A 25-year-old Caucasian woman presents to the university

student clinic with complaints of intermittent crampy

abdominal pain and four to five loose stools per day. She

describes some visible mucus and blood in the stool and

states that these symptoms have been present for 6 to

8 weeks. She also has intermittent lower back pain, fatigue,

fever, and a 10-lb (4.5 kg) weight loss. The back pain started

about the same time as her gastrointestinal symptoms. She

denies any sick contacts and has not eaten any take-out

or restaurant food over the last 2 months. She takes nonprescription

naproxen as needed for aches and pains. She

has been using more naproxen recently because of the back

pain. She also takes an oral contraceptive pill once daily.

She consumes alcohol socially and currently smokes 1/2 to

1 pack of cigarettes per day.

• What symptoms are suggestive of IBD in this patient?

• Are these symptoms more suggestive of UC or CD?

• What factors may be contributing to her IBD symptoms?

• What additional information would you acquire prior to

recommending drug therapy?

Inflammatory bowel disease (IBD) encompasses both Crohn’s disease (CD) and ulcerative colitis (UC). Both disorders are associated with inflammation of various regions within the gastrointestinal (GI) tract.

Differences exist between UC and CD with regard to

the regions of the GI tract that may be affected

the distribution and depth of inflammation.

Some patients with IBD may also have inflammation involving organs other than the GI tract, known as “extraintestinal” manifestations.

Symptoms of IBD are associated with significant morbidity, reduction in quality of life, and substantial costs to the health care system.

**EPIDEMIOLOGY**

Inflammatory bowel disease is most common in westernized

countries such as the United States. Ulcerative colitis affects up

to 500,000 people and Crohn’s disease affects up to 480,000

people in the United States.2−4 The age of initial presentation of

IBD is bimodal, with patients typically diagnosed between the

age ranges of 20 to 40 years or 60 to 80 years.5 The peak incidence

of CD occurs in the second and third decades of life,with

a smaller peak in the fifth decade.2,5 Peak incidence of UC

occurs between the ages of 15 and 25 years.6

Men and women are approximately equally affected by IBD.

In general, whites are affected more often than blacks, and persons

of Jewish descent also have higher reported incidences of

IBD. One of the greatest risk factors for development of IBD is a

positive family history of the disease. The incidence of IBD is 10

to 40 times greater in patients with a first-degree relative who

has IBD compared to the general population.4,5,7 A positive family

history may be more of a contributing factor for development

of CD than UC.7−9**ETIOLOGY**

The exact cause of IBD is not fully understood. Processes

thought to be involved in its development include genetic predisposition,

dysregulation of the inflammatory response within

the GI tract, or perhaps environmental or antigenic factors.3

The fact that a positive family history is a strong predictor of

IBD supports the theory that genetic predisposition may be

responsible in many cases. Many potential candidate genes

have been identified. An example is a gene found on chromosome

16 that encodes for nucleotide oligomerization

domain 2 (NOD2). NOD2 is a cytoplasmic protein expressed in

macrophages, monocytes, and gut epithelial cells thought to be

involved in recognition and degradation of bacterial products

by the gut wall. Presence of NOD2 mutations has been shown

to predispose patients to development of CD.9,10 Less is known

about genetic alterations that may predispose patients to UC,

but UC may share common genetic features with CD.

An alteration in the inflammatory response regulated by

intestinal epithelial cells may also contribute to development of

IBD. This may involve inappropriate processing of antigens presented

to the GI epithelial cells.3 The inflammatory response in

IBD may actually be directed at bacteria that normally colonizethe GI tract. Products derived from these bacteria may translocate

across the mucosal layer of the GI tract and interact with

various cells involved in immunologic recognition. The result is

T-cell stimulation, excess production of proinflammatory

cytokines, and persistent inflammation within the GI tract.

The intestinal mucosa of patients with CD has a preponderance

of CD4+ type 1 helper T cells, while patients with UC

have more CD4+ lymphocytes with atypical type 2 helper T

cells.9 Likewise, drugs such as non-steroidal anti-inflammatory

drugs (NSAIDs) that disrupt the integrity of the GI mucosa

may facilitate mucosal entry of intestinal antigens and lead to

disease flares in patients with IBD.11

The role of antigens derived from dietary intake in the

development of IBD is less well defined. There is some speculation

that ingestion of large quantities of refined carbohydrates

or margarine leads to higher rates of CD. Use of oral

contraceptives has been associated with increased development

of IBD in some cohort studies, but a strong causal relationship

has not been proven.7

Lastly, positive smoking status has been shown to have protective

effects in UC, leading to reductions in disease severity.

