Welcome to the IBD Nurse Fellowship Program!

The program consists of 13 modules:

Module 1 – Ulcerative Colitis
Module 2 – Crohn's Disease
Module 3 – Ulcerative Colitis vs. Crohn's Disease
Module 4 – Management of Ulcerative Colitis
Module 5 – Management of Crohn's Disease
Module 6 – IBD and Surgery
Module 7 – Medication Adherence in IBD
Module 8 – Health Promotion and Maintenance in IBD
Module 9 – Nutrition and IBD
Module 10 – Extra-intestinal Manifestations of IBD
Module 11 – Anemia in IBD
Module 12 – Fatigue in IBD
Module 13 – Anxiety and Depression in IBD

Each module is divided into sections, all of which are listed in the Table of Contents. The Table of Contents allows you to click on the page numbers to navigate to each section. Each page has a Home Button on the bottom right-hand corner that will take you back to the Table of Contents.

The learning objectives are at the beginning and end of each module. Before completing the module, you will have the opportunity to take a self-directed quiz, which will test your knowledge on several of the key concepts and takeaways from the module. It is recommended that you take the quiz and accomplish all of the learning objectives before moving on to the next module.

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csgna
Canadian Society of Gastroenterology Nurses & Associates
Société canadienne des infirmières et infirmiers en gastroentérologie et travailleurs associés

CANIBD
Canadian Nurses IBD Group

Module 10

Extra-intestinal manifestations of IBD

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Learning objectives

After completing Module 10 you will be able to:

- Explain what extra-intestinal manifestations (EIMs) are and how they occur
- List the organ systems affected by EIMs associated with inflammatory bowel disease (IBD)
- Describe different types of EIMs and their prevalence in IBD
- Outline the pathophysiology of EIMs of IBD
- Discuss treatment options for EIMs of IBD

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Section 1

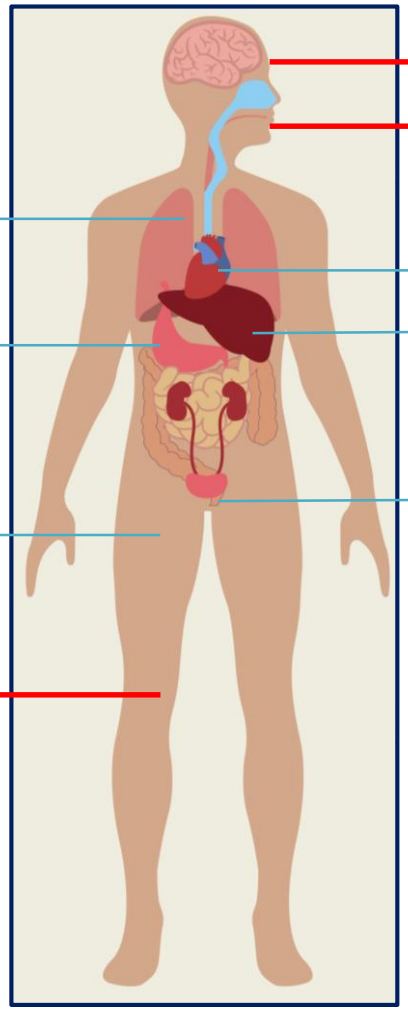
Extra-intestinal manifestations in IBD

What are extra-intestinal manifestations?

- Inflammatory bowel disease (IBD) predominantly affects the gastrointestinal system, but is associated with many extra-intestinal manifestations (EIMs)
  - Associated with the presence of active colonic inflammation
  - Have a potentially detrimental impact on the patient's functional status and quality of life
- EIMs can occur:
  - In patients with either ulcerative colitis (UC) or Crohn's disease (CD)
  - In any organ system
  - Before, in parallel, or up to 30 years after diagnosis of IBD
- EIMs are reported with frequencies ranging from 6% to 47% in patients with IBD
- Multiple EIMs may occur concomitantly, and the presence of one EIM confers a higher likelihood of developing other EIMs
- Some EIMs are related to increased intestinal disease activity, while other EIMs may or may not be related to IBD disease activity at all

