## Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overview</td>
<td>5</td>
</tr>
<tr>
<td>Recognition, diagnosis and differential diagnosis</td>
<td>8</td>
</tr>
<tr>
<td>Referral</td>
<td>10</td>
</tr>
<tr>
<td>Appropriate early tests</td>
<td>11</td>
</tr>
<tr>
<td>Identifying patients in need of early help or aggressive therapy</td>
<td>14</td>
</tr>
<tr>
<td>Medical management</td>
<td>14</td>
</tr>
<tr>
<td>Initial therapy and therapy for disease flares</td>
<td>15</td>
</tr>
<tr>
<td>S-ASA: mesalazine preparations</td>
<td>15</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>16</td>
</tr>
<tr>
<td>Maintenance therapy</td>
<td>16</td>
</tr>
<tr>
<td>Immunosuppressant therapy</td>
<td>16</td>
</tr>
<tr>
<td>Biological therapy</td>
<td>17</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>18</td>
</tr>
<tr>
<td>Surgery</td>
<td>18</td>
</tr>
<tr>
<td>Maintenance therapy</td>
<td>16</td>
</tr>
<tr>
<td>Routine follow-up</td>
<td>19</td>
</tr>
<tr>
<td>Special situations</td>
<td>19</td>
</tr>
<tr>
<td>Iron deficiency with or without anaemia</td>
<td>19</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>21</td>
</tr>
<tr>
<td>Psychological issues</td>
<td>22</td>
</tr>
<tr>
<td>Smoking</td>
<td>22</td>
</tr>
<tr>
<td>Vaccinations</td>
<td>22</td>
</tr>
<tr>
<td>Bone health</td>
<td>23</td>
</tr>
<tr>
<td>Travel</td>
<td>24</td>
</tr>
<tr>
<td>Complementary and alternative medicine</td>
<td>25</td>
</tr>
<tr>
<td>Abbreviations</td>
<td>27</td>
</tr>
<tr>
<td>References</td>
<td>27</td>
</tr>
</tbody>
</table>
Inflammatory bowel disease (IBD) is a general diagnostic term that describes conditions with idiopathic, chronic, relapsing and remitting inflammation of the gastrointestinal tract. Crohn’s disease (CD) and ulcerative colitis (UC) are the two most common types of IBD. UC is limited to the colon (large intestine); CD can involve any part of the gastrointestinal tract from the mouth to the anus, although it most commonly affects the small intestine or the colon. About 5-15% of patients with IBD affecting the colon have some features of both conditions. Where a clear distinction cannot be made, the disorder is now referred to as IBD unclassified (IBD-U). The previously used term, indeterminate colitis, should be reserved for cases where colectomy has been performed and the pathologist is unable to classify the disease after a full examination.

IBD leads to significant morbidity and impaired quality of life, generally without affecting mortality. It is estimated that at least 61 000 Australians are living with IBD: 28 000 with CD and 33 000 with UC. Over 1622 new cases are diagnosed every year, 776 with CD and 846 with UC. Australia has among the highest reported incidence of IBD worldwide. In high-incidence areas of the world such as northern Europe, North America, Australia and New Zealand, the occurrence of IBD is beginning to stabilise however numbers are rising in low-incidence areas such as southern Europe, Asia and much of the developing world. The causes of IBD are not completely understood. Genetic, infectious and other environmental factors may play a role in the dysregulation of intestinal immunity, leading to gastrointestinal injury. Research is underway to identify causal factors in the development of IBD, including finding a specific gene or a group of genes that makes a person more susceptible to IBD.
Both CD and UC involve inflammation of the gastrointestinal tract. The main difference between the two diseases is the area of the gut affected and the thickness of the gut wall involved by the inflammation. In CD, the inflammation can involve any part of the gastrointestinal tract, from the mouth to the anus, although it occurs mostly in the ileum, the lower part of the small bowel (ileitis), in the large bowel (colitis) or in both (ileo-colitis). However, in any given person, it is usually stable in location over time. In UC, the inflammation affects only the colon. In CD, the whole thickness of the gut wall can be inflamed whereas UC affects only superficial layers, being confined to the colon mucosa.

### Crohn's disease

The European Crohn's and Colitis Organisation (ECCO) has attempted to standardise terms used internationally to define CD so that results of clinical trials can be applied to clinical decision making. Best's Crohn's Disease Activity Index (CDAI) is an estimate of the clinical severity of the disease and not of the activity of inflammation.

#### The following terms are recommended:

**Disease activity:** is grouped into mild (CDAI 150 - 220), moderate (CDAI 220 - 450) and severe (CDAI > 450).

**Remission:** complete resolution of symptoms and endoscopic mucosal healing.

**Relapse:** a flare of symptoms in a patient with established UC who is in clinical remission, either spontaneously or after medical treatment. Some definitions include rectal bleeding as an essential component of relapse; others include a combination of rectal bleeding with an increase in stool frequency and abnormal mucosa at sigmoidoscopy.

#### Table 1. Features for differentiating between ulcerative colitis and Crohn's disease

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Typical ulcerative colitis feature</th>
<th>Typical Crohn's disease features</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequent small-volume diarrhoea with urgency</td>
<td>Diarrhoea accompanied by abdominal pain and malnutrition</td>
</tr>
<tr>
<td></td>
<td>Predominantly bloody diarrhoea</td>
<td>Stomatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abdominal mass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perianal lesions</td>
</tr>
<tr>
<td>Endoscopic and radiological</td>
<td>Diffuse superficial colonic inflammation. Involvement of rectum, but this can be patchy</td>
<td>Discontinuous transmural asymmetric lesions</td>
</tr>
<tr>
<td></td>
<td>Shallow erosions and ulcers</td>
<td>Mainly involving ileum and right sided colon</td>
</tr>
<tr>
<td></td>
<td>Spontaneous bleeding</td>
<td>Cobblestone appearance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Longitudinal ulcer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deep fissures</td>
</tr>
<tr>
<td>Histopathological</td>
<td>Diffuse inflammation in mucosa or submucosa</td>
<td>Granulomatous inflammation</td>
</tr>
<tr>
<td></td>
<td>Crypt architecture distortion</td>
<td>Fissures or aphthous ulcers can be seen; often transmural inflammation</td>
</tr>
<tr>
<td>Serological markers</td>
<td>Antineutrophil cytoplasmic antibodies</td>
<td>Anti-Saccharomyces cerevisiae antibodies</td>
</tr>
</tbody>
</table>

#### Table 2. The Montreal classification of disease activity in ulcerative colitis

<table>
<thead>
<tr>
<th></th>
<th>S0</th>
<th>S1</th>
<th>S2</th>
<th>S3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stools/day</td>
<td>Remission</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Blood</td>
<td>Asymptomatic</td>
<td>May be present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Pulse</td>
<td>All normal</td>
<td>Minimal, or no signs of systemic toxicity</td>
<td>&gt;90 bpm or</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>All normal</td>
<td>Minimal, or no signs of systemic toxicity</td>
<td>&gt;37.5 °C or</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>All normal</td>
<td>Minimal, or no signs of systemic toxicity</td>
<td>&lt;10.5 g/dL, or</td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>All normal</td>
<td>Minimal, or no signs of systemic toxicity</td>
<td>&gt;30 mm/h</td>
<td></td>
</tr>
</tbody>
</table>

bpm: beats per minute

ESR: erythrocyte sedimentation rate

**Inflammatory bowel disease unclassified (IBD-U)**

When a definitive distinction between UC, CD or other causes of colitis cannot be made after the history, endoscopic appearances, histopathology of multiple mucosal biopsies and appropriate radiology have been taken into account, the condition is referred to as inflammatory bowel disease unclassified (IBD-U).
In IBD, symptoms range from mild to severe during relapses and decrease or may disappear during remissions. Symptoms depend on the location and amount of the intestinal tract involved in the disease. However, symptoms and lesions do not always match well, and reinvestigation may be required to confirm objective inflammation before treatment intensification.

