Livestream: How Low Can You Go? Targeting of Deep Remission in the Management of Crohn's Disease

SYLLABUS & COURSE GUIDE

A Free, 90-Minute Live Activity
Premiere Date: Sunday, October 27, 2024
6:00 AM - 7:30 AM ET

Login:
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Faculty:
Bruce E. Sands, MD, MS (Moderator)
Marita Kametas, MSN, APN, FNP-BC, CMSRN, COCN
Millie D. Long, MD, MPH

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Information for Participants

Statement of Need

Crohn's disease (CD) can cause progressive bowel damage, impaired quality of life, and permanent disability. Severity and presentation can vary widely from person to person, necessitating an individualized treatment approach. The use of more readily available imaging modalities such as intestinal ultrasound and magnetic resonance enterography can be added to standard monitoring practices to improve disease management. Additionally, targeting deeper remission at a histological level is an emerging treatment target for patients with CD. Clinicians in collaboration with a multidisciplinary care team must become knowledgeable on individualized care and novel imaging modalities to optimize treatment for patients with CD.

In this CME Outfitters livestream symposium, expert faculty will guide learners on how to integrate knowledge of the heterogeneity of CD in severity and manifestation into patient assessment and treatment. Learners will be instructed on utilizing alternative diagnostic and evaluation tools beyond colonoscopy for evaluating symptoms in patients with CD. Faculty will model incorporation of histopathologic treatment targets as an objective measure of inflammation in CD to inform clinical decision-making.

Learning Objectives

At the conclusion of this activity, learners will be able to better:

- Integrate knowledge of the heterogeneity of CD in severity and manifestation into patient assessment and treatment
- Utilize alternative diagnostic and evaluation tools beyond colonoscopy for evaluating symptoms in patients with CD
- Incorporate histopathologic treatment targets as an objective measure of inflammation in CD to inform clinical decision-making

Financial Support

This activity is supported by an independent educational grant from Lilly.

Target Audience

U.S. and international gastroenterologists, and gastroenterology nurse practitioners (NPs) and physician associates (PAs) (with the exception of HCPs in the United Kingdom)

Faculty

BRUCE E. SANDS, MD, MS (MODERATOR)
Dr. Burrill B. Crohn Professor of Medicine
Chief, Division of Gastroenterology
Icahn School of Medicine at Mount Sinai
Mount Sinai Health System
New York, NY

Bruce E. Sands, MD, MS, is the Dr. Burrill B. Crohn Professor of Medicine in the Icahn School of Medicine at Mount Sinai in New York City and Chief of the Division of Gastroenterology in the Mount Sinai Health System. He is an expert in the management of inflammatory bowel disease (IBD) and has earned an international reputation for his care of patients with complex and refractory disease.

Dr. Sands was awarded his BA and MD from Boston University in Massachusetts, and he trained in internal medicine at the Hospital of the University of Pennsylvania in Philadelphia. After completing a gastrointestinal fellowship at Massachusetts General Hospital (MGH) in Boston, he joined the faculty of Harvard Medical School in Cambridge and served as the Acting Chief of the Gastrointestinal Unit at MGH. He moved to Mount Sinai in 2010 as Chief of the Dr. Henry D. Janowitz Division of Gastroenterology.

Dr. Sands is a past Chair of the Clinical Research Alliance of the Crohn's & Colitis Foundation of America, and served as Chair of the Immunology, Microbiology, and Inflammatory Bowel Disease Section of the American Gastroenterological Association. Additionally, Dr. Sands was the Chair of the International Organization for the Study of IBD (IOIBD). In 2016, Dr. Sands was awarded the Dr. Henry Janowitz Lifetime Achievement Award from the Crohn's & Colitis Foundation, that organization's highest honor. In 2023, Dr. Sands was the recipient of the Jacobi Medallion, Mount Sinai's most prestigious award for distinguished contributions to the field of medicine or extraordinary service to the hospital, health system, School of Medicine, or alumni community.

Dr. Sands is widely recognized for his innovative treatment of Crohn's disease and ulcerative colitis and for his expertise in the clinical investigation of new therapeutics. His research also explores IBD epidemiology and includes the creation of a population-based IBD cohort in Rhode Island, a project funded by both the National Institute of Health and the Centers for Disease Control and Prevention. He has served as an associate editor for the journal *Gastroenterology,* and has published more than 300 original manuscripts in leading journals such as *Gut*, *Gastroenterology*, and the *American Journal of Gastroenterology*. He was the lead investigator of the landmark studies ACCENT 2, UNIFI, and VARSITY, all published in the *New England Journal of Medicine,* and SEAVUE, published in *The Lancet*.

Dr. Sands reports the following relationships:

Consultant: Abbvie Inc.; Amgen Inc.; AstraZeneca; Boehringer-Ingelheim; Bristol Myers Squibb Company; Celltrion Inc.; Lilly; Galapagos; Genentech, Inc.; Gilead Sciences, Inc.; GSK; Janssen Pharmaceuticals, Inc.; Merck & Co., Inc.; Pfizer Inc.; Takeda Pharmaceuticals U.S.A., Inc.; Teva Pharmaceuticals USA, Inc.; and Ventyx Biosciences, Inc.

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Manager of Gastroenterology Advanced Practice Provider Services
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Chicago, IL

Marita Kametas, MSN, APN, FNP-BC, CMSRN, COCN, is a family nurse practitioner and ostomy specialist who treats adult patients with inflammatory bowel disease (IBD). She serves as the manager for the Advanced Practice Gastroenterology Service at the University of Chicago in Illinois. She volunteers her time as a mentor for the Crohn's and Colitis Advanced Practice Provider (APP) mentorship program and delivers empowering lectures to APPs to optimize their care of patients with IBD. She was awarded the honor of Distinguished APP of 2023 at the University of Chicago. She is currently pursuing a doctorate in nursing practice and a master's degree in public health at Johns Hopkins University in Baltimore, Maryland with an emphasis on diversity, equity, and inclusion.

Ms. Kametas reports the following financial relationships:

Advisory Board: Lilly and Pfizer Inc.

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Speakers Bureau: Abbvie Inc.; Janssen. Pharmaceuticals, Inc.; and Pfizer Inc.

MILLIE D. LONG, MD, MPH
Professor of Medicine
Vice-Chief for Education
Director, Gastroenterology and Hepatology Fellowship Program
Division of Gastroenterology and Hepatology
University of North Carolina
Chapel Hill, NC

Millie D. Long, MD, MPH, is board certified in internal medicine, preventive medicine, and gastroenterology. Dr. Long received her medical degree from University of Virginia in 2002. She then completed residency in internal medicine and a chief residency at University of Alabama at Birmingham. She completed fellowships in gastroenterology and hepatology, preventive medicine, and inflammatory bowel disease, all at University of North Carolina. She is currently Professor of Medicine in the Department of Medicine and Director of the Gastroenterology and Hepatology Fellowship Program at University of North Carolina at Chapel Hill.

