

Overview On Inflammatory Bowel Disease

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Abstract: Ulcerative colitis (UC) and Crohn's disease (CD) (collectively termed inflammatory bowel disease (IBD)) are complex disorders reflected by wide variation in clinical practice. Ulcerative colitis is characterized by diffuse mucosal inflammation limited to the colon. Crohn's disease is characterized by patchy, trans mural inflammation, which may affect any part of the gastrointestinal tract. It may be defined by location (terminal ileal, colonic, ileocolic, upper gastrointestinal), or by pattern of disease (inflammatory, fistula ting, or structuring). About 5% of patients with IBD affecting the colon are unclassifiable after considering clinical, radiological, endoscopic, and pathological criteria, because they have some features of both conditions. This can be termed indeterminate colitis (IC) (1).

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Introduction:

The etiologies of both UC and CD remain unknown. The consensus is that both diseases are an immunological response to environmental triggers (infection, drugs, or other agents) in genetically susceptible individuals. The genetic component is stronger in CD than in UC. Smoking increases the risk of CD, but decreases the risk of UC through unknown mechanisms(2).

Clinical features

The cardinal symptom of UC is bloody diarrhea. Associated symptoms of colicky abdominal pain, urgency, or tenesmus may be present, a severe attack of UC is a potentially life threatening illness. The clinical course of UC is marked by exacerbation and remission. About 50% of patients with UC have a relapse in any year. An appreciable minority has frequently relapsing or chronic, continuous disease and, overall, 20–30% of patients with pan colitis come to colectomy. Symptoms of CD are more heterogeneous, but typically include abdominal pain, diarrhea, and weight loss. Systemic symptoms of malaise, anorexia, or fever are more common with CD than UC. CD may cause intestinal obstruction due to strictures, fistulae (often perianal), or abscesses. The clinical course of CD is also characterized by exacerbations and remission. CD tends to cause greater disability than UC. Both ulcerative and Crohn's colitis are associated with an increased risk of colonic carcinoma(3).

Extra intestinal manifestations of IBD

1. Disorders that usually parallel (ie, wax and wane with) IBD flare-ups: These disorders include peripheral arthritis, episcleritis, aphthous stomatitis, erythema nodosum, and pyodermagangrenosum. Arthritis tends to involve

large joints and be migratory and transient. One or more of these parallel disorders develops in more than one third of patients hospitalized with IBD(4,5).

2. Disorders that are clearly associated with IBD but appear independently of IBD activity:

These disorders include ankylosing spondylitis, sacroiliitis, uveitis, and primary sclerosing cholangitis. Ankylosing spondylitis occurs more commonly in IBD patients with the HLA-B27 antigen. Most patients with spinal or sacroiliac involvement have evidence of uveitis and vice versa. Primary sclerosing cholangitis, which is a risk factor for cancer of the biliary tract, is strongly associated with UC or Crohn colitis. Cholangitis may appear before or concurrently with the bowel disease or even 20 yr after colectomy. Liver disease (eg, fatty liver, autoimmune hepatitis, pericholangitis, cirrhosis) occurs in 3 to 5% of patients, although minor abnormalities in liver function tests are more common. Some of these conditions (eg, primary sclerosing cholangitis) may precede IBD by many years and, when diagnosed, should prompt an evaluation for IBD(4,5).

3. Disorders that are consequences of disrupted bowel physiology:

These disorders occur mainly in severe Crohn disease of the small bowel. Malabsorption may result from extensive ileal resection and cause deficiencies of fat-soluble vitamins, vitamin B12, or minerals, resulting in anemia, hypocalcemia, hypomagnesemia, clotting disorders, and bone demineralization. In children, malabsorption retards growth and development. Other disorders include kidney stones from excessive dietary oxalate absorption, hydronephrosis and hydroureter from ureteral compression by the intestinal inflammatory process, gallstones from

impaired ileal reabsorption of bile salts, and amyloidosis secondary to long-standing inflammatory and suppurative disease.

Thromboembolic disease may occur as a result of multiple factors in all 3 categories(4,5).

