

Extraintestinal Manifestations in Patients With Inflammatory Bowel Disease

Contents



[EIMs in Patients With IBD](#)



[Commonly Occurring EIMs in Patients With IBD](#)



[Management of EIMs in Patients With IBD](#)



[References](#)

EIMs in Patients With IBD

Definition of Extraintestinal Manifestations^a

- An inflammatory pathology in a patient with inflammatory bowel disease (IBD) that is **located outside the gut** whose pathogenesis is either
 - Dependent on extension or translocation of immune responses from the intestine
 - An independent inflammatory event perpetuated by IBD or that shares a common environmental or genetic predisposition with IBD
- True extraintestinal manifestations (EIMs), as described above, exclude pathologies (such as associated autoimmune conditions) or complications of IBD and its treatment
- EIMs are difficult to define because their underlying mechanisms are poorly defined

Organ Systems Commonly Affected by EIMs in Patients With IBD^b

System	EIMs
Musculoskeletal	Spondyloarthritis
Cutaneous	Erythema nodosum Pyoderma gangrenosum Sweet syndrome Metastatic CD
Ocular	Episcleritis Uveitis Scleritis
Oral	Oral CD Orofacial granulomatosis Metastatic CD

^aAs defined by the European Crohn's and Colitis Organisation. ^bComplete list can be found within publication.
CD=Crohn's disease; EIM=extraintestinal manifestation; IBD=inflammatory bowel disease.
Hedin CRH, et al. *J Crohns Colitis*. 2019;13(5):541-554.

Prevalence of EIMs in Patients With IBD

- Up to 50% of patients with IBD are thought to experience at least one EIM¹⁻⁴
 - Patients may experience their first EIM prior to their diagnosis of IBD³
 - The presence of a single EIM confers a higher probability to develop additional EIMs^{3,4}
- EIMs were reported to occur more commonly in patients with CD than in those with UC⁵⁻⁷
 - A population-based European cohort study (N=1145) found that 20.1% of patients with CD and 10.4% of patients with UC experienced an EIM (CD, n=364; UC, n=781)⁵

Note: This ex-US cohort study may be limited by an absence of an independent review board for on-site investigators. This analysis included immune-mediated EIMs (peripheral arthritis, plantar fasciitis, ankylosing spondylitis, sacroiliitis, erythema nodosum, pyoderma gangrenosum, anterior uveitis, iridocyclitis, and sclerosing cholangitis) as well as non-immune-mediated complications (gallstones and kidney stones)
 - A retrospective, multicenter, cross-sectional study based on patients identified from the Spanish ENEIDA registry (N=31,077) found that 23.5% of patients with CD and 13.7% of patients with UC experienced an EIM⁶

Note: In this ex-US study, diagnoses of EIMs were done by different physicians using a wide range of diagnostic criteria. The registry also did not include EIM dates, treatments, appearances prior to diagnosis, or chronology of EIMs in patients with multiple manifestations
 - A population-based Danish study based on patients identified from the Danish National Patient Register (N=32,446) found that 27.4% of patients with CD and 20.0% of patients with UC experienced an EIM⁷

Note: This ex-US study relied on information from a registry that lacked measures of disease-state severity and included a risk of misclassification during identification of CD, UC, and EIMs/comorbidities

CD=Crohn's disease; EIM=extraintestinal manifestation; ENEIDA=Estudio Nacional en Enfermedad Inflamatoria intestinal sobre Determinantes genéticos y Ambientales; IBD=inflammatory bowel disease; UC=ulcerative colitis.

1. Olpin JD, et al. *Radiographics*. 2017;37(4):1135-1160. 2. Hedin CRH, et al. *J Crohns Colitis*. 2019;13(5):541-554. 3. Harbord M, et al. *J Crohns Colitis*. 2016;10(3):239-254. 4. Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992. 5. Isene R, et al. *Scand J Gastroenterol*. 2015;50(3):300-305. 6. Algaba A, et al. *Dig Dis Sci*. 2021;66(6):2014-2023. 7. Vadstrup K, et al. *Crohns Colitis* 360. 2020;2(3):otaa070.