The opposite is true in CD, as smoking may lead to increases in

symptoms or worsening of the disease**Ulcerative Colitis**

The inflammatory response in UC is propagated by atypical

type 2 helper T cells that produce proinflammatory cytokines

such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor

(TNF).7 As discussed previously, a genetic predisposition to

UC may partially explain the development of excessive colonic

and rectal inflammation. The finding of positive perinuclear

antineutrophil cytoplasmic antibodies (pANCA) in association

with the human leukocyte antigen (HLA)-DR2 allele in a

large percentage of patients with UC supports this theory.4,12

The role of an immune response to intestinal bacteria in the

development of UC may not be as strong a contributing factor

as it is in CD. The potential role of environmental factors in the

development of UC implies that the immune response is

directed against an unknown antigen. The findings that development

and severity of UC are reduced in patients who smoke,

or in those with appendectomies, may support the theory that

these factors may somehow modify either the genetic component

or phenotypic response to immunologic stimuli.11,13

NSAID use is also implicated in disease flares in patients

with UC. NSAIDs may affect production of both nuclear

factor κβ and peroxisome proliferator activated receptors

(e.g., PPAR-γ), both of which are involved in regulating the

intestinal responses.11

The inflammatory process within the GI tract is limited to the

colon and rectum in patients with UC (Fig. 16–1).Most patients

with UC have involvement of the rectum (**proctitis**) or both therectum and sigmoid colon (proctosigmoiditis). Inflammation

involving the majority of the colon is referred to as **pancolitis**.

Left-sided disease, defined as inflammation extending from the

rectum to the splenic flexure, occurs in 30% to 40% of patients.4

A small number of cases of UC involve mild inflammation of the

terminal ileum, referred to as “backwash ileitis.”

The pattern of inflammation in UC is continuous and confluent

throughout the affected areas of the GI tract. The

inflammation is also superficial and does not typically extend

below the submucosal layer of the GI tract (Fig. 16–2).

Ulceration or erosion of the GI mucosa may be present and

varies with disease severity. The formation of **crypt abscesses**

within the mucosal layers of the GI tract is characteristic of UC

and may help to distinguish it from CD. Severe inflammation

may also result in areas of hypertrophied GI mucosa, which

may manifest as **pseudopolyps** within the colon.12 The inflammatory

response may progress in severity, leading to mucosal

friability and significant GI bleeding.

**Crohn’s Disease**

As with UC, the immune activation seen in CD involves the

release of many proinflammatory cytokines. Cytokines

thought to play major roles in CD are derived from T-helper

type 1 cells and include interferon-γ, TNF-α, and IL-1, IL-6,

and IL-12. TNF-α is a major contributor to the inflammatory

process seen in CD. Its physiologic effects include activation

of macrophages, procoagulant effects in the vascular

endothelium, and increases in production of matrix metalloproteinases

in mucosal cells.9,15 Excessive production of bothinterferon-γ and TNF-α may account for the excessive clinical

evidence of granulomatous disease in patients with CD.10

TNF-α is also thought to induce production of nuclear factor

κβ, which stimulates further production of TNF-α and other

proinflammatory cytokines.3,14

The role of an immune response directed against endogenous

bacteria as the initiating factor is more evident in CD, as

evidenced by the apparent strong T-helper 1 activation against

bacteria seen in animal models of this disease. Likewise, bacteria

are often found deep in the intestinal mucosal layer of

patients with CD. As mentioned previously, the finding of

genetic mutations in NOD2 may result in excessive production

of IL-12 and inhibition of intestinal phagocytes to break

down bacterial antigens.10

Dysregulation of cytokines that normally downregulate

inflammatory responses, such as transforming growth factor-

β,may also be involved in the excessive inflammatory response

seen in CD. As in UC, patients with CD may have disease flares

due to ingestion of NSAIDs. The role of dietary antigens in the

development of CD compared to UC is also another potential

initiating factor. Excess ingestion of refined sugars or margarine

may be higher in patients who develop CD.7

The distribution of inflammation in CD differs from that

seen in UC, as any part of the entire GI tract may be affected

in CD. The small intestine is the site most commonly involved.

