Case Number 14
Crohn's Disease

Franklin Abela & Anthony Pio Dimech
Reviewed by: Ms. Josephine Psaila FRCS(Edin)

Case summary:

Demographic details:
G.J., married housewife.
Referred from: home and admitted to Surgical Ward 5.

G.J, 44-year-old female known case of Crohn's disease and depression who presented with a few hours' history of severe abdominal pain and multiple episodes of vomiting faeculant matter. An inflamed terminal ileum and ascending colon were found at laparatomy and resection of terminal ileum and caecum (right hemicolectomy) was carried out.

Presenting complaint:

Few hours' history of: Severe abdominal pain
Vomiting faeculent matter

History of presenting complaint:

The pain was initially epigastric and then migrated to the periumbilical region. She reported multiple episodes of vomiting faeculant matter and had passed loose stools. There was also marked abdominal distension.

Past medical and surgical history:

Past medical history:

Crohn's disease (diagnosed 8 years ago in 2004).
Clinical depression.

Past surgical history:

Never had surgery.
Never had anaesthesia.
Drug History: Allergic to penicillin.

Drug	Dosage	Frequency	Type	Reason
Mirtazapine	30mg	nocte	Noradrenergic and specific serotonergic antidepressant (NaSSA)	For treatment of depression[1]
Paroxetine	40mg-20mg-0	BD	SSRI (selective serotonin reuptake inhibitor)	For treatment of depression

Bromazepam	3mg 2-2-2	TDS	Benzodiazepine	For the treatment of anxiety
Esomeprazole	20mg	once daily	Proton pump inhibitor	To treat symptoms of gastroesophageal reflux disease (GORD)
Hydroxocobalamin	1mg	once daily	A synthetic injectable form of vitamin B12	To treat low levels (deficiency) of vitamin B12
Folic acid	5mg	once daily	Water-soluble B vitamin	To treat low levels of folic acid and anaemia
Mesalazine	500mg 2-2-2	TDS	Anti-inflammatory agent	To treat inflammatory bowel disease
Prednisolone	30mg (tailing dose since last admission)	once daily	Corticosteroid	To treat inflammatory disease

Information on type of drug and indications was obtained from BNF, 2011[1]

Family History:

Nil of note.

Social History:

The patient was a non-smoker who lived with her husband and had no relevant history of recreational drug use/abuse.

Systemic enquiry:

- General Health: unwell, afebrile, pale and visibly in pain.
- Cardiovascular System: haemodynamically stable. Heart sounds: S1 + S2 + 0.
- Respiratory System: clear breath sounds heard bilaterally.
- Gastrointestinal System: distended abdomen, soft with tenderness in the epigastrium (which did not radiate to the back), left iliac fossa and infraumbilical region.
- Genitourinary System: nil of note.
- Central nervous System: nil of note.
- Musculoskeletal System: no abnormality detected.
- Endocrine System: no abnormality detected.

Treatment on admission:

Intravenous infusion of Hartmann's solution was set up to prevent dehydration from vomiting since the patient was unable to tolerate oral fluids.

Nasogastric tube – to empty stomach contents in an attempt to reduce the bouts of vomiting.

Urinary catheter – to monitor fluid output and detect dehydration as early as possible.

Discussion of results of general and specific examinations:

Crohn's disease can affect the whole gastrointestinal system. Inflammation may occur at any point in the bowel, from the mouth to the anus. Tenderness over the left iliac fossa and infraumbilical region may have been due to the inflamed bowel, but peritonitis due to perforation of the bowel should be excluded. Since the patient was apyrexic, peritonitis was unlikely; however one must remember that she was on steroids and therefore may not have pyrexia in spite of peritonitis.

Epigastric pain may follow straining due to recurrent vomiting as well as irritation of the lower oesophagus by gastric acid. It can also be caused by gallbladder disease, peptic ulceration and pancreatitis. However, the latter was unlikely because pain did not radiate to the back[2]. Blood tests to detect any hepatic involvement were taken which turned out negative.

