Guidelines for the management of inflammatory bowel disease in adults

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RIEPILOGO DEGLI STATEMENTS

2.0 SERVICE DELIVERY

Recommendation for service delivery

Hospitals involved in the care of patients with IBD should model their service as far as possible to meet the IBD Service

Standards (EL5, RG D).

It is suggested that an IBD service is delivered within the following basic framework:

The IBD team

- Patients with IBD should be cared for by a defined IBD team with named personnel comprising gastroenterologists, colorectal surgeons, clinical nurse specialists, a dietician, pharmacist, pathologist and GI radiologist (IBD Standard A1). The roles and responsibilities of an IBD nurse specialist are outlined within Royal College of Nursing guidance, (http://www.rcn.org.uk/__data/assets/pdf_file/0007/107746/ 003194.pdf (last accessed Oct 2010)). The IBD team should have access to the following essential supporting services: a psychologist/counsellor, rheumatologist, ophthalmologist, dermatologist, obstetrician, nutrition support team, a paediatric gastroenterology clinical network, general practise (IBD Standard A2).

Multi-disciplinary care (IBD Standard A3)

- The IBD team should have regular meetings to discuss patients with complex needs
- Patients should have access to a joint or parallel Gastroenterology surgical clinic that is held at least monthly in a unit that meets the standards set out in this document.

Patient management (IBD Standard A4)

- Local protocols should be developed to facilitate referral of symptomatic patients in whom IBD is suspected.
- All patients with IBD who are admitted to hospital should be notified to the IBD specialist nurse (IBD Standard A10).
- Newly diagnosed patients for whom surgery is not an immediate consideration should be transferred to the care of the medical gastroenterology team.
- IBD inpatients should, wherever possible, be cared for in a specialist ward area with 24 h access to intensive care facilities on site.
- IBD surgery should be undertaken by recognised colorectal surgeons, who are core members of the IBD team, or their supervised trainees, in a unit performing such operations regularly (IBD Standard A7).
- All IBD outpatients should have an annual review and basic information recorded. This may be in a hospital/community clinic, or by telephone follow-up, and should be done by a healthcare professional with recognised competence in IBD (Standard A11).
- Patients with IBD should have access to a dedicated telephone service supported by an answer-phone, which can provide a response by the end of the next working day (Standard A11).
- Patients experiencing a possible relapse of their IBD should have access to specialist review within a maximum of five working days (Standard A11).
- There must be a defined policy and protocol for transitional care of adolescents with IBD (Standard A12).

3.0 INFLAMMATORY BOWEL DISEASE

3.1 Definitions

Definition of ulcerative colitis phenotype according to the Montreal classification

Maximal extent of inflammation observed at colonoscopy

Proctitis	E1
Left-sided e extending up to splenic flexure	E2
More extensive disease	E3

Definition of Crohn's disease phenotype according to the Montreal classification

Age of onset	Location	Behaviour
#16 years (A1)	Ileal (L1)	Non-stricturing, Non-penetrating (B1)
17-40 years (A2)	Colonic (L2)	Stricturing (B2)
>40 years (A3)	Ileo-colonic (L3)	Penetrating (B3)
	*Isolated upper GI disease (L4)	+ 'p' if peri-anal disease

*L4 is a modifier that can be added to L1 e 3 when concomitant upper gastrointestinal (GI) disease is present.

3.3 Diagnosis and investigation

Recommendations

All patients with diarrhoea should have stools sampled for culture and C difficile toxin. Four samples are required for 90% sensitivity. (EL4, RGC).

- Imaging techniques may be constrained by availability and local expertise. In general, attempts should be made to minimise exposure to ionising radiation.
- For imaging the small bowel, MRI is the preferred technique where available (EL 2b).
- All new patients should have their disease phenotype classified in accordance with the Montreal Classification (EL 5, RG D).

IBD Service Standards for diagnosis and investigation: (IBD standard A)

- Local guidelines/referral pathways should be in place for rapid referral of new/suspected cases of IBD.
- The patient's weight and body mass index (BMI) should be measured at each attendance.
- Outpatients should wait no more than 4 weeks for radiological endoscopic investigations.
- Inpatients with severe disease should wait no more than 24 h for necessary imaging or endoscopy.
- Processing of biopsies should be rapid (2e5 days maximum according to need).

