

ENDOSCOPY AND DIAGNOSTIC IMAGING

Part 2

Colon and Hepatobiliary

COMPLEMENTING GI PRACTICE REVIEW

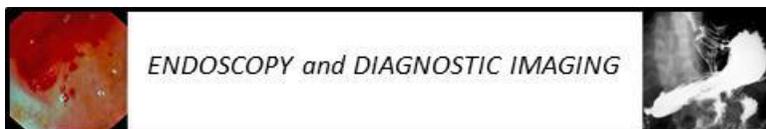
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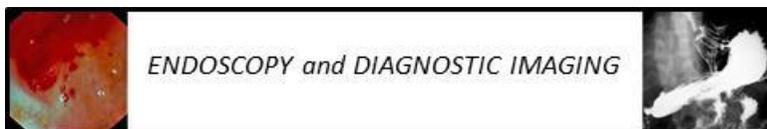
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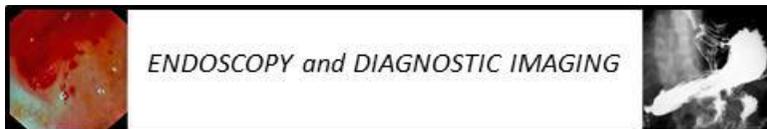
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ARE YOU PREPARING FOR EXAMS IN GASTROENTEROLOGY AND HEPATOLOGY?

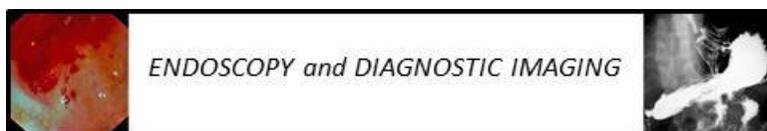
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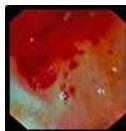
Gastroenterology and Hepatology

- First Principles of Gastroenterology and Hepatology, 6th edition
- GI Practice Review, 2nd edition
- Endoscopy and Diagnostic Imaging, Part I
- Scientific Basis for Clinical Practice in Gastroenterology and Hepatology

General Internal Medicine

- Mastering the OSCEs in Internal Medicine. Part I. Cardiology to Nephrology
- Mastering the OSCEs in Internal Medicine. Part II. Neurology to Rheumatology
- Bits and Bytes for Rounds in Internal Medicine
- Mastering the Boards and Clinical Examinations. Part I. Cardiology to Nephrology
- Mastering the Boards and Clinical Examinations. Part II. Neurology to Rheumatology



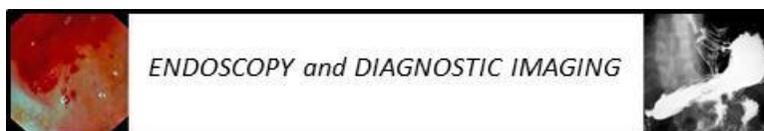


ENDOSCOPY and DIAGNOSTIC IMAGING



TABLE of CONTENTS

	Page
Endoscopy and Diagnostic Imaging and the CanMed Objectives	iii
Prologue	v
Dedication	viii
Acknowledgments	ix
Colon	
Defecation	3
Perianal disease	10
Motility disorders	13
Irritable bowel syndrome	25
Chronic Intestinal Pseudo-obstruction	28
Constipation	43
Laxatives	49
Inflammatory Bowel disease	65
UC cancer	122
Diverticular disease	179
Ischemic bowel disease	214
Colonic polyp and cancer	251
Lower gastrointestinal bleeding	268
Endometriosis	282
Diagnostic imaging	284
Endoscopic imaging	300
Hepatobiliary	
Fatty liver disease	342
Cholestasis	343
Portal hypertension	348
Diagnostic imaging	379
Index	403



Endoscopy and Diagnostic Imaging and the CANMED Objectives

Medical expert

The discussion of complex cases provides the participants with an opportunity to comment on additional focused history and physical examination. They would provide a complete and organized assessment. Participants are encouraged to identify key features, and they develop an approach to problem-solving.

The case discussions, as well as the discussion of cases around a diagnostic imaging, pathological or endoscopic base provides the means for the candidate to establish an appropriate management plan based on the best available evidence to clinical practice. Throughout, an attempt is made to develop strategies for diagnosis and development of clinical reasoning skills.

Communicator

The participants demonstrate their ability to communicate their knowledge, clinical findings, and management plan in a respectful, concise and interactive manner. When the participants play the role of examiners, they demonstrate their ability to listen actively and effectively, to ask questions in an open-ended manner, and to provide constructive, helpful feedback in a professional and non-intimidating manner.

Collaborator

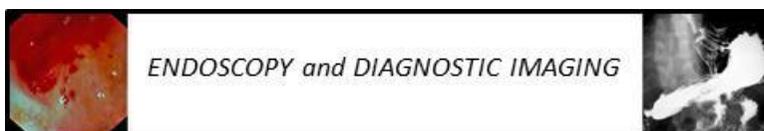
The participants use the “you have a green consult card” technique of answering questions as fast as they are able, and then to interact with another health professional participant to move forward the discussion and problem solving. This helps the participants to build upon what they have already learned about the importance of collegial interaction.

Manager

Some of the material they must access demands that they use information technology effectively to access information that will help to facilitate the delineation of adequately broad differential diagnoses, as well as rational and cost effective management plans.

Health advocate

In the answering of the questions and case discussions, the participants are required to consider the risks, benefits, and costs and impacts of investigations and therapeutic alliances upon the patient and their loved ones.



Scholar

By committing to the pre- and post-study requirements, plus the intense three day active learning Practice Review with colleagues is a demonstration of commitment to personal education. Through the interactive nature of the discussions and the use of the “green consult card”, they reinforce their previous learning of the importance of collaborating and helping one another to learn.

Professional

The participants are coached how to interact verbally in a professional setting, being straightforward, clear and helpful. They learn to be honest when they cannot answer questions, make a diagnosis, or advance a management plan. They learn how to deal with aggressive or demotivated colleagues, how to deal with knowledge deficits, how to speculate on a missing knowledge byte by using first principals and deductive reasoning. In a safe and supportive setting they learn to seek and accept advice, to acknowledge awareness of personal limitations, and to give and take 360⁰ feedback.

Knowledge

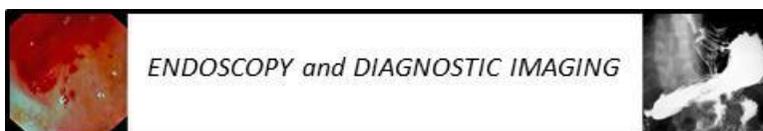
The basic science aspects of gastroenterology are considered in adequate detail to understand the mechanisms of disease, and the basis of investigations and treatment. In this way, the participants respect the importance of an adequate foundation in basic sciences, the basics of the design of clinical research studies to provide an evidence-based approach, the designing of clinical research studies to provide an evidence-based approach, the relevance of their management plans being patient-focused, and the need to add “compassionate” to the Three C’s of Medical Practice: competent, caring and compassionate.

“They may forget what you said, but they will never forget how you made them feel.”

Carl W. Buechner, on teaching.

“With competence, care for the patient. With compassion, care about the person.”

Alan B. R. Thomson, on being a physician.

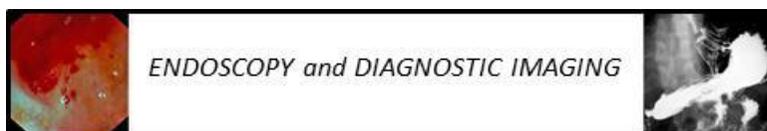


Prologue

Like any good story, there is no real beginning or ending, just an in-between glimpse of the passing of time, a peek into a reality of people's minds, thoughts, feelings, and beliefs. The truth as I know it has a personal perspective which drifts into the soul of creation. When does life begin, when does an idea become conceived, when do we see love or touch reality? A caring, supportive, safe, and stimulating environment creates the holding blanket, waiting for the energy and passion of those who dream, invent, create – disrupt the accepted, challenge the conventional, ask the questions with forbidden answers. Be a child of the 60's. Just as each of us is a speck of dust in the greater humanity, the metamorphosis of the idea is but a single sparkle in the limitlessness of the Divine Intelligence. We are the ideas, and they are us. No one of us is truly the only parent of the idea, for in each of us is bestowed the intertwined circle of the external beginning and the end....

...during a visit to the Division of Gastroenterology at the University of Ottawa several years ago, the trainees remarked how useful it would be to have more than two hours of learning exchange, a highly interactive tutorial with concepts, problem solving, collegial discussion, the fun and joys of discovery and successes. Ms. Jane Upshall of BYK Canada (Atlanta, Nycomed), who had sponsored two of these visiting Professorships, encouraged the possibility of the development of a longer program. Her successor, Lynne Jamme-Vachon, supported the initial three day educational event for the trainees enrolled in the GI training program at the University of Ottawa. With her entrepreneurial foresight, wisdom, and enthusiasm, the idea began. Lynne's commitment to an event which benefited many of the future clinicians, who will care for ourselves and our loved ones, took hold. Then, thanks to the GI program directors in Ottawa and the University of Western Ontario, Nav Saloojee and Jamie McGregor, more trainees were exposed, future GI fellows talked with other trainees, and a grass roots initiative began. Had it not been for Nav and Jamie's willingness to take a risk on something new, had they not believed in me, then there would have been no further outreach. Thank you, Lynne, Nav, and Jamie. You were there at the beginning. I needed you.

By 2008, all but one GI program in the country gave their trainees time off work to participate in the three day event, GI Practice Review (GI-PR). The course is 90% unsponsored, and is gratis to the participants, (except for the



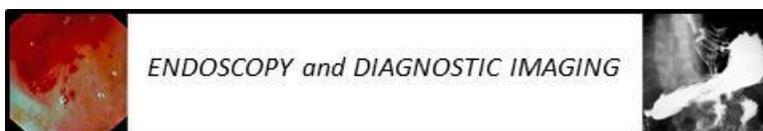
cost of their enthusiastic participation!) I am happy to give back to the subspecialty that gave me so much for 33 years. I hope GI-PR is helpful to all trainees. I know that from these future leaders there will arise those who will continue to dedicate and donate their time, energy, and ability to the betterment of those who contribute to the continued improvement of our medical profession. The clinicians, the teachers, the researchers.

In the short span of six years, more than 250 fellows, coming from all the 14 training programs in Canada, have participated in the small group sessions in the GI practice review. I thank the training program directors who have supported GI-PR. Special appreciation as well to their many staff physicians who worked without their trainees for the three days of each program.

The idea for the electronic and hard copy summary of the “list of facts” came from the trainees who wished for an aide memoir. But the GI-PR is about more than lists and facts - it is about problem formulation, case discussions, review of endoscopy, histopathology, motility, diagnostic imaging. It is about having fun working together to learn. The subterfuge to gain interest in the basic sciences is the use of clinical scenarios to show the way to the importance of first principles. While the lists are here, the experience is in the performance.

The child will grow, the images will expand, the learning of all aspects of our craft will develop and flourish amongst persons of good will. Examinations will become second nature, as each clinical encounter, each person, each patient, becomes our test, the determination of clinical competence, of caring, of compassion. May these three C's become part of each of our live's narrative. And from this start comes Capstone Academic Publishing, an innovation for the highest quality and value in educational material, made available at cost, speaking in tongues, in the languages of many cultures, with the dialect of the true North strong and free, so that knowledge will be free at last.

Outstanding medical practice and true dedication to those from whom we receive both a privilege and pleasure of care, comes from much more than the GI-PR can give you, much more than Q & As, descriptions of diagnostic imaging or endoscopy stills or videos, histopathology or motility. True, we need all of these to jump over a very high bar. But to be a truly outstanding physician, you need to care for and care about people, and you must respect the dignity and rights of all others. You must strike a balance

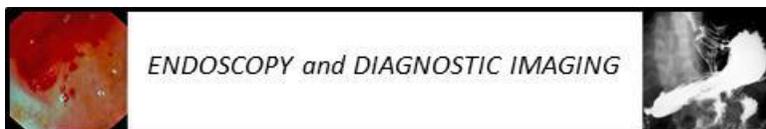


between love and justice, and you place your family and friends at the top of your wish-list of lifetime achievements.

For the skeptics who ask “What do you want from me?” I simply say “You are the future; I trust that in time you too will help young people to be the best they can be.”

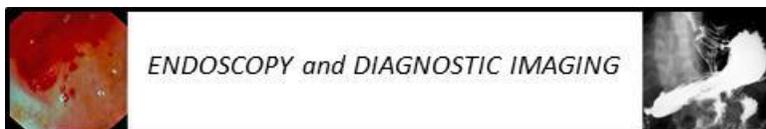
May good luck, good health, modesty, peace, and understanding be with you always. Through medicine, all persons of the world may come to share caring, respect, dignity, and justice.

Sincerely,



Dedication

We dedicate this book to all gastroenterologists
in training or starting a gastrointestinal career.

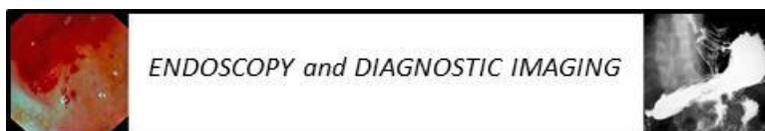


Acknowledgments

Patience and patients go hand in hand. So also does the interlocking of young and old, love and justice, equality and fairness. No author can have thoughts transformed into words, no teacher can make ideas become behavior and wisdom and art, without those special people who turn our minds to the practical - of getting the job done!

Thank you, Naiyana and Duen, for translating those terrible scribbles, called my handwriting, into the still magical legibility of the electronic age. My most sincere and heartfelt thanks go to the excellent persons at JP Consulting, and CapStone Academic Publishers. Jessica, you are brilliant, dedicated and caring. Thank you.

When Rebecca, Maxwell, Megan Grace, Henry and Felix ask about their Grandad, I will depend on James and Anne, Matthew and Allison, Jessica and Matt, and Benjamin to be understanding and kind. For what I was trying to say and to do was to make my professional life focused on the three C's - competence, caring, and compassion - and to make my very private personal life dedicated to family - to you all.



COLON

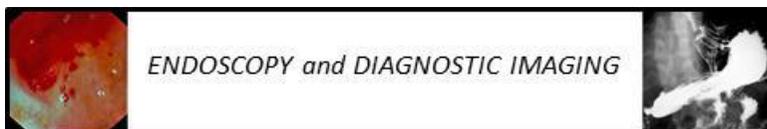
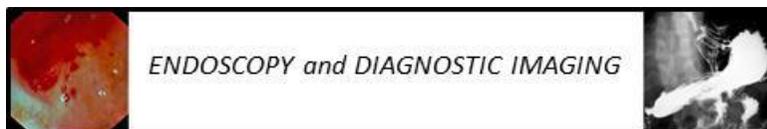


TABLE of CONTENTS

	Page
Defecation	3
Perianal disease	10
Motility disorders	13
Irritable bowel syndrome	25
Chronic Intestinal Pseudo-obstruction	28
Constipation	43
Laxatives	49
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COLON

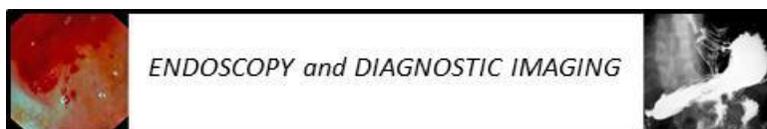
“Sharpening Knowledge to Enhance Clinical Skills”

DEFECATION

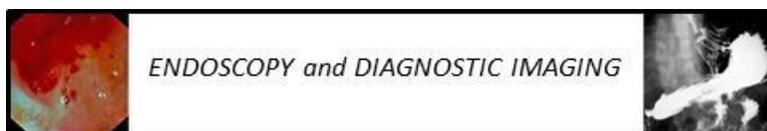
- Give the components of defecation, and their changes with passing stool.
- Components
 - Sensory
 - rectal sensation
 - rectal ampulla
 - pelvic floor
 - Structural
 - canal sensation
 - anorectal angle
 - flutter valve
 - mucosal rosette
 - Motor
 - puborectalis
 - striated muscle
 - internal and sphincter
 - smooth muscle
 - external and sphincter
 - striated muscle

Practice Pointers: Fecal incontinence

- Definition: The recurrent uncontrolled passage of fecal material for at least one month duration (Rao 09)
- Subtypes
 - Passive – involuntary release of stool or flatus
 - Urge – release of fecal contents despite voluntary attempts to retain contents
 - Seepage – leakage of small amounts of stool following an evacuation
- Value of rectal examination in the person with fecal incontinence
 - Perianal sensation
 - Sphincter tone at rest or voluntary contraction, and election of perineum
 - Sphincter tone
 - Length of anal canal
 - Anorectal angle
- Psyllium has been shown in a RCT to reduce the number of episodes of fecal incontinence by 50%; uncontrolled studies suggest a benefit for cholestyramine or amitriptyline (Rao 09)



- The operant conditioning techniques of biofeedback training using visual, auditory or verbal feedback, are meant to improve; the strength of the anal sphincter muscles, anorectal sensory perception, and coordination of anal sphincter, gluteal and abdominal muscles following rectal perception (balloon dilation) or voluntary squeeze
- Both biofeedback training and Kegal exercises each produce a 50% reduction in fecal incontinence, and one study has shown a superior improvement with biofeedback as compared to exercises, on a per protocol but not an intention-to-treat basis. A third study (Hegmen et al, GE 2007;132:A-83) showed 77% of persons with fecal incontinence showing improvement versus 40% treated with Kegal exercises ($p < 0.001$), with 66% versus 48%, respectively, being totally content.
- RCTs have shown a benefit of sacral nerve stimulation for fecal incontinence when the anal sphincter is intact
- The Malone procedure (antegrade continent enema procedure – cecostomy or appendicostomy for antegrade washing of the colon) gives a 61% success rate for fecal incontinence over 39 months
- Biofeedback defecation is also of benefit for dyssynergic defecation, providing sustained 12 month improvement in 80% as compared with 22% in the standard care (laxative [PEG] and counseling group), with improved ability to expel a test balloon, and standard care correction of dysynergy in 79% of the active biofeedback group versus 4% in the sham group (Rao 09) (Rao SSC, et al. *Clin Gastroenterol Hepatol* 2007:331-8.), and in second study, 70% improvement at 3 months, with biofeedback vs 23% with diazepam and 28% with placebo (Heymen S, et al. *Gastroenterology* 2007:A-83.)
- Biofeedback is also of benefit in persons with solitary rectal ulcer syndrome (Rao SSC, et al. *Clin Gastroenterol Hepatol* 2007:331-8.)
- Give anatomical structures and the mechanism by which they contribute to normal fecal continence.
- Nerves – pudendal nerve/sacral segments S2 – S4/brain: The pudendal nerve has both afferent and efferent limbs, sensing stool entry into the rectum and delivering the impulse through the sacral nerves, spinal cord, to the brain. The efferent limb carries the sensation of distension which causes central pathways to send signals via the afferent limb to allow for conscious contraction of external sphincter to maintain continence.
- Muscles
 - Internal anal sphincter (IAS)
 - External anal sphincter (EAS)
 - Levator ani complex: The internal anal sphincter is tonically contracted providing continence at rest. When stool enters the



rectum the IAS relaxes, however, continence is maintained if consciously desired by contraction of the EAS. The IAS returns to resting tone, the rectum demonstrates compliance allowing intrarectal pressure to decrease and the urge to defecate to pass. The levator ani muscles provide additional support to the EAS. As well, they form a sling around the anal canal, forming an acute angle during rest, creating a mechanical barrier for continence. Inability to distend without substantial rise in pressure thus not overwhelming resting anal tone.

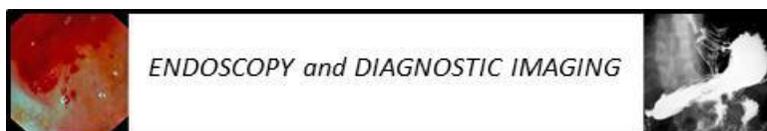
- Rectum - reservoir

Abbreviations: EAS, external anal sphincter; IAS, internal anal sphincter

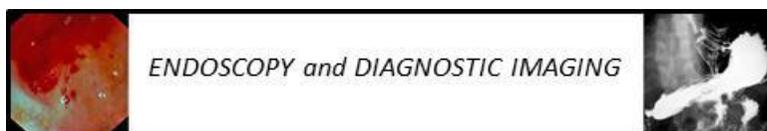
Adapted from: Schiller LR. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 200-201.

- Give the tests/procedures which are useful to investigate the patient with fecal incontinence.
 - Clinical
 - History, physical examination
 - Sensory and motor (DRE) testing
 - Perianal descent (normally 1.5-3.0 cm)
 - Mucosa
 - Endoscopy
 - Muscle
 - Pressure
 - Anorectal manometry
 - Function
 - Defecography
 - Balloon expulsion test
 - Pellet retention
 - Endoscopy, EUS
 - Colon transit study
 - MRI, CT
 - Nerve
 - Pudendal nerve terminal latency

Abbreviations: DRE, digital rectal examination; EUS, endoscopic ultrasound



- Give the medical and surgical treatments of fecal incontinenc
- Treat underlying cause (s)
- Supportive therapy
 - Education/counseling/habit training
 - Trained defecation
 - Diet (fiber; lactose, fructose, reduce caffeine intake)
 - Incontinence pad
 - Perianal hygiene/skin care
- Pharmacological
 - Fiber
 - loperamide
 - lomotil
 - Codeine
 - Cholestyramine/colestipol
 - Estrogen
 - Phenylephrine
 - Sodium valproate
- Biofeedback therapy
 - Anal sphincter muscle strengthening
 - Rectal sensory conditioning
 - Recto-anal coordination training
- Perianal
 - Anal plugs
 - Pessary
 - Kegal exercises
 - Sphincter bulking (collagen, silicone)
 - Anal electrical stimulation
 - Injection sclerotherapy
 - Sacral nerve stimulation
- Surgery
 - Artificial anal sphincter
 - Sphincteroplasty
 - Anterior repair (rectocele)
 - Gracilis/gluteus muscle transposition +/- stimulation
 - Colostomy
 - Pelvic reconstruction
 - Options: rubber band ligation
 - Surgical excision
 - PPH-Stapled Hemorrhoidopexy



Adapted from: Schiller L. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 207

- Give the affected structure and pathophysiology of disorders causing functional anorectal outlet obstruction.

Affected structure	Pathophysiology
○ Internal sphincter: Hirschsprung's disease	- No relaxation - Paradoxical contraction
○ External sphincter: Pelvic floor dyssynergia ('anismus')	- Luminal obstruction
○ Rectal wall, circumferential: Intussusception	- Loss of pressure
○ Rectal wall, mostly anterior: Rectocele	- Loss of pressure
○ Pelvic floor: Pelvic floor descent	

Printed with permission: Müller-Lissner S. *Best Practice & Research Clinical Gastroenterology* 2007; 21(3): pp. 474.

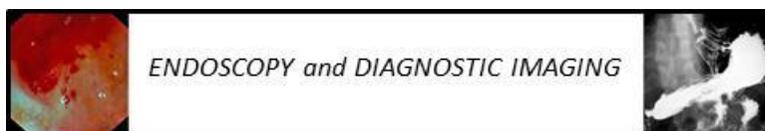
- Give the FDA classification of the safety of laxatives in pregnancy.

Safe (B)	Caution (C)	Unsafe (D)
➤ Lactulose	○ Saline osmotic laxatives	- Anthraquinones - 5HT agonists
➤ Glycerine	○ Castor oil	- Prostaglandins (misoprostol)
➤ Polyethylene glycol (PEG)	○ Senna	
➤ Bulking agents	○ Docusate sodium	
➤ Bisacodyl		

Adapted from: Cullen G, and O'Donoghue D. *Best Practice & Research Clinical Gastroenterology* 2007; 21(5): pg. 815; and Thukral C, and Wolf JL. *Nature Clinical Practice Gastroenterology & Hepatology* 2006; 3(5): pg. 260.; printed with permission: Kane SV. *AGA Institute 2007 Spring Postgraduate Course Syllabus*:511.

- Give the causes of constipation in pregnancy.

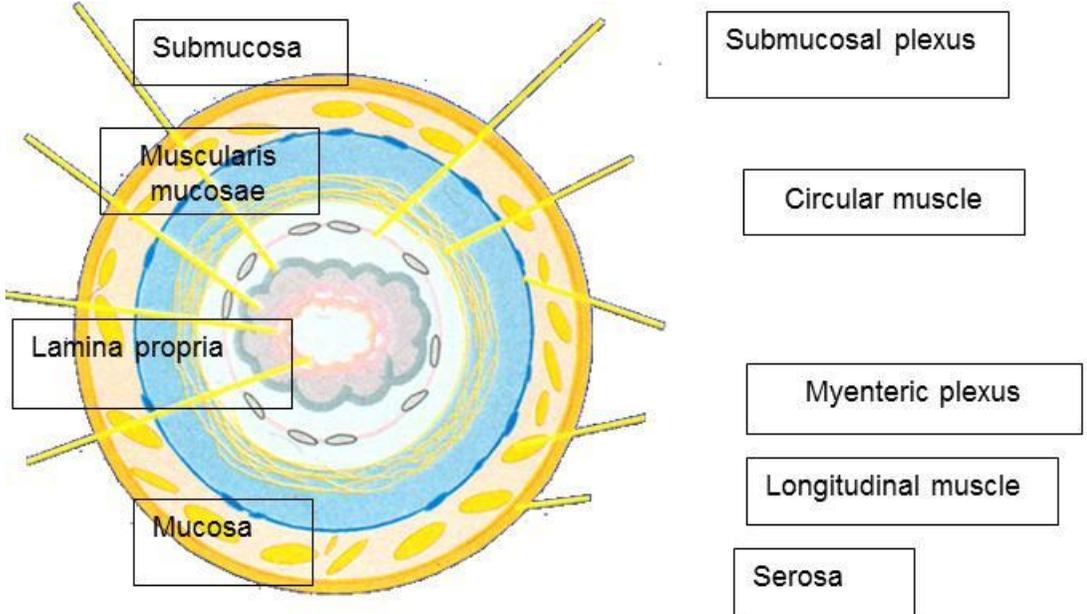
- Hormonal – slow transit
- Mechanical
- Medications
- Lifestyle
 - Reduced exercise
 - Dietary changes



- Pre-existing disease:
 - Chronic slow-transit constipation
 - Irritable bowel syndrome
 - Congenital or acquired megacolon
 - Chronic idiopathic intestinal pseudo-obstruction

Adapted from: Quigley EMM. *Best Practice & Research Clinical Gastroenterology* 2007;21(5): pg. 882.; and Cullen G, and O'Donoghue D. *Best Practice & Research Clinical Gastroenterology* 2007; 21(5): pg. 810.

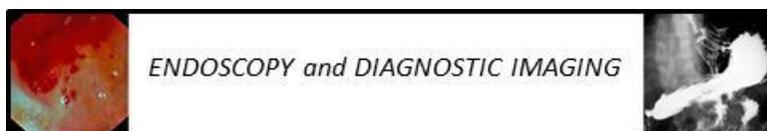
BASIC STRUCTURES OF THE GI TRACT



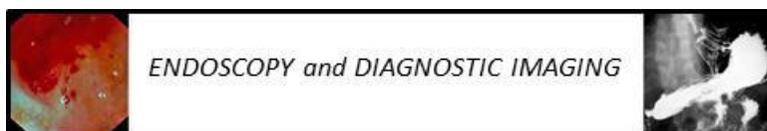
- Autonomic Nervous System
 - Parasympathetic nervous system
 - Sympathetic nervous system
 - Enteric nervous system
- Enteric Nervous System
 - Controls motility and secretory functions
 - Semi-autonomous
 - may function independently
 - Contains many neurotransmitters including 5-HT

Fecal Continence

- Anatomical structures and the mechanism by which they contribute to normal fecal continence



- Nerves – pudendal nerve/sacral segments S2 – S4/brain: The pudendal nerve has both afferent and efferent limbs, sensing stool entry into the rectum and delivering the impulse through the sacral nerves, spinal cord, to the brain. The efferent limb carries the sensation of distension which causes central pathways to send signals via the afferent limb to allow for conscious contraction of external sphincter to maintain continence.
- Muscles
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- Affected structure and pathophysiology of disorders causing functional anorectal outlet Obstruction

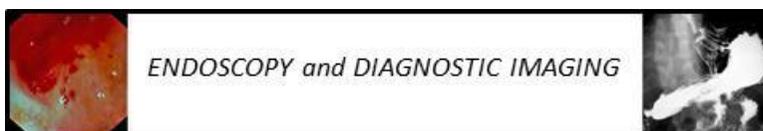
Affected structure	Pathophysiology
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○ Rectal wall, mostly anterior: Rectocele	- Loss of pressure
○ Pelvic floor: Pelvic floor descent	- Loss of pressure

Adapted from: Müller-Lissner, Stefan. *Best Practice & Research Clinical Gastroenterology* 2007; 21(3): pp. 474.

PERIANAL DISEASE

- Give the anatomical structures and mechanisms by which they contribute to normal fecal continence.
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 - Internal anal sphincter (IAS)
 - External anal sphincter (EAS)
 - Levator ani complex: The internal anal sphincter is tonically contracted providing continence at rest. When stool enters the rectum the IAS relaxes, however, continence is maintained if consciously desired by contraction of the EAS. The IAS returns to resting tone, the rectum demonstrates compliance allowing intrarectal pressure to decrease and the urge to defecate to pass. The levator ani muscles provide additional support to the EAS. As well, they form a sling around the anal canal, forming an acute angle during rest, creating a mechanical barrier for continence. Inability to distend without substantial rise in pressure thus not overwhelming resting anal tone.
 - Rectum - reservoir

Abbreviations: EAS, external anal sphincter; IAS, internal anal sphincter
Adapted from: Schiller LR. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 200-201.



Hematochezia

- Give the causes of hematochezia in adults.

Causes	Approximate frequency (%)	Comments
➤ Diverticular disease	30	<ul style="list-style-type: none"> ○ Stops spontaneously in 80% of patients ○ In one series, the need for surgery may be unlikely if <4U red cell transfusion given in 24 h, but is required in 60% of patients receiving >4U in 24h
➤ Colonic vascular ectasia (AV malformation, angiodysplasia)	25	<ul style="list-style-type: none"> ○ Frequency of these lesions vary widely in clinical series ○ Acute bleeding appears to be more frequently due to lesion in proximal colon
➤ Colitis	10	<ul style="list-style-type: none"> ○ Ischemic colitis often presents with pain and self-limited haematochezia. Colitis is segmental, most often affecting splenic flexure

Causes	Approximate frequency (%)	Comments
		<ul style="list-style-type: none"> ○ Bleeding may also occur from other types of colitis, such as Crohn disease or ulcerative colitis (see Small Bowel question 40) ○ Bloody diarrhoea is most frequent symptom of infectious colitis and inflammatory bowel disease of the colon
➤ Colonic neoplasia/post-polypectomy	10	<ul style="list-style-type: none"> ○ Post-polypectomy bleeding is frequency self-limited, and may occur ≤ 14 days after polypectomy
➤ Anorectal causes (including hemorrhoids, varices)	5	<ul style="list-style-type: none"> ○ Anoscopy/proctoscopy should be included in the rectal initial evaluation of these patients

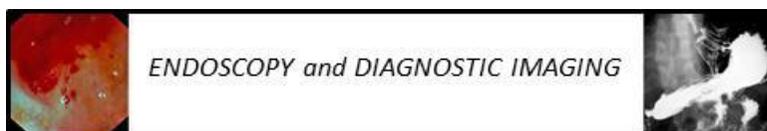


- Upper gastrointestinal sites (including duodenal/gastric ulcer, esophageal/gastric varices) 5
 - A negative nasogastric aspirate does not exclude this possibility
- Small bowel sites (including Crohn ileitis, Meckel's diverticula, tumours, vascular ectasia) 10
 - Frequency diagnosed by radiologic studies or enteroscopy after the acute bleeding episode has resolved.
- 5
 - In about 5% of patients, no site of bleeding is found

Adapted from: Zuccaro G. *Best Practice & Research Clinical Gastroenterology* 2008; 22(2): pg. 227.

Hemorrhoids

- Give the medical and surgical treatment of chronic internal hemorrhoids.
- Treat underlying associated causes
 - Diarrhea/constipation, prolapse, bleeding, deficient intake of fibre and fluids
- Supportive therapy
 - Avoid straining and limit time on commode
- Pharmacological
 - Barrier creams: zinc oxide, Lanolin (limit contact of stool and mucus with sensitive anoderm)



- Surgery
 - Repair fissures to limit further trauma
 - Surgery – rubber band ligation, injection sclerotherapy, surgical excision, PPH-stapled hemorrhoidopexy

Adapted from: Hull T L. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 2836-2839.

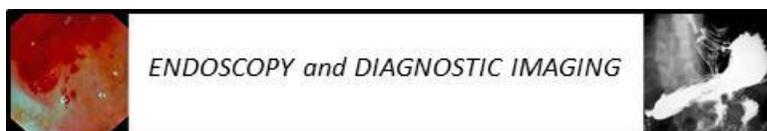
- Give the causes of anorectal disease in the person with HIV/AIDs.
 - Anal fistula
 - Anal fissure
 - Condylomata accuminata
 - Kaposi sarcoma
 - Hodgkin disease
 - Intraepithelial anal carcinoma
 - Lymphoma
 - Small cell carcinoma of the rectum

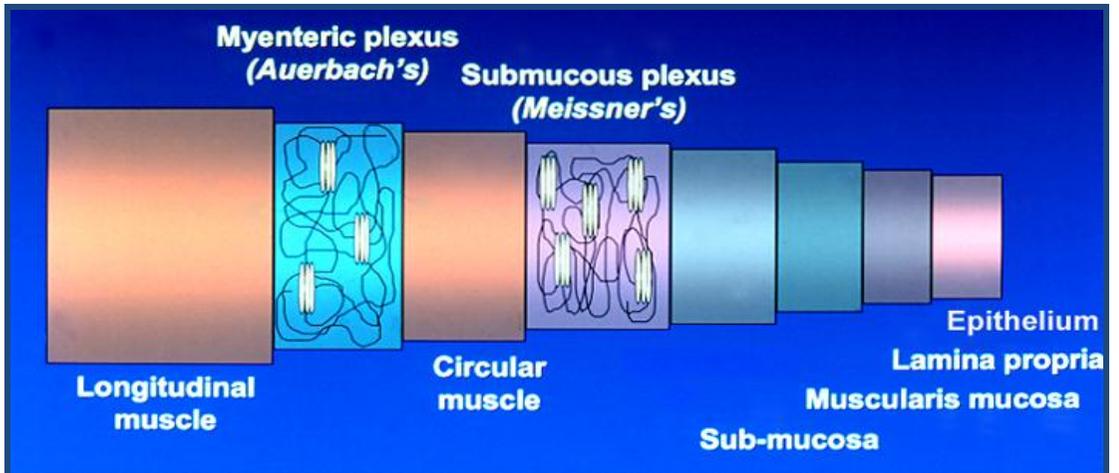
MOTILITY DISORDERS

- Both propagating and non-propagating pressure waves
- Only one third of the propagating pressure waves are propulsive
- Most propagating and propulsive pressure waves occur in the proximal colon (mixing and storage)
- Transport of colonic content over long distances mediated by propagating pressure waves

Enteric Nervous System

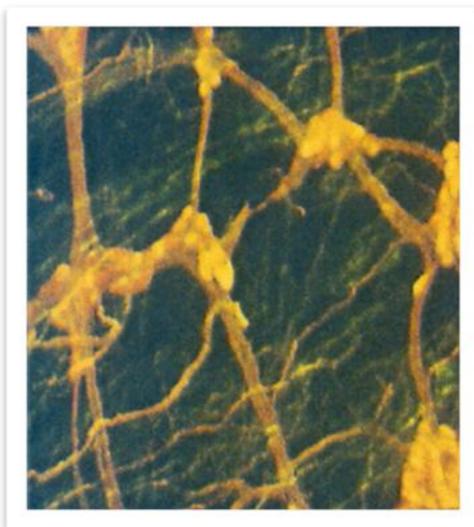
- Controls motility and secretory functions of the intestine
- Semi-autonomous
 - Actions modified by parasympathetic and sympathetic nervous systems
 - May function independently
- Contains many neurotransmitters including 5-hydroxytryptamine (5-HT)



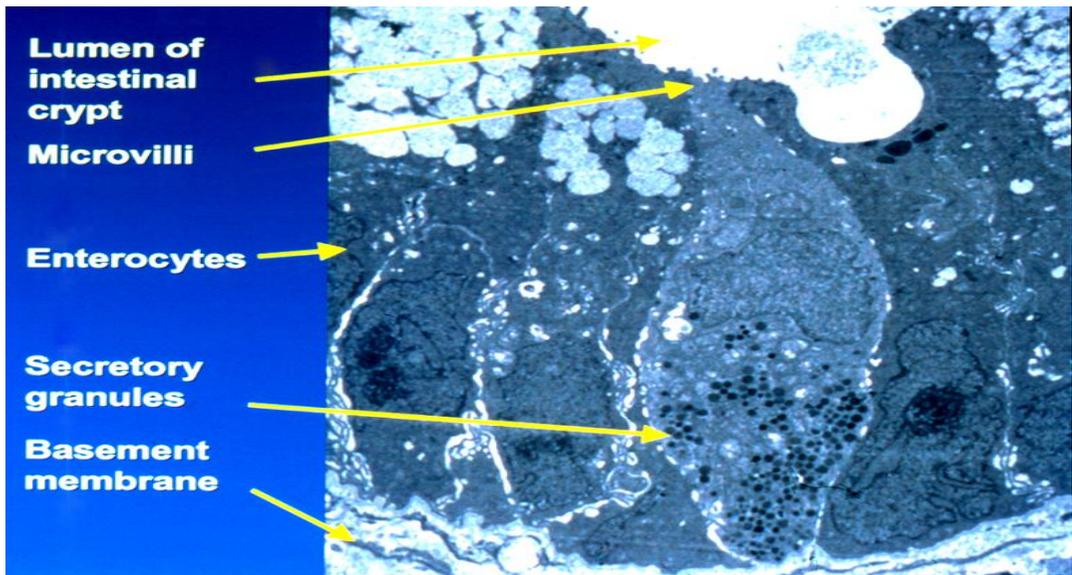


- Controls motility and secretory functions
- Semi-autonomous
 - may function independently
- Contains many neurotransmitters including 5-HT

Courtesy of Professor D Grundy
Sheffield, UK



Enterochromaffin Cell



Dr RC Spiller

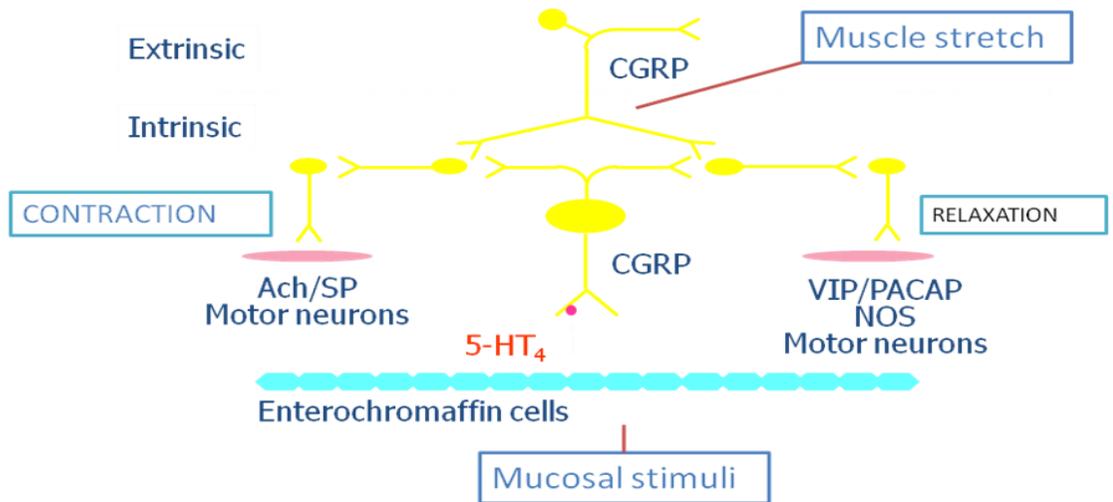
➤ Normal Colonic Motility

- Both propagating and non-propagating pressure waves
- Only one third of the propagating pressure waves are propulsive
- Most propagating and propulsive pressure waves occur in the proximal colon (mixing and storage)
- Transport of colonic content over long distances mediated by propagating pressure waves

Cook et al., 2000

Normal Motility

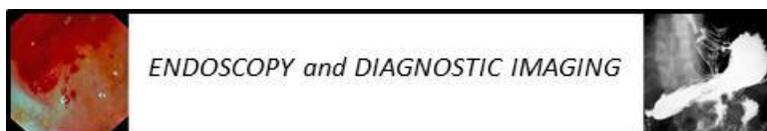
- Cornerstone of normal motility is the peristaltic reflex



- Normal Motility
 - Wide variety of functions:
 - Storage of luminal contents (gastric fundus, proximal colon)
 - Mixing and grinding of ingested food
 - Transport of chyme at rate allowing and promoting absorption of nutrients
 - Expulsion of undigested material
 - Achieved by contractions and relaxations organized into well distinguished motor patterns
 - Motor patterns are stored in the enteric nervous system (= software of the gut)

The Enteric Nervous System: The Little Brain of the Gut

- Complex integrative functions
- Several subsets of neurons
 - sensory neurons, interneurons, motor neurons
- Multiple neurotransmitters and synaptic mechanisms



- Isolated from blood vessels
- No connective tissue
- CNS-like glial elements

Acetylcholine binds to muscarinic receptors on the smooth muscle cell membrane

↓

Sodium channels open

↓

Sodium ions accumulate in the cell

↓

Calcium channels open

↓

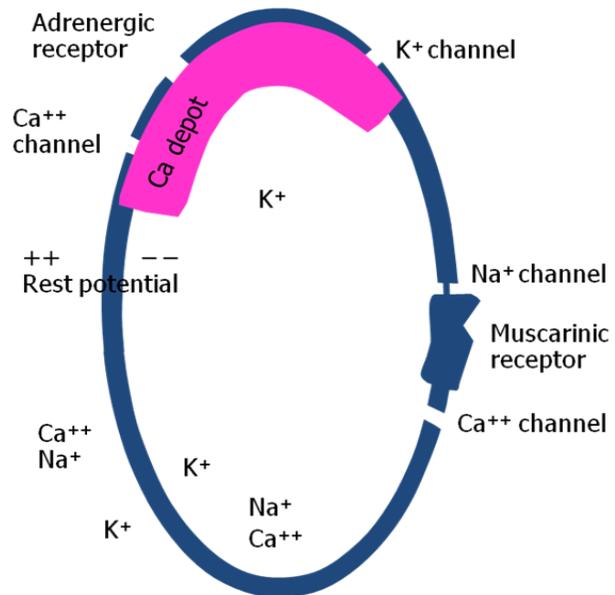
Calcium ion influx

↓

Calcium ions interact with actin and myosin in the muscle cell

↓

Muscle contraction

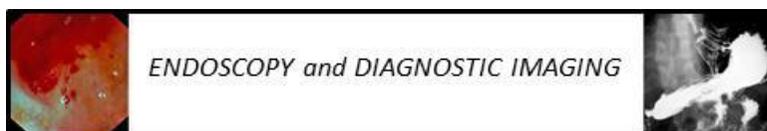


Chronic Intestinal Pseudo-Obstruction

- Differential Diagnosis
 - Mechanical obstruction
 - more pronounced abdominal pain
 - often constipation, less common diarrhea
 - rarely chronic or intermittent
- Functional bowel disease (mild form of CIIP?!)