Dr. Long's clinical practice is at the UNC Multidisciplinary Inflammatory Bowel Diseases (IBD) Center. Her research interests include prevention of complications of IBD, women's health, and clinical epidemiology. Dr. Long has contributed to over 200 peer-reviewed publications, book chapters, and review articles and to the medical literature. She is the current co-Editor in Chief of the *American Journal of Gastroenterology*. She also serves as an invited reviewer for journals such as *Inflammatory Bowel Diseases* and *Gastroenterology.*

Dr. Long is a fellow of the American College of Gastroenterology, where she serves on the Board of Trustees. She is also a fellow of the American Gastroenterological Association and the Crohn's and Colitis Foundation, where she co-chairs the Clinical Research Alliance.

Dr. Long reports the following financial relationships:

Consultant: AbbVie Inc.; Bristol Myers Squibb Company; Intercept Pharmaceuticals, Inc.; Janssen Pharmaceuticals, Inc.; Lilly; Pfizer Inc.; Prometheus Biosciences, Inc.; Takeda Pharmaceuticals U.S.A., Inc.; and Target RWE

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Targeting of Deep Remission in the Management of Crohn's Disease
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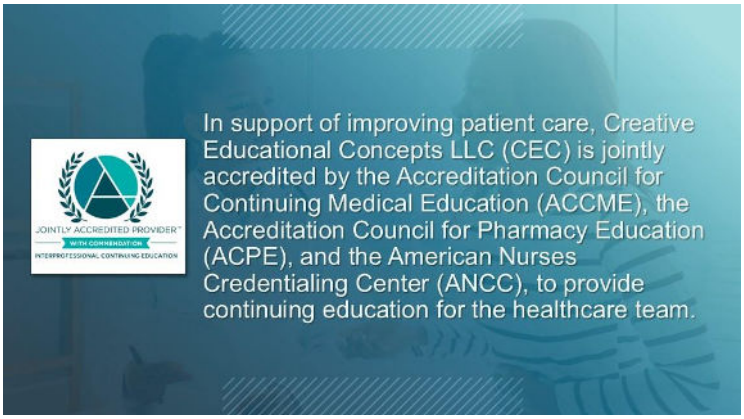
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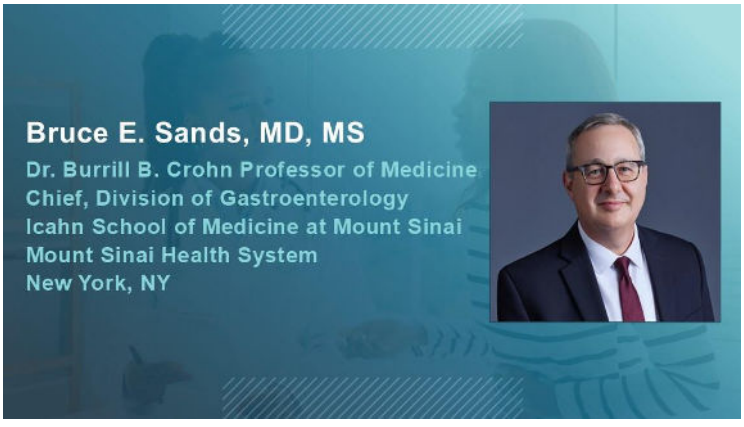
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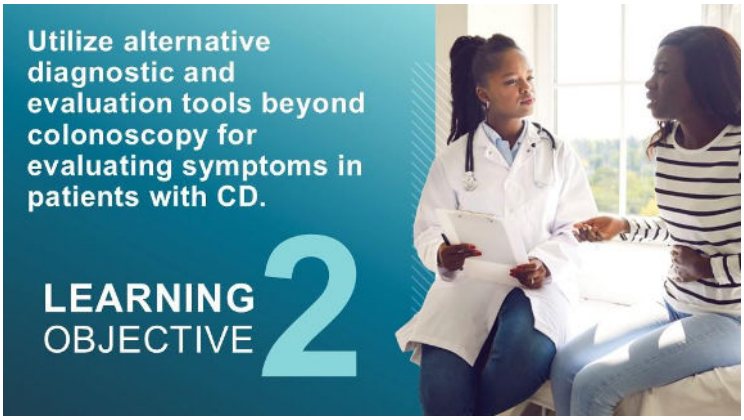
Integrate knowledge of the heterogeneity of CD in severity and manifestation into patient assessment and treatment.
LEARNING OBJECTIVE 1


Utilize alternative diagnostic and evaluation tools beyond colonoscopy for evaluating symptoms in patients with CD.
LEARNING OBJECTIVE 2

Incorporate histopathologic treatment targets as an objective measure of inflammation in CD to inform clinical decision-making.

LEARNING OBJECTIVE 3

Disease Heterogeneity in CD

Marita Kametas, MSN, APN, FNP-BC, CMSRN, COCN

CD Classification and Risk Factors for Severe Disease

Risk Factors for Severe Disease

- Under age 30 at diagnosis
- Extensive anatomic involvement
- Perianal disease
- Severe rectal disease
- Deep ulcers
- Previous surgical resection
- Stricturing behavior
- Penetrating behavior

Montreal Classification

- Age at diagnosis
  - < 17
  - 17-40
  - > 40
- Location-terminal ileum +/- limited cecal disease, colonic, ileocolonic, isolated upper
- Behavior: stricturing, penetrating or perianal involvement

Santiago P, et al. Am J Gastroenterol. 2024;119(1):147-154.

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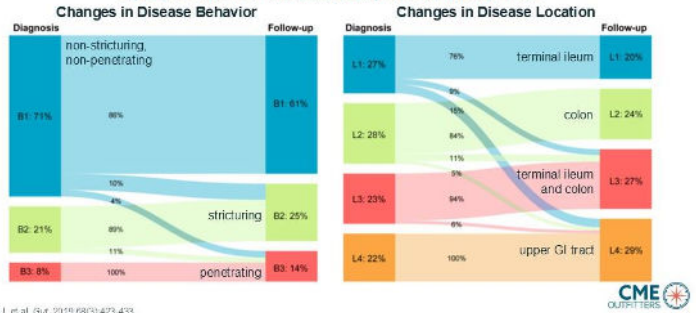
Disease Course Frequently Changes in CD

Epi-IBD Cohort: 5-Year Follow-Up of Patients with CD



Rieder F, et al. Gut. 2019;68(3):472-477.