5.0 MANAGEMENT OF ULCERATIVE COLITIS

Recommendations for the treatment of active (left-sided or extensive) ulcerative colitis:

- Oral mesalazine 2.4-4.8 g daily or balsalazide 6.75 g (delivering 2.4 g mesalazine) daily are effective first-line therapy for mild-moderately active disease (EL 1a, RG). Topical mesalazine combined with oral mesalazine >2 g/day is more effective than oral therapy alone for both left-sided (EL 1b, RG B) and extensive colitis (EL1b, RG A).
- Once daily dosing with mesalazine is at least as effective as twice or three times daily regimes.
- Prednisolone 20-40 mg daily is appropriate for those patients with moderately active disease, in whom mesalazine in appropriate dose and route has been unsuccessful (EL1b, RG C).
- Prednisolone should be reduced gradually according to severity and patient response, generally over 8 weeks. More rapid reduction is associated with early relapse.

Recommendations for the treatment of active proctitis

- In mild-moderate disease, topical mesalazine 1-2 g daily (in appropriate form for extent of disease) may be effective alone.
- Combination with oral mesalazine 2-4 g daily, or balsalazide 6.75 g daily, may be useful in resistant cases. (EL1b, RG B).
- Topical corticosteroids are less effective than topical mesalazine, and should be reserved as second-line therapy for patients who are unresponsive to topical mesalazine (EL 1b, RG B).
- Patients who have failed to improve on a combination of oral mesalazine with either topical mesalazine or topical corticosteroids should be treated with oral prednisolone 40 mg daily. Topical agents may be used as adjunctive therapy in this situation (EL1b, RG A).
- In the management of proximal faecal loading associated with distal colitis, non-stimulant osmotic laxatives such as a PEG-based preparation are often helpful (EL 3, RG C).
- Refractory proctitis should prompt exclusion of alternative pathology, consideration of drug compliance, change of formulation, associated irritable bowel, and further escalation of therapy.

Acute severe ulcerative colitis

- The IBD service should have arrangements in place to admit known patients with IBD direct to the specialist Gastroenterology ward or area.
- Patients admitted with known or suspected IBD should discussed with and normally be transferred to the care of a consultant gastroenterologist/colorectal surgeon within 24 h of admission.
- Where these facilities are not available (especially where there is no dedicated colorectal surgical service on site), patients should be transferred to appropriate centre for on-going joint medical-surgical management.

Important steps in the initial management include:

- Patients should be weighed and their nutritional needs assessed (IBD Standard A10). If the patient is malnourished nutritional support by the enteral route is associated with fewer complications than the parenteral route in acute coiitis
- Full blood count, urea and electrolytes, liver function tests, serum albumin, glucose and CRP, and haematinics (iron, B12, folate).
- Stool culture and C difficile toxin assay. Microbiological testing for C difficile. Toxin in addition to standard organisms in increasingly important. C difficile infection has a higher prevalence in patients with IBD through unknown mechanisms, may not be confined to the colon, and is associated with increased mortality. A minimum of four stool samples are required to detect 90% of cases. Cytomegalovirus (CMV) should be considered in severe or refractory colitis as reactivation is common in patients with IBD on immunosuppression and the presentation can mimic ulcerative colitis or Crohn's disease. CMV colitis is associated with a poor outcome and high colectomy rate. A combination of colonic histology and PCR for viral DNA confirms the diagnosis rapidly. Immunosuppressants should be discontinued in favour of intravenous Gancyclovir for 2 weeks or the more expensive but equally effective oral agent Valgancyclovir. Further management is described in the ECCO consensus statement on prevention, diagnosis and management of opportunistic infections in IBD.
- Intravenous fluid and electrolyte replacement to correct and prevent dehydration or electrolyte imbalance, with blood transfusion to maintain a haemoglobin >10 g/dl.
- Intravenous antibiotics only if infection is considered, or immediately prior to surgery. Withdrawal of anticholinergic, antidiarrhoeal agents, opioid drugs, which risk precipitating colonic dilatation.
- Subcutaneous heparin to reduce the risk of thromboembolism.
- Intravenous corticosteroids Either hydrocortisone 100 mg four times a day or methylprednisolone 60 mg/day (EL1b, RGB). higher doses of steroids offer no greater benefit, but lower doses are less effective.
- If there is evidence of toxic megacolon (diameter >5.5 cm, or caecum >9 cm), the urgency with which surgery is undertaken after recognition of colonic dilatation depends on the condition of the patient: the greater the dilatation and the greater the degree of systemic toxicity, the sooner surgery should be undertaken, but signs may be masked by steroid therapy. In selected patients with mild dilatation, expectant management may be undertaken.
- Any clinical, laboratory or radiological deterioration mandates immediate colectomy.
- Flexible sigmoidoscopy and biopsy should be available within 72 h (ideally within 24 h) and a histological diagnosis within 5 days to confirm diagnosis and exclude CMV. (IBD Standard A9)