Burden of EIMs in Patients With IBD

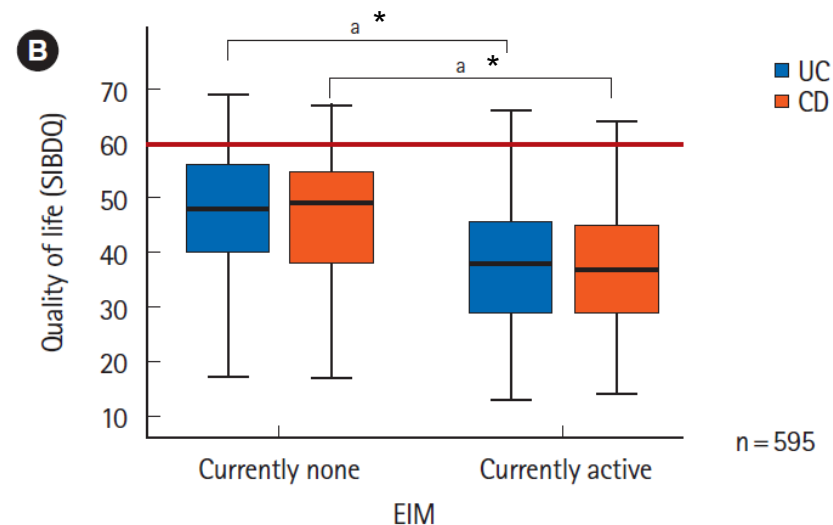
- EIMs can substantially impair quality of life (QoL) and functional status and also affect morbidity and mortality in patients with IBD^{1,2}

- In a study that used the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), EIMs were found to have a significant negative impact on patients (N=595)^{3,a}

Note: This is an ex-US study based on questionnaire data collected via the internet, which may result in a degree of interpretation bias

- Multidisciplinary care is critical to manage the additional disease burden that EIMs place on patients with IBD⁴

QoL is significantly reduced in patients with active EIM in IBD^{3,a}



* $P < 0.001$.

^aSIBDQ is a 10-item shortened version of the original Inflammatory Bowel Disease Questionnaire, which included 32 items. It measures QoL in 4 domains: bowel symptoms, emotional health, systemic systems, and social function.⁵ Cutoff of the score for QoL was 60 points in the SIBDQ and is depicted by a red line (normal QoL, ≥ 60 ; moderately to severely reduced QoL, < 60).

CD=Crohn's disease; EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; QoL=quality of life; SIBDQ=Short Inflammatory Bowel Disease Questionnaire; UC=ulcerative colitis.

1. Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992. 2. Vavricka SR, et al. *Am J Gastroenterol*. 2011;106:110-119. 3. Keller R, et al. *Intest Res*. 2021;19(1):45-52. 4. Ghosh S, et al. *J Crohns Colitis*. 2020;13(suppl 1):S314-S315. 5. Crohn's and Colitis Foundation. <https://www.crohnscolitisfoundation.org/sites/default/files/legacy/science-and-professionals/programs-materials/ibd-nurses/best-practices/ibd-patient-intake-data-sheet-2.pdf>. Accessed September 21, 2021.

Relationship Between EIMs and IBD Disease Activity

- Most EIMs characteristically parallel the course of IBD disease activity¹⁻³
- EIMs that parallel the course of IBD disease activity may occur with flare, and they improve with successful treatment of intestinal inflammation¹

Relationship Between EIM Activity and Intestinal Activity^{1,a}

EIM	Parallels course of IBD	Separate course from IBD	May or may not parallel IBD disease activity
Axial arthropathy		✓	
Peripheral arthropathy	✓ (Type I)	✓ (Type II)	
Erythema nodosum	✓		
Pyoderma gangrenosum			✓
Sweet's syndrome	✓		
Oral aphthous ulcers	✓		
Episcleritis	✓		
Uveitis			✓

^aTable modified from Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992.

EIM=extraintestinal manifestation; IBD=inflammatory bowel disease.

1. Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992. 2. Olpin JD, et al. *Radiographics*. 2017;37(4):1135-1160. 3. Harbord M, et al. *J Crohns Colitis*. 2016;10(3):239-254.