II. Disorders of the Smooth Muscle

- Primary
 - Familial visceral myopathies
 - autosomal dominant
 - autosomal recessive (with ptosis and external ophthalmoplegia)
 - autosomal recessive with total GI tract dilatation
 - Sporadic visceral myopathies
- Secondary

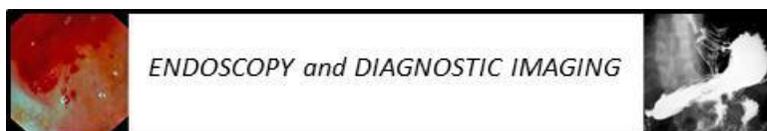


- Progressive systemic sclerosis/polymyositis
 - Myotonic dystrophy
 - Progressive muscular dystrophy
 - Amyloidosis
 - Ceroidosis?
- Diffuse lymphoid infiltration
- III. Small Intestinal Diverticulosis
- With muscle resembling visceral myopathy
 - With muscle resembling progressive systemic sclerosis
 - With visceral neuropathy and neuronal intranuclear inclusions
 - Secondary to Fabry disease
- Chronic Intestinal Pseudo-Obstruction
- Chronic idiopathic intestinal pseudo-obstruction (CIIP/Naish)
 - Scleroderma
 - Myxedema
 - Hypoparathyroidism – hyperparathyroidism
 - Severe celiac disease and electrolyte imbalance
 - Mesenteritis, mesenteric lesions, celiac ganglion lesions
 - Amyloidosis
 - Chagas disease
 - Myotonia dystrophica
 - Hirschsprung disease
 - Drug toxicity (morphine, heroine, anticholinergics, ganglionic blockers, etc)
 - Autonomic nervous system disorders
 - Glucagon-secreting tumor
- Transient Intestinal Pseudo-Obstruction
- Colonic intestinal pseudo-obstruction (Ogilvie Syndrome)
 - Renal failure
 - Pancreatitis
 - Pneumonia
 - Congestive heart failure
 - Spinal injury
 - Electrolyte imbalance

Chronic intestinal pseudo-obstruction

Acute, recurrent or chronic symptoms suggestive of obstruction of small or large intestine without any radiological, surgical or endoscopic evidence of mechanical obstruction

- Disordered GI motility – muscle - ICC – neuron

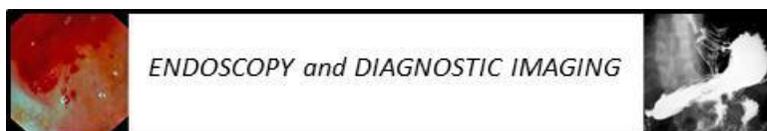


➤ Classification

- Pathophysiological criteria
 - neuropathic CIP
 - myopathic CIP
 - unclassified
- Etiological criteria
 - congenital / familial
 - acquired (systemic diseases, post-infectious, drug-induced,)

➤ Classification

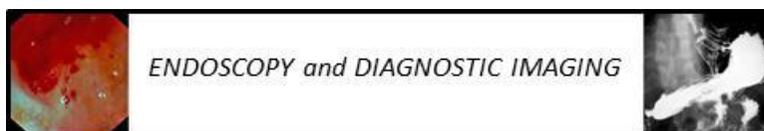
Type	Myopathic	Neuropathic
➤ Infiltrative neurologic disease	<ul style="list-style-type: none"> ○ Scleroderma, amyloidosis ○ Myotonic and other dystrophies, mitochondrial myopathy (MNGIE) 	<ul style="list-style-type: none"> - Early scleroderma, amyloidosis - Diabetes, porphyria, brain stem tumor, MS, spinal cord transection, dysautonomias (Shy Drager)
➤ Neoplaastic		<ul style="list-style-type: none"> - Paraneoplastic (small cell lung tumor), mammary CA, pancreas CA
➤ Endocrine	<ul style="list-style-type: none"> ○ Hypothyroidism, diabetes, hypoparathyroidism, pheochromocytoma (MEN IIB) 	
➤ Drug-induced infectious		<ul style="list-style-type: none"> - Anti-depressants, narcotics, anticholinergics, laxative abuse, smooth muscle relaxants, vincristine - Chagas, viral (CMV, EBV, HSV)
➤ Idiopathic	<ul style="list-style-type: none"> ○ Non-familial hollow visceral myopathy 	<ul style="list-style-type: none"> - Hirschsprung disease, chronic idiopathic intestinal pseudo-obstruction
➤ Familial	<ul style="list-style-type: none"> ○ Familial visceral myopathies (AD or AR), MNGIE (AR) 	<ul style="list-style-type: none"> - Familial visceral neuropathies, von Recklinghausen disease



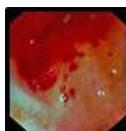
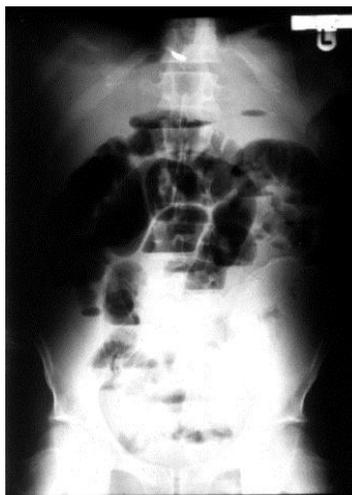
I. Disorders of the myenteric plexus

- Familial visceral neuropathies
 - Recessive, with intranuclear inclusions
 - Recessive, with mental retardation and calcification of the basal ganglia
 - Dominant, with neither of above
- Sporadic visceral neuropathies
 - Degenerative, non-inflammatory
 - Degenerative, inflammatory
 - Paraneoplastic
 - non-paraneoplastic (Chagas, cytomegalovirus, idiopathic)
 - isolated axonopathy
- Developmental abnormalities
 - Hirschsprung disease
 - Total colonic aganglionosis (sometimes with small intestinal aganglionosis)
 - Maturational arrest
 - with mental retardation
 - with other neurological abnormalities
 - isolated to myenteric plexus, without the above
 - Neuronal intestinal dysplasia
 - with neurofibromatosis
 - with MEA II
 - isolated to intestine, without above
- Severe, idiopathic constipation
- Drug-induced /toxic damage
- Chronic idiopathic intestinal pseudo-obstruction
 - Recurrent bouts of intestinal pseudo-obstruction
 - Mimicks mechanical ileus (without organic occlusion)
 - Gross distension particularly of small bowel, ineffective peristalsis, pronounced segmental non-propulsive motor activity
 - Bacterial overgrowth, malnutrition, cachexia
 - Functional and morphological disturbance of myenteric plexus or muscle layer

Naish, Gut 1960,1:62
- Diagnostic evaluation
 - When to suspect pseudo-obstruction?
 - Coexistence of vomiting, abdominal distention, constipation, weight loss

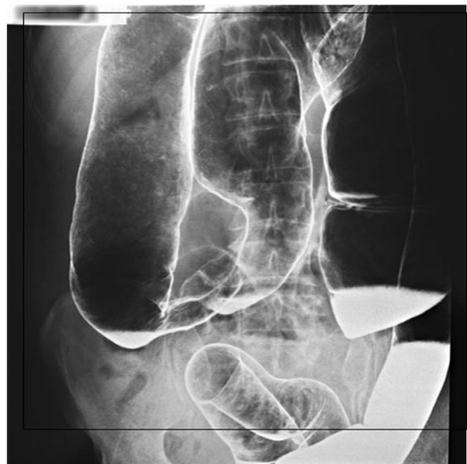
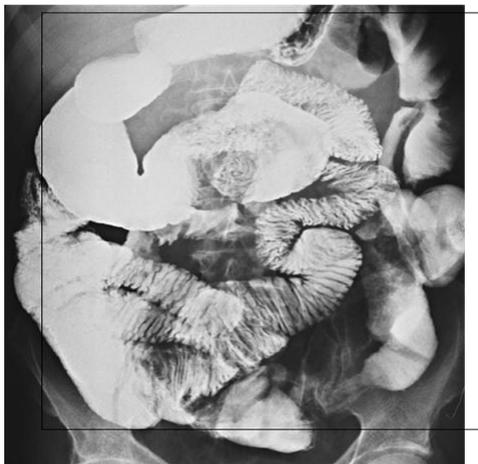
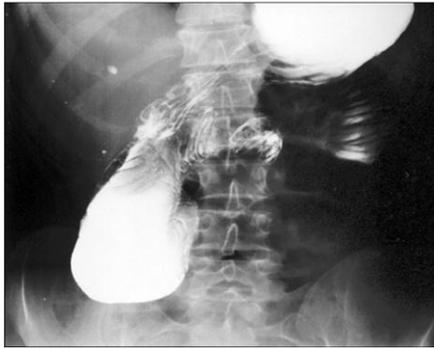


- chronic symptoms, no symptom-free intervals
 - abdominal pain is not the only symptom
 - urinary symptoms (bladder distention, frequent urinary infections)
 - familial history
 - several non-diagnostic laparotomies
 - autonomic nervous system dysfunction (postural dizziness, sweating abnormalities)
 - radiological studies (no obstruction, megaduodenum)
 - muscle weakness, ptosis, ophthalmoplegia, deafness, mental retardation, lactate acidosis
 - Laboratory
 - Electrolytes (K, Ca), thyroid function, glycemia
 - Lactate, pyruvate, muscle enzymes (MNGIE)
 - Urinary analysis (amyloidosis)
 - EBV, CMV HSV
 - ANA (systemic disease)
 - X-ray
 - Abdominal flat film
 - Small intestine: megaduodenum?, obstruction?, diverticulosis
 - Chest (small cell carcinoma)
- Differential diagnosis
 - Mechanical obstruction
 - more pronounced abdominal pain
 - often constipation, less common diarrhea
 - rarely chronic or intermittent
 - Functional bowel disease (mild form of CIIP?!)
 - Obstruction

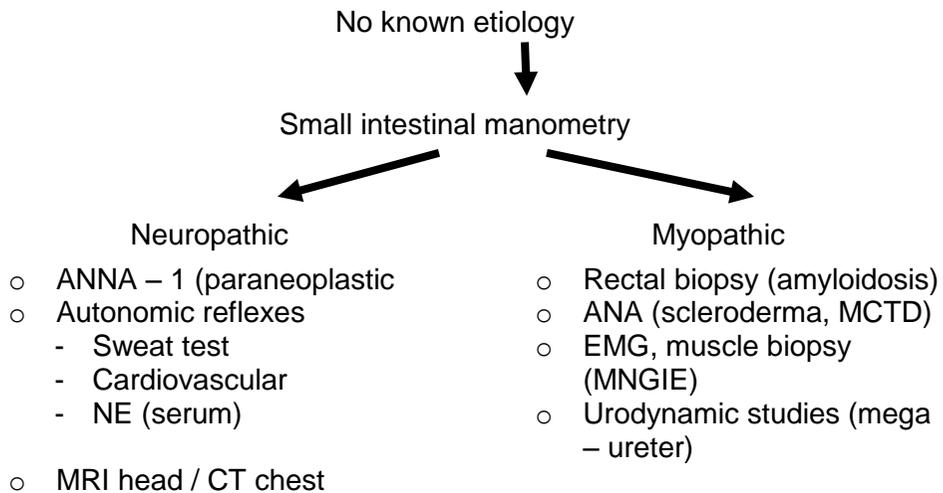


- Marked distension usually of both large and small bowel with air-fluid levels throughout the abdomen
- Massive duodenal dilatation with abnormal motility
- Hypomotility or disorganized ineffective peristaltic activity
- Extensive dilution of contrast material
- Occasional abnormalities of the fold pattern depending on the underlying cause

➤ Radiological findings



➤ Diagnostic evaluation



➤ Assess type of pseudo-obstruction (myogenic vs neurogenic)

➤ Assess segment involved (intestinal - colonic)

➤ Assess extra-intestinal disease

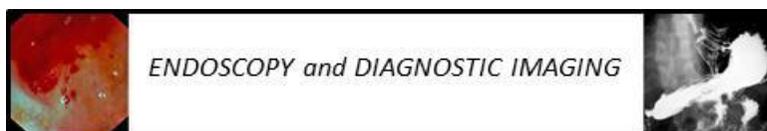
- urinary tract (megaureter, urinary bladder dysfunction)
- signs of autonomic neuropathy
- striated muscle disease (mitochondrial disease)
- systemic disease (amyloidosis, CREST, neoplasm)
- CNS disease

➤ Transient causes

- Intra-abdominal / extra / abdominal inflammation
- Electrolyte imbalance
- Drug toxicity

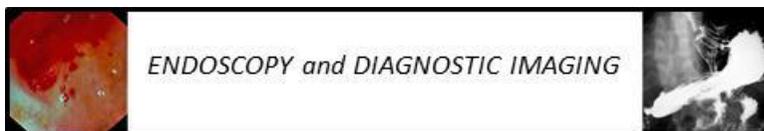
➤ Chronic causes

- Diseases involving intestinal smooth muscle
 - Collagen vascular disease
 - Muscular dystrophias
 - Amyloidosis
- Neurological diseases
 - Hirschsprung disease
 - Chagas disease
 - Parkinson disease
 - Ganglioneuromatosis



- Multiple sclerosis

- Neurotrophins and the Gut
 - Neurotrophins and their receptors are present in the adult ENS
 - The neurotrophins BDNF and NT-3 display significant prokinetic effects on gastrointestinal and colonic transit
 - The neurotrophin NT-3 restores colonic transit and defecation parameters in patients with constipation
 - Transport of colonic contents over long distances requires coordinated motor activity
 - Motor patterns underlying this propulsive motor activity are preprogrammed in the enteric nervous system
 - Intervention with neurotransmission in the neural circuit involved may enhance colonic transit
 - Multigene family: nerve growth factor, brain-derived neurotrophic factor, neurotrophin-3, neurotrophin-4
 - Neurotrophin-3 and brain-derived neurotrophic factor promote survival and maturation of sensory and motor neurons
 - Therapeutic potential in treatment of human neurodegenerative disorders such as ALS and peripheral neuropathies
 - In clinical trials in patients with diabetic neuropathy, recombinant human NT-3 (r-HuNT-3) induces diarrhea
- Give the disorders of the Myenteric Plexus
- Familial visceral neuropathies
 - Recessive, with intranuclear inclusions
 - Recessive, with mental retardation and calcification of the basal ganglia
 - Dominant, with neither of above
- Sporadic visceral neuropathies
 - Degenerative, non-inflammatory
 - Degenerative, inflammatory
 - Paraneoplastic
 - non-paraneoplastic (Chagas, cytomegalovirus, idiopathic)
 - isolated axonopathy
- Developmental abnormalities
 - Hirschsprung disease
 - Total colonic aganglionosis (sometimes with small intestinal aganglionosis)
 - Maturation arrest
 - with mental retardation
 - with other neurological abnormalities
 - isolated to myenteric plexus, without the above
 - Neuronal intestinal dysplasia



- with neurofibromatosis
- with MEA II
- isolated to intestine, without above

➤ Severe, idiopathic constipation

➤ Drug-induced /toxic damage

IRRITABLE BOWEL SYNDROME (IBS)

➤ Colonic dysmotility

- Increased amplitude of colonic contractions
- Abnormally prolonged gastrocolonic motor response to food
- Abnormal contractility upon balloon distension
- Abnormal contractility upon CCK stimulation?
- Abnormal colonic transit in ascending colon?
- Consistent pathognomonic colonic motility changes, coinciding with IBS symptoms have not been established (3c/min myoelectric rhythm?)
- Hypercontractile episodes often not temporally related to symptoms
- Usually short-term recordings available often in rectosigmoid only

➤ Other smooth muscle irritability

- Lung
 - Bronchus and trachea
- GU
 - Bladder
 - Vagina
- GI
 - Esophagus
 - Stomach
 - Small bowel

➤ Alteration of visceral sensitivity in IBS

- Heightened sensitivity to gut nociceptive stimuli
- Heightened and more diffusely projected perception to mechanoreceptor stimulation
- Suprareceptor sensory disturbance contributing to distorted focalization of abnormal sensation
- Alteration of pain perception confined to GI-tract; somatosensory pain perception normal

➤ Stress associations

- IBS patients recall more stressful events than asymptomatic controls
- Stressful life events precede the onset of IBS in 50% of patients
- Stressful events exacerbate bowel symptoms



- IBS patients show a greater increase in colon motility in response to emotional arousal than healthy controls
- ROME III criteria for IBS
 - Symptom onset at least 6 months prior to the diagnosis of recurrent abdominal pain or discomfort for at least 3 days of the month in the last 3 months
- Association with at least 2 of the following:
 - Improvement with defecation
 - Onset associated with change in stool frequency
 - Onset associated with change in stool form

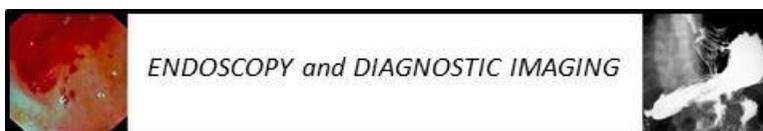
Adapted from: Longstreth GF, Thompson WG, Chey WD, et al. *Gastroenterology* 2006;130(5):1480-1491.

- Pathophysiological abnormalities associated with post-infectious IBS.
 - ↑ intestinal permeability
 - ↑ intestinal IL-1b
 - ↑ enterochromafin cells
 - ↑ serotonin blood levels after food

Adapted from: Connor BA. *Clin Infect Dis* 2005;41 suppl 8:S577-86.; and Spiller RC. *Gastroenterology* 2003;124(6):1662-1671.

Practice Pointers: IBS and prebiotics, antibiotics and Mesalamine

- For benefit, NNT=4 (Moayyedi P, et al. The efficacy of probiotics ***in the treatment of*** irritable bowel syndrome: a systematic review. *Gut* 59(3), 325–332 (2008).
 - Systematic Review: many sub-optimal study designs; 2 high quality studies suggested that only *Bifidobacter infantis* 35,624 showed benefit in IBS (Brenner DM, Moeller MJ, Chey WD et al. The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Am J Gastroenterol* 2009;104(4):1033-49).
 - Rifaximin increases IBS improvement from 20% with placebo, to about 40% (Pimentel M, Park S, Mirocha J et al. The effect of a nonabsorbed oral antibiotic (rifaximin) on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med.* 2006 Oct 17;145(8):557-63)



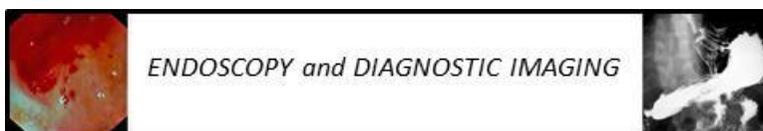
Recent Updates: Irritable Bowel Syndrome (IBS)

- Persons with IBS (particularly diarrhea-predominant or mixed diarrhea/constipation) may have diverticulitis (9% of males and 17% of females with IBS), but the presence of IBS is not associated with an increased risk of diverticulitis (Jung et al., 2010; 105: 652-661).
- Traditionally, constipation has been classified into normal transit, slow transit, and functional defecatory disorders. This is not an ideal approach, since the changes in slow transit do not necessarily reflect problems with motor function, and colonic tone and compliance (presence-volume relationships) were not taken into account. Addressing these issues, a new mechanistic classification is suggested based on 1) fasting phasic activity and tone; 2) phasic activity and tonic postprandial high amplitude contractions, and responses (Ravi et al., GE 2010; 138: 89-97).
- A number of new features have been suggested in the pathogenesis of IBS (Ohman & Finzen, 2010):
 - Innate immunity – increased numbers or altered functions of innate immunity cells (innate cells, monocytes/macrophages, CD3+ or CD4+ T cells, CD8+ T cells, or B-cells in the small and/or large intestine, and in the blood).
 - Intestinal permeability – decreased expression in the jejunum of the tight junction protein ZO1 (aka zonula occludens protein)
 - Neuroimmune interactions – increased number of sensory nerve fibres expressing the capsaicin receptor TRPV1
 - Microbiota – increased risk of IBS after enteric infection, abnormalities in fecal microbiota

Practice Pointers: Diagnostic criteria for functional abdominal pain syndrome (FAPS)

- Presence for at least 3 months, with onset of at least 6 months before diagnosis of:
 - Continuous or nearly continuous abdominal pain; and
 - No or only occasional relationship of pain with physiologic events (e.g. eating, defecation, or menses); and
 - Some loss of daily functioning; and
 - The pain is not feigned (e.g. malingering); and
 - Insufficient symptoms to meet criteria for another disorder of gastrointestinal function that would explain the pain

Adapted from: Drossman D. *Clinical Gastroenterology and Hepatology* 2008;6:pg 979.



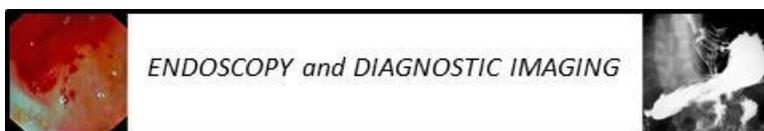
CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (CIPO)

- Definition
 - Acute, recurrent or chronic symptoms suggestive of obstruction of small or large intestine without any radiological, surgical or endoscopic evidence of mechanical obstruction
 - Disordered GI motility
 - muscle - ICC – neuron
- Pathophysiological criteria
 - neuropathic CIP
 - myopathic CIP
 - Unclassified (ICC's [interstitial cell of cajal]??)
- Etiological criteria
 - congenital / familial
 - acquired (systemic diseases, post-infectious, drug-induced,)
- Outline when to suspect CIPO, the types and associations
- When to suspect pseudo-obstruction
 - Coexistence of vomiting, abdominal distention, constipation, weight loss
 - chronic symptoms, no symptom-free intervals
 - abdominal pain is not the only symptom
 - urinary symptoms (bladder distention, frequent urinary infections)
 - familial history
 - several non-diagnostic laparotomies
 - autonomic nervous system dysfunction (postural dizziness, sweating abnormalities)
 - radiological studies (no obstruction, megaduodenum)
 - muscle weakness, ptosis, ophthalmoplegia, deafness, mental retardation, lactate acidosis
- Type of Chronic intestinal pseudo-obstruction

Type	Myopathic	Neuropathic
➤ Infiltrative	Scleroderma, amyloidosis	Early scleroderma, amyloidosis
➤ Neurologic Disease	Myotonic and other dystrophies, mitochondrial myopathy (MNGIE)	Diabetes, porphyria, brain stem tumor, MS, spinal cord transection, dysautonomias (Shy Drager)

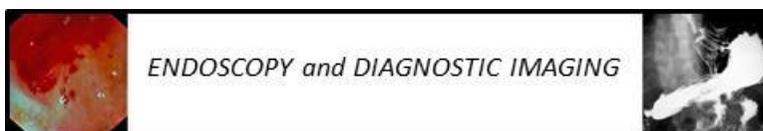


- Neoplastic
 - Paraneoplastic (small cell lung tumor), mammary ca, pancreas ca
- Endocrine
 - Hypothyroidism, diabetes, hypoparathyroidism, pheochromocytoma (MEN II B)
- Drug-induced
 - Anti-depressants, narcotics, anti cholinergics, laxative abuse, smooth muscle relaxants, vincristine
- Infectious
 - Chagas, viral (CMV, EBV, HSV)
- Idiopathic
 - Non-familial hollow visceral myopathy
 - Hirschsprung disease, chronic idiopathic intestinal pseudo obstruction
- Familial
 - Familial visceral myopathies (AD or AR), MNGIE (AR)
 - Familial visceral neuropathies, von Recklinghausen disease
- Conditions associated with chronic intestinal pseudo-obstruction-like clinical presentation
 - Scleroderma
 - Myxedema
 - Hypoparathyroidism – hyperparathyroidism
 - Severe celiac disease and electrolyte imbalance
 - Mesenteritis, mesenteric lesions, celiac ganglion lesions
 - Amyloidosis
 - Chagas disease
 - Myotonia dystrophica
 - Hirschsprung disease
 - Drug toxicity (morphine, heroine, anticholinergics, ganglionic blockers, etc)
 - Autonomic nervous system disorders
 - Glucagon-secreting tumor



Practice Pointers: Ogilvie Syndrome

- Definition: Acute colonic pseudo-obstructive
- Clinical
 - Acute dilation of the colon without evidence of mechanical obstruction
 - Associated with an underlying medical condition or postoperative state in >90 %
 - >50 % in relation to surgery
 - 45 % with an acute or chronic medical disorder
 - Risk factors:
 - advanced age (sixth decade)
 - obesity
 - male gender
- Causes
 - Surgical
 - Orthopedic (hip)
 - Intra-abdominal
 - Cardiothoracic
 - Neurosurgical
 - Laminectomy
 - epidural anesthesia
 - spinal anesthesia
 - myelography
 - Medical
 - Electrolytes (hypoNa, hypoK, hyperCa, hypoCa, hypoMg)
 - AMI, congestive heart failure
 - COPD, pulmonary embolism
 - Parkinson, dysautonomia
 - Amyloidosis, MEN IIB
 - Burns
 - GI (cholecystitis, pancreatitis, peritonitis,...)
 - Retroperitoneal disorders (hemorrhage, hematoma, malignancy,...)
 - Medications
 - Infections (CMV, HSV)
- Conditions associated with transient Intestinal pseudo-obstruction
 - Colonic intestinal pseudo-obstruction (Ogilvie Syndrome)
 - Renal failure
 - Pancreatitis
 - Pneumonia
 - Congestive heart failure
 - Spinal injury
 - Electrolyte imbalance



Acute Colonic Pseudo-Obstruction Ogilvie Syndrome

- Acute dilation of the colon without evidence of mechanical obstruction
- Associated with an underlying medical condition or postoperative state in >90 %
 - >50 % in relation to surgery
 - 45 % with an acute or chronic medical disorder
- Risk factors:
 - advanced age (sixth decade)
 - obesity
 - male gender
- Causes

Surgical

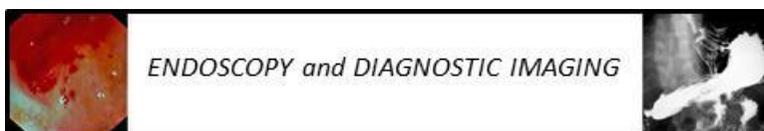
- Orthopedic (hip)
- Intra-abdominal
- Cardiothoracic
- Neurosurgical
 - Laminectomy
 - Epidural anesthesia
 - Spinal anesthesia
 - Myelography

Medical

- Electrolytes (hypoNa, hypoK, hyperCa, hypoCa, hypoMg)
- AMI, congestive heart failure
- COPD, pulmonary embolism
- Parkinson, dysautonomia
- Amyloidosis, MEN IIB
- Burns
- GI (cholecystitis, pancreatitis, peritonitis,...)
- Retroperitoneal disorders (hemorrhage, hematoma, malignancy,...)
- Medications
- Infections (CMV, HSV)

➤ Symptomatology

- progressive abdominal distention
- postoperatively: typically by the 4th day
- lower abdominal pain
- obstipation
- low grade fever
- hypoactive or absent bowel sounds (40%)



➤ Radiology

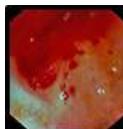
- dilation of cecum, ascending and transverse colon (70–90 %)
- paucity of gas in the left colon
- preservation of haustral markings (vs mechanical obstruction)



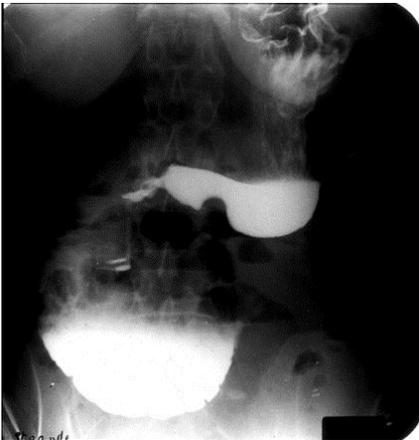
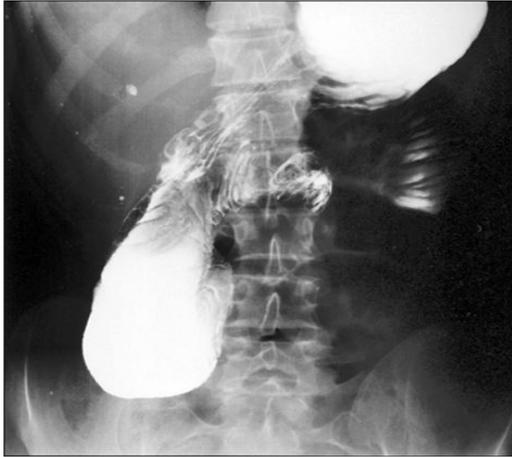
➔ **Monitor cecal distention !!**

> 9 cm = abnormal

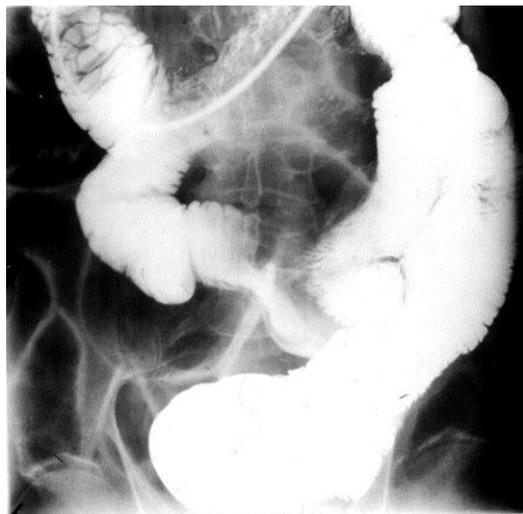
>12 cm: risk of perforation!!

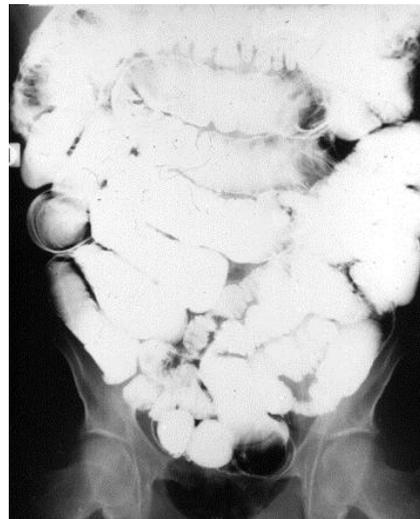
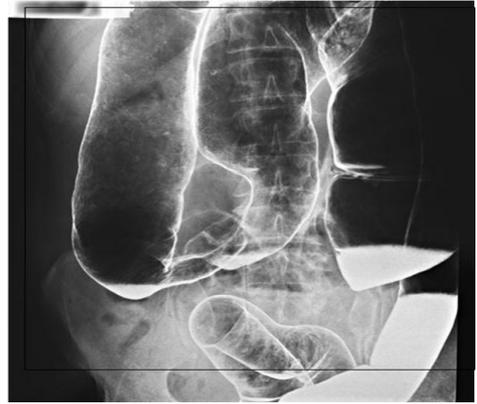


➤ Chronic intestinal pseudo-obstruction: Radiological findings

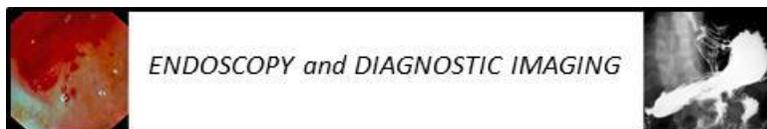
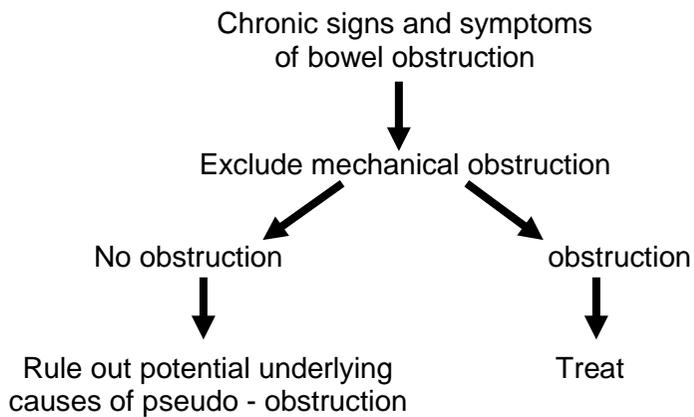








➤ Diagnostic evaluation



- Chronic intestinal pseudo-obstruction associated with small cell carcinoma of the lung – histopathology
 - Visceral neuropathy of the myenteric plexus (esophagus-stomach-bowel)
 - Neuron and axon degeneration
 - Lymphoplasmacytic infiltration
 - Glial cell proliferation
 - Smaller number of neurons

Chinn JS, Schuffler MD, Gastroenterology 1988;95:1279-1286

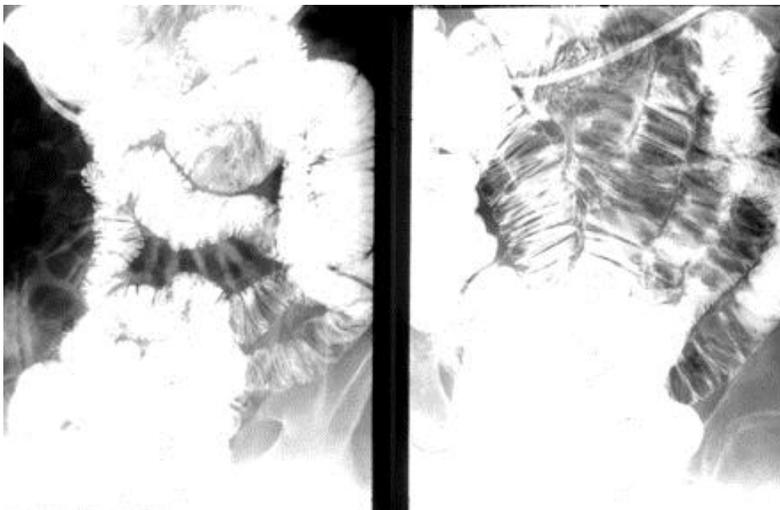
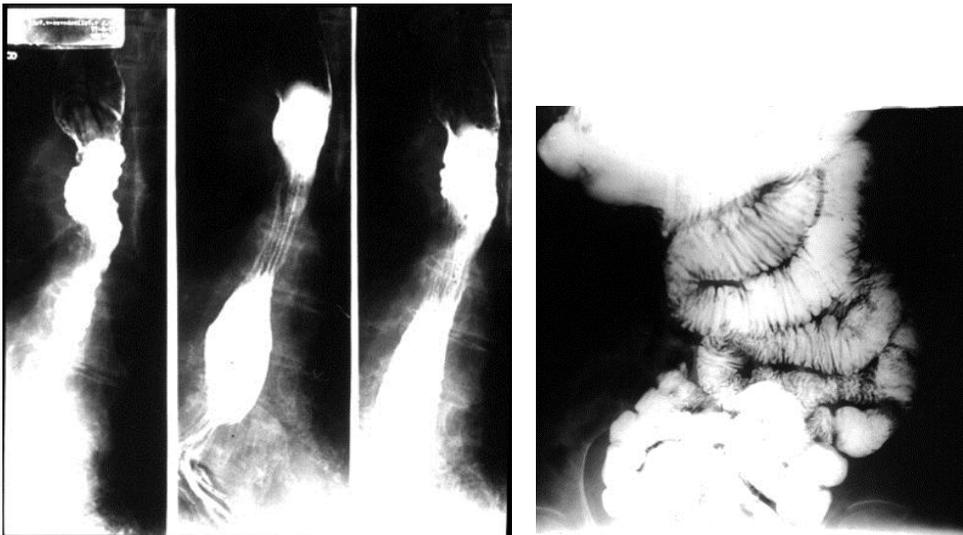
- Scleroderma
 - Skin changes
 - Raynaud phenomenon
 - Aperistalsis of esophagus
 - Duodeno-jejunal dilatation and hypomotility with straightening of enlarged folds, closely set and parallel to one another
 - Abnormalities of small bowel biopsy
 - Dilatation of the colon with formation of wide-mouthed pseudo diverticula
 - Dilated esophagus with abnormal esophageal motility – achalasia
 - Dilatation of small bowel
 - Dilatation of left colon
- Scleroderma-associated colonic diverticulae
 - Sacculations – wide mouthed pseudodiverticulae on antimesenteric border
 - Haustral markings: lost
 - Dilation
 - Localized narrowing
 - Elongation

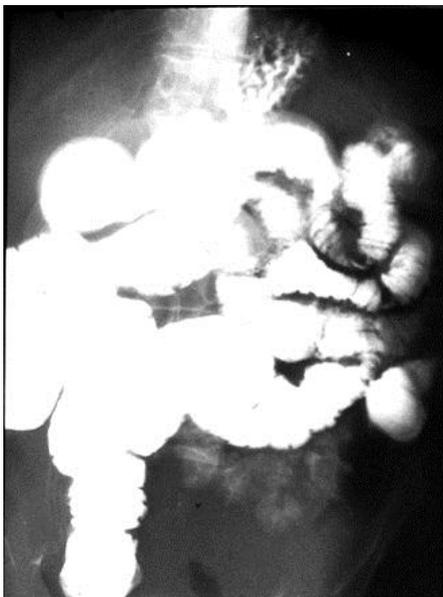
Distinguishing diagnosis: scleroderma colon vs Crohn colitis

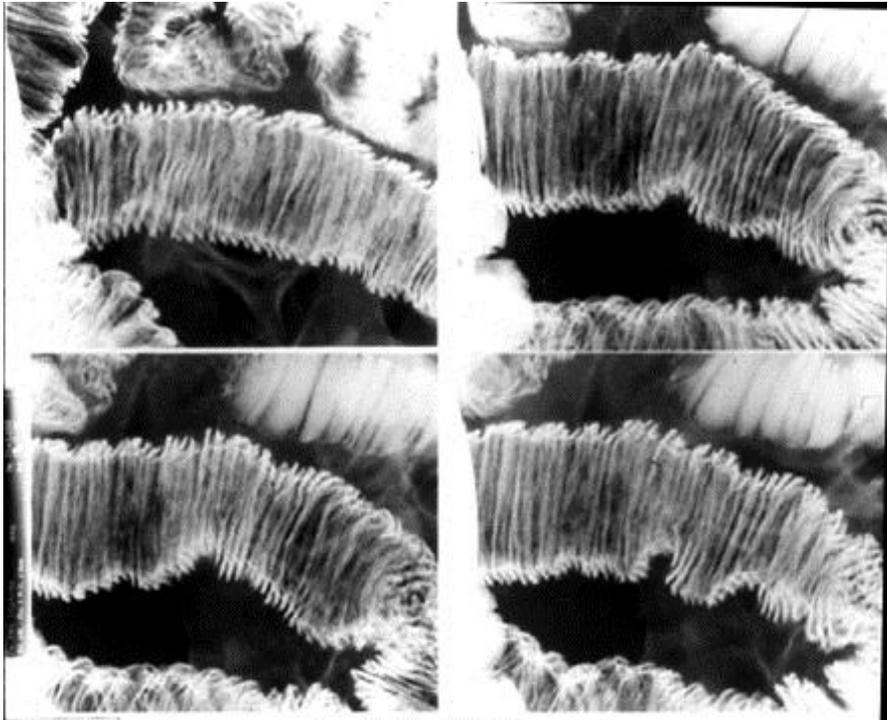
	Scleroderma colon	Crohn colitis
○ Patchy (segmental)	+	+
○ Mesenteric border	+	-
○ Antimesenteric border	+	+

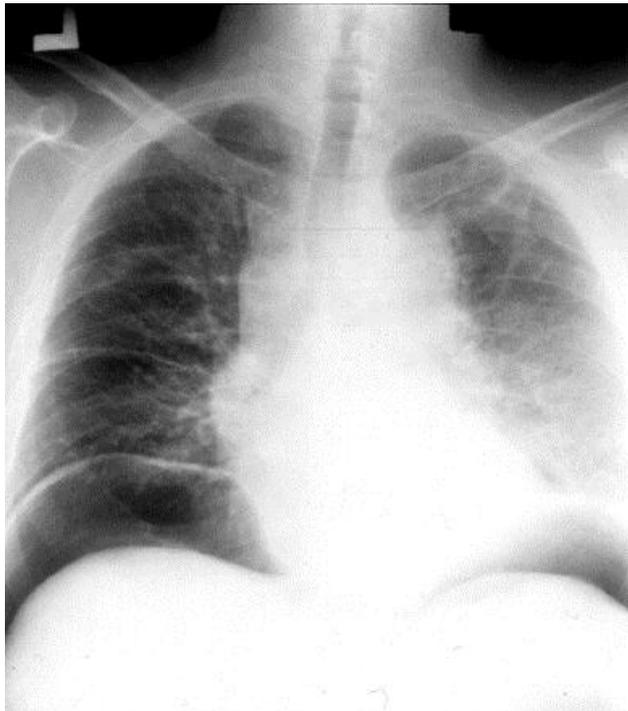


- Mastocytosis of colon
 - Segmental
 - Non-specific
 - Folds haustra
 - Thick
 - Distorted
 - Mucosa
 - Fine, nodular, “sand-like” pattern
 - Skeleton
 - Sclerosis

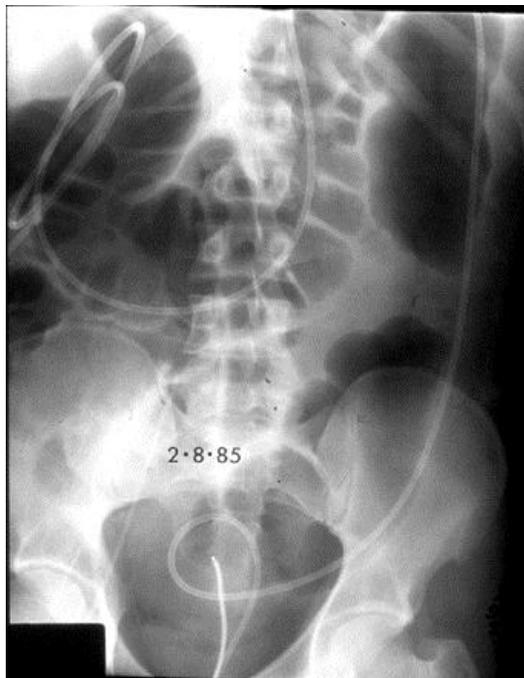




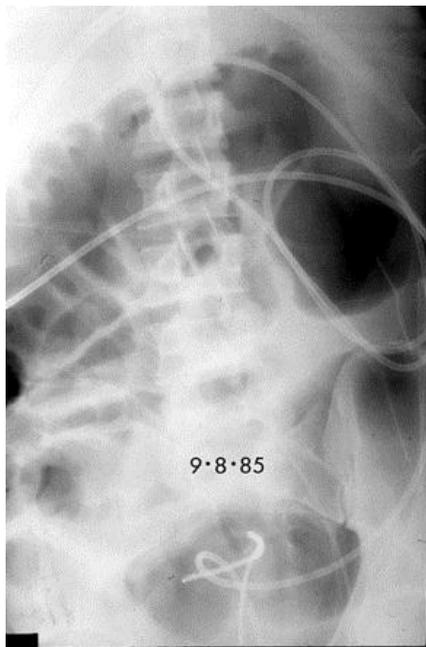




➤ Endoscopic decompression of acute colonic pseudo-obstruction



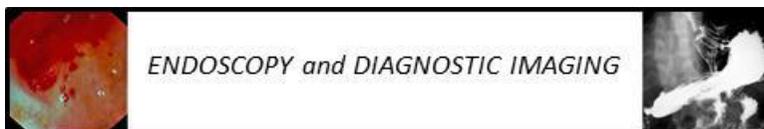
CONSTIPATION



- Causes of constipation may be classified as neurogenic, drug-associated, and metabolic.
 - Central
 - Multiple sclerosis
 - Parkinson's disease
 - Cerebral infarction (CVA)
 - Medullary trauma
 - Spinal
 - Cognitive challenge
 - Dementia
 - Meningocele
 - Spinal cord lesions (trauma, tumor)
 - Cauda equina lesions

Printed with permission: Müller-Lissner, Stefan. *Best Practice & Research Clinical Gastroenterology* 2007; 21(3): pg. 475.

