abscesses or fistulas in Crohn patients
Laboratory Evaluation	
Blood studies	Complete blood count, ferritin, iron, total iron-binding capacity Chemistry panel Acute phase reactants including ferritin, erythrocyte sedimentation rate (ESR), and C-reactive protein Liver function tests Albumin and prealbumin Cytomegalovirus (CMV) quantitative polymerase chain reaction

Initial diagnostic evaluation of suspected flare or complication of inflammatory bowel disease

Stool studies	*Clostridium difficile* testing, parasite screening, stool cultures, Shiga toxin evaluation, *Escherichia coli* O157:H7 assays Fecal calprotectin and lactoferrin
Imaging Evaluation	
In ulcerative colitis	Consider plain film of abdomen (evaluate for toxic megacolon)
In Crohn disease	Consider plain film of abdomen, computed tomography (CT) of abdomen/pelvis, CT or MRI enterography (evaluate for obstruction, strictures, fistulas, abscesses)
Endoscopy Evaluation	
In ulcerative colitis	Consider colonoscopy or flexible sigmoidoscopy (evaluate for mucosal inflammation and rule out CMV colitis)
In Crohn disease	Consider colonoscopy (evaluate location and severity of mucosal inflammation in colon, terminal ileum)

Differential diagnosis of abdominal pain in patients with inflammatory bowel disease

- Abscess (Crohn disease)
- Cholangitis
- Cholelithiasis
- Inflammatory bowel disease flare
- Intestinal obstruction (due to adhesions or strictures)
- Nephrolithiasis
- Pancreatitis

MANAGEMENT

Assessing Severity of Disease

Assessing clinical severity of ulcerative colitis

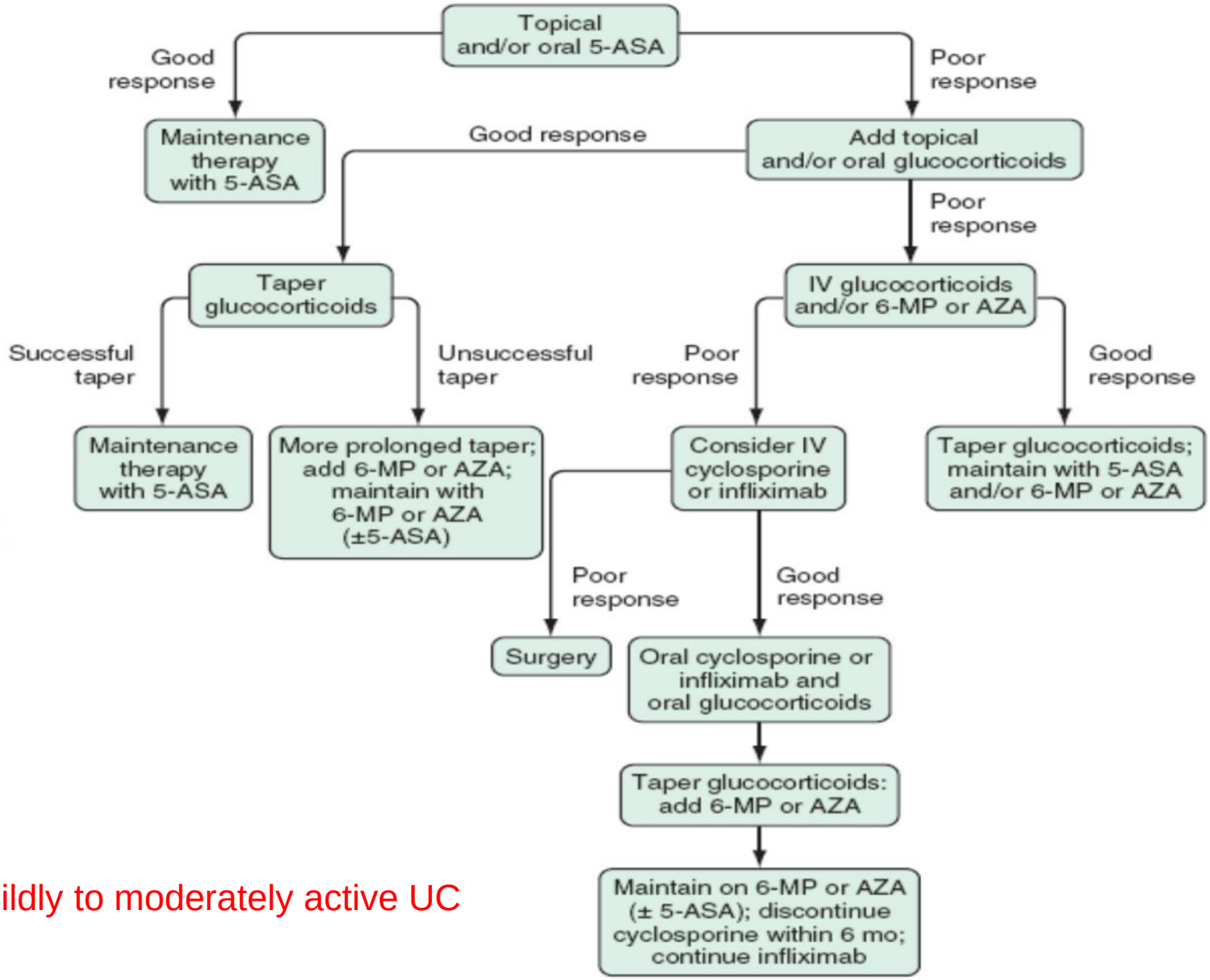
Disease Severity	Mild	Moderate	Severe	Fulminant
No. of bowel movements (BMs) per day	<4 BMs, with or without hematochezia	>4 BMs	>6 BMs, bloody	>10 BMs with continuous bleeding
Additional clinical characteristics	No systemic toxicity, normal ESR	Minimal evidence of systemic toxicity	Evidence of systemic toxicity including fever, tachycardia, anemia, or elevated ESR	Evidence of systemic toxicity, abdominal tenderness, abdominal distention, colonic dilatation on imaging, need for blood transfusions