Mechanisms Linking Inflammation to EIMs

- Two links between inflammation in the intestine and occurrence of EIMs have been proposed
 - Independent inflammatory events may be initiated or perpetuated in the presence of IBD or shared genetic/environmental risk factors
 - EIMs may arise from an extension of an immune response from the intestine to nonintestinal sites
- Multiple mechanisms may contribute to each of these processes, and these mechanisms are not mutually exclusive

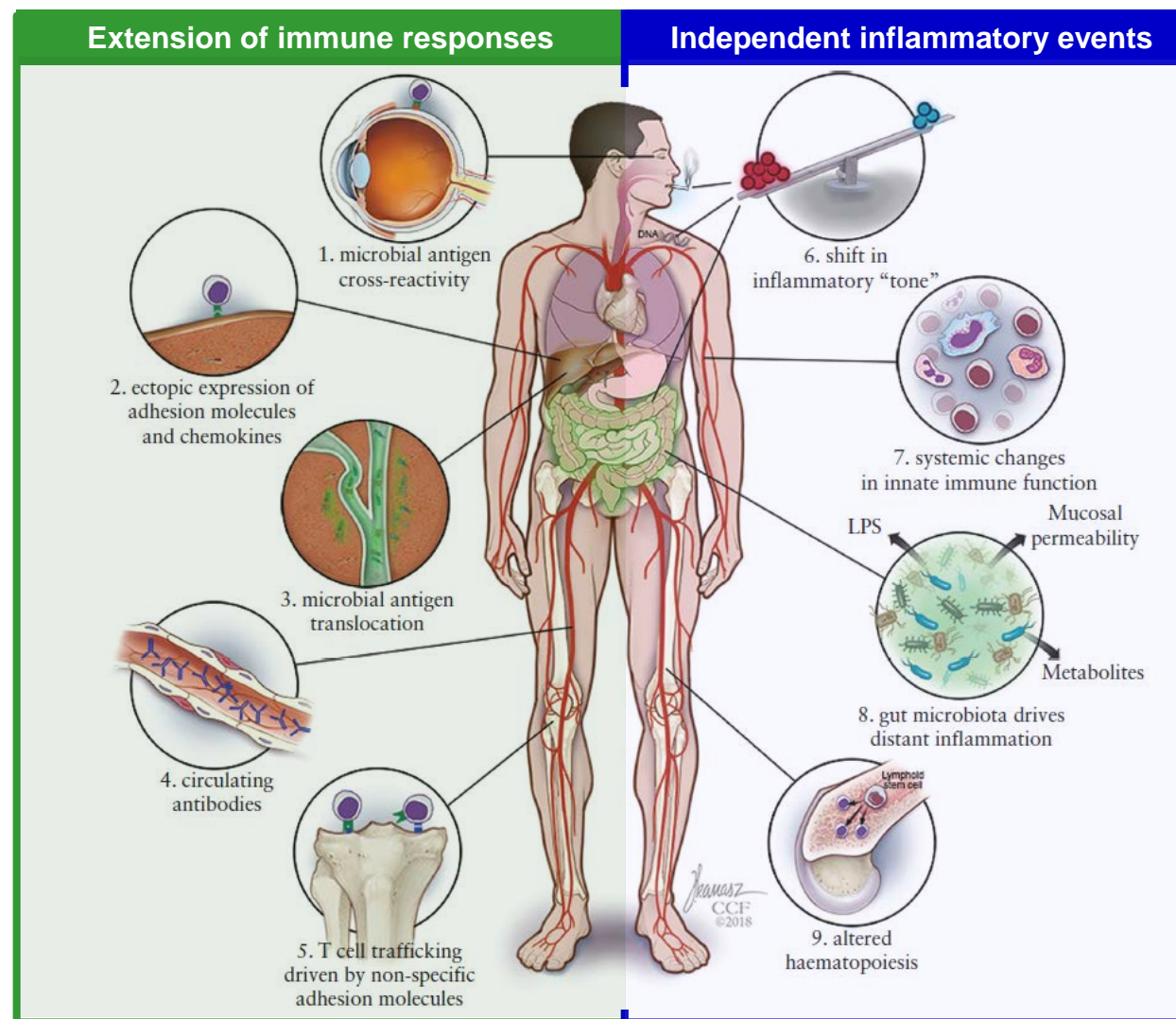


Figure from Hedin CRH, et al. The pathogenesis of extraintestinal manifestations: implications for IBD research, diagnosis, and therapy. *J Crohn's Colitis*. 2019;13(5):541-554, by permission of the European Crohn's and Colitis Organisation.

EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; LPS=lipopolysaccharide.

Hedin CRH, et al. *J Crohn's Colitis*. 2019;13(5):541-554.