- Gut
 - Autonomic neuropathy (paraneoplastic, pseudoobstruction, diabetes)
 - Aganglionosis: congenital (Hirschsprung's) or acquired
 - Cathartic colon (laxative abuse)
 - Narcotic bowel syndrome



➤ Metabolic

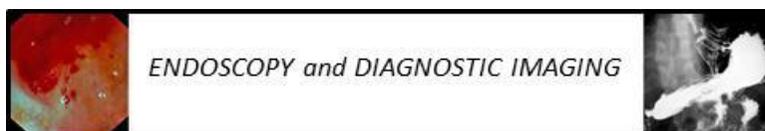
- Diabetes mellitus
- Glucagonoma
- Hypothyroidism
- Hypoparathyroidism
- Hypopituitarism (panhypopituitarism)
- Hypocalcemia
- Hypomagnesium
- Hypokalemia
- Heavy metal poisoning
- Pregnancy
- Progesterone level cyclic fluctuation (just before menses)
- Porphyria
- Low intake of water

➤ Drugs

- Analgesic: narcotics e.g. opiates (“cathartic colon”), non-narcotics
- Antacid (aluminum)
- Anticholinergics (dopaminergics)
- Anti-Parkinson drugs
- Antipsychotics
- Antidepressants (tricyclics, but not SSRIs – serotonin reuptake inhibitors)
- Antidiarrheals
- Antihypertensives (calcium channel blockers, clonidine)
- Antiseizure medications
- Bile acid sequestrants
- Chemotherapeutic agents
- Nutrient supplements: calcium, iron
- 5-HT₃ antagonists
- Somatostatin analogs

➤ Appropriate investigations for the investigation of persons with constipation

- History and Physical – social, laxative and drug use, psychological assessment, stool chart; full examination including digital rectal exam (DRE)
- Lab tests – Ca⁺⁺, glucose, TSH, electrolytes, CBC, Mg⁺⁺
- 3 views of the abdomen
- Colonoscopy, defecating proctogram (defecogram), colonic transit study, EUS, Colonic manometry
- Diagnostic Imaging
- Manometry, anorectal manometry (rectoanal inhibitory reflex)
- Functional testing, Balloon expulsion



- Non-pharmacological treatments of constipation
 - Treat underlying conditions
 - Bowel management techniques
 - Psychological management
 - Avoid constipating medications
 - Exercise
 - Adequate water intake
 - Dietary measures
 - Biofeedback (pelvic floor retraining)
 - Total colectomy with ileorectal anastomosis

Secondary Intestinal Pseudo-Obstruction

- Transient causes
 - Electrolyte Disturbances
 - Drugs Immotility
- Chronic causes
 - Diseases involve intestinal smooth muscle
 - Neurological diseases
 - Endocrine disorders
 - Diabetes mellitus
 - Myxoedema
 - Pheochromocytoma
 - Hypoparathyroidism

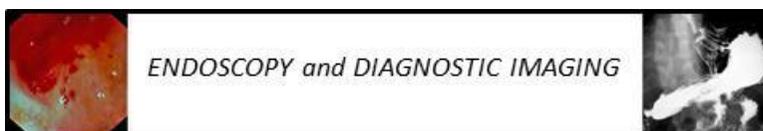
Megacolon

Colon persistently increased in diameter associated with longstanding constipation, differentiation between colon inertia and outlet

- obstruction necessary
 - Aganglionosis
 - Underlying causes
 - Medical conditions
 - Antipsychotic drugs
 - Neurological disturbances
 - Idiopathic disease

Causes of Constipation in Pregnancy

- Hormonal – slow transit
- Mechanical
- Medications
- Lifestyle
 - Reduced exercise
 - Dietary changes



- Pre-existing disease:
 - Chronic slow-transit constipation
 - Irritable bowel syndrome
 - Congenital or acquired megacolon
 - Chronic idiopathic intestinal pseudo-obstruction
- Risk factors for the development of incontinence post-partum
 - Vaginal delivery
 - Instrumental delivery
 - Emergency cesarean section
 - Epidural anesthesia
 - Perineal laceration
 - Obstetric genital fistula

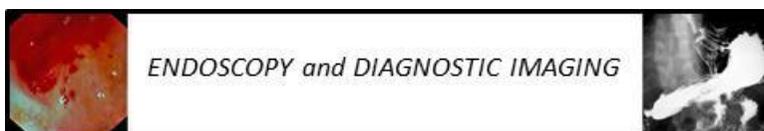
Printed with permission: Quigley, Eamonn MM. *Best Practice & Research Clinical Gastroenterology* 2007;21(5): pg. 885.

Diagnostic imaging

- Mechanical Obstruction
 - Distention to level of obstruction
 - No distal air contents
 - Air
 - Fluid
 - Stool
 - Ileum
 - Gaseous distention of ileocecal valve is open
 - Causes of acute obstruction
 - Carcinoma
 - Diverticulitis
 - Extramural compression (metastases)
 - Impaction
 - Hernia
 - Adhesion
 - Chronic obstruction
 - Haustra thickened
 - Luminal contents “grey, “granular”-appearing fluid

Obstruction

- Volvulus
- Sigmoid
 - Dilated, inverted, U-shaped loop
 - Twisted loop of bond at the obstruction (“beaking”)
- Cecal



- Abdominal film, barium
 - Dilation (> 9 cm)
 - Cecum in middle left side, especially LUQ
 - Distal colon no air
 - Distal small bowel
 - Air
 - Dilation
 - Perforation
 - Free air
 - Decompression of air in volvulus
 - Ischemia
 - Cecal
 - Intramural air
 - Air in portal vein

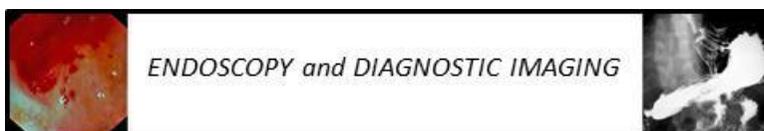
- CT
 - Cecum in middle or left side
 - Cecum and mesentery
 - Twisted (whorled appearance of the mesentery)
 - Encircle each other

- Perforation
 - Plain abdominal radiograph: air
 - Peritoneal
 - Retroperitoneal
 - Intramural
 - Perirectal
 - Paraspinal

- CT: most helpful

- Innominate grooves (lines)
 - When colon is only partially distended, spiculations that look like ulcers are seen along the colonic wall from barium collected in the crevices; these spiculations disappear with further colonic distention.

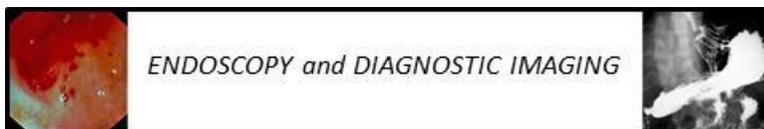
- Thickened Fold
 - Diverticulitis
 - Colitis
 - UC, CD
 - PMC
 - Neurogenic
 - Ischemic
 - Radiation
 - Pancreatitis



- Appendicitis
- Mastocytosis

Filling Defects

- Single
 - Ileocecal valve
 - Lipoma
 - Endometrioma
 - Appendicitis
 - Mucocele
 - Stool
 - Bubbles / cysts
- Single or multiple
 - Polyp multiple polyposis syndrome
 - Adenocarcinoma
 - Lymphoma
 - Metastases
 - Stool
 - Pneumatosis coli
 - Lymphoid follicles
 - Amebiasis
 - Colitis cystica profunda
- Narrowing
 - Spasm
 - Diverticulitis
 - Adenocarcinoma
 - Metastases
 - Colitis
 - UC, CD
 - Ischemia
 - Radiation
 - Pancreatitis
 - Endometriosis
 - Cathartic colon
 - Pelvic lipomatosis

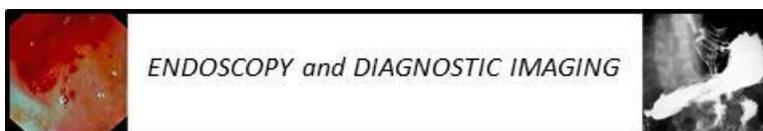


LAXATIVES

Classify drugs used to treat constipation(laxative), and give their site as well as mechanism of action.

Class	Examples	Site of action	Mechanism of Action
➤ Bulk or hydrophilic	<ul style="list-style-type: none"> ○ Plantain derivatives ○ Methylcellulose ○ Psyllium ○ Isphagula ○ Bran 	Small intestine and large intestine	Holds water in stool, mechanical distension
➤ Osmotic	<ul style="list-style-type: none"> ○ Salinic osmotic ○ Lactulose ○ Sorbitol 	Small intestine and large intestine	Attracts/retains water in intestinal lumen, increasing intraluminal pressure
➤ Surfactant or softener or wetting	<ul style="list-style-type: none"> ○ Docusate ○ Poloxalcol 	Small intestine and large intestine	Softens stool by facilitating admixture of fat and water to agents to soften stool
➤ Irritant or peristaltic stimulant	<ul style="list-style-type: none"> ○ Senna ○ Cantron ○ Cascara ○ Bisacodyl 	Large intestine	Direct action on mucosa, stimulates myenteric plexus, alters water and electrolyte secretion
➤ Other	<ul style="list-style-type: none"> ○ Cisapride ○ Prucalopride 	Small intestine and large intestine	Stimulates motility of the lower GI tract

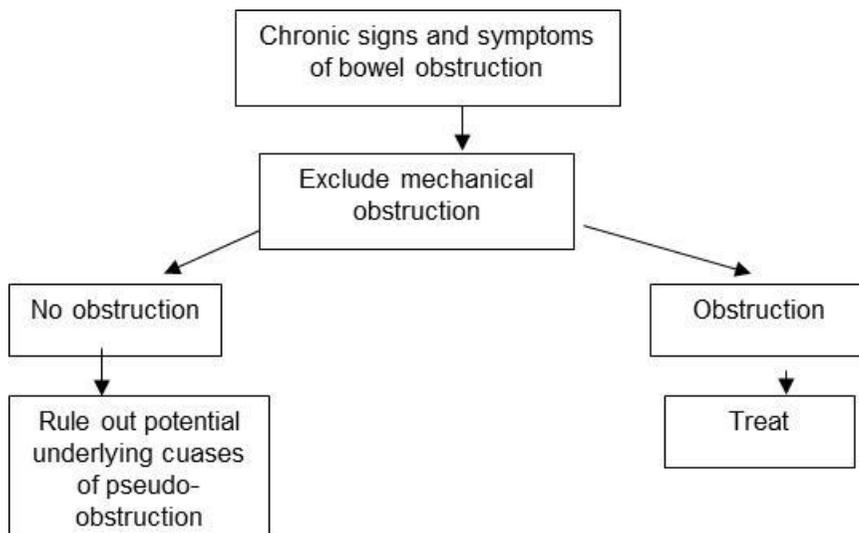
- Classify drugs used to treat constipation in persons with constipation-predominant IBS (IBC-C)
 - Bulking agents – psyllium, methylcellulose, fiber
 - Osmotic laxatives – M of M (“milk of magnesia”), lactulose, PEG, sorbitol, mannitol
 - Stimulant laxatives – Senna, Bisacodyl, castor oil
 - Lubricant – mineral oil
 - CFTR stimulants
 - Chloride- channel agonists



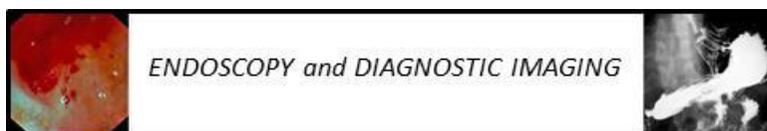
- Prostaglandins
- Cholinergics: neostigmine, bethanecol
- 5HT4 agonist
- Prokinetics - dopamine
- Motilin agonist
- Colchicine

Abbreviation: IBC-C, constipation-predominant IBS

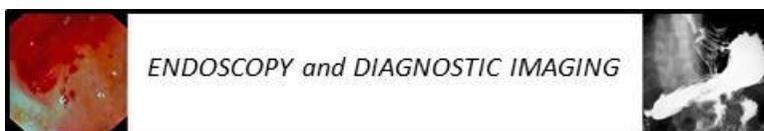
Outline a diagnostic evaluation in the person with constipation



- Assess type of pseudo-obstruction (myogenic vs neurogenic)
 - Assess segment involved (colonic vs rectosigmoid, vs anal)
 - Assess extra-intestinal disease
 - urinary tract (megaureter, urinary bladder dysfunction)
 - signs of autonomic neuropathy (eg diabetes mellitus)
 - striated muscle disease (mitochondrial disease)
 - systemic disease (amyloidosis, CREST, neoplasm)
 - CNS disease
- Constipation: definition using objective criteria
- Defecation frequency less than 3 times per week
 - Fecal consistency: 40–60% water instead of 75–80%
 - Fecal weight: less than 30 gram per day
 - Evacuation of 80% of markers after 5 days
- Spincteric changes and altered patterns of defecation



- Internal anal sphincter
 - Increased activity
 - Idiopathic
 - Hemorrhoids
 - fissure-in-ano
 - Diminished relaxation
 - Hirschsprung disease
 - Tendency to constipation
 - External anal sphincter
 - Decreased activity (tendency to cause incontinence)
 - Idiopathic
 - rectal prolapse
 - neurological lesions
 - result of injury
- Give the causes of constipation
 - Neurogenic
 - Central
 - Multiple sclerosis
 - Parkinson's disease
 - Cerebral infarction (CVA)
 - Medullary trauma
 - Spinal
 - Cognitive challenge
 - Dementia
 - Meningocele
 - Spinal cord lesions (trauma, tumor)
 - Cauda equina lesions
 - Gut
 - Autonomic neuropathy (paraneoplastic, pseudoobstruction, diabetes)
 - Aganglionosis: congenital (Hirschsprung's) or acquired
 - Cathartic colon (laxative abuse)
 - Narcotic bowel syndrome
 - Drugs
 - Analgesic: narcotics e.g. opiates ("cathartic colon"), non-narcotics
 - Antacid (aluminum)
 - Anticholinergics (dopaminergics)
 - Anti-Parkinson drugs
 - Antipsychotics
 - Antidepressants (tricyclics, but not SSRIs – serotonin reuptake inhibitors)
 - Antidiarrheals
 - Antihypertensives (calcium channel blockers, clonidine)
 - Antiseizure medications



- Bile acid sequestrants
- Chemotherapeutic agents
- Nutrient supplements: calcium, iron
- 5-HT₃ antagonists
- Somatostatin analogs

➤ Metabolic

- Diabetes mellitus
- Glucagonoma
- Hypothyroidism
- Hypoparathyroidism
- Hypopituitarism (panhypopituitarism)
- Hypocalcemia
- Hypomagnesium
- Hypokalemia
- Heavy metal poisoning
- Pregnancy
- Progesterone level cyclic fluctuation (just before menses)
- Porphyria
- Low intake of water

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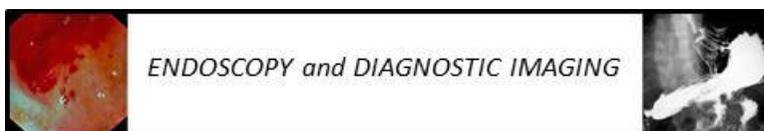
- Give the choices for the investigation of persons with constipation.
 - History and physical– social, laxative and drug use, psychological assessment, stool chart; digital rectal exam (DRE)
 - Lab tests – Ca⁺⁺, glucose, TSH, electrolytes, CBC, Mg⁺⁺
 - 3 views of the abdomen
 - Colonoscopy, defecating proctogram (defecogram), colonic transit study, EUS, colonic manometry, CT colonoscopy
 - Diagnostic imaging
 - Manometry, anorectal manometry
 - Functional testing, balloon expulsion

Abbreviation: DRE, digital rectal exam

- Give the non-pharmacological and pharmacologic treatments of constipation (ie, classify laxatives):

➤ Non-pharmacological

- Treat underlying conditions
- Bowel management techniques
- Psychological management
- Avoid constipating medications
- Exercise



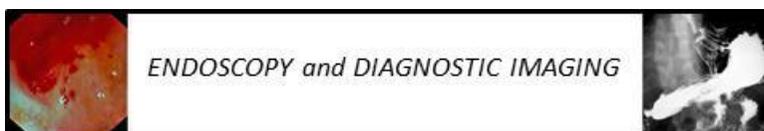
- Adequate water intake
 - Dietary measures
 - Biofeedback (pelvic floor retraining)
 - Total colectomy with ileorectal anastomosis
- Pharmacological agents
- Opiates
 - Osmotic laxatives
 - Stimulants
 - Enemas
 - Lubricants
 - 5HT₃ agonists
 - α₂- agonists
 - Octreotide
 - Bile salt binders
 - Bulking agents
 - Anticholinergics
 - Tight junction enhancers
 - Selective intestinal calcium channel blocker
 - Peripheral κ-opiate antagonist

Practice Pointers: Osmotic laxatives

- Poorly absorbed polyvalent ions (magnesium sulphate, hydroxide, carbonate, oxide, citrate) (sodium sulphate and phosphate) (sodium potassium tartrate)
- Retain fluid in intestinal lumen
- Magnesium sulphate release cholecystokinin from intestinal mucosa
 - gallbladder contraction
 - pancreatic secretion
 - stimulation of small and large bowel motor activity
 - stimulation of intestinal secretion

Practice Pointers: Why to avoid certain laxatives: Anthraquinone – induced alterations of intestinal intrinsic innervations

- Initially myenteric neurones enlarge
- Later on myenteric neurones degenerate
- Ultimately there is atrophy and even loss of neurones with increase in Schwann cells in myenteric ganglia



- Give the approximate median frequency of undesirable outcomes after colectomy for chronic constipation.

Undesirable outcomes	Approximate frequency (%)
○ Abdominal pain	40
○ Small bowel obstruction	15
○ Reoperation	10
○ Fecal incontinence	10
○ Diarrhoea	10
○ Recurrent constipation	10
○ Stoma dysfunction	5

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- Give the cause of Megacolon

➤ Definition

- Colon persistently increased in diameter associated with longstanding constipation.
- Differentiate between colon inertia and outlet obstruction necessary

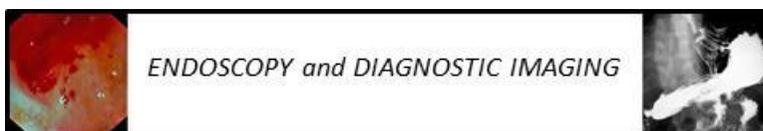
➤ Causes

- Aganglionosis
- Underlying causes
- Medical conditions
- Antipsychotic drugs
- Neurological disturbances
- Idiopathic disease

FDA classification of the safety of laxatives in pregnancy.

Safe (B)	Caution (C)	Unsafe (D)
➤ Lactulose	○ Saline osmotic laxatives	- Anthraquinones
➤ Glycerine	○ Castor oil	- 5HT ₃ agonists
➤ Polyethylene glycol (PEG)	○ Senna	- Prostaglandins (misoprostol)
➤ Bulking agents	○ Docusate sodium	
➤ Bisacodyl		

Adapted from: Cullen G, and O'Donoghue D. *Best Practice & Research Clinical Gastroenterology* 2007; 21(5): pg. 815; and Thukral C, and Wolf JL. *Nature Clinical Practice Gastroenterology & Hepatology* 2006; 3(5): pg. 260.; printed with permission: Kane SV. *AGA Institute 2007 Spring Postgraduate Course Syllabus*:511.



- Give the colonic complications of chronic laxative use (cathartic colon)
 - Pseudomelanosis Coli
 - Sharp demarcation at ileocecal valve
 - Pigmentation often more marked in cecum and ascendens, sometimes more in recto-sigmoid
 - Pigment-loaded macrophages in lamina propria and superficial submucosa
 - Pigment has staining characteristics of lipofuscin and not of melanin
 - Mode of formation of pigment is unknown
 - Radiological Abnormalities of the Cathartic colon
 - Present in 10–30% of patient with laxative abuse
 - Terminal ileum appears as smooth tube-like structure
 - Ileocecal sphincter becomes wide and gaping
 - At first mainly the right colon becomes dilated, distensible and featureless; losing its normal haustral and mucosal pattern; no rectal changes; no ulceration or pseudopolyps
 - Transient areas of narrowing or pseudo-strictures appear
 - Final shortening and retraction of colon
 - Pathological abnormalities
 - Pseudomelanosis coli
 - Mild mucosal infiltration with inflammatory cells
 - Hypertrophy of muscularis mucosae
 - Myenteric plexus damage
 - Atrophy of outer muscle layer
 - Proximal colon worse than distal colon

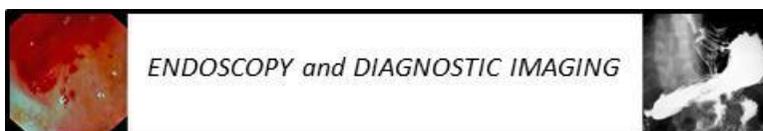
Cathartic Laxatives

- Osmotic laxatives - salines
 - magnesium salts (MgSO_4 , MgO , $\text{Mg}(\text{OH})_2$) $\text{Na}_2 \text{SO}_4$
 - lactulose (beta galactosidofructose), sorbitol
- Bulk producers
 - methylcellulose, psyllium seeds (metamucil), sterculia (normacol)
 - bran



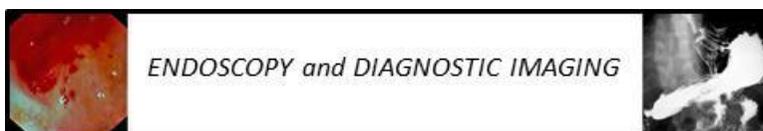
- Lubricants
 - liquid paraffin
 - dioctyl sodiumsulphosuccinate (DSS), poloxalcol
- Stimulants - irritants
 - anthraquinones (senna, cascara, aloe)
 - diphenylmethanes
 - phenolphthaleine
 - bisacodyl (dulcolax)
 - castor oil (ricinoleic acid)

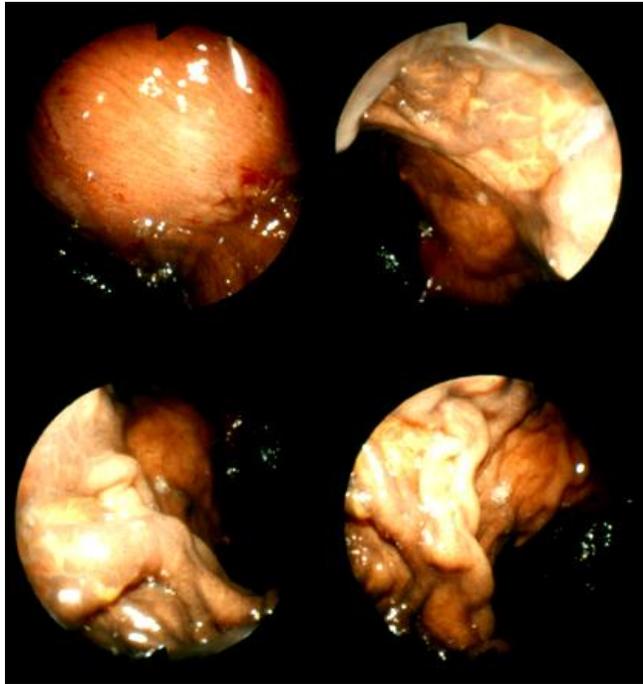
Class	Example
➤ Anthracene	○ Senna, aloe, rhubarb, cascara, frangula, danthron
➤ Salts	○ $MgSO_4$, Na_2SO_4 , $Mg(OH)_2$, Na_2HPO_4
➤ Phenylmethanes	○ Phenophtalein, bisacodyl, oxyphenisatin
➤ Polysaccharides	<ul style="list-style-type: none"> - Cellulose and derivatives - Gums – sterculia - Mucilages – ispaghula, psyllium - Agar – agar, alginates - Bran
➤ Detergents	○ Dioctyl sodium sulphosuccinate, blie salts, poloxalcol
➤ Miscellaneous	○ Lactulose, liquid paraffin, castor oil
➤ Anthraquinone – Induced alterations of intestinal intrinsic innervation	<ul style="list-style-type: none"> ○ Initially myenteric neurons enlarge ○ Lateron myenteric neurones degenerate ○ Ultimately there is atrophy and even loss of neurones with increase in Schwann cells in myenteric ganglia
➤ Pseudomelanosis Coli	<ul style="list-style-type: none"> ○ Sharp demarcation at ileocecal valve ○ Pigmentation often more marked in cecum and ascendens, sometimes more in recto-sigmoid ○ Pigment-loaded macrophages in lamina propria and superficial submucosa ○ Pigment has staining characteristics of lipofuscin and not of melanin ○ Mode of formation of pigment is unknown
➤ Pathological changes in cathartic colon	<ul style="list-style-type: none"> ○ Pseudomelanosis ○ Mild mucosal infiltration with inflammatory cells ○ Hypertrophy of muscularis mucosae ○ Myenteric plexus damage

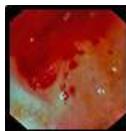
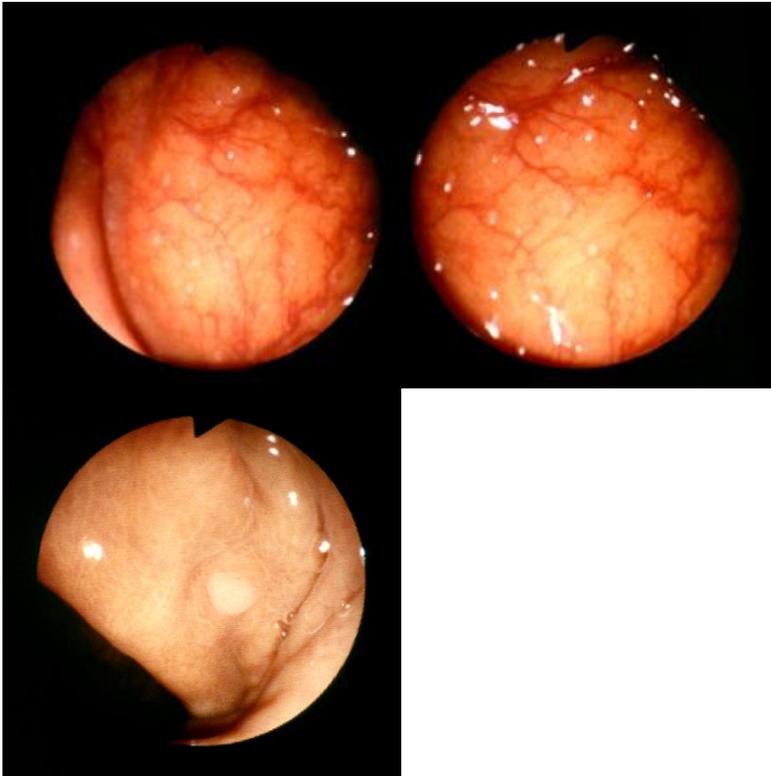


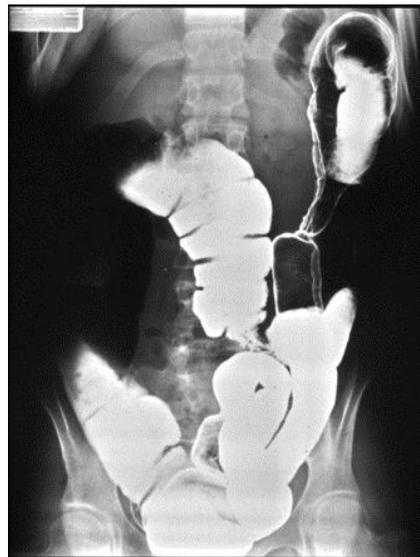
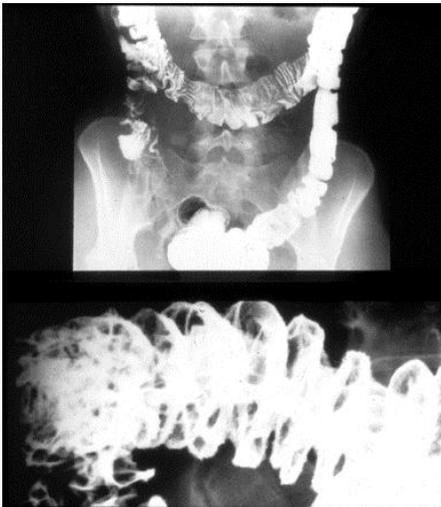
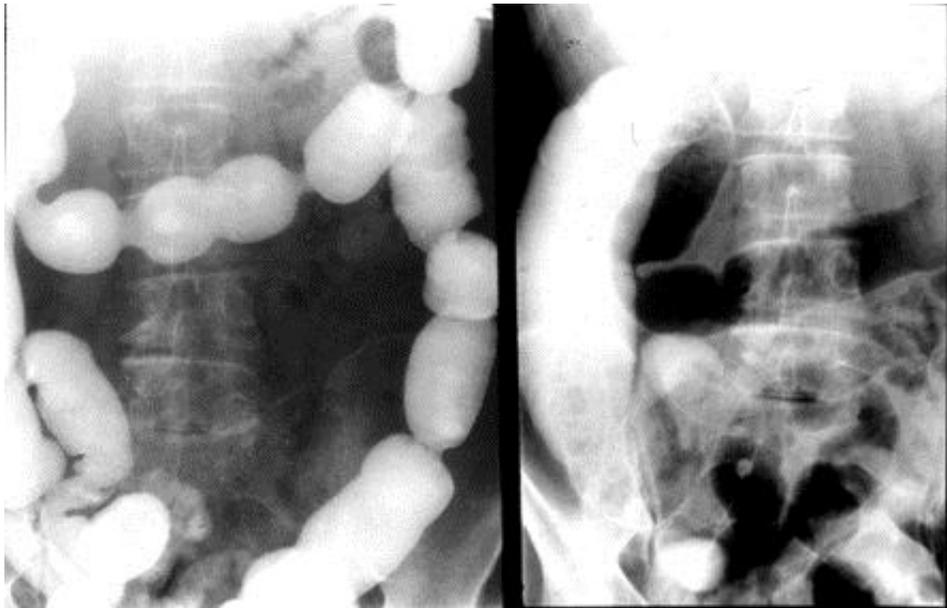
- Atrophy of outer muscle layer
- Proximal colon worse than distal colon
- Clinical presentation
 - Nearly always female
 - Usually excessive laxative use for years
 - Chief complaint

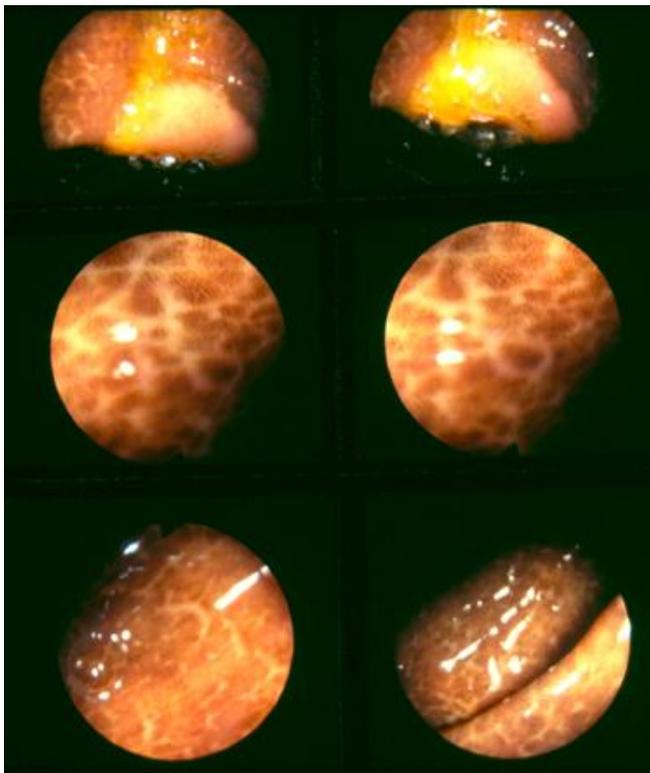
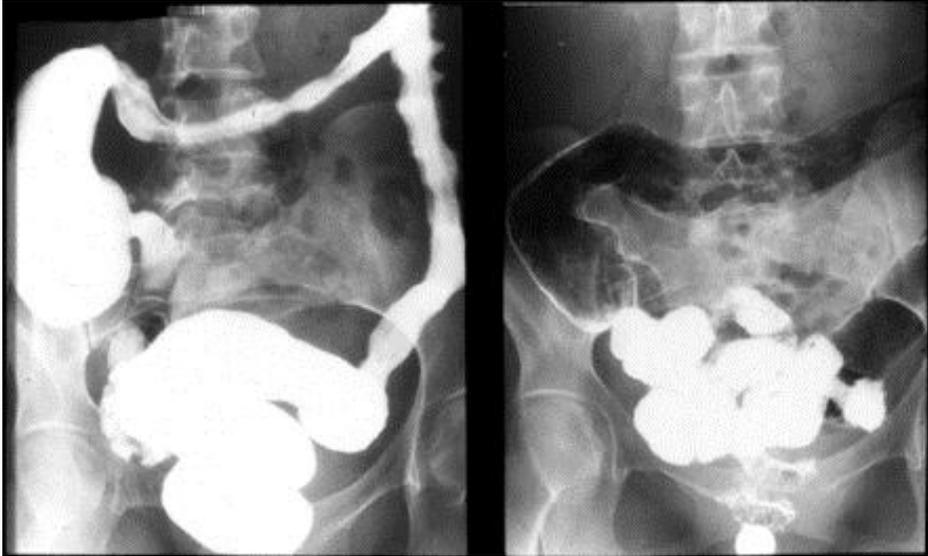
– diarrhea	60%
– constipation	40%
 - Nausea, vomiting, abdominal discomfort 90%
 - Fatigability and exhaustion 100%
 - Psychological disturbances (depression, hysteria) 90%
 - Recurrent ileus, exploratory laparotomies 30%
 - Hypokalemia 70%
 - Hypocalcemia 40%
 - Elevated creatinine 50%
 - Rx – cathartic colon
- Cathartic colon – Diagnosis
 - History
 - Electrolyte abnormalities
 - Characteristic endoscopic findings
 - Characteristic radiologic findings
 - Detection of laxatives in stool or urine
- Radiological abnormalities of the cathartic colon
 - Present in 10–30% of patient with laxative abuse
 - Terminal ileum appears as smooth tube-like structure
 - Ileocecal sphincter becomes wide and gaping
 - At first mainly the right colon becomes dilated, distensible and featureless; losing its normal haustral and mucosal pattern; no rectal changes; no ulceration or pseudopolyps
 - Transient areas of narrowing or pseudo-strictures appear
 - Final shortening and retraction of colon

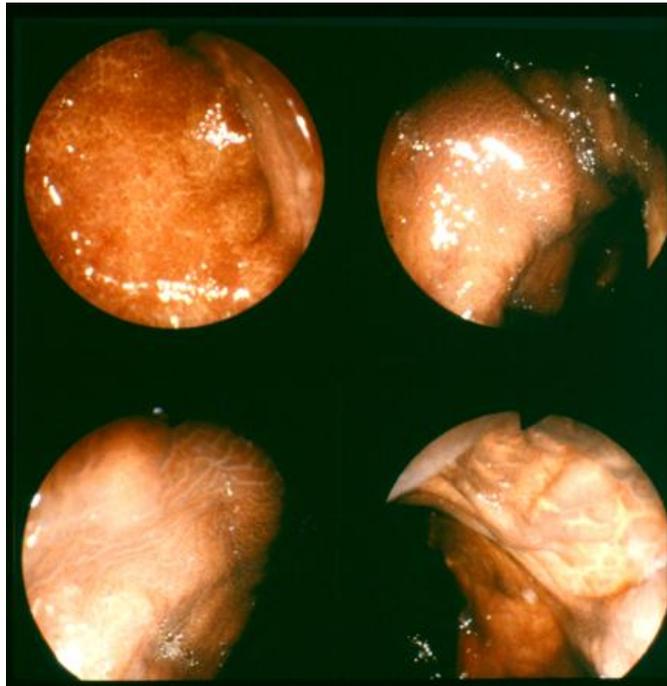
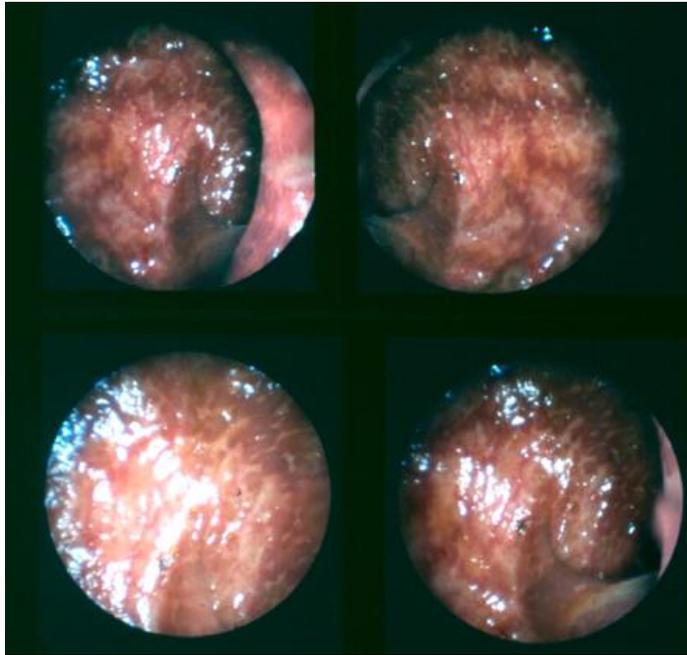


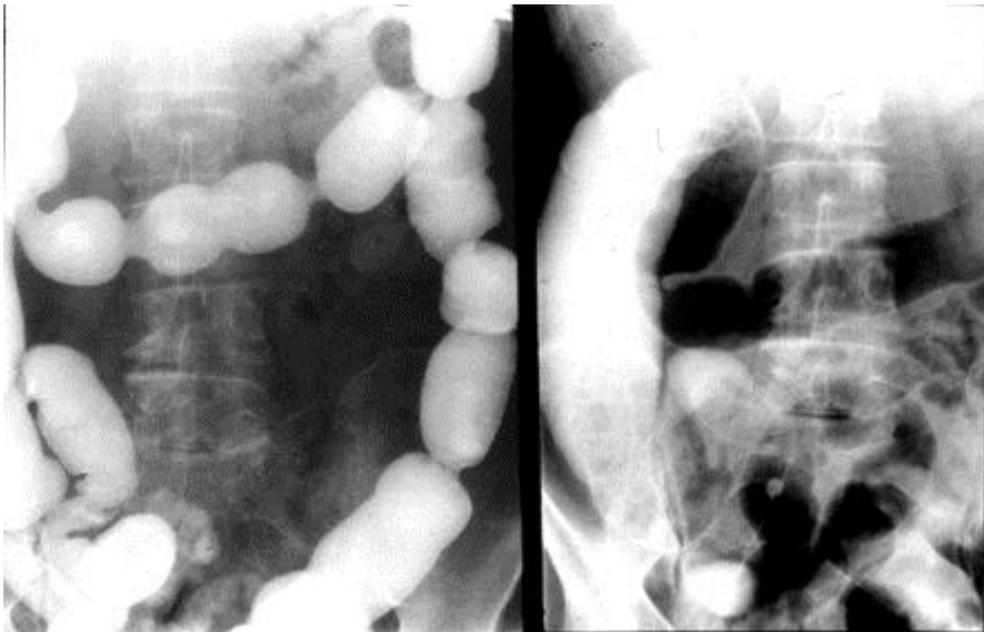


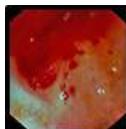
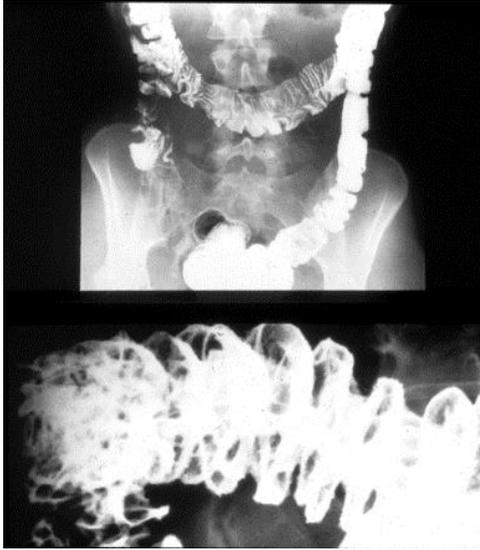


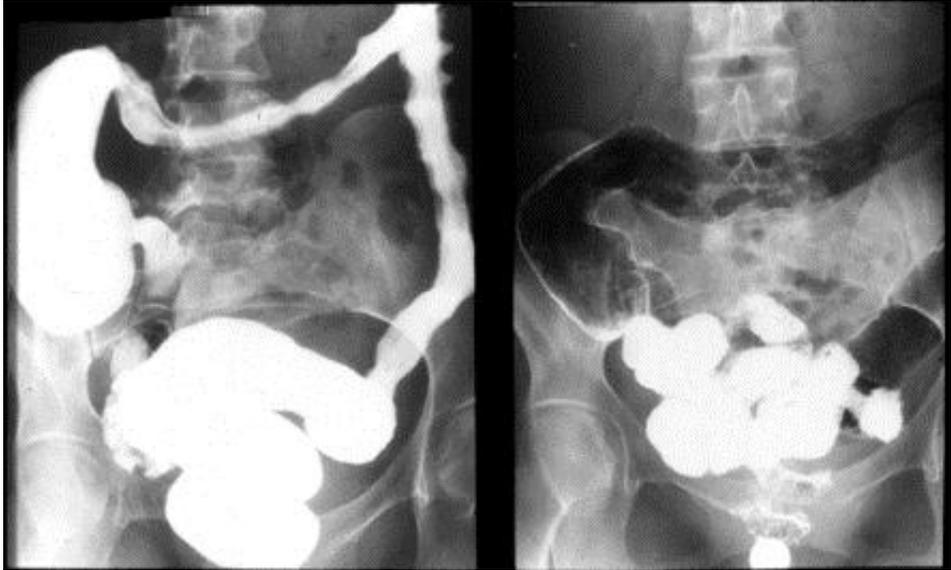












INFLAMMATORY BOWEL DISEASE: Ulcerative colitis (UC) and Crohn colitis (CC)

➤ Serology

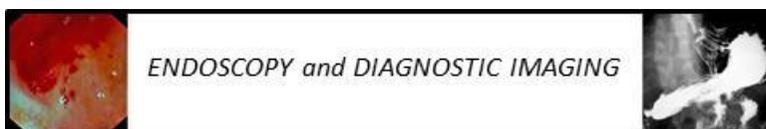
ASCA and pANCA in persons with Crohn disease and UC

Marker	Diagnosis	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
➤ ASCA	CD	50-65	70-85	80	64
➤ pANCA	UC	65-80	70-85	64	80

Abbreviations: NPV, negative predictive value; PPV, positive predictive value
Adapted from: Targan SR. *AGA Institute PostGraduate Course book*. pg. 47.

