Module 1958

Inflammatory bowel diease: Crohn's disease

From this CPD module you will learn about:

- The condition inflammatory bowel disease, presenting as both ulcerative colitis and Crohn's disease
- Typical symptoms and investigations used for diagnosis
- Crohn's disease management and monitoring requirements for disease progression and pharmacological treatments
- Information that pharmacists and pharmacy technicians can provide to patients

JOSHUA WELLS, PHARMACIST

Inflammatory bowel disease (IBD) is the collective definition for chronic inflammatory gastrointestinal conditions, which are classified as ulcerative colitis (UC) and Crohn's disease (CD). Bowel inflammation results in ulceration of the gastrointestinal mucosa in IBD, however the presentation of UC and CD are distinct from one another based on a number of factors that will be discussed below.

Crohn's disease

CD affects the entirety of the gastrointestinal tract from mouth to anus. Often, regions of inflammation along the mucosa are 'patchy', creating areas of both healthy and diseased bowel tissue. CD can also affect the entire thickness of the bowel wall, which can result in changes to the bowel lumen and epithelium. CD can be classified into the following types depending on the area affected: ileocolitis (ileum and colon), ileitis (ileum), gastroduodenal (stomach and duodenum), jejunoileitis (jejunum) and granulomatous (colon).[1,2]

Ulcerative colitis

Unlike CD, UC refers to inflammation restricted to the large intestine (colon) and rectum. Classification of UC is also dependent on the location of the area affected extending from the rectum, categorised as one of the following sub-types: proctitis (rectum only), left-sided colitis, proctosigmoiditis (rectum and sigmoid colon) and extensive colitis, which includes pancolitis (whole colon involvement). It is estimated that 50% of people with proctitis or proctosigmoiditis will develop more extensive disease. Of patients initially diagnosed with proctitis, 10% will go on to eventually develop extensive colitis.[1,3,4]

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is another form of chronic gastrointestinal condition, which can present with similar symptoms to IBD. However, IBS does not cause changes in gastrointestinal tissue and therefore should not be confused with or classified under IBD.

What is the prevalence of IBD?

Prevalence of IBD in the Western world is estimated at approximately 0.5% of the general population,[5] with 300,000 people diagnosed with IBD in the UK alone.[1] Rising prevalence of IBD over the last few decades is a major cause for concern. Expenditure related to direct healthcare costs of IBD diagnosis and management within Europe alone is valued between €4.6-5.6 billion annually.[5]

Risk factors and causes in CD

Risk factors for CD include:[1,3]

- **Age**: CD can start at any age, however first symptoms often appear between 10 and 40 years of age.
- **Sex**: CD is more common in women than men.
- Ethnicity: IBD is more common in white Eastern Europeans.
- **Genetics**: research has identified genes that are associated with IBD – having a parent who has IBD puts the child at greater risk.
- **Smoking**: Crohn's disease is more likely to occur in those who smoke, and cessation can reduce the severity of symptoms.

Although not fully understood, the causes of CD include environmental, genetic and immunogenic factors, eg an abnormal response to bacteria in the gut.

Signs, symptoms and complications

Symptoms of UC and CD are very similar, so further diagnostic tests are required for disease classification. IBD is an incurable chronic relapsing-remitting condition, and treatment focuses on symptom management.

The term remission is used to identify a period of symptom control. Alternatively, flare-ups refer to acute or chronic deterioration in disease management. Flare-ups can vary from mild to severe. Common symptoms for recognition of IBD are listed below:[1,6]

- diarrhoea, often with blood or pus – the presence of blood or pus can often be used to differentiate between IBS and IBD
- abdominal pain and cramping
- rectal pain
- rectal bleeding — passing small amount of blood with stool

Crohn's disease is a chronic inflammatory condition that affects the entire gastrointestinal tract

- urgency to defecate
- inability to defecate despite urgency (tenesmus)
- weight loss and fatigue – often due to poor absorption of nutrients as well as development of anaemia (anaemia can be caused by blood loss or malabsorption of dietary iron, vitamin B-12 and folate, which are all essential for effective red blood cell function)
- mouth ulcers – true oral CD is rare, however mouth ulcers may indicate deficiencies in iron, folate and/or Vitamin B12
- fever
- failure in children to grow as a result of poor nutrient absorption.

There are several symptoms that would warrant referral for both diagnosed and undiagnosed patients presenting in a community setting such as:

- severe abdominal pain
- hypotension
- blood in the stool (especially for patients without an IBD diagnosis)
- treatment unresponsive diarrhoea
- nocturnal waking as a result of diarrhoea
- fever that does not resolve within 24-48 hours (this can often indicate an acute flare-up or relapse in IBD patients).