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CD Activity Versus Disease Severity

Activity
- Current inflammatory burden
- Current symptom burden
- Objective and subjective assessments of current activity

Severity
- Historical disease behavior
- Need for surgery
- Extent of bowel involvement
- Complications

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Cockburn E, et al. Clin Med (Lond). 2021;21(6):549-557.

Complexity Complicates CD Monitoring and Treatment

- Age of diagnosis
- Extra-intestinal manifestations
- Past surgeries
- Disease location
- Previous treatments
- History of nutritional deficiencies
- Disease behavior
- Concomitant inflammatory conditions
- Historical disease behavior vs today

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Cushing K, et al. JAMA. 2021;326(2):169-170.

Extraintestinal Manifestations (EIMs) are Unpredictable but Frequent in CD

- EIMs occur in varying frequency
  - Up to 50% of patients with IBD have at least 1 EIM
- EIMs can occur before or after diagnosis of IBD
  - One in four patients develop an EIM before diagnosis
- Can be dependent on or independent of intestinal inflammation

Extraintestinal manifestation of IBD	Inflammatory pathology located outside the gut
Extraintestinal complication of IBD	Sequelae of intestinal inflammation

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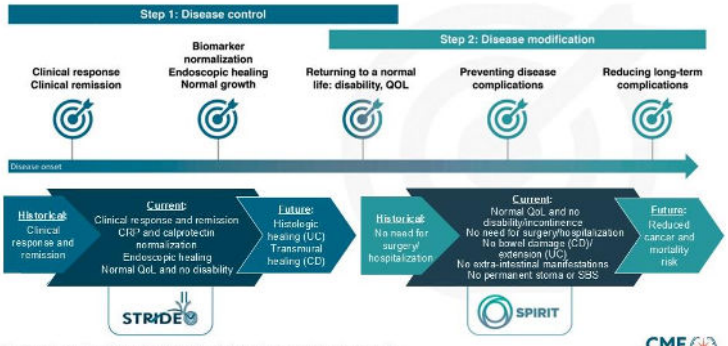
Gordon H, et al. Journal of Crohn's and Colitis. 2023;18(1):1-37. Rieder G, et al. Gastroenterology. 2021;161(4):1118-1132.

Treat-to-Target (T2T) Approach in IBD



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CRP = C-reactive protein; QoL = quality of life; SBS = short bowel syndrome; UC = ulcerative colitis.

Le Berre C, et al. Gastroenterology. 2022;162(6):1424-1438.

Outcomes Associated with Mucosal and Transmural Healing in CD

- Lower rates of corticosteroid utilization
- Lower rates of hospitalization
- Decreased rates of relapse or need for treatment escalation
- Decreased rate of surgical intervention

Rubin DT, et al. *Inflamm Bowel Dis*. 2024;[Epub ahead of print]. In press.

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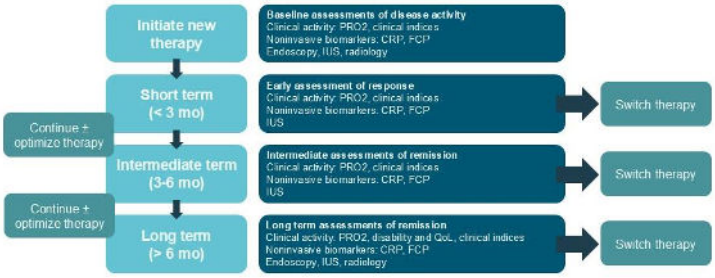
Evaluating Response Using a T2T Approach



PRO2 = patient reported outcome 2; FCP = fecal calprotectin; IUS = intestinal ultrasound.
Srinivasan AR. *World J Gastroenterol*. 2024;30(11):59-69.

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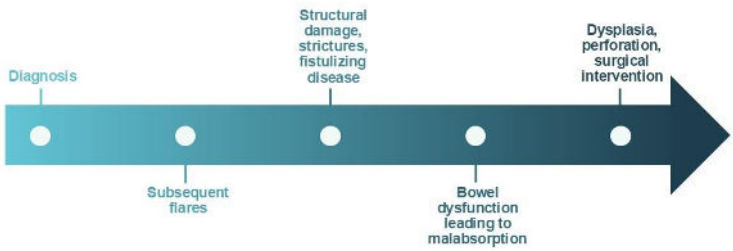
Consequences of Recurrent Inflammatory Activity



Cockburn E, et al. *Clin Med (Lond)*. 2022;22(6):549-557.

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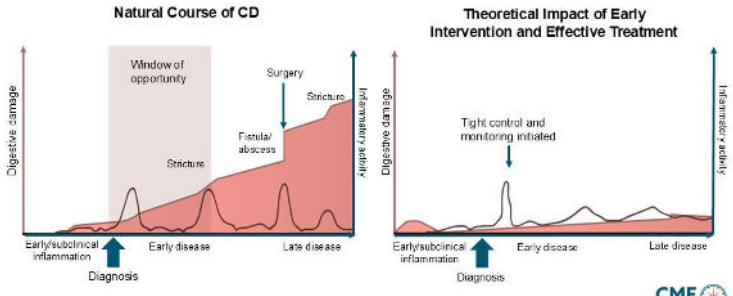
Early Diagnosis and Early Treatment are Key to Preventing Complications



Adapted from Colombel JF, et al. *Gastroenterology*. 2017;152(2):351-361.

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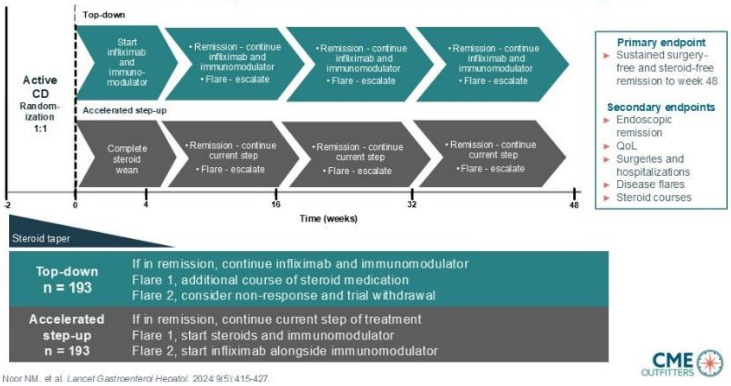
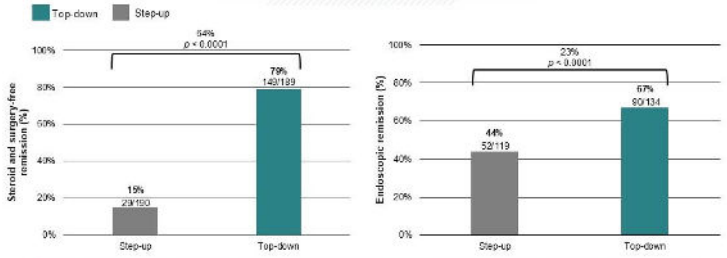
PROFILE: Comparison of Two CD Treatment Strategies



