

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Faecal Incontinence and Autoimmune Diseases

*Batool Mutar Mahdi*

## Abstract

Anal and rectal continence depend on many factors such as consistency of stool, integrity of neuromuscular sphincter complex, rectal capacity, sensation of defecation, higher cerebral function, and mobility. Any disturbance to these parameters may lead to various degrees of faecal incontinence. Continence may also be affected by immunological disorders that cause vasculitis as well as gastrointestinal mucosal and smooth muscle damage due to the formation of autoantibodies and immune complexes in autoimmune disease. A thorough knowledge of the gastrointestinal manifestations of autoimmune disease is important in order to be able to manage patients' symptoms optimally.

**Keywords:** autoimmunity, immune tolerance, inflammasomes, cytokines, faecal incontinence

## 1. Introduction

Faecal incontinence is characterized by inability to control bowel motions, causing the unexpected leakage of flatus and feces per rectum [1]. It may adversely affect the quality of one's life. Faecal incontinence may be precipitated by conditions such as diarrhea, constipation, pelvic muscle damage, nerve damage, and vaginal delivery. Faecal continence depends on many factors; for example, consistency of faecal substance, neuromuscular sphincter complex, rectal capacity, and sensation of defecation [2]. Other causes of faecal incontinence include immunological disorders that cause muscle damage due to formation of autoantibodies in autoimmune diseases [3, 4].

## 2. What is autoimmunity?

Autoimmunity is a disorder of the immune system. It is characterised by the absence of immune tolerance (tolerance is the absence of an immune response in an immunologically competent person), be it central tolerance in the thymus or peripheral tolerance through Treg cell CD4<sup>+</sup> and CD25<sup>+</sup> (T regularity). It is due to a defect in immune regulatory and signaling mechanisms; genetic factors like single-gene defects or gene mutation can also cause an immune dysregulation and autoimmunity [5].

### 3. Causes of autoimmunity

#### 3.1 Epigenetic alterations

Epigenetic alterations like DNA methylation, histone modification, and microRNAs alter the transcription and activity of genes that are involved in autoimmune responses and disease pathogenesis. These lead to aberrant epigenetic modifications in CD4 T helper cells' function through deregulations in several transcriptional genes like *Ifng*, *Cd70*, *Tnf*, *Dnmt3a*, and *Foxp3* that determine T cell identity. Adding to this, epigenetics target regulatory genes like *Tim-3*, *cereblon*, protein kinase C  $\theta$ , octamer transcription factor 1, basic leucine zipper transcription factor ATF-like, p70 kinase, and lactate dehydrogenase A that influence T cell activation, differentiation, and metabolism [6].

#### 3.2 Genetic mutation in inflammasome

Inflammasomes are multi-protein complexes that consist of NOD-like receptor (NLR) and AIM-like receptor (ALR) and apoptosis-associated speck-like protein that contains a CARD and caspase-1. The active caspase-1 cleaves pro-IL-1 $\beta$  and pro-IL-18 to IL-1 $\beta$  and IL-18, resulting in inflammation. Genetic mutations in inflammasomes result in autoimmune diseases. NOD-like receptor family, pyrin domain containing 1 (NLRP1) haplotypes contributes to susceptibility to autoimmune disease and single nucleotide polymorphisms (SNPs) that alter the susceptibility and severity of autoimmune disease. IL-1 $\beta$  and IL-18 maintain Th17 responses and endothelial cell damage, which potentiate autoimmune diseases. Autoimmunity is mediated in part by innocent bystander cells, augmented by inflammasomes [7].

#### 3.3 HLA-associated autoimmune diseases

Autoimmune diseases have associations with particular HLA alleles through displaying the autoantigens targeted by self-reactive T cells that escape thymic deletion because most HLA alleles are capable of presenting self-antigens even in healthy individuals [8].

#### 3.4 Cytokines pathway

Cytokine and cytokine receptor genetic polymorphisms have been associated with many different autoimmune diseases like *IL23R* and IL-23 that augment the pro-inflammatory action of Th17 cells that leads to tissue damage, and anti-cytokine therapy can be nicely used as a target to treat autoimmune diseases [9–11].

### 4. Mechanism of autoimmunity

The mechanism of autoimmune reactions is due to an imbalance between two immune responses, effector and regulatory, that develop through stages of initiation and propagation, and often show phases of resolution or remissions and exacerbations or flares. The mechanism of autoimmunity is defective elimination and/or control of self-reactive lymphocytes. A major goal of treatment is reestablishing the normal balance between effector and regulatory immune responses [12] (**Figure 1**).