Within the small intestine, the terminal ileum and cecum are

almost always affected. Approximately 20% of patients have

isolated colonic involvement, whereas inflammation proximal

to the small intestine is almost never seen without the presence

of small or large intestinal disease. In contrast to UC, the pattern of inflammation in CD is

described as discontinuous. Areas of inflammation are intermixed

with areas of normal GI mucosa, resulting in characteristic

“skip lesions.” Superficial **aphthous ulcers** may also

develop in the GI mucosa. These ulcers may coalesce into larger

linear ulcers, resulting in fissure formation as they increase in

depth, giving rise to the characteristic “cobblestone” pattern

observed upon examination of the mucosa.

Furthermore, the inflammation may be **transmural**, penetrating

to the muscularis or serosal layers of the GI tract

(Fig. 16–2). The propensity for transmural involvement may

lead to serious complications of CD, such as **strictures**, **fistulae**,

and abscesses.4,12 While rectal inflammation is typically less

common in CD than UC, several types of perianal lesions may

be observed in patients with CD. These include skin tags,

hemorrhoids, fissures, anal ulcers, abscesses, and fistulae

**CLINICAL PRESENTATION AND DIAGNOSIS**

❷ *Differentiation of ulcerative colitis and Crohn’s disease is*

*based on signs and symptoms as well as characteristic endoscopic*

*findings, including the extent, pattern, and depth of inflammation*

*(see Presentation Box in second column)*.

**Presentation of Inflammatory Bowel**

**Disease**

**General**

• Patients with CD or UC may present with similar symptoms.

• The onset may be insidious and subacute.

• Some patients present with extraintestinal manifestations

before GI symptoms occur.

• In approximately 10% of cases it may not be possible to

distinguish between UC and CD. These patients are

described as having “indeterminate colitis.”

**Symptoms**

*• Ulcerative colitis*: Diarrhea (bloody, watery, or mucopurulent),

rectal bleeding, abdominal pain/cramping,

weight loss and malnutrition, tenesmus, constipation

(with proctitis)

*• Crohn’s disease*: Diarrhea (less bloody than UC), rectal

bleeding (less than UC), abdominal pain/cramping,

weight loss and malnutrition (more common than UC),

fatigue/malaise

**Signs**

*• Ulcerative colitis*: Fever, tachycardia (with severe disease),

dehydration, arthritis, hemorrhoids, anal fissures, perirectal

abscesses

*• Crohn’s disease*: Fever, tachycardia (with severe disease),

dehydration, arthritis, abdominal mass and tenderness,

perianal fissure or fistula

**Laboratory Tests**

*• Ulcerative colitis*: Leukocytosis, decreased

hematocrit/hemoglobin, elevated erythrocyte sedimentation

rate (ESR), guaiac-positive stool, (+) perinuclear antineutrophil

cytoplasmic antibodies (pANCA; up to 70% of

patients)

*• Crohn’s disease*: Leukocytosis, decreased

hematocrit/hemoglobin, elevated ESR, guaiac-positive

stool, (+) anti–*Saccharomyces cerevisiae* antibodies (up to

50% of patients), hypoalbuminemia with severe disease

**Extraintestinal Manifestations and Complications**

**of IBD**

❸ *Patients may manifest signs and symptoms of disease in*

*areas outside the GI tract. These extraintestinal manifestations*

*may occur in various body regions.5,8* Painful joint complications

associated with IBD include sacroiliitis and ankylosing

spondylitis. Ocular involvement with episcleritis, uveitis, or

iritis may manifest as blurred vision, eye pain, and photophobia.

Associated skin findings include pyoderma gangrenosum

(involving papules and vesicles that develop into painful

ulcerations) and erythema nodosum (red nodules of varying

size typically found on the lower extremities). Nephrolithiasis

may also develop at a higher rate in patients with IBD.Oxalate

stones are more common in CD, and uric acid–containing

stones are more common in UC.

Liver and biliary manifestations of IBD include an

increased incidence of gallstone formation in patients with

CD and development of sclerosing cholangitis or cholangiocarcinoma

in patients with UC. Patients with UC are also at

increased risk for development of colorectal cancer. Ongoing

inflammation due to active IBD may induce a hypercoagulable

state, resulting in higher rates of both arterial and venous

thromboembolism. Likewise, inflammation and recurrent

blood loss may result in the development of chronic anemia.