Top-down n = 193	If in remission, continue infliximab and immunomodulator Flare 1, additional course of steroid medication Flare 2, consider non-response and trial withdrawal
Accelerated step-up n = 193	If in remission, continue current step of treatment Flare 1, start steroids and immunomodulator Flare 2, start infliximab alongside immunomodulator

Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

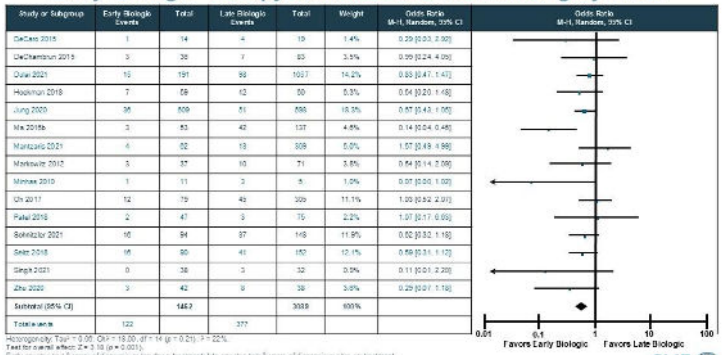
PROFILE: Top-Down Treatment Strategy of Infliximab + Immunomodulator Led to Improved Remission Rates



Requiring failure of conventional step therapy prior to advanced therapy is not recommended

Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

Early Biologic Therapy Decreases the Risk of Surgery in CD



Heterogeneity: Tau² = 0.00; Chi² = 18.00, df = 14 (p = 0.21); I² = 22%.
Test for overall effect: Z = 3.18 (p = 0.001).
Early was less than 3 years of diagnosis on top-down treatment; late was less than 3 years of diagnosis on step-up treatment.

CI = confidence interval
Law CCY, et al. *Inflamm Bowel Dis*. 2024;30(7):1080-1086.

Summary

- Disease severity that considers a patient's overall disease course should drive treatment selection rather than current disease activity
- Tight control of inflammation can prevent complications in CD
- Early advanced therapy is appropriate without requiring failure of conventional step therapy

Faculty Discussion

What are some unmet needs in clinical practice or practice areas not addressed by guidelines?

Monitoring Beyond Endoscopy: Noninvasive Monitoring Tools in Gastroenterology Practice

Millie D. Long, MD, MPH

Limitations of Endoscopy in CD

- Variability in scoring between observers
- Disease activity below mucosal surface is not captured
- Utility limited by patient's ability to access care and resources
- Patients require preparation, time off work, and post-procedure support
- Time-consuming
- Delays can occur for many reasons (scheduling, cost, etc.)

CME OUTFITTERS

Schoeuien KM, et al. J Clin Med. 2023;12(5):1995. Rahabinsky N, et al. Crohns Colitis 360. 2023;5(2):otad012.

Noninvasive Monitoring

- Biomarkers
- Cross-sectional imaging
  - Magnetic resonance enterography (MRE)
  - Intestinal ultrasound (IUS)
  - Computed tomography enterography (CTE)
- Capsule endoscopy

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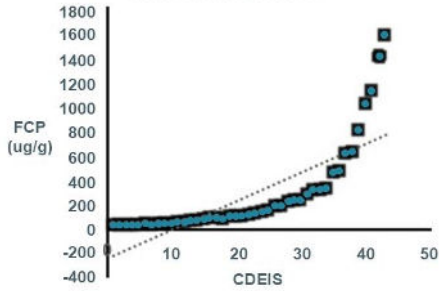
Schoeuien KM, et al. J Clin Med. 2023;12(5):1995.

FCP Levels Significantly Correlate with MRE Disease Activity in Colonic CD



CDEIS = Crohn's Disease Endoscopic Index of Severity.
Somwaru AS, et al. *BMC Gastroenterol*. 2019;19:210.

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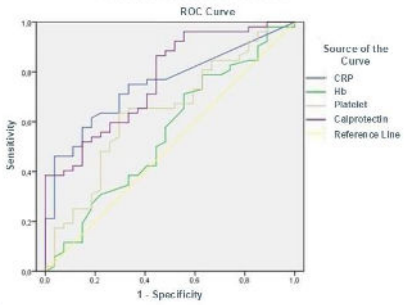
Fecal Calprotectin is the Best Biomarker for Assessing Overall CD Activity



Diagonal segments are produced by ties.
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FCP Levels Significantly Correlate with MRE Disease Activity in Colonic CD

- 27-year-old female with colonic CD and abdominal pain of increasing severity
- FCP of 436 µg/g, MaRIA score of 15 on MRE (severe), and CDEIS of 26 on colonoscopy

MaRIA = Magnetic Resonance Index of Activity.
Somwaru AS, et al. *BMC Gastroenterol*. 2019;19:210.

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FCP < 50 µg/g in Post-Ileocolonic Resection Associated with Low Risk of Recurrence

	FCP < 50 µg/g (*n* = 15)	FCP ≥ 50 µg/g (*n* = 22)	*p*-value
Low-risk, n (%)	7 (47%)	13 (59%)	0.51
High-risk received prophylaxis, n (%)	8 (53%)	9 (41%)	
Median time to endoscopic recurrence, days	-	145 (56-217)	N/A
Ever endoscopic recurrence, n (%)	**0 (0%)**	**9 (36%)**	**0.006**
Median time to surgical recurrence, days	-	1416 (839-1677)	N/A
Ever surgical recurrence, n (%)	0 (0%)	3 (14%)	0.26

LI T, et al. *Crohns Colitis 360*. 2024;6(1):otae016.

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Multiple Factors and Conditions are Associated with Elevated FCP Levels

Infectious	Inflammatory Conditions
Bacterial dysentery	Inflammatory bowel disease
Giardia lamblia	Autoimmune enteropathy
Helicobacter pylori gastritis	Cirrhosis
Infectious diarrhea	Cystic fibrosis
Viral gastroenteritis	Diverticulitis
Neoplasms	Eosinophilic colitis/enteritis
Colonic and gastric polyps	Gastroesophageal reflux disease
Colorectal cancer	Juvenile polyp
Gastric carcinoma	Microscopic colitis
Intestinal lymphoma	Peptic ulcer
	Untreated celiac disease
Drugs	**Other**
NSAIDs	Age < 5 years
PPIs	Untreated food allergy

NSAIDs = nonsteroidal anti-inflammatory drugs; PPIs = proton pump inhibitors.
Rispens R, et al. Can J Gastroenterol Hepatol. 2015;29(7):368-379.