Diagnosis and investigation

The diagnosis of IBD is confirmed by clinical evaluation and a combination of biochemical, endoscopic, radiological, histological, or nuclear medicine based investigations. In the case of UC the diagnosis should be made on the basis of clinical suspicion supported by appropriate macroscopic findings on sigmoidoscopy or colonoscopy, typical histological findings on biopsy, and negative stool examinations for infectious agents. For CD the diagnosis depends on demonstrating focal, asymmetric, and often granulomatous inflammation but the investigations selected vary according to the presenting manifestations, physical findings, and complications.

History and examination: A full history should include recent travel, medication, smoking, and family history. Details should include the stool frequency and consistency, urgency, rectal bleeding, abdominal pain, malaise, fever, weight loss, and symptoms of extra intestinal (joint, cutaneous, and eye) manifestations of IBD.

General examination includes general wellbeing, pulse rate, blood pressure, temperature, checking for anemia, fluid depletion, weight loss, abdominal tenderness or distension, palpable masses, and perineal examination(4).

Initial investigations

Laboratory investigations should include full blood count, ESR, CRP, liver function tests and microbiological testing for infectious diarrhoea including *Clostridium difficile* toxin. Abdominal radiography is essential in the initial assessment of patients with suspected severe IBD.

Colonoscopy: Macroscopic features of UC are loss of the vascular pattern, granularity, friability, and ulceration of the rectal mucosa. A rectal biopsy is best taken for histology even if there are no macroscopic changes.

For suspected CD, colonoscopy to the terminal ileum and small bowel barium studies to define extent and site of disease are appropriate. A terminal ileal biopsy performed at colonoscopy documents the extent of examination and may find microscopic evidence of CD.

Other investigations

Double contrast barium enema and small bowel radiology by follow through or intubation (small bowel enema) is the current standard for assessing the small intestine. The role of capsule endoscopy is at present unclear.

White cell scanning is a safe, non-invasive investigation, but lacks specificity.

Ultrasound in skilled hands is a sensitive and non-invasive way of identifying thickened small bowel loops in CD and may identify abscesses or free fluid in the peritoneum.

Computed tomography and magnetic resonance imaging help evaluate activity and complications of disease.

Laparoscopy may be necessary in selected patients, especially where the differential diagnosis of intestinal tuberculosis is being considered.

The serologic panel for IBD is rapidly expanding. So far, ASCA and atypical P-ANCA are the most widely studied markers and remain the best characterized markers in IBD. The ASCA+ve/atypical P-ANCA-ve phenotype is characteristic of CD, while the ASCA -ve/atypical P-ANCA+ve phenotype is seen primarily in UC(6).

The fecal markers lactoferrin and calprotectin are able to differentiate active IBD from inactive IBD as well as from IBS. None of these stool markers is consistently superior in its ability to reflect endoscopic inflammation, but all three are superior to CRP in their diagnostic accuracy. A combination of the stool markers with the CRP and a disease-specific activity index in a categorical comprehensive activity index can increase the diagnostic accuracy with reference to the endoscopic inflammation in UC(7).

Drugs used in the treatment of IBD

Aminosalicylates

5-Aminosalicylic acid (5-ASA, mesalamine): 5-ASA blocks production of prostaglandins and leukotrienes and has other beneficial effects on the inflammatory cascade. Adverse effects (eg, nausea, dyspepsia, headache), interferes with folate (folic acid) absorption, and occasionally causes serious adverse reactions (eg, hemolytic anemia or agranulocytosis and, rarely, hepatitis or pneumonitis). Reversible decreases in sperm count and motility occur in up to 80% of men. Sulfasalazine should be given with food, initially in a dose of 1 to 2 g bid to tid. Patients should take daily folate supplements (1 mg po) and have CBC and liver tests every 6 to 12 mo. Newer drugs that complex 5-ASA with other vehicles seem almost equally effective but have fewer adverse effects. Olsalazine (a 5-ASA dimer) and balsalazide (5-ASA conjugated to an inactive compound) are cleaved by bacterial azoreductases (as is sulfasalazine). These drugs are activated mainly in the colon and are less effective for proximal small-bowel disease. Olsalazine dosage is 500 to 1500 mg po bid, and balsalazide is 2.25 g potid. Asacol (typical dose 800 to 1200 mg potid) is 5-ASA coated with an acrylic polymer whose pH solubility delays release of the drug until entry into the distal ileum

and colon. Pentasa (1 g poqid) is 5-ASA encapsulated in ethylcellulosemicrogranules that release 35% of the drug in the small bowel. 5-ASA is also available as a suppository (500 or 1000 mg at bedtime or bid) or enema (4 g at bedtime or bid) for proctitis and left-sided colon disease(8).