Patients with IBD also have higher rates of osteopenia, osteoporosis,

and fractures.16

A serious complication of UC is toxic megacolon, defined as

dilation of the transverse colon of greater than 6 cm. Patientswith toxic megacolon typically manifest systemic signs of

severe inflammation such as fever, tachycardia, and abdominal

distention.3 Surgical intervention, including colonic resection,

may be necessary to acutely manage toxic megacolon.

Formation of strictures, abscesses, fistulae, and obstructions

in patients with CD is possible. Patients with CD may

develop significant weight loss or nutritional deficiencies secondary

to malabsorption of nutrients in the small intestine,

or as a consequence of multiple small- or large-bowel resections.

Common nutritional deficiencies encountered in IBD

include vitamin B12, fat-soluble vitamins, zinc, folate, and

iron. Malabsorption in children with CD may contribute to

significant reductions in growth and development. **Diagnosis**

Because patients often present with nonspecific GI symptoms,

initial diagnostic evaluation includes methods to characterize

the disease and rule out other potential etiologies.

This may include stool cultures to examine for infectious

causes of diarrhea.

Endoscopic approaches are typically used and may include

colonoscopy, proctosigmoidoscopy, or possibly upper GI

endoscopy in patients with suspected CD. Endoscopy is useful

for determining the disease distribution, pattern and depth of

inflammation, and to obtain mucosal biopsy specimens.

Supplemental information from imaging procedures, such as

computed tomography (CT), abdominal x-ray, abdominal

ultrasound, or intestinal barium studies may provide evidence

of complications such as obstruction, abscess, perforation, or

colonic dilation.3

After the diagnosis is made, the information derived from

diagnostic testing and the patient’s medical history and symptoms

are used to gauge disease severity. The severity of active

UC is generally classified as mild, moderate, severe, or fulminant.

1 Mild UC typically involves up to four bloody or watery

stools per day without systemic signs of toxicity or elevation of

ESR.Moderate disease is classified as more than four stools per

day with evidence of systemic toxicity. Severe disease is considered

more than six stools per day and evidence of anemia,

tachycardia, or an elevated ESR. Lastly, fulminant UC may

present as more than 10 stools per day with continuous bleeding,

signs of systemic toxicity, abdominal distention or tenderness,

colonic dilation, or a requirement for blood transfusion.

A similar classification scheme is used to gauge the severity

of active CD.2 Patients with mild to moderate CD are typically

ambulatory and have no evidence of dehydration, systemic

toxicity, loss of body weight, or abdominal tenderness, mass,

or obstruction. Moderate to severe disease is considered in

patients who fail to respond to treatment for mild to moderate

disease, or those with fever, weight loss, abdominal pain or

tenderness, vomiting, intestinal obstruction, or significant

anemia. Severe to fulminant CD is classified as the presence of

persistent symptoms or evidence of systemic toxicity despite

outpatient corticosteroid treatment, or presence of cachexia,

rebound tenderness, intestinal obstruction, or abscess.

**TREATMENT**

**Desired Outcomes**

Pharmacologic interventions for IBD are designed to target

the underlying inflammatory response. Treatment goals

involve both management of active disease and prevention of

disease relapse.❹ *Major treatment goals include alleviation of*

*signs and symptoms and suppression of inflammation during*

*acute episodes and maintenance of remission thereafter*.

Addressing active IBD in a timely and appropriate manner

may prevent major complications such as perforation and may

reduce the need for hospitalization or surgical intervention.Once

control of active disease is obtained, treatment regimens are

designed to achieve the following long-term goals: (1) maintenance

of remission and prevention of disease relapse;

(2) improvement in the patient’s quality of life; (3) prevention

of surgical intervention or hospitalization; (4) management of

extraintestinal manifestations; (5) prevention of malnutrition;

and (6) prevention of treatment-associated adverse effects.

**General Approach to Treatment**

❺*When designing a drug regimen for treatment of IBD, several*

*factors should be considered, including the patient’s symptoms,*

*medical history, current medication use, drug allergies, and*

*location and severity of disease.* A thorough patient history may

also help to identify a family history of IBD or potential exacerbating

factors, such as tobacco or NSAID use.