Daily monitoring:

- Physical examination daily to evaluate abdominal tenderness and rebound tenderness. Joint medical and surgical management is appropriate (EL5, RG D).
- Recording of vital signs four times daily and more often if deterioration noted.
- 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, CRP, serum electrolytes, serum albumin, liver function tests and glucose every 24 h.
- Consider need for daily AXR especially if there are signs of colonic distension and/or there is significant deterioration in clinical condition or blood parameters.

Further decision making:

- A stool frequency of >8/day or CRP >45 mg/l at 3 days appears to predict the need for surgery in 85% of cases.
- Surgical review and input from specialist colorectal nurse or stoma therapist is appropriate at this stage.
- Intravenous steroids are generally given for up to 5 days. There is no benefit beyond 7e10 days.
- Consideration of colectomy or rescue therapy with either intravenous ciclosporin (CsA) 2 mg/kg/day OR infliximab (IFX) if there is no improvement by day 3 or there is subsequent deterioration (EL1b, RG B). NICE recommends CsA as first-line (and IFX use only if CsA is contraindicated) based on health economic analyses and the paucity of data to support the use of IFX over CsA (http://www.nice.org.uk/ nicemedia/pdf/TA163Guidance.pdf (accessed Oct 2010)). For patients already on immunosuppressive therapy such as AZA/MP at the time of presentation, surgery should be considered as the first option (EL4, grade D).
- Rescue with intravenous CsA:
  - 2 mg/kg/day is as effective as 4 mg/kg/day with decreased toxicity.
  - Magnesium, cholesterol and creatinine should be measured within 48 h of starting CsA eBeware contraindications (Mg2+<0.5 mM or cholesterol <3.0 mM) and be vigilant for toxicity
  - Following induction of remission, oral CsA for 3e6 months is appropriate. (EL 1b, RG B).
  - Intravenous CsA alone may be as effective as methylprednisolone, but potential side effects mean that it is rarely an appropriate single first line therapy (EL1b, RG C).
- Rescue with IFX:
  - dose induction of 5 mg/kg (0, 2 and 6 weeks). The sideeffects of IFX, including therapy associated risk of mortality, should be discussed fully prior to its initiation (EL2, grade C).
  - IFX maintenance therapy in ulcerative colitis is not recommended because of the low corticosteroid-free remission rates after 1 year, and the limited data on subsequent need for colectomy (EL1b, grade C).
  - IFX should be given as a 'bridge' to longer term immunosuppressive therapy such as AZA/MP.
  - If no response to rescue therapy is seen within 4e7 days, colectomy is recommended (EL5, RG D). Specifically, we do not recommend CsA after IFX or vice versa (EL5, RG B).

Other factors to consider:

- The long-term follow-up of patients following an attack of acute severe ulcerative colitis reveals 50% of those who do not enter complete remission with steroids will require colectomy within 1 year.
- Patients who avoid surgery should be considered for maintenance therapy with a thiopurine.
- On discharge, oral steroids should be tapered over 8 weeks. Supplementation with calcium and vitamin D is recommended.