Bowel obstruction in Crohn's is mainly caused by strictures due to the inflamed bowel. At times, the inflammation itself can reduce the diameter of the lumen enough to cause obstruction[3]. Bowel obstruction is a major cause of morbidity in patients with Crohn's disease[4]. They often present with faecal vomiting if the stricture is in the lower gastrointestinal tract, as well as marked abdominal distension.

Loose stools and diarrhoea in Crohn's mainly originate due to malabsorption in the large intestine. It may or may not be bloody[7]. At times, it can arise from side effects of the drugs used in Crohn's, for example sulfasalazine and mesalazine[1].

Differential diagnosis:

- Intestinal obstruction[5]
- Peritonitis
- Peptic ulceration[6]
- Appendicitis
- Diverticulitis
- Bowel tuberculosis
- Small bowel cancer
- Coeliac sprue
- Lymphoma
- Behcet's disease
- Ischemic colitis
- Ulcerative colitis
- Infectious enteritis
- Non-steroidal drug enteropathy[7]

Diagnostic procedures:

Laboratory exams:

Test: Blood test.
Justification for test: The reason behind doing a full blood count in Crohn's disease is because of the predisposition towards anaemia due to iron deficiency (malabsorption), anaemia of chronic disease, blood loss from the gastrointestinal tract and drug-induced (e.g. mesalazine). Anaemia may also be due to folate or vitamin B12 deficiency. Thus knowing the levels of these substances in blood is important[8]. A high white cell count may also show signs of infection.

Measurement of the erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) is done to determine whether there is inflammation. CRP is known as an acute phase protein. All these tests can be altered by steroids and disease-modifying drugs.

Liver function tests are required whenever a patient complains of epigastric pain, especially if there is associated vomiting. The results can confirm or exclude biliary involvement. Serum albumin tends to be low in Crohn's disease. It was also noted in a study that pre-operative hypoalbuminaemia was one of several factors associated with early postoperative complications in inflammatory bowel diseases[9]. Thus, its measurement is important. Liver function tests help to exclude any liver pathology which can be a cause of low albumin.

The reason for measuring serum magnesium levels is because of the tendency towards malabsorption of the mineral. This may cause additional problems that need to be dealt with separately, including functional hypoparathyroidism, by reducing the synthesis of parathyroid hormone (PTH). Low PTH can affect adversely the kidneys and the skeleton[10].

Results: Hb: 9.35g/dL (11.5-16)
MCV: 90.3fL (79-96)
Platelets: 280 x 10^9/L (150-400)
Reticulocytes: 48.2 x 10^9/L (20-130)
WBC: 4.2 x 109/L (3.5-11)
Neutrophils Abs (Absolute Value): 8.64 x 109/L (2.5-7.5)

Ferritin (serum): 116ng/mL (15-200)
Vitamin B12: >738pmol/L (200-900)16
Folate (serum): >54.4nmol/L (7-30)17

ESR: 81mm/hr (30)
CRP: 78mg/L (<0.8)

Alkaline phosphatase (serum): 33U/l (30-150)
Alanine aminotransferase (serum): 6U/l (5-35)
Gamma glutamyl transferase (Abs): 14U/L (5-36)
Total protein (serum): 53.1g/L (60-80)
Albumin (serum): 32.1g/l (35-50)

Globulin: 21.4g/l
Magnesium (serum/plasma): 0.83mmol/l (0.75-1.2)

Conclusion: Haemoglobin levels were slightly lower than the normal range for a female. However, all other blood cell parameters, as well as ferritin, vitamin B12 and folate, were normal. The cause may be anaemia of chronic disease[11]. The ESR and CRP were high, indicating an inflammatory process. Liver function was normal and there was no indication of biliary pathology. A low serum protein and albumin level is a common finding in long-standing cases of Crohn's disease, mostly due to malabsorption of nutrients from the intestine. Another rare cause is protein-losing enteropathy, which is a severe complication of Crohn's disease. It is a diagnosis of exclusion, done after eliminating malnutrition and liver or kidney failure. The pathogensis of protein-losing enteropathy implies excessive leakage of protein through the injured intestinal mucosa[12].