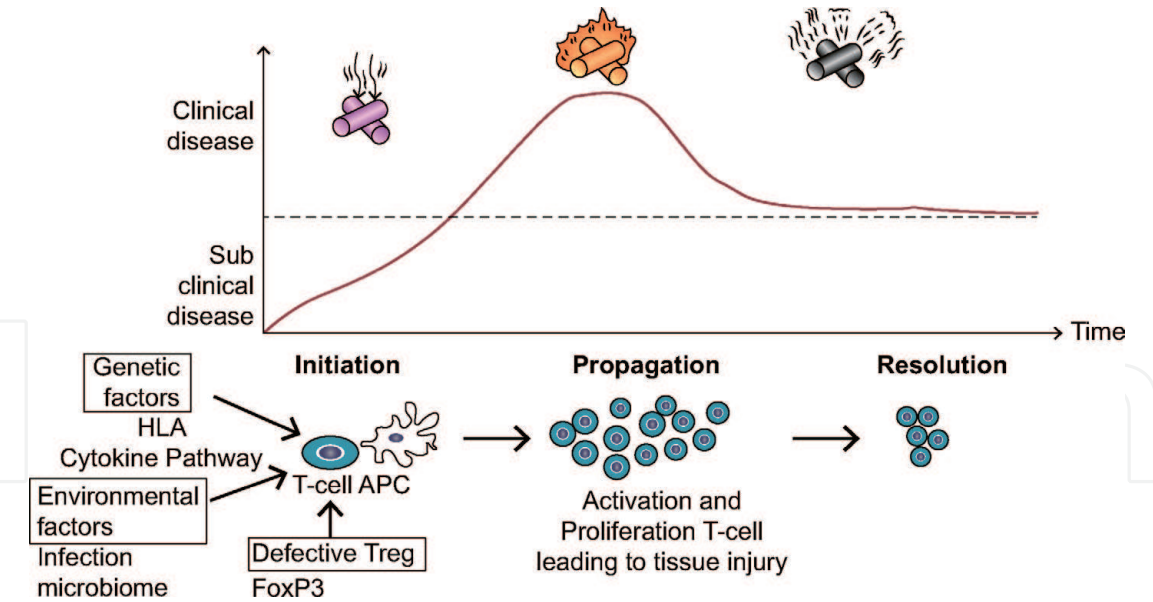


Figure 1.  
Mechanism of autoimmunity.

## 5. Gastrointestinal manifestations in systemic autoimmune diseases

The systemic autoimmune diseases include different diseases like collagen vascular diseases, systemic vasculitides, Wegener granulomatosis, and Churg-Strauss syndrome that involve any part of gastrointestinal tract, hepatobiliary system, and pancreas. Patients with these diseases had different gastrointestinal symptoms like oral ulcers, dysphagia, gastroesophageal reflux diseases, abdominal pain, constipation, diarrhea, faecal incontinence, pseudo-obstruction, perforation of GIT tract, and bleeding [13].

### 5.1 Effects of autoimmune diseases on the gastrointestinal tract

Some autoimmune diseases are characterized by autoreactive T cells attacking body's own tissues. One of the manifestations of these diseases is gastrointestinal manifestation, which is either the initial presentation or the complications of the disease.

#### 5.1.1 Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology, characterized by deposition of autoantibodies and immune complexes in tissues (type III hypersensitivity). Gastrointestinal manifestations of SLE are due to primary gastrointestinal disorders, complications of therapy, and SLE itself. Any part of the gastrointestinal tract may become involved in SLE. Many GI conditions can be mimicked by SLE [14]. Lupus enteritis, a distinct subset of SLE, is defined as either vasculitis or inflammation of the small bowel. The clinical manifestations include decreased salivation, buccal mucosal ulcers, dysphagia, oesophageal ulceration, gastric ulceration, pseudo-obstruction, and faecal incontinence [15–17].

#### 5.1.2 Rheumatoid arthritis

It is also a type III hyper sensitivity reaction due to deposition of immune complexes in the synovium of small interphalangeal joints of hands. Gastrointestinal

manifestations are common and variable. It involves the esophagus resulting in decreased peristalsis, decreased lower esophageal sphincter tone, hiatal hernia, and esophageal ulcer. It may also result in peptic ulcer and chronic atrophic gastritis. Colonic inflammation such as collagenous colitis with secondary amyloidosis may also occur, leading to diarrhea and faecal incontinence [18].