Commonly Occurring EIMs in Patients With IBD

Musculoskeletal EIMs

- Musculoskeletal EIMs, especially joint pain, are the most common EIMs in patients with IBD^{1,2}
- IBD-related arthropathies are a subtype of seronegative spondyloarthritis (SpA) and are termed IBD-SpA^{1,3,a}
 - IBD-SpA is an EIM that can involve both peripheral and axial joints²
- Suspicion of IBD-SpA should be prompted by the presence of chronic back pain (>3 months), peripheral joint pain/swelling, signs of enthesitis, and the presence or history of dactylitis or other types of tenosynovitis³

Peripheral arthropathy^{2,3}

- Reported in up to 34.6% of patients with IBD
- Higher prevalence in CD than in UC

Type 1 (knee joint)

- Associated with IBD disease activity
- Affects ≤4 joints

Type 2 (MCP joint)

- Not associated with IBD disease activity
- Affects ≥5 joints

Axial arthropathy^{2,3}

- Reported in up to 16% of patients with IBD
- Higher prevalence in CD than in UC
- Not associated with IBD disease activity
- Includes inflammatory back pain, isolated sacroiliitis, and ankylosing spondylitis

^aSpA also includes reactive arthritis, psoriatic arthritis, ankylosing spondylitis, and undifferentiated SpA.

CD=Crohn's disease; EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; MCP=metacarpophalangeal; SpA=spondyloarthritis; UC=ulcerative colitis.

1. Longman RS, Scherl EJ. In: *Medical Therapy of Ulcerative Colitis*. New York, NY: Springer Science+Business Media; 2014:377-391. 2. Wiens J, et al. *Gastroenterol Nurs*. 2017;40(6):496-503.

3. Gionchetti P, et al. *J Rheumatol Suppl*. 2015;93:21-23.

Cutaneous EIMs

- Major cutaneous manifestations, including erythema nodosum (EN) and pyoderma gangrenosum (PG), have been reported to occur in 2% to 34% of patients with IBD¹

Erythema nodosum

- EN lesions are tender, painful, and symmetric nodules that present on the surface of lower extremities^{1,2}
 - Bluish-red discoloration can persist for weeks but does not ulcerate or scar
 - Usually self-limiting, although reoccurrence is common
- Reported in 15% of patients with CD and 10% of patients with UC³
- Treatment is largely supportive, with or without analgesics¹
- Parallels IBD disease course; 90% of IBD-associated EN occurs in the setting of a relapse¹

Pyoderma gangrenosum

- PG lesions are usually painful ulcerations with sharp borders and a necrotic base that present on the surface of lower extremities^{1,2}
 - Most commonly appear as pustules but can also be red papules or nodules
 - May appear anywhere on the body
- Reported in 1% to 2% of patients with CD and 5% to 20% of patients with UC³
- Treatment includes supportive care, occlusive wound management, systemic immunomodulatory therapy, and analgesics as needed¹
- Does not parallel IBD disease course; often manifests near the time of a bowel exacerbation^{1,4}

Erythema nodosum⁴

Pyoderma gangrenosum⁴



CD=Crohn's disease; EIM=extraintestinal manifestation; EN=erythema nodosum; IBD=inflammatory bowel disease; PG=pyoderma gangrenosum; UC=ulcerative colitis.

1. Longman RS, Scherl EJ. In: *Medical Therapy of Ulcerative Colitis*. New York, NY: Springer Science+Business Media; 2014:377-391. 2. Olpin JD, et al. *Radiographics*. 2017;37(4):1135-1160. 3. Marotto D, et al. *Pharmacol Res*. 2020;161:105206. 4. Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992.

Ocular EIMs

- Ocular manifestations have been reported to occur in 0.3% to 13% of patients with IBD and often occur with concomitant musculoskeletal manifestations^{1,2}
 - Ocular manifestations may be more common in patients with CD than in those with UC¹
 - Episcleritis is the most common ocular manifestation in IBD, followed by uveitis^{1,2}

Episcleritis²



Episcleritis¹⁻³

- Occurs in ~2%-5% of patients
- Usually painful, with acute hyperemia but no photophobia, blurring of vision, or vision loss
- Treatment includes controlling intestinal flare and symptom management with lubricant eye drops, cold compresses, or topical steroids

- Parallels IBD activity

Uveitis¹⁻³

- Occurs in ~0.5%-3.5% of patients
- Usually painful, with headache, photophobia, blurring of vision, or vision loss
- Treatment includes topical and/or systemic steroids or immunomodulatory therapies

- Does not parallel IBD activity

Scleritis¹⁻³

- Occurs in <1% of patients
- Usually painful, with tenderness, edema, visual impairment, or visual loss
- Treatment includes controlling intestinal flare with systemic steroids or immunomodulatory therapies and NSAIDs

