Figure 1: Recurrent abdominal pain/discomfort with disordered bowel habit

1. Patient with recurrent abdominal pain/discomfort associated with disordered bowel habit

2. Medical and psychosocial history, physical examination

3. Alarm features?
   - No: Consider limited screening tests
   - Yes: Investigations as indicated: eg colonoscopy, blood & stool tests, duodenal biopsy

4. Investigations as indicated: eg colonoscopy, blood & stool tests, duodenal biopsy

5. Any abnormality identified?
   - No: Evaluation of stool consistency (using Bristol Stool Form Scale)
   - Yes: Any abnormality identified?

6. Celiac disease, giardiasis, inflammatory bowel disease, microscopic colitis, small intestinal bacterial overgrowth, colorectal neoplasia

7. Consider limited screening tests

8. Any abnormality identified?
   - No: Evaluation of stool consistency (using Bristol Stool Form Scale)
   - Yes: Any abnormality identified?

9. Irritable bowel syndrome (IBS)

10. Evaluation of stool consistency (using Bristol Stool Form Scale)

11. IBS with constipation (IBS-C)

12. Mixed IBS (IBS-M)

13. IBS with diarrhea (IBS-D)
Recurrent abdominal pain/discomfort with disordered bowel habit

Case history

A 32 year old businesswoman is referred to a gastroenterologist because of recurrent episodes of abdominal pain associated with a disordered bowel habit (Box1, Fig 1). The symptoms have been present intermittently for about five years, but have become more frequent and severe over the past four months. The pain occurs every two or three weeks, and lasts for several days at a time. It is usually situated in the left iliac fossa or periumbilical region and is often brought on by eating and relieved by a bowel movement. Her stools usually become looser and more frequent at the onset of the pain. She may have up to four loose mushy stools within a period of two hours in the morning. At other times she may not have a bowel movement for three or four days, and the stool is then hard and lumpy. She experiences urgency accompanying the loose bowel movements, straining with the hard bowel movements and often experiences a sensation of incomplete evacuation. She also has an uncomfortable sensation of bloating and her abdomen is often visibly distended, especially in the afternoon and evening (Box 2). There are no alarm features, with no blood or mucus in her stools, no weight loss, nor any pain during the night (Box 3). She has no nausea, vomiting or anorexia, but feels tired for much of the time. Her periods are heavy, often lasting six or more days. She has no significant past medical history apart from longstanding migraine. There is no family history of gastrointestinal disease (Box 3).

The patient is a non-smoker and eats a balanced diet with no known food intolerances. Her milk intake is less than 240ml per day. Caffeine, fiber, and fructose intake are not excessive. Her only medications are the oral contraceptive pill and infrequent sumatriptan tablets for migraine headaches. She has not taken antibiotics recently. She has tried a number of herbal preparations for her symptoms with no improvement. Physical examination is negative with no pallor or abdominal mass. She demonstrates the location of her pain with both hands spread open over the umbilicus. Perianal and rectal examination are normal (Boxes 2, 3). Given her tiredness and heavy periods the gastroenterologist arranges a complete blood count (CBC); he also suggests
checking celiac serology (Box7). The CBC is normal (Hb 11.7 gm/dl, MCV 88 fl) and tissue transglutaminase is negative (Box 8).

The gastroenterologist makes a diagnosis of **irritable bowel syndrome (IBS)** (Box 9). He discusses the diagnosis of IBS, including the possible causes and how the symptoms may occur, and reassures her that IBS does not lead to more serious disease. He uses the Bristol Stool Form Scale (BSFS) to help the patient describe her usual pattern of stool consistency (without laxatives or anti-diarrheal preparations) (Box 10). This discussion confirms that her stool form, according to the BSFS, varies from Type 1 or 2 (hard/lumpy) to Type 6 or 7 (mushy/watery) in approximately equal proportions of time (at least 25% of the time for each pattern). On this basis a diagnosis of mixed IBS (IBS-M) is made (Box 12).
1. The features of the abdominal pain or discomfort should be further characterized in terms of frequency, site, character, duration, radiation (if any), and precipitating and relieving factors. In this context discomfort means an uncomfortable sensation not described as pain \(^7\). The bowel pattern should be characterized in terms of pattern and frequency, consistency and ease or difficulty of passage of stool. The temporal relationship, if any, between the abdominal pain and the altered bowel habit should be established. Any rectal bleeding or passage of mucus, and the presence of nocturnal symptoms, should be noted, as per alarm features outlined below.