Recommendations for the maintenance of remission in ulcerative colitis:

- Patients with ulcerative colitis should normally receive maintenance therapy with aminosalicylates, azathioprine, or mercaptopurine to reduce the risk of relapse.
- Oral mesalazine 1.2-2.4 g daily or balsalazide 4.5 g daily should be considered as first-line therapy (EL1b, RG A).
- Topical mesalazine 1 g daily may be used in patients with distal disease with/without oral mesalazine, but patients are less likely to be compliant. (EL1b, RG B).
- For patients on maintenance aminosalicylates, annual measurement of creatinine is sensible, although there is no evidence that monitoring is necessary or effective at preventing renal impairment. Aminosalicylates should be stopped if renal function deteriorates.
- Long-term treatment with steroids is unacceptable. If steroids cannot be withdrawn, surgery should be considered.
- AZA 2-2.5 mg/kg/day, or MP 0.75-1.5 mg/kg/day are the first line agents of choice for steroid-dependent disease. AZA is significantly more effective than mesalazine at inducing clinical and endoscopic remission in the treatment of steroid dependent ulcerative colitis. (EL1b, RG A) These drugs should be considered in the following situations:
  - any patient who has a severe relapse or frequently relapsing disease
  - those who require two or more corticosteroid courses within a 12 month period
  - those whose disease relapses as the dose of steroid is reduced below 15 mg
  - relapse within 6 weeks of stopping corticosteroids
  - following ciclosporin (CsA) for induction of remission of severe ulcerative colitis
- All patients should have measurement of thiopurine methyltransferase (TPMT) levels before starting thiopurines, mainly to avoid administration to a patient with no functional TPMT in whom thiopurine administration may be fatal (EL4, RG B)
- For patients in remission, cessation may be considered after 4 years of full remission (EL2, RG C), but a small treatment benefit persists even after 6 years (EL1b, RG B). Benefits and risks of continuing thiopurines should be discussed with individual patients.
- Methotrexate may be considered in the treatment of patients who do not respond to or are intolerant of thiopurines (EL4, RGC). Optimal duration of therapy is not established.
- If first-line immunosuppressive therapy fails, several factors (patient's wishes, fecundity, patient age and extent of disease)need to be taken into account and a suitable therapeutic strategy to achieve steroid free remission discussed. In many cases this may necessitate surgery.

IBD service standards

- There must be local protocols for prescribing and monitoring of thiopurines. Local practice should be audited (IBD Standard A6).

Surgery for ulcerative colitis

Indications

- Disease not responding to intensive medical therapy
- Presence of dysplasia or carcinoma (see section 7.2)
- Poorly controlled disease
- Recurrent acute on chronic episodes of ulcerative colitis
- Retained rectal stump following previous colectomy.

Recommendations for surgery in ulcerative colitis

- surgical units undertaking IAPP should be performing at least 10 cases per year as a minimum (EL5, RG D).

IBD Service Standards: (A7)

- expert pathological assessment before surgery is important < IBD surgery should be undertaken by colorectal surgeons in a unit where the operations are performed regularly
- pouch failure and salvage should be managed in a high-volume specialist unit

Recommendations for pouchitis

- The diagnosis of pouchitis should normally be made on clinical and endoscopic and histological criteria (EL1a, RG A).
- Metronidazole 400 mg three times a day (EL1a, RG A) or ciprofloxacin 250 mg bd (EL1b, RG B) for 2 weeks is the first-line therapy of choice for pouchitis.
- Long-term, low-dose metronidazole or ciprofloxacin are potentially effective for chronic pouchitis (RG B).
- VSL#3 probiotic therapy may be used to treat and prevent pouchitis (EL2b, RG B). Its efficacy is lost soon after stopping the treatment.

6.0 MANAGEMENT OF CROHN'S DISEASE

Recommendations for active ileal, ileocolonic, or colonic Crohn's disease

- Initial treatment of active ileal or ileo-colonic Crohn's disease should be tailored to the severity of disease and must take the views of the patient into account.
- For patients with moderately active disease requiring treatment, oral corticosteroids such as prednisolone 20-40 mg, or budesonide 9 mg daily is appropriate (EL1a). Prednisolone should be reduced gradually according to severity and patient response, generally over 8 weeks. More rapid reduction is associated with early relapse. If steroids are given, concomitant bone protection is recommended. Budesonide 9 mg daily is appropriate for patients with isolated ileo-caecal disease with moderate disease activity. Although marginally less effective than prednisolone, its side-effect profile is substantially better (EL1b).
- Failure to wean corticosteroids is common, and should be regarded as a treatment failure necessitating further intervention.
- In patients with severe active Crohn's disease, or disease refractory to corticosteroids, anti-TNF therapy may be used in induction of remission, and in subsequent maintenance (see sections 4.4.7 and 6.2 for a detailed discussion of evidence, treatment strategies, and uncertainties that need to be addressed).
- AZA, MP and MTX are efficacious in inducing remission, but each limited by time to response, side-effects, and uncertainties regarding drug withdrawal (see section 6.2)(EL1b, RG A).
- Refractory active Crohn's disease remains an area for clinical trials of new therapies, supported by the National Institute of Health Research Portfolio, (http://www.crncc.nihr.ac.uk/ (accessed Oct 2010)).