The principal symptom of UC is bloody diarrhoea. Associated symptoms of colicky abdominal pain, urgency or tenesmus may be present as UC gets more severe. The rectum is always involved and inflammation spreads proximally in a continuous fashion. The clinical course is marked by exacerbation and remission. About 50% of patients have a relapse in any year.

Symptoms of CD are more heterogeneous, but typically can include abdominal pain, diarrhoea and weight loss. Systemic symptoms of malaise, anorexia or fever are more common than in UC. CD may cause intestinal obstruction due to strictures, fistulae (often perianal) or abscesses. The presentation of CD depends on the location affected. It can present as a colitis with bloody diarrhoea and abdominal pain. When there is only ileal involvement, it may present with right iliac fossa (RF) pain and obstructive symptoms. In the case of diffuse small bowel involvement, CD may have a more systemic presentation with weight loss, nutritional deficiencies and possibly fever with few specific gut symptoms.

The biggest delay in making a diagnosis of IBD is as a result of not suspecting it.

While IBD shares many symptoms with other more common conditions such as irritable bowel syndrome (IBS), other functional bowel disorders and infectious gastroenteritis including travellers’ diarrhoea, it should be suspected after a careful history and some basic investigations.

The time course of the illness, along with the presence or absence of alarm features, are the best discriminators when delineating among these common differential diagnoses. Infectious gastroenteritis is common, and usually short-lived, with an abrupt onset, with symptoms at their worst soon after starting. Contacts with similar symptoms are often identified. IBD usually has a more gradual, insidious onset with a crescendo or fluctuating pattern. If the patient is questioned carefully, symptoms are usually found to have been present for longer than initially acknowledged. IBD, especially CD, is frequently associated with some constitutional symptoms such as weight loss or anorexia and, as IBD worsens, the need to pass stool at night: awakening from sleep is a symptom of concern. IBS is approximately 50 times more common than IBD in Australia (10-15% of the community with IBS compared to 0.3% for IBD); it is therefore the most likely important differential diagnosis. IBS is typically longstanding, with fluctuating severity, but without alarm features or abnormal blood tests.

Where diarrhoea (without blood) is the predominant feature, with or without evidence of malabsorption (iron, vitamin D or folate deficiency), coeliac disease should always be excluded, as it is also far more common than IBD (1-1.5% of the community).

Because the symptoms of CD and UC are similar, it is sometimes difficult to distinguish between them, although the precise distinction between CD and UC is often not necessary, as many treatment decisions are made on disease severity and location, rather than strictly by diagnosis. However, now that biological therapies such as infliximab and adalimumab are available in Australia on the Pharmaceutical Benefits Scheme (PBS), on strict criteria only for patients with CD, the distinction between diagnoses has become more important especially with more severe disease.

Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) Many intestinal disorders have similar symptoms, which can delay an accurate diagnosis. Irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) (both Crohn’s disease and ulcerative colitis) have several symptoms in common but the differences between IBD and IBS are significant. They require different management.

Symptoms in common between IBD and IBS
- chronic abdominal pain and discomfort
- urgency and bloating
- diarrhoea
- constipation
- alternating bouts of diarrhoea and constipation
- changes in bowel habits.
• Sexual history
• Food intolerances. All doctors (general practitioners [GPs] and specialists) caring for patients with IBD should assess the patient’s vaccination status at diagnosis (and on first contact when patients change doctors), and ensure necessary vaccines are kept up to date (where possible) even if the patient is on treatment. As more immunosuppression therapy is being used to treat these patients, and used earlier in the disease course, it is helpful for specialists if an accurate record of a patient’s vaccination history is sent with the initial referral from the GP.

In patients on immunosuppression therapy, killed or inactivated vaccines can be used with safety, and it is recommended that IBD patients receive the ‘flu vaccine every year. Live vaccines should not be given to patients on (recently ceasing or about to start) IBD patients receive the ‘flu vaccine every year. Live vaccines should not be given to patients on (recently ceasing or about to start) immunosuppressants; patients on immunosuppression therapy or other immunosuppressants; live vaccines can only be safely used in IBD patients who are on aminosalicylate (5-ASA) medication without any immunomodulators.

Physical examination
• General wellbeing
  - weight
  - body mass index
  - pulse rate
  - blood pressure
  - temperature
  - signs of anaemia
  - fluid depletion
• Abdominal region
  - tenderness
  - distension
  - palpable masses
• Perianal region
  - tags
  - fissures
  - fistulas
  - abscess
  - digital rectal examination
• Oral inspection

• Extraintestinal inspection of the eyes, skin and joints. The physical examination should be complemented by simple blood tests and a stool specimen analysis to check for: signs of acute and/or chronic inflammatory response, anaemia, fluid depletion, signs of malnutrition or malabsorption and to exclude an enteric infection (see the following section).

REFERRAL
Endoscopy / colonoscopy with histology and radiology are all used to establish the diagnosis of IBD and to assess its severity and extent. These tests should only be ordered in discussion with a gastroenterologist to ensure they are necessary and, in the case of imaging, to prevent young patients from unnecessary exposure to ionising radiation. It is now understood that many patients with IBD receive high levels of radiation due mainly to computed tomography (CT) scanning.

Barium studies should no longer be ordered before referral as they are insensitive and unnecessary in most cases. Many procedures are ordered by non-gastroenterologists, and are frequently not needed to guide specialist management. Where detailed cross-sectional anatomy needs to be defined, magnetic resonance imaging (MRI) is preferred, but as it is not currently rebated on the Medicare Benefits Schedule (MBS), it may therefore need to be accessed via a specialist at a teaching hospital where specialised IBD services exist.

For suspected IBD, colonoscopy and ileoscopy with multiple biopsy specimens is well established as the first-line procedure to establish the diagnosis and extent of disease.2,14,15

Endoscopy
• Colonoscopy (visual exam of the lining of the entire large intestine)
  - Examine for ulcers, inflammation, bleeding, stenoses
  - Take multiple biopsies from the colon and terminal ileum

- Where there is a lack of response to usual therapy, assess for cytomegalovirus (CMV) infection (test biopsies using light microscopy, immunochemistry and polymerase chain reaction [PCR]); if the patient is receiving chronic immunosuppressant therapy or appearances suggest C. difficile infection
  - A screening colonoscopy for dysplasia surveillance is indicated after 8 years of colonic IBD.
  - Upper gastrointestinal endoscopy (gastroscopy or oesophago-gastro-duodenoscopy) for upper gastrointestinal symptoms (nausea, vomiting, epigastric pain).