2. A careful history of the current symptoms, including what the patient believes is causing his/her symptoms, should be obtained, together with past medical, surgical, psychosocial and drug history. The pain of IBS is typically diffuse, poorly localized, and either central or lower abdominal in site. It typically occurs in bouts lasting several days \(^3\) during which time the pain is intermittent. The pain is often precipitated by eating \(^{18}\) and may resolve with fasting. A common feature of the bowel habit in IBS is that it is unpredictable, and that the stool frequency or form changes with the onset of pain. Some patients report that the abdominal pain is relieved by defecation, strongly suggesting it originates in the colon. The disturbance in bowel habit may include urgency, often but not always associated with loose stools or the passage of small hard stools. Characteristically, patients with mixed IBS may describe the passage of both hard and soft stools on the same day, often starting with formed stool and passing progressively softer stool as the contents are emptied in sequence from distal to proximal colon.

The physical examination includes palpation for abdominal masses and digital rectal examination to reveal evidence of inflammatory bowel disease and to assess stool consistency. Depending on the precise pattern of symptoms, particularly if there is a linkage between the abdominal pain and altered bowel habit as discussed below, the age of the patient, and the presence or absence of other alarm features (see below), a provisional diagnosis of IBS can be entertained even at this stage.
3. A systematic enquiry should be made during the initial consultation to exclude alarm features. Identification of these features indicates the need to carefully consider the differential diagnosis and undertake appropriate investigations. The American College of Gastroenterology and The British Society of Gastroenterology have recently published guidelines 19, 20 which include the following ‘red flags’: 

- Documented weight loss
- Nocturnal symptoms
- Family history of colon cancer
- Blood mixed with stool
- Recent antibiotic use
- Relevant abnormalities on physical examination
- Age >50 years
- Short history of symptoms
- Male sex

Some of these red flags were first employed in the Kruis scoring system for IBS 21 in which the presence of “abnormal physical findings or features suggestive of other disease”, ESR (erythrocyte sedimentation rate) > 10 mm/hr, WBC >10 x 109/l, anemia or a history of blood in the stool generated a negative score that substantially reduced the probability of IBS. This system performed better than the Manning criteria with a positive likelihood ratio of 4.6 compared with 2.9 for any three Manning criteria 4. The value of red flags was confirmed in an outpatient study of 154 patients with symptoms suggestive of IBS who were fully investigated. The combination of Rome criteria and the absence of red flags had a sensitivity of 0.65 but a specificity of 100%. A subsequent prospective study of 95 patients who met Rome I criteria in the absence of red flags showed a true positive rate of 93% with only two false positives 22. Thus, in the absence of red flags, a clinical diagnosis of IBS is a safe one. Moreover, several series confirm that once established, this diagnosis rarely needs to be revised 23.
4-5. If one or more alarm features are present, further investigations are required. Relevant blood tests include CBC (complete blood count), ESR/CRP (C-reactive protein), together with calcium, and tissue transglutaminase (tTGA) or endomysial antibodies (EMA), and thyroid stimulating hormone (TSH). Anemia or raised inflammatory markers (ESR / CRP) may be due to occult Crohn’s disease. In older patients, anemia may be due to a large colonic polyp or cancer. A low serum calcium level suggests malabsorption. These simple inexpensive tests are usually normal (1-2% abnormal in a patient meeting the Rome II symptom criteria for IBS who has no alarm features). A positive tTGA or EMA suggests celiac disease (around 95% sensitivity and specificity in secondary care). Several studies suggest that the detection of thyroid abnormalities in IBS patients is no greater than by chance and only rarely will correction of the abnormality resolve the IBS symptoms. Stool examination may demonstrate cysts in giardiasis. However, one examination is only 65% sensitive and 3 samples are needed to reach 85% sensitivity. Fecal antigen testing of stool is superior to microscopic examination. Stool examination for other parasites in studies largely carried out in the USA have been unrewarding but this may not be true in other countries where parasites are more common. Weight loss and chronic diarrhoea should raise the possibility of HIV infection and the patient should be questioned about intravenous drug abuse or unprotected sexual intercourse with multiple partners. If relevant, serological testing for HIV infection and CD4 T cell count should be performed. A history of recent antibiotic preceding the onset of symptoms should prompt consideration of the possibility of C. difficile infection.