- Parallels IBD activity

Oral EIMs

- Oral manifestations can occur in patients with IBD and may have some correlation with disease activity¹⁻³
 - Presentation of oral lesions may be more severe with flare; however, up to 30% of patients may continue to experience oral manifestations despite IBD disease control²
 - In ~5%-10% of patients, oral lesions may present earlier than gastrointestinal symptoms²
 - Oral aphthous ulcers have been estimated to occur at a frequency of ~4%-5% in patients with IBD and occur more frequently in patients with CD compared with UC and among males^{1,2}
- Dental manifestations, such as periodontitis, may also be related to IBD disease activity¹

Spectrum of Oral Manifestations in IBD^{1,a}

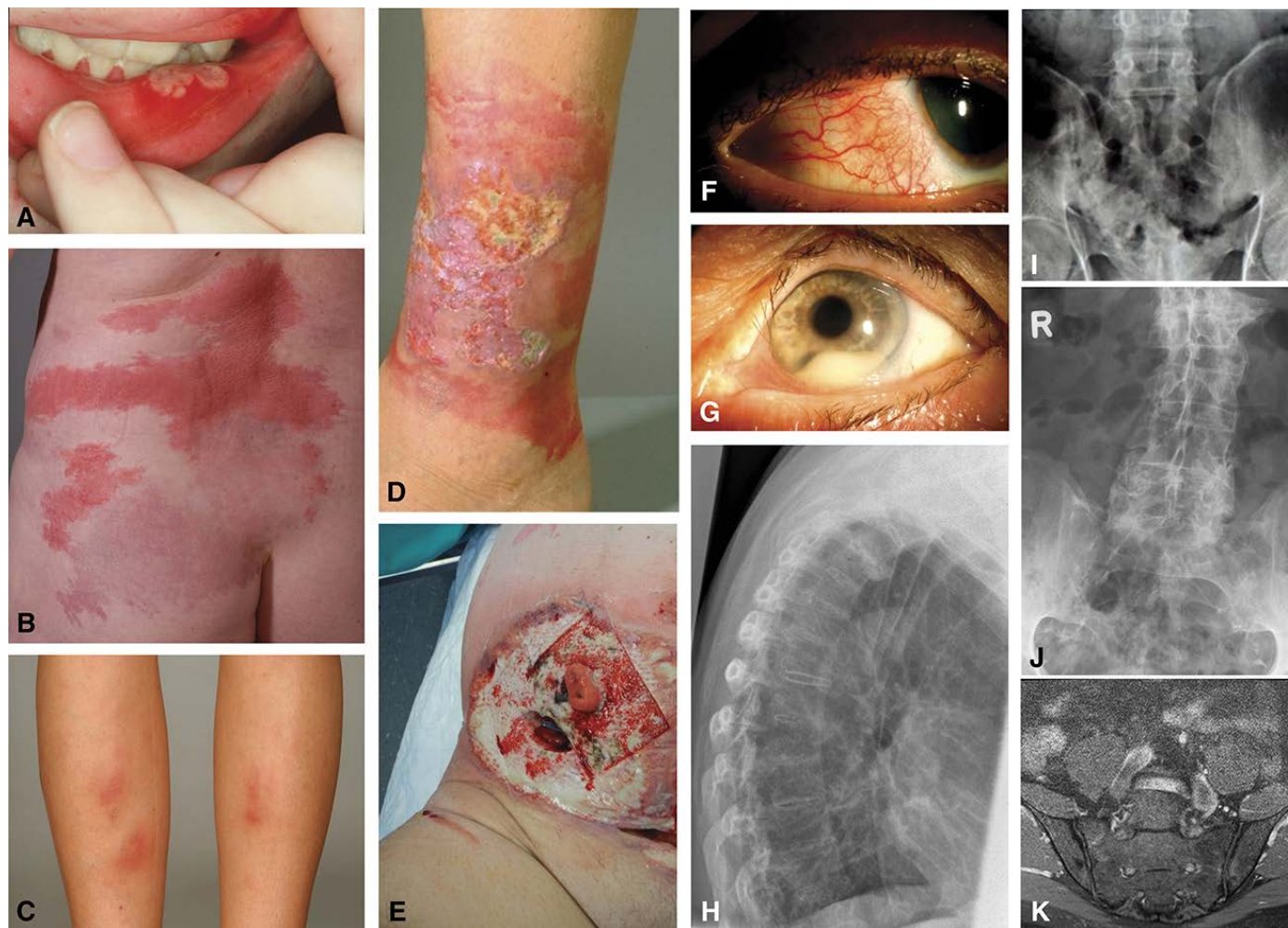
Crohn's disease		Ulcerative colitis	
Highly specific	Highly suspicious	Nonspecific oral lesions (IBD and non-IBD)	Highly specific
<ul style="list-style-type: none"> Metastatic CD of the face Orofacial Granulomatous cheilitis: subacute involvement of the area of the mouth, mostly focal granulomatous inflammation of the lower lip 	<ul style="list-style-type: none"> Taglike lesions Cobblestoning Mucogingivitis Lip swelling and vertical fissuring Deep linear oral ulcers 	<ul style="list-style-type: none"> Malabsorption related Medication related Other 	<ul style="list-style-type: none"> Pyostomatitis vegetans: erythematous and thickened oral mucosa with multiple pustules and superficial erosions