MANAGEMENT

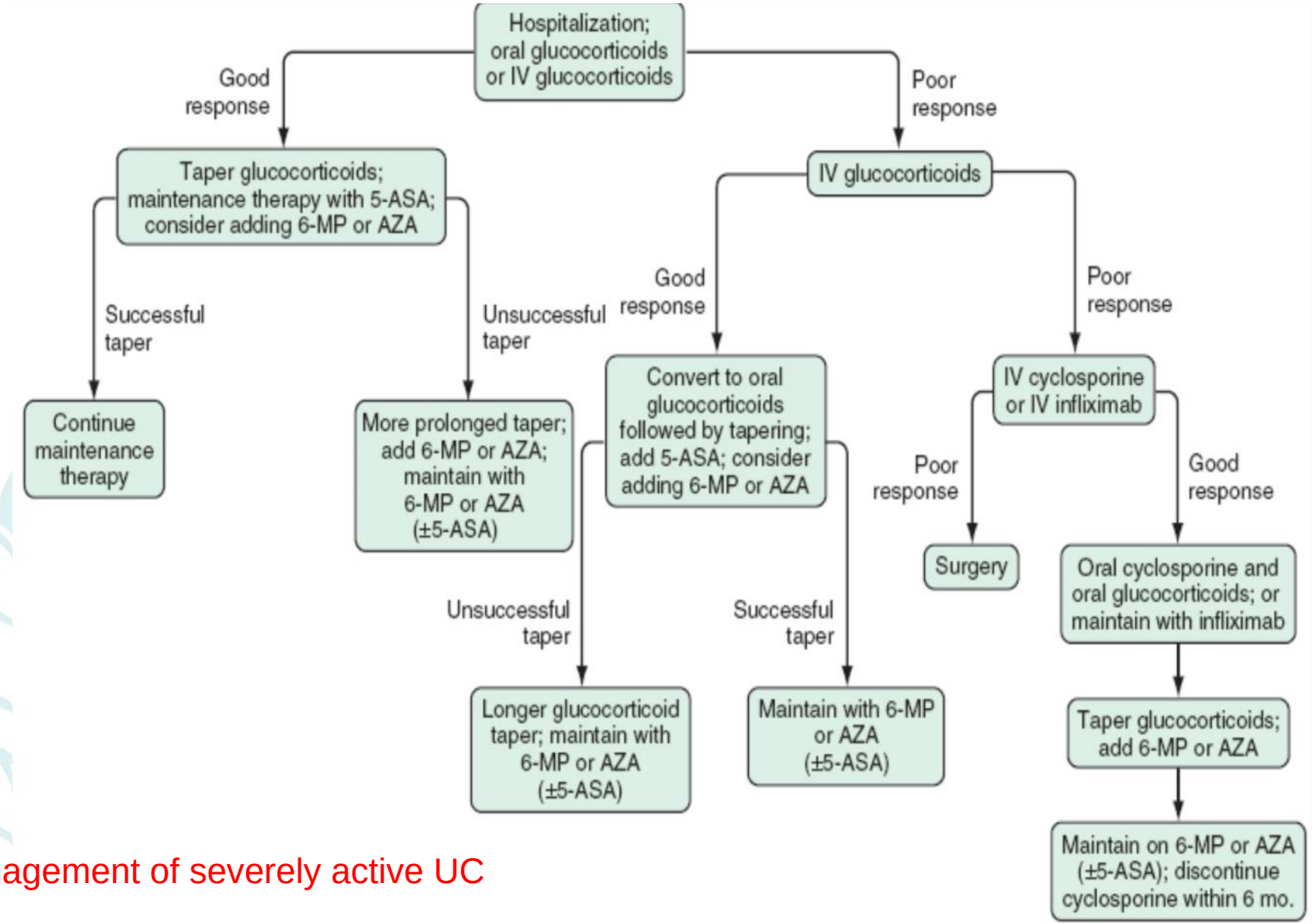
Assessing Severity of Disease

Assessing clinical severity of Crohn disease

	Mild to Moderate	Moderate to Severe	Severe to Fulminant
Crohn disease activity index (CDAI) correlation	CDAI 150–220	CDAI 220–450	CDAI >450
Clinical characteristics	Ambulatory, tolerating an oral diet, without significant morbidities	Failed therapy for mild-moderate disease; systemic toxicity including fever, weight loss, abdominal pain or tenderness, nausea or vomiting (without obstruction), or significant anemia	Persistent symptoms even with outpatient corticosteroid or biologic agent use; cachexia; severe systemic toxicity including high fevers; persistent vomiting; intestinal obstruction; peritoneal signs including guarding, rebound tenderness; evidence of abscess



management of mildly to moderately active UC



management of severely active UC

Conventional therapy of IBD

5-ASA-Derivatives

Mesalazine
Sulfasalazine
Olsalazine
Balsalazide
MMX-Mesalazine

Supportive therapy

Loperamide
Cholestyramine
Spasmolytics
Pain medication
Vitamins

Steroids

Hydrocortisone
Prednisone
Methylprednisone
Beclomethasone
Budesonide
other

Nutrition therapy

parenteral
enteral

Immunmodulator & Biologics

Azathioprine/6-MP
MTX
Infliximab/Adalimumab/Certolizumab
Cyclosporine/Tacrolimus

Antibiotics/ Probiotics

Ciprofloxacin
Metronidazole
ECN/VSL
other

Medical Therapeutics: step-up approaches vs. step-down

- Corticosteroids
  - systemic (methylprednisolone and prednisone), enteric (budesonide), and topical (enema)
- 5-Aminosalicylates
  - mesalamine (oral, enemas, suppositories), sulfasalazine (a mesalamine prodrug), olsalazine, and balsalazide
- Immunomodulators
  - thiopurines (6-mercaptopurine, azathioprine) and methotrexate
- Antibiotics
  - ciprofloxacin and metronidazole
- Biologics
  - Infliximab, adalimumab, and certolizumab