Vavricka et al., 2015; Levine et al., 2011

Extra-intestinal organ systems involved with IBD



- Ocular system
- Dermatologic and oral systems
- Pulmonary system
- Cardiac system
- Endocrine and metabolic systems
- Hepatobiliary system
- Genitourinary system
- Vascular and hematologic systems
- Musculoskeletal system

More common

Less common

IBD, inflammatory bowel disease

Ardizzone et al., 2008

Examples of IBD-associated extra-intestinal manifestations

System	Examples
Musculoskeletal system	• Arthritis: colitic type, ankylosing spondylitis, isolated joint involvement • Hypertrophic osteoarthropathy: clubbing, periostitis • Miscellaneous manifestations: osteoporosis, aseptic necrosis, polymyositis
Dermatological and oral lesions	• Reactive lesions: erythema nodosum, pyoderma gangrenosum, aphthous ulcers, necrotizing vasculitis, Sweet's syndrome • Specific lesions: fissures, fistulas, oral Crohn's disease, drug rashes • Nutritional deficiencies: acrodermatitis enteropathica, purpura, glossitis, hair loss, brittle nails • Associated diseases: vitiligo, psoriasis, amyloidosis
Ocular system	• Uveitis/iritis, episcleritis, scleromalacia, corneal ulcers, retinal vascular disease
Hepatobiliary system	• Primary sclerosing cholangitis (PSC), bile-duct carcinoma (cholangiocarcinoma) • Associated inflammation: autoimmune chronic active hepatitis, pericholangitis, portal fibrosis, cirrhosis, granulomatous disease • Metabolic manifestations: fatty liver, gallstones associated with ileal Crohn's disease
Metabolic system	• Growth retardation in children and adolescents, delayed sexual maturation
Renal system	• Calcium oxalate stones

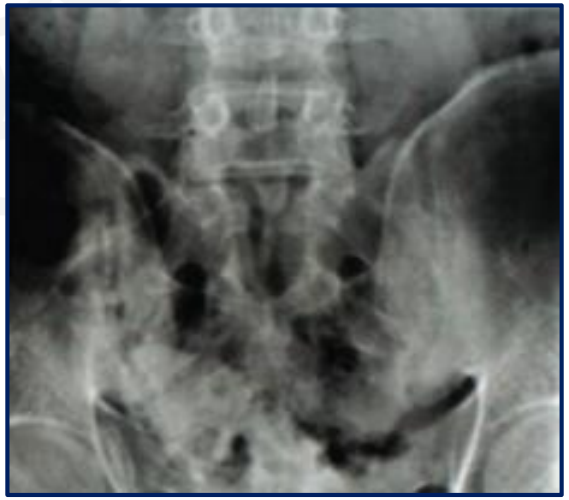
IBD, inflammatory bowel disease

Levine et al., 2011.

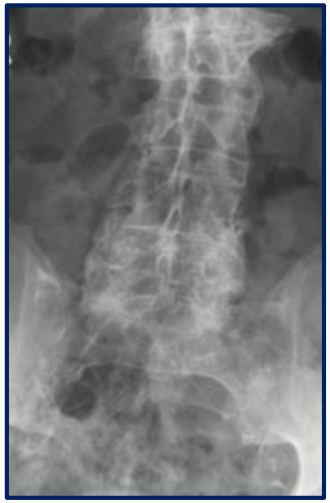
Musculoskeletal extra-intestinal manifestations

- Musculoskeletal EIMs are considered the most common EIMs in IBD patients (occurring in 9% to 53%), and include:
  - Articular involvement
  - Periarticular involvement
  - Muscular involvement
  - Osteoporosis and related fractures
  - Fibromyalgia

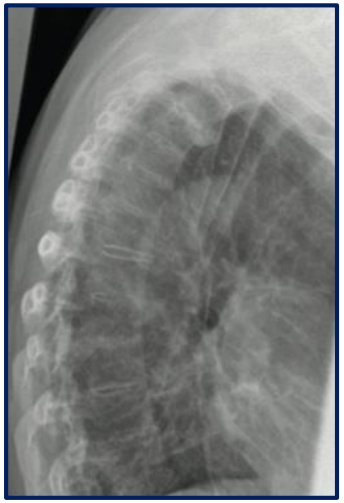
Joint symptoms affecting peripheral large and small joints or the axial joints occur in up to 40% of patients with IBD