^aIndex of suspicion for IBD (UC or CD) is increased with the increasing intensity of the color.

CD=Crohn's disease; EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; UC=ulcerative colitis.

- Katsanos KH, et al. *Aliment Pharmacol Ther.* 2015;42(1):40-60.
- Lankarani KB, et al. *World J Gastroenterol.* 2013;19(46):8571-8579.
- Vavricka SR, et al. *Inflamm Bowel Dis.* 2015;21(8):1982-1992.
- Papageorgiou SN, et al. *J Clin Periodontol.* 2017;44(4):382-393.

Physical Manifestations of EIMs



- (A) Oral aphthous ulcers
- (B) Sweet's syndrome
- (C) Erythema nodosum
- (D) Pyoderma gangrenosum
- (E) Peristomal pyoderma gangrenosum
- (F) Episcleritis
- (G) Uveitis with hypopyon and dilated iris vessels
- (H) Conventional x-ray of the lateral spine demonstrating syndesmophytes (bamboo spine)
- (I) Plane radiograph of the iliosacral joints with bilateral sacroiliitis
- (J) Plane radiography of the sacrum with bilateral ankylosis
- (K) Coronal magnetic resonance image of the sacroiliac joints with active inflammation mainly on the left side and chronic inflammatory changes on both sides

Management of EIMs in Patients With IBD

Management of EIMs: Guidance for Patients With IBD

- Patient awareness of and education about EIMs of IBD are important aspects of disease management^{1,2}
 - Awareness of EIMs and complications related to IBD is associated with increased treatment adherence and follow-up¹
 - Because IBD-associated arthropathy is the most common EIM of IBD (reported to occur in up to half of patients), healthcare providers, including nurses, can include a basic physical assessment when examining a patient²⁻⁴
- Standardized criteria for the diagnosis and monitoring of EIMs in patients with IBD are lacking⁵
 - However, at the time of diagnosis of IBD, presence of EIMs (including joint, skin, ocular, and oral manifestations) should be assessed^{6,a}
- For patients with pronounced EIMs, such as skin or joint problems, systemic UC treatments (TNF blockers and Janus kinase inhibitors) may be preferable over gut-selective therapies (integrin blockers)^{6,a}
- Management of EIMs, particularly those that are complex, may necessitate the collaboration of a multidisciplinary team⁷

^aAs recommended by the American College of Gastroenterology.

EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; TNF=tumor necrosis factor; UC=ulcerative colitis.

1. Huang V, et al. *J Crohns Colitis*. 2013;7(8):e318-e324. 2. Wiens J, et al. *Gastroenterol Nurs*. 2017;40(6):496-503. 3. Longman RS, Scherl EJ. In: *Medical Therapy of Ulcerative Colitis*. New York, NY: Springer Science+Business Media; 2014:377-391. 4. Olpin JD, et al. *Radiographics*. 2017;37(4):1135-1160. 5. Hedin CRH, et al. *J Crohns Colitis*. 2019;13(5):541-554. 6. Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413. 7. Harbord M, et al. *J Crohns Colitis*. 2016;10(3):239-254.