#### 5.1.3 Sjögren's syndrome

Sjögren syndrome is a common autoimmune disease due to B cell activation and invasion of T and B lymphocytes to affected exocrine glands. This disease affects the gastrointestinal tract resulting in dry mouth, difficulty in swallowing, esophageal atrophy, epigastric pain, dyspepsia, chronic atrophic gastritis, chronic pancreatitis, jejunitis, sigmoiditis, and inflammatory bowel disease [19, 20].

#### 5.1.4 Progressive systemic sclerosis (scleroderma)

It is one of the connective tissue diseases of unknown etiology that affects females more than males. It is characterized by vasculopathy, tissue fibrosis, and autoimmunity. It causes overproduction of collagen due to autoimmune dysfunction that leads to fibrosis of many visceral organs. The immune system attacks the kinetochore of the chromosomes that leads to genetic malformation of nearby genes. Patients experience gastrointestinal tract symptoms like thinning of the lips, tightening of the perioral skin, impaired taste sensation, atrophy of the mucous membrane and tongue papilla, dysphagia and dyspepsia, gastroesophageal reflux, peptic esophagitis, Barrett's metaplasia, gastric antral vascular ectasia (GAVE) or watermelon stomach, and dysmotility of small intestine leading to chronic pseudo-obstruction. As scleroderma progresses, it may lead to decreased motility of the intestine and to progressive fibrosis and scarring of the small intestine leading to bacterial overgrowth and malabsorption of nutrients and growth in stagnant intestinal fluid. Large intestine and colon will be involved, causing pseudo-obstruction or ischemic colitis [21, 22]. Anorectal involvement causes faecal incontinence and rectal prolapse. Gastrointestinal tract involvement greatly affects morbidity and mortality in this disease and therapy aims to relieve these symptoms [23, 24].

#### 5.1.5 Polyarteritis nodosa

The gastrointestinal manifestations of systemic vasculitis that results from mesenteric ischemia are vague nonspecific abdominal pain, hematemesis, melena, hematochezia, jejunal ulceration, and perforation. Liver may be involved with acalculous cholecystitis, appendicitis, pancreatitis, and biliary strictures [25–27].

#### 5.1.6 Kawasaki disease

This is a syndrome that is characterized by oral mucosal changes, fever, lymphadenopathy, and polyarteritis in addition to gastrointestinal symptoms like abdominal pain, vomiting, diarrhea, small bowel obstruction, jaundice, and paralytic ileus [28].

#### 5.1.7 Inflammatory muscle disorders: polymyositis and dermatomyositis

These are systemic autoimmune diseases characterized by inflammation of striated and smooth muscle of the body. Patients had a progressive weakness of



proximal striated muscles and skin rash with dermatomyositis. The whole gastrointestinal tract may be affected but the proximal esophagus is more common affected. Gastric and esophageal emptying and peristalsis are affected in many patients, so they complain of dysphagia, aspiration, nasal regurgitation, early satiety, bloating, reduced gastrointestinal motility, hiatal hernia, gastroesophageal reflux disease (GERD), stricture, dilated atonic esophagus associated with delayed gastric emptying, and intestinal mucosal thickening. In addition to that, there are colonic pseudodiverticulosis and pneumatosis coli. Neurological dysfunction and diminished smooth muscle contractility due to muscle atrophy and fibrosis lead to bowel wall oedema, ulceration, and perforation [29].

#### *5.1.8 Giant cell arteritis*

This is a granulomatous inflammation of the arteries, particularly cranial and temporal, leading to narrowing the lumen of the arteries. The main symptoms are headache and fever. Blindness may occur suddenly. There are associations with intestinal manifestations like bowel ischemia and gangrene, acute pancreatitis, liver granulomas, lymphocytic infiltration, and dilated bile canaliculi. The erythrocyte sedimentation rate is high [30, 31].

#### *5.1.9 Henoch-Schönlein purpura*

This is an IgA-mediated immune complex deposit resulting in systemic vasculitis in small vessels. Gastrointestinal signs and symptoms are common such as periumbilical pain with nausea and vomiting. Sometimes ulceration of the mucosa of the second part of the duodenum and less commonly in the colon and rectum may occur [32].