Instrumental exams:

Test: Chest X-ray
Justification for test: Patient was tachypnoeic.
Result: Poor respiratory effort. No obvious pulmonary lesion is seen. There was cardiomegaly and lung congestion.
Conclusion: This finding had to be taken care of separately. Medications and procedures that could worsen chest signs had to be avoided.

Test: Abdominal X-ray
Justification for test: This non-invasive test is often done to evaluate pathology in the small intestine and colon. Its importance in Crohn's is to detect the presence of ulceration, strictures, cobblestoning, string signs (narrow lumen), fissures and loss of haustrations[7].
Result: The contrast coating of the oesophagus, stomach and duodenal bulb showed no stricture, mass or wall abnormality. There was no hiatus hernia. There was a stricture of a long segment of the terminal ileum, in keeping with Crohn's disease. Faecal loading was visible. A slightly widened loop of the small bowel was noted in the left mesogastric region.
Conclusion: The strictures visible on barium follow-through were causing the obstruction, explaining the faecal vomiting and abdominal distension.

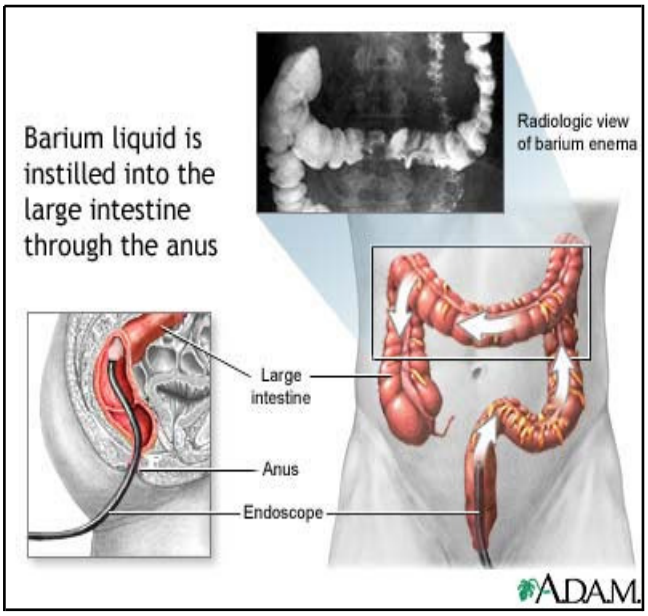

Figure 1

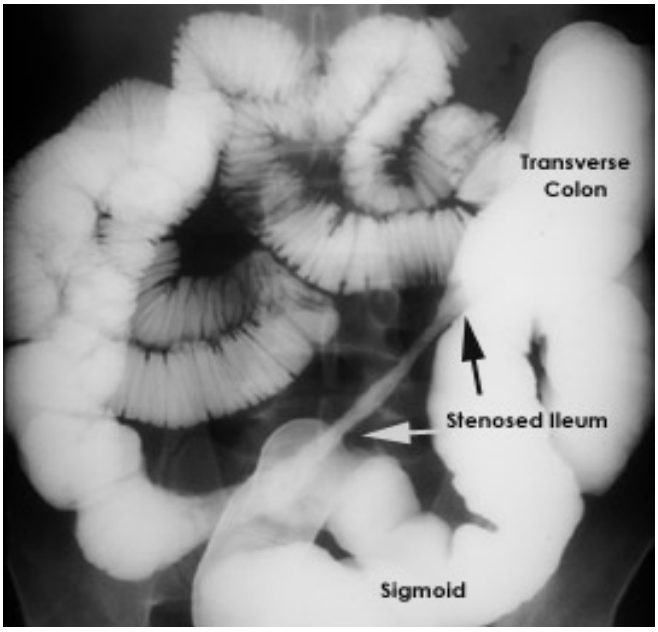

Figure 2

Figures 1,2: Barium Enema

Test: CT abdomen and pelvis
Justification for test: To exclude bowel obstruction and examine the cause of abdominal distension.
Result: Ascites and free fluid in pelvis were noted. Several sections of the small bowel showed contrast-enhancing oedematous walls which also involved the terminal part of the ileum. Some small bowel loops (particularly in the lower abdomen) also showed distension. A radial hyper-dense fluid collection containing small air bubbles was seen near the terminal ileum. This might have possibly been a sign of incipient abscess formation. The colon was collapsed, the intestines in the left abdominal part were moderately distended and fluid filled. No lymphadenopathy was noted. No free gas was identified.
Conclusion: These findings were compatible with Crohn's disease of the small bowel complicated by abscess formation and bowel obstruction.