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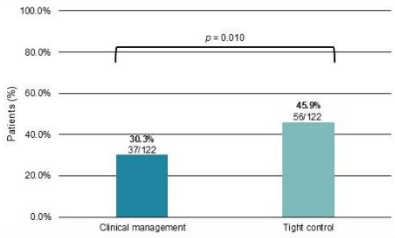
CALM: Tight Control Monitoring with Biomarkers is Better Than Symptoms Alone

Primary outcome: CDEIS < 4 and no deep ulcers at week 48



More than half of patients in the tight control arm did not achieve mucosal healing

Colombel JF, et al. *Lancet*. 2017;390(10114):2779-2789.

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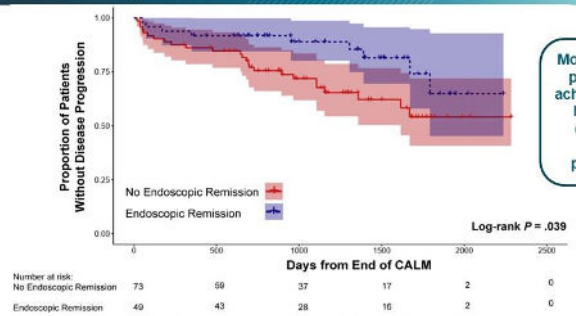
Patients Who Achieve Mucosal Healing Are Less Likely to Have Disease Progression



More than 1/4 of patients who achieve mucosal healing still experience disease progression

Deep remission defined as CD endoscopic index of severity scores < 4, with no deep ulcerations or steroid treatment, for 8 or more weeks.
Ungaro R. Gastroenterology. 2020;159(1):129-147.

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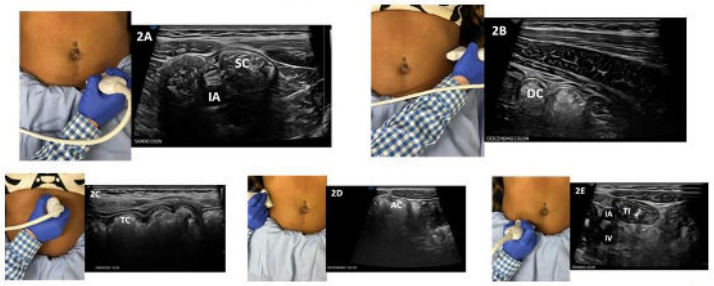
Noninvasive Monitoring to Achieve Tight Control

IUS Quickly Visualizes the Colon and Terminal Ileum



Kellar A, et al. *J Pediatr Gastroenterol Nutr*. 2023;76(2):142-148.

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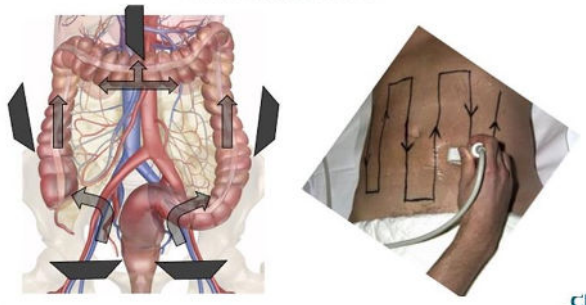
IUS Technique Follows the Same Standardized Approach Regardless of Disease Location



Images courtesy of Dr. Long.

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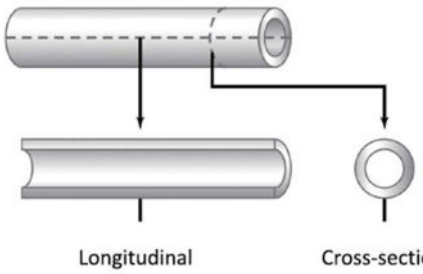
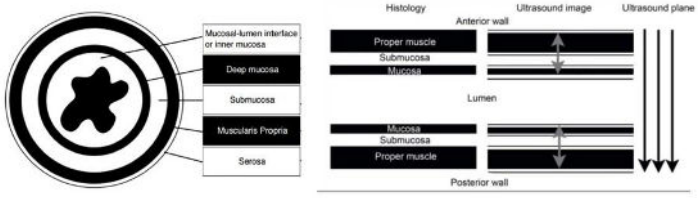
Two Major Scan Planes on IUS



Images courtesy of Dr. Long.

CME OUTFITTERS

Bowel Layers on IUS



Nylund K, et al. *Ultraschall Med*. 2012;33(7):E225-E232.

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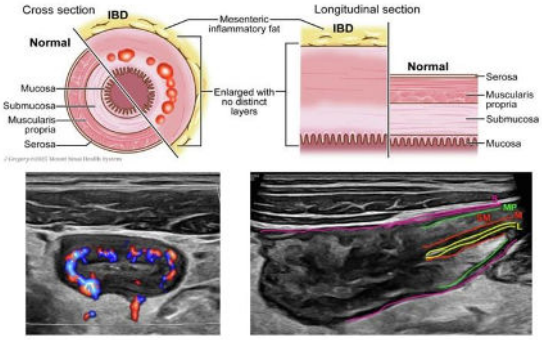
Bowel Wall Layers and IUS Features of Active Disease



Chavannes M, et al. *Clinical Gastroenterology and Hepatology*. 2024;22(9):1780-1795.

CME OUTFITTERS

ARS Question

What are the measures of inflammation on IUS?

A. Bowel wall thickness
B. Bowel wall stratification
C. Inflammatory fat stranding
D. Bowel wall hyperemia
E. All of the above
F. I don't know

Goodsell TM, et al. *J Crohns Colitis*. 2021;15:125-142.

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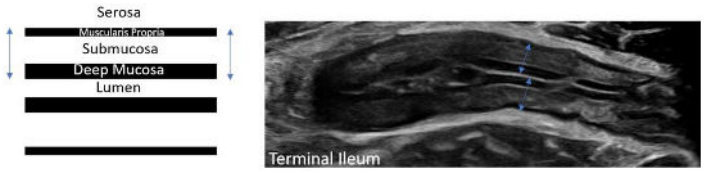
Bowel Wall Thickness is the Most Important Measure of IBD Activity



Kellar A, et al. *J Pediatr Gastroenterol Nutr*. 2023;76(2):142-148.