Corticosteroids

(Oral prednisolone, prednisone, budesonide (among others), or intravenous hydrocortisone, methylprednisolone.) Topical suppositories, foam or liquid enemas include hydrocortisone, prednisolone metasulphobenzoate, betamethasone, budesonide). Choice and mechanism

Corticosteroids are potent anti-inflammatory agents for moderate to severe relapses of both UC and CD. They have no role in maintenance therapy for either disease. They act through inhibition of several inflammatory pathways— suppressing interleukin transcription, induction of I κ B that stabilises the NF κ B complex, suppression of arachidonic acid metabolism, and stimulation of apoptosis of lymphocytes within the lamina propria of the gut.

Efficacy for active UC

A combination of oral and rectal steroids is better than either alone. Adverse events are significantly more frequent at a dose of 60 mg/day compared with 40 mg/day, without added benefit. Too rapid reduction can be associated with early relapse and doses of prednisolone.

Efficacy for active CD

In active Crohn's prednisone 1 mg/kg/day should be given.

Adverse effects of steroids

Early effects due to supraphysiological doses include cosmetic (acne, moon face, oedema), sleep and mood disturbance, dyspepsia, or glucose intolerance.

Effects associated with prolonged use (usually 12 weeks, but sometimes less) include posterior subcapsular cataracts, osteoporosis, osteonecrosis of the femoral head, myopathy, and susceptibility to infection.

Effects during withdrawal include acute adrenal insufficiency (from sudden cessation), a syndrome of myalgia, malaise, and arthralgia (similar to recrudescence of CD), or raised intracranial pressure.

Complete steroid withdrawal is facilitated by early introduction of azathioprine, adjuvant nutritional therapy, or timely surgery(9).

Thiopurines

(Azathioprine (AZA) and mercaptopurine (MP). Purine antimetabolites inhibit ribonucleotide synthesis, but the mechanism of immunomodulation is by inducing T cell apoptosis by modulating cell (Rac1) signalling. Azathioprine is metabolised to

mercaptopurine and subsequently to 6-thioguanine nucleotides. Thiopurines are effective for both active disease and maintaining remission in CD and UC. The main role for thiopurines is steroid sparing. Thiopurines should be considered for patients who require two or more corticosteroid courses within a calendar year; those whose disease relapses as the dose of steroid is reduced below 15 mg; relapse within 6 weeks of stopping steroid. Thiopurines are effective as maintenance therapy for CD for up to 4 years then stop, except in those with evidence of continuing disease activity. Maintenance dose of AZA of 2–2.5 mg/kg/day and 6-MP of 1–1.5 mg/kg/day in both UC and CD.

Monitoring thiopurinetherapy:Manufacturers recommend weekly FBCs for the first 8 weeks of therapy followed by blood tests at least every 3 months.

Side effects

Leucopenia can develop, hepatotoxicity and pancreatitis are uncommon (<5%). Thiopurines can reasonably be continued during pregnancy if UC or CD has been refractory. There is no increased risk of lymphoma or other cancers in IBD patients treated with AZA(10).

Methotrexate

(Oral, subcutaneous or intramuscular injection, unlicensed therapy for IBD.)Polyglutamated metabolites of methotrexate inhibit dihydrofolatereductase, but this cytotoxic effect does not explain its anti-inflammatory effect. Inhibition of cytokine and eicosanoid synthesis probably contribute.

Efficacy

Methotrexate (MTX) is effective for inducing remission or preventing relapse in CD. At present, the role of MTX is in the treatment of active or relapsing CD in those refractory to or intolerant of AZA or MP. For CD and 25 mg/week is standard. No comparable trials have addressed the role of MTX in the induction or maintenance of remission in UC.

Duration of therapy is debated. The 3 year remission rate for methotrexate in one series was 51%, which compares with data on azathioprine from the same centre (69% 3 year remission rate for azathioprine).