A Multidisciplinary Team Approach to Manage IBD and EIMs

Primary care physician¹⁻³

- Makes initial diagnosis and referral to specialist
- Provides routine appointments and treatment of non-IBD-related illnesses
- Provides basic management of IBD symptoms
- May perform routine screenings

Gastroenterologist^{2,4,5}

- Manages medical oversight of team
- Authorizes treatment decisions and care plans
- May perform routine screenings

Rheumatologist^{2,6}

- Assists in the diagnosis of joint disease, such as SpA
- Provides assistance in the treatment of joint symptoms

Dermatologist^{2,6,7}

- Performs routine screening for skin cancer
- Assists in the diagnosis of cutaneous manifestations
- Provides treatment of skin symptoms if required

Ophthalmologist^{6,8}

- Performs routine ophthalmic check-ups and screening
- Provides assistance with treatment of ophthalmologic symptoms as needed

Dentist⁹

- Performs routine dental care
- Also provides screening, diagnosis, and treatment of oral symptoms

EIM=extraintestinal manifestation; IBD=inflammatory bowel disease; SpA=spondyloarthritis.

1. Bennett AL, et al. *World J Gastroenterol*. 2015;21:4457-4465. 2. IBD Standards Group. Available at: <http://s3-eu-west-1.amazonaws.com/files.crohnsandcolitis.org.uk/Publications/PPR/ibd-standards.pdf>. Accessed September 9, 2021. 3. Kane SV. *Gastroenterol Hepatol (N Y)*. 2017;13:500-503. 4. Regueiro M, et al. *Clin Gastroenterol Hepatol (N Y)*. 2017;15:1148-1153. 5. Moss A, Pham NV. *Gastrointest Endoscopy*. 2015;82:715-717. 6. Jansen FM, et al. *United European Gastroenterol J*. 2020;8(9):1031-1044. 7. Siao D, Velayos F. *Clin Gastroenterol Hepatol*. 2014;12:274-276. 8. Troncoso LL, et al. *World J Gastroenterol*. 2017;23(32):5836-5848. 9. Mays JW, et al. *J Evid Based Dent Pract*. 2012;12(3 suppl):265-282.

Summary

EIMs can occur in up to 50% of patients with IBD

- EIMs have been found to occur more frequently in patients with CD vs UC
- EIMs can affect multiple organ systems

Multiple mechanisms linking inflammation to EIMs have been proposed

- These mechanisms are not yet clearly defined and may not be mutually exclusive

Musculoskeletal, cutaneous, ocular, and oral EIMs are commonly reported among patients with IBD

- Many of these EIMs characteristically parallel the course of IBD disease, and these EIMs may improve with successful treatment of intestinal inflammation

Management of EIMs, particularly those that are complex, may necessitate the collaboration of a multidisciplinary team

References

References

- Algaba A, Guerra I, Ricart E, et al; Spanish GETECCU Group (ENEIDA Project). Extraintestinal manifestations in patients with inflammatory bowel disease: study based on the ENEIDA registry. *Dig Dis Sci.* 2021;66(6):2014-2023.
- Bennett AL, Munkholm P, Andrews JM. Tools for primary care management of inflammatory bowel disease: do they exist? *World J Gastroenterol.* 2015;21:4457-4465.
- Crohn's and Colitis Foundation. IBD surveys/questionnaires for clinical practice. <https://www.crohnscolitisfoundation.org/sites/default/files/legacy/science-and-professionals/programs-materials/ibd-nurses/best-practices/ibd-patient-intake-data-sheet-2.pdf>. Accessed September 21, 2021.
- Ghosh S, Casellas F, O'Shea C, et al. Extraintestinal manifestations and quality of life in patients with ulcerative colitis: 1-year data from ICONIC. *J Crohns Colitis.* 2019;13(suppl 1):S314-S315.
- Gionchetti P, Calabrese C, Rizzello F. Inflammatory bowel diseases and spondyloarthropathies. *J Rheumatol Suppl.* 2015;93:21-23.
- Harbord M, Annese V, Vavricka SR, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. *J Crohns Colitis.* 2016;10(3):239-254.
- Hedin CRH, Vavricka SR, Stagg AJ, et al. The pathogenesis of extraintestinal manifestations: implications for IBD research, diagnosis, and therapy. *J Crohns Colitis.* 2019;13(5):541-554.
- Huang V, Mishra R, Thanabalan R, Nguyen GC. Patient awareness of extraintestinal manifestations of inflammatory bowel disease. *J Crohns Colitis.* 2013;7(8):e318-e324.
- IBD Standards Group. Standards for the healthcare of people who have inflammatory bowel disease (IBD), 2013 update. Available at: <http://s3-eu-west-1.amazonaws.com/files.crohnsandcolitis.org.uk/Publications/PPR/ibd-standards.pdf>. Accessed September 9, 2021.
- Isene R, Bernklev T, Hoie O, et al. Extraintestinal manifestations in Crohn's disease and ulcerative colitis: results from a prospective, population-based European inception cohort. *Scand J Gastroenterol.* 2015;50(3):300-305.
- Jansen FM, Vavricka SR, den Broeder AA, de Jong EM, Hoentjen F, van Dop WA. Clinical management of the most common extra-intestinal manifestations in patients with inflammatory bowel disease focused on the joints, skin and eyes. *United European Gastroenterol J.* 2020;8(9):1031-1044.
- Kane SV. Health maintenance assessment for patients with inflammatory bowel disease. *Gastroenterol Hepatol (N Y).* 2017;13:500-503.
- Katsanos KH, Torres J, Roda G, Brygo A, Delaporte E, Colombel JF. Review article: non-malignant oral manifestations in inflammatory bowel diseases. *Aliment Pharmacol Ther.* 2015;42(1):40-60.
- Keller R, Mazurak N, Fantasia L, et al. Quality of life in inflammatory bowel diseases: it is not all about the bowel. *Intest Res.* 2021;19(1):45-52.
- Lankarani KB, Sivandzadeh GR, Hassanpour S. Oral manifestation in inflammatory bowel disease: a review. *World J Gastroenterol.* 2013;19(46):8571-8579.