Imaging
Radiation exposure should be considered when selecting imaging techniques. All imaging should be discussed with a specialist to minimise the potential risk of radiation-induced malignancy.13

- Plain abdominal radiography (X&R):
  - Can establish whether colitis (UC) is present, and in some cases its extent
  - May give an impression of a mass in the right iliac fossa, or show evidence of small bowel dilatation (CD)
  - Can exclude toxic megacolon, with acute severe colitis
  - Is not a diagnostic test for CD.14

- Barium double-contrast enema/barium small-bowel radiography
  - Barium imaging of the gut is now rarely used in IBD and has been replaced by colonoscopy. Small bowel barium studies are too insensitive and unreliable and have been replaced by enterography (where contrast is swallowed) or enteroclysis (where the contrast is infused via a nasogastric tube) with imaging via CT or MRI.
  - Barium enemas may be helpful in areas in rare situations when colonoscopy is incomplete, or to delineate the length of a stricture.
  - Cross-sectional imaging: (CT, ultrasonography, magnetic resonance imaging (MRI) including CT enterography and MRI enterography)

- To determine the disease extent and severity and to assess for perforating complications. Ultrasound and MRI are preferred, as the patients are often young and are likely to require repeat imaging over time.

- Dual-emission X-ray absorptiometry (DXA): to assess bone mineral density where needed
- Chest radiography
  - to exclude pulmonary tuberculosis (TB)
  - to look for free air under the diaphragm in case of suspected perforation.

APPROPRIATE EARLY TESTS
There is no one test that can reliably diagnose all cases of IBD, and many people require a number of tests (or testing on more than one occasion), which may delay diagnosis, particularly where disease is mild. In mild disease, the delay is usually not overly harmful, however abnormal blood test results should always result in referral to a specialist gastroenterologist with a view to endoscopic examination. Fortunately, more severe cases usually present more obviously and delays should be minimal. In suspected IBD, tests are aimed at differentiating IBD from infectious gastroenteritis, IBS and coeliac disease. Investigations also help in defining disease activity and severity. Initial investigations when patients present with suggestive symptoms should include the following:

Laboratory tests
Laboratory investigations should include blood and stool examination to rule out other causes of diarrhoea and inflammation.

Blood examination
Blood tests are not specific for IBD but may be done to determine and evaluate the severity of inflammation, anaemia and vitamin or mineral deficiencies associated with IBD.

- Full blood count (FBC): a thorough review of FBC can reveal a lot of information. It may show anaemia (sign of chronic disease or iron deficiency); a low mean corpuscular volume (MCV) (suggesting iron deficiency); a high MCV (suggesting B12 or folate deficiency); a normal MCV with a high red cell distribution width (RDW)

- To determine the disease extent and severity and to assess for perforating complications. Ultrasound and MRI are preferred, as the patients are often young and are likely to require repeat imaging over time.

- Dual-emission X-ray absorptiometry (DXA): to assess bone mineral density where needed
- Chest radiography
  - to exclude pulmonary tuberculosis (TB)
  - to look for free air under the diaphragm in case of suspected perforation.

APPROPRIATE EARLY TESTS
There is no one test that can reliably diagnose all cases of IBD, and many people require a number of tests (or testing on more than one occasion), which may delay diagnosis, particularly where disease is mild. In mild disease, the delay is usually not overly harmful, however abnormal blood test results should always result in referral to a specialist gastroenterologist with a view to endoscopic examination. Fortunately, more severe cases usually present more obviously and delays should be minimal. In suspected IBD, tests are aimed at differentiating IBD from infectious gastroenteritis, IBS and coeliac disease. Investigations also help in defining disease activity and severity. Initial investigations when patients present with suggestive symptoms should include the following:

Laboratory tests
Laboratory investigations should include blood and stool examination to rule out other causes of diarrhoea and inflammation.

Blood examination
Blood tests are not specific for IBD but may be done to determine and evaluate the severity of inflammation, anaemia and vitamin or mineral deficiencies associated with IBD.

- Full blood count (FBC): a thorough review of FBC can reveal a lot of information. It may show anaemia (sign of chronic disease or iron deficiency); a low mean corpuscular volume (MCV) (suggesting iron deficiency); a high MCV (suggesting B12 or folate deficiency); a normal MCV with a high red cell distribution width (RDW)
• Elevated serum ferritin

• Biochemistry: low albumin (indicating inflammation and malnutrition); elevated creatinine and/or urea (evidence of dehydration); electrolyte disturbances (low magnesium, selenium, potassium, zinc) related to poor diet and/or long-standing diarrhoea.

• Iron studies: elevated serum ferritin (marker of inflammatory state); low ferritin (indicates iron deficiency). Note, if ferritin < 100 μg/L with raised CRP level, iron deficiency is still likely.

• Inflammatory markers: erythrocyte sedimentation rate (ESR) test and the CRP test may be helpful in confirming the inflammatory activity suspected on the FBC but may correlate imperfectly with inflammation and disease activity. Useful indicator if elevated, but normal values do not exclude inflammation.

• Coeliac antibody testing: do this unless history or physical examination reveals obvious nontropical features such as fistulas, perianal disease and bloody stool.

• Special antibody tests: are not helpful in the initial assessment of a suspected case and their value in routine management is yet to be determined. They are not recommended for initial testing. Anti-saccharomyces cerevisiae antibodies (ASCA) and atypical perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) serological tests can help discriminate CD from UC in some situations and are being studied for their ability to predict poor prognosis in known IBD cases. They may become more helpful if multi-antibody positivity or high positive titres are validated as a prognostic marker in the future.

Stool examination

Routine stool examination in patients with suspected IBD is valuable for differential diagnoses and because there is an increased risk of enteric infections such as **Cclostridium difficile** with IBD.

- A stool examination and routine culture screens are warranted to exclude the possibility of bacterial, viral or parasitic cause of diarrhoea. Microbiological testing (at diagnosis, with any new flare or with bloody diarrhoea) for infectious diarrhoea should specifically include **C. difficile** toxin (May be seen following antibiotic therapy). **C. difficile** super-infection has a high prevalence in patients with IBD. Treatment of IBD with immunosuppression without addressing infectious pathogens can be extremely dangerous, leading to a greater risk for emergency colectomy. A minimum of four stool samples is required to detect 90% of **C. difficile** cases.

- White blood cells (WBC) in stool sample indicates an inflammatory disease.

- Faecal markers to identify gut inflammation: calprotectin and lactoferrin (neutrophil-derived proteins) can detect colonic inflammation and help discriminate it from functional diarrhoea. However, they will also be positive where there is infectious diarrhoea, and thus are more useful to discriminate the cause of diarrhoea if their use is restricted to clinical scenarios where diarrhoea has been present for more than 1 month. Although not yet widely available in Australia (and not funded by MBS), faecal testing may be useful in distinguishing mild IBD from IBD and in predicting relapses in established IBD. Faecal testing for calprotectin and lactoferrin is not useful where there is obvious bloody diarrhea.

- Faecal occult blood testing (FOBT) can reveal traces of blood that cannot be seen with the naked eye. However, FOBT is a screening test for colorectal cancer and should not be used for diagnosis of IBD.

- Additional special stool cultures may be needed for patients who have travelled abroad (seek advice from infectious diseases specialists).

Tests in established disease

Tests used will depend on a patient’s therapy and clinical state.

- Well patients not on immunosuppression: an annual FBC and biochemistry only is required, along with checking their weight and asking about general health.
  - If they have had symptomatic periods in the preceding year, consideration of treatment intensification is indicated
  - If patients have had prior low bone density or new steroid use, bone density monitoring should be considered in addition to treatment to protect bone health
  - All patients should have at least an annual review with their GP and specialist to manage their disease before problems arise and to optimise their wellbeing.

- Well patients on immunosuppression: need more regular consultations and should also be having routine blood tests (FBC, electrolytes [sodium/potassium/chloride]/urea/creatinine/EUC/liver function test [LFT]). These regular visits are an opportunity to detect complications related to disease or treatment at an early stage, and to detect and treat recurrent symptoms early. The frequency varies between guidelines and usual practice in different locations, but a minimal regime would be blood tests 3 monthly and visits 6 monthly. A formal recall system is advisable: patients (and results) not seen regularly tend to be more likely to encounter problems.