Monitoring therapy: Measurement of full blood count and liver function tests are advisable before and within 4 weeks of starting therapy, then monthly. Side effects: Early toxicity from methotrexate is primarily gastrointestinal (nausea, vomiting, diarrhoea, and stomatitis) and this may be limited by co-prescription of folic acid. The principal concerns are hepatotoxicity and pneumonitis(11). Ciclosporin (Oral or intravenous, unlicensed therapy for UC.)Ciclosporin (CsA) is an inhibitor of calcineurin,

preventing clonal expansion of T-cell subsets. its main role is a bridge to thiopurine therapy. It has a rapid onset of action and is effective in the management of severe UC. Intravenous CsA is rapidly effective as a salvage therapy for patients with refractory colitis, who would otherwise face colectomy, but its use is controversial because of toxicity and long term failure rate. Its only well-documented use in Crohn disease is for patients with refractory fistulas or pyoderma. Initial dose is 4 mg/kg IV in continuous infusion over 24 h; responders are converted to an oral dose of 6 to 8 mg/kg once/day with early introduction of azathioprine or 6-mercaptopurine. Long-term use (> 6 mo) is contraindicated.

Monitoring therapy: Measurement of blood pressure, full blood count, renal function, and CsA concentration (aim 100–200 ng/ml) are advisable at 0, 1, and 2 weeks, then monthly. Measurement of blood cholesterol and magnesium are appropriate before starting therapy.

Side effects

Tremor, paraesthesiae, malaise, headache, abnormal liver function, gingival hyperplasia, hirsutism, renal impairment, infections, and neurotoxicity(12).

Infliximab

Infliximab (Remicade) is an anti-TNF-alpha monoclonal antibody that is administered by infusion for the treatment of active and fistulating Crohn disease. Infliximab is FDA approved for both ulcerative colitis and Crohn disease; it appears to have a higher efficacy rate in Crohn disease. Infliximab is generally administered as 3 separate infusions of 5 mg/kg over 2 h for the induction of remission of moderate to severe IBD at weeks 0, 2, and 6, followed by infusions every 8 weeks for maintenance of remission. the dose needs to be increased or the interval needs to be shortened within a year or so(13).

Adalimumab is given with an initial loading dose of 160 mg sc and then 80 mg sc at wk 2. After that dose, 40 mg sc is given every 2 wk. A third anti-TNF agent, certolizumab, is also approved for use in Crohn disease. Monotherapy with anti-TNF agents is clearly effective for both induction and maintenance of remission, but some studies suggest better results when patients received an immunomodulator (AZA, MP, or MTX) unless these cannot be tolerated, as these probably extend the interval and reduce development of antibodies to IFX that in turn reduce efficacy and increase side effects. certolizumabpegol (Cimzia), which is given by SC injection every 4 weeks. Natalizumab (Tysabri), an agent aimed at preventing the accumulation of lymphocytes in the diseased bowel by blocking the effects of integrin,

has been approved by the FDA, but it is only available through a restricted distribution program. Natalizumab is an intravenous medication that has shown efficacy in Crohn disease, but there have been 3 reports of progressive multifocal leukoencephalopathy, a potentially fatal opportunistic viral infection. Risk is typically apparent in those with prior immunosuppressant exposure or with a duration of infusion for longer than 2 years(14,15).

Side effects

Infusion reactions, anaphylactic reactions and delayed reaction of joint pain and stiffness, fever, myalgia, and malaise may occur. Active sepsis (for example, an abscess) is an absolute contraindication, as this risks overwhelming septicemia. Reactivation or development of tuberculosis. IFX may exacerbate existing cardiac failure. The theoretical risk of lymphoproliferative disorders or malignancy (in view of the role of endogenous TNF in tumor suppression) has not been confirmed. Before anti-TNF agents are administered, screening should be done for coexistent infection with perianal and abdominal abscess (including *Mycobacterium tuberculosis*), and caution is advised if a patient is a carrier for the hepatitis B virus(16).