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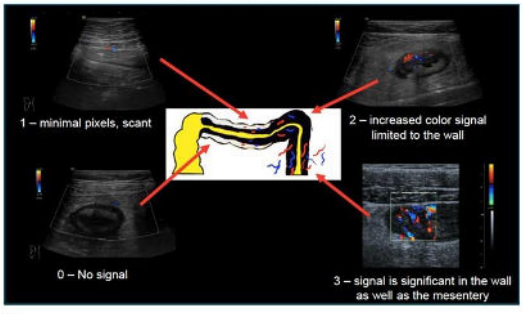
Bowel Wall Hyperemia is Graded by a Modified Limberg Score



Images courtesy of Dr. Long.

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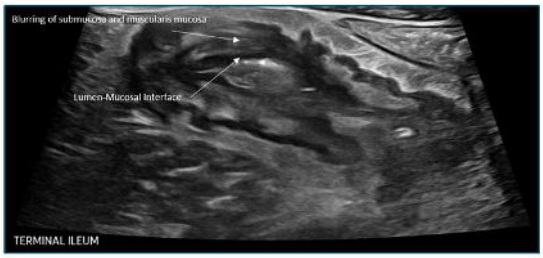
Loss of Preservation of Bowel Wall Layer Stratification



Kellar A, et al. *J Pediatr Gastroenterol Nutr*. 2023;76(2):142-148.

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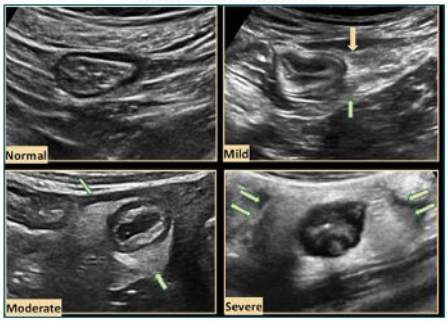
Inflammatory Fat Presence on IUS as a Marker of IBD Activity and Chronicity



Images courtesy of Dr. Lone.

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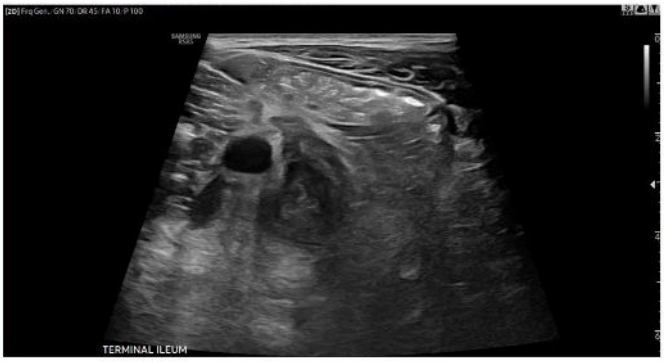

Images courtesy of Dr. Lone.

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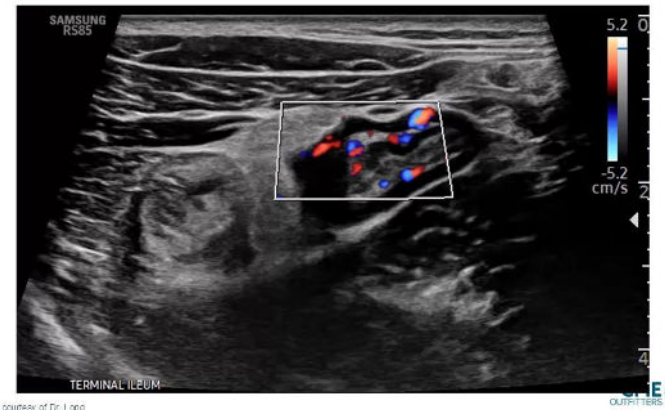

Images courtesy of Dr. Lone.

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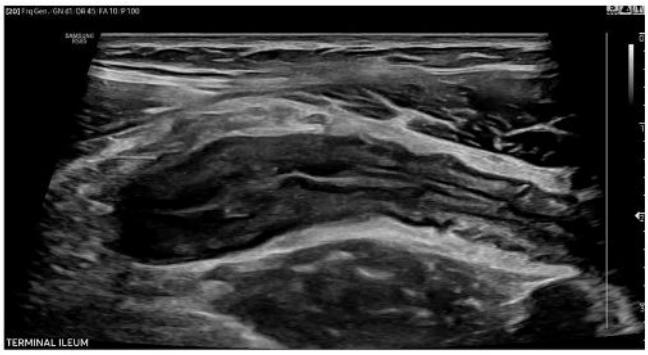

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Who Should IUS Be Performed On?

Best Performance	Most Difficult
Terminal ileum/ileum	Rectum
Sigmoid colon	Left flexure
Transverse colon	Duodenum
Ascending colon/cecum	Jejunum

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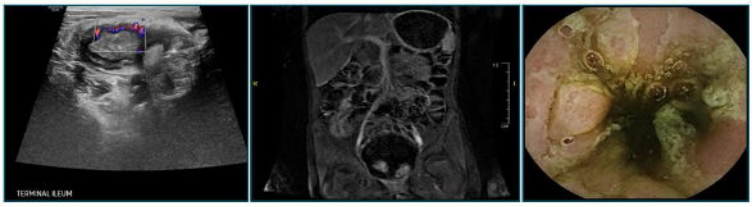
IUS is Accurate When Compared to MRI and Endoscopy



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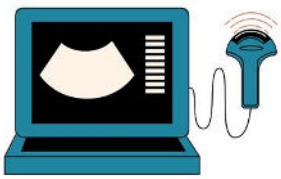
Advantages for IUS Evaluation of Disease Activity in CD

- Noninvasive
- Accurate
- Reproducible results
- Well-tolerated by patients
- Patient able to see scan results in real time
- No radiation exposure (monitoring option in pregnancy)



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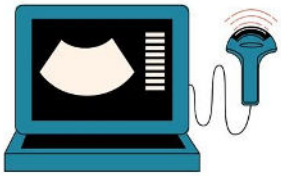
Limitations and Barriers for IUS

- Needs specialized equipment
- Image interpretation requires training
- Scheduling and cleaning protocols
- Poorer image quality in patients with obesity (cannot use high frequency transducer)
- Cannot evaluate proximal small bowel