- Patients with longstanding (> 8 years) substantial colitis (proximal to splenic flexure) should be referred for colorectal cancer surveillance. Although this was previously recommended to be with colonoscopy every 1–2 years, more recent British Society of Gastroenterology (BSG) guidelines now stratify patients at the first surveillance exam at 10 years according to whether they have a normal or abnormal appearance to their colon, whether they have ongoing inflammation, dysplasia or intercurrent primary sclerosing cholangitis (PSC) and then vary the surveillance interval according to a more targeted assessment of their individual colorectal cancer risk. Under these guidelines, many patients are having fewer colonoscopies, but those with an abnormal-appearing colon and those with PSC have enhanced surveillance.

- Patients with known significant small intestinal Crohn’s disease (≥30 cm): should have a screen for malabsorption each year, including BI2, folate, iron studies, international normalised ratio (INR) and vitamin D. This screen is to avoid undiagnosed complications from malnutrition, which are easier avoided than treated.

- Patients who are unwell: tests are aimed at defining disease activity and severity.

Role of the GP in early tests

IBD is a chronic disease. Its management requires multidisciplinary care by IBD gastroenterologists, colorectal surgeons, GPs. IBD nurses, radiologists, dieticians and psychologists. Currently, most medical management is focused on acute flares of disease, although there is a push to change this approach: it is increasingly recognised that maintaining remission and anticipating problems and thereby preventing complications is a more effective strategy.

With more intensive medical therapy and the development of biological therapy, management risks becoming even more narrowly focused on acute care, directed only at those with more severe disease, rather than encompassing all sufferers and addressing important non-acute issues. It is important to remember that all IBD patients warrant attention to optimise health and quality of life.

GPs have a key role in early diagnosis, supporting the patient with psychological comorbidities, assisting with smoking cessation and managing intercurrent issues such as maintenance therapy, monitoring and adherence, sexuality, fertility, family planning and pregnancy, iron deficiency and anaemia. GPs are encouraged to call for advice from a local gastroenterologist or IBD service if they are uncertain about what tests are necessary before referral. If clinical
suspected and the results of the initial routine laboratory tests indicate IBD, the patient should be referred to a hospital specialist for further tests.

Due to the delay in obtaining a routine outpatient gastroenterologist appointment in most areas, a fixed or posted referral is inadequate for any patient who is unwell. A personal phone call to the local gastroenterology hospital unit, a regional IBD service or a local gastroenterologist is recommended as most of these patients require review within 1-2 weeks. Most gastroenterologists will ensure priority for these patients.

IDENTIFYING PATIENTS IN NEED OF EARLY HELP OR AGGRESSIVE THERAPY

It is important to identify patients at high risk of poor outcomes when assessing for known or possible IBD. Signs indicating current severe disease or a poor prognosis can be determined from a brief history and simple clinical examination. A judgment on severity and the need for urgent referral to a gastroenterologist and possible hospitalisation can frequently be made without laboratory testing. An appropriate referral for specialist or hospital care should not be delayed while waiting for test results.

The following patients are at high risk of a poor outcome and need prompt referral for specialist gastroenterology care to prevent avoidable adverse outcomes (such as resection or colectomy):

- weight loss of more than 5 kg at presentation
- poor appetite: decreased oral intake
- unable to manage usual activities
- the need for steroids at first visit
- hospital admission at first visit.

Early intensification of therapy may be needed in the following high-risk patients:

- young age at onset (< 40 years)
- widespread disease (e.g. ileal and perianal disease in CD or extensive colitis in UC).

As the disease is highly variable between affected individuals, it is important to follow newly diagnosed patients closely, with frequent face-to-face visits, to allow both the patient and the treating doctor to get an understanding of the disease behaviour and severity. This approach also enables doctors to promptly identify at-risk patients:

- those in whom the disease is responding poorly to therapy
- those who have progressive disease
- those with intolerance or non-compliance to therapy
- those needing early treatment intensification.

This approach should minimise accumulated morbidity, which often results from delayed decision making.

MEDICAL MANAGEMENT

There is no cure for IBD. It is a chronic disease requiring lifetime care, usually starting in early adulthood in otherwise healthy, active people.

The goals of treatment are to:

- treat acute disease:
  - reduce or control intestinal inflammation and if possible heal the mucosa
  - minimise side-effects and long-term adverse effects
  - eliminate symptoms (abdominal pain, diarrhoea and rectal bleeding)
- improve and maintain the patient’s general wellbeing (optimising the quality of life)
- correct nutritional deficiencies
- maintain steroid-free remissions (decreasing the frequency and severity of recurrences and reliance on steroids)
- prevent complications, hospitalisation and surgery.

The therapeutic approach is similar with CD and UC, even though UC can be cured technically by surgical removal of the large intestine (although this option is reserved for patients who are refractory to all medical treatments as it often leads to a different set of symptoms, due to the loss of the large intestine along with either stoma or pouch formation).

The medical management of IBD is determined by:

- location of inflammation within the gastrointestinal tract
- degree of involvement
- severity of symptoms
- extra-intestinal complications
- response or lack of response to previous treatment.

Historically, IBD has been treated with a limited choice of drugs or combination of drugs. Treatment decisions have been based on a standard step-up approach: at diagnosis mild anti-inflammatory therapy is initiated; if these measures fail, patients are offered immunomodulating agents. When active disease persists, biological agents such as anti-tumour necrosis factor (TNF) drugs are added. If all of these measures fail, surgery is considered as a last resort.

However, therapy for IBD is rapidly evolving. This treatment paradigm is being challenged with the acceptance of the need to treat beyond symptoms and aim for mucosal healing and sustained remission, and avoid repeated use of immunomodulators. New research suggests that the use of immunomodulators and anti-TNF agents can be more effective if used earlier in the course of the disease (within the first 1-3 years).

Due to the availability of stronger and better immunomodulatory therapies, initial assessment and management are now recommended to be directed by a specialist gastroenterologist. Although IBD is a chronic illness, most medical management has been previously directed at acute flares of disease. Now that it is recognised that a chronic care model is better, GPs are ideally placed to monitor the treatment plan once it is in place; they have a critical role in ensuring treatment adherence and are often the first point of call for the management of new symptoms and the management of lifestyle and nutritional modifications for improving the wellbeing of patients. However, all members of the care team should work together and patients should be encouraged to participate actively in therapeutic decisions.

Initial therapy and therapy for disease flares

Treatment is directed not only at relieving the symptoms of IBD but also at healing the mucosa, preventing the next flare and reducing the chances that complications may develop. Treatment to control the inflammation to give the gastrointestinal tract an opportunity to heal belongs to five main categories:

- aminosalicylates (5-ASA)
- corticosteroids
- immunomodulators (azathioprine, 6-mercaptopurine and methotrexate)
- biological agents (infliximab and adalimumab)
- antibiotics (metronidazole, ampicillin, ciprofloxin, others).

5-ASA: mesalazine preparations

These agents are more useful in UC than CD, and are the mainstay of maintaining remission in UC.7 They are typically also used to treat mild to moderate symptoms of active colonic IBD. 5-aminosalicylic acid (5-ASA) is the active ingredient that is delivered to the colon in a number of ways. It must be bound to a carrier molecule or embedded in a matrix to prevent its rapid absorption in the proximal gut. These agents are more effective for colonic (as opposed to small bowel) disease. While they do relieve acute symptoms in mild to moderate colitis, their main use is for long-term maintenance of remission.