IBD Service Standards

- Access to a dietician and nutritional support should be available to all patients with IBD (Standard A5).
- Nutritional assessment should be performed on diagnosis and each hospital admission. Adolescents should have regular monitoring with height and weight centile charts and 6-monthly assessment of pubertal status (Standard A10).

Recommendations for maintenance of remission of Crohn's disease

- AZA or MP should be considered as first line treatment for patients in the following situations (see section 4.4.4 for details):
  - any patient who has a severe relapse or frequently relapsing disease
  - those who require two or more corticosteroid courses within a 12 month period
  - those whose disease relapses as the dose of steroid is reduced below 15 mg
  - a relapse within 6 weeks of stopping corticosteroids
- MTX is effective for patients whose active disease has responded to IM methotrexate (EL1b, RG A). It is appropriate or those intolerant of, or who have failed to respond to thiopurines (EL2, RG B) once potential toxicity and other options, including surgery, have been discussed with the patient (see section 4.4.5 for details).
- Anti-TNF therapy is effective in maintaining remission in Crohn's disease (EL1a, RG A), although long-term data are lacking. It is best used as part of treatment strategy including immunomodulation once other options, including surgery, have been discussed with the patient. Treatment with ADA or IFX should only be started and reviewed by clinicians with experience of managing Crohn's disease with anti-TNF therapy (http://guidance.nice.org.uk/TA187 (accessed Oct 2010)). Concurrent infection/sepsis should be excluded and treatment delayed until appropriate investigations (eg, cultures/imaging/examination under anaesthesia) and treatment (eg, antibiotics/surgical drainage) concluded.

Practical guidance in the use of anti-TNF therapies in induction and maintenance strategies

- For IFX, the dosing regimen is as follows:
  - A dose of 5 mg/kg IFX is used with loading doses at 0, 2 and 6 weeks:
  - If no evidence of initial response after two doses (primary non-responders), reconsider overall medical and surgical
  - management of patient. Switch to ADA or dose intensification to 10 mg/kg can be considered but with caution as data supporting these strategies are not strong (EL4, grade C).
  - If there is evidence of initial response, scheduled maintenance therapy will usually be appropriate. This is given initially at 8-weekly intervals (EL1b, RG B). Where response is lost, a valid initial strategy is to decrease infusion interval (initially to 6 weeks; no more frequent than 4-weekly) or to dose intensify by a single dose of 10 mg/kg or to switch to ADA (EL4, RG C).
- IFX should be used for fistulating Crohn's disease only after ensuring that all sepsis is actively draining; this requires appropriate cross sectional imaging (eg, MRI pelvis) and close collaboration with experienced colo-rectal surgeons (EL3, RG B).
- Pre-dosing with hydrocortisone is not usually required with the recommended scheduled maintenance IFX therapy.
- Initial infusions of IFX should be given over 2 h with close monitoring in a dedicated infusion facility, by trained personnel. Subsequent doses can be given over 1 h (EL4, RG D).
- If re-treatment with IFX is required after a significant 'drug holiday' (>12 months) following initial IFX therapy, high vigilance is required for acute and chronic infusion reactions. Consider switching to alternative agent (ie, ADA) (EL5, RG D).
- For ADA the induction regimen can be 80 mg/40 mg sc on successive weeks, or 160 mg/80 mg (EL1b, grade B). The 80 mg/40 mg loading regimen is associated with a high requirement for subsequent does escalation. (EL4, grade C). The alternative of 160/80 mg may be more effective in patients who have lost response/intolerant to IFX. (EL2, grade C)
  - Maintenance therapy is 40 mg every other week
  - If response is lost, then escalate to 40 mg every week
  - If response is regained, it may then be possible to decrease dosing back to 40 mg every other week (EL5, RG D)
- For ADA therapy, the patient or relative/carer should be taught appropriate injection technique by an IBD nurse practitioner. Patients should be given clear advice about intercurrent illness (especially infection), when to delay treatment and who to contact for further advice.
- A medical history of demyelinating illness or optic neuritis is a relative contraindication for anti-TNF therapy (EL2b, RG C). In patients with a family history of demyelination, anti- TNF therapy should be used with caution or avoided if possible. In this context, the risk of subsequent demyelinating episode is unclear. Expert neurological advice may be sought.
- The initiation of anti-TNF therapy during pregnancy should only be considered following full risk counselling with patient (and partner) particularly its unknown long-term effects. This should also be counterbalanced against risk of active disease in pregnancy and be applicable in patients already on maintenance anti-TNF therapy in Crohn's disease (see section 7).
- Anti-TNF therapy should only be used with caution in older patients (>65 years old) with significant smoking histories. If used in this situation, we suggest a CXR every 6-12 months (EL2b, RG C).
- We suggest particular caution in the use of anti-TNF therapy in patients with a medical history of malignancy.
- Anti-TNF therapy should be avoided in patients with congestive cardiac failure (EL2, RG B). In elderly patients or those with pre-existing ischaemic heart disease, the presence of cardiac failure should be screened (EL1b, RG B).
- NICE recommends that maintenance with anti-TNF therapy should continue until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter: The disease should then be reassessed. Maintenance therapy should only then be continued if there is clear evidence of ongoing active disease as determined by clinical symptoms and investigation (http://guidance.nice. org.uk/TA187 (accessed Oct 2010)).