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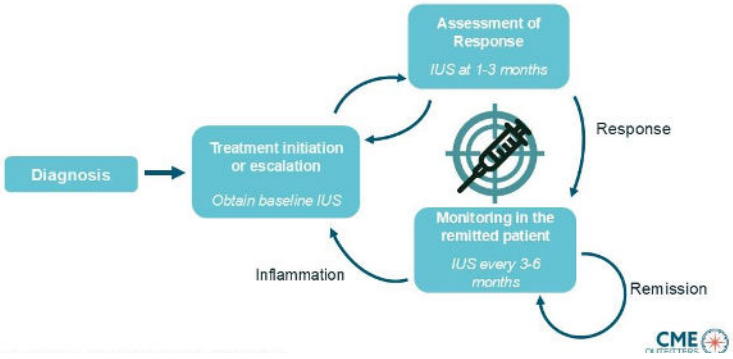
Monitoring Disease Activity in Practice Utilizing IUS



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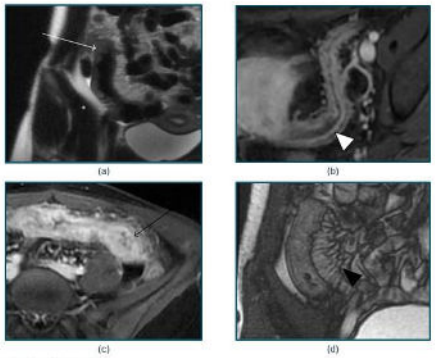
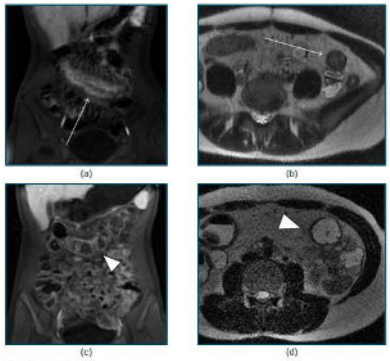
MRE Features of Active CD



CME OUTFITTERS

MRE Mucosal Healing in CD



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MRE is Not Accurate for the Colon

Ileocolonoscopy		MaRIA score 0	MaRIA score 1	MaRIA score ≥ 2
Transverse colon (n = 140)	Absence of lesions (n = 70)	70 (100)	0	0
	Inflammatory lesions without ulceration (n = 52)	49 (94)	1(2)	2 (4)
	Severe lesions (n = 18)	14 (78)	1 (5)	3 (17)
Descending colon (n = 140)	Absence of lesions (n = 63)	61 (96)	1 (2)	1 (2)
	Inflammatory lesions without ulceration (n = 59)	49 (83)	1 (2)	9 (15)
	Severe lesions (n = 18)	12 (67)	1(5)	5(28)
Sigmoid colon (n = 140)	Absence of lesions (n = 61)	58 (95)	0 (0)	3 (5)
	Inflammatory lesions without ulceration (n = 63)	51 (81)	0 (0)	12 (19)
	Severe lesions (n = 16)	10 (63)	1 (6)	5 (31)
Rectum (n = 140)	Absence of lesions (n = 62)	50 (81)	2 (3)	10 (16)
	Inflammatory lesions without ulceration (n = 65)	49 (75)	2 (3)	14 (22)
	Severe lesions (n = 13)	7 (54)	1 (8)	5 (38)

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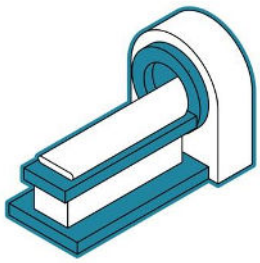
Advantages of MRE in CD

- Identifies mural and extramural complications
- No radiation exposure
- Differentiates inflammation, stricturing, and penetrating disease
- Useful for treatment/intervention planning



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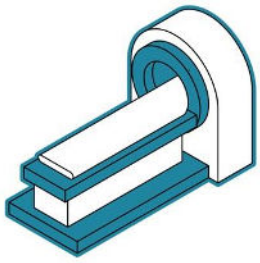
Limitations and Barrers for MRE

- Cost
- Limited accuracy in colonic disease
- Time requirement
- Difficult for patients with claustrophobia
- Differentiation of inflammation from fibrosis can be difficult



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Video Capsule Endoscopy in CD

- Can be used in surveillance and diagnosis
- Particularly beneficial in patients with proximal small bowel disease and a normal ileocolonoscopy
- Risk of capsule retention with strictures
- Capsule endoscopy can support CD diagnosis in patients with normal upper and lower endoscopy studies
  - Ge et al. – 13/20 (65%) of patients examined
  - Herrerías et al. – 9/21 (43%) of patients examined

Levartovsky A, et al. *Diagnostics (Basel)*. 2023;13(8):1507. Ge ZZ, et al. *World J Gastroenterol*. 2004;10:1349-1352. Herrerías JM, et al.

CME

Summary

- Favor calprotectin over CRP in biomarker monitoring
- IUS can be utilized in point-of-care assessment in patients with CD
- Noninvasive monitoring through IUS, MRE, and capsule endoscopy is effective in tight control

Faculty Discussion

How have you incorporated noninvasive monitoring strategies into practice?

Histopathologic Remission in CD

Bruce E. Sands, MD, MS

Defining Histopathologic Remission

ARS Question

Which of the following parameters can be measured by histopathologic evaluation in CD?

A. Fibrosis
B. Disease distribution
C. Fistula formation
D. Duration of disease
E. I don't know

CME

Geboes Score and Derived RHI

GS	Morphology	RHI
Grade 0: Architectural changes	0.0 No abnormality	0
	0.1 Mild abnormality	0
	0.2 Mild/moderate diffuse or multifocal abnormalities	0
	0.3 Severe diffuse or multifocal abnormalities	0
Grade 1: Chronic inflammatory infiltrate	1.0 No increase	0
	1.1 Mild but unequivocal increase	1
	1.2 Moderate increase	2
	1.3 Marked increase	3
Grade 2A: Eosinophils in lamina propria	2A.0 No increase	0
	2A.1 Mild but unequivocal increase	0
	2A.2 Moderate increase	0
	2A.3 Marked increase	0
Grade 2B: Neutrophils in lamina propria	2B.0 No increase	0
	2B.1 Mild but unequivocal increase	2
	2B.2 Moderate increase	4
	2B.3 Marked increase	6

GS = Geboes score; RHI = Roberts histopathological index; GS: histological remission ≤ 2.0, histological response ≤ 3.0; RHI: histological remission ≤ 3, histological response ≤ 9

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Geboes Score and Derived RHI

GS	Morphology	RHI
Grade 3: Neutrophils in epithelium	3.0 None	0
	3.1 < 5% crypts involved	3
	3.2 < 50% crypts involved	6
	3.3 ≥ 50% crypts involved	9
Grade 4: Crypt destruction	4.0 None	0
	4.1 Probable - local excess of neutrophils in part of the crypts	0
	4.2 Probable - marked attenuation	0
	4.3 Unequivocal crypt destruction	0
Grade 5: Erosions and ulcerations	5.0 No erosion, ulceration or granulation tissue	0
	5.1 Recovering epithelium + adjacent inflammation	5
	5.2 Probable erosion – focally stripped	5
	5.3 Unequivocal erosion	10
	5.4 Ulcer or granulation tissue	10