Sacroiliitis



Sacrum with bilateral ankylosis



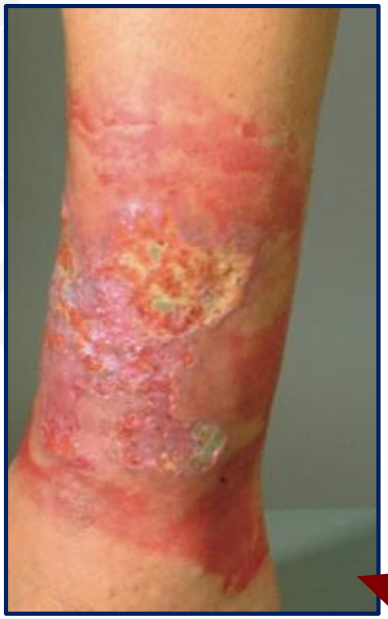
Syndesmophytes (bamboo spine)

EIM, extra-intestinal manifestation; IBD, inflammatory bowel disease

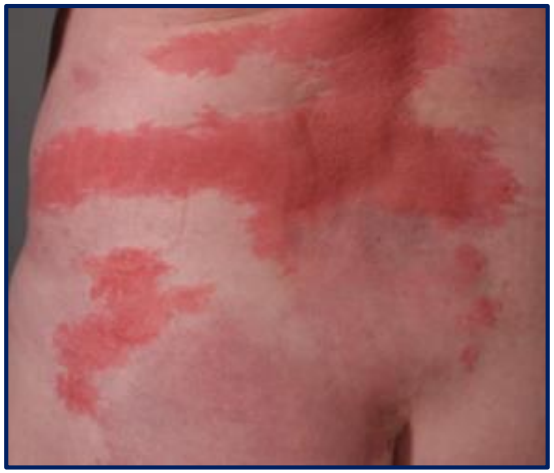
Vavricka et al., 2015; Levine et al., 2011.

Dermatological and oral extra-intestinal manifestations

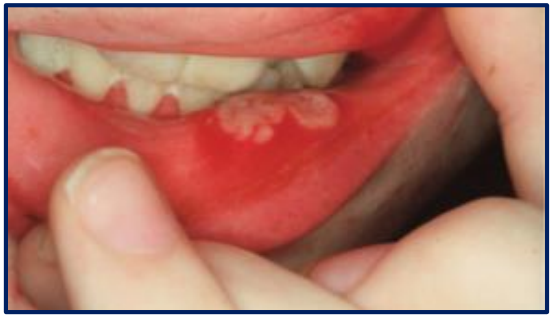
- Major dermatologic manifestations have been reported in 2% to 34% of IBD patients
- A broad spectrum of skin diseases may occur, and patients may develop multiple dermatologic manifestations concurrently



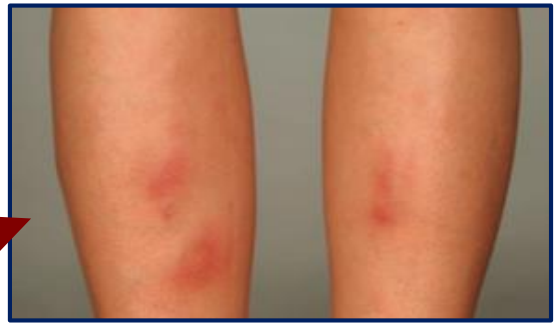
Pyoderma gangrenosum



Sweet's syndrome



Aphthous ulcers



Erythema nodosum

Erythema nodosum and pyoderma gangrenosum are the most common cutaneous manifestations

IBD, inflammatory bowel disease

Vavricka et al., 2015; Levine et al., 2011.