They act topically on the colonic mucosa to suppress the production of numerous pro-inflammatory mediators and control inflammation.

5-ASAs can be given rectally or orally as they are essentially a topical therapy. 5-ASA preparations available in Australia for oral use include sulphasalazine, olsalazine, balsalazine and numerous mesalazine preparations. Those available for rectal use include mesalazine enemas (liquid or foam) and suppositories. Due to PBS regulations, patients must be treated first with sulphasalazine. If this is not tolerated or causes an allergy, patients may be offered other mesalazine-containing 5-ASA agents which do not have the sulphasalazine (generally responsible for side-effects).
Corticosteroids

For patients with acute flare-ups who are either too sick or who fail to respond to adequate doses of 5-ASA therapy or who cannot tolerate the side-effects, oral steroid therapy should be considered (prednisone). Corticosteroids are used for moderate to severe active IBD. They usually provide significant suppression of inflammation and rapid relief of symptoms. However, significant side-effects including greater susceptibility to infection exclude their recurrent use or their use for long-term maintenance therapy.

The decision to treat with steroids depends on the severity of the disease and how quickly one wants to get the symptoms under control. If a really sick patient does not respond to oral steroids within a few days, hospital admission is necessary for the administration of intravenous corticosteroids. Oral steroids should not be continued as an outpatient if a patient does not respond to oral steroids within a few days, hospital admission is necessary for the administration of intravenous corticosteroids. Oral steroids are not recommended for maintenance of medically induced remission in Crohn's disease.6

Maintenance therapy

It is now well accepted that maintenance therapy is of benefit in the maintenance of remission in both CD and UC, thus adherence to long-term therapy is relevant for all but the mildest cases.5 Immunosuppressant therapy

Drugs that modulate or suppress the immune system (especially azathioprine, 6-mercaptopurine and methotrexate) are commonly used to help control inflammation and maintain disease remission. However, they are not agents for induction of remission due to their slow onset of action (may take 2 to 3 months for response). These agents are used to prevent or reduce corticosteroid dependence in IBD:

- Thiopurines: oral 6-mercaptopurine or azathioprine (8-12 weeks from reaching full dose to see efficacy) or Methotrexate: usually commenced subcutaneously, weekly (4-6 weeks to see efficacy). They are started when:
  - disease is predicted to be severe at onset
  - steroid dependence occurs
  - a second course of steroids for a relapse (within 12 months of first course) is needed

- patient has important reason to avoid further steroids (obesity, osteoporosis, diabetes).
- Calcium antagonist inhibitors: cyclosporin A or tacrolimus. These agents are generally reserved for rescue therapy when there is a severe episode of disease not responding to high dose intravenous steroids in hospital. These agents should only be used for safety under the supervision of an expert along with prior colorectal surgical consultation as a lack of satisfactory response to these agents would necessitate a colectomy.

The aim of commencing one of these immunomodulating drugs is to be able to withdraw steroid therapy. These drugs may cause side-effects like nausea, vomiting and diarrhoea. Their use has been associated with a number of complications including pancreatitis, hepatitis, reduced white blood cell count and increased risk of infection. Starting at a low dose and up-titrating the dose weekly until the target dose is reached may overcome the nausea and non-specific side-effects of thiopurines. Pre-medicating patients on methotrexate with metoclopramide or other anti-nausea agent is also recommended to minimise intolerance. Regular weekly blood tests (FBC and EUC/LFT) should be done while adjusting the dose, and regular 3-monthly monitoring needs to continue while the patient is on therapy. Patients on methotrexate should also be given folate on the other 6 days of the week or 5 mg weekly.

As C. difficile has a higher prevalence in patients with IBD, treatment of the disease with immunosuppression without addressing bacterial pathogens can be extremely dangerous, leading to a greater risk for emergency colectomy.

Biological therapy

In IBD, biological agents can only be prescribed by a specialist gastroenterologist.

TNF-alpha inhibitors (infliximab and adalimumab)

There are two anti-tumour necrosis factor (TNF) antibodies licensed by the TGA for treatment of IBD: infliximab (Remicade) and adalimumab (Humira).

Both agents are supported on the PBS for the treatment of selected cases of IBD. Biological agents are effective in patients with both CD and UC, but are only supported on the PBS for CD at present. The current criteria specify that they are only available to patients who have failed standard therapy (with a high CDAI, stoma or extensive small intestinal disease) or to those with complex refractory fistulizing disease. Infliximab is also useful in patients who are hospitalised with acute severe colitis not improving with corticosteroids.20 Even though the PBS does not support this indication, many hospitals allow compassionate access. These agents block the immune system's production of TNF, a cytokine that intensifies inflammation. Infliximab is given by intravenous infusion whereas adalimumab is given by subcutaneous injection only.

In studies, these drugs have been shown to be highly effective in selected patients as first-line therapy for the treatment of IBD.21,22 More data are needed on whether early aggressive therapy or a step-up approach is better in the long term for the treatment of IBD and whether early aggressive therapy has any role in altering the natural history of the disease.22

While some specialists in Australia believe that early aggressive therapy in IBD should not be offered, it is worth noting that, if patients with poor prognostic features are identified early, biological therapy can be offered in the 12th week after commencing standard therapy, or sooner if thiopurines are not tolerated and methotrexate is inappropriate (patients intending to conceive). A proactive stance is recommended when assessing new patients and planning ahead.

The value of concomitant immunosuppression is contentious, given the contradictory results of the Study of Biological and Immunomodulator Naïve Patients in Crohn's Disease (SONIC) and the Combination of Maintenance Methotrexate-Infliximab Trial (COMMIT) studies.23,24 Australian guidelines recommend that, if a concomitant immunosuppressive therapy improves clinical outcome for IBD patients who are treated with short courses or episodic anti-TNF therapy, the benefits of continuing immunosuppressive agents in
patients receiving regular, maintenance anti-TNF agents for refractory Crohn’s disease are still uncertain.26 These decisions are best taken by specialists with an ongoing interest in IBD therapy as new information is rapidly emerging.

Anti-TNF therapy has the potential to be associated with various adverse effects such as infection, malignancy and immunogenicity.27 The following adverse effects have been reported with the use of biological agents for IBD:

- opportunistic infection
- reactivation of viral infection
- malignancy and lymphoma
- infectious complications (tuberculosis)
- infusion reactions such as pruritus, flushing and nausea
- psoriasis
- demyelinating disorders
- biological therapy may have adverse effects if a patient has congestive heart failure, or if used with certain medications, such as some for rheumatoid arthritis because they may increase the risk for infection.

It is worth noting that most serious infectious complications in Australian IBD patients on an anti-TNF agent occurred early in their treatment, and the majority were associated with steroid co-therapy.28 These data are consistent with reports from the TREAT Registry which identifies steroid co-therapy.29

Commencing anti-TNF therapy are reviewed in Connell et al 2010.24

Special situations

Antibiotics

Antibiotic therapy (metronidazole, ciprofloxacin and others) may be useful for induction of remission in CD but not for maintenance. They are used for the treatment of CD complications (perianal disease, fistulas, inflammatory mass, bacterial overgrowth in the presence of strictures). There are no data showing that any antibiotics are effective in UC, but they are used prophylactically in the setting of fulminant colitis in many centres.

There is an increased risk for C. difficile-associated disease; patients presenting with any new flare of diarrhoeal disease should be checked for faecal pathogens.