- chronic steroids such as prednisone should not be used as maintenance therapy.
- 5-Aminosalicylate agents are generally less effective in Crohn disease than in ulcerative colitis.
- Surgery should also be considered for appropriate clinical cases before emergent situations arise

Review of medical therapies in inflammatory bowel disease

Medication	Adverse Effects	Monitoring Recommendations
Corticosteroids		
Systemic Corticosteroids		
Prednisone, hydrocortisone, methylprednisolone	Iatrogenic Cushing syndrome (moon facies, fat redistribution, etc), opportunistic infections, adrenal suppression, diabetes, weight gain, striae, impaired wound healing, osteopenia, osteoporosis, avascular necrosis, glaucoma, cataracts	Blood pressure Blood glucose Electrolytes Dual-energy x-ray absorptiometry if patients have indications as detailed in Routine Health Maintenance Annual ophthalmologic examination

Review of medical therapies in inflammatory bowel disease

Enteric Corticosteroids		
Budesonide	Although budesonide is less systemically available, it has a similar adverse effect profile if used for a prolonged period of time	See above

Review of medical therapies in inflammatory bowel disease

5-Aminosalicylates (5-ASA)		
5-ASA in its original form is highly absorbed in the small bowel. Several formulations have been developed to deliver 5-ASA to more distal areas of the gastrointestinal tract		
Azo compounds: sulfasalazine, balsalazide, olsalazine Mesalamine: Pentasa, Asacol, Apriso, Lialda, Rowasa enema, Canasa suppository	5-ASA agents are generally well tolerated but can rarely lead to nephrotoxicity, pancreatitis, hypersensitivity reactions. Sulfasalazine can cause gastrointestinal upset, folate deficiency, abnormal sperm counts	Complete blood count with differential periodically Chemistry panel, specifically renal function, periodically Liver function tests periodically Urinalysis periodically