IBD service standards

- there must be local protocols for prescribing and monitoring of thiopurines. Local practice should be audited (IBD Standard A6).
- Treatment with anti-TNF therapy should only be initiated by clinicians with expertise in their use for IBD (IBD Standard B1).
- *Multi-disciplinary team meeting (IBD Standard A3).* Where maintenance anti-TNF therapy is considered, it is recommended that the patient's case is discussed at multidisciplinary IBD meeting where colorectal surgeons are also present. Of note, it should be considered at this stage whether or not surgery represents a more appropriate intervention for a particular patient.
- *Counselling (IBD Standard C3)* The risks and benefits of treatment should be discussed with the patients and documented in the medical case records. In view of insufficient evidence with respect to several key issues surrounding the long-term use of immunosuppressive therapy and anti-TNF therapy, limitations in knowledge need to be discussed with each patient. One mechanism of formalising such a discussion is the provision of formal consent. It is recommended that this conversation include the discussion of:
  - Efficacy
  - Alternative treatment options, including surgery
  - Risks of infection, infusion reactions, malignancy (including hepatosplenic T cell lymphoma), demyelination and drug-Induced lupus
  - Written information should be provided (IBD Standard D1)

Recommendations for perianal Crohn's disease

Medical treatment

- Metronidazole 400 mg three times a day and/or ciprofloxacina 500 mg bd are appropriate first-line treatments for simple perianal fistulae (EL4, RG D) (see section 4.2).
- AZA 2-2.5 mg/kg/day or MP 0.75-1.5 mg/kg/day are potentially effective for simple perianal fistulae or enterocutaneous fistulae where distal obstruction and abscess have been excluded (EL4, RG D).
- Anti-TNF therapy may be used in patients with severe perianal or enterocutaneous fistulae or who are refractory to other treatment, and should be used as part of a pathway that includes immunosuppression and surgery.

Surgical treatment.

- Surgery should be used in conjunction with best medical therapy. Seton drainage can be a useful technique to provide symptom control and can be used as a prelude to medical treatment. Other surgical approaches such as advancement flaps, and fistula plugs may be appropriate for persistent or complex fistulae in combination with medical treatment.

There is insufficient evidence to recommend other agents such as tacrolimus ointment and local infliximab outside clinical trials or specialist centres.