➤ Extra-intestinal manifestations of IBD

- Skin disorders
 - Erythema nodosum
 - Pyoderma gangrenosum
- Joint disorders
 - Peripheral arthritis
 - Sacroiliitis
 - Ankylosing spondylitis
- Ocular disorders
 - Iritis, uveitis, and episcleritis
- Hepatobiliary
 - Gallstones
 - Sclerosing cholangitis
 - Cholangiocarcinoma



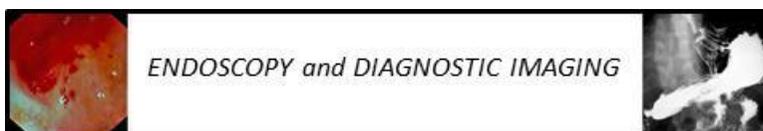
- Renal
 - Renal stones
 - Amyloidosis
- Other manifestations
 - Aphthous stomatitis

Practice Pointers:

- Ankylosing spondylitis (in IBD)
 - Clinical Criteria
 - Limitation of lumbar spine in anterior and lateral flexion and extension
 - Pain at dorsolumbar junction or in lumbar spine
 - Chest expansion <1 inch (measured at 4° intercostal space)
 - Radiological Criteria
 - grade 1, suspicious
 - grade 2, abnormal – erosions or sclerosis
 - grade 3, moderate or advanced sacroilitis with erosions, sclerosis, widening, narrowing, partial ankylosis
 - grade 4, total ankylosis

- Spondyloarthropathy (peripheral arthritis) in IBD
 - Monoarticular/pauci-articular; asymmetrical; large > small joints especially of lower limbs (knees, hips, shoulders)
 - arthralgia, effusion, tenderness
 - No synovial destruction; no subcutaneous nodules; seronegative
 - frequently associated enthesiopathies at the Achilles tendon and insertion of fascia plantaris
 - No increased incidence of HLB-B27 antigen
 - Frequently transient, migratory, non-deforming; may become chronic and erosive in 10%
 - May respond to steroids
 - Mild forms respond to SASP and/or NSAIDs

- Erythema nodosum in IBD
 - More in males
 - CD >>UC
 - Septal panniculitis; Tender subcutaneous nodules, preferably on lower legs, preferably on extensor side: avoid biopsy!
 - Usually parallel IBD activity or heralds exacerbation; Repeated attacks infrequent
 - Mimicry with bacterial antigens? Response to particular cytokines? Often in HLA-B27 positives
 - DD- sarcoidosis (chest X-ray)
 - Px:
 - rest. Leg elevation, support stockings & wraps



- potassium iodide (300 mgx3/d/15d), dapsone colchicine (2mg/d/3d); 1mg/d/15-30d), thalidomide
 - steroids, immunosuppressives (azathioprine, methotrexate, cyclosporine)
 - hyperbaric oxygen? Resection of diseased bowel
 - no NSAIDs
- Pyoderma gangrenosum (vesiculopustular eruption, Sweet syndrome, afebrile neutrophilic dermatitis)
- Variable or absent parallelism with IBD activity
 - Often associated with other EIMS /eye, arthritis)
 - DD tuberculosis, herpetic infections, fungal infections, squamous cancer
 - Recurrence is infrequent
 - Px: local/intralesional steroids; silver nitrate dressings
 - sulfon dapsone, metronidazole, minocycline (200 mg/d)
 - thalidomide (200 mg/d), immunosuppressive (azathioprine, cyclosporine)
 - nicotine?, povidone iodine, cromoglycate, nicotinamide
 - Special circumstances
 - pyoderma adjacent to ileostomy
 - may reoccur at relocated stoma
 - medical therapy preferable
 - pyoderma of head and face common in children
- Aphthous stomatitis
- CDCD>>UC
 - Small punched out erosions(ulcers, surrounded by red halo)
 - May Parallel IBD activity
 - DD pemphigus, herpetic infection (common cold sores)
 - Px:
 - Pentoxifylline, colchicine, dapsone, thalidomide, plaquenil
 - systemic steroids, topical steroids (triamcinolone in orabase, steroid mouth rinse), intralesional steroids
 - topical anaesthetic, nicotine gum
 - antiviral therapy for herpetic sores
 - correction of folate, iron, B12 and zinc deficiencies
- Relationship of extraintestinal complications with IBD activity and response to medical therapy
- Strong
 - Erythema nodosum
 - Peripheral arthritis
 - Moderate
 - Pyoderma gangrenosum
 - Uveitis



- Weak
 - Anklosing spondylitis
 - Sacroiliitis
 - Primary sclerosing
 - Cholangitis

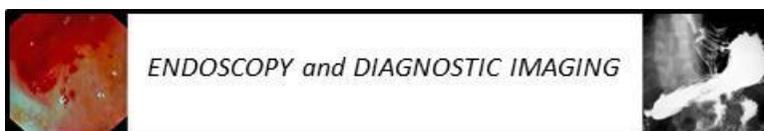
- Diagnostic imaging: barium enema
 - Normal pattern
 - Loss of haustration – spasm and irritability
 - Contraction and decreased distensibility (widening of retrorectal space)
 - Abundant secretions of blood, mucus and pus
 - flocculent barium
 - Minute ulcerations or spicules
 - Large ulcers (collar-button)
 - Hazy fuzzy or grossly ragged contour
 - Pseudopolyps
 - Backwash ileitis

- Ulcerative Colitis: Endoscopy
 - Superficial ramifying blood vessels normal throughout, patchy, none
 - Spontaneous bleeding ahead of instrument: none; present
 - Granularity: normal smoothness/granular
 - Mucosal surface: normal mat; dull lustreless; wet and shiny
 - Ulceration: no ulcers – ulcers
 - Valves: normal thin sharp crescent; swollen; absent
 - Scoring of Endoscopic Severity

- Ulcerative colitis (UC)
 - Mucosa is granular
 - Rectal involvement
 - Mucosal ulcerations affects bowel wall in a symmetrical manner
 - Ulcers are linear, fine, stippled (“sandpaper” – like)
 - Involvement extends proximally
 - Symmetry of bowel wall is normal
 - No skip lesions (continuous, symmetrical thickening of bowel wall)
 - Polyps
 - Pseudopolyps, areas
 - Normal mucosa surrounded by denuclear inflamed mucosa
 - Seen with severe UC
 - Inflammatory polyp
 - Loss of haustral pattern (“lead-pipe” appearance)
 - Diffuse shortening
 - Narrow lumen
 - Area of normal mucosa surrounded by granulation tissue
 - Sessile / pedunculated



- Seen with milder UC
 - Megacolon
 - Associated with pseudopolyps
 - Bowel wall thickening
 - Haustral thickening
 - Dilation (> 6 cm in transverse colon, > 9 cm in cecum)
 - Perforation
 - Air in
 - Bowel wall (intramural air [aka pneumatosis])
 - Peritoneum (pneumoperitoneum)
 - Strictures
 - R/O colitis-associated adenocarcinoma
 - Benign ulcers from
 - Muscle hypertrophy
 - Severe inflammation
 - “backwash ileitis”
 - Nodules / dysplastic plaques
 - Single / multiple
 - Clusters, with opposed flat edge (in ½)
 - Colitis-associated adenocarcinoma
 - Often associated with narrowing of colonic lumen (annular, constricting lesion)
 - Strictures (in ¼)
 - Multiple
- CT in UC
- Mild disease
 - Moderate / severe disease
 - Wall thickening
 - Pericolonic fat stranding
 - “backwash” ileitis (acute inflammation)
 - Hyperenhancement of colonic wall
 - Enlargement of vasa recti
 - Fat attenuation in thickened bowel wall
- Amebiasis
- Barium
- Narrow
 - Irregular contour
- CT
- Wall thickening
 - Liver multiloculated
 - Low-density (fluid-filled) mass (abscess)
 - Mass



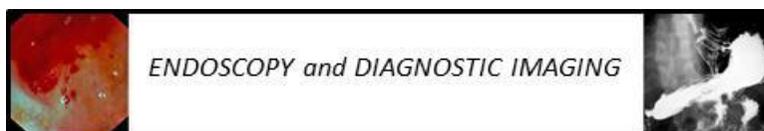
- Ameboma
- Ulcerations
 - Multifocal
 - Confluent
 - Perforation
 - Fistula
 - Pericolonic abscess
 - Distant intraperitoneal abscess
 - Peritonitis
- Strictures
- Cannot be distinguished for CRC (colorectal cancer) on diagnostic imaging

➤ Ulcerative colitis – Endoscopy

0. Normal mucosa, ramifying vascular pattern clearly visible throughout, no spontaneous bleeding, no bleeding to light touch
1. Abnormal but not hemorrhagic appearance (between 0–2)
2. Moderately hemorrhagic-bleeding to light touch but no spontaneous bleeding seen ahead of instrument on initial inspection
3. Severely hemorrhagic – spontaneous bleeding seen ahead of instrument of initial inspection and bleeding to light touch
4. Spontaneous bleeding and spotty ulceration

➤ Ulcerative colitis: Scoring of endoscopic severity

	0	1	2
➤ Colour	○ Normal	- Red	Deeply red
➤ Vascular pattern	○ Normal	- Partially absent	Totally absent
➤ Friability	○ normal	- Slight	Severe
➤ Granularity	○ Absent	- Fine	Coarse
➤ Rectal valves	○ Sharp	- Swollen	Absent
➤ Ulcers	○ absent	- Few	Multiple
➤ Spontaneous bleed	○ Absent	- Discrete	Severe
➤ Mucopurulent exudate	○ absent	- Little	Much



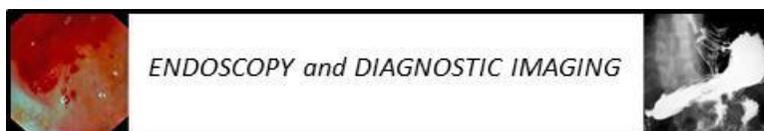
➤ Endoscopic features distinguishing between Ulcerative Colitis and Crohn Colitis

	Ulcerative Colitis	Crohn Colitis
○ Rectal involvement	- Present	- May be absent
○ Skip areas/symmetry	- Absent always, symmetrical and continuous	- Common; asymmetric and discontinuous disease common
○ Ulceration	- Always in areas of mucosal inflammation; large (>1cm) ulcers in severe disease	- Discrete ulcers in normal mucosa; aphthous and linear ulcers pathognomonic - Large and serpiginous ulcers and deep, longitudinal ulcers are common
○ Cobblestoning	- Absent	- Pathognomonic
○ Mucosal Bridging	- Occasional	- Occasional
○ Vascular pattern	- Blurred or lost	- Often normal
○ Granularity	- Common	- Less common
○ Mucosal friability and granularity	- Frequent in early UC	- Unusual

Recent Updates:

➤ Treatment

- Locally acting steroids (oral budesonide) are of no value to reduce the post operative rate of CD (³⁶ Hollers et al., 1999).
- Treatment without steroid may be predictive of mucosal healing
- Early immunosuppression and TNFBs in adults with CD may provide superior outcomes (D'Haens, 2010)
- New diagnosis of CD, naive to steroids and/or immunomodulators given IFX plus AZA (combined), or steroids plus AZA if needed for relapse or steroid dependency (standard): clinical remission at 6 months: standard, 36%; combined, 60%; 12 months: standard 42%; combined, 62%; median time to clinical relapse, 174 vs 329 days,



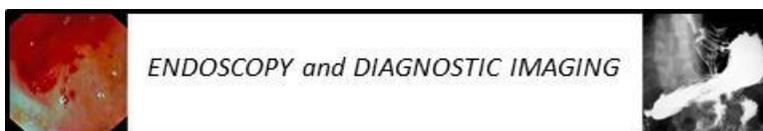
respectively; mucosal healing at 2 years, 73% vs 30%, respectively (D'Haens, 2008).

- The clinical response rates to certolizumab pegol (CER) (PRECISE2, Schreiber, 2006) or to Adalimumab (ADA) (CHARM; Schreiber, 2007) are less effective with longer duration of CD. For example with CD duration of 1 year, TNF blocker response rate is approximately 75%, but with CD duration of 4 year or longer, response to CER and ADA is less than 50%.
- Maintainance with IFX (Accent I) is associated with fewer hospitalizations and surgery if there was mucosal healing (Rulgeerts, 2004)
- Stopping IFX plus AZA in persons in clinical remission is associated with fewer future symptomatic relapses if there was mucosal healing (STORI) (Louis, 2008).
- Starting newly diagnosed CD patients who were naïve to immunomodulators to TNFB might be advantageous (“start high”). Treatment was with IFX, or AZA, or IFX plus AZA (Sonic; Colombel et al, 2009). Those on IFX alone or IFX plus AZA combined therapy had higher clinical remission not on steroids, and no mucosal ulcers on endoscopy.

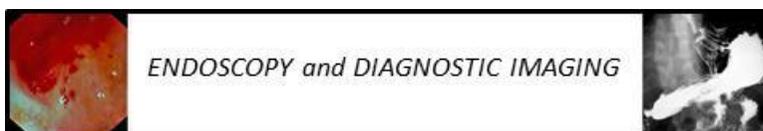
At 6 months	Clinical Remission, Not on steroids	Endoscopic remission (no ulcer in mucosa)
AZA alone	30%	16%
IFX alone	45%	30%
IFX plus AZA	57%	44%

Interestingly, this superior outcome was only in persons with an elevated blood CRP concentration, or mucosal ulcers at their colonoscopy. Also differences were not seen at 12 months. This challenges the “start high” approach of using IFX or IFX plus AZA early in the course of patient’s CD to modify the disease course. Furthermore, in the COMMITT trial of IFX vs IFX plus MTX in CD patients who had failed initial steroids (and 25% had failed AZA), there was no difference in outcomes between the two treatment groups (Feagan et al., 2008).

- Following an ileocecal resection, IFX lowers the endoscopic recurrence rate from 85% to 9%, a therapeutic gain of 76%)⁽³⁴⁾ (Regueiro, et al, 2009).
- Predictors of future severe CD
- Clinical: the presence of perianal disease at the time of diagnosis, the need to use steroids, and age under 40 years all suggested a future severe course of CD (Beaneugerie et al, 2006)



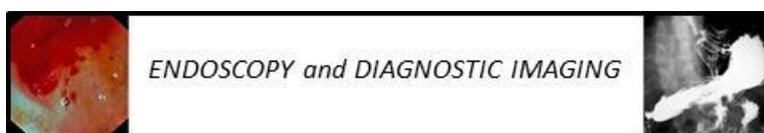
- Mutation in NOD₂/CARD 15 (ileal stricture, future need for surgical resection)
 - HLA-DRB1* 0103 allele
 - Increasing number of abnormal serological markers (such as pANCA, ASCA, AMCA, ALCA, anti-omp-c, anti-CB_{1R1}, anti-I₂)
- Adverse Effects (AEs) of anti—TNFs (TNF blockers [TNFB])
- In the IFX Accent I and II trials in CD (¹⁶ Hanauer et al., 2002; ⁸ Sands et al., 2004), in the IFX ACT1 and 2 trials in UC (Rutgeerts et al., 2006), and in the CER PRECISE 2 trials, the incidences of infections in both the IFX and the placebo groups was about 30%.
 - In the TREAT registry, the rate of infection with IFX or IFX plus AZA were similar (Lichtenstein et al., 2008). This suggests that the use of an immunosuppressant with the TNFB does not further increase the risk of infection.
 - The ENCORE European Registry showed that it was not the use of IFX but rather age over 65, disease severity, and the use of prednisolone which predicted the occurrence of serious infections (34 D' Haens et al., 2008). Thus, any increased risk of infection may be the IBD itself or factors other than or in addition to TNFBs, such as the use of steroids.
- Pharmacoeconomics, There is a subgroup of IBD patients who have more severe disease requiring hospitalization, surgery and biological agents such as TNF Blockers, TPN therapy, and are on prolonged disability. These persons represent the group with high cost impact, and any therapy which would reduce hospitalizations and surgery would have a major impact on costs in this subgroup with more severe disease (*Nature Review:GI/Hep. 61/Hep* (page 104 and 108).
- In the USA and Canada, 80% of the overall costs were attributed to 20% of IBD patients (Feagan et al., 2000).
- Surgery
- In the USA and Canada, surgeries account for nearly half of the admissions for IBD, most of the hospital days, and most of the costs (Cohen et al., 2000; Bernstein et al., 2000 and 2006; Bickston et al., 2005).
- Hospitalization
- In the UK, the 14% of IBD patients who required hospitalization accounted for half of the costs.
 - In Canada, about half the hospitalizations for CD and UC resulted in major IBD-related surgery; about a third of IBD patients who were hospitalized were readmitted at least once in the next seven years,



- and at least a fifth of CD or UC patients had more than one admission per year (Berstein et al, 2006)
- In the USA and other Western countries, hospitalization accounts for a half to two thirds of the direct medical costs for CD (Yu et al, 2008).
 - In the Scandinavian countries, hospitalization accounts for 58% of the direct costs of IBD (Blomquist et al., 1997).
 - Hospitalization accounts for 60% of the costs for CD patients with fistula (Cohen et al., 2008).
- TNFB reduce serious health utilization in persons with IBD
Reduction (%) of health service utilization in CD patients treated with IFX)

	All CD patients (Rubenstein et al., 2002)	CD fistula patients (Rubenstein et al., 2002)	(Harrison et al., 2003)
ER visits	66	64	372
All surgery	38	66	
GI surgery	18	59	
Hospitalizations		59	37
Endoscopies	43		52
Radiographs	12	40	58-147
Outpatient visits	16	27	22-33

- Similar benefits of IFX on rate of hospitalization, surgery and procedures were described in the Accent I and II trails (Han Aher et al., 2002; Lichtenstein et al., 2004).
- This reduction in health serious utilization could be partially offset by the high cost of biologics, so that cost effectiveness and cost-utility analysis are necessary. A UK cost-utility analysis reported that maintenance treatment with IFX every 8 weeks was cost-effective for patients with luminal and fistula CD (Lindsay, et al., 2008). For example, for luminal CD, an incremental cost per quality adjusted year (QALY) gained for IFX was £26, 128 (using the exchange rate at the time of publication of this paper, this equates to approximately \$70,000 Cdn).
- However, the use of QALY for the measurement of cost-effectiveness is of questionable value for diseases such as IBD, which have a young patient base and low mortality rate but high morbidity (Cohen, 2010). Also, indirect costs are high in persons with IBD: In Sweden or Scotland, about two thirds of the costs are indirect (Blomquist, et al. 1997; Ferguson et al; 1994), and in the Accent I trial of IFX, about half the patients at baseline were not employed



(Han Aher et al., 2002). Because of this the result of studies of cost-effectiveness and cost-utility need to be challenged, since direct costs are often not taken into consideration (Lewis et al., 2002).

➤ CD versus TB

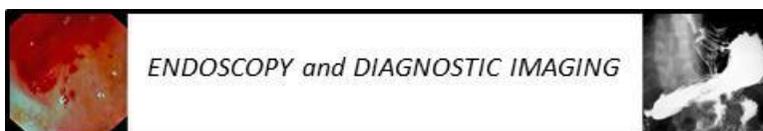
- It may be challenging to distinguish between CD and intestinal tuberculosis (Makharia et al., AJG 2010; 105 642-651).
- Because the intestinal permeability is defective (“leaky”) in CD, there is an increase in bacterial load or altered types of bacteria in the tissue, worsening the adaptive mucosal response. Intestinal macrophages secrete cytokines and chemokines in response to intestinal bacteria. This process of post-translational modification may be impaired in some persons with CD, as well as there being a reduced recruitment of neutrophils to the tissue for destruction and removal of the organisms in the autophagolysosomes.
- This may possibly be associated with NOD₂ receptor mutations which reduce the acute inflammatory response to enteric organisms, and thereby exacerbating and amplifying the chronic response (Fava Dannese, Nat Rev. 61; GI/Hep 2010; 7: 126-128).
- NOD₂ mutations are also associated with higher loads of bacterial colonization of the crypts, and thereby higher bacterial loads.

➤ CD and Functional GI Symptoms

- A defect in the transport of vesicles in the macrophage may be linked to mutations in IREM and ATE 16L1, autophagy related genes which may be abnormal in CD. The NOD₂ mutations are associated with reduced transcription of IL-10, leading to an enhancement of the granulomatous reaction, which in course is a feature of CD.
- It has been estimated that approximately 50% of persons with inactive Crohn disease, and 26% to 50% of those with inactive UC will have functional GI symptoms (Ohman & Simran, 2010).

➤ Diagnostic distinctions: chronic vs. acute colitis

	Chronic	Acute	Shortening
○ Featureless mucosa		+	-
○ Lead-pipe mucosa		+	-
○ Narrow lumen (hypertrophic of circular and longitudinal)	+		-
○ CT: fat attenuation (darker) in thickened colonic wall	+		-



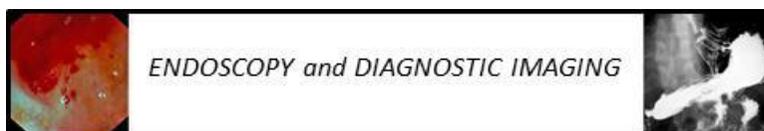
- Crohn Colitis (CC)
 - Large lymph follicles → small nodules
 - Ulcers surrounded by “hab” of edema (“aphthous” ulcers; central “umbilication”)
 - Poorly defined borders
 - Variation in size of central umbilication
 - Aphthous ulcers coalesce → deep, serpiginous, linear ulcers
 - Ulcers are circumferentially asymmetric
 - Discontinuous disease
 - May see solitary deep ulcers
 - Segmental narrowing
 - Inflammatory polyps
 - Fistulae
 - Rectal sparing
 - Cobblestone appearance of mucosa (longitudinal and transverse collections of barium from deep ulcers)

- MRI in CC
 - T₁- weighted
 - Thickening of wall
 - Stranding of soft tissue
 - T₂- weighted
 - High-signal intensity in pericolonic fat
 - Abscess, fistula (best test)

➤ Characteristics of Ulcerative Colitis (UC) and Crohn Disease (CD)

	UC	CD
○ Location	- Colon	- Entire GI tract
○ Extent of inflammation	- Mucosal and submucosal	- transmural
○ Peak age of onset (years)	- 15-20	- 15-25
○ Prevalence (per 100.000)	- 35-100	- 10-100
○ Surgery/resection	- curative	- Not curative

Adapted from: Stenson WF: In: Textbook of Gastroenterology. 2nd Ed. 1995:1748-1805



➤ Activity of UC

Variable	Clinical disease activity	
	Mild	Severe
➤ Stool frequency	Minimal	>6/d
➤ Blood in stool	Absent	Continuous
➤ Fever	Mean rate \leq 90 bpm	Mean evening $T > 37.5^{\circ}\text{C}$ or $> 37.7^{\circ}\text{C}$ for at least 2/4 days (any time of day)
➤ Pulse	Mild	>90 bpm
➤ Anemia	<30 mm/h	Hgb \leq 7.5 mg/dL (compared) with normal values
➤ Erythrocyte sedimentation rate (ESR)		>30 mm/h

Abbreviation: T, temperature; Hgb, hemoglobin

Adapted from: Truelove SC, Witts LJ. Br Med J. 1955;2:1041-1048

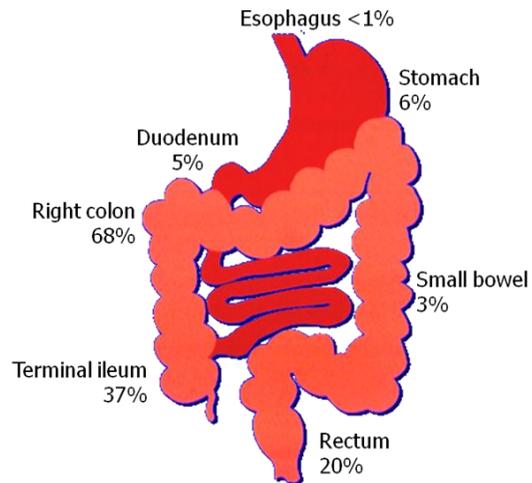
➤ Ulcerative Colitis: Assessment of Severity

Feature	Mild	Moderate	Severe
➤ Motions per day	<4	4-6	>6
➤ Rectal bleeding	Little	moderate	Large amounts
➤ Temperature	Apyrexial	intermediate	$> 37.8^{\circ}\text{C}$ for 2 of 4 days
➤ Pulse rate	normal	intermediate	>90 beats/minute
➤ Haemoglobin	normal	intermediate	<10.5 g/dL
➤ ESR	normal	intermediate	>30 mm/hour



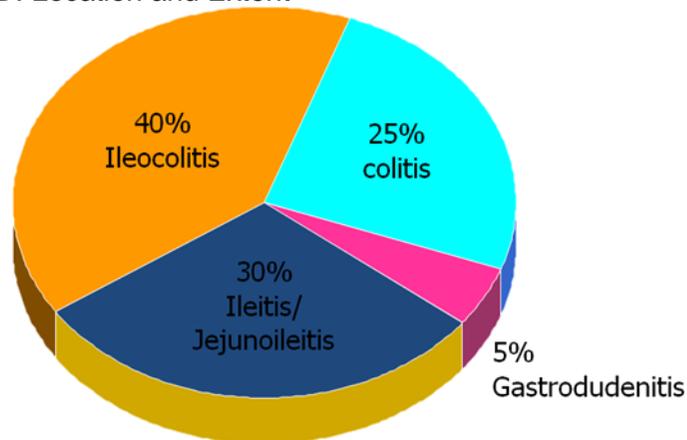
Presentation of IBD

- Crohn Disease
 - Diarrhea
 - Chronic abdominal pain and tenderness
 - Weight loss
 - Fever
 - Perianal disease
 - Symptoms vary with location of disease
 - Extraintestinal manifestations
- Sites of Involvement of Crohn Disease



Adapted from: Farmer RG, et al: Gastroenterology 1975; 68:1818-1825.

- CD: Location and Extent



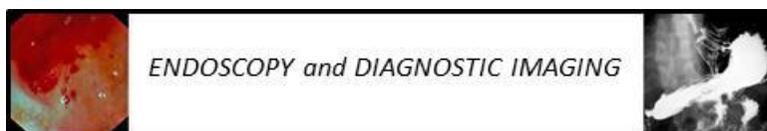
Crohn Disease Activity

- Maximum score
- Remission
- Moderate activity
- Severe activity

Index: Scoring

- 600
- < 150
- 200–450
- > 450

Adapted from: Best WR et al. Gastroenterology. 1976;70:439-444.



- The Simple index of Crohn Disease Activity
 1. General well-being: 0=very well, 1=slightly below par, 2=poor, 3=very poor, 4=terrible
 2. Abdominal pain: 0=none, 1=mild, 2=moderate, 3=severe
 3. Number of liquid stools per day
 4. Abdominal mass: 0=none, 1=dubious, 2=definite, 3=definite and tender
 5. Complications: arthralgia, uveitis, erythema nodosum, aphthous ulcers, pyoderma gangrenosum, anal fissure, new fistula, abscess
(score one per item)

- Crohn Disease: Different causes of diarrhea
 - Active disease
 - Small intestinal bacterial overgrowth
 - Bile salt malabsorption after ileal resection
 - Hypolactasia
 - Short bowel after resection
 - Other disease (celiac, chronic pancreatitis)
 - Co-existent irritable bowel syndrome

- Factors that lead to malnutrition in IBD
 - Decreased oral intake
 - Increased caloric requirements
 - Malabsorption of nutrients
 - Loss of proteins and electrolytes
 - Drug-induced nutritional complications
 - Down regulation of metabolism by pro-inflammatory cytokines

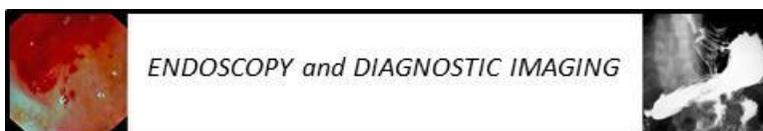
Adapted from: Stenson WF. In: Textbook of Gastroenterology. 2nd Ed. 1995:1748-1806.

- Ulcerative Colitis – Endoscopy
 - Superficial ramifying blood vessels normal throughout, patchy, none
 - Spontaneous bleeding ahead of instrument: none; present
 - Granularity: normal smoothness/granular
 - Mucosal surface: normal mat; dull lustreless; wet and shiny
 - Ulceration: no ulcers – ulcers
 - Valves: normal thin sharp crescent; swollen; absent

- Molecular mechanisms of steroid resistance in a hospitalized patient having severe UC
Showing No Response to Oral Steroids
 - Abnormalities in absorption/metabolism (liver disease)
 - Altered number of GCS receptors or altered numbers of isoforms (α , β , δ)



- Altered affinity of GCS for GCS receptors
 - Reduced affinity of the GCS receptor ligands to bind DNA
 - Altered expression of transcription factors (AP-1, NF- κ B) and/or cytokines (IL-2, IL-4, p38 activated MAP kinase)
 - Genetic factors (primary steroid resistance, MDR-1 [P-glycoprotein 170], HLA class II allele DRB1*0103)
- Clinical causes of steroid resistance in patients with “Colitis”
- Infection - C. difficile, CMV
 - NSAIDs
 - Smoking discontinuation
 - Drug interactions
 - UC with CD-like features – discontinuous disease, superficial fissuring ulcers, aphthous ulcers, ileal involvement, involvement of the upper GI tract, granulomas
 - CD with UC-like features – pancolitis, superficial colitis
 - IBD complicated by infections – PMC, C. difficile, CMV, etc
 - Other forms of “colitis” that may mimic UC
 - Development of colorectal cancer (CRC)
- A clinical strategy for dealing with steroid resistance in patients with IBD
- Adjust dose, route of steroids
 - Higher dose of 5-ASA, or different targeted 5-ASA (enemas)
 - Cyclosporine
 - Azathioprine, 6-MP
 - Methotrexate
 - Biologics – anti TNF α
 - Probiotics
 - Fish oil, nicotine patch
 - Colectomy
- The biopsy features of acute self-limiting colitis(AC)
Which help to Distinguish it from Chronic Idiopathic Ulcerative Colitis (UC)
- Crypts are straight, parallel, close
 - No lymphoplasmacytosis at base of crypts
 - Large, bulging, cystic dilation with a “necklace” of cells around any crypt abscess
 - PML are abundant, and scattered in the lamina propria (LP)

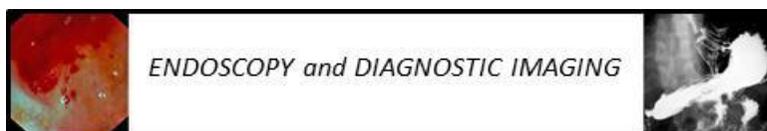


➤ Conditions that cause “Colitis” and may Mimic UC

Infection

- Bacterial
 - Clostridium difficile
 - Salmonella species
 - Shigella species
 - Yersinia enterocolitica
 - Campylobacter jejuni
 - Vibrio parahaemolyticus
 - Aeromonas hydrophila
 - Neisseria gonorrhoeae
 - Listeria monocytogenes
 - Chlamydia trachomatis
 - Syphilis
 - Staphylococcus aureus
 - Escherichia coli 0157:H9
- Protozoan
 - Amebiasis (ENT amoeba histolytica)
 - Balantidiasis
 - Schistosomiasis
- Viral
 - Cytomegalovirus (CMV)
 - Herpes (HSV)
- Fungal
 - Histoplasmosis
 - Candidiasis
- Iatrogenic (drugs)
 - Enemas
 - Laxatives
 - OCA
 - Ergotamine
 - Amphetamines
 - Phenylephrine
 - Cocaine
 - Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Penicillamine
 - Gold
 - Methyl dopa

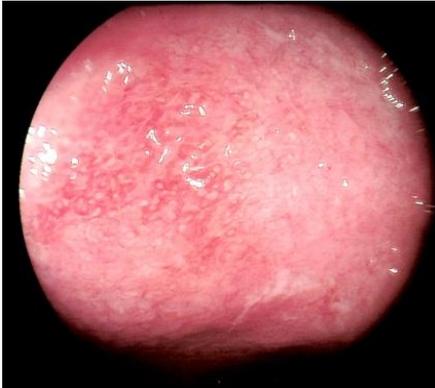
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- Diagnostic Distinctions: aphthous ulcers
- Crohn disease
 - Yersinia-associated colitis
 - Amebic colitis
-

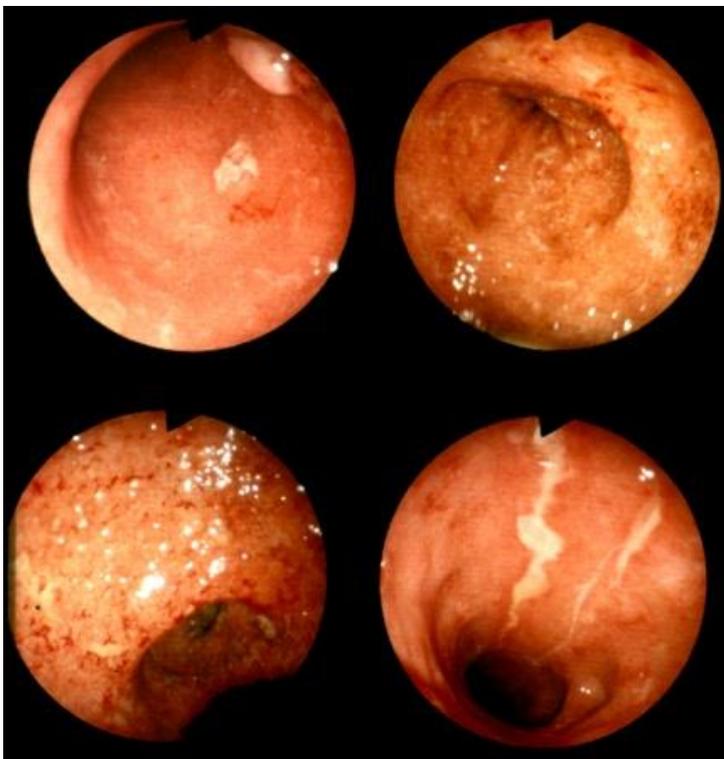
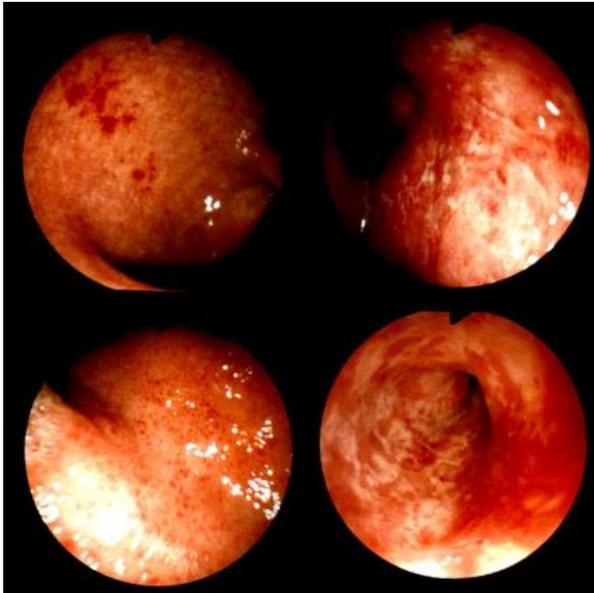