Complications related to CD include: strictures (bowel narrowing), perforations (rupture of the bowel wall) and fistulae (abnormal channels that develop between internal organs, primarily starting in the intestine).

Other complications can include anaemia, problems with blood circulation (people with CD are twice as likely to develop blood clots) and problems with the liver and kidneys.

Furthermore, other complications referred to as extra-intestinal manifestations (EIMs) can affect up to 50% of patients with an IBD diagnosis.[7] There are numerous EIMs that present in IBD, affecting the eyes, joints and skin, which is not an exhaustive list. Further information can be found on the Crohn's and Colitis UK website.

Mouth ulcers may indicate deficiencies in iron, folate or vitamin B12 due to malabsorption in Crohn's disease

CD diagnosis

Clinical history

A GP will usually be the first point of contact for further investigation of a CD diagnosis. An appointment will include an in-depth history of the patient's symptoms, diet, family history and general health. A medical history is important to rule out other conditions such as IBS.[8,9]

Physical examination and blood tests

A physical examination to investigate abdominal tenderness and paleness will be used to identify signs of gastrointestinal inflammation or anaemia. Furthermore, if the patient's symptoms suggest a potential infection, a stool sample can be taken to rule out gastroenteritis/clostridium difficile. Blood samples may be taken to review nutritional deficiencies such as iron, vitamin D or B12. Other tests such as platelet count and C-reactive protein are valuable in determining potential blood loss and non-specific inflammation.[8,9]

Endoscopy and biopsy

If further investigation is warranted, patients may undergo an endoscopic procedure. Given the extent to which CD affects the gut, patients may undergo both a colonoscopy and gastroscopy to explore both the upper and lower GI tract. These procedures may also involve taking a biopsy of bowel tissue to support a clinical diagnosis and/or evaluate the extent of inflammation in the bowel.[8,9]

Imaging

In order to rule out potential complications, imaging techniques such as an x-ray or CT scan can be used to provide a detailed examination of a patient's gastrointestinal tract.[8,9]

Management

Treatment for CD focuses on both inducing remission and prevention of relapses. There is an array of treatment options available for patients with further detail provided in the Nice guidance.[10]

Pharmacological Treatment

Inducing remission

Monotherapy with one of the following treatments should be initiated in patients for whom this is their first presentation, or only presentation within the past 12 months to induce remission:[10]

1. **Prednisolone, methylprednisolone or IV hydrocortisone**
2. **Budesonide*** – If glucocorticoids are contraindicated or declined, and the patient has one or more of distal ileal, ileocaecal or right-sided colonic disease.
3. **Enteral nutrition** – Can be considered for young people or children for whom there is a concern regarding growth and/or side-effects.
4. **Aminosalicylates** – Can be offered if other treatments either contraindicated or not tolerated.

Patients should be informed that both budesonide and aminosalicylates are less effective than glucocorticoids as monotherapy to induce remission, however, may have fewer side-effects.

Add-on treatment with one of the following agents can be initiated in patients for whom tapering of glucocorticoids is not feasible, or if they have had two or more exacerbations within the previous 12 months:

1. **Azathioprine/mercaptopurine** – Add-on therapy to either conventional glucocorticoid or budesonide therapy.
2. **Methotrexate** – Can be offered for those unable to tolerate or with a contraindication to azathioprine/mercaptopurine in addition

The aim of CD treatment is to induce disease remission and prevent disease relapses

to conventional glucocorticoid or budesonide therapy.

Thiopurine Methyltransferase (TPMT) is an enzyme required for azathioprine/mercaptopurine activity. If activity is low, lower doses may be used. For those who are deficient, treatment with azathioprine/mercaptopurine should not be initiated and methotrexate may be considered as an alternative.

For patients with severe or treatment resistant disease following conventional therapy, monoclonal antibodies including infliximab, adalimumub, ustekinumab and vedolizumab may have a certain role in CD treatment. These treatments may not show up on a summary care record or be provided by a GP practice so it's important to check with patients if they receive any medication from a hospital source.

Maintaining remission

When initiating maintenance therapy, the following options should be considered:

1. Azathioprine/mercaptopurine – When previously used in addition to conventional glucocorticoid or budesonide therapy, as well as patients who have not used either drug but have adverse prognostic factors including early onset age of onset for diagnosis and perianal disease.