#### *5.1.10 Takayasu arteritis*

This is a chronic vasculitis of unknown etiology. The inflammatory processes cause thickening, narrowing, and eventual occlusion of the walls of the affected arteries. Patients usually experience gastrointestinal symptoms such as abdominal pain, nausea, diarrhea, and hemorrhage due to the involvement of the descending abdominal aorta [33].

#### *5.1.11 Cogan's syndrome*

This is a chronic inflammatory disorder characterized by interstitial keratitis, audiovestibular system involvement, aortitis, mesenteric vasculitis, weight loss, fever, lymphadenopathy, hepatosplenomegaly, abdominal pain, nausea, and vomiting [34].

#### *5.1.12 Churg-Strauss syndrome*

This is an allergic angiitis that occurs mostly in asthmatic patients, and is associated with granulomatous necrotizing vasculitis. Patients have eosinophilia, fever, and allergic rhinitis. Sometimes gastrointestinal involvement occurs in about 50% of patients, leading to eosinophilic gastroenteritis associated with abdominal pain, bloody diarrhea due to multiple ulcers, nausea, and vomiting. Perforation of the small intestine and colon may commonly occur. Necrotizing granulomatous vasculitis of the mesenteric artery leads to mucosal ischemia [35].

#### 5.1.13 Wegener granulomatosis

This is a systemic autoimmune disease characterized by granulomatous vasculitis of the upper and lower respiratory tracts leading to infection, glomerulonephritis, and small-vessel necrotizing vasculitis with granuloma formation. Gastrointestinal manifestations of Wegener granulomatosis are oropharyngeal mucosal lesions, gingivitis, ulcer of gastric mucosa, small intestinal perforation, colonic ulceration, non-healing perianal ulcers, cholecystitis, recurrent acute pancreatitis, and splenic necrosis [25].

#### 5.1.14 Antiphospholipid antibody syndrome

This is a disorder characterized by recurrent vascular thrombosis, abortion, and thrombocytopenia due to increased antiphospholipid antibodies. The gastrointestinal manifestations of antiphospholipid antibody syndrome lead to vasculopathy and tissue ischemia. Antiphospholipid antibodies in SLE patients are associated with Budd-Chiari syndrome, with patients presenting with abdominal pain, ascites, and hepatic failure [36–38].

#### 5.1.15 Spondyloarthropathies

These are a group of interconnected chronic inflammatory rheumatic diseases including ankylosing spondylitis, arthritis associated with inflammatory bowel disease and reactive arthritis. The spondyloarthropathies are associated with the HLA-B27 gene. About 36% of patients have reactive arthritis secondary to a dysenteric infection were positive for HLA-B27. Subclinical gut inflammation, ulcerative colitis, and Crohn's disease are frequent types of idiopathic IBD that are associated with arthritis or spondylitis [39–43].

#### 5.1.16 Behçet's disease

This is a widespread autoimmune vasculitis of unknown origin occurring in all ages resulting in a damage to blood vessels in all the body. Patients usually had uveitis with oral and genital ulcers. Clinical manifestations also include vascular, neurological, articular, renal, and gastrointestinal manifestations. Gastrointestinal Behçet's disease symptoms are similar to those caused by inflammatory bowel diseases, and include nausea, abdominal pain, and bloody diarrhea. In addition, ulceration in the mouth, gastrointestinal tract, or genitalia may occur, the ulcers typically being painful, shallow and round with discrete borders. Segmental mucosal ulceration in the ileocecal and colonic area leads to perforation and bloody diarrhea [44].

## 6. Mechanisms of how autoimmune disorders cause faecal incontinence

The precise cause and mechanism how autoimmune diseases cause faecal incontinence are unknown, but multiple factors are probably involved. These factors include deterioration and destruction of collagen framework by the effect of autoantibodies, resulting in inflammation, reduced compliance of rectal muscles with consequent urgency, and urge faecal incontinence. Diarrhea is one of GIT manifestation of autoimmune connective tissue diseases, and this in itself may lead to incontinence even in the presence of normal sphincters.

## 7. Conclusion

Continence usually requires normal functioning of both the muscles of the lower digestive tract and pelvic floor, and the nervous system. There are many causes of faecal incontinence. In this chapter, we have discussed the various autoimmune disorders and their involvement in the disruption of the continence mechanism. Further studies are necessary in this field, focusing on targeted therapies to minimize the effect of these diseases on the gastrointestinal tract.