Review of medical therapies in inflammatory bowel disease

Antimetabolites		
Thiopurines		
Azathioprine, 6-mercaptopurine	Opportunistic infections, gastrointestinal intolerance, macrocytic anemia, hepatic toxicity, bone marrow suppression with leukopenia, anemia, thrombocytopenia. Hypersensitivity reactions can cause fever, rash, pancreatitis. Increased risk of lymphoma, including non-Hodgkin lymphoma and hepatosplenic T-cell lymphoma	Thiopurine methyltransferase (TPMT) level before initiation of therapy. Absent TPMT contraindicates thiopurine use Complete blood count with differential, weekly on initiation and then regular monitoring Chemistry panel, including renal function, periodically Liver function tests periodically Monitor for signs of infection or malignancy

Review of medical therapies in inflammatory bowel disease

Medication	Adverse Effects	Monitoring Recommendations
Folate Antagonists		
Methotrexate	Bone marrow suppression (including leukopenia), nausea, opportunistic infections, hepatic toxicity, hypersensitivity pneumonitis	Pregnancy category X medication. Contraception required Complete blood count with differential periodically Liver function tests periodically Chest radiograph at baseline

Anti–Tumor Necrosis Factor (TNF) Therapy

Infliximab, adalimumab, certolizumab pegol	Opportunistic infections including tuberculosis, hepatitis B reactivation, others. Hepatotoxicity, demyelinating disorders, hematologic reactions, worsening congestive heart failure in patients with preexisting heart disease, development or exacerbation of multiple sclerosis. Development of antibodies to the antibody, serum sickness-like reaction, lupus-like syndrome, development of antinuclear antibodies, anti–double-stranded DNA. May increase risk of lymphoma. The combination of immunomodulators with anti-TNF monoclonal antibodies has been associated with hepatosplenic T-cell lymphomas in young males	Tuberculosis screening (tuberculin skin testing or interferon-γ release assay) before treatment and annually during treatment Complete blood counts with differential periodically Chemistry panel periodically Liver function tests Hepatitis B screening before treatment Chest radiograph before treatment Monitor for symptoms of infection, heart failure, lupus-like syndromes, and malignancy