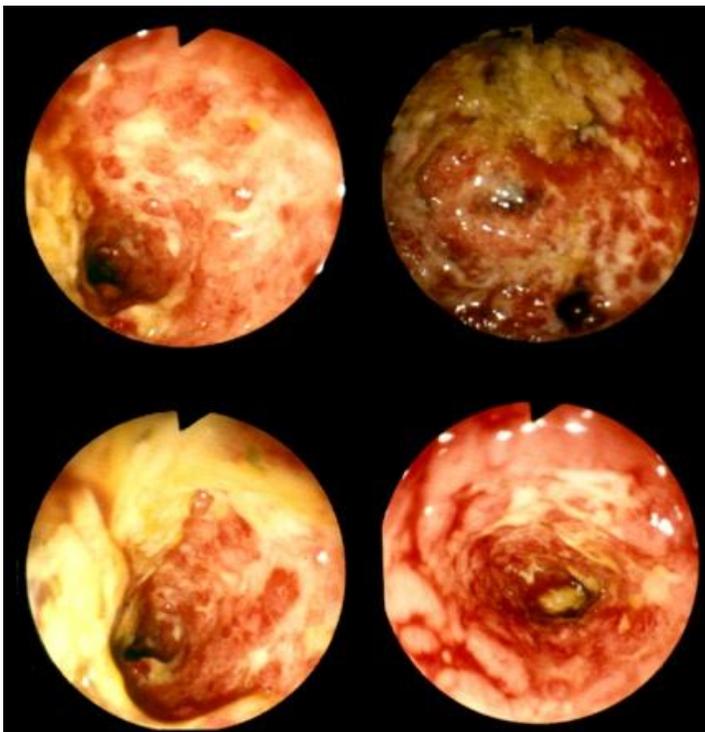
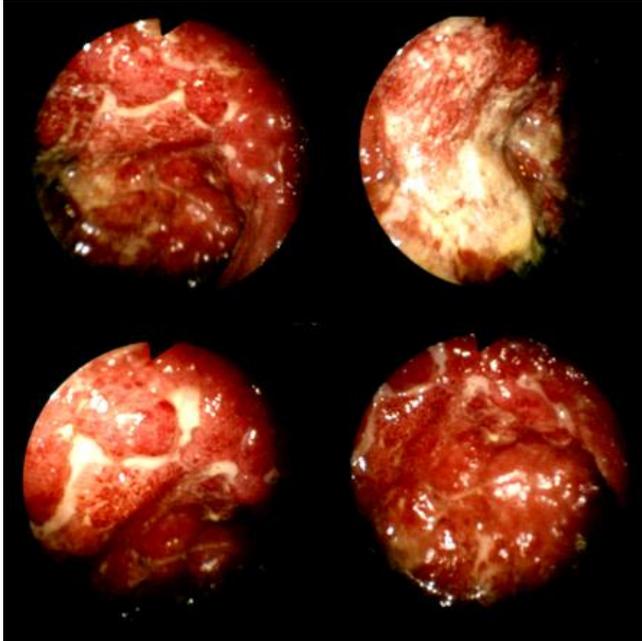
➤ Vasculature in UC

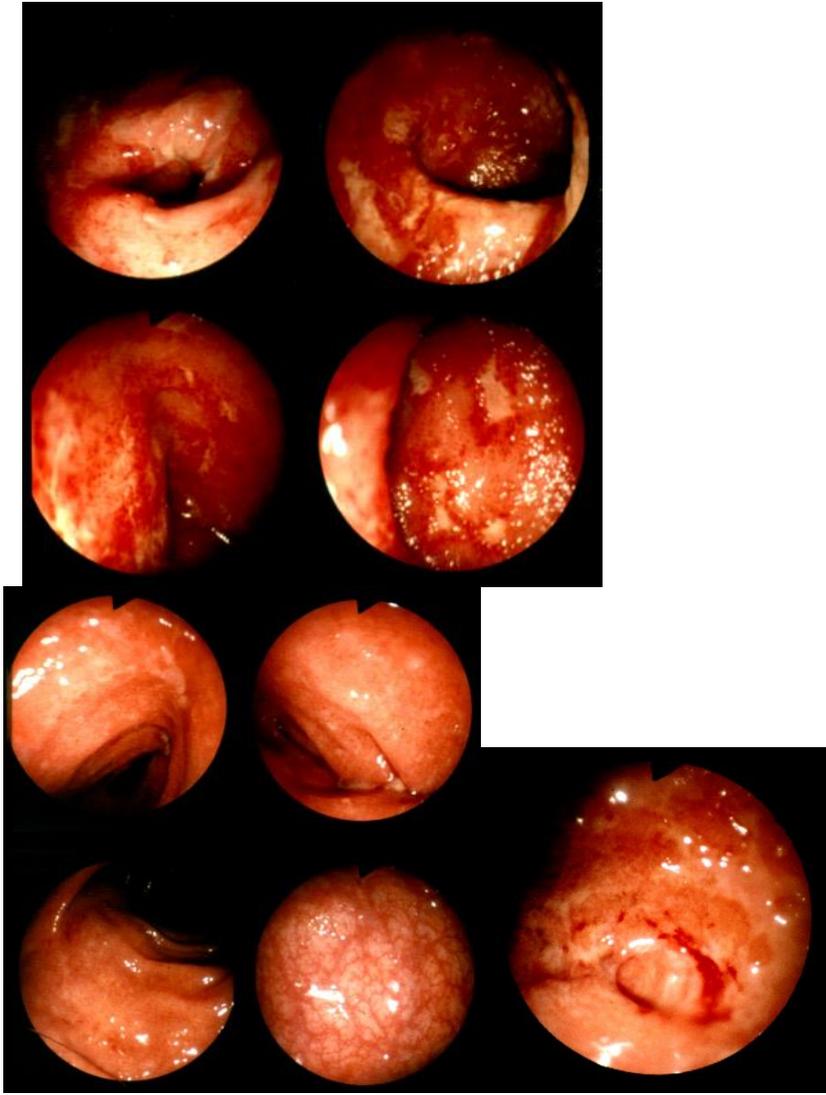


➤ Crypt abscesses

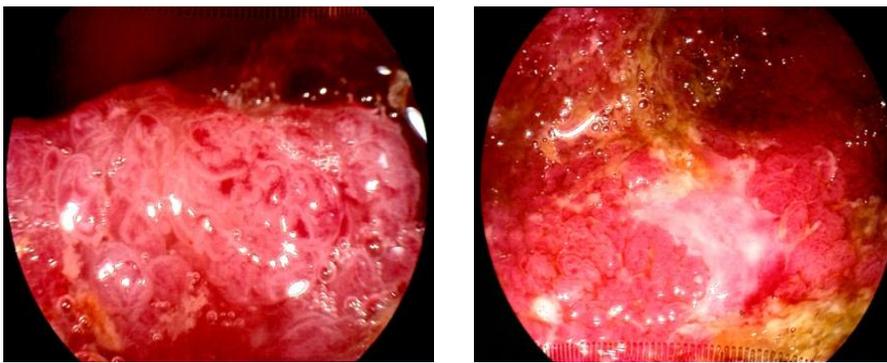


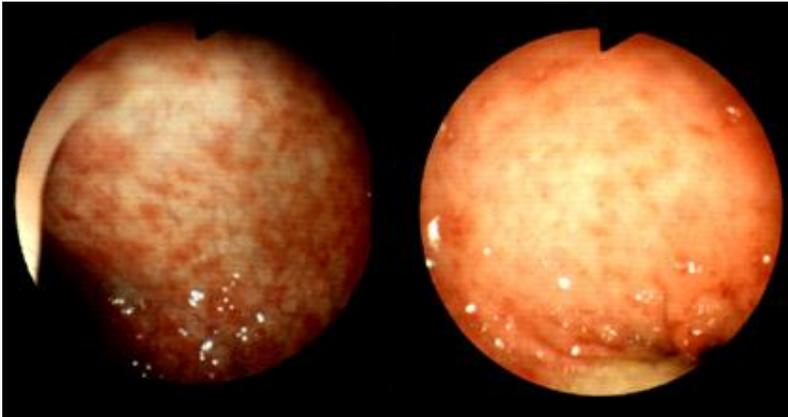


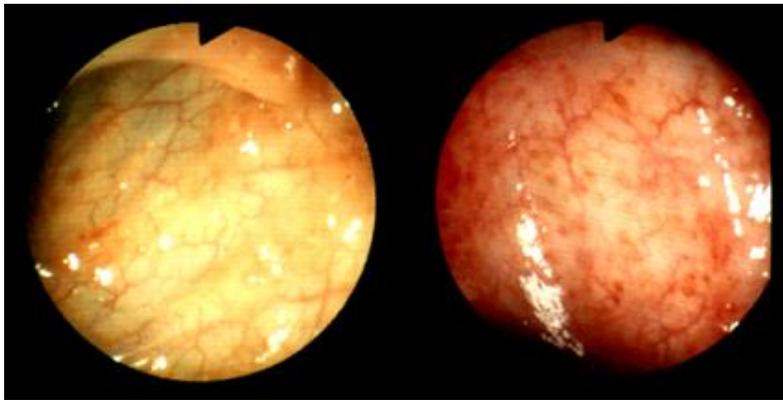
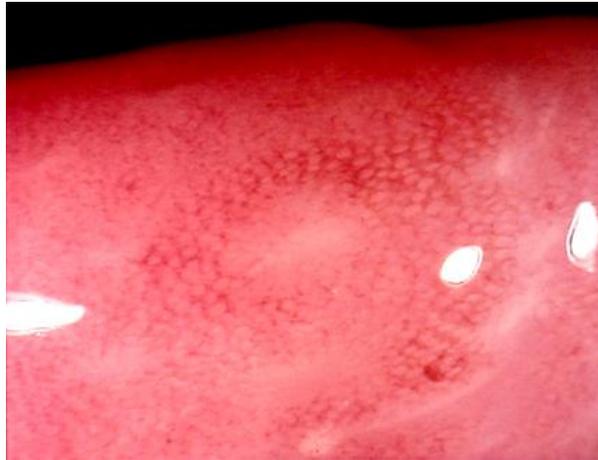


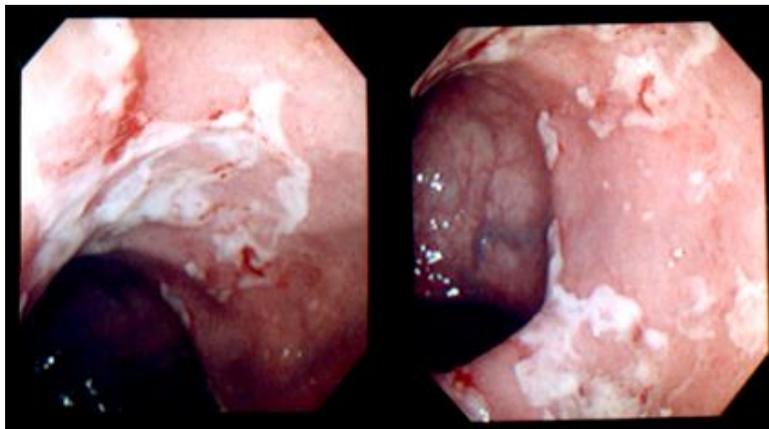
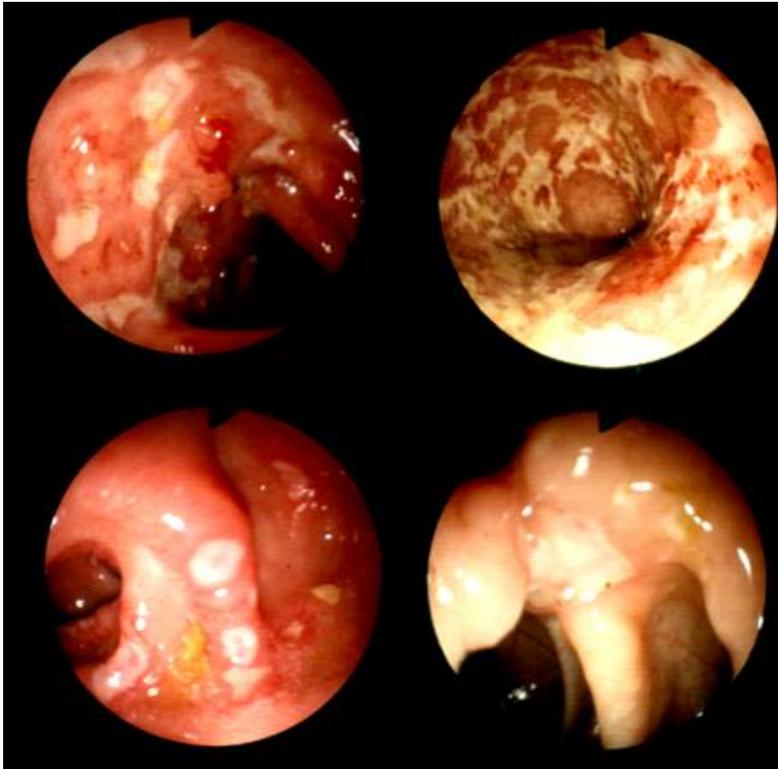


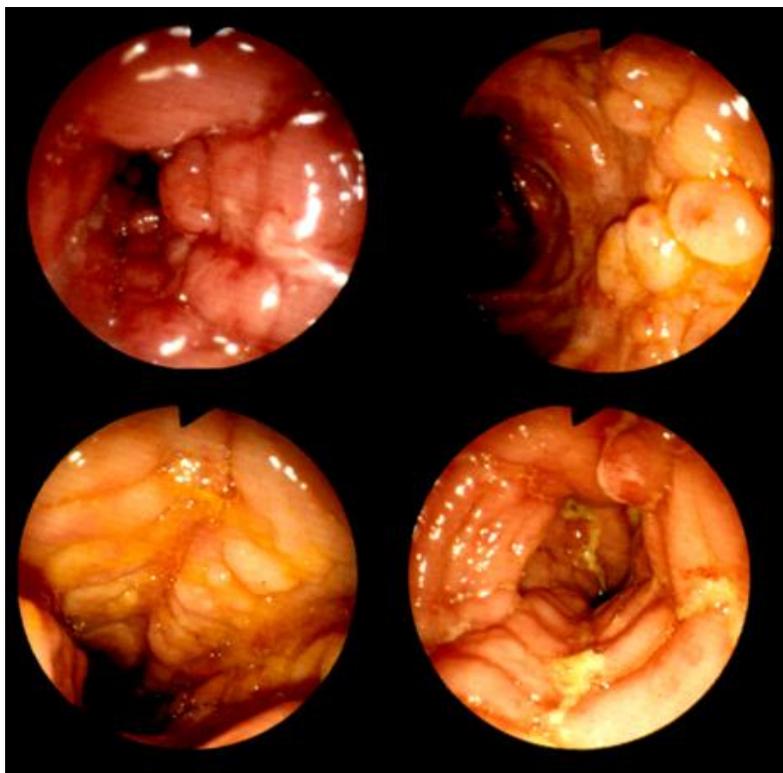
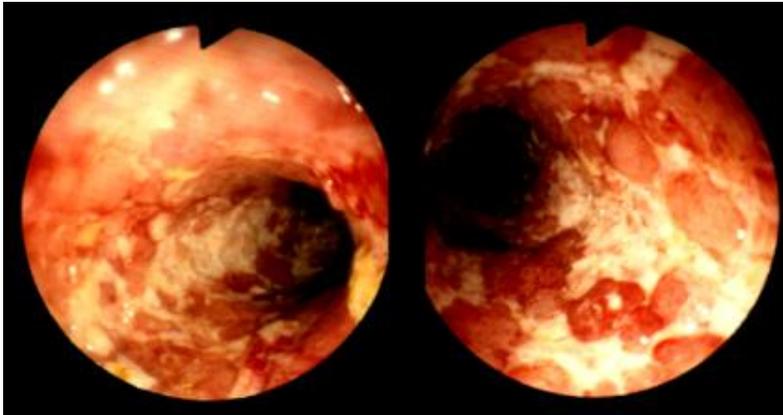
➤ Crohn disease: Aphthoid lesions

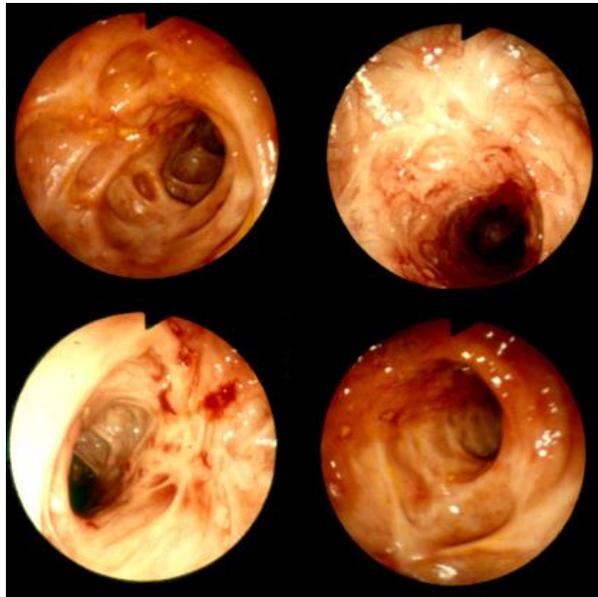


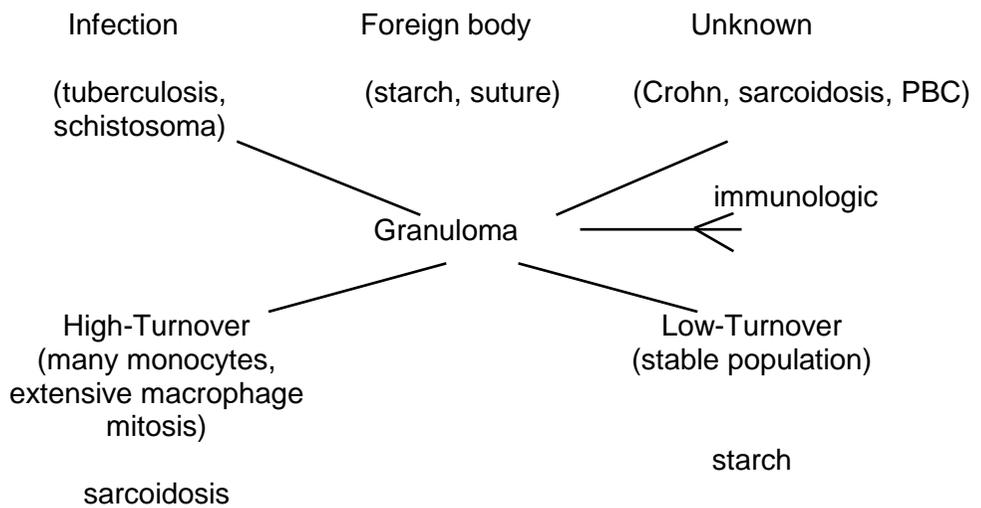
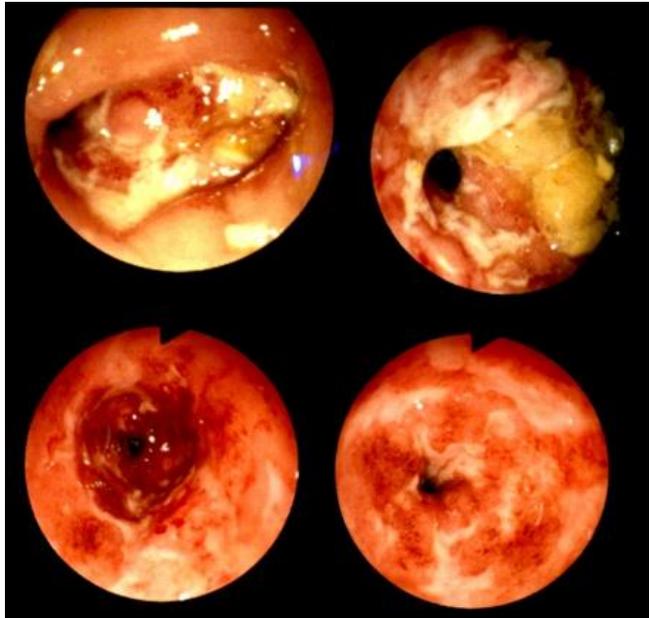












➤ Endoscopic features of ulcerative and Crohn disease colitis

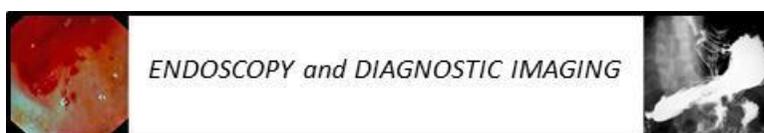
	Ulcerative Colitis	Crohn Disease
➤ Rectal involvement	Present	May be present
➤ Skip areas/symmetry	Absent always, symmetrical and continuous	Common; asymmetric & discontinuous disease common

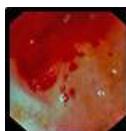
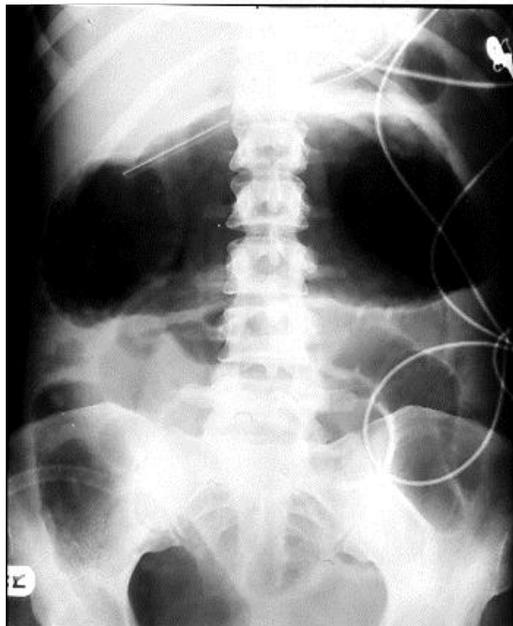
➤ Ulceration	Always in areas of mucosal inflammation; large (> 1 cm) ulcers in severe disease	Discrete ulcers in normal mucosa; Aphthous and linear ulcers pathognomonic Large and serpiginous ulcers and deep longitudinal ulcers common
➤ Cobblestoning	Absent	Pathognomonic
➤ Mucosal bridging	Occasional	Occasional
➤ Vascular pattern	Blurred or lost	Often normal
➤ Granularity	Common	Less common
➤ Mucosal friability and granularity	Frequent in early UC	Unusual

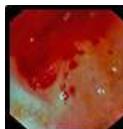
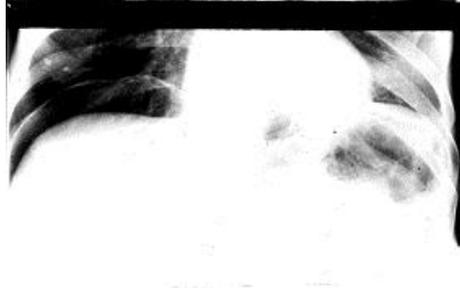
➤ Differential diagnosis: Colonoscopic biopsy

UC	CD
○ All samples inflamed	○ Normal samples
○ Distal biopsy specimens most	○ No pattern of inflammation severe
○ Mucosal disease	○ Transmural disease
○ Goblet cells reduced	○ Goblet cells may be normal
○ Crypt abscess	○ Mononuclear infiltrate
○ Capillary and venule engorgement	○ Lymphangiectasia
○ No granulation tissue/fibrosis	○ Granulation tissue/fibrosis
○ No granulomata	○ Granulomata

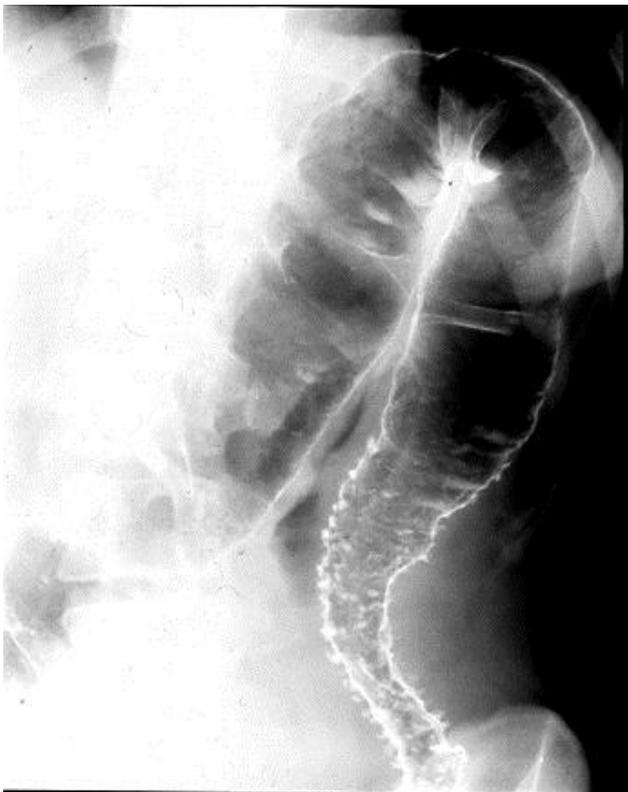
Adapted from: Geller SA. In: Inflammatory Bowel Disease. From Bench to Bedside. 1994:336-351.

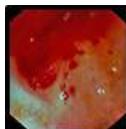
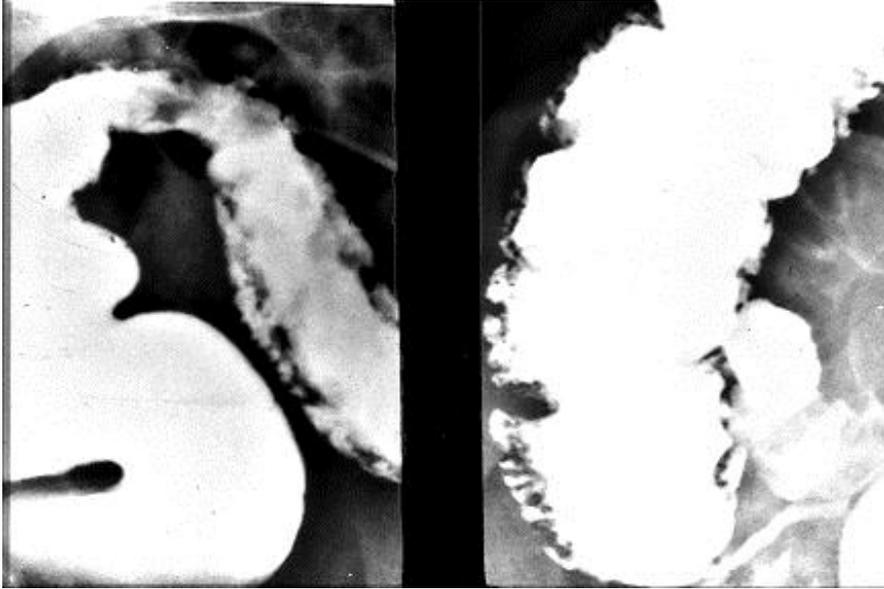


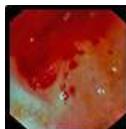
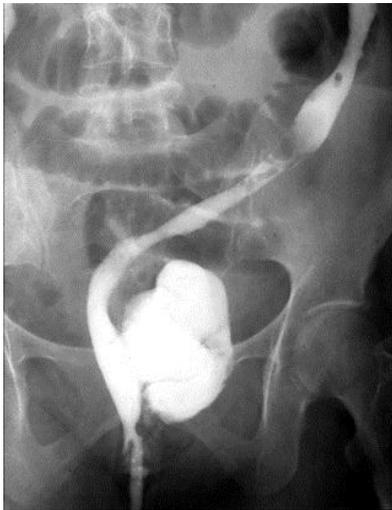


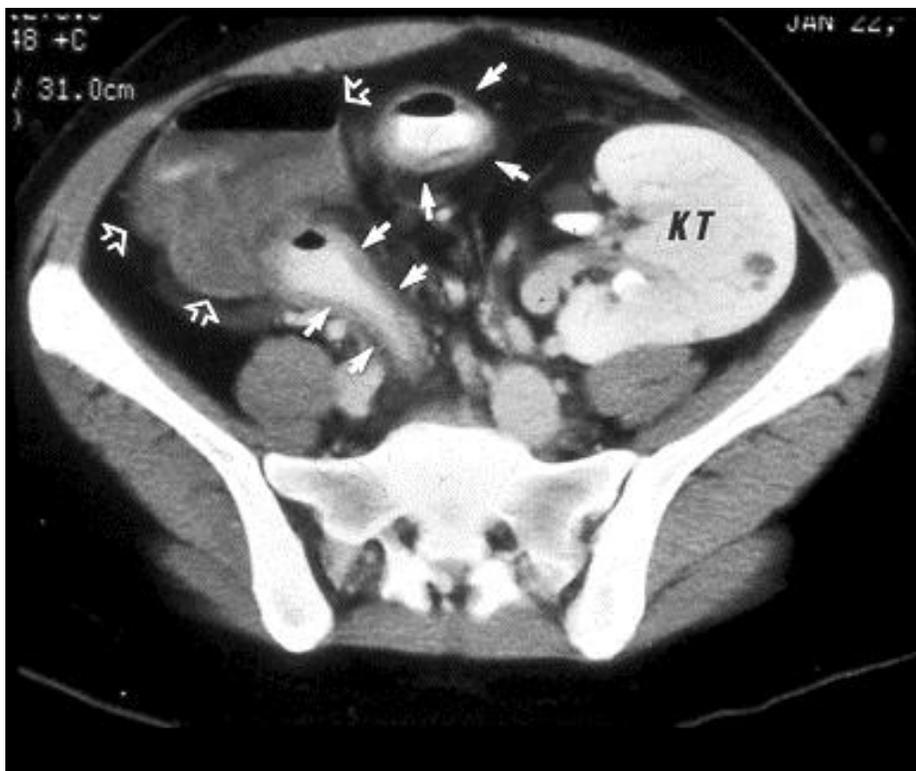


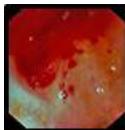
- Ulcerative colitis – Barium enema
 - Normal pattern
 - Loss of haustration – spasm and irritability
 - Contraction and decreased distensibility (widening of retrorectal space)
 - Abundant secretions of blood, mucus and pus
 - flocculent barium
 - Minute ulcerations or spicules
 - Large ulcers (collar-button)
 - Hazy fuzzy or grossly ragged contour
 - Pseudopolyps
 - Backwash ileitis

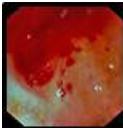
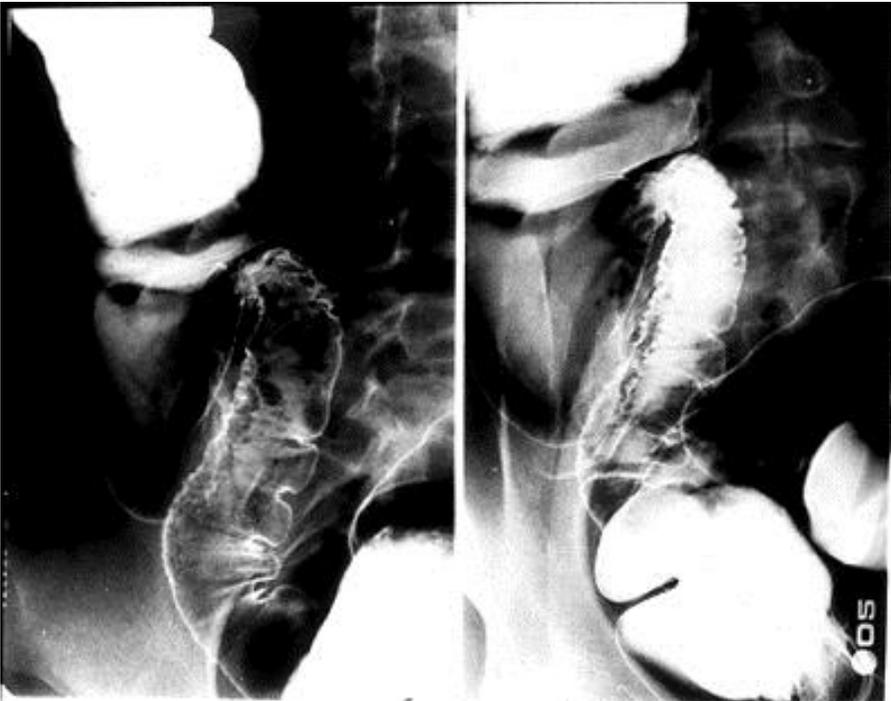


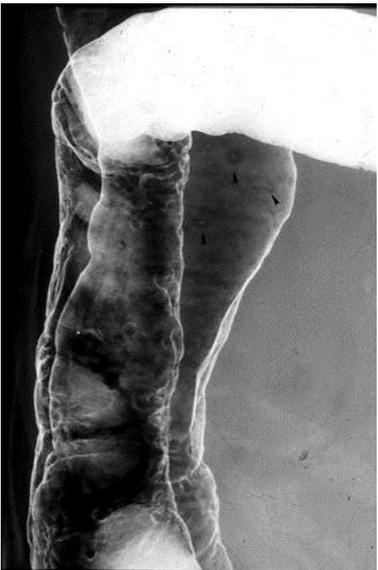
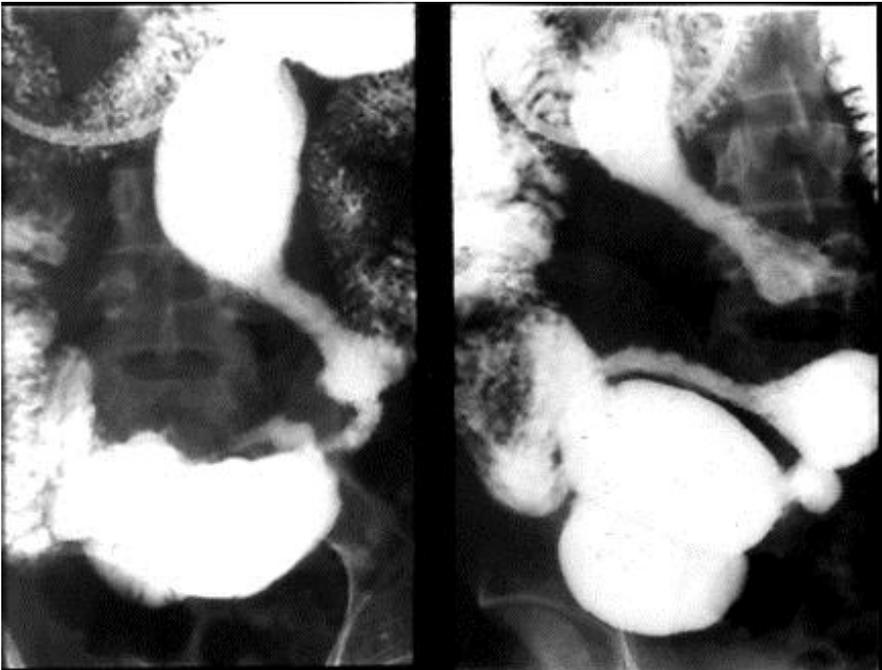


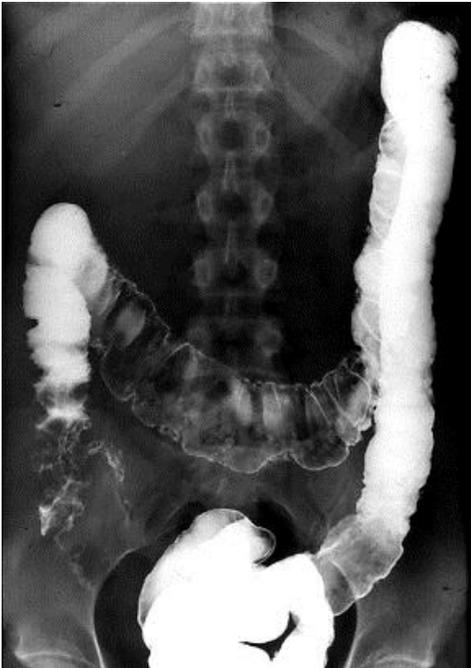




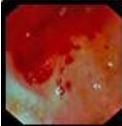
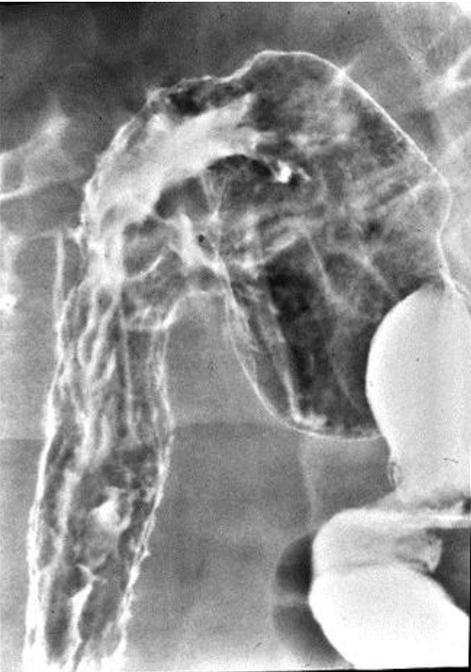


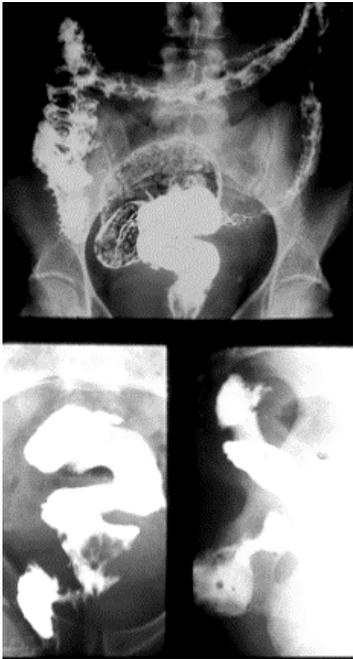


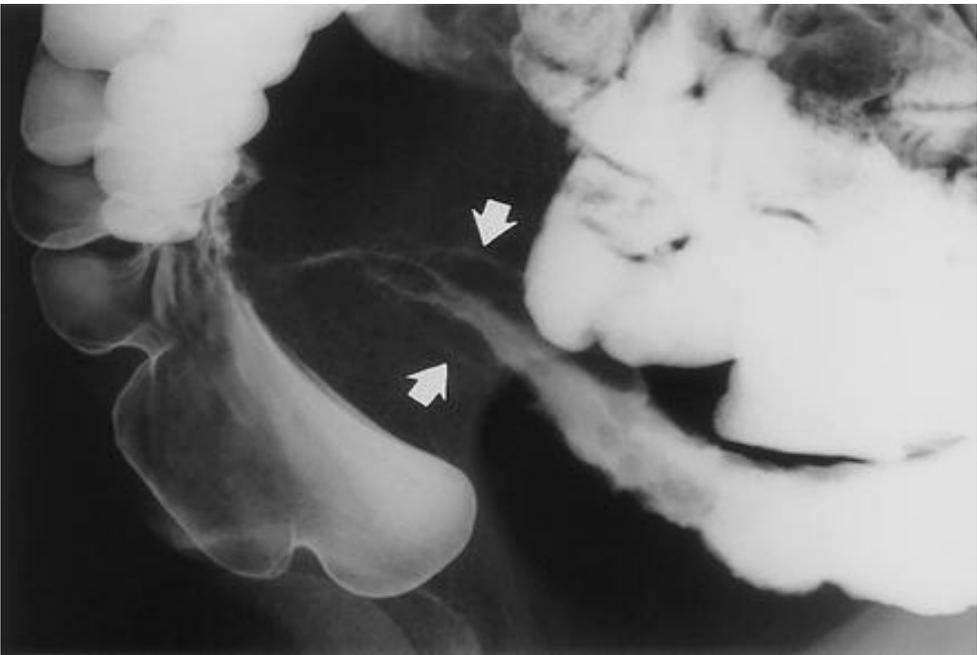


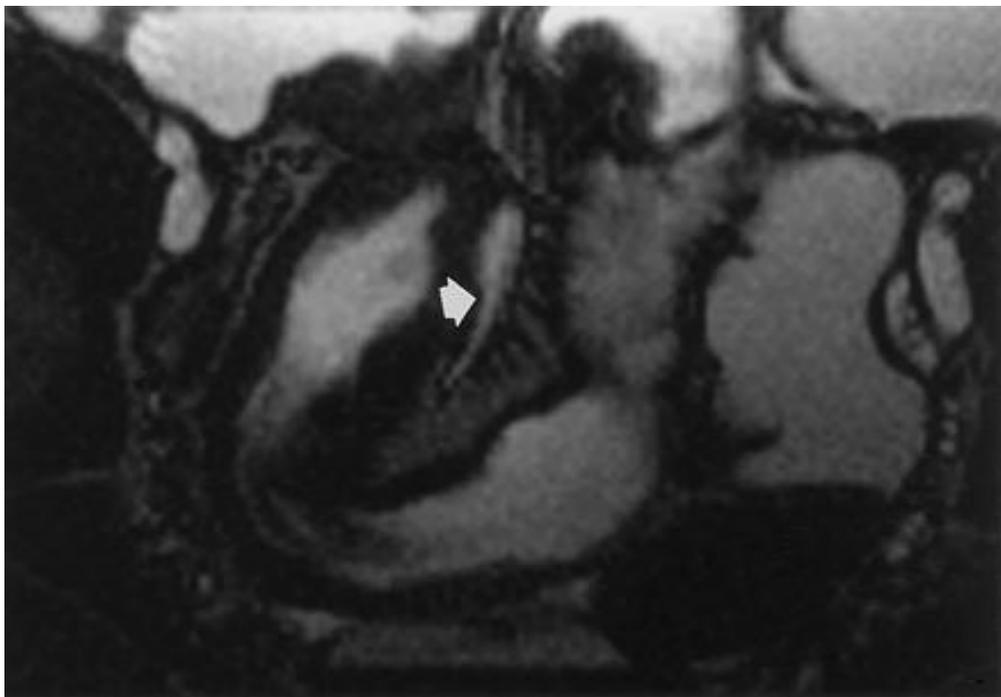












Differential diagnosis of UC

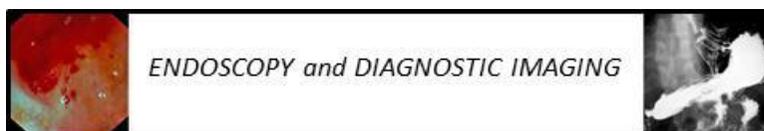
- Infection
- Ischemia
- Diversion, pseudomembranous, or radiation colitis
- Physical agent
- Immunologic etiologies
- Systemic disease
- CD
- Irritable bowel syndrome

Differential diagnosis of CD

- Lymphoma
- Infectious etiologies
- Appendicitis
- Diverticulitis
- Carcinoma
- UC
- Celiac disease

Extraintestinal Manifestations of IBD

- Skin disorders
 - Erythema nodosum
 - Pyoderma gangrenosum
- Joint disorders
 - Peripheral arthritis
 - Sacroiliitis
 - Ankylosing spondylitis