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Nancy Index (NI)

Grade	Morphology
0	No or only mild increase in chronic inflammatory cells
1	Moderate or severe increase in chronic inflammatory cells (lymphocytes, plasma cells, and eosinophils) defined as presence of an increase in chronic inflammatory cells that is easily apparent
2	Mild increase in neutrophils defined as few or rare neutrophils in lamina propria or in the epithelium that are difficult to see
3	Moderate or severe increase in neutrophils defined as presence of multiple clusters of neutrophils in lamina propria and/or in epithelium that are easily apparent
4	Ulcers or erosions defined as loss of colonic crypts replaced with "immature" granulation tissue (disorganized blood vessels with extravasated neutrophils) or the presence of fibrinopurulent exudate

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Histologic Healing is Associated with Better Long-Term Outcomes in CD

Study	Type of Study	Disease	N Patients	Endoscopic Activity	Histological Index	Outcome
Brennan et al.	Retrospective cohort study	CD	82 patients, follow-up for at least 6 months. A total of 103 patients with CD underwent elective colonoscopies during clinical remission.	55 patients (53%) in endoscopic healing, 48 patients (47%) with active disease.	A semiqualitative score (0 to 3) was assigned for the histologic characteristics in each of the biopsy samples.	At 12 months, the rate of relapse was 25.5% in patients with histologic activity, compared with only 2.4% of patients without histologic activity at baseline. The presence of histological activity was associated with higher flare rates ($p < 0.05$).
Christensen et al.	Retrospective study	CD	101 patients, follow-up for a median of 21 months.	63% of patients with endoscopic remission.	55% of patients achieved histologic remission.	CR occurred in 42% (n = 42) of patients. Histologic healing was associated with a decreased risk of CR (HR 2.05, 95% CI, 1.07-3.94; $p = 0.031$).

Association between histological activity and the risk of clinical relapse. A p-value < 0.05 is considered statistically significant.

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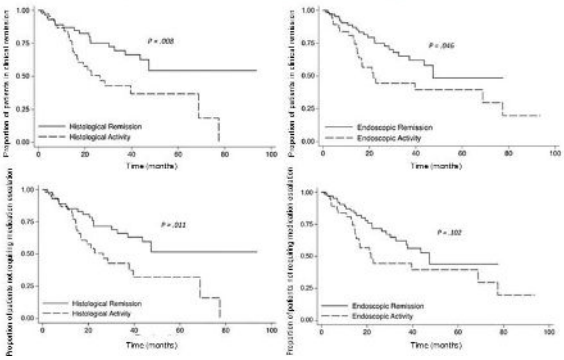
Improved Outcomes with Endoscopic and Histologic Healing in Ileal CD



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Global Histologic Disease Activity Score (GHAS)

Epithelial damage	0 - Normal
	1 - Focal pathology
	2 - Extensive pathology
Architectural changes	0 - Normal
	1 - Moderately disturbed (< 50%)
	2 - Severely disturbed (> 50%)
Infiltration of mononuclear cells in the lamina propria	0 - Normal
	1 - Moderate increase
	2 - Severe increase
Infiltration of polymorphonuclear cells in the lamina propria	0 - Normal
	1 - Moderate increase
	2 - Severe increase
Polymorphonuclear cells in epithelium	1 - In surface epithelium
	2 - Cryptitis
	3 - Crypt abscess

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Components of the IBD-DCA Score

Variable	Classification
Distribution (D)	0 = Normal 1 = < 50% of the time tissue per same biopsy site 2 = ≥ of tissue affected per same biopsy site
Chronic features (C)	0 = Normal 1 = Crypt distortion *and/or* mild lymphoplasmacytosis 2 = Marked lymphoplasmacytosis *and/or* marked basal plasmacytosis
Activity features (A)	0 = Normal 1 = Two or more neutrophils in lamina propria in one high-power field (HPF) *and/or* intraepithelial neutrophils (any number) 2 = Crypt abscesses, erosions, ulcers

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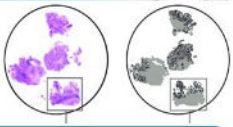
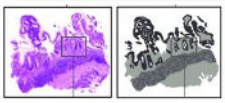
IBD-DCA Scoring Example

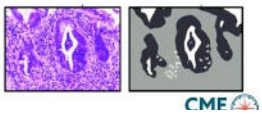
Distribution "D": overall affected tissue in scanning magnification (2.5-4x). Ex. four biopsies, affected by inflammatory and architectural changes in > 50% of tissue = D2





Chronicity "C": Assess in magnification 4 to 10x.
Ex. shows architectural distortion as and prominent bandlike (lympho-) plasmacytosis = C2

Activity "A": assess in higher magnification.
Ex. shows cluster of neutrophilic granulocytes in tunica propria and some granulocytes in crypt epithelium = A1



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Summary

- Several histopathologic indices exist for scoring disease activity in CD
- Several important long-term outcomes have been associated with histologic healing in CD

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Faculty Discussion

What is the current state of incorporating histopathologic activity measures in patients with CD in practice?

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Consider disease severity and a patient's overall disease course when making choices regarding treatment selection
- Utilize advanced therapies in patients with CD without first requiring failure or intolerance of conventional therapies
- Incorporate noninvasive monitoring strategies into the routine care of patients with CD

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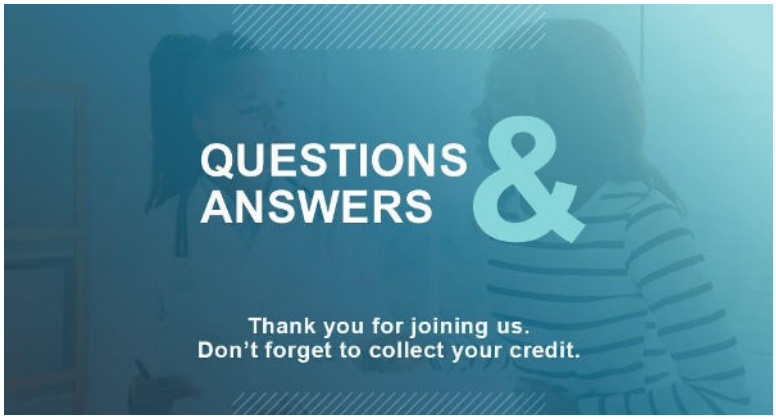
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