Antibiotics and probiotics: Antituberculosis therapy, macrolides, fluoroquinolones, 5-nitroimidazoles, and rifaximin (alone or in combination) have not consistently been shown to induce remission in selective active Crohn disease and have rarely been shown to induce remission in ulcerative colitis. Antibiotics may be helpful in Crohn disease but are of limited use in UC. Metronidazole 500 to 750 mg po tid for 4 to 8 wk may control mild Crohn disease and help heal fistulas. Ciprofloxacin 500 to 750 mg po bid may prove less toxic. Many experts recommend metronidazole and ciprofloxacin in combination. Rifaximin, a nonabsorbable antibiotic, at a dose of 200 mg po tid or 800 mg po bid may also be beneficial as treatment for active Crohn disease. Antibiotics have potential adverse effects, including nausea, anorexia, diarrhea, and monilial (candidal) infections. Peripheral neuropathy can be observed in association with metronidazole and, when present, requires discontinuation of therapy with that drug. Finally, antibiotics can also increase the risk of *Clostridium difficile* colitis.

Various nonpathogenic microorganisms (eg, commensal *Escherichia coli*, *Lactobacillus* species, *Saccharomyces*) given daily serve as probiotics and may be effective in preventing pouchitis, but other therapeutic roles have yet to be clearly defined. Therapeutic infestation with the parasite *Trichuris suis* has been tried in an effort to stimulate T2-helper cell

immunity and may decrease disease activity in UC (17).

Medical management of inflammatory bowel disease.

Therapeutic decisions depend on the age of the onset of the disease, patient gender and race, mode of the disease presentation, disease location, disease activity disease-associated complications such as perianal disease/fistula, and serology and genetic markers can all help to individualize disease

treatment. These factors can help to determine whether one should start with 5-ASA/antibiotic/steroid [step-up where there is no risk factors for aggressive disease course] or whether one should initiate biologic therapy at diagnosis [top-down approach], and whether it is most advisable to use monotherapy with biologic treatment [e.g. in young, Caucasian male or elderly] or use a combination therapy with a biologic and an immunomodulator (18).

Table (1): Truelove and Witts for U/C(19) Symptoms	Mild Activity	Severe Activity
Daily BMs	< 4	>6
Rectal Bleeding	infrequent	frequent
Temperature	normal	normal to elevated
Heart Rate	<90 bpm	>90 bpm
Hemoglobin	>10gm/100mL	< 10g/100mL
Sed Rate	< 30 mm/h	>30 mm/h

The CDAI The index consists of eight factors, each summed after adjustment with a weighting factor. The components of the CDAI and weighting factors are the following: Clinical or laboratory variable	Weighting factor
Number of liquid or soft stools each day for seven days	x 2
Abdominal pain (graded from 0-3 on severity) each day for seven days	x 5
General wellbeing, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days	x 7
Presence of complications*	x 20
Taking Lomotil or opiates for diarrhea	x 30
Presence of an abdominal mass (0 as none, 2 as questionable, 5 as definite)	x 10
Hematocrit of <0.47 in men and <0.42 in women	x 6
Percentage deviation from standard weight	x 1

*One point each is added for each set of complications: the presence of joint pains (arthralgia) or frank arthritis inflammation of the iris or uveitis presence of erythema nodosum, pyodermagangrenosum, or aphthous ulcers anal fissures, fistulae or abscesses other fistulae fever during the previous week.

The *Harvey-Bradshaw index* is a simpler version of the CDAI for data collection purposes. It consists of only clinical parameters: general well-being (0 = very well, 1 = slightly below average, 2 = poor, 3 = very poor, 4 = terrible) abdominal pain (0 = none, 1 = mild, 2 = moderate, 3 = severe) number of liquid stools per day abdominal mass (0 = none, 1 = dubious, 2 = definite, 3 = tender) complications, as above, with one point for each. Remission of Crohn's disease is defined as a fall in the CDAI of less than 150 or HBI less than 5, mild disease is defined with a CDAI value between 150 and 220 or with a HBI value between 5 and 7. Moderate disease is defined with a CDAI value between 220 and 450 or with a HBI value between 8 and 16. Severe disease is defined with a CDAI value > 450 or with a HBI value > 16.

Treatment of mild to moderate disease

Topical management is appropriate for those with proctitis and often the case if the disease extends into the sigmoid. For those with more extensive

disease, oral or parenteral therapy are the mainstays of treatment, although some of these patients may get additional benefit from topical therapy.

Step 1: Topical mesalazine 1 g daily combined with oral mesalazine 2-4 g daily, olsalazine 1.5-3 g daily, or balsalazide 6.75 g daily. Topical corticosteroids for patients who are intolerant of topical mesalazine.