Test: Colonoscopy

Justification for test: Direct vision of the large bowel and terminal ileal mucosa, with the possibility of taking biopsies[7].

Result: Oedematous colonic mucosa. There was severe inflammation of a large segment of the terminal ileum, caecum and ascending colon up to the hepatic flexure.

Conclusion: These findings match Crohn's disease of the terminal ileum with extension to the proximal colon.

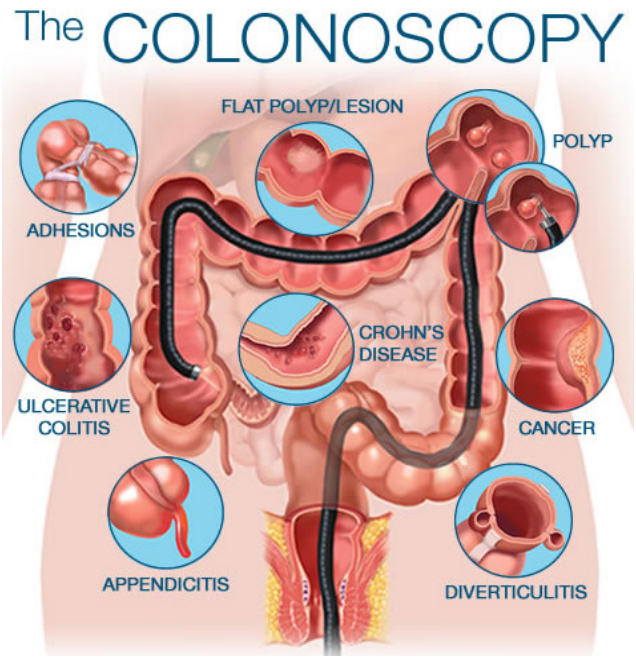

Figure 3: Colonscopy

Therapy:

Drug therapy:

Drug	Dose	Frequency	Type	Reason
Metoclopramide	10mg IV	TDS	Dopamine receptor antagonist	To reduce the nausea and vomiting
Rantidine	50mg IVI	6-8 hourly	H2-receptor antagonist	To inhibit stomach acid production
Paracetamol	1g IVI	4-6 hourly	Non-opioid analgesic	Pain relief
Ciprofloxacin	400mg IV	8-12 hourly	Quinolone antibiotic	Prophylaxis against possible gastrointestinal infection (Gram negative and Gram positive)
Metronidazole	500mg	8 hourly	Antibiotic	Prophylaxis against anaerobic organisms and protozoa which can cause gastroenteritis

Information on type of drug and indications was obtained from BNF, 2011[1]

Surgical therapy:

Pre-operative: The patient was kept nil by mouth in hospital. She was admitted for surgery as soon as all the investigations were carried out.

Operation: The surgical site was disinfected and a median laparotomy incision was made. On gross examination, an inflamed terminal ileum, was identified. A section of colon distal to the ileocaecal valve was collapsed.

The right part of the colon and caecum were mobilised. The mesentery was divided to demarcate the dissection margins. Resection of terminal ileum and caecum with primary bowel anastomosis was carried out. Bowel specimens were sent for histology. The anastomosis was hand sewn using polydioxanone (PDS) absorbable sutures. Haemostasis was confirmed before closing. Lavage of the area was necessary. A Nelaton drain was inserted and secured via a nylon suture. The skin was closed with metal staples.