2. Methotrexate – Can be offered for those who meet the following criteria:

- Previously required methotrexate to induce remission.
- Do not tolerate azathioprine/mercaptopurine therapy as maintenance therapy.
- Have contraindications to therapy with azathioprine/mercaptopurine. This may include TPMT deficiency.

Conventional glucocorticoid or budesonide therapy should not be initiated as a method for maintaining remission owing to poor long-term tolerability and side effects.

Some patients may opt not to receive maintainence treatment. For these patients, it is important that they are aware of symptoms which may suggest a relapse (including unintended weight loss, abdominal pain, diarrhoea and general ill-health), and when they should see a healthcare professional. These patients should also be counselled on the importance of not smoking.[10]

Non-pharmacological treatment

Surgery is an option for patients with CD limited to the distal ileum in the early course of their disease. This option should also be considered for young people, children and those before or early in puberty who have growth impairment despite optimised therapy and/or refractory disease.

Dietary treatment includes enteral nutrition as a method to provide the bowel with time to rest. Usual course durations range from 2-8 weeks and can be particularly valuable in paediatric patients, whereby nutritional absorption can help to improve growth.[7]

Monitoring in the community

There are a number of monitoring points that can be addressed with patients to ensure the safe and effective use of their treatment.

Immunosuppressants (eg azathioprine, mercaptopurine)[11]

- Regular blood tests should be used to monitor for neutropenia and thrombocytopenia. Patients should be educated on recognising signs of blood disorders such as bruising, bleeding and infections. These medicines can affect liver and kidney function, so local guidelines may suggest liver function tests and urea and electrolytes are also checked along with a full blood count.
- Nausea is a common side effect and can be mitigated with divided daily dosing and taking these medicines after food.

Corticosteroids (eg prednisolone, hydrocortisone)[12]

- Corticosteroids should be used as part of a time-limited course, with high dose/long courses requiring tapered dose reductions in order to prevent adrenal insufficiency upon withdrawal.
- There are multiple side effects with both short-term and long-term use of steroids. Some that may be more evident in the community setting include fluid retention, immunosuppression (eg increased reporting of infections), gastro-intestinal upset and mood changes. More information can be found in the British National Formulary at ***tinyurl.com/BNFsteroids.***
- For high dose or courses lasting more than three weeks, patients should receive a steroid card. This can be a useful tool in monitoring steroid courses in the community pharmacy.

Aminosalicylates (eg sulfasalazine, mesalazine)(13)

- Patients should be made aware of the potential for blood disorders (dyscrasia). Signs and symptoms include any unexplained bruising, bleeding, sore throat, malaise and fever. These disorders occur primarily within the first 3-6 months of treatment.
- Patients should be advised to report any changes in their condition when switching brands of mesalazine.
- Different manufacturers of mesalazine may recommend different monitoring tests and these should be reviewed in line with local shared care policy guideance.

Methotrexate[14]

- Patients should be made aware of the potential for blood disorders. Signs and symptoms include any unexplained bruising, bleeding, sore throat, malaise and fever.
- Signs of hepatotoxicity include nausea,

vomiting, loss of appetite, abdominal pain and fatigue. Jaundice is more prominent in patients with more developed liver damage.
- Other symptoms to monitor include increased infections, respiratory changes, mouth ulcers and dermatological reactions – this list is not exhaustive.
- Methotrexate requires weekly dosing; hence, this should be monitored as part of on-going treatment. Folic acid is usually given to reduce anti-folate side effects associated with treatment. Patients should be advised not to take their folic acid on the same day as their methotrexate.
- More information can be found in the National patient safety guidance for safer use of oral methotrexate.

Further Advice

CD is a lifelong condition that requires multidisciplinary management however, the community pharmacy team can provide important advice, including:

- **Stoma management** – community pharmacies can help to support patients with complaints relating to their stoma. This may include the integrity of the patient's skin and their stoma output. Often, over-the-counter remedies to prevent skin irritation and reduce high-output eg loperamide, can be used to support patients.
- **Diet and lifestyle** – patients should be encouraged to use a food diary to highlight certain foods that may exacerbate their condition. All patients should be advised so seek specialist support from a dietician if they are struggling with this aspect of the disease management and supplements may be required due to higher risk of nutritional deficiency
- **Smoking cessation** – evidence suggests smoking contributes to both the prevalence and severity of CD, therefore, adequate steps should be taken to support patients with cessation.
- **Frequent episodes of diarrhoea or constipation** – patients could be directed to the Crohn's and colitis information sheet for diarrhoea and constipation.
- **Frequent mouth ulcers** – patients may be recommended specialist treatment.
- Patients with CD should be advised that absorption of **emergency hormonal contraception** will be affected and should be referred to their GP or family planning clinic.