Infliximab

Chimeric

CD
UC
RA

Adalimumab

humanized

CD
UC
RA

Etanercept

humanized
Receptor/ Fc
Fusion protein

RA

Certolizumab

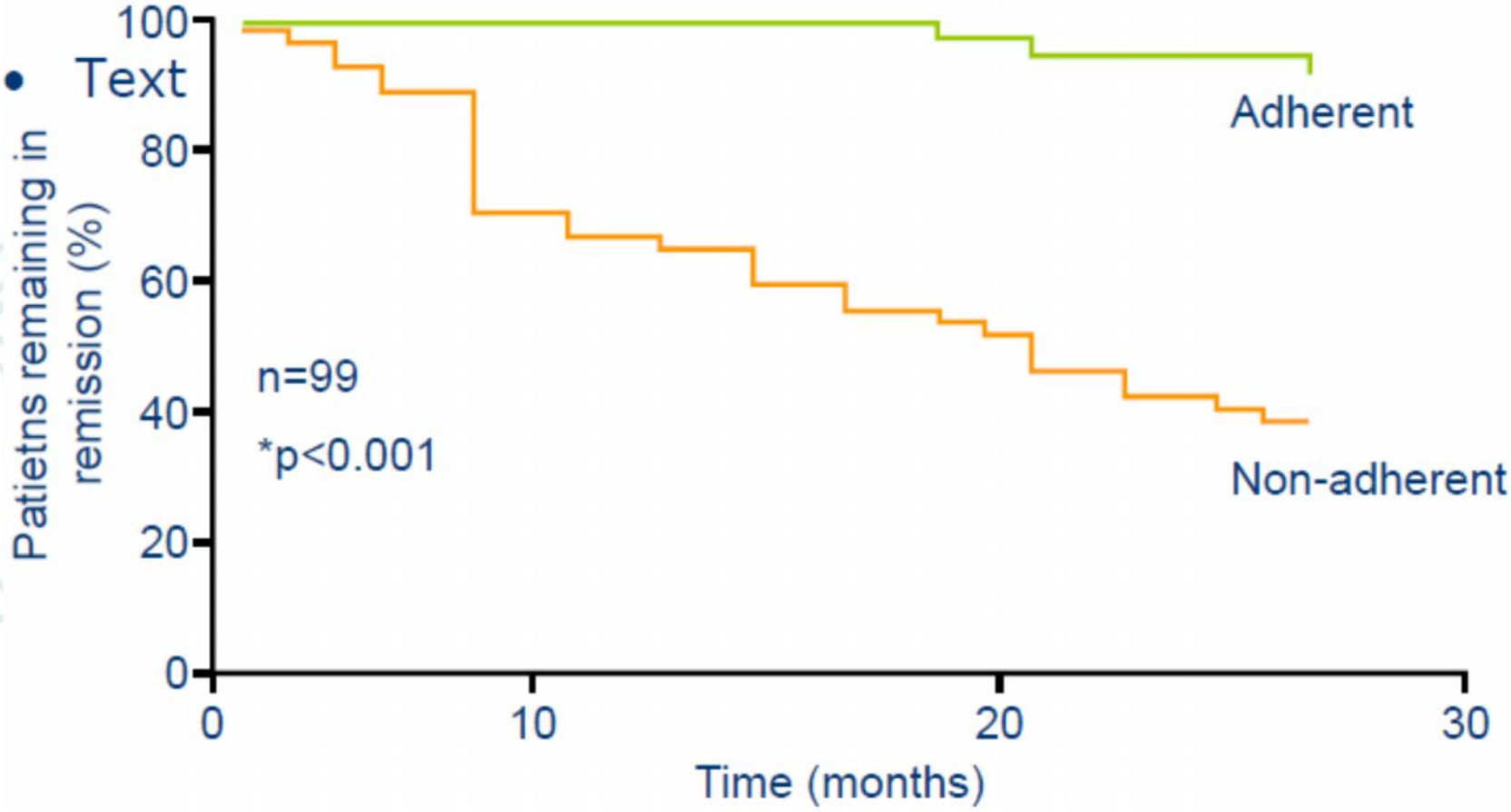
humanized
Fab' Fragment

CD (US, CH)