Post-operative period: The following instructions were given to the nursing staff in the post-operative period:

- Keep nil by mouth with nasogastric tube in situ
- IV fluids
- Analgesia : Paracetamol 1g IV 6 hourly , Pethidine 75mg IM 6 hourly
- DVT prophylaxis: Enoxaparin sodium 40mg SC daily and stockings
- Antibiotics: Ciprofloxacin 250mg IV
- Oxygen must also be given to the patient

On examination, the patient was stable, afebrile and not in pain. Parameters were stable (Sp O_2 was 99% on air, blood pressure 110/80mmHg).

Diagnosis:

The formal diagnosis in this case was that of Crohn's disease with involvement of the terminal ileum, caecum and ascending colon.

Crohn's disease is one of the two forms of chronic inflammatory bowel diseases, the other being ulcerative colitis. Crohn's is relatively common in Western Europe, compared to the rest of the world and its incidence has increased over the past half century. Onset of the disease is early in life (at approximately 20 years of age) with little preference between the two sexes. The aetiology of the disease is unknown, but there is a familial tendency towards inflammatory bowel disease in general, making scientists believe that it must be polygenic and genetically heterogenous. The genes involved in Crohn's include NOD2 and CARD15, but this remains an active area of research[5].

Another, hypothesis suggests that the activation of Crohn's disease is caused by a rapid and severe immunological stimulus in the bowel, such as severe gastroenteritis. The effect of this is a rapid activation of resting macrophages with the release of many cytokines, including interleukin-1 (IL-1). Interleukins bind to cellular receptors and promote an inflammatory reaction in the bowel, with all its consequences of tissue damage. Genetic and environmental predisposition towards the exaggerated activation of the immune system plays a very important role in the pathophysiology of Crohn's. Furthermore, tobacco smoking predisposes to Crohn's, but somehow exhibits a degree of protection against ulcerative colitis[7].

Crohn's disease affects any part of the gastrointestinal tract sparing some areas in between. Thus the disease is patchy, forming skip lesions, unlike ulcerative colitis. The following table shows the relative incidence of Crohn's in different areas of the bowel:

Area of bowel	**Incidence Rate**
Small intestine (mainly terminal ileum)	50%
Large intestine	20%
Both large and small intestine	30%

The mouth, oesophagus, stomach and duodenum are also occasionally involved. The disease can also affect the perianal area, with or without influencing the large bowel[5].

In Crohn's disease, the inflammation of the bowel is transmural, i.e. involving the whole thickness of the bowel wall. The consequences of this include obstruction, fistulation and perforation. Several interspersed fissured ulcers which extend deep into the muscle layer are common, producing a cobblestone appearance. Granulomas (often non-caseating) are also present. They contain multinucleate giant cells. Fibrosis may follow prolonged inflammation, producing bowel strictures which can lead to obstruction[5].

The effects of mucosal inflammation are varied. If the colon is involved, the patient may pass diarrhoea streaked with blood. In small bowel involvement, partial obstruction may occur, which causes colicky abdominal pain. Diarrhoea and malabsorption may predispose to protein-calorie malnutrition, anaemia (reduced iron and folate absorption) and failure to thrive (in children). If the terminal ileum is involved, the patient may suffer from vitamin B12 malabsorption, and if bile salts are not reabsorbed in the ileum, they can irritate the colon, causing more diarrhoea. In addition, lack of bile salts in the circulation predisposes to gallstones[5].