### Author details

Batool Mutar Mahdi  
HLA Research Unit, Department of Microbiology, Al-Kindy College of Medicine,  
University of Baghdad, Baghdad, Iraq

\*Address all correspondence to: [abas\\_susan@yahoo.com](mailto:abas_susan@yahoo.com)

### IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 



## References

- [1] Ditah I, Devaki P, Luma HN, Ditah C, Njei B, Jaiyeoba C, et al. Prevalence, trends, and risk factors for fecal incontinence in United States adults, 2005-2010. *Clinical Gastroenterology and Hepatology*. 2014;**12**:636-643.e2
- [2] Landenfeld CS, Bowers BJ, Feld AD, Hartmann KE, Hoffman E, Ingber MJ, et al. National Institutes of Health State-of-the-Science Conference statement: Prevention of fecal and urinary incontinence in adults. *Annals of Internal Medicine*. 2008;**148**:449-458
- [3] Chirkin VV, Martynova TI, Dul'tsev IV. Immunological disorders and their correction in patients with incompetence of the anal sphincter. *Khirurgiia (Mosk)*. 1983;**3**:88-92
- [4] Coura MM, Silva SM, Almeida RM, Forrest MC, Sousa JB. Is digital rectal exam reliable in grading anal sphincter defects? *Arquivos de Gastroenterologia*. 2016;**53**:240-245
- [5] Schmidt RE, Grimbacher B, Witte T. Autoimmunity and primary immunodeficiency: Two sides of the same coin? *Nature Reviews Rheumatology*. 2017;**14**:7-18
- [6] Wang Z, Chang C, Lu Q. Epigenetics of CD4+ T cells in autoimmune diseases. *Current Opinion in Rheumatology*. 2017;**29**:361-368
- [7] Yang CA, Chiang BL. Inflammasomes and human autoimmunity: A comprehensive review. *Journal of Autoimmunity*. 2015;**61**:1-8
- [8] Goris A, Liston A. The immunogenetic architecture of autoimmune disease. *Cold Spring Harbor Perspectives in Biology*. 2012;**4**:a007260
- [9] Ghoreschi K et al. Generation of pathogenic T(H)17 cells in the absence of TGF- $\beta$  signalling. *Nature*. 2010;**467**(7318):967-971
- [10] Vandebroek K. Cytokine gene polymorphisms and human autoimmune disease in the era of genome-wide association studies. *Journal of Interferon & Cytokine Research*. 2012;**32**:139-151
- [11] Elliott M et al. Ustekinumab: Lessons learned from targeting interleukin-12/23p40 in immune-mediated diseases. *Annals of the New York Academy of Sciences*. 2009;**1182**:97-110
- [12] Rosenblum MD, Remedios KA, Abbas AK. Mechanisms of human autoimmunity. *The Journal of Clinical Investigation*. 2015;**125**:2228-2233
- [13] Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Gastrointestinal manifestations in systemic autoimmune diseases. *Maedica (Buchar)*. 2011;**6**:45-51
- [14] Rich RR, Fleisher TA, Shearer WT, et al. *Clinical Immunology. Principles and Practice*. 2nd ed. London: Mosby International Limited; 2001
- [15] Mok MY, Wong RWS, Lau CS. Intestinal pseudo-obstruction in systemic lupus erythematosus an uncommon but important clinical manifestation. *Lupus*. 2000;**9**:11-18
- [16] Tian X-P, Zhang X. Gastrointestinal involvement in systemic lupus erythematosus: Insight into pathogenesis, diagnosis and treatment. *World Journal of Gastroenterology*. 2010;**16**:2971-2977
- [17] Alves SC, Fasano S, Isenberg DA. Autoimmune gastrointestinal complications in patients with systemic lupus erythematosus: Case

series and literature review. *Lupus*. 2016;**25**:1509-1519

[18] Wordsworth P. Arthritis and inflammatory bowel disease. *Current Rheumatology Reports*. 2000;**2**:87-88

[19] Shahzad HS, Shaw-Stiffel TA. The gastrointestinal manifestations of Sjögren's syndrome. *The American Journal of Gastroenterology*. 1995;**90**:9-14

[20] Popov Y, Salomon-Escoto K. Gastrointestinal and hepatic disease in Sjogren syndrome. *Rheumatic Diseases Clinics of North America*. 2018;**44**:143-151

[21] Ponge T, Bruley des Varannes S. Digestive involvement of scleroderma. *La Revue du Praticien*. 2002;**52**: 1896-1900