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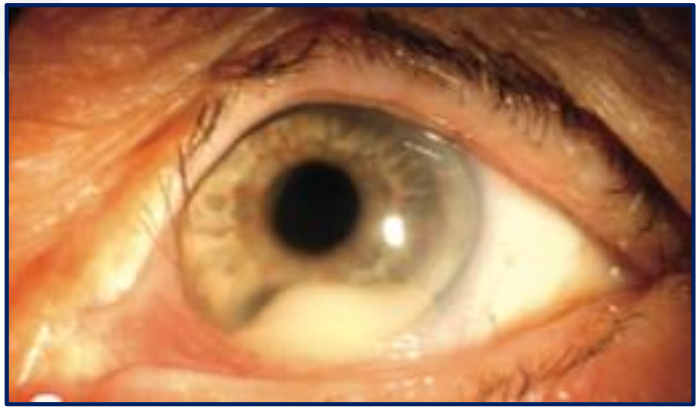
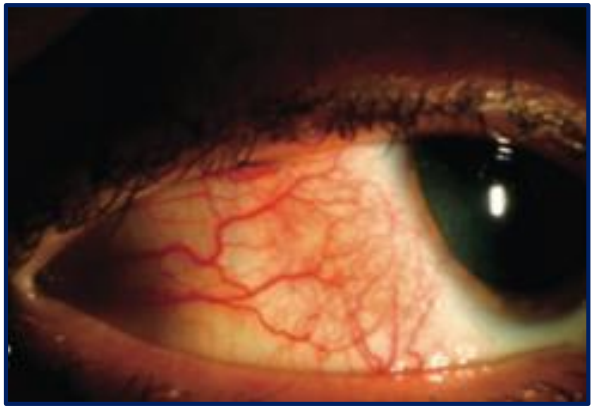
Ocular extra-intestinal manifestations

- Ocular manifestations occur in 0.3% to 5% of all IBD patients
- Patients with colitis or ileocolitis are affected more frequently than patients with isolated small-bowel disease
- Ocular complications often present concurrently with other EIMs, particularly peripheral arthritis and erythema nodosum



Uveitis



Episcleritis

The most common ocular manifestation is episcleritis, or inflammation of the blood-rich episclera

EIMs, extra-intestinal manifestations; IBD, inflammatory bowel disease

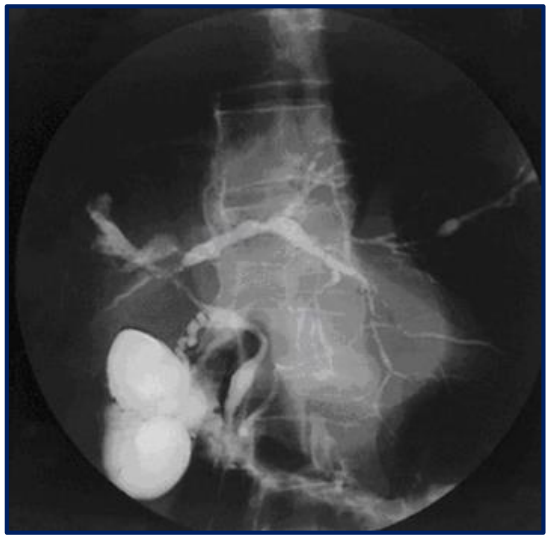
Ardizzone et al., 2008; Levine et al., 2011.

Image source: Vavricka et al., 2015.

Hepatobiliary extra-intestinal manifestations

- Although the reported incidence of hepatobiliary disorders in patients with IBD ranges from 5% to 95%, a more realistic figure is about 5% to 15%
- The most important hepatobiliary complication of IBD is primary sclerosing cholangitis (PSC), a chronic, progressive disorder that manifests as inflammation, stricturing, and fibrosis of medium and large intra- and extra-hepatic bile ducts
  - At least 75% of PSC patients have coexisting UC
  - 5% to 10% of PSC patients have CD
- PSC is most common in male patients 30 to 59 years of age

The clinical course of PSC bears no relationship to underlying bowel disease. PSC can develop either years before or after the development of bowel symptoms.



Primary sclerosing cholangitis

CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis

Vavricka et al., 2015; Levine et al., 2011; Worthington et al., 2006.