Colonoscopy is indicated to exclude colon cancer or inflammatory bowel disease in a patient with one or more of the first four alarm features. During colonoscopy, biopsies should be performed even if the mucosa is macroscopically normal since these may reveal microscopic colitis or melanosis coli (indicating anthraquinone laxative use). The prevalence of microscopic colitis increases markedly with age being rare under 40 years but accounting for around 1 in 10 of unexplained diarrhea in patients aged > 70 years. The term microscopic colitis includes collagenous colitis, 87% of which are female, and lymphocytic colitis, which shows no obvious
gender bias. If Crohn’s ileitis is suspected (because of e.g. anemia, elevated CRP), the diagnosis may be confirmed by inspection or biopsy of the terminal ileum during colonoscopy. Barium follow-through or CT enterography are alternatives. Imaging should be kept to a minimum to avoid irradiation in patients of childbearing age. Capsule endoscopy should be reserved for those with a high probability of Crohn’s disease in whom other tests are unsuccessful.

Small intestinal bacterial overgrowth (SIBO) is rare in the absence of achlorhydria, “blind loops”, diverticula, strictures or severe small intestinal motility disorders (chronic intestinal pseudo-obstruction). Proton pump inhibitors and pernicious anemia are the most common causes of achlorhydria. Whether or not primary SIBO (presumably due to abnormal motility) contributes to IBS is controversial but seems unlikely in most individuals. It may be diagnosed in specialist centers by culture of jejunal aspirate. Using this highly specific test the incidence of SIBO in Rome criteria positive IBS patients is only 4%. The glucose breath hydrogen test is much easier for the patient but much less reliable with a poor sensitivity and specificity at 41.7 and 44.4% respectively.

Bile acid malabsorption (BAM) is also rare and most reliably diagnosed by measuring the percent retention of Selenium75 homo-cholic acid taurine 7 days after dosing (SeHCAT test). Values <5% are often seen with acute onset, often in post infectious BAM and such low values predict a good response to cholestyramine. Values between 5-10% are also abnormal but only 50% respond to cholestyramine. If SeHCAT is unavailable a trial of cholestyramine is a reasonable alternative. BAM is characterised by nocturnal symptoms with stool weights over 250 gm.

6. The precise incidence of celiac disease and giardiasis depends upon where the patient lives or originated from, but in many countries these diseases are more prevalent than inflammatory bowel disease. Colon cancer is rare below the age of 40 years, and in Asia.
7. If there are no alarm features then a limited screen for disorders that may accompany or masquerade as IBS may still be required. Most guidelines\textsuperscript{19, 20} recommend a CBC, and serological testing for celiac disease especially in patients with diarrhea or mixed bowel habit. The cause of any anemia should be fully elucidated before a diagnosis of IBS is made. In many adult females, anemia will be related to menstrual loss but other causes should be excluded. In children a CBC is highly sensitive and moderately specific for inflammatory bowel disease\textsuperscript{36}. CRP >5 mg/l has low sensitivity (50%) but good specificity (81%) for inflammatory bowel disease and should also be measured if diarrhea is present\textsuperscript{37}. The value of screening for celiac disease depends on the prevalence in the underlying population. In North West Europe, the prevalence is around 1% of the population and in an unselected IBS population meeting Rome II criteria the prevalence was 4.6\%\textsuperscript{38}. If celiac disease is present, the response to a gluten free diet may indicate the extent to which the disease was causing the IBS-like symptoms.

8. If the limited screen reveals one or more positive test results, then further investigations are required (as per box #4).

9. If the patient’s symptoms fulfill the Rome III criteria for IBS (see below), there are no alarm features (see annotation #3 above), and the results of the limited screening investigations are negative, then a diagnosis of IBS can be made.

The Rome III diagnostic symptom criteria for IBS are:

1) recurrent abdominal pain or discomfort at least three days a month in the last three months with two or more of the following:

   i) improvement with defecation

   ii) onset associated with a change in frequency of stool

   iii) onset associated with a change in form (appearance) of stool, and
2) criterion fulfilled for the last three months with symptom onset at least six months prior to diagnosis.