Surgery

Surgery in IBD is generally reserved for when medical therapy can no longer control symptoms or to deal with mechanical complications such as stricture, obstruction, perforation, abscess or bleeding. However, up-front, early resection can also be a reasonable option in patients with isolated short segment ileal Crohn’s disease.

Resection of part of the intestine can be of benefit in CD, but it is not a cure; the disease can recur after surgery. Close postoperative surveillance is recommended to detect recurrence early. There is currently debate about how aggressively one should treat postoperatively when all macroscopic disease is resected. Expert opinion recommends metronidazole for 12 weeks and thiopurine therapy for those at high recurrence risk. Many also advocate a colonoscopy at 6-12 months to see if a step up in therapy is warranted before a second resection becomes necessary. These strategies are being evaluated in clinical trials. UC is said to be cured after surgery that involves the removal of the colon; however patients then have to cope with either a stoma or an ileal pouch life long.

Routine follow-up

Care and follow-up of patients with IBD is a complex task requiring a multidisciplinary team and a long-term approach in treatment decisions. IBD is a lifelong condition that is optimally managed as a chronic disease. Planning treatment for patients with IBD should take into account long-term outcomes as well as acute care.27,29

Follow-up should be individualised and should focus on those patients with signs of chronic inflammation in their mucosa.28

GP follow-up

- Ensure patients do enter remission; if not, work harder to reduce intestinal inflammation and if possible heal the mucosa
- Check adherence to medication as most non-adherence starts early after new agents are prescribed
- Identify and minimise side-effects and long-term adverse effects
- Specifically enquire about psychosocial problems
- Consider the need for symptomatic therapy and supplements
- Simplify drug dosing regimes (once daily is generally preferable)
- For patients on immune modifiers (azathioprine, 6-mercaptopurine), do regular weekly blood tests (FBC and EUC/LFT) while adjusting the dose, and regular 3-monthly monitoring while the patient is on therapy
- In cases of weight loss or long-term steroid use, refer for dual-energy X-ray absorptiometry (DXA) to assess bone mineral density
- Ensure vaccinations are up to date
- Give annual influenza vaccine if on immune modifiers
- Annual PAP smear for females patients on any immunosuppression
- Conduct annual gastroenterologist review, even if patients appear well, to ensure all eligible patients have access to new therapies and to ensure patients are truly well

While surgery may not be appropriate for everyone, especially where widespread disease cannot be completely resected without compromising gut length, it is a valuable part of the overall management of IBD and should be seen as a useful component of therapy NOT simply as a last resort.

Special situations

Iron deficiency

Anaemia caused by iron deficiency and also by chronic inflammation is a common systemic complication of IBD and can be one of the earliest indicators of the disease. Any patient with gastrointestinal symptoms and iron deficiency warrants specialist referral for investigation. Iron deficiency is by far the most common nutritional problem in IBD.25

Multiple factors in patients with IBD can lead to the development of anaemia, including chronic blood loss (often occult), inadequate nutrient intake or absorption, and the effect of inflammation on the bone marrow.
Screening for anaemia

IBD patients should be regularly assessed for the presence of anaemia, and deficiencies treated when necessary.29 Simple tests and interventions can be highly successful in improving the patient’s quality of life.

The usual WHO definition of anaemia also applies to patients with IBD. Minimum haemoglobin and haematocrit levels used to define anaemia in people living at sea level30

<table>
<thead>
<tr>
<th></th>
<th>Haemoglobin (g/dL)</th>
<th>Haematocrit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 6 months to 5 years</td>
<td>11.0</td>
<td>33</td>
</tr>
<tr>
<td>Children 5-11 years</td>
<td>11.5</td>
<td>34</td>
</tr>
<tr>
<td>Children 12-13 years</td>
<td>12.0</td>
<td>36</td>
</tr>
<tr>
<td>Nonpregnant women</td>
<td>12.0</td>
<td>36</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>11.0</td>
<td>33</td>
</tr>
<tr>
<td>Men</td>
<td>13.0</td>
<td>39</td>
</tr>
</tbody>
</table>

Source: WHO 199831

Treatment of iron deficiency

Iron replacement should always be undertaken when found, even before establishing a specific cause.31 Treatment may be with oral iron (e.g. ferrous sulphate 200 mg twice a day or another preparation with no more than 100 mg elemental iron daily) if tolerated, or intravenous iron with the intravenous route preferred when:

- iron deficiency is severe
- significant anaemia is present (haemoglobin <10 g/dL)
- active inflammation is present
- there is poor tolerance to oral iron
- there are problems with adherence.

To evaluate the response to therapy, haemoglobin should be measured within 4 weeks in asymptomatic patients and sooner in symptomatic patients in order to ensure haemoglobin is responding appropriately and to adjust treatment. When monitoring oral iron supplementation, a serum ferritin above 100 µg/L indicates appropriate iron stores in patients with IBD.34

Caution

- Oral iron therapy: nonabsorbed ferrous iron has the potential to worsen IBD symptoms and to aggravate intestinal inflammation.
- As there are now many well-tolerated forms of iron for intravenous use, intramuscular iron is not generally endorsed.

Pregnancy

As IBD is most commonly diagnosed in the 20s to 40s, many women with IBD will be of child-bear age and receiving treatment for IBD. Studies show a lower birth rate among both men and women with IBD which suggests avoidance of pregnancy rather than inability to conceive.34 The South Australian IBD cohort reported that people considering pregnancy were concerned about adverse fetal effects of IBD medication and surgery, adverse effects of disease activity on pregnancy outcome, adverse effects of pregnancy on disease activity, congenital abnormalities and IBD inheritance.35 Importantly, most children born to parents with IBD are unaffected, even when both parents have IBD.

Inactive IBD does not appear to affect the fertility of either women or men, although active CD and previous pelvic surgery or sepsis (women) have been shown to decrease fertility. None of the usual medicines for IBD is known to decrease fertility, except sulphasalazine (men), and methotrexate (women and men). These effects are reversible once the agents are ceased.

For women with IBD, overall pregnancy outcomes are slightly worse than the general population, with slightly higher rates of spontaneous abortion, preterm birth, low birth weight, intrauterine growth retardation, small-for-gestational age, congenital anomalies and stillbirth. The risk of complications during pregnancy is not increased when IBD is in remission, but is increased with active disease at conception (see Andrews 2010 and Mountifield 2009 for an overview of common pregnancy concerns).35,36

Women with IBD considering conception should discuss their situation with their specialist well before pregnancy. They should be in remission before pregnancy. Combined care with good communication between GPs, gastroenterologists and obstetricians is essential. Optimal disease control is necessary before and during pregnancy for both maternal and fetal health.1

Treatment

Most of the adverse outcomes in pregnancy are related to active disease rather than the medicines given to control IBD.

Extremely important

Treating doctors should discuss continuing therapy and adherence with all potentially pregnant IBD patients (i.e. all women not yet postmenopausal).

- 5-ASA and thiopurines should be continued during pregnancy.
- Methotrexate is potentially teratogenic and should NEVER be used in those attempting conception.

Early data suggest biological agents are relatively safe in pregnancy; however, long-term experience is limited, and ongoing data are being collected due to some early concerns about rare syndromal congenital malformations.3 Previously, where possible, women were generally advised to suspend anti-TNF therapy before conception and during pregnancy because of clinical uncertainty about the potential fetal toxicity.3 However, many more exposed pregnancies have now been reported and there does not appear to be any greater risk to the infants than with thiopurines. If the mother’s disease has recently been severe enough to warrant anti-TNF therapy, it is probably unwise to cease therapy pre-conception as active disease may recur and loss of pregnancy, or pre-term delivery, may result. In patients where disease has been in true remission (with endoscopically documented healing) for some time, a drug holiday under close monitoring may be considered.