MANAGEMENT OF NON-PERIANAL FISTULATING CROHN'S DISEASE

Recommendations for entero-gynaecological fistulae

- Low anal-introital fistula may be almost asymptomatic and not need surgical treatment (EL5, RG D).
- If the patient has a symptomatic fistula, surgery is usually necessary (including diverting ostomy) (EL5, RG D).
- Rectovaginal fistulae failing conservative treatment should have surgery with an advancement flap and/or diverting ostomy if they are associated with unacceptable symptoms (EL5, RG D).
- Intestinal small bowel or sigmoid-gynaecological fistulae can usually be treated with resection of the diseased bowel segment (EL5, RG D).

Recommendations for enterovesical fistulae

- Surgery is the preferred approach for enterovesical fistulae (EL5, RG D). Only in high-risk patients (after multiple operations and\or severely shortened bowel), should medical therapy be the first option (EL5, RG D).

Recommendations for enterocutaneous fistulae

- Post-surgical enterocutaneous fistulae should initially be treated with nutritional support and anatomical definition (EL5, RG D). Surgery after an interval is appropriate once nutrition is restored.
- Primary enterocutaneous fistulae can be treated medically but will generally require surgical management (by resecting the diseased bowel segment) (EL5, RG D).

Indications for surgery

- There are few randomised data to support decisions about surgery in Crohn's disease and multidisciplinary meetings to discuss these issues are invaluable. Surgical intervention Is governed by the extent of the disease, the response to medical treatment and the presence or absence of complications. Fibrostenotic and fistulating intestinal disease with or without associated sepsis respond poorly to medical therapy; in the presence of a limited ileocolic distribution surgery is a good therapeutic option. In more extensive disease, preservation of bowel length is critically important. Limiting the resection to macroscopic disease and the use of strictureplasty have revolutionised surgery in this scenario.

Recommendations for surgery in Crohn's disease (IBD Service Standards: A7)

- Expert pathological assessment before surgery is important. This may involve referral to a recognised expert in the differential diagnosis of IBD.
- IBD surgery should be undertaken by colorectal surgeons (or their supervised trainees), who are core members of the IBD team in a unit where the operations are performed regularly.

Recommendations for prevention of postoperative recurrence of Crohn's disease

- Patients who smoke should be strongly advised to stop and offered help to achieve this (EL2b, RG C).

7.0 ASSOCIATED ASPECTS OF INFLAMMATORY BOWEL DISEASE

Surveillance for colonic carcinoma

Patients with extensive colitis (ulcerative colitis or Crohn's disease) can be risk stratified as follows:

- Lower risk: 5-yearly colonoscopy
  - no endoscopic/histological active inflammation on the previous colonoscopy (histological chronic or quiescent changes acceptable) **or**
  - left-sided colitis (any grade of inflammation) **or**
  - Crohn's disease colitis affecting <50% surface area of the colon (any grade of inflammation).
- Intermediate risk: 3-yearly colonoscopy
  - mild endoscopic/histological active inflammation on the previous surveillance colonoscopy **or**
  - presence of post-inflammatory polyps **or**
  - family history of colorectal cancer in a first-degree relative aged 50 years or over.
- Higher risk: yearly colonoscopy
  - moderate or severe endoscopic/histological active inflammation on the previous surveillance colonoscopy or stricture within past 5 years **or**
  - confirmed dysplasia within past 5 years in a patient who declines surgery or primary sclerosing cholangitis/post-orthotopic liver transplant for PSC **or**
  - family history of colorectal cancer in a first-degree relative aged <50 years

Recommendations for the surveillance of colonic carcinoma

- The appropriateness of surveillance should be discussed with patients who have ulcerative colitis or Crohn's disease colitis and a joint decision made on the balance of benefit to the individual. The risk arising from ulcerative colitis and Crohn's disease colitis is similar.
- Index (screening) colonoscopy is advised for all patients with ulcerative colitis or Crohn's disease colitis at approximately 10 years after onset of symptoms to reassess disease extent (EL2, RG C).
- Surveillance colonoscopies should be performed, where possible, when the disease is in remission. However, a surveillance procedure should not be unduly delayed if remission cannot be achieved.
- Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended. (EL2, RG A). If chromoendoscopy is not used, the strategy of random biopsy outlined in the 2002 surveillance guidelines should be followed.
- If a dysplastic polyp is detected within an area of inflammation and can be removed in its entirety, it is not necessary to recommend colectomy. Absence of dysplasia in surrounding tissue should be confirmed.