On factor analysis of patients and the general population, these criteria cluster together 39. There are associated symptoms that occur in IBS but are not specific enough to be included in the criteria. These include the sensations of bloating, incomplete evacuation, straining or urgency, and the presence of increased passage of gas and burping. The presence of extra-intestinal symptoms, common in IBS, should also be assessed, as they must be managed as well. They include symptoms such as lethargy, headache, palpitation, dyspnea, backache, dyspareunia and dysmenorrhea. Around 10% of IBS patients report their symptoms began with an acute bacterial enteric infection 40.

The significance of the diagnosis of IBS should be explained to the patient, emphasizing that other diagnoses are very unlikely now and/or in the future. The pattern of symptoms and their relation to certain precipitants may indicate the influence of stress or diet. Many patients ask if their diet is important, particularly whether they might be lactose intolerant. The prevalence of lactose intolerance differs greatly by race (90% in Chinese, 60% in Asians, 40% in Eastern Mediterranean people). In northwest Europe only 10% of people are lactose intolerant 41. Many sufferers recognize the link with dairy products and avoid them. Symptoms of lactose intolerance include abdominal pain, flatulence and diarrhea. However, the incidence of lactose intolerance in IBS patients is similar to that of healthy people 42. The effects of lactose are dose-related and unless subjects take more than 240ml of milk or its equivalent daily, lactose intolerance is unlikely to be the cause of their symptoms 43. It is important to also consider the potential role of fructose and related substances. There has been a recent substantial increase in ingestion of fructose particularly in soft drinks. Since fructose is poorly absorbed, large amounts can overwhelm the absorptive capacity of the small intestine leading to flatulence and diarrhea 44. Exclusion diets sometimes indicate that wheat and dairy products cause diarrhea or bloating and dietary adjustments can lead to long term improvements 45, 46.

10. In many cases, it is useful to determine the subtype of IBS, according to the bowel habit, at the time of the visit. In the Rome III classification this is based on the BSFS (Diagram 1). The accompanying diagram (Diagram
2) illustrates how the Scale may be used to identify IBS with diarrhea, IBS with constipation, mixed IBS (IBS-M), where both are present at different times, and untyped IBS (IBS-U), where neither are present. Patients with IBS show great variability in the timing of defecation and in the consistency of stool\textsuperscript{47}. There may be uncertainty about bowel pattern since IBS symptoms typically fluctuate with flares averaging 5 days\textsuperscript{3}. In such a case a two-week diary using the BSFS can help determine the predominant bowel pattern, and thus guide treatment.

![Bristol Stool Form Scale](image_url)

Diagram 1
Diagram 2

Diagram 2 illustrates how the Scale may be used to identify IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) where both loose and hard stool are often (>25% of the time) present, and unsubtyped IBS (IBS-U) in whom loose or hard stools are infrequent (<25%). The stool forms are illustrated in the appropriate segments of the diagram to indicate the predominant (>25%) stool form at the time of the visit, or from a diary. This permits subtyping of patients with IBS into IBS-C, IBS-D, IBS with a mixed pattern and an undetermined group where no bowel habit pattern dominates. Serial observations are necessary to determine those with an alternating pattern where bowel habit changes over weeks or months (IBS-A).

[IBS-C = IBS with constipation; IBS-D = IBS with diarrhea; IBS-M = IBS with a mixed pattern (that is IBS with both stool types 1/2 and 6/7 >25% of the time) and IBS-U = Unsubtyped IBS, with neither > 25% of the time]

11-13. The BSFS is used in the Rome III diagnostic criteria to identify the stool form of IBS patients. Repeated use of this scale over longer periods can identify patients whose bowel habit alternates IBS (IBS-A). The precise distribution of the IBS subtypes varies in different populations. In one large survey the most frequent subtype
was IBS-M at 46%, IBS-C 17%, IBS-D 32% and 3.9% being unclassified. This is important because approximately one third patients switch subtypes between IBS-D and IBS-C over 1 year (IBS-A), and up to 75% switch from diarrhea or constipation to a mixed pattern. However, since several proposed IBS drugs target altered bowel habit, this subtyping can help the gastroenterologist choose the appropriate treatment at the time of consultation. Since the subtype can change, the patient and doctor should be prepared to change the drug or other treatment over time.