Image source: https://openi.nlm.nih.gov/detailedresult.php?img=1636629_1750-1172-1-41-1&query=primary+sclerosing+cholangitis&lic=by&req=4&npos=1.

Pathology of extra-intestinal manifestations

- The pathogenesis of extra-intestinal manifestations (EIMs) in IBD is not well understood, there are several current hypotheses:
  - Some systemic disorders may be of immunologic origin and are likely related to the pathophysiology of the intestinal disease
  - Intestinal bacterial overgrowth across a leaky intestinal mucosa may cause an adaptive immune response leading to inflammation
  - Complications of the therapy used to control bowel inflammation may contribute to EIMs
- Triggers of the autoimmune responses in certain organs seem to be influenced by:
  - Genetic susceptibility
  - Antigenic display of auto-antigen
  - Aberrant self-recognition
  - Immunopathogenetic auto-antibodies against organ-specific cellular antigen(s) shared by colon and extra-colonic organs

IBD, inflammatory bowel disease.
Vavricka et al., 2015; Ardizzone et al., 2008.

Section 2

Treatment of extra-intestinal manifestations

Joint manifestations

Peripheral arthritis (mainly seronegative arthralgia/arthritis) occurs in in 10-20% of patients with CD and 5-10% of patients with UC

Joint manifestations	Prevalence in IBD (%)	Association with disease activity	Treatment options
Peripheral arthritis joint manifestation Type 1	CD 6-11% versus UC 2.7-3.6%	• Parallels with disease activity • Occurs more frequently in females with CD-pancolitis and penetrating disease	• Treatment of underlying IBD • NSAIDs • Sulfasalazine
Peripheral arthritis joint manifestation Type 2	2-4% in IBD	• Independent from disease activity • Associated with uveitis, female gender, and colonic CD	• NSAIDs • Sulfasalazine • Corticosteroids
Axial arthritis	CD 1% versus UC 3%	• Independent from disease activity • Associated with female gender, colonic CD, and pancolitis	• Physiotherapy • NSAIDs • Anti-TNF biologic therapy

CD, Crohn's disease; IBD, inflammatory bowel disease; NSAIDs, non-steroidal anti-inflammatory drugs; TNF, tumor necrosis factor; UC, ulcerative colitis

Lakatos et al., 2012; Voulgari, 2011.

Skin manifestations

Skin manifestations	Prevalence in IBD (%)	Association with disease activity	Treatment options
Erythema nodosum	CD 10-15% versus UC 3-10%	• Parallels with disease activity • Associated with female gender • May be associated with joint and ocular manifestations, colonic CD, and pancolitis	• Treatment of underlying IBD • Aspirin • NSAIDs
Pyoderma gangrenosum	1-2% in IBD	• May be independent from disease activity • Associated with female gender • May be associated to uveitis and pancolitis	• Corticosteroids • Cyclosporine • Anti-TNF biologic therapy
Aphthous stomatitis	5-10% in IBD	• Parallels with disease activity	• Treatment of underlying IBD • Viscous lidocaine

CD, Crohn's disease; IBD, inflammatory bowel disease; NSAIDs, non-steroidal anti-inflammatory drugs; TNF, tumor necrosis factor; UC, ulcerative colitis

Lakatos et al., 2012.

Ocular manifestations

Ocular manifestations	Prevalence in IBD (%)	Association with disease activity	Treatment options
Episcleritis	2-3% in IBD	• Parallels with disease activity • Associated with female gender • May be associated with joint and cutaneous manifestations, pancolitis	• Often self-limiting • Treatment of underlying IBD • Topical steroids • NSAIDs
Uveitis	2-6% in IBD	• May be independent from disease activity • Associated with female gender • May be associated with joint and cutaneous manifestations, pancolitis	• Topical or systemic steroids • Anti-TNF biological therapy

IBD, inflammatory bowel disease; NSAIDs, non-steroidal anti-inflammatory drugs; TNF, tumor necrosis factor.
Lakatos et al., 2012.