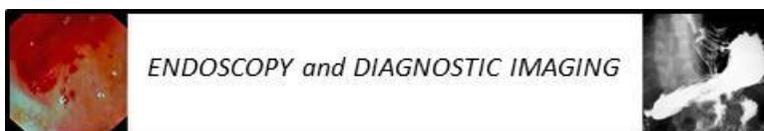
- Ocular disorders
 - Iritis, uveitis, and episcleritis
- Hepatobiliary
 - Gallstones
 - Sclerosing cholangitis
 - Cholangiocarcinoma
- Renal
 - Renal stones
 - Amyloidosis
- Other manifestations
 - Aphthous stomatitis

IBD – Extraintestinal Complications

- Spondyloarthropathy – Central (Axial) Arthritis – (Ankylosing) Spondylitis
 - Incidence 2–6% of UC
 - Incidence of HLA-B27 antigen varies between 50–75%
 - Inflammatory low back pain radiating into the buttocks, especially at night, plus morning stiffness ± peripheral synovitis
 - Gradual progression with restriction of spinal movement and chest expansion
 - Diagnosis is clinical
 - Onset and evolution independent of IBD course
- Sacroilitis
 - Incidence 15%
 - No increased incidence of HLA-B27 antigen
 - Frequently asymptomatic; asymptomatic sacroilitis stage 2 or more seen in 25% of patients
 - Diagnosis is radiological

Ankylosing Spondylitis

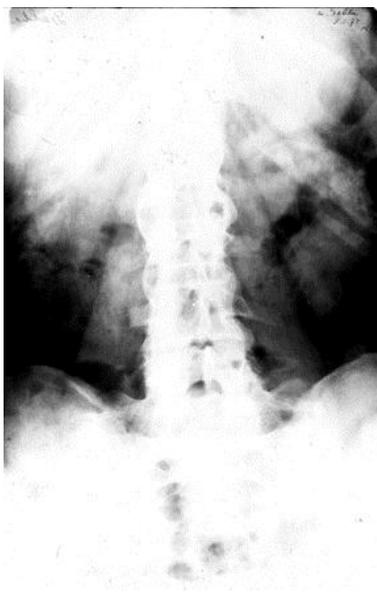
- Clinical Criteria
 - Limitation of lumbar spine in anterior and lateral flexion and extension
 - Pain at dorsolumbar junction or in lumbar spine
 - Chest expansion ≤ 1 inch (measured at 4^o intercostals space)
- Radiological Criteria
 - Grade 1 suspicious
 - Grade 2 abnormal – erosion or sclerosis

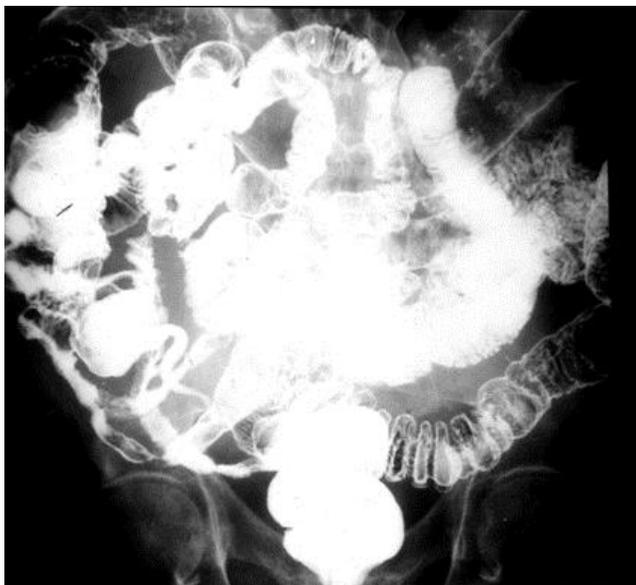


- Grade 3 moderate or advanced sacroilitis with erosions, sclerosis, widening, narrowing, partial ankylosis
- Grade 4 total ankylosis
- Definite Ankylosing Spondylitis
 - XR grade 3 or 4 bilateral sacrolitis and one clinical criterion
 - XR grade 2 bilateral sacrolitis or grade 3 or 4 unilateral sacrolitis plus either clinical criterion 2 or both 2 and 3

IBD – Extraintestinal Manifestations: Spondyloarthropathy – Peripheral Arthritis

- Monoarticular/pauci-articular; asymmetrical; large > small joints especially of lower limbs (knees, hips, shoulders)
 - arthralgia, effusion, tenderness
- No synovial destruction; no subcutaneous nodules; seronegative
 - frequently associated enthesiopathies at the Achilles tendon and insertion of fascia plantaris
- No increased incidence of HLB-B27 antigen
- Frequently transient, migratory, non-deforming; may become chronic and erosive in 10%
- Tx: steroids

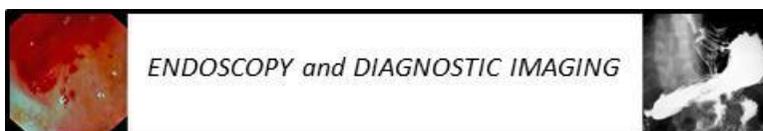




IBD – Extraintestinal manifestations

- Spondyloarthropathy
 - Most patients respond to short courses of NSAIDs
 - Maximally intense anti-inflammatory therapy for peripheral arthritis → sulphasalazine maintenance (?)
 - Sulphasalazine for axial disease (?)
 - Azathioprine / 6-mercaptopurine, methotrexate, anti-TNF (?) for severe forms

- Erythema nodosum
 - More in males
 - CD >>UC
 - Septal panniculitis; Tender subcutaneous nodules, preferably on lower legs, preferably on extensor side: avoid biopsy!
 - Usually parallel IBD activity or heralds exacerbation; Repeated attacks infrequent
 - Mimicry with bacterial antigens? Response to particular cytokines? Often in HLA-B27 positives
 - DD- sarcoidosis (chest X-ray)

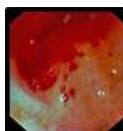


- Tx:
 - rest. Leg elevation, support stockings & wraps
 - potassium iodide (300 mgx3/d/15d), dapsone colchicine (2mg/d/3d); 1mg/d/15-30d), thalidomide
 - steroids, immunosuppressives (azathioprine, methotrexate, cyclosporine
 - hyperbaric oxygen? Resection of diseased bowel
 - no NSAIDs



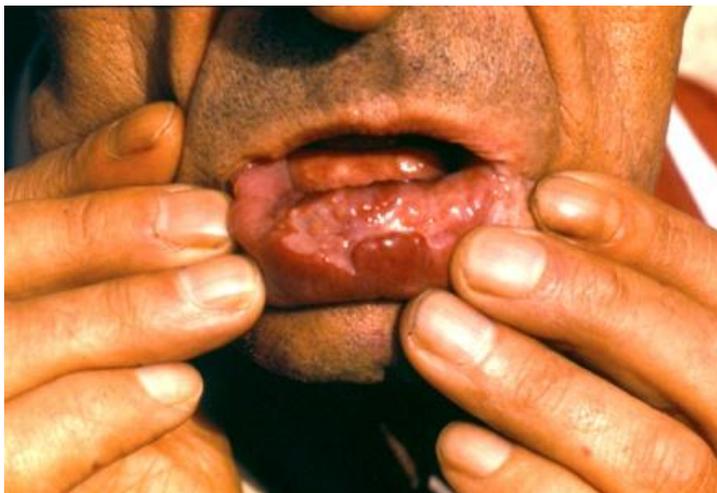


- Pyoderma Gangrenosum (vesiculopustular eruption, sweet syndrome, afebrile neutrophilic dermatitis) [2]
 - Variable or absent parallelism with IBD activity
 - Often associated with other EIMS /eye, arthritis)
 - DD tuberculosis, herpetic infections, fungal infections, squamous cancer
 - Recurrence is infrequent
 - Tx: local/intralesional steroids; silver nitrate dressings
 - sulfon dapsone, metronidazole, minocycline (200 mg/d)
 - thalidomide (200 mg/d), immunosuppressive (azathioprine, cyclosporine)
 - nicotine?, povidone iodium, cromoglycate, nicotinamide



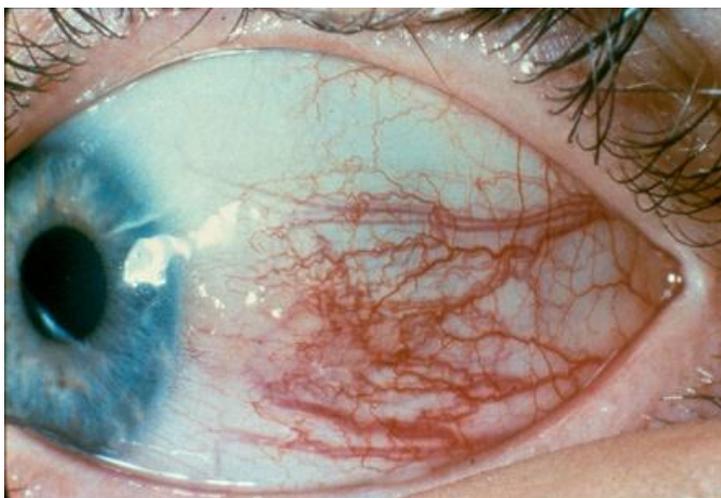


- Pyoderma gangrenosum: Special circumstances
 - pyoderma adjacent to ileostomy
 - may reoccur at relocated stoma
 - medical therapy preferable
 - pyoderma of head and face common in children



- Aphthous stomatitis
 - CDCD>>UC
 - Small punched out erosions(ulcers, surrounded by red halo
 - ? Parallels IBD activity
 - DD pemphigus, herpetic infection (common cold sores)
 - Tx:
 - pentoxifylline, colchicine, dapsone, thalidomide, plaquenil
 - systemic steroids, topical steroids (triamcinolone in orabase, steroid mouth rinse), intralesional steroids
 - topical anaesthetic, nicotine gum
 - antiviral therapy for herpetic sores
 - correction of folate, iron, B₁₂ and zinc deficiencies

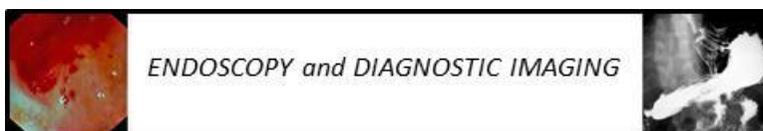




- Uveitis (anterior uveitis, iritis, iridocyclitis)
 - Retinal vasculitis (rare)
 - Incidence 0.5–3% UC>>>CD
 - Diagnosis with split lamp examinations prompt diagnosis necessary to preventing scarring
 - Tx:
 - azathioprine, cyclosporine, methotrexate
 - local/systemic steroids (cave glaucoma, posterior synechiae, cataract)



- Primary sclerosing cholangitis
 - May affect both intra- and extrahepatic bile ducts
 - Asymptomatic, cholestasis, bacterial cholangitis, cirrhosis cholangiocarcinoma
 - Incidence 5% of UC; 2/3 of PSC have UC
 - No parallel disease activity
 - Diagnosis: cholangiography (MRCP/ERCP), biopsy
 - Tx:
 - ursodeoxycholic acid, D-penicillamine, colchicine;
 - steroids?
 - immunosuppressives, methotrexate
 - short time stenting of dominant stenosis
 - liver transplantation



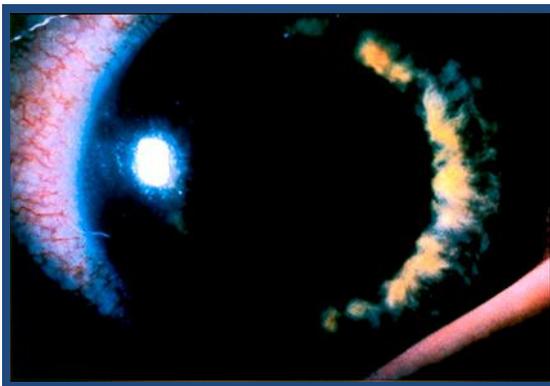
- Pyoderma Gangrenosum in IBD



Courtesy of J-F Colombel, MD

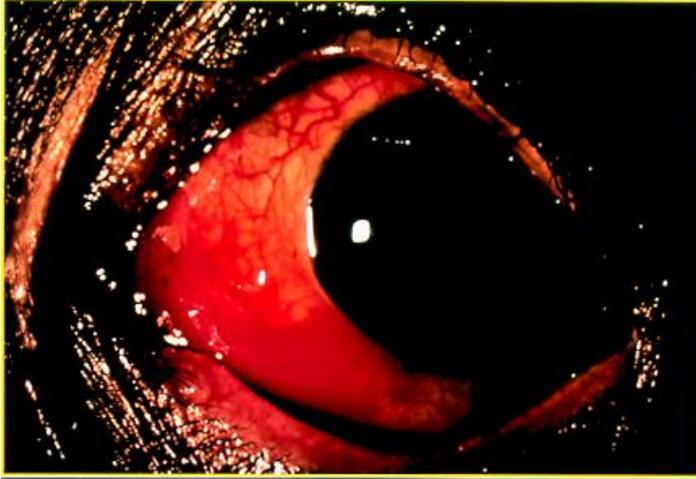


- Uveitis in IBD



Courtesy of J-F Colombel, MD

- Scleritis in IBD



- Sclerosing Cholangitis in IBD



Courtesy of J-F Colombel, MD

- Perianal CD – Anal fissures
 - Often multiple, also located laterally or centrally
 - Often wide with undermined edges
 - Limited pain, lack of reactive sphincter spasm
 - Covered with indurated firm cap-like skin fold
 - Reddish violet edematous perianal skin with radial pronounced furrows
 - Limited tendency to healing





- Perianal fistulas in Crohn disease
 - 20–30 % of patients with CD has fistulas
 - Decreased quality of life
 - 50% of patients with Crohn colitis and perianal fistula's end with ileostomy
 - Few effective therapeutic approaches

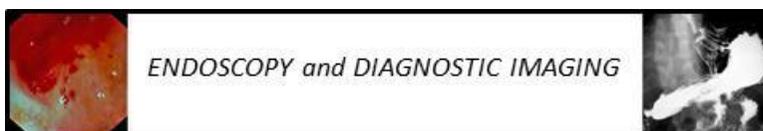
- Clinical classification of perianal CD: Simplified (U-F-S) clinical classification system

U. Ulceration	F. Fistula/abscess	S. Stricture
0. Not present	0. Not present	0. Not present
1. Superficial fissure	1. Low/superficial	1. Spasm/membranous
2. Cavitating ulcer	2. High complex	2. Severe fibrotic

Adapted from: Hughes LE. Dis Colon Rectum. 1992;35:928-932

- Cardiff classification of perianal Crohn Disease (UFS)

U. Ulceration	F. Fistula/abscess	S. Stricture
0. Not present	0. Not present	
1. Superficial	1. Low/Superficial	



fissures

- | | | |
|------------------------------|-------------------------|--------------------------------------|
| a) Posterior and/or anterior | a) Perianal | a) anal canal-spasm |
| b) Lateral | b) Anovulval anoscrotal | b) low rectum-membranous |
| c) With gross skin tags | c) Intersphincteric | c) spasm with severe pain, no sepsis |
| | d) anovaginal | |

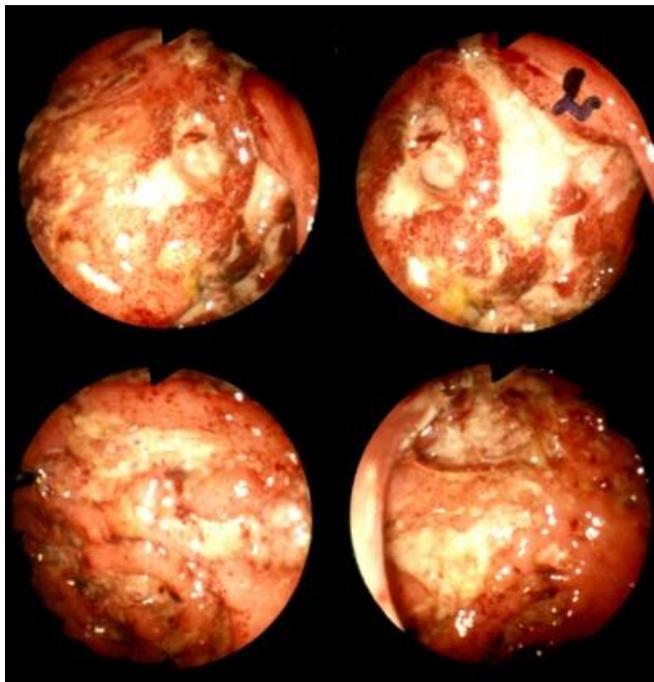
2.Cavitating ulcers

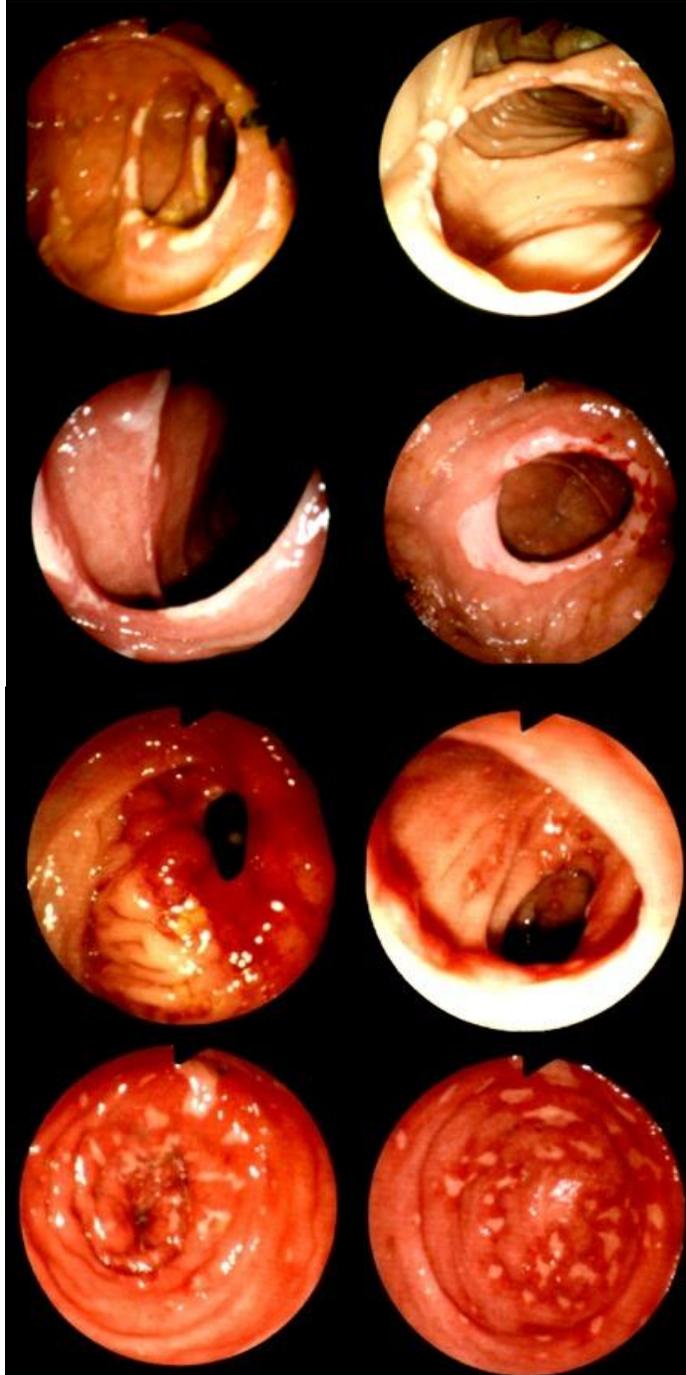
- a) anal canal
- b) lower rectum
- c) with extension to perineal skin (aggressive ulceration)

2.High

- | | |
|----------------------------|--------------------------|
| a) blind supralelevator | a) anal stenosis |
| b) high direct (anorectal) | b) extrarectal stricture |
| c) high complex | |
| d) rectovaginal | |
| e) ileoperineal | |

UC CANCER



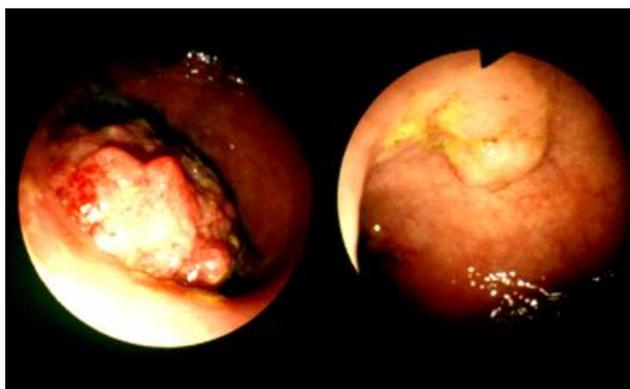


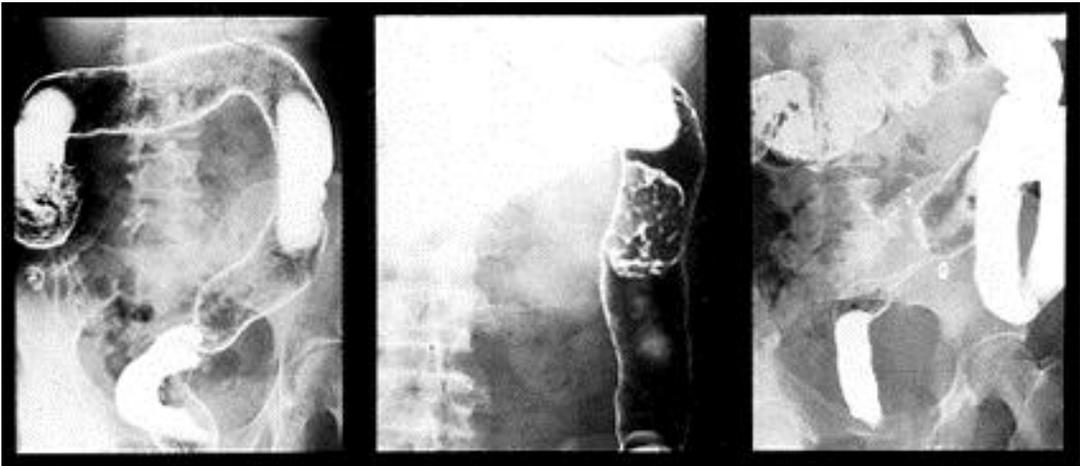
UC-Dysplasia/Carcinoma Surveillance:

- How often should surveillance be repeated
 - Recommendations are empiric, determined by presence /absence of dysplasia
 - Every 1–2 years if initial BX's are negative
 - Every 3–6 months if initial BX's are indefinite or low grade dysplasia in the absence of Dalm or CA at colonoscopy
 - Every 3–6 months if BX's show multifocal low grade dysplasia on repeated exams
 - Low grade dysplasia progresses to high-grade dysplasia/CA in 13-18% of patients during surveillance

- Who is eligible for surveillance
 - Patients with usually quiescent disease without need otherwise for colectomy
 - Pancolitis of >8–10 years duration
 - Left-sided colitis of >15–20 years duration

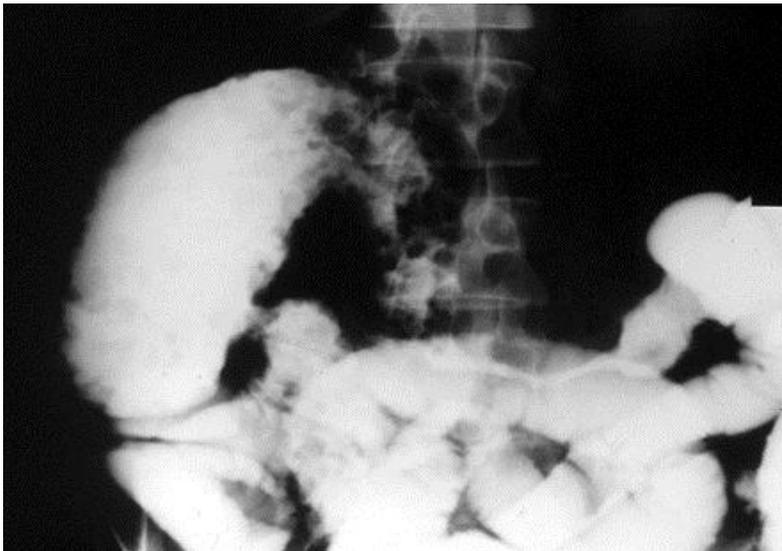
- How should surveillance be done
 - Pancolonoscopy
 - Multiple biopsies of any suspect abnormality:
 - heaped-up, thickened, plaque-like or nodular mucosa
 - villous appearance
 - polypoid mass >1 cm (Dalm)
 - bizarre 'pseudopolyps' with altered mucosal colour and texture
 - isolated flat/slightly raised ulcer
 - any stricture with/without ulceration
 - focal erythematous indurated mucosa
 - 2–3 BX's every 10–12 cm, submitted separately

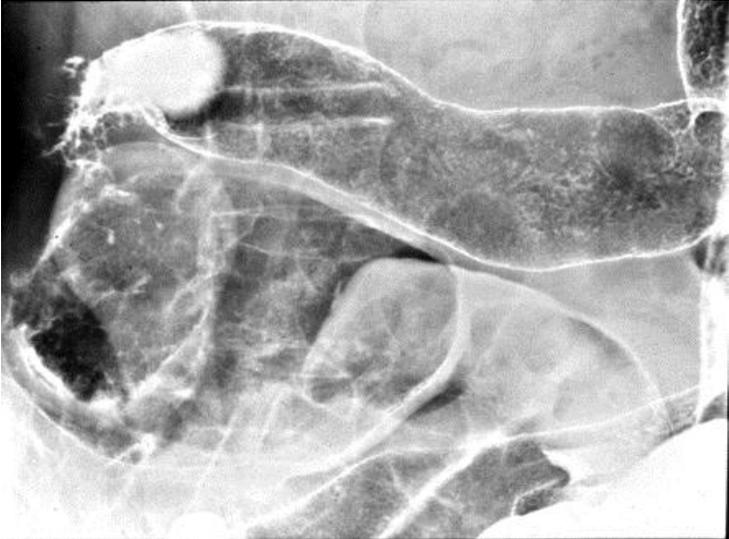




- Who is at risk?
 - Patients with entire colon involvement
 - Duration of colitis for over 8 years
 - Lesser risk with left-sided colitis
 - Risk not related to:
 - severity of initial attack
 - disease activity
 - age at onset

- Colorectal cancer in chronic ulcerative colitis
 - Cancer develops at younger age
 - Cancer tends to be more advanced at diagnosis
 - Cancer tends to be less differentiated
 - Cancer tends to be more in the proximal colon
 - Cancer is more frequently multiple







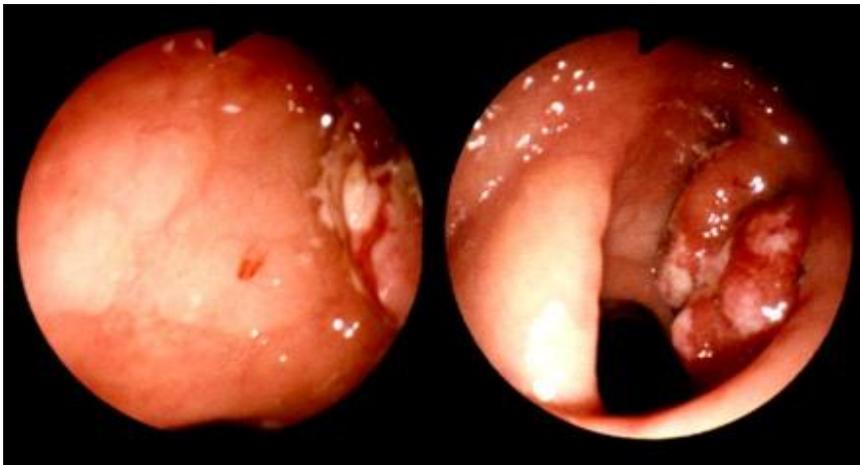
➤ Dysplasia

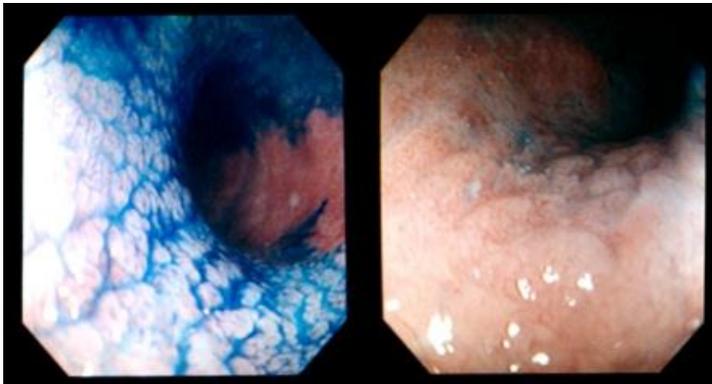
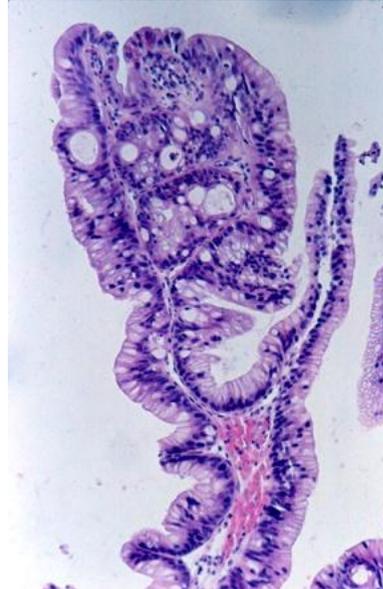
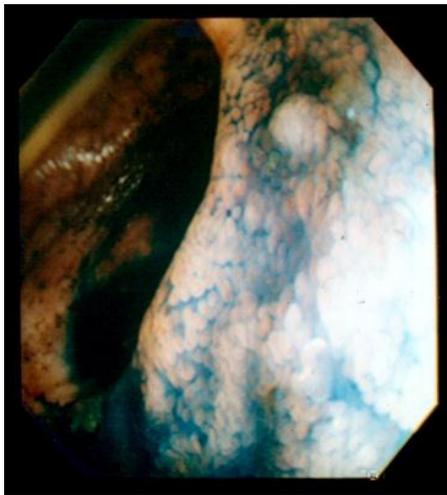
- An unequivocally neoplastic proliferation
- Essentially equivalent to an adenoma
- Excludes all equivocal or regenerative lesions
- May be the superficial part of a carcinoma
- Often multifocal
- May occasionally be visible to endoscopist

IBD - Cancer – Surveillance: Macroscopic classification

- Flat dysplasia
 - Endoscopically undetectable
 - Endoscopically visible suspicious alterations
 - Discoloration
 - velvety/villous appearance
 - irregular fine nodularity

- Raised dysplasia
 - Discrete polypoid lesion or nodular mass
 - Irregular plaque-like lesion/wart-like thickening
 - Conglomerate of polypoid lesions in a finite colonic segment





IBD - Cancer – Surveillance: Macroscopic classification

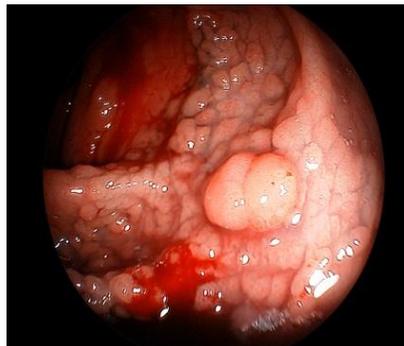
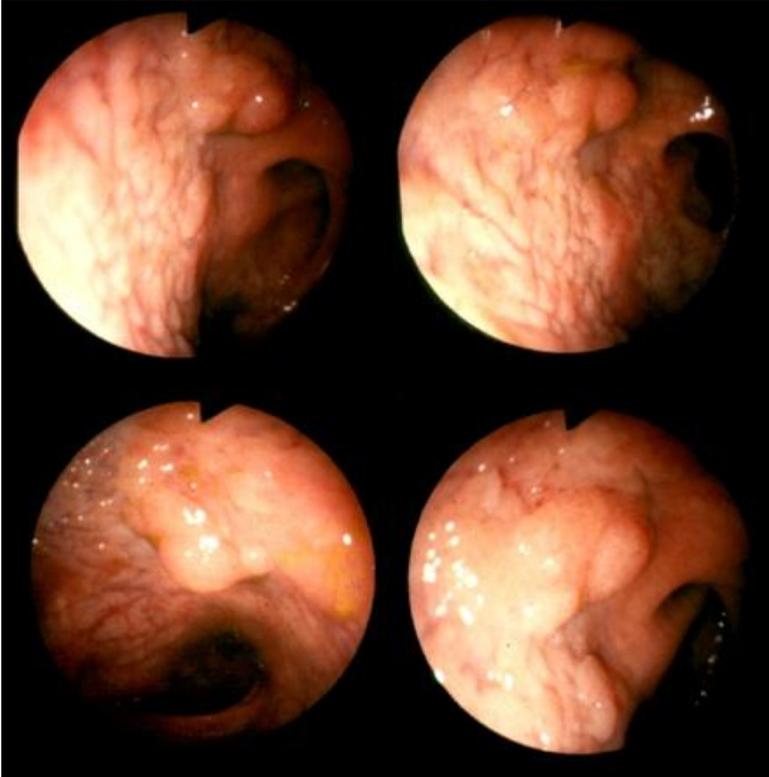
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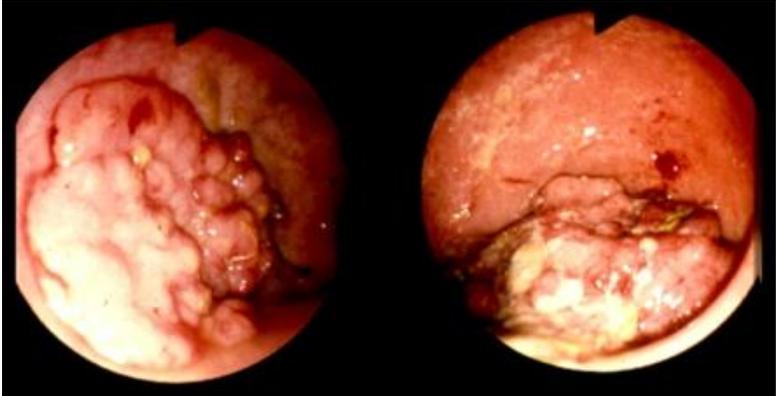
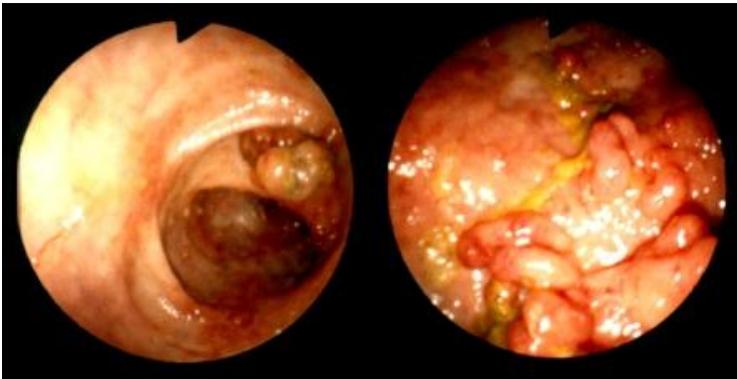
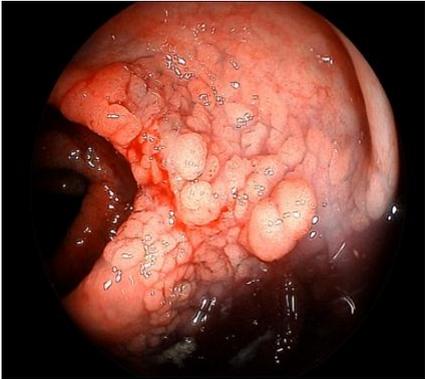


UC-Dysplasia/Carcinoma Surveillance

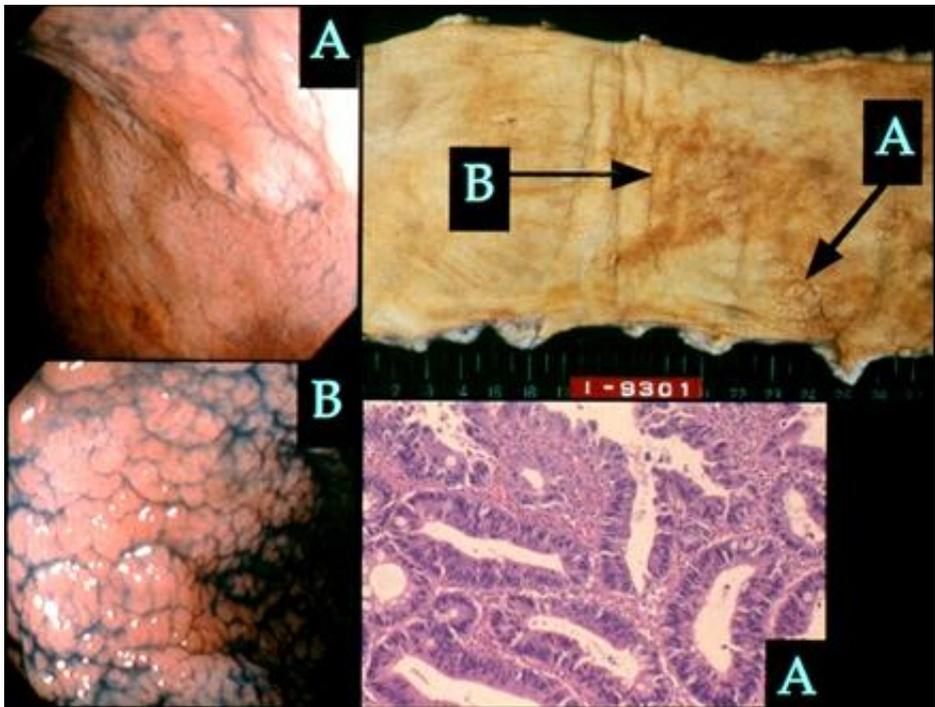
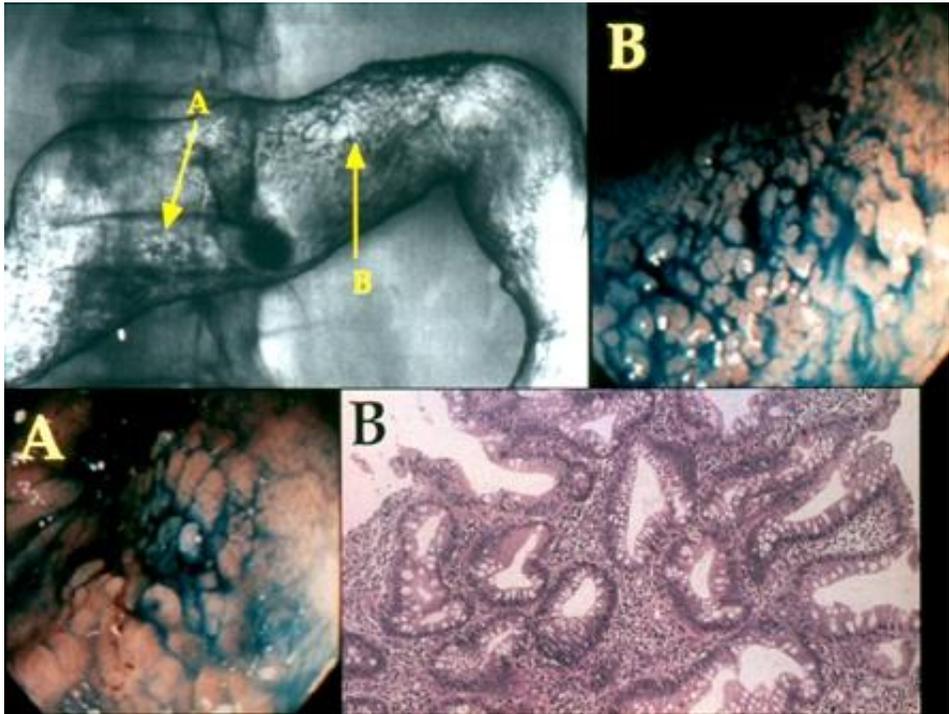
- The problem of DALM (dysplasia-associated lesion or mass)
 - Dalms are rather uncommon
 - Difficult/impossible to distinguish from 'ordinary' sessile adenoma
 - Occasionally difficult to distinguish from bizarre pseudopolyps
 - Occasionally difficult to distinguish from early cancer

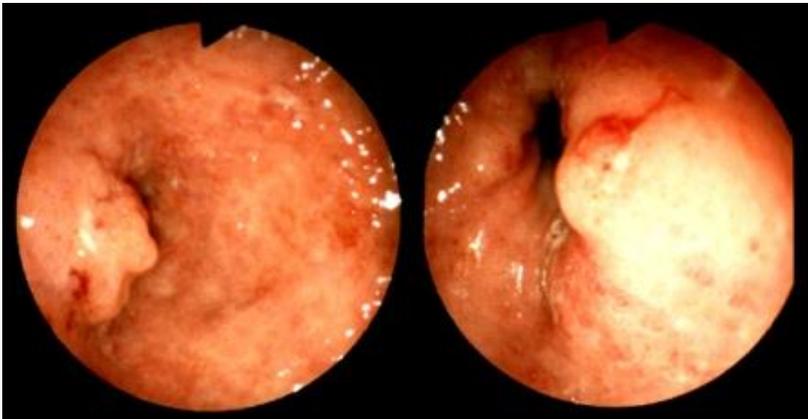
- Dalms may be of larger size, irregular shape, conspicuous discoloration and firmer consistency
- May occur in uninvolved colon
- May have same significance as (high grade) dysplasia