Step 1 A: Antibiotics

Step 2: Oral prednisolone 40 mg daily. Prednisolone should be reduced gradually according to severity and patient response, generally over 8 weeks. In CD concomitant intravenous metronidazole is often advisable, because it may be difficult to distinguish between active disease and a septic complication

Step 3: Patients with chronic active steroid dependent disease should be treated with azathioprine 1.5-2.5 mg/kg/day or mercaptopurine 0.75-1.5 mg/kg/day. In CD Methotrexate (15-25 mg IM

weekly) is effective for patients whose active disease has responded to IM methotrexate. It is appropriate for those intolerant of, or who have failed, azathioprine/mercaptopurine Therapy.

Step 4: Infliximab is administered as 3 infusions of 5 mg/kg for the induction of remission(22).

Treatment of severe IBD

Physical examination daily to evaluate abdominal tenderness and rebound tenderness. Joint medical and surgical management is appropriate. Recording of vital signs four times daily and more often if deterioration noted. A stool chart to record number and character of bowel movements, including the presence or absence of blood and liquid versus solid stool. Measurement of FBC, ESR, or CRP, serum electrolytes, serum albumin, and liver function tests every 24–48 hours. Daily abdominal radiography if colonic dilatation (transverse colon diameter >5.5 cm) is detected at presentation. Intravenous fluid and electrolyte replacement to correct and prevent dehydration or electrolyte imbalance, with blood transfusion to maintain a haemoglobin.10 g/dl. Subcutaneous heparin to reduce the risk of thromboembolism. Nutritional support (by enteral or parenteral route) if the patient is malnourished. Intravenous corticosteroids (hydrocortisone 400 mg/day or methylprednisolone 60 mg/day), biological therapy. Withdrawal of anticholinergic, antidiarrhoeal agents, NSAID and opioid drugs, which risk precipitating colonic dilatation. Continuation of aminosalicylates once oral intake resumes, although these have not been studied in severe

disease. Topical therapy (corticosteroids or mesalazine) if tolerated and retained. Intravenous antibiotics only if infection is considered, or immediately before surgery. Immediate surgical referral if there is evidence of toxic megacolon (diameter.5.5 cm, or caecum.9 cm). Consideration of colectomy or intravenous ciclosporin 2 mg/kg/day if there is no improvement during the first 3 days. Following induction of remission, oral ciclosporin for 3–6 months is appropriate. Surgery should be considered for those who have failed medical.

Maintenance of remission

A general rule of thumb is that once remission is achieved, the medications used to achieve remission should be continued, except steroids, which should be tapered off, because they have no role in maintaining remission[8] and their use may lead to debilitating illness(23)

Oral Crohn's disease. This is best managed in conjunction with a specialist in oral medicine. Topical steroids, topical tacrolimus, intra-lesional steroid injections, enteral nutrition, and infliximab may have a role in management.

Gastroduodenal disease. Symptoms are often relieved by proton pump inhibitors. Surgery is difficult and may be complicated by fistulation.

Diffuse small bowel disease. Stricture dilatation or strictureplasty with or without triamcinolone injection should be considered. Nutritional support before and after surgery is usually essential. Other approaches, including the combination of infliximab with surgery for residual strictures, are evolving.

Patients who have a poor response to steroids can be divided into steroid refractory and steroid dependent.

Steroid-refractory disease may be defined as active disease in spite of an adequate dose and duration of prednisolone (>20 mg/d for >2 weeks) and steroid dependence as a relapse when the steroid dose is reduced below 20 mg/day, or within 6 weeks of stopping steroids. Such patients should be considered for treatment with immunomodulators if surgery is not an immediate consideration. Azathioprine 1.5–2.5 mg/kg/day, or mercaptopurine 0.75–1.25 mg/kg/day are the first line agents of choice for steroid dependent disease.

Methotrexate IM 25 mg weekly for up to 16 weeks followed by 15 mg weekly is effective for chronic active disease. Infliximab (5 mg/kg) should be reserved for patients with moderate to severe CD, who are refractory to or intolerant of treatment with steroids, mesalazine, azathioprine/mercaptopurine, and methotrexate, and where surgery is considered inappropriate (24).

SURGERY FOR INFLAMMATORY BOWEL DISEASE of treatment with steroids, mesalazine, azathioprine/mercaptopurine, and methotrexate, and where surgery is considered inappropriate(24).