Post-colectomy

There is no clear evidence that pouch surveillance is beneficial and thus it cannot be strongly recommended. However, if a clinician wishes to offer surveillance, the following surveillance policy would seem reasonable:

- Higher-risk post-colectomy patients: consider yearly flexible sigmoidoscopy of pouch/rectal mucosa in patients with:
  – previous rectal dysplasia or dysplasia **or**
  – colorectal cancer at the time of pouch surgery **or**
  – primary sclerosing cholangitis **or**
  – type C mucosa in the pouch (mucosa exhibiting permanent persistent atrophy and severe inflammation).
- Lower-risk post-colectomy patients: consider 5-yearly flexible sigmoidoscopy of pouch/rectal mucosa in patients with none of the risk factors above.

Recommendations for pouch surveillance

- Biopsies should be taken from pre-pouch ileum, the pouchanal anastomosis and the body of the pouch with four biopsies from each site. Pouch surveillance should be started early after pouch formation.

MANAGEMENT OF PREGNANCY

Recommendations for drugs used in pregnancy

- Sulfasalazine should be stopped if there is suspected neonatal haemolysis.
- AZA should in general be continued during pregnancy, as the risks to the fetus from disease activity appear to be greater than continued therapy. Babies born to mothers on AZA may be lighter than normal and the risk-benefit should be discussed with patients.
- Corticosteroids can be used for active disease, as the risks to the pregnancy from disease activity are greater than from continued therapy.
- MTX is absolutely contra-indicated in pregnancy.
- Physicians should exercise caution when considering the elective use of anti-TNF therapy in pregnant patients with IBD until further data become available regarding the frequency of congenital abnormalities and long-term outcomes. Conception should be discussed with women of childbearing age at the start of anti-TNF therapy. If treated patients present having become pregnant the treatment should be stopped after the second trimester.

Recommendations for the management of IBD in pregnancy

- A gastroenterologist and obstetrician should manage pregnant women with IBD jointly.
- Maintaining adequate disease control during pregnancy is essential for both maternal and fetal health. If planning pregnancy, patients should be counselled to conceive during remission and advised to continue their maintenance medication. Prior to conception patients should be well nourished and take folate supplements.
- Flexible sigmoidoscopy may be used safely where the information provided will significantly alter management. The least extensive procedure possible should be employed.
- Patients with acute severe colitis or other life-threatening complications of disease should be managed as for the nonpregnant 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. Patients with perianal Crohn's disease or ileoanal pouch formation may best have a caesarean section to avoid the risk of damage to the anal sphincter.
- Absolute indications for surgery are unaltered by pregnancy and surgery should only be delayed where aggressive medical therapy may allow critical foetal maturation.
- Intestinal resection should be covered by a defunctioning stoma. Primary anastomosis is best avoided.

Recommendations for osteoporosis and osteomalacia:

- Supplementation of calcium and vitamin D is recommended when systemic steroid use is necessary (EL3, RG C).
- Co-administration of bisphosphonates with steroids is recommended for patients aged over 65 years or with known osteoporosis/osteopenia. Unless advised on other grounds, the bisphosphonate should only be given while the patient is on steroids (EL4, RG C).

VACCINATIONS

Recommended vaccinations

- Influenza, pneumococcal and HPV (females) vaccination is generally recommended for immunosuppressed adults and is best considered for all patients with IBD, given the frequent need for steroid and immunosuppressive therapy. Booster vaccinations are appropriate for influenza (annually) and pneumococcus (after 3 years).418
- Hep B vaccinations should be considered prior to immunosuppressive or anti-TNF monoclonal antibody therapy in the non immune high-risk patient.
- Live vaccines should be avoided in patients on immunosuppression or steroids (MMR, oral polio, yellow fever, live typhoid, varicella, BCG).
- Varicella vaccination before treatment with steroids or immunosuppressants is now a possibility and has been recommended in Europe and the USA in the non-immune.

Recommendations for vaccinations

- A vaccination and infection history should be taken in all patients with IBD (EL5, RG D).
- Primary and booster vaccination for influenza and pneumococcus should be offered to immunosuppressed patients with IBD.

Psychological aspects

IBD service standard

- Psychological support should be available to patients with IBD (IBD Standard A2).