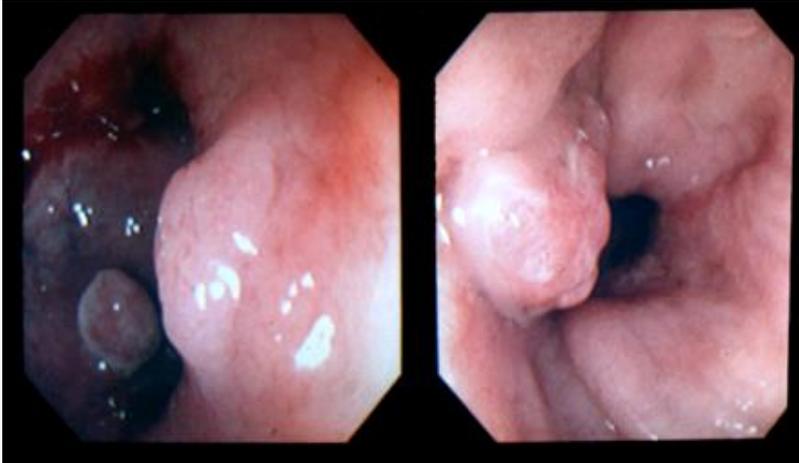




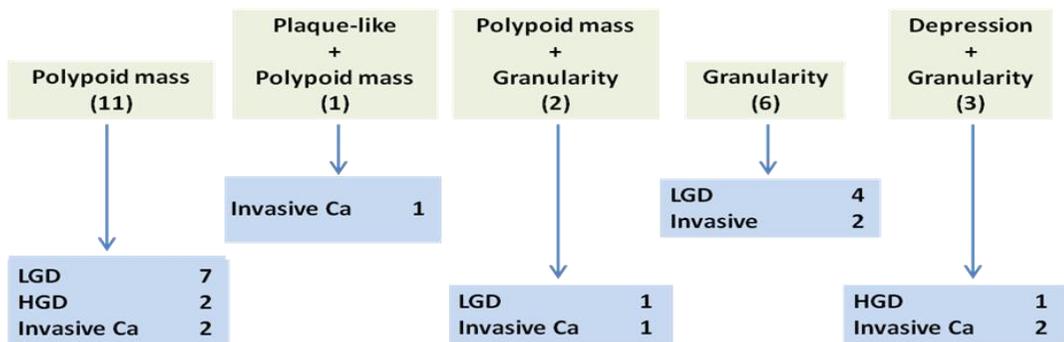
A Case of Low Grade Dysplasia







Correlation Between Endoscopic Findings and Histology



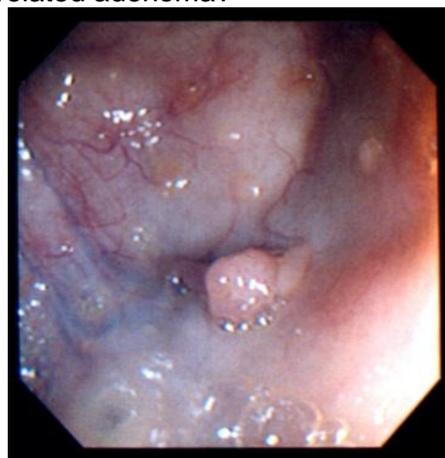
LGD; low-grade dysplasia, HGD; high-grade dysplasia
 One HGD could not be detected by colonoscopy

Adapted from: Matsumoto T, Iida M, et al: Radiology, 1996



IBD – Surveillance

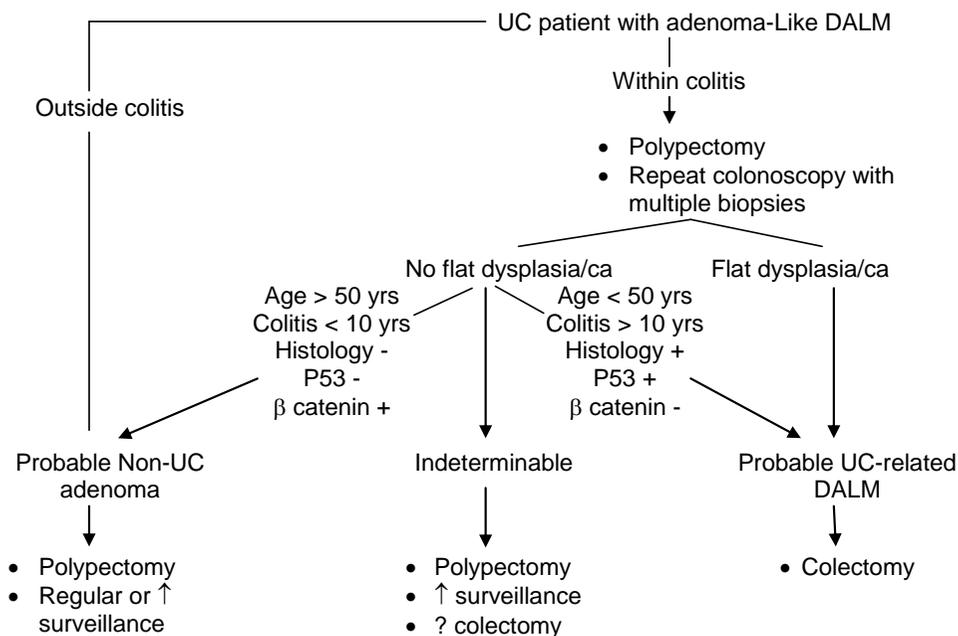
- Distinction between DALM and inflammatory pseudopolyp may be impossible
- Pointers towards DALM
 - mass lesion over 1 cm in diameter
 - friable
 - firm consistency
 - different coloration than other pseudopolyps
 - surface irregularity
 - lack of exudate cap
- The problem of the polypoid lesion
 - corresponding to colitis-related raised dysplasia?
 - corresponding to sporadic non-colitis related adenoma?
- Sporadic pedunculated or small sessile (>1 cm) adenomas, found during surveillance, not accompanied by mucosal dysplasia elsewhere in the colon are considered incidental and not colitis related. Endoscopic removal suffices
- Adenomatous polyps, especially large sessile (<1 cm) lesions, accompanied by dysplasia elsewhere are considered precancerous and colitis-related. Colectomy is mandatory



Adenomas in IBD

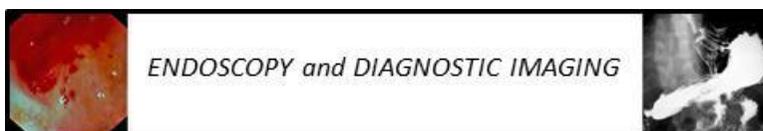
1. No reason why they should not occur, but
2. May be impossible to distinguish from DALM
3. If
 - i) completely excised,
 - ii) adjacent mucosa is not dysplastic,
 - iii) patient is in adenoma age group.

Lesions may be treated by local excision only but careful follow-up is required



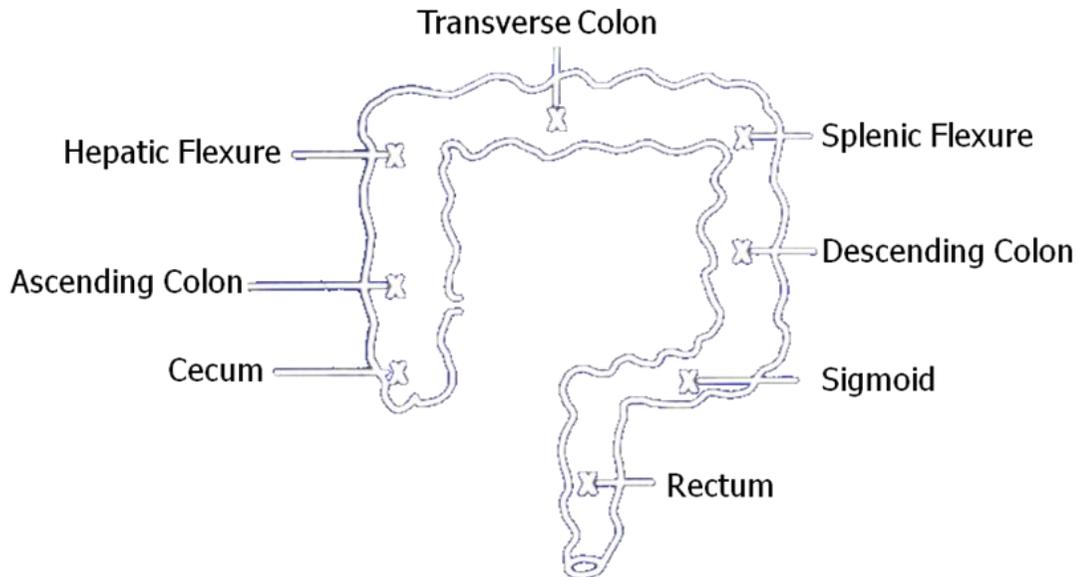
Odze AJGE
1999;94:1746.

- Colonoscopic examination for dysplasia
 - Direct special attention to any mass lesion (additional biopsies should be obtained)
 - Dysplasia associated with a lesion or mass (DALM) has a high incidence of cancer
 - No need to routinely biopsy pseudopolyps unless:
 - greater than 1 cm in diameter
 - friable
 - different coloration than other pseudopolyps
 - have surface irregularities
 - Multiple biopsies of all strictures



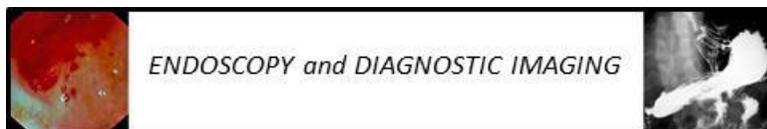
Colonoscopic Surveillance for Dysplasia/Cancer

Recommendation: biopsy every 10 cm

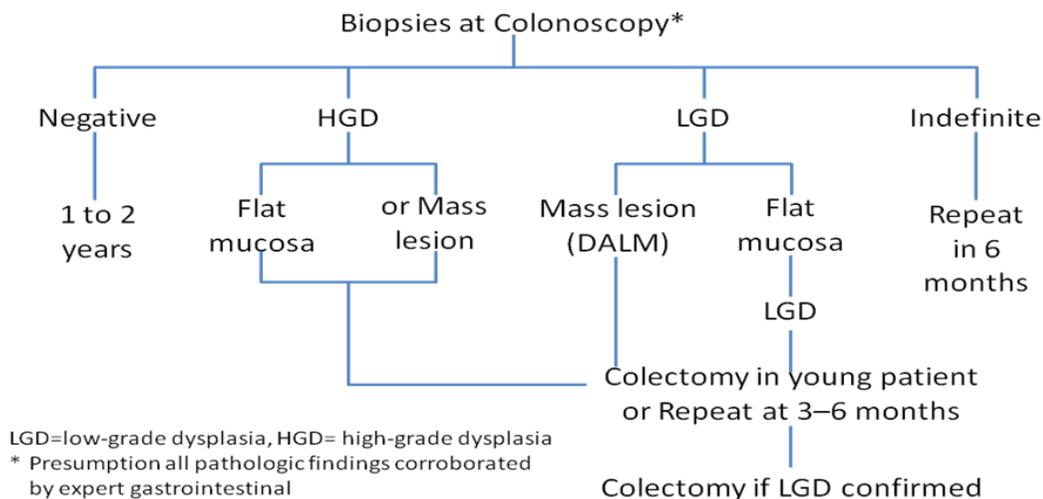


UC-Dysplasia/ Cancer Surveillance

- Shortcomings
 - There is no proof that development of cancer can be averted
 - There is no firm proof that cancer mortality is decreased
 - Cancer may develop without the discovery of dysplasia



Chronic Inflammatory Bowel Disease Algorithm for Patient Management

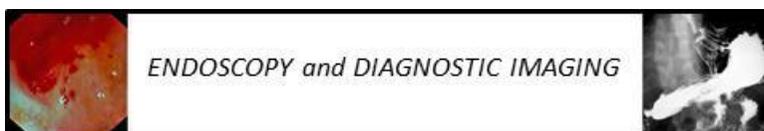
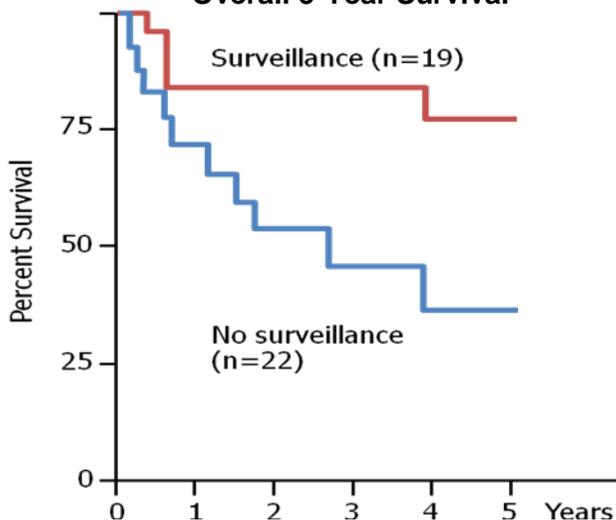


IBD Surveillance

- Low-grade dysplasia may be associated with cancer in 19% of cases
- Low-grade dysplasia may progress to high-grade dysplasia or cancer in 35–50% of cases

➔ Colectomy instead of enhanced surveillance

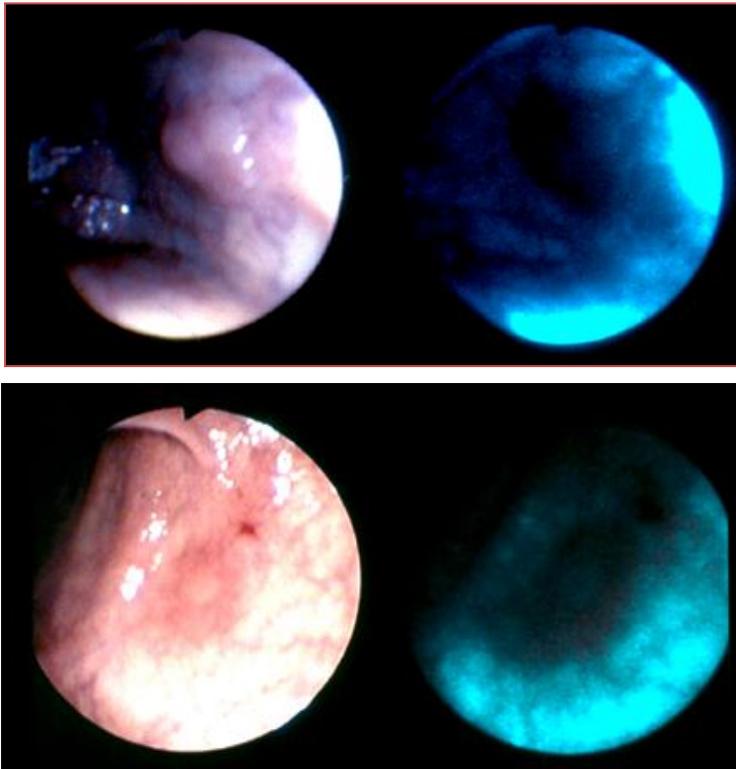
Overall 5-Year Survival

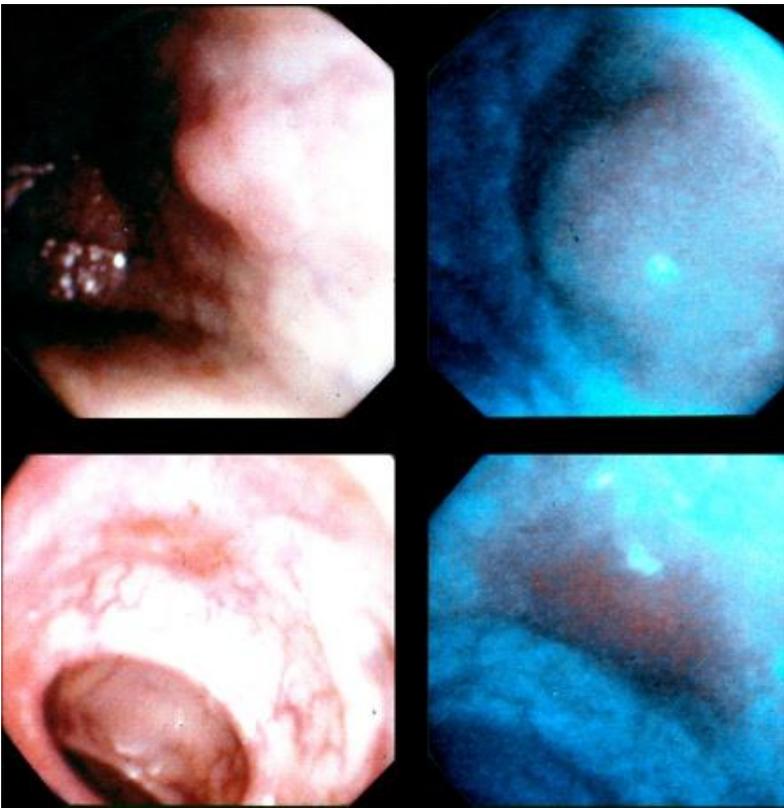
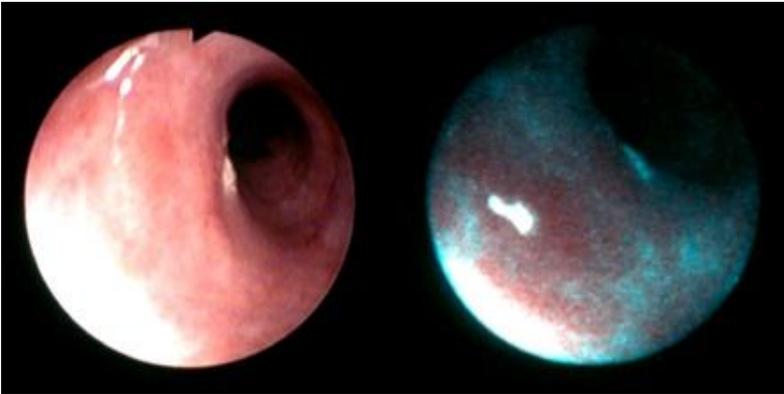


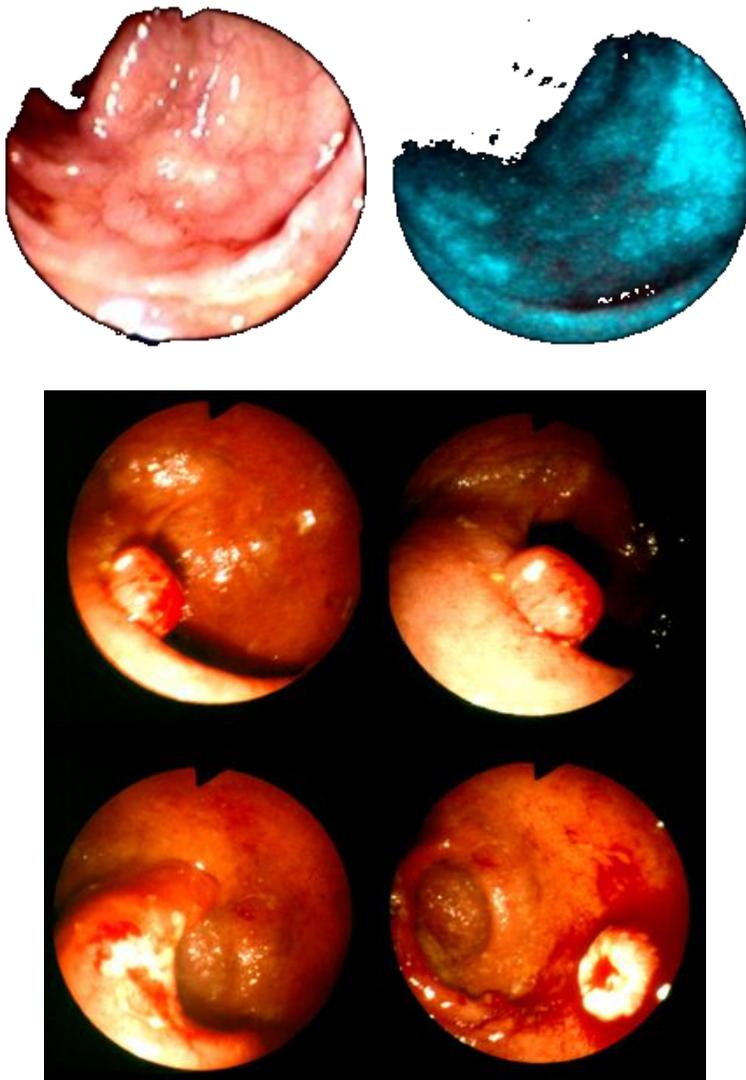
UC-Dysplasia/Cancer Surveillance

- Other biomarkers
 - Flow cytometry for DNA aneuploidy
 - Sucrase/isomaltase immunostaining
 - Sialomucins
 - Pectin binding
 - Carcino embryonic antigen expression
 - Endoscopic autofluorescence tissue spectroscopy

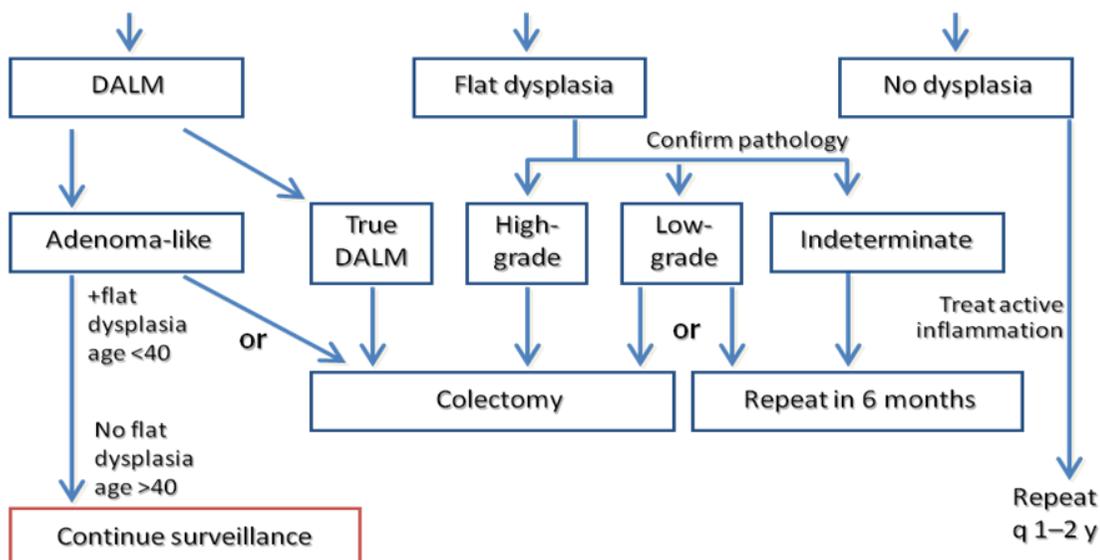
Ulcerative Colitis: Dysplasia







Technique: Colonoscopy to the cecum with four quadrant biopsies every 10 cm, removal of all DALMs when feasible. Candidates: pancolitis >7 y, left-sided >15 y, with PSC at time of diagnosis

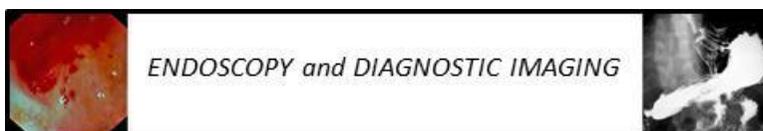


Practice Points:

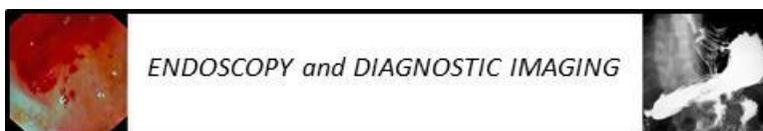
- Main targets for therapeutic activity in Crohn disease
 - T-cell activation
 - Pro-inflammatory cytokines
 - CD4+ T-cells and T-helper subsets
 - Adhesion molecules and leukocyte recruitment
 - Nonspecific mediators of injury and repair
- Therapeutic endpoints of acute therapy for Crohn disease
 - CDAI score <150 (absence of inflammatory symptoms)
 - Endoscopic evidence of mucosal response (reduction in CDEIS score)
 - highest score = 14.9
 - lowest score = 0
 - Corticosteroid withdrawal
 - Improved quality of life

Define common terms

- Steroid dependent disease
 - Disease relapsing as soon as systemic steroids are tapered to less than 15 (20?) mg prednisolone-equivalent: three relapses during 12 months;
 - CD: CDAI >200 after 12 weeks steroid therapy
 - UC: relapse despite optimal oral (4.8g/d) and/or rectal (4 g/d) mesalazine therapy to maintain remission



- Steroid refractory disease
 - Disease that cannot be controlled by currently-used steroid regimens within 12 weeks
 - Currently-used regimens:
 - 60 mg prednisolone-equiv. tapered to 10 mg over 6 weeks, 10 mg for another 6 weeks
 - 40 mg prednisolone-equiv. tapered to 0 over 12 weeks
 - Exclusion (pain due to fibrous stenosis; diarrhea due to bile salt malabsorption; anemia due to inadequate nutrition; overlapping infectious disease)
 - Steroid refractory or dependent disease that cannot be controlled by a “currently used steroid regimen”, and additional azathioprine/6MP in a sufficient dose (>2 mg/kg/d/4 months) or need for other interventions;
 - CDAI >200 after 4 months azathioprine/6MP
- Give the cyclosporin toxicity
 - Gastrointestinal: nausea, altered taste
 - Hepatic toxicity
 - Stomatitis
 - Renal: increase in creatinine
 - CNS: seizures, tremor
 - Skin: Lanugo hair, rashes, facial edema
 - Bone marrow suppression
 - Flu-like symptoms
 - Allergic reactions
 - Herpes zoster
 - Seizures with low serum cholesterol
- Give the clinical features of methotrexate toxicity
- Major
 - Hepatic
 - Myelosuppressive
 - Pulmonary
 - Fertility-related
 - Teratogenic
 - Enteritic/colitic
- Minor
 - Gastrointestinal
 - Alopecia-inductive
 - Allergic
 - Neurologic
- UC surgical treatment: Indications



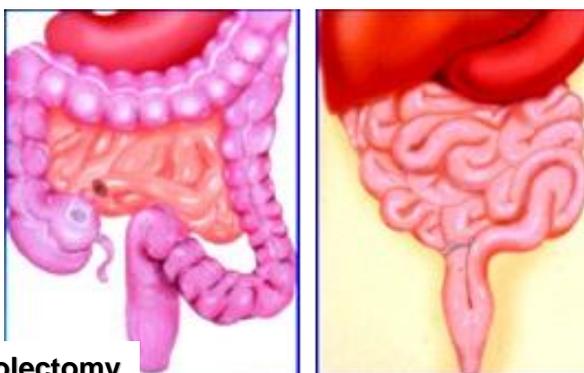
Elective

- Disease resistant to treatment (intractability)
- Cancer risk (dysplasia)/development
- Growth retardation
- Systemic complications

Emergency

- Failure of medical therapy in acute severe colitis
- Hemorrhage
- Toxic dilatation
- Perforation

Surgical Options



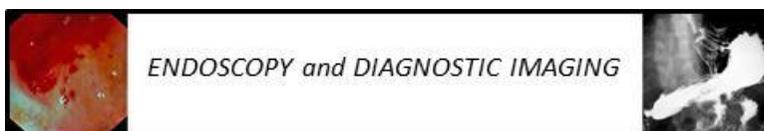
**Proctocolectomy
with permanent
ileostomy**

**Total colectomy &
subsequent ileal
anastomosis with
pouch formation**

Pouchitis

- Give the predictive factors for the development of pouchitis following total colectomy and IPAA surgery.
 - Positive association
 - Extraintestinal manifestations
 - Primary sclerosing cholangitis
 - Antineutrophil cytoplasmic antibody with a perinuclear staining pattern (pANCA)
 - Extent of pre-operative UC
 - Negative association
 - Smoking

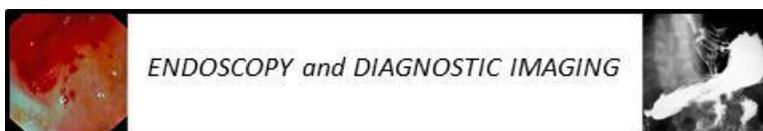
Printed with permission: Gionchetti P, et al. *Best Practice & Research Clinical Gastroenterology* 2004;18(5): pg 995.



- Give a differential diagnoses for late pouch-related symptoms in a patient who has an ileoanal pouch after proctocolectomy for UC:
 - Cuffitis
 - Pouchitis
 - Irritable pouch syndrome
 - Crohn disease
 - NSAID-induced damage (especially with isolated afferent limb ulcers)
 - Poor reservoir capacity
 - Adhesions
 - Stricture
 - Unrelated infections
 - Pelvic floor dysfunction
 - Anastomotic leak
 - Bacterial overgrowth syndrome
 - Malignancy (squamous cell cancer) of anus, small bowel cancer
 - Unmasked celiac disease

Practice Points: Pouchitis

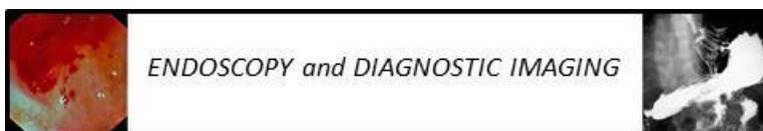
- The likelihood of developing chronic pouchitis in a UC patient having an IAPP is over 80% if serological testing shows high levels of panca (Fleshner P, et al. *Clin Gastroenterol Hepatol* 2008:561-8.)
 - Persons who fail to respond to one antibiotic for pouchitis may respond to two
 - Some persons will require chronic continuous antibiotics to maintain remission (antibiotic dependent chronic pouchitis)
 - For antibiotic dependent chronic pouchitis one option is to alternate 3 or 4 antibiotics every week
 - The 9 month relapse rate of pouchitis when using VSL #3 is 15%, no 100% for placebo
 - The efficacy of budesonide enemas is comparable with metronidazole tablets
 - Topical or oral mesalamine, or anti-TNF therapy may also be effective for pouchitis
- Predictive factors for the development of pouchitis
 - Positive association
 - Extraintestinal manifestations
 - Primary sclerosing cholangitis



- Antineutrophil cytoplasmic antibody with a perinuclear staining pattern (p-ANCA)
 - Extent of pre-operative UC
- Negative association
- Smoking

Adapted from: Gionchetti Paolo et al. *Best Practice & Research Clinical Gastroenterology* 2004;18(5): pg 995.

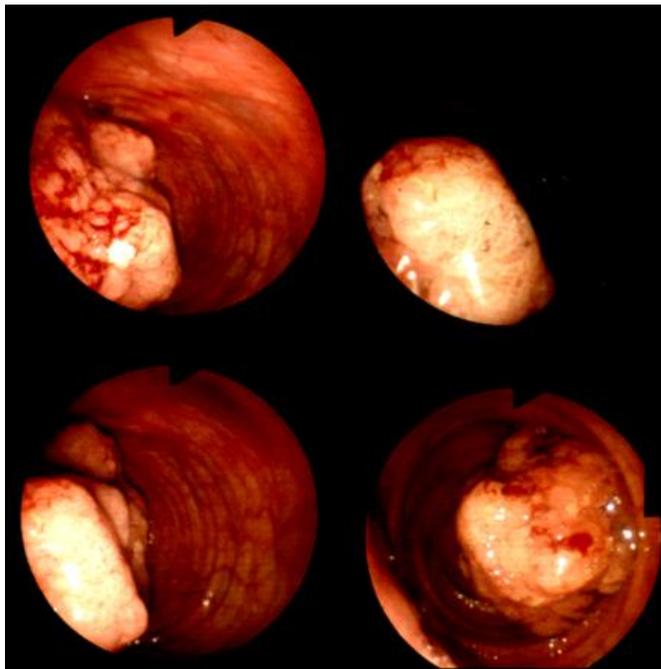
- Mechanisms by which *Clostridium Difficile* cause Pseudomembranous Colitis in a patient with a History of Antibiotic Use
- Antibiotics deplete regular gut microbionta, which normally outnumber *C. difficile* which is present
 - *C. difficile* can resist antibiotics as a spore and then will outgrow normal microbionta when antibiotics are discontinued
 - Toxins A and B are produced by the great numbers of *C. difficile* cause diarrhea
- Differential diagnoses for late pouch-related symptoms
- Cuffitis
 - Pouchitis
 - Irritable pouch syndrome
 - Crohn disease
 - NSAID-induced damage (especially with isolated afferent limb ulcers)
 - Poor reservoir capacity
 - Adhesions
 - Stricture
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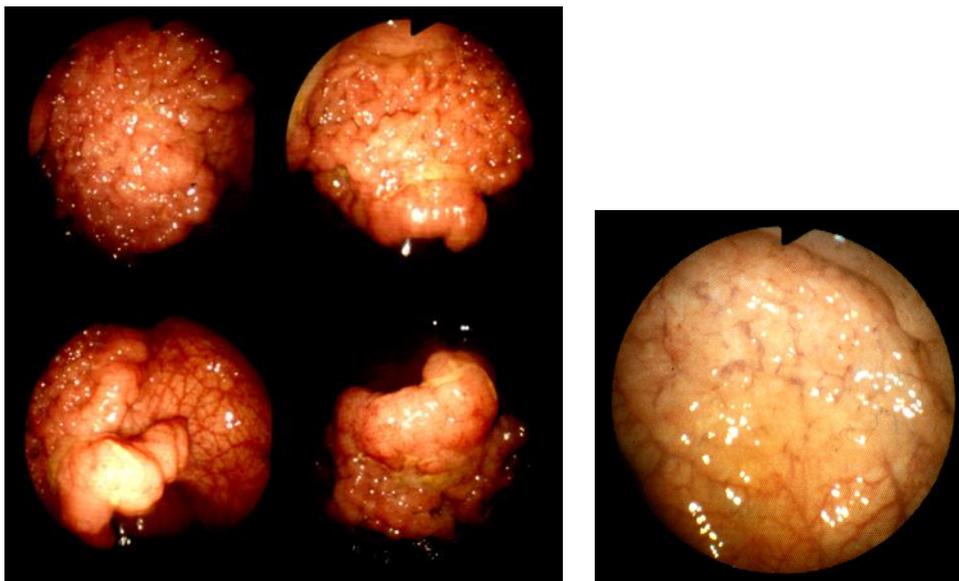
Colonic Polyps and Cancer



- Giant villous adenoma – invaginating

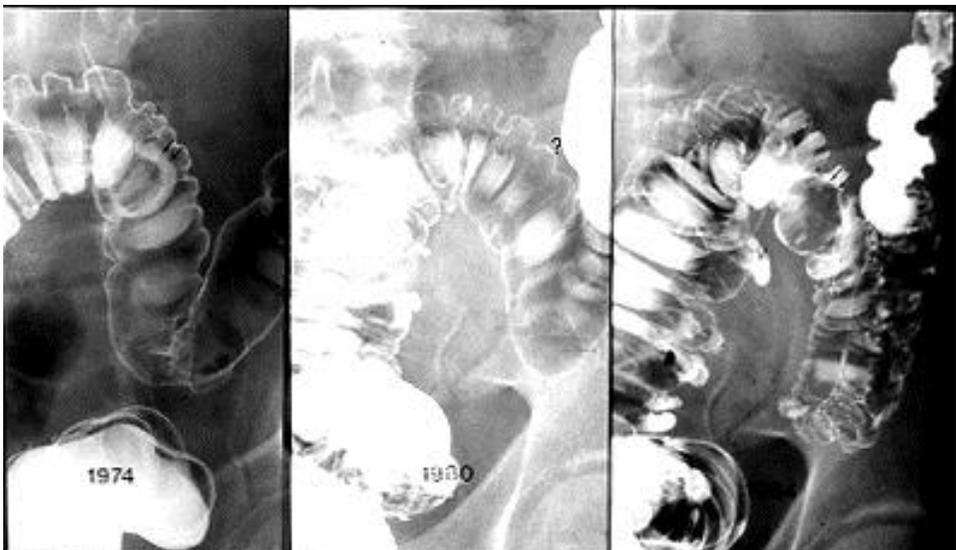


➤ Rectal villous adenoma

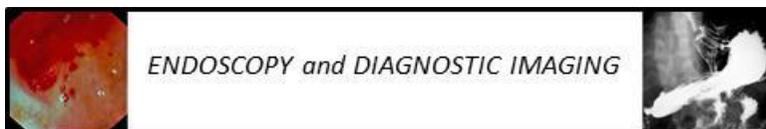


➤ Histological classification of polyps of the large intestine

Type	Single or isolated Multiple polyps	Polyposis
Neoplastic	Adenoma	Adenomatosis (familial polyposis)
➤ Hamartomas	<ul style="list-style-type: none"> ○ Juvenile polyp ○ Peutz-Jegher Polyp 	<ul style="list-style-type: none"> ○ Juvenile polyposis ○ Peutz-Jegher Syndrome
➤ Inflammatory polyp	<ul style="list-style-type: none"> ○ Benign lymphoid 	<ul style="list-style-type: none"> ○ Benign lymphoid polyposis
➤ Unclassified	<ul style="list-style-type: none"> ○ Metaplastic (hyperplastic polyp) 	<ul style="list-style-type: none"> ○ Inflammatory polyposis eg in inflammatory bowel disease ○ Metaplastic polyposis



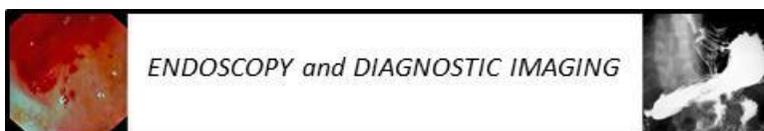
- Risk factors for colorectal cancer
 - Age over 50 years
 - High-fat, low-fibre diet, smoking
 - Excess caloric intake or alcohol
 - Personal history of colorectal adenomatous polyps or cancer
 - Chronic inflammatory bowel disease ulcerative colitis, Crohn colitis)

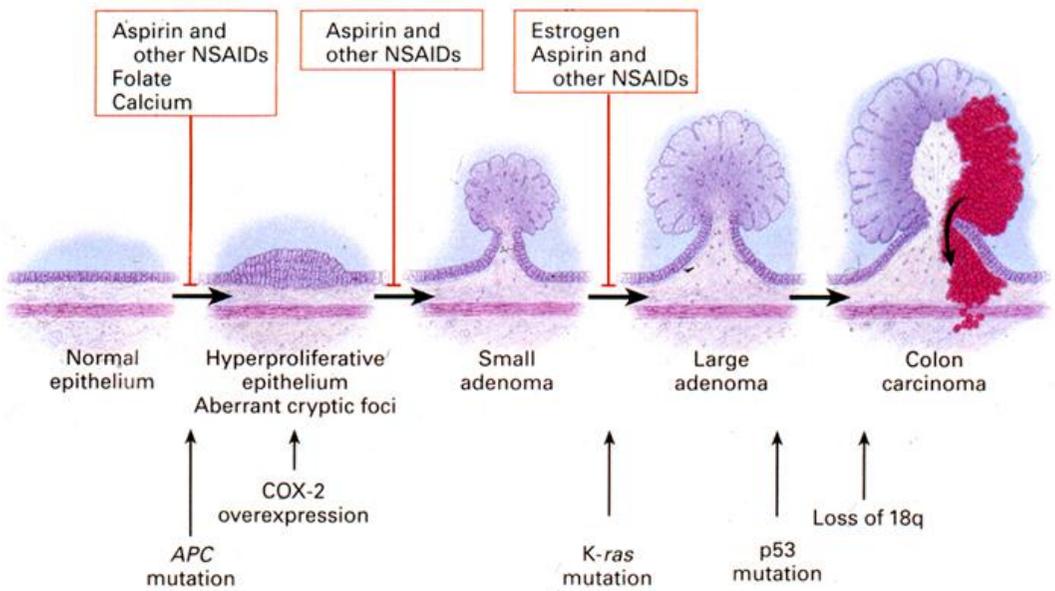
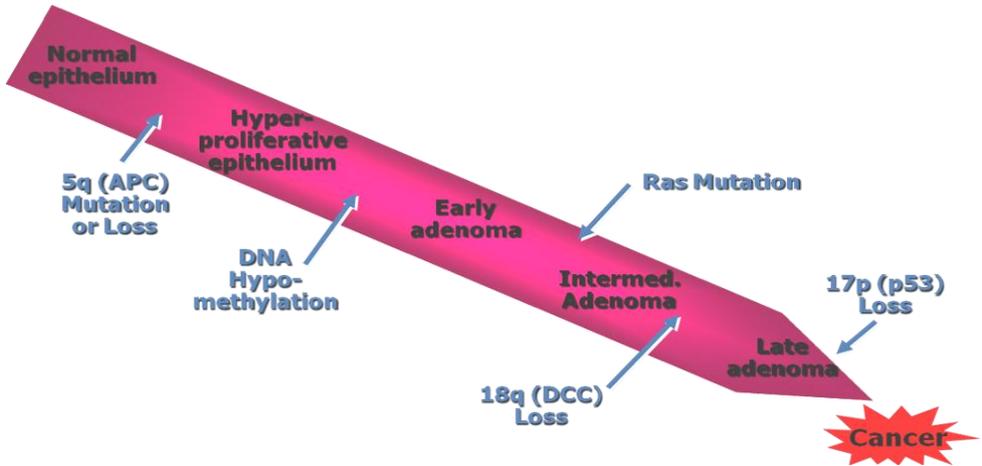