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SURGERY FOR INFLAMMATORY BOWEL DISEASE

For UC, surgery should be advised for disease not responding to intensive medical therapy. The decision to operate is best taken by the gastroenterologist and colorectal surgeon in conjunction with the patient. Other patients with dysplasia or carcinoma, poorly controlled disease, recurrent acute on chronic episodes of UC should be counseled regarding surgical options.

For CD, surgery should only be undertaken for symptomatic rather than asymptomatic, radiologically identified disease, because it is potentially panenteric and usually recurs following surgery. Resections should be conservative(25).

Surveillance for colonic carcinoma is important to discuss with individual patients their risk of

colorectal cancer, the implications should dysplasia be identified, the limitations of surveillance (which may miss dysplasia), and the small, but definable, risks of colonoscopy.

It is advisable that patients with UC should have a colonoscopy after 8–10 years to re-evaluate disease extent. Colonoscopies should be conducted every 3 years in the second decade, every 2 years in the third decade, and annually in the fourth decade of disease. Four random biopsies every 10 cm from the entire colon are best taken with additional samples of suspicious areas.

Patients with primary sclerosing cholangitis appear to represent a subgroup at higher risk of cancer, and they should have more frequent (perhaps annual) colonoscopy. If dysplasia (of any grade) is detected colectomy is usually advisable(26). The regular 5-ASA use is associated with some reduction in the risk of CRC developing in ulcerative colitis(27). NSAID use increases the risk of hospitalizations due to complications in the lower gastrointestinal tract. By inhibiting COX-2 or other tumorigenic targets, NSAIDs, especially aspirin or new aspirin derivatives, may prevent colon cancer in selected populations(28).

Management of pregnancy

Maintaining adequate disease control during pregnancy is essential for both maternal and fetal health. If planning pregnancy, patients should be counseled to conceive during remission and advised to continue their maintenance medication. Before conception, patients should be well nourished and take folate supplements. Patients with acute severe colitis or other life threatening complications of disease should be managed as for the non-pregnant patient, including abdominal radiograph. The best interests of the fetus are served by optimal management of maternal IBD. The mode of delivery should be carefully considered. It may be best for patients with perianal CD or ileoanal pouch formation to have a Caesarian section to avoid the risk of damage to the anal sphincter. Sulphasalazine should be stopped if there is suspected neonatal haemolysis. Azathioprine should in general be continued during pregnancy, as the risks to the fetus from disease activity appear to be greater than continued therapy. Corticosteroids can be used for active disease, as the risks to the pregnancy from disease activity are greater than from continued therapy. Methotrexate is absolutely contraindicated in pregnancy. Anti-TNF α therapies are considered category B drugs for pregnancy. To date, there is no evidence that TNF α antagonists are associated with embryo toxicity, teratogenicity or increased pregnancy loss. However, caution should be taken when anti-TNF α agents are used during pregnancy, as experience in humans, with regard to safety for the developing foetus, is still limited. Absolute indications for surgery

are unaltered by pregnancy and surgery should only be delayed where aggressive medical therapy may allow critical fetal maturation(29).

Nutrition

There is no evidence that artificial nutritional support alters the inflammatory response in UC, in contrast to CD. For CD, nutrition should be considered an integral component of the management of all patients. Specific attention should be paid to vitamin B12 status, especially after ileal resection. Nutritional support is appropriate as adjunctive therapy for any malnourished patients, or for those with intestinal partial obstruction awaiting surgery, or severely symptomatic perianal disease, or those with postoperative complications. Enteral nutrition is preferred when the patient's condition permits(30).

Management of extraintestinal manifestations

Extraintestinal manifestations are more common in Crohn's colitis and ileocolitis than in exclusively small bowel those that are associated with active intestinal disease largely respond to therapy aimed at controlling disease activity(31).

Recent literature supports an association between inflammatory bowel disease and coronary artery disease. While hypertension increases the risk of coronary artery disease in inflammatory bowel disease patients, other typical risk factors have not been confirmed, and markers of inflammation may predict coronary artery disease risk in this population. Common cardiovascular drugs such as statins and angiotensin-converting enzyme inhibitors may have dual potential for controlling inflammatory bowel disease and preventing or treating coronary artery disease(32).

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