**Nonpharmacologic Therapy**

No specific dietary restrictions are recommended for patients

with IBD, but avoidance of high-residue foods in patients with

strictures may help to prevent obstruction.Nutritional strategies

in patients with long-standing IBD may include use of vitamin

and mineral supplementation. Administration of vitamin B12,

folic acid, fat-soluble vitamins, and iron may be needed to prevent

or treat deficiencies. In severe cases, enteral or parenteral

nutrition may be needed to achieve adequate caloric intake. Patients with IBD, particularly those with CD, are also at

risk for bone loss. This may be a function of malabsorption or

an effect of repeated courses of corticosteroids. Patients with

IBD should receive a baseline bone density measurement prior

to receiving corticosteroids. Vitamin D and calcium supplementation

should be used in all patients receiving long-term

corticosteroids. Oral bisphosphonate therapy may also be

considered in patients receiving prolonged courses of corticosteroids

or in those with osteopenia or osteoporosis.

Surgical intervention is a potential treatment option in

patients with complications such as fistulae or abscesses, or in

patients with medically refractory disease. Ulcerative colitis is

curable with performance of a total colectomy. Patients with

UC may opt to have a colectomy to reduce the chance of developing

colorectal cancer. Patients with CD may have affected

areas of intestine resected. Unfortunately, CD may recur following

surgical resection. Repeated surgeries may lead to significant

malabsorption of nutrients and drugs consistent with

development of short-bowel syndrome. **Pharmacologic Therapy**

Several pharmacologic classes are available for the treatment

and maintenance of IBD. Because there may be differences in

the underlying disease process, distribution, and severity

between CD and UC, response rates to drugs in the same pharmacologic

class may differ between these two diseases.

Therefore, initial selection of an appropriate agent for patients

with active IBD should be designed to deliver maximum efficacy

while minimizing toxicity. Response rates to individual

classes of medications for both UC and CD will be discussed

within the specific treatment section for each disease.

***Symptomatic Interventions***

Patients with active IBD often have severe abdominal pain and

diarrhea.Medications used to manage these types of symptoms

may have adverse consequences in patients with active IBD.

❻*Antidiarrheal medications that reduce GI motility, such as loperamide,*

*diphenoxylate/atropine, and codeine should be avoided*

*in patients with active IBD due to the risk of precipitating acute*

*colonic dilation (toxic megacolon).8* Drugs with anticholinergic

properties, such as hyoscyamine and dicyclomine, are often

used to treat intestinal spasm and pain, but these drugs may

also reduce GI motility and should generally be avoided in

active IBD. Once active disease is under control, antidiarrheal

agents may be used with caution as adjunctive treatment.

Patients who have had multiple intestinal resections due to

CD may have diarrhea related to the inability to reabsorb bile

salts. Cholestyramine has been demonstrated to improve diarrheal

symptoms in this population.8,15 NSAIDs should be

avoided for pain management due to their ability to worsen

IBD symptoms. Narcotic analgesics should be used with caution,

as they may significantly reduce GI motility.

**Aminosalicylates**

The aminosalicylates are among the most commonly used drugs

for inducing and maintaining remission in patients with IBD

(Table 16–1). These drugs are designed to deliver 5-aminosalicylate

(5-ASA, mesalamine) to areas of inflammation within

the GI tract. While the mechanism of mesalamine is not fully

understood, it appears to have favorable anti-inflammatory

effects. These effects may include reducing prostaglandin and

leukotriene production, inhibiting bacteria-induced chemotaxis,

scavenging of free radicals, and inhibiting nuclear factor

κβ.9 The delivery of mesalamine to the affected sites is accomplished

by either linking mesalamine to a carrier molecule or

altering the formulation to release drug in response to changes

in intestinal pH. Topical suppositories and enemas are designed

to deliver mesalamine directly to the distal colon and rectum.17,18

The prototypical aminosalicylate is sulfasalazine, which is

comprised of mesalamine linked by a diazo bond to the carrier

molecule sulfapyridine. This linkage prevents premature

absorption of mesalamine in the small intestine. Once sulfasalazine

is delivered to the colon, bacterial degradation ofthe diazo bond frees mesalamine from sulfapyridine.

Sulfapyridine is then absorbed and excreted renally, while

mesalamine acts locally within the GI tract.