Emerging evidence suggests women with IBD on immunosuppression have a higher risk of an abnormal Pap smear associated with human papillomavirus (HPV) infection.36 HPV vaccination should be offered to these women and they should have yearly Pap tests.37

There is accumulating evidence of the protective role that breastfeeding has on IBD.37
Psychological issues

It is well recognised that patients with IBD are at high risk of psychological comorbidities, especially anxiety and depression, which increases relapse rates during disease flares.2,3 A cross-sectional Australian study in gastroenterology outpatients has shown a significant impairment of quality of life due to anxiety and depression.4 A history of psychological comorbidity has been shown to be a poor prognostic factor in IBD,5,6 however it is still unclear how it exerts its influence mechanistically. It is controversial whether stress and anxiety specifically worsen IBD’s inflammatory activity and overall behaviour7 but it is also generally agreed that improving patients’ psychological state will improve their quality of life, independent of IBD activity, and thus should be specifically addressed as recommended elsewhere.8 Australian data indicate that IBD patients are disadvantaged with respect to employment, education and income, often due to disease activity impairing function during their young adult years.9 These considerations should be carefully assessed in the management of patients with a chronic disease, particularly with respect to private or public care and treatment decisions. Studies are underway to examine specifically whether therapies targeting patients’ psychological state improve their IBD activity. While awaiting these results, it appears sensible to consider whether patients would benefit from support or counselling where anxiety and depression are an issue. Patients with a chronic disease and a care plan may be referred for MBS-supported psychological services if they meet certain criteria.

Smoking

The strongest environmental factor so far identified in IBD is cigarette smoking.10 There is consistent evidence that smoking increases the risk for the development of CD, and worsens its outcome; conversely, smoking is a protective factor in UC. (Mahd 2006).11 Smoking in CD is associated with greater disease activity, more flares, worse postoperative relapse rates, and possibly decreases the effectiveness of biological therapies.12 However, why smoking is an important environmental factor in the pathogenesis of IBD remains uncertain.

The single most effective approach patients can take to reduce recurrence in CD is to quit smoking. Smoking cessation is associated with a 65% reduction in the risk of a relapse as compared with continuing smokers, a similar magnitude to that obtained with immunosuppressive therapy.13 IBD clinicians should actively promote smoking cessation as therapy. Highly dependent smokers with IBD should be offered support and treatment for smoking cessation similar to other smokers in the general population.14

Vaccinations

Research has suggested that the efficacy of immunisation can be diminished in people with IBD whose immune status is compromised by immune suppression (drugs or chronic inflammation). Immunosuppressive treatment like corticosteroids, immunomodulators and biologicals are the mainstay of therapy to suppress or modify the immune response and limit the abnormal inflammatory process.15 As the immune system is important for fighting infections, these treatments potentially increase the risk from various bacterial, viral and fungal infections, many of which are preventable by prior vaccination.16 People with IBD may also be at risk of infections due to underlying disease, malnutrition and surgery.

Except for live agent vaccines, most denatured protein, carbohydrate and killed virus vaccines may be safely given to people with IBD even when immune compromised.17 Encouragingly, data are now emerging that even when on immunosuppression, patients are capable of mounting a satisfactory immune response to vaccines such as the influenza and HPV vaccines. Infection and immunisation history should be taken when a person is diagnosed with IBD. Even if a newly diagnosed person is not currently taking immunosuppressive treatment, he or she may be on these treatments in the future. It is important to adopt a proactive strategy and consider vaccinations early on in the disease course, before people with IBD start immunosuppressive therapy.

Immunisation in people with IBD follows the recommended schedules. For specific recommendations see The Australian Immunisation Handbook 9th Edition 2008.18

In addition the following five vaccines should be considered for all people with IBD:19

- Influenza vaccine (trivalent inactivated vaccine) (annually)
- Pneumococcal vaccine (booster may be needed after 3-5 years)
- HPV vaccine (consider in adult women on immunosuppressive medication; women with IBD have a higher risk for HPV and abnormal Pap smears)
- Hepatitis B: but beforehand, all IBD patients should be screened for hepatitis B infection (to include hepatitis B core antibody (HBcAb), hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (HBsAb)) before initiating immunosuppressive or anti-TNF therapy
- Varicella zoster virus (if there is no medical history of chickenpox, shingles, or varicella zoster virus and varicella zoster virus serology is negative).

Caution

The following live vaccines should be avoided in patients on immunosuppression or steroids or in those about to start these therapies:

- measles-mumps-rubella (MMR)
- oral polio
- yellow fever
- live typhoid
- varicella
- Bacille Calmette-Guérin (BCG).

Measles-mumps-rubella (MMR)

In 1998, there was concern internationally that the MMR vaccine might have been causally linked with IBD and autistic spectrum disorder. However, the World Health Organization and many other international scientific organisations have now concluded that there is no link between autism or IBD and the MMR vaccine.19,20

Bone health

The most serious consequence of osteoporosis is fracture, resulting from low bone mineral density (BMD). Both men and women with IBD are at risk of low bone mass and osteoporosis because of poor nutrition, low BMI, chronic inflammation, corticosteroid treatment, extensive small bowel disease or resection, age, smoking and low physical activity.10 The management of osteoporosis prevention in people with IBD involves the effective control of the underlying disease and maintaining remission of disease, along with education on the importance of lifestyle changes such as:

- avoiding excessive alcohol
- ceasing smoking
- taking regular weight-bearing exercise
- ensuring good nutrition
- avoiding steroids as far as possible.20

People with IBD on corticosteroid therapy or those with reduced BMD should receive calcium and vitamin D supplements. Treatment with calcium 1000 mg/day and vitamin D (800–1000 IU/day) increases bone density in patients with IBD although it is not yet known if calcium and vitamin D prevent fracture in this group.21
Australian recommended dietary intake

Calcium (dietary and supplements): 1000 mg/day for women and men over 19 years

Vitamin D (sunlight exposure and supplement): 1500 IU/day (25-OH D) levels should remain above 275 nmol/L for younger adults aged 19-50 years

Calcium and vitamin D: to optimise clinical efficacy, calcium should be taken in conjunction with vitamin D

Source: Nutrient reference values for Australia and New Zealand including recommended dietary intakes. Canberra: Commonwealth of Australia, 2006.47

The diagnosis of osteoporosis is based on bone densitometry (dual energy X-ray absorptiometry [DXA] scanning). Osteoporosis is defined as a T-score of less than –2.5 (people over 50 years of age) and low bone mass is defined by a Z-score of less than 2.0 (people under 50 years of age).4.52 Patients with a low BMD and other risk factors for osteoporosis should be referred to a specialist for anti-osteoporosis treatment. Treatment should be offered if there is a reduced BMD together with other risk factors for fracture.

Travel

Often, the ability to travel is compromised by IBD because of concerns about flare-ups while travelling, about receiving medical attention in another country, being too unwell to travel and difficulties with travel insurance.

Preventive measures are necessary to minimise the risk of infection while travelling, since people with IBD are exposed to the same infections as the general population as well as opportunistic infections related to immunosuppression.15.16 These strategies include being in remission before travel, good control of environmental exposure, chemoprophylaxis when indicated and the use of a specific vaccination program to prevent endemic infections.