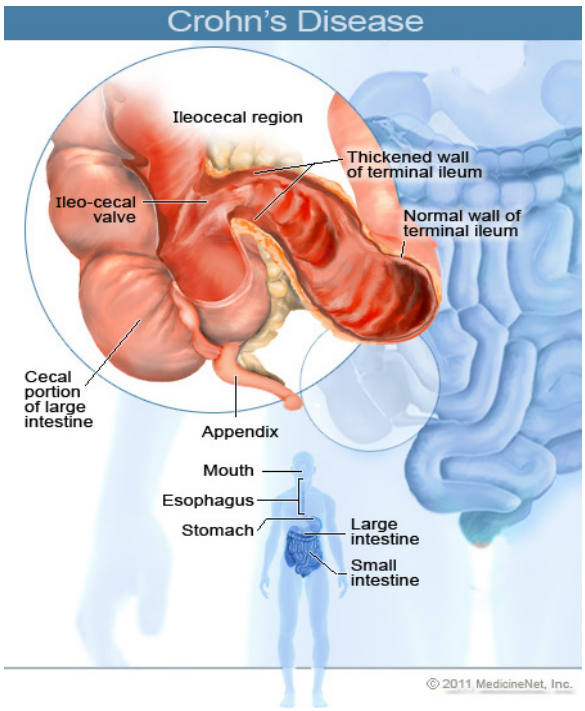

Figure 4: General overview of Crohn's Disease

Transmural inflammation in Crohn's may cause peritonitis, with severe, localised pain. In the terminal ileum, it may mimic appendicitis. Rarely, toxic megacolon may ensue. If the serosa is breached, adhesions may form to adjacent organs. However, these are rarely symptomatic. Bowel perforation may be free (with contents spilling out in the abdominal cavity) or contained (forming localised abscesses). Fistulae between the bowel and nearby hollow viscera may form. Some examples and clinical manifestations of these fistulae are listed in the table below[5].

Type of fistula	**Structures involved**	**Clinical features**
Gastro-colic	Colon and stomach	Faecal vomiting
Ileo-rectal	Ileum and rectum	Exacerbation of diarrhoea
Entero-vesical	Bowel and bladder	Recurrent UTIs and pneumaturia
Entero-vaginal	Bowel and vagina	Passage of faeces through vagina
Entero-cutaneous	Bowel and skin	Passage of soft stools through skin opening

Perianal involvement can occur in patients with Crohn's disease, especially if there is small bowel involvement[5]. This can manifest itself as multiple abscesses, piles, hypertrophied skin tags, anal fissures, numerous fistulae between the rectum and perianal skin (pepper-pot perineum), and perineal scarring[7].

Extraintestinal manifestations of Crohn's disease may be severe and correlate with the intestinal activity of the condition. The joints (e.g. ankylosing spondylitis, sacroilitis), skin (e.g. erythema nodosum, pyoderma gangrenosum), eyes (e.g. uveitis, episcleritis), and hepatobiliary system (primary sclerosing cholangitis) may be implicated[7].

Fact Box 14:

Title: Crohn's Disease

Description: Crohn's is a chronic inflammatory bowel disorder of unknown aetiology which can affect the whole gastrointestinal system (from mouth to anus) and is typified by asymmetric, focal, transmural inflammation and sometimes granuloma formation in the bowel wall. Signs of extraintestinal manifestation can be marked. The life-long disease is punctuated by periods of exacerbation and remission[15]. Genetic and environmental contributors, as well as immunological factors are implicated in the pathogenesis and severity of Crohn's disease.

Risk factors:

- Genetic factors (family history)
- Immune system
- Infection (mycobacteria, paramyxovirus, cytomegalovirus)[7,13]
- Diet (high intake of meat, fats and polyunsaturated fatty acids)[14]
- Smoking
- Perhaps other risk factors not yet identified

Histological features of bowel wall:

- Transmural inflammation of bowel wall
- Thickened, oedematous, fibrotic submucosa
- Lymphoid aggregates (may extend deep to the muscularis propria)
- Non-caesating granulomas (not always present)[7]

Clinical features:[7]

Gastrointestinal involvement:

- Nausea
- Vomiting
- Dysphagia
- Odynophagia
- Aphthous ulcers over the hard palate
- Postprandial fullness
- Abdominal pain
- Weight loss
- Anorexia
- Abdominal mass
- Diarrhoea (may or may not be bloody)