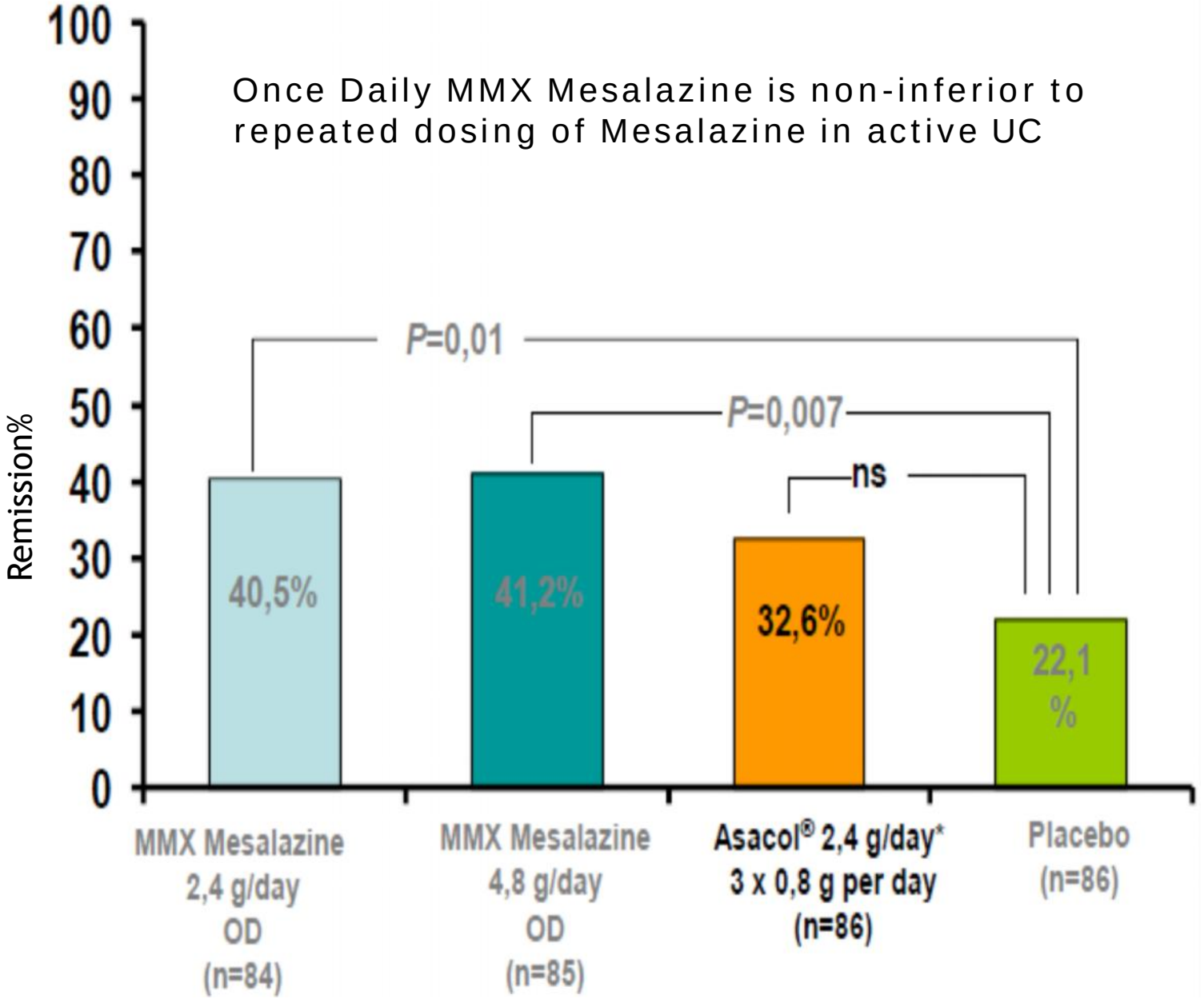
RA

Increased risk of relapse in patients non-adherent to mesalazine

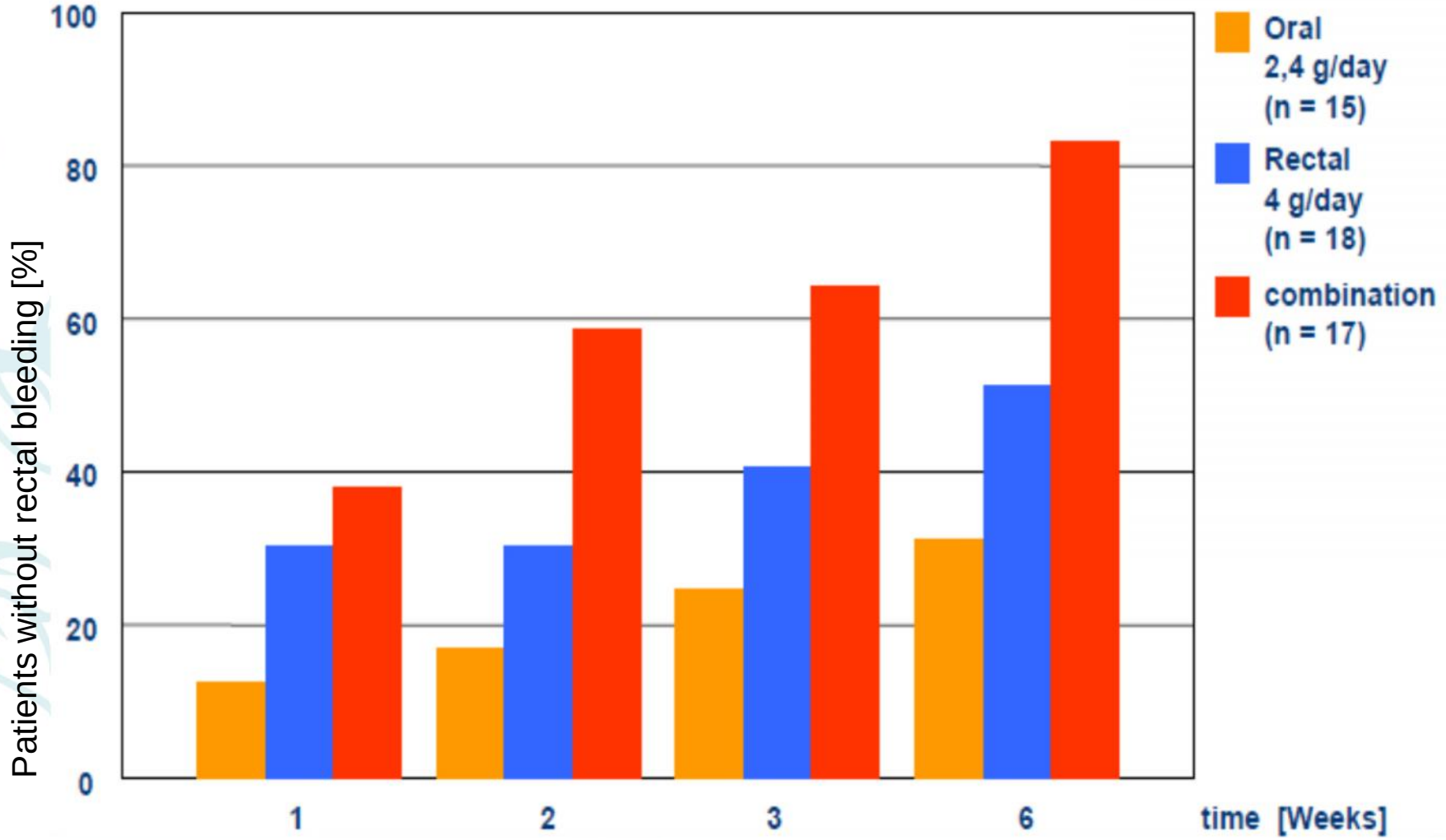
- Text



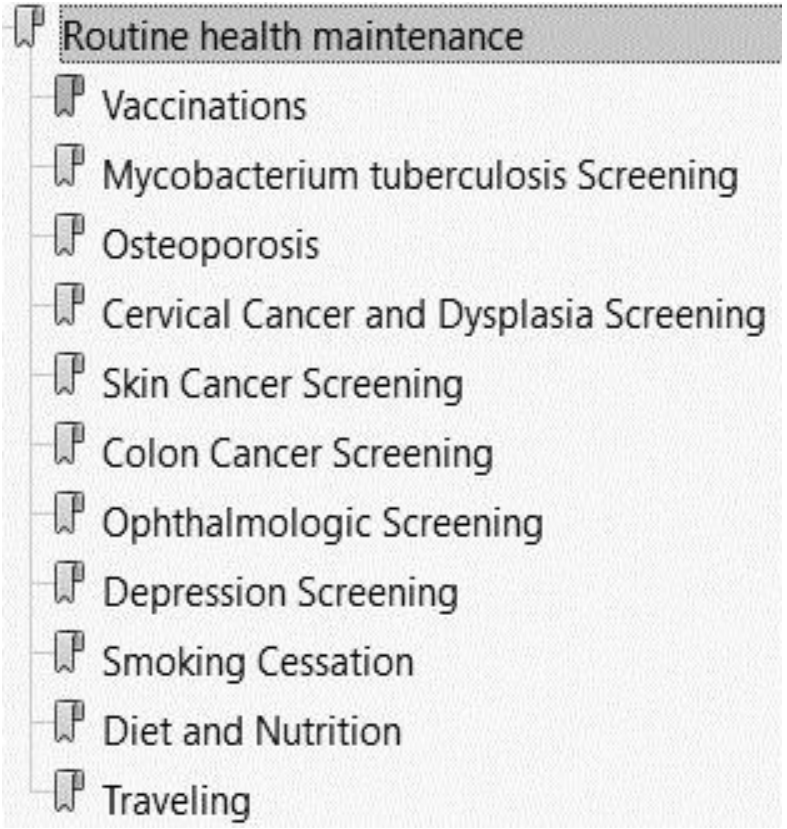
Once Daily MMX Mesalazine is non-inferior to repeated dosing of Mesalazine in active UC



combined treatment with oral and rectal Mesalazine induces a more efficacious in distal active UC



ROUTINE HEALTH MAINTENANCE



ROUTINE HEALTH MAINTENANCE
vaccinations

- Immunosuppressed patients
  - on corticosteroids, immunomodulators, or biologic agents,
  - patients who have received such therapies in the last 3 months
  - Patients with significant protein-calorie malnutrition
- live vaccines should **not** be administered for 3 months after immunosuppressive therapy has been stopped
- waiting at least 12 to 24 weeks after administering a live vaccine before beginning immunosuppressive therapy has been suggested?

ROUTINE HEALTH MAINTENANCE
Live vaccines

- Live bacterial vaccines
  - BCG (bacillus Calmette-Gue´rin) and oral Ty21a Salmonella Typhi vaccine
- Live viral vaccines
  - MMR (measles, mumps, and rubella), MMRV (measles, mumps, rubella, and varicella), OPV (oral polio vaccine), LAIV (live, attenuated influenza vaccine), yellow fever, zoster, rotavirus, varicella, and vaccinia (smallpox)

- Do not administer live vaccines to immunosuppressed patients.

ROUTINE HEALTH MAINTENANCE
vaccinations

- In general, patients with IBD should receive
  - influenza vaccine annually,
  - pneumococcal vaccine if chronically immunosuppressed,
  - tetanus and diphtheria vaccine every 10 years

- When age-appropriate, the human papillomavirus (HPV) vaccine should be administered.
- Furthermore, patients must be screened for hepatitis B before starting biologic therapy.