Preventive measures before travel

• Provide advice regarding travel (avoid areas where tuberculosis is endemic especially if taking an anti-TNF agent)

Yellow fever special considerations

• Vaccination against yellow fever is mandatory when visiting 16 countries and strongly recommended for all endemic countries.

• The yellow fever vaccine contains live attenuated virus and is contraindicated for IBD patients who cannot stop immunosuppressants for at least 4 months.

• With planning, the long-lasting immunity of yellow fever vaccine allows its administration at any time that is convenient for immunosuppressant discontinuation

Preventive measures before travel

• Avoidance of insect bites

• Strict food and water precautions (IBD patients should pay particular attention to preventing traveller’s diarrhoea; there is no evidence for chemoprophylaxis for IBD travellers to prevent diarrhoea).

Checks after travel

• People with IBD on immunosuppressant therapy must be carefully assessed in case of fever, diarrhoea, abdominal pain or rectal bleeding when returning from or coming from developing countries

• People on maintenance therapy with steroids, immunomodulators or biological agents who travel to developing countries are at increased risk for opportunistic infections. Intending travellers with IBD need to think carefully about the wisdom of travel to these countries. Additionally, those on maintenance steroid therapy should be discussing with their specialist strategies to get off steroids.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

There is at present no internationally agreed complementary and alternative medicine (CAM) definition nor classifications of CAM therapies and modalities, which makes comparison of the findings of different studies difficult.14 The ECCO guidelines define complementary therapy as being used together with conventional medicine, while alternative therapy is used in place of conventional medicine.15.16 Refer to these guidelines for a list of alternative therapies such as antibiotics, helminthes, heparin, interferon-alpha and leucytapheresis whose roles remain to be established in IBD.16 Many people with IBD have used some form of CAM for a number of reasons:

• a perception that gastrointestinal disorders can be righted with diet and lifestyle changes

• some CAM have anti-inflammatory properties or alter the bacterial flora in the bowel

• these products are often seen as being natural, which does not however necessarily mean safe

• anxiety about actual or potential side-effects of standard therapy

• ineffectiveness of conventional therapies

• anxiety about continuing symptoms when taking conventional therapy.

Generally, the use of complementary medicine is considered safe. However, evidence of efficacy and safety is often unavailable. Many CAMs remain unregulated as they have not yet been investigated in well-designed scientific studies. Currently, few CAMs have good evidence supporting their use in treating IBD, but, after rigorous testing, some may eventually prove beneficial. To date E. coli Nissle and fish oil have shown some efficacy in maintenance of remission in UC, and VSL#3 for maintenance of remission in pouchitis (see below).

Herbal and nutritional supplements

Herbal remedies are commonly used for IBD and IBS symptoms including abdominal pain, constipation and diarrhoea. Much of the research on these remedies has been done in China. As yet, there is only limited evidence from poor quality studies that any herbal remedies might help improve IBD symptoms.16 Even natural herbs and supplements can have side-effects and cause dangerous interactions, for example, St John’s Wort can interact with immunosuppressive agents.

New approaches to IBD are being investigated in randomised controlled trials with bromelain, an enzyme derived from pineapple stems and green tea polyphenols to reduce inflammation in IBD.16

Peppermint oil (Mentha x piperita)

Peppermint oil is used for stomach and bowel conditions (IBD and IBS). Results from several studies suggest that enteric-coated peppermint oil capsules may improve symptoms of abdominal pain, bloating and gas, and used in small doses it appears to be safe. Possible side-effects include allergic reactions and heartburn.

Prebiotics

Unlike probiotics — which are beneficial live bacteria that are consumed — prebiotics are natural compounds found in plants, such as artichokes, that help fuel beneficial intestinal bacteria. An initial study on prebiotics had promising results. More studies are under way. Early research suggests that prebiotics may play a role in treating UC, possibly by enhanced butyrate production.
Probiotics

Probiotics are live microorganisms (in most cases, bacteria) that are similar to beneficial micro-organisms found in the human gut. They are available mainly in the form of dietary supplements and foods. The most common types of these beneficial bacteria are lactobacilli and bifidobacteria. A randomised controlled trial of the probiotic drug Escherichia coli Nissle 1917 (multiflor) has shown efficacy and safety in maintaining remission equivalent to mesalazine in patients with UC. Studies have also been undertaken showing high dose probiotic VSL#3 is effective in maintaining antibiotic-introduced remission for at least a year in patients with recurrent or refractory pouchitis. It is thought that probiotics may have a role in treating gastrointestinal conditions, boosting immunity and preventing or slowing the development of certain types of cancer.

Although some probiotics have been investigated in clinical studies, these publications are considered of insufficient power to recommend their use.

Acupuncture

Trials indicate that acupuncture has some positive effect on quality of life in people with IBD and IBS; however systematic reviews have concluded that there is no convincing evidence to support the use of acupuncture for the treatment of these symptoms.

Omega-3 free fatty acids

Omega-3 fatty acids are a group of polyunsaturated fatty acids that are important for a number of functions in the body. They are found in foods such as fatty fish and vegetable oils and are also available as dietary supplements (include fish oil, flaxseed oil and walnut oil). Studies show that fish oil supplements may be effective in reducing several cardiovascular disease risk factors and may help with some aspects of rheumatoid arthritis. Evidence for the health effects of omega-3s for other conditions is limited. A recent Cochrane review concluded that there is no significant benefit for omega-3 free fatty acids in the treatment of CD.

Omega-3s appear to be safe for most adults at low-to-moderate doses.

However, fish oil supplements may cause minor gastrointestinal upset (diarrhoea, heartburn, indigestion and abdominal bloating) and at high doses can interact with certain medications, including blood thinners and drugs used for high blood pressure.

Other CAM approaches that have not been well studied for IBD but which are commonly used include:

- Hypnotherapy
- Meditation
- Reflexology
- Relaxation therapies
- Yoga

In order to coordinate safe and effective care for people with IBD, treating clinicians should always ask about the use of CAM and advise about any potential drug interactions. Check if a particular therapy has been studied in reputable trials by looking on the following websites:

Further information on CAM


The Therapeutic Goods Administration (TGA) maintains the Australian Register of Therapeutic Goods (ARTG), a database that includes details of all therapeutic goods, including complementary medicines that may be legally supplied in Australia. Available at: http://www.tga.gov.au/industry/artg-searching.htm


ABBREVIATIONS

S-ASA 5-aminosalicylic acid
AXR Abdominal radiography
BCG Bacille Calmette-Guérin
BMD Bone mineral density
CAM Complementary and alternative medicine
CDAI Crohn’s Disease Activity Index
CMV Cytomegalovirus
CT Computed tomography
CRP C-reactive protein
DXA Dual-emission X-ray absorptiometry
ESR Erythrocyte sedimentation rate
EUC Electrolytes (sodium/potassium/chloride)/urea/creatinine
FBC Full blood count
FOBT Faecal occult blood testing
Hb Haemoglobin
HPV Human papillomavirus
IBD Inflammatory bowel disease
IBS Irritable bowel syndrome
INR International normalised ratio
LFT Liver function test
MBS Medicare Benefits Schedule
MCV Mean corpuscular volume
MMR Measles-mumps-rubella vaccine
MRI Magnetic resonance imaging
NSAID Nonsteroidal anti-inflammatory drug
PBS Pharmaceutical Benefits Scheme
PCR Polymerase chain reaction
PSC Primary sclerosing cholangitis
RDW Red cell distribution width
TB Tuberculosis
TGA Therapeutic Goods Administration
TNF Tumour necrosis factor
WBC White blood cells
WCC White cell count

REFERENCES