Other manifestations

Other manifestations	Prevalence in IBD (%)	Association with disease activity	Treatment options
Primary sclerosing cholangitis (PSC)	CD 1-2% versus UC 2-4%	• Independent from disease activity • Risk for developing colorectal and biliary cancers	• Ursodeoxycholic acid (at 10–15 mg/kg) • Endoscopic retrograde cholangiopancreatography (ERCP) • Liver transplantation
Osteoporosis/ Osteopenia	18-42%	• Both independent and dependent factors associated with disease activity • Risk factors include age and cumulative steroid use	• Calcium and Vitamin D supplementation • Bisphosphonates • Anti-TNF biologic therapy
Thrombo-embolism	1.2-6.7%	• Parallels with disease activity, comorbidities and age • Risk is high in hospitalized patients	• Low-molecular-weight heparin and Vitamin K antagonist for treatment (and prophylaxis)

IBD, inflammatory bowel disease; NSAIDs, non-steroidal anti-inflammatory drugs; TNF, tumor necrosis factor.
Lakatos et al., 2012.

Section 3

Self-assessment quiz

Self-assessment quiz

- Now that you have reviewed the module content, you have the opportunity to test your knowledge and understanding of the material by completing a self-assessment
- The assessment consists of 5 multiple choice questions
- Please attempt each question before looking at the answer key, which is located on page 26
- The answer key provides the rationale for each answer and indicates where the correct answer can be found in the module

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Question 1

Extra-intestinal manifestations can occur in which of the following situations?

a) In any organ system, in patients with ulcerative colitis or Crohn's disease

b) Concomitantly with other extra-intestinal manifestations

c) Before, in parallel, or up to 30 years after diagnosis of IBD

d) All of the above

Question 2

Which organ systems are affected by extra-intestinal manifestations associated with inflammatory bowel disease?

a) Metabolic, renal and ocular systems

b) Cardiovascular and lymphatic systems

c) Hepatobiliary and dermatological systems

d) Both a) and c)

Question 3

Which of the following is/are considered one of the most common forms of extra-intestinal manifestations?

a) Osteoporosis

b) Erythema nodosum

c) IBD arthritis

d) Both a) and c)

Question 4

Non-steroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, and corticosteroids may be used to treat which form of extra-intestinal manifestation?

a) Thrombo-embolism

b) Peripheral arthritis joint manifestation Type 1

c) Primary sclerosing cholangitis

d) Axial arthritis

Question 5

Which extra-intestinal manifestations may be remedied by treating the underlying inflammatory bowel disease?

a) Erythema nodosum

b) Aphthous stomatitis

c) Episcleritis

d) All of the above

Answer key

1. **The correct answer is d.** Extra-intestinal manifestations may occur in any organ system in patients with ulcerative colitis or Crohn's disease. They may also occur concomitantly with other extra-intestinal manifestations. Additionally, they may occur before, in parallel, or up to 30 years after diagnosis of IBD. See page 6 for more information on this topic.

2. **The correct answer is d.** Metabolic, renal, ocular, hepatobiliary and dermatological systems are affected by extra-intestinal manifestations associated with IBD. See page 8 for more information on this topic.

3. **The correct answer is d.** Osteoporosis and IBD arthritis are both examples of musculoskeletal extra-intestinal manifestations (EIMs), which are considered the most common EIMs in IBD. See pages 8 & 9 for more information on this topic.

4. **The correct answer is b.** Peripheral arthritis joint manifestation Type 1 may be treated with NSAIDs, sulfasalazine, and corticosteroids. See page 15 for more information on this topic.

5. **The correct answer is d.** Treatment of underlying IBD can help to treat erythema nodosum, aphthous stomatitis and episcleritis. See pages 16 & 17 for more information on this topic.

Congratulations!

You have completed the 10th module of the program.

Based on what you learned in Module 10, you should be able to:

- Explain what extra-intestinal manifestations (EIMs) are and how they occur
- List the organ systems affected by EIMs associated with inflammatory bowel disease (IBD)
- Describe different types of EIMs and their prevalence in IBD
- Outline the pathophysiology of EIMs of IBD
- Discuss treatment options for EIMs of IBD

If you have answered the quiz questions correctly and achieved the learning objectives, you are ready to move on to Module 11, which will focus on anemia in IBD.

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