- When patients are diagnosed with IBD, it is important to check and update their vaccination histories

Mycobacterium tuberculosis Screening

- Patients with IBD in whom the use of TNF-a inhibitors is being considered require testing for latent tuberculosis (TB) before the initiation of therapy
  - Tuberculin skin test or interferon-γ release assay (IGRA)
- chest radiograph in patients who have a history suggestive of tuberculosis, positive skin test, or positive IGRA

Osteoporosis

- Patients with IBD are at increased risk for osteopenia and osteoporosis.
- The reported rates of osteoporosis in IBD patients ~ 15%
- The etiology seems to be multifactorial
  - effect of inflammation on bone,
  - corticosteroid use,
  - calcium and vitamin D malabsorption,
  - other factors such as low body mass index

bone mineral density screening with (DXA) scanning

- AGA recommends :
  - postmenopausal women or men older than 50 years,
  - patients with prolonged corticosteroid use (>3 consecutive months or recurrent courses)
  - patients with a history of a low trauma fracture,
  - patients with hypogonadism
- ACG recommended whenever :
  - smoking, low body mass index, sedentary lifestyle, nutritional deficiencies, or family history of bone density abnormalities

- general preventive measures include
  - lifestyle modifications
    - *smoking cessation, regular weight-bearing exercise, and minimizing alcohol.*
    - *Adequate calcium intake and vitamin D intake*
    - *minimizing corticosteroid use*

Cervical Cancer and Dysplasia Screening

- undergo annual gynecologic examinations,
- annual cervical cancer screening,
- receive HPV vaccination when appropriate

Skin Cancer Screening

- ✓ increased risk of nonmelanoma skin cancer,
  - particularly in those who have been treated with thiopurines
- ✓ Risk of melanoma was increased by the use of biologic

1. Patients should be advised to use broad-spectrum sun protection
2. Annual skin examinations may be warranted in patients who are taking immunomodulators or biologics

Colon Cancer Screening

- increased risk of developing colorectal cancer
- IBD patients should undergo a screening colonoscopy at a maximum of 8 years after onset of symptoms
  - obtain biopsies throughout the colon, to assess the microscopic extent of inflammation
- extensive or left-sided colitis should begin surveillance within 1 to 2 years after initial screening colonoscopy.
- These same recommendations for Crohn colitis who have disease involving at least one-third of the colon
- but after 2 negative examinations with no dysplasia, further surveillance colonoscopy should be performed every 1 to 3 years.

Risk Factors for Colorectal Carcinoma in Ulcerative Colitis

- Age at onset of disease
- Anatomic extent of disease
- Disease activity
- Duration of disease
- Family history of colorectal cancer
- Primary sclerosing cholangitis

Colon Cancer Screening

- Surveillance colonoscopy ideally should be performed when the colonic disease is in remission
- In IBD + PSC should begin surveillance colonoscopy at the time when PSC is diagnosed, and undergo yearly colonoscopy thereafter
- more frequent surveillance in Patients? :
  - have a history of colorectal cancer in first-degree relatives,
  - ongoing active inflammation,
  - anatomic abnormalities such as a foreshortened colon, stricture, or pseudopolyps

Ophthalmologic Screening

- Annual ophthalmologic screening for:
  - Drugs side effects and extraintestinal manifestations
- any patient with IBD
  - who complains of eye pain or vision changes should be referred for ophthalmologic soon

Depression Screening

- may affect up to 15% -35% of IBD patients
- MDD was more than **twice** as high in IBD
  - aggressive screening and support for depression should be pursued
- Cause ?
  - chronic and relapsing nature of IBD,
  - social ramifications of unpredictable bowel patterns,
  - burden of medication and medical care
  - Steroid therapy
- It may also affect the patient's adherence to medication

Smoking Cessation

- smoking has a deleterious effect on the course of Crohn disease
  - linked to ileal involvement and complications
- **active** smoking leads to a protective effect against ulcerative colitis.
- however, **former** smokers have a 70% **increased** risk of developing ulcerative colitis.

Diet and Nutrition

- Crohn's are more susceptible micronutrient deficiencies that include vitamins, minerals, and trace elements.
  - Iron deficiency is common in the IBD population
- Folate deficiency may be less common given widespread supplementation in food products.
- Vitamin B12 deficiency is an important consideration in Crohn disease

Suggested travel instructions for patients with inflammatory bowel disease

- Before travel
  - Explore potential medical providers at travel destinations
  - Avoid live vaccines if immunosuppressed
  - Ensure travel or health insurance provides for emergency health concerns including evacuation by air
- During travel
  - Carry health history and home medical providers' information in carry-on baggage
  - Carry prescription medications and copies of scripts in carry-on baggage
  - Brush teeth with and only drink sterilized water (ideally bottled water with the seal intact)
  - Avoid insect bites
- After travel
  - Screen for latent tuberculosis if indicated