[22] Sallam H, McNearney TA, Chen JD. Systematic review: Pathophysiology and management of gastrointestinal dysmotility in systemic sclerosis (scleroderma). *Alimentary Pharmacology & Therapeutics*. 2006;**23**:601-712

[23] Marie I. Gastrointestinal involvement in systemic sclerosis. *Presse Médicale*. 2006;**35**:1952-1965

[24] Stelle M, Chizzolini C. Gastrointestinal features in systemic sclerosis. *Revue Médicale Suisse*. 2014;**10**:860-863

[25] Pagnoux C, Mahr A, Cohen P, et al. Presentation and outcome of gastrointestinal involvement in systemic necrotizing vasculitides: Analysis of 62 patients with polyarteritis nodosa, microscopic polyangiitis, Wegener granulomatosis, Churg-Strauss syndrome, or rheumatoid arthritis-associated vasculitis. *Medicine (Baltimore)*. 2005;**84**:115-128

[26] Levine SM, Hellmann DB, Stone JH. Gastrointestinal involvement in

polyarteritis nodosa (1986-2000): Presentation and outcomes in 24 patients. *The American Journal of Medicine*. 2002;**112**:386-391

[27] Ebert EC, Hagspiel KD, Nagar M, et al. Gastrointestinal involvement in polyarteritis nodosa. *Clinical Gastroenterology and Hepatology*. 2008;**6**:960-966

[28] Chen WT, Huang SR, Wang JK. Kawasaki disease presenting with hepatitis and prolonged fever. Report of one case. *Acta Paediatrica Taiwanica*. 2003;**44**:174-176

[29] Ebert EC. Review article: The gastrointestinal complications of myositis. *Alimentary Pharmacology & Therapeutics*. 2010;**31**:359-365

[30] Annamalai A, Francis ML, Ranatunga SKM, et al. Giant cell arteritis presenting as small bowel infarction. *Journal of General Internal Medicine*. 2007;**22**:140-144

[31] Trimble MA, Weisz MA. Infarction of the sigmoid colon secondary to giant cell arteritis. *Rheumatology (Oxford, England)*. 2002;**41**:108-110

[32] Chang W-L, Yang Y-H, Lin Y-T, et al. Gastrointestinal manifestations in Henoch-Schönlein purpura: A review of 261 patients. *Acta Paediatrica*. 2004;**93**:1427-1431

[33] Zamani F, Shakeri R, Modiramani O, et al. *Medscape General Medicine*. 2006;**8**:69

[34] Gluth MB, Baratz KH, Matteson EL, et al. Cogan syndrome: A retrospective review of 60 patients throughout a half century. *Mayo Clinic Proceedings*. 2006;**81**:483-488

[35] Vaglio A, Corradi D, Ronda N, et al. Large bowel obstruction heralding Churg-Strauss syndrome. *The American Journal of Gastroenterology*. 2004;**99**:562-563

[36] Braham A, Safer L, Bdioui F, et al. Antiphospholipid antibodies in digestive diseases. *Presse Médicale*. 2001;**30**:1890-1897

[37] Asherson RA, Cervera R. Unusual manifestations of the antiphospholipid syndrome. *Clinical Reviews in Allergy and Immunology*. 2003;**25**:61-78

[38] Spencer HL. Primary antiphospholipid syndrome as a new cause of autoimmune pancreatitis. *Gut*. 2004;**53**:468

[39] Hannu T, Mattilla L, Siitonen A, et al. Reactive arthritis attributable to *Shigella* infection: A clinical and epidemiological nationwide study. *Annals of the Rheumatic Diseases*. 2005;**64**:594-598

[40] Orlando A, Renna S, Perricone G, et al. Gastrointestinal lesions associated with spondyloarthropathies. *World Journal of Gastroenterology*. 2009;**15**:2443-2448

[41] Rudwaleit M, Baeten D. Ankylosing spondylitis and bowel disease. *Best Practice & Research. Clinical Rheumatology*. 2006;**20**:451-466

[42] Smale S, Natt RS, Orchard TR. Inflammatory bowel disease and spondylarthropathy. *Arthritis and Rheumatism*. 2001;**44**:2728-2736

[43] De Keyser F, Baeten D, Van den Bosch F, et al. Gut inflammation and spondyloarthropathies. *Current Rheumatology Reports*. 2002;**4**:525-532

[44] Yurdakul S, Tuzuner N, Yardakul I, et al. Gastrointestinal involvement in Behçet's syndrome: A controlled study. *Annals of the Rheumatic Diseases*. 1996;**55**:208-210