Extraintestinal involvement:

- Fever
- Uveitis
- Episcleritis
- Erythema nodosum
- Pyoderma gangrenosum
- Ankylosing spondylitis
- Sacroiliitis

- Seronegative polyarteritis
- Primary sclerosing cholangitis

Complications:[5]

- Strictures
- Fistulae (intestinal, anal)
- Anal and perianal lesions
- Haemorrhage
- Intestinal obstruction
- Intestinal perforation
- Toxic megacolon (very rare)

Treatment:[15]

- 5-aminosalicylic acid compounds e.g. mesalazine, sulfasalazine (modified for local release)
- Corticosteroids e.g. prednisolone and budesonide (local or systemic)
- Immunomodulators e.g. azathioprine, 6-mercaptopurine, methotrexate, infliximab
- Supportive treatment: antidiarrhoeal drugs, antispasmodics, dietary modification, vitamin and mineral supplements
- Surgery

References:

1. Royal Pharmaceutical Society of Great Britain. British National Formulary 62, September 2011. London: BMJ Publishing and RPS Publishing (joint publication); 2011.
2. Ojetti V, Migneco A, Manno A, et al. Management of acute pancreatitis in emergency. European Review for Medical and Pharmacological Sciences. 2005; 9:133-140
3. Martens T, Sas S. Enteroliths in Crohn's disease: a case report. Acta Chir Belg. 2010; 110(5):552-4.
4. Gustavsson A, Magnuson A, Blomberg B, et al. Endoscopic dilation is an efficacious and safe treatment of intestinal strictures in Crohn's disease. Aliment Pharmacol Ther. 2012; 36(2):151-8.
5. Burkitt HG, Quick CRG., Reed J B. Essential Surgery: Problems, diagnosis and management. 4th ed. UK and Australia: Churchill Livingstone; 2007. p.416-429.
6. Baser MJ.Microbial causation of the chronic idiopathic inflammatory bowel diseases.Inflam Bowel Dis.1997; 3(3):225-9.
7. Parray FQ, Wani ML, Bijli AH, et al. Crohn's Disease: A Surgeon's Perspective Saudi J Gastroenterol. 2011; 17(1): 6–15.
8. Bayraktar UD, Bayraktar S. Treatment of iron deficiency anaemia associated with gastrointestinal tract diseases. World J Gastroenterol. 2010; 16(22): 2720–2725
9. Yang SS, Yu CS, Yoon YS et al. Risk factors for complications after bowel surgery in Korean patients with Crohn's disease. J Korean Surg Soc. 2012; 83(3):141-8.
10. Kelly AP, Robb BJ, Gearry RB. Hypocalcaemia and hypomagnesaemia: a complication of Crohn's disease. N Z Med J. 2008; 121(1287):77-9.
11. Wians FH, Urban JE, Keffer JH, et al. Discriminating Between Iron Deficiency Anemia and Anemia of Chronic Disease Using Traditional Indices of Iron Status vs Transferrin Receptor Concentration. Am J Clin Pathol. 2001; 115:112-118.
12. Ferrante M, Penninckx F, De Hertogh G, et al. Protein-losing enteropathy in Crohn's disease. Acta Gastroenterol Belg. 2006; 69(4):384-9.
13. Yi F, Zhao J, Luckheeram RV, et al. The prevalence and risk factors of cytomegalovirus infection in inflammatory bowel disease in Wuhan, central China. Virol J. 2013; 10(1):43.
14. Yamamoto T. Nutrition and diet in inflammatory bowel disease. Curr Opin Gastroenterol. 2013; 29(2):216-21
15. Lichtenstein GR, Hanauer SB, Sandborn WJ. Management of Crohn's disease in adults. Am J Gastroenterol. 2009; 104(2):465-483.
16. http://www.nlm.nih.gov/medlineplus/ency/article/003705.htm accessed on 6th January 2013
17. http://www.webmd.com/diet/folic-acid?page=2 accessed on 6th January 2013