Patients and their carers can find out more information about the above and about UC management from charities or online sources such as:

- Crohn's and Colitis UK at ***tinyurl.com/Crohnsdisease001***
- Guts at ***tinyurl.com/Crohnsdisease002***
- NHS website at ***tinyurl.com/Crohnsdisease003***

C+D Update Plus

CPD 5-minute test

1. Crohn's disease (CD) affects the entirety of the GI tract from mouth to anus.
   True or false
2. CD is more common in men than women.
   True or false
3. Smoking is a risk factor for both the incidence and severity of CD.
   True or false
4. Oral CD is a common presentation in most patients.
   True or false
5. Extra-intestinal manifestations affect up to 95% of CD patients.
   True or false
6. Nocturnal waking as a result of diarrhoea is common and does not require further referral.
   True or false
7. Strictures, perforations and fistulae are all complications associated with CD.
   True or false
8. Enteral nutrition is only suitable for paediatric patients.
   True or false
9. Patients may be expected to undergo exploratory procedures such as a colonoscopy as part of their CD diagnosis.
   True or false
10. Methotrexate can be used as an adjunct in inducing CD remission, as well as part of maintenance therapy.
    True or false

References

1. Crohn's and Colitis UK (2019) About inflammatory bowel disease
2. Spiller, R. and Major, G. (2016) IBS and IBD—separate entities or on a spectrum? Nature reviews Gastroenterology & hepatology, 13(10), p.613.
3. British Society of Gastroenterology (2019) BSG consensus guidelines on the management of inflammatory bowel disease in adults.
4. British National Formulary (2020) Ulcerative colitis.
5. Kaplan, G.G. (2015) The global burden of IBD: from 2015 to 2025. Nature reviews Gastroenterology & hepatology, 12(12), p.720.
6. Mayo Clinic (2019) Crohn's disease.
7. Crohn's and Colitis UK (2019) All about Crohn's and colitis.
8. NHS UK (2018) Crohn's disease: diagnosis.
9. Crohn's & Colitis Foundation of America (2010) Diagnosing Crohn's Disease and ulcerative colitis.
10. National Institute of health and Care Excellence (2019) Crohn's disease: management.
11. British National Formulary (2019) Mercaptopurine.
12. BNF (2019) Prednisolone.
13. BNF (2019) Sulfasalazine.
14. BNF (2019) Methotrexate.

Crohn's disease CPD planned learning

What are you planning to learn?

I want to learn more about Crohn's disease (CD) and the variety of treatments involved in disease management. We have a number of patients taking methotrexate who visit our pharmacy, therefore managing their needs and supporting monitoring is a major priority for our team.

I often provide medicines for patients with CD, as well as over-the-counter support for patients with stomas. I want to better understand the rationale for choice of treatment in these patient groups to better support their future care.

How are you planning to learn it?

- I plan to improve my knowledge of CD prevalence and diagnosis through the use of this article.
- I plan to read the Nice guidance available on Crohn's disease available at ***www.nice.org.uk/guidance/ng129***
- I will also discuss the main treatments we use within our pharmacy with my colleagues to ensure we can all recognise patients with inflammatory bowel disease, particularly CD, to enable shared learning.
- I also plan to complete the five-minute test at ***www.chemistanddruggist.co.uk/update-plus*** to test my knowledge and confirm what I have learned.

Give an example of how this learning has benefited the people using your services.

A patient in our pharmacy was recently prescribed methotrexate as part of their maintenance therapy for CD. The patient is well known to the pharmacy and has a number of issues at home, including a recent bereavement that has caused them a great deal of stress and anxiety.

The patient came in complaining of a sore throat, unexplained bruising and severe abdominal pain linked with gastrointestinal upset. The patient seemed particularly unwell at a glance and I decided to ask some brief questions to decide about the most appropriate referral. It quickly became known that the patient had been taking their methotrexate on a daily basis as opposed to weekly. Their family often support the use of their medicines however, because of the bereavement the usual home routines were not in place. The patient was referred for immediate medical attention.

Two weeks later the patient came back with their son to collect another prescription and reported feeling well again. The patient's son informed me that suitable care had been taken to ensure appropriate adherence of the patient's methotrexate at home and thanked the pharmacy team for their intervention.