References

- Longman RS, Scherl EJ. Medical management of extraintestinal manifestations of ulcerative colitis. In: Lichtenstein G, ed. *Medical Therapy of Ulcerative Colitis*. New York, NY: Springer Science+Business Media; 2014:377-391.
- Mady R, Grover W, Butrus S. Ocular complications of inflammatory bowel disease. *ScientificWorldJournal*. 2015;2015:438402.
- Marotto D, Atzeni F, Ardizzone S, Monteleone G, Giorgi V, Sarzi-Puttini P. Extra-intestinal manifestations of inflammatory bowel diseases. *Pharmacol Res*. 2020;161:105206.
- Mays JW, Sarmadi M, Moutsopoulos NM. Oral manifestations of systemic autoimmune and inflammatory diseases: diagnosis and clinical management. *J Evid Based Dent Pract*. 2012;12(3 suppl):265-282.
- Moss A, Pham NV. Guidelines for screening and surveillance in inflammatory bowel disease: just a “rough guideline” or a cornerstone of high-quality modern medical practice? *Gastrointest Endoscopy*. 2015;82:715-717.
- Olpin JD, Sjoberg BP, Stilwill SE, et al. Beyond the bowel: extraintestinal manifestations of inflammatory bowel disease. *Radiographics*. 2017;37(4):1135-1160.
- Papageorgiou SN, Hagner M, Nogueira AV, Franke A, Jäger A, Deschner J. Inflammatory bowel disease and oral health: systematic review and a meta-analysis. *J Clin Periodontol*. 2017;44(4):382-393.
- Regueiro M, Click B, Holder D, Shrank W, McAnallen S, Szigethy E. Constructing an inflammatory bowel disease patient-centered medical home. *Clin Gastroenterol Hepatol (N Y)*. 2017;15:1148-1153.
- Rubin DT, Ananthkrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
- Siao D, Velayos F. Avoiding rash decision making: skin cancer screening of patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol*. 2014;12:274-276.
- Troncoso LL, Biancardi AL, de Moraes HV, Jr., Zaltman C. Ophthalmic manifestations in patients with inflammatory bowel disease: a review. *World J Gastroenterol*. 2017;23(32):5836-5848.
- Vadstrup K, Alulis S, Borsi A, et al. Extraintestinal manifestations and other comorbidities in ulcerative colitis and Crohn disease: a Danish nationwide registry study 2003–2016. *Crohns Colitis 360*. 2020;2(3):otaa070.
- Vavricka SR, Brun L, Ballabeni P, et al. Frequency and risk factors for extraintestinal manifestations in the Swiss inflammatory bowel disease cohort. *Am J Gastroenterol*. 2011;106(1):110-119.
- Vavricka SR, Schoepfer A, Scharl M, et al. Extraintestinal manifestations of inflammatory bowel disease. *Inflamm Bowel Dis*. 2015;21(8):1982-1992.
- Wiens J, Rankin JA, Then KL. Arthropathies in inflammatory bowel disease: a review for clinicians. *Gastroenterol Nurs*. 2017;40(6):496-503.