Newer mesalamine products utilize non-sulfapyridine methods

for drug delivery.Olsalazine uses two mesalamine molecules

linked together, while balsalazide uses the inert carrier molecule

4-aminobenzoyl-β-alanine. Both drugs use a diazo bond similar

to sulfasalazine. Other mesalamine formulations are pHdependent

formulations that release mesalamine at various

points throughout the GI tract.

Sulfasalazine is associated with various adverse effects, most

of which are thought to be due to the sulfapyridine component.

Common adverse effects that may be dose related

include headache, dyspepsia, nausea, vomiting, and fatigue.19

Idiosyncratic effects include bone marrow suppression, reduction

in sperm counts in males, hepatitis, and pulmonitis.

Hypersensitivity reactions may occur in patients allergic to

sulfonamide-containing medications.

The use of non-sulfapyridine–based aminosalicylates has

led to greater tolerability. Although the adverse effects are similar

to those of sulfasalazine, they occur at a much lower rate.

Olsalazine, in particular, is associated with a higher incidence

of secretory diarrhea. These agents can also be used safely in

patients with a reported sulfonamide allergy.

**Corticosteroids**

Corticosteroids have potent anti-inflammatory properties and

are used in active IBD to rapidly suppress inflammation.

Corticosteroids have favorable effects in modulating several

cell types involved in the inflammatory process.20,21 They may

be administered systemically or delivered locally to the site of

action by altering the drug formulation (Table 16–2). Because

these drugs usually improve symptoms and disease severity

rapidly, they should be restricted to short-term management

of active disease. Long-term use of systemic corticosteroids is

associated with significant adverse effects, including cataracts,

skin atrophy, hypertension, hyperglycemia, adrenal suppression,

osteoporosis, and increased risk of infection, among others.19,22

Budesonide is a high-potency glucocorticoid used in CD that

has low systemic bioavailability when administered orally.23 The

formulation releases budesonide in the terminal ileum for treatment

of disease involving the ileum or ascending colon. Due to its

reduced bioavailability, budesonide may prevent some long-term

adverse effects in patients who have steroid-dependent IBD.23,24

**Immunosuppressants**

Agents targeting the excessive immune response or cytokines

involved in IBD are potential treatment options (Table 16–3).

Azathioprine and its active metabolite 6-mercaptopurine (6-MP)

are inhibitors of purine biosynthesis and reduce IBD-associated GI

inflammation. They are most useful for maintaining remission of

IBD or reducing the need for long-term use of corticosteroids.Use

in active disease is limited by their slow onset of action, which

may be as long as 3 to 12 months.Adverse effects associated with

azathioprine and 6-MP include hypersensitivity reactions resulting

in pancreatitis, fever, rash, hepatitis, and leukopenia.25

Methotrexate is a folate antagonist used primarily for maintaining

remission of CD. It may be administered orally, subcutaneously,

or intravenously and may result in a steroid-sparing

effect in patients with steroid-dependent disease.26,27 Long-term

methotrexate use may result in serious adverse effects, including

hepatotoxicity, pulmonary fibrosis, and bone marrow suppression.

Methotrexate is teratogenic and should not be used in

pregnant women or those who plan to become pregnant.

Cyclosporine is a cyclic polypeptide immunosuppressant typically

used to prevent organ rejection in transplant patients. Its use

is restricted to patients with fulminant or refractory symptoms

in patients with active IBD. Significant toxicities associated with

cyclosporine are nephrotoxicity, risk of infection, seizures,

hypertension, and liver function test abnormalities

**Biologic Agents**

Infliximab is the only biologic agent routinely used for managing

IBD. It is a murine-human IgG1 antibody directed against

TNF-α.14 Reduction in TNF-α activity in patients with IBD is

associated with improvement in the underlying inflammatory

process. Disadvantages of infliximab include need for intravenous

administration, significant drug cost, and potential for

adverse effects.Adverse effects include infusion-related reactions

such as fever, chest pain, hypotension, and dyspnea.29 Infliximab

has also been associated with reactivation of serious infections,

particularly intracellular pathogens such as tuberculosis.19,30 For

this reason, infliximab should not be used in patients with current

infections, and patients should be screened for tuberculosis

prior to initiating therapy. Infliximab may also lead to the development

or exacerbation of heart failure; it should be avoided in

patients with advanced or decompensated heart failu