- Family history of colorectal adenomatous polyps or cancer
- Hereditary syndromes
 - Hereditary nonpolyposis colorectal cancer (Lynch Syndrome)
 - Familial Adenomatous Polyposis
 - Gardner syndrome
 - Turcot syndrome
 - Peutz-Jeghers syndrome
 - Familial Juvenile Polyposis
- Familial adenomatous polyposis & hereditary nonpolyposis colon cancer
 - FAP
 - Germline mutation = APC gene
 - Autosomal dominant
 - 100's–1,000's of colonic adenomas
 - Age of Dx=early teens (flex sig w/bx)
 - Tx=colectomy
 - 10% risk duodenal ca
 - HNPCC
 - Germline mutation = DNA Mismatch Repair Genes
 - Autosomal dominant
 - Few if any polyps
 - Right-sided colon ca
 - Other ca: uterine, gastric, pancreatic, ovarian, urinary, small bowel
 - Early average age of colon cancer dx:
 - FAP = 39 years of age
 - HNPCC = 44 years of age
 - Genetic tests:
 - Should be done w/ genetic counselor
 - FAP=APC protein Truncation Test
 - HNPCC = MSI → MLH1, MSH2
 - Median Age of Onset of CRC in the 4 Phenotypes of FAP

Phenotype	Age, yrs
○ Profuse	39
○ Intermediate	39-50
○ Attenuated (AFAP)	>50 (R colon)
○ MYH (MAP)	>60 (recessive)

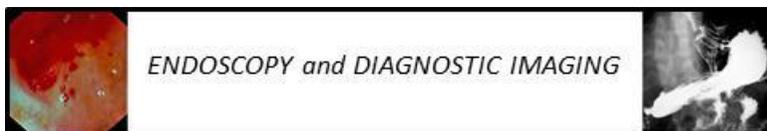
- Adenoma-Carcinoma Sequence





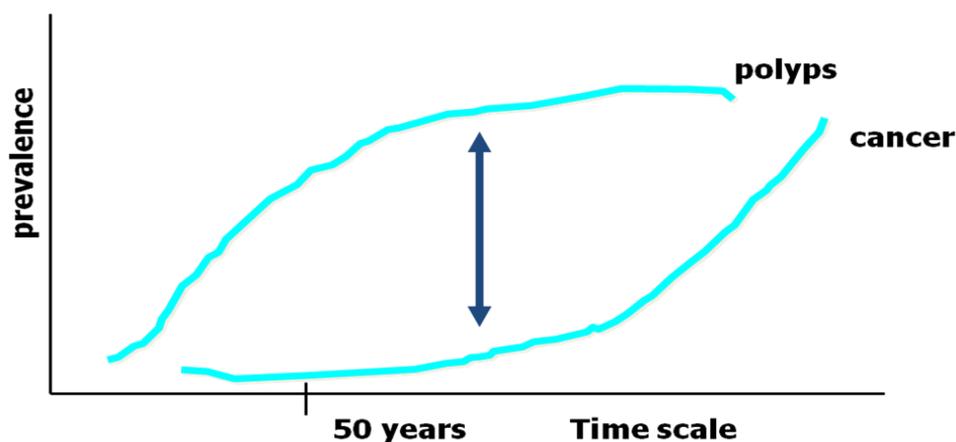
Risk Stratification

Risk level	% of CRC	Recommendations for testing
➤ High risk Familial polyposis	1	Sigmoidoscopy in teenage years Consider genetic screening Total colectomy if detected



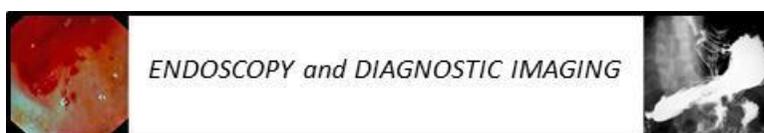
HNPCC	5	Colonoscopy in 3 rd /4 th decade at 2-years intervals
Chronic ulcerative colitis	< 1	Colonoscopy for universal colitis every 2 years beginning 8-10 years after onset
➤ Moderate risk		
Familial risk	15-20	Begin screening at an age 10 years younger than age of index case. Consider colonoscopy screening
- First degree		
Personal history of breast, uterine, ovarian	< 1	No specific recommendation
➤ Average risk		
Age > 50 years	70-75	Begin screening at age 50

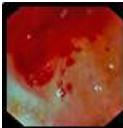
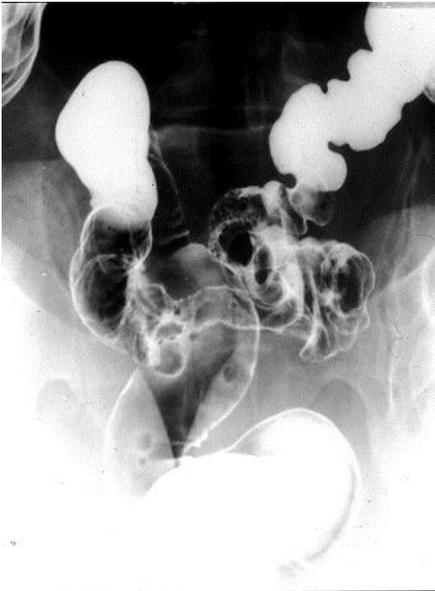
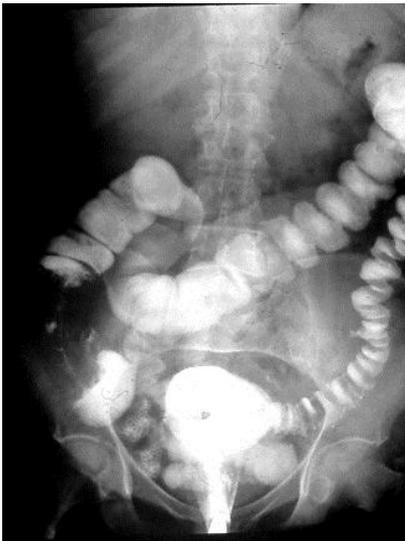
Colon Polyp – Cancer Sequence – Window of Opportunity



Colorectal Cancer: Mass Screening Programs – Fecal Occult Blood Problems:

- Compliance varies from 35–90%
- <30% of larger polyps and cancers bleed sufficiently to be detected by fecal occult blood testing

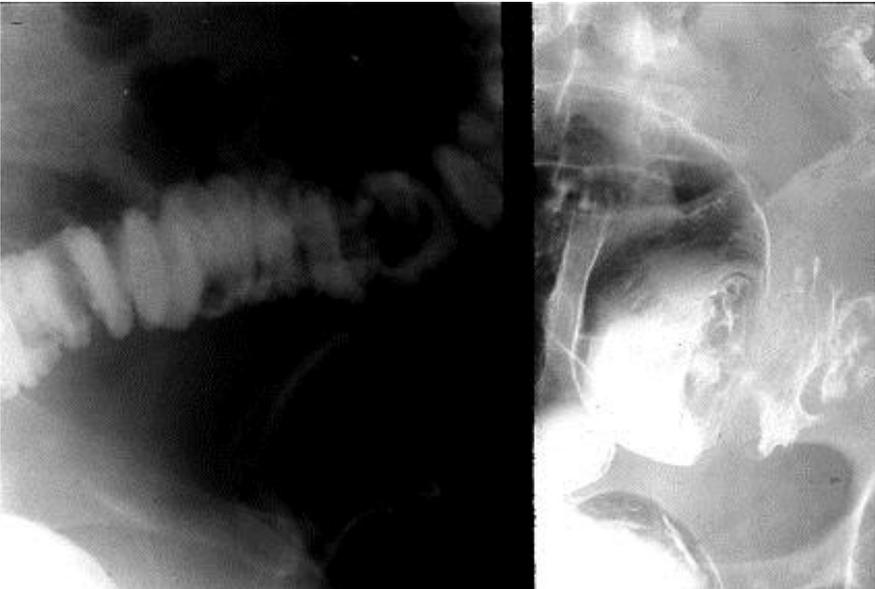


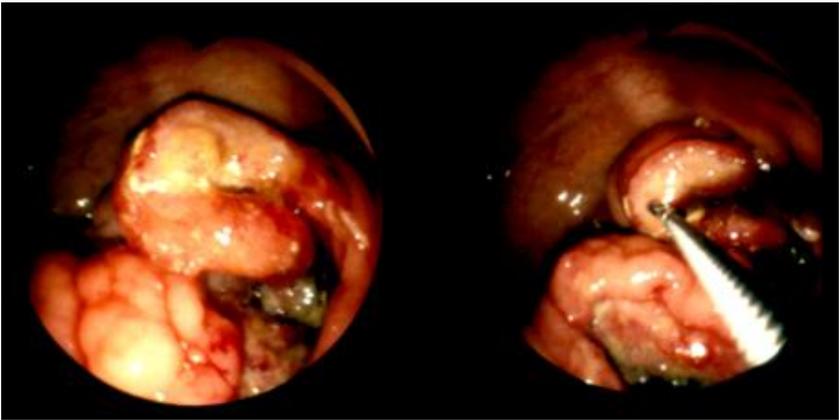
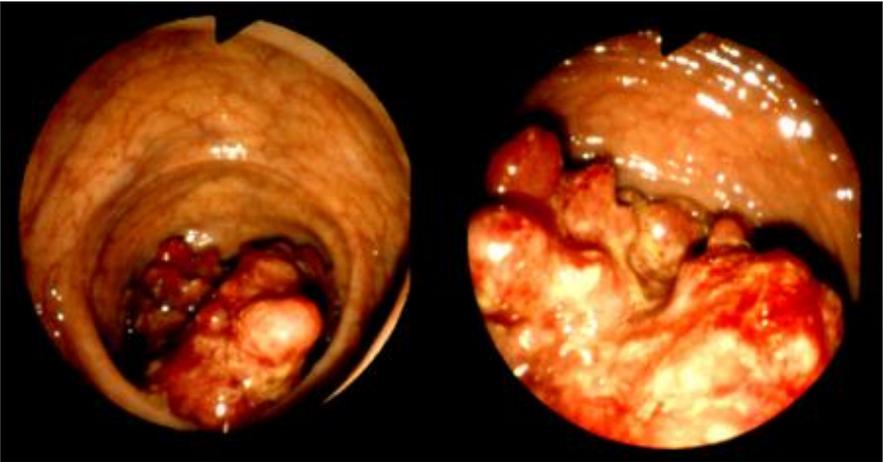


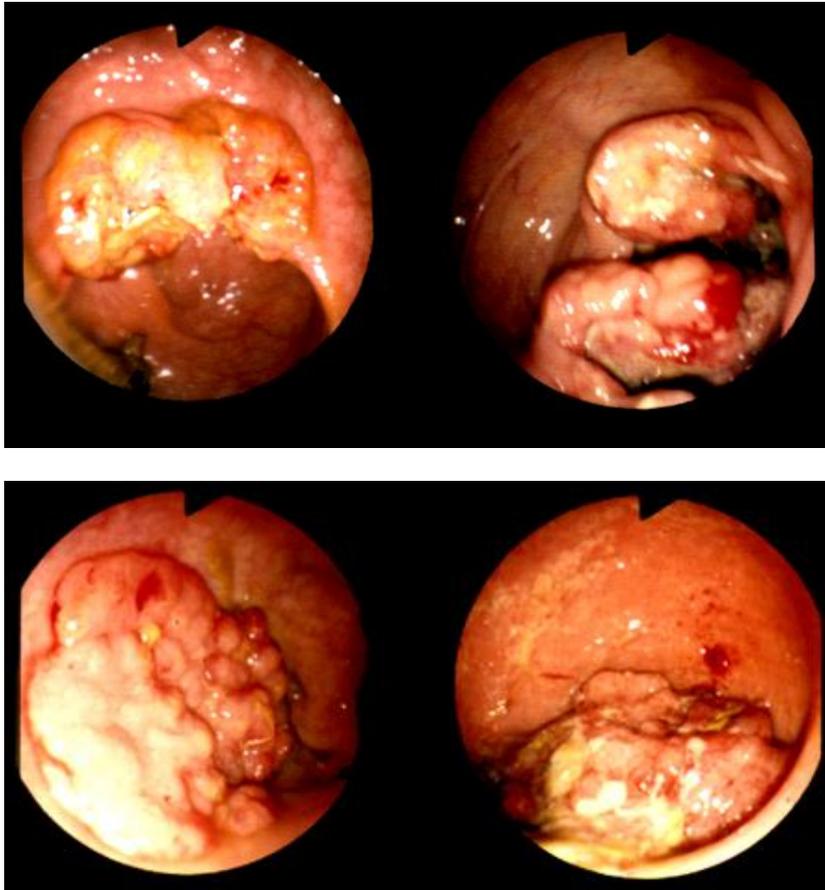
➤ Radiologic differentiation between colonic cancer and diverticulitis

	Diverticulitis	Cancer
○ Segment length	Long	Short
○ Mucosa	Intact	Destroyed
○ Contour	Bizarre, "picket fence"	Irregular, nodular
○ Bowel spasm	Present	Absent
○ Presence of diverticula in remainder of colon	Usual	Occurs
○ Appearance of ends of deformity	Tapered or cone	Blunt, shelf, abrupt transition



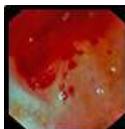
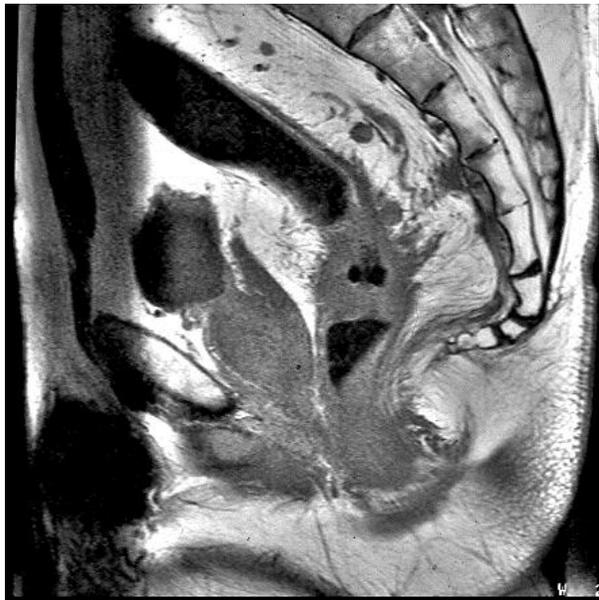


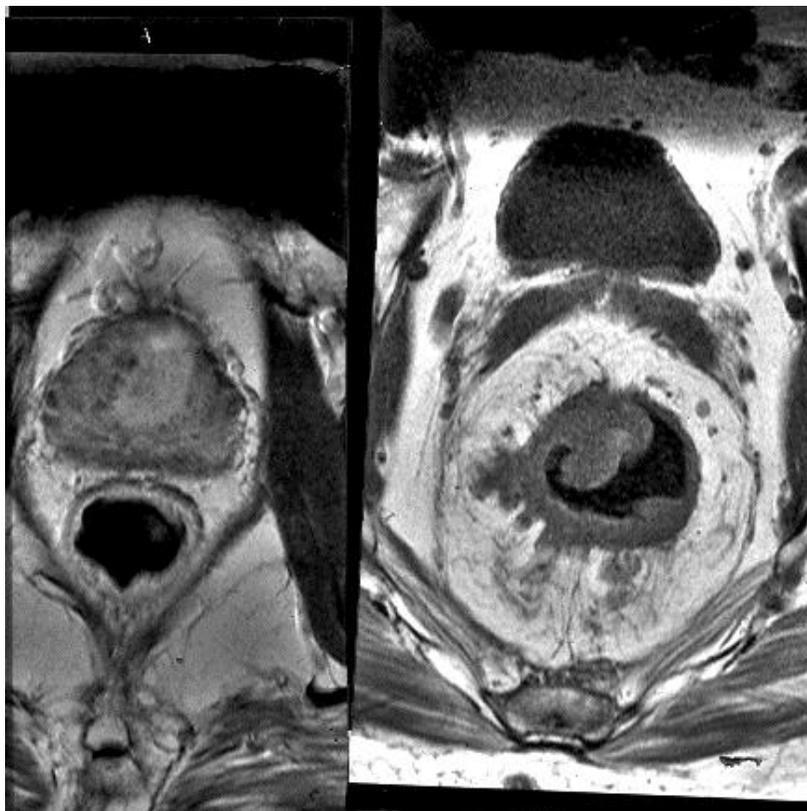




CT-Scan Staging in Rectal Malignancy

- | | |
|--|--------|
| ○ Overall tumor detection | 65–70% |
| ○ Perirectal fat infiltration | 50–60% |
| ○ Absent perirectal fat infiltration | ~80% |
| ○ Lymph node involvement | ~20% |
| ○ Absent lymph node involvement | ~100% |
| <hr/> | |
| ○ Overall staging accuracy of invasiveness | 35–95% |





T: Tumor

TX: primary tumor cannot be assessed

T0: no evidence of primary tumor

Tis: carcinoma in situ

T1: tumor invades submucosa

T2: tumor invades muscularis propria

T3: tumor invades through muscularis propria into subserosa or into non - peritonealized pericolic or perirectal tissues

T4: tumor perforates the visceral peritoneum or directly invades other organs or structures

N: Regional Lymph Nodes

The regional lymph nodes are the pericolic and perirectal and those located along the ileocolic, right colic, middle colic, left colic, inferior mesenteric and superior rectal (hemorrhoidal) arteries

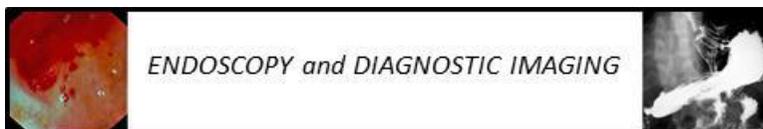
NX: regional lymph nodes cannot be assessed

N0: no regional lymph node metastasis

N1: metastasis in 1 to 3 pericolic or perirectal lymph nodes

N2: metastasis in 4 or more pericolic or perirectal lymph nodes

N3: metastasis in any lymph node along the course of a named vascular trunk



M distant Metastasis

MX: presence of distant metastasis cannot be assessed

M0: no evidence of distant metastasis

M1: distant metastasis

Pre-operative staging

I: T₁₋₂, N_x, M₀

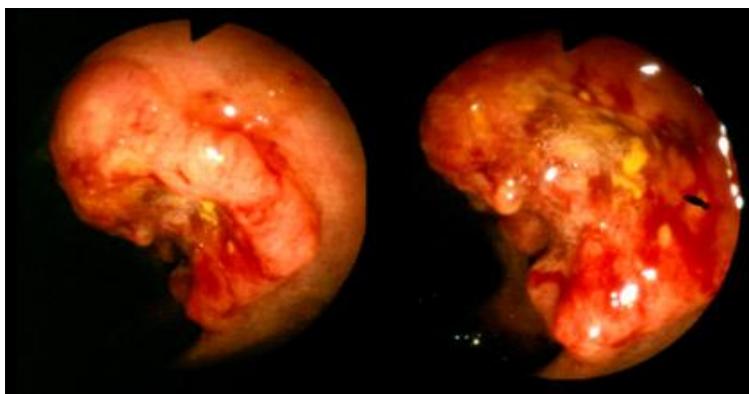
II: T₃, operable T₄, N_x, M₀

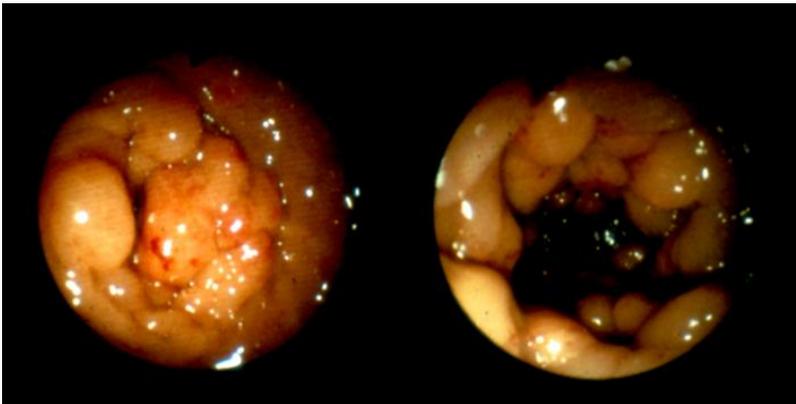
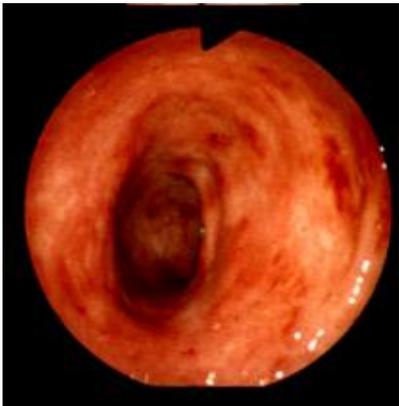
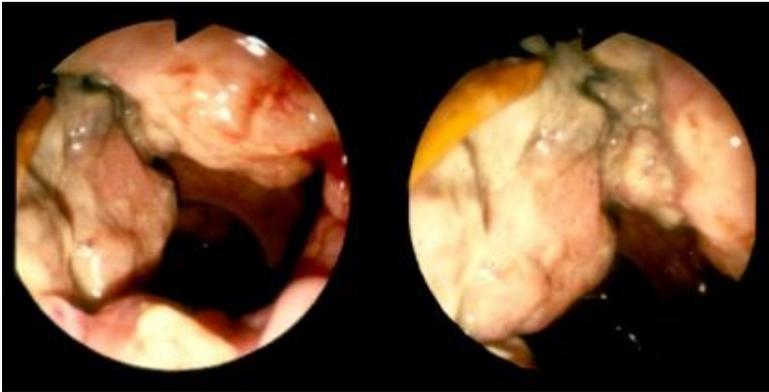
III: any T, N₁, M₀

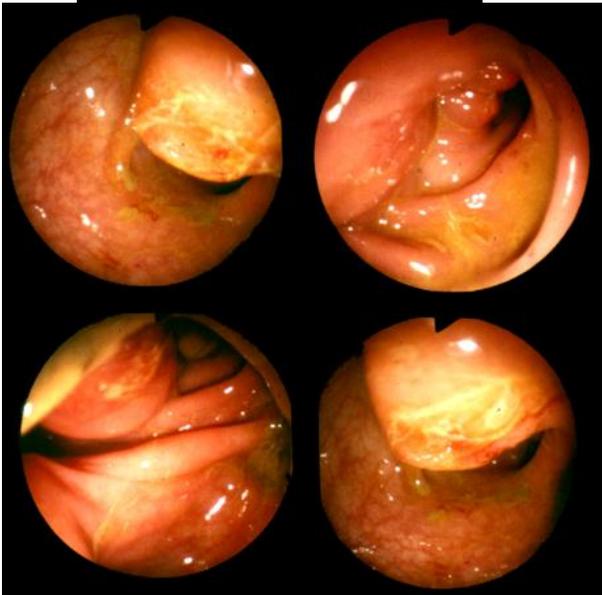
IV: any T, any N₁, M₁ or inoperable T₄, NX, M0

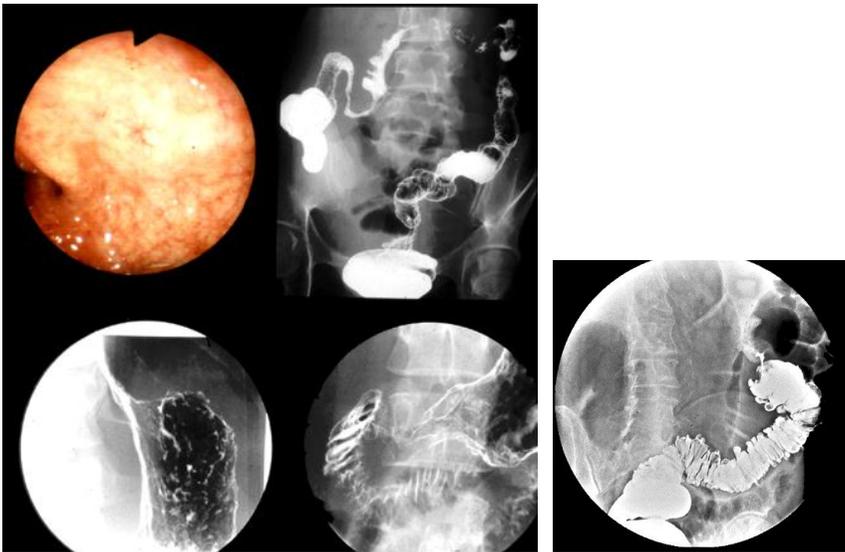
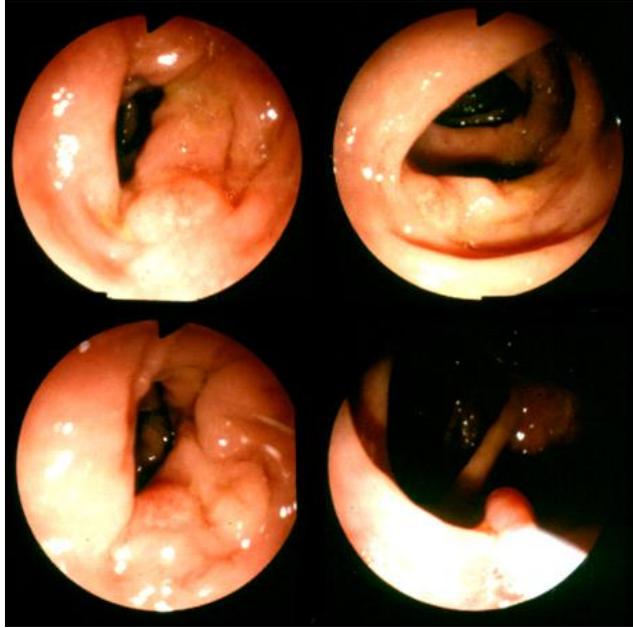
Stage	TN	M	5 – years overall survival
Stage I	T1, T2 N0	M0	80-95%
Stage IIA	T3 N0	M0	72-75%
Stage IIB	T4 N0	M0	65-66%
Stage IIIA	T1, T2 N1	M0	55-60%
Stage IIIB	T3, T4 N1	M0	35-42%
Stage IIIC	Any T N2	M0	25-27%
Stage IV	Any T Any N	M1	0-7%

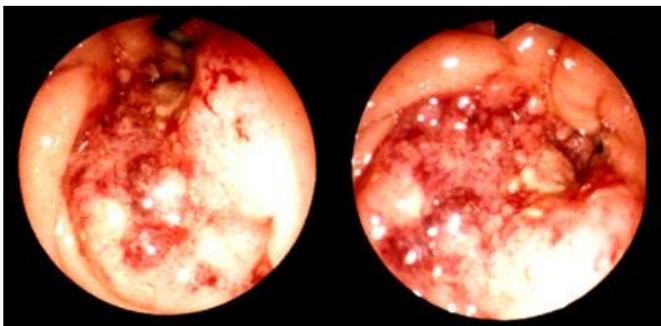
Tejpar, Sabine. *Best Practice & Research Clinical Gastroenterology* 2007; 21(6): pp. 1074.











Staging and survival of colorectal cancers

TMM classification (%)	Modified Duke's Classification	Survival
➤ Stage 0 – Carcinoma insitu	A	90 - 100
➤ Stage I – No nodal involvement, no metastases; tumor invades submucosa (T1, N0, M0); tumor invades		
➤ Stage II – No nodal involvement, no metastases; tumor invades into subserosa (T3, N0, M0); tumor invades other organs (T4, N0, M0)	B	75 - 85
➤ Stage III – Regional lymph nodes involved (any T, N1, M0)	C	30 - 40
➤ Stage IV – Distant metastases	D	< 5

Colonic Polyps & Cancer: Non Familial Forms

- Factors which must be taken into account when stratifying screening for colorectal cancer
 - Age >50 yrs
 - Family history - of polyps, CBC, Lynch/FAP associated tumours
 - High risk groups
 - IBD patients
 - African-Canadians
 - Smokers
 - Obesity (BMI>30, waist circumference>32-34")
 - The absolute risk of CRC (In a 55 year old patient whose:)
 - Father developed proven CRC at age 59
 - 50 year old brother had an adenomatous colonic polyp
 - Grandmother and an aunt of unknown age had CRC

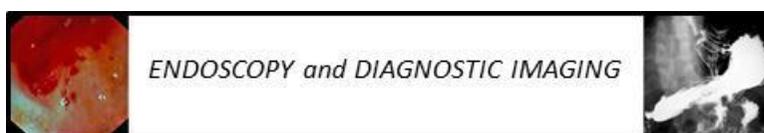
Familial Risk of Colorectal Neoplasia (CRC)

Familial Setting	RR	95% CI
○ One first-degree relative with CRC	2.25	2.00 – 2.53
○ < 45 yrs	3.87	2.40 – 6.22
○ 45 – 59 yrs	2.25	1.85 – 2.72
○ > 59 yrs	1.82	1.47 – 2.25
○ Two or more first-degree relatives with CRC	4.25	3.01 – 6.02
○ Only two first-degree relatives with CRC	3.76	2.56 – 5.51
○ One second – or third – degree relative with CRC	1.5	
○ Two second – degree relatives with CRC	2.3	
○ One first – degree relative with an adenoma < 60 yrs	1.99	1.55 – 2.55

RR, relative risk

RR = (2.25 × 1.99 × 2.3) = 10.3; Absolute risk for average risk person, 5%; absolute risk for this person, RR × AR = 10.3 × 5% = 51.5%!

Printed with permission: Winawer, Sidney J. *Best Practice & Research Clinical Gastroenterology* 2007; 21(6): PP.1035.



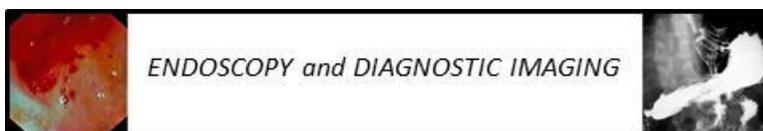
- The recommended follow-up interval for post-polypectomy colonoscopic surveillance

Finding on screening	Follow-up interval
○ 1-2 tubular adenomas < 1 cm	5-10 yrs
○ 3-10 adenomas, or any adenoma with villous elements, high-grade dysplasia or ≥ 1 cm in size	3 yrs
○ Patients with prior advanced adenomas after normal follow-up examination, or only 1-2 small tubular adenomas	< 3 yrs

Finding on screening	Follow-up interval
➤ 10 adenomas (possible familial syndrome)	
○ Large sessile adenoma removed piecemeal	2-6 months to confirm complete removal
○ Small distal hyperplastic polyps without adenomas (suspect hyperplastic polyposis syndrome)	10 yrs
○ Proximal colon hyperplastic polyps	Interval uncertain

Adapted from: Rex, Douglas K. *2008 ACG Annual Postgraduate course book*: pp. 90; and printed with permission: Levin B, Lieberman DA, McFarland B et al. *Gastroenterology* 2008;134(5): pg. 1588.

- Endoscopic techniques or technical improvements which enhance the colonoscopic sensitivity for CRC screenin
 - Improve performance skills of colonoscopist
 - Documented incubation of cecum > 9
 - Withdrawal time > 7
 - Personal detection rate of adenomatous polyps on screening colonoscopy of average risk persons > 50 years of age
 - Improve bowel cleansing
 - Improve insertion
 - Cap-fitted colonoscopy
 - Overtubes
 - Imaging
 - Wide-angle colonoscopy
 - Narrow-band imaging
 - Chromoendoscopy

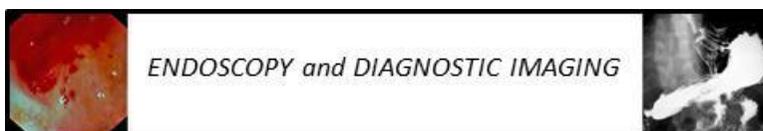


- Confocal laser microscopy
- Pharmacological or nutritional agents shown to be effective chemoprevention to reduce the risk of development of colorectal adenomas/CRCs
 - Drugs
 - ASA
 - Coxibs
 - 5-ASA in IBD
 - Hormone replacement therapy (HRT) in post menopausal women
 - Nutrients
 - Selenium
 - Calcium (+ vitamin D)
 - Non-western diet (low intake of saturated fats in red meat)
 - High intake of green leafy vegetables
 - Possibly folate, vitamins C, E, B-carotene
 - Probably not dietary fiber
 - Exercise

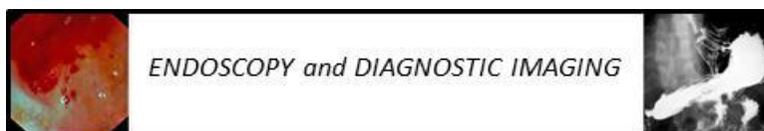
Adapted from: Arber N and Levin B. *Gastroenterology* 2008;134(4): 1224-1237; and Meyerhardt JA, Niedzwiecki D, Hollis D. *JAMA* 2007;298(7): 754-764.

- Guidelines for screening and surveillance for the Early Detection of Colorectal Adenomas and Cancer in Individuals at Increased Risk or High Risk

Risk category	Age to begin	Recommendation	Comment
Increased risk – patients with history of polyps at prior colonoscopy			
➤ Patients with small rectal hyperplastic polyps	-	○ Colonoscopy or other screening options at intervals recommended for average-risk individuals	○ An exception is patients with a hyperplastic polyposis syndrome. They are at increased risk for adenomas and colorectal cancer and need to be identified for more intensive



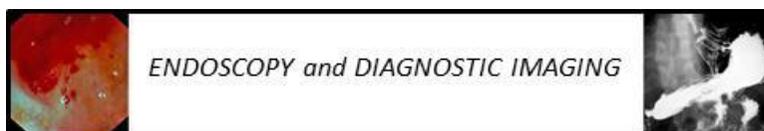
- | | | | |
|---|---|---------------|--|
| ➤ Patients with 1 or 2 small tubular adenomas with low-grade dysplasia | ○ 5 to 10 years after the initial polypectomy | ○ Colonoscopy | follow-up
○ The precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician) |
| ➤ Patients with 3 to 10 adenomas, or 1 adenoma > 1 cm, or any adenoma with villous features or high-grade dysplasia | ○ 3 years after the initial polypectomy | ○ Colonoscopy | ○ Adenomas must have been completely removed. If the follow-up colonoscopy is normal or shows only 1 or 2 small tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be 5 years. |
| ➤ Patients with > 10 adenomas on a single examination | ○ < 3 years after the initial polypectomy | ○ Colonoscopy | ○ Consider the possibility of an underlying familial syndrome. |
| ➤ Patients with sessile adenomas that are removed piecemeal | ○ 2 to 6 months to verify complete removal | ○ Colonoscopy | ○ Once complete removal has been established subsequent surveillance needs to be individualized based on the endoscopist's judgment. Completeness of |



removal should be based on both endoscopic and pathologic assessments.

- Guidelines for screening and surveillance for the Early Detection of Colorectal Adenomas and Cancer in Individuals at Increased Risk or High Risk (Cont'd)

Risk category	Age to begin	Recommendation	Comment
Increased risk – patients with colorectal cancer			
➤ Patients with colon and rectal cancer should undergo high-quality perioperative colonoscopy to ensure there is no synchronous CRC	○ 3 to 6 months after cancer resection, if no unresectable metastases are found during surgery; alternatively, colonoscopy 1 year after the resection, or 1 year following the performance of the colonoscopy that was performed to clear the colon of synchronous disease	○ Colonoscopy	○ In the case of nonobstructing tumors, this can be done by preoperative colonoscopy. In the case of obstructing colon cancers, CTC with intravenous contrast or DCBE can be used to detect synchronous neoplasms in the proximal colon.
➤ Patient undergoing curative resection for colon or rectal cancer		○ Colonoscopy	○ This colonoscopy at 1 year is in addition to the perioperative colonoscopy for synchronous tumors. If the examination performed at 1 year is normal, then the interval before the next



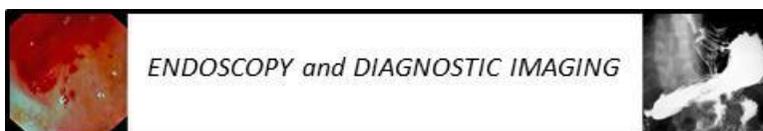
subsequent examination should be 3 years. If that colonoscopy is normal, then the interval before the next subsequent examination should be 5 years. Following the examination at 1 year, the intervals before subsequent examinations may be shortened if there is evidence of HNPCC or if adenoma findings warrant earlier colonoscopy. Periodic examination of the rectum for the purpose of

- Guidelines for screening and surveillance for the Early Detection of Colorectal Adenomas and Cancer in Individuals at Increased Risk or High Risk (Cont'd)

Risk category	Age to begin	Recommendation	Comment
---------------	--------------	----------------	---------

Increase risk- patients with a family history

- | | | | |
|---|--|---------------|-----------------|
| ➤ Either colorectal cancer or adenomatous polyps in a first-degree relative before age 60 years or in 2 or more first-degree relatives at any age | ○ Age 40 years, or 10 years before the youngest case in the immediate family | ○ Colonoscopy | ○ Every 5 years |
|---|--|---------------|-----------------|

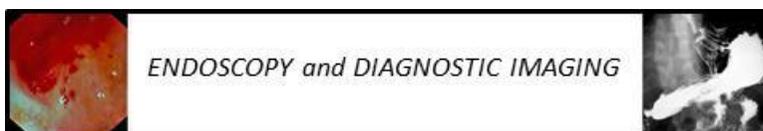


- Either colorectal cancer or adenomatous polyps in a first – degree relative age 60 or older or in 2 second – degree relatives with colorectal cancer
 - Age 40 years
 - Screening options at intervals recommended for average – risk individuals
 - Screening should be at an earlier age, but individuals may choose to be screened with any recommended form of testing

High risk

- Genetic diagnosis of FAP or suspected FAP without genetic testing evidence
 - Age 10 to 12 years
 - Annual FSIG to determine if the individual is expressing the genetic abnormality and counseling to consider genetic testing
 - If the genetic test is positive, colectomy should be considered

- Genetic or clinical diagnosis of INPCC or individual at increased risk of INPCC
 - Age 20 to 25 years, or 10 years before the youngest case in the immediate family
 - Colonoscopy every 1 to 2 years and counseling to consider genetic testing
 - Genetic testing for HNPCC should be offered to first-degree relatives of persons with a known inherited MMR gene mutation. It should also be offered when the family mutation is not already known, but 1 of the first 3 of the modified Bethesda criteria is present.

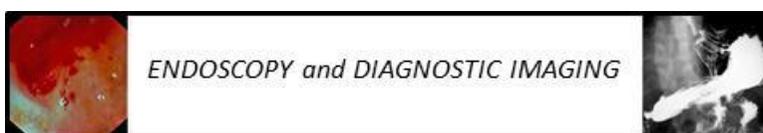


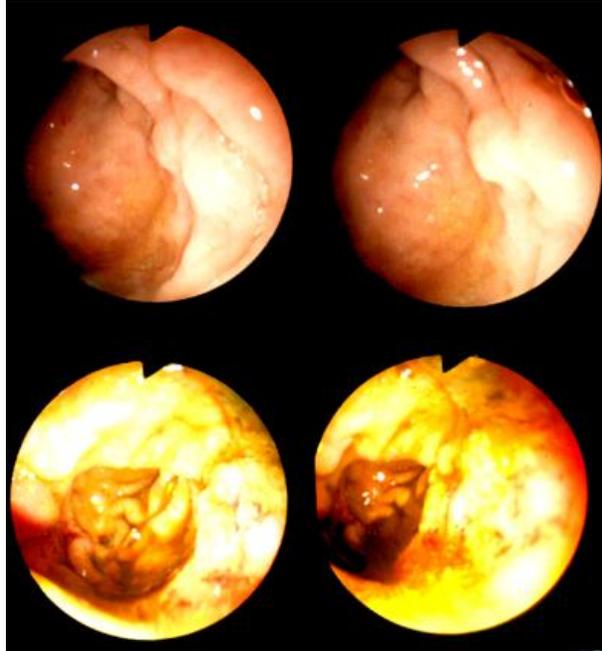
- Guidelines for screening and surveillance for the Early Detection of Colorectal Adenomas and Cancer in Individuals at Increased Risk or High Risk (Cont'd)

Risk category	Age to begin	Recommendation	Comment
➤ Inflammatory bowel disease, chronic ulcerative colitis and Crohn colitis	○ Cancer risk begins to be significant 8 years after the onset of pancolitis or 12 to 15 years after the onset of left-sided colitis (UC or CC)	○ Colonoscopy with biopsies for dysplasia	○ Every 1 to 2 years; these patients are best referred to a center with experience in the surveillance and management of inflammatory bowel disease

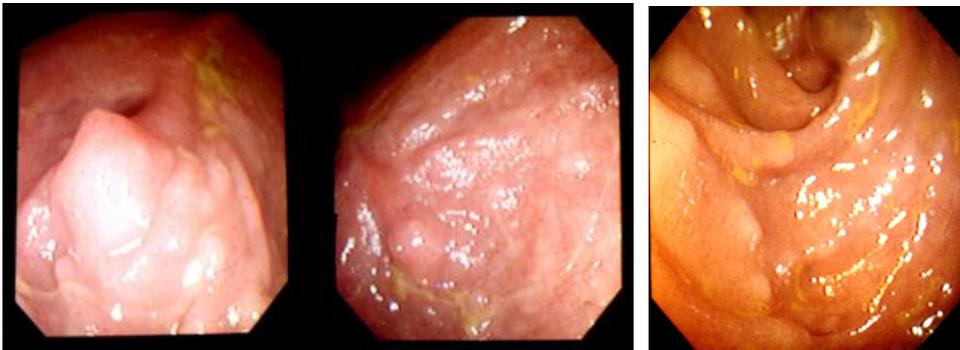
CRC, colorectal cancer; CTC, computed tomographic colography; DCBE, double-contrast barium enema; FAP, familial adenomatous polyposis; FSIG, flexible sigmoidoscopy; HNPCC, hereditary nonpolyposis colon cancer (Lynch syndrome); MR, mismatch repair; UC, ulcerative colitis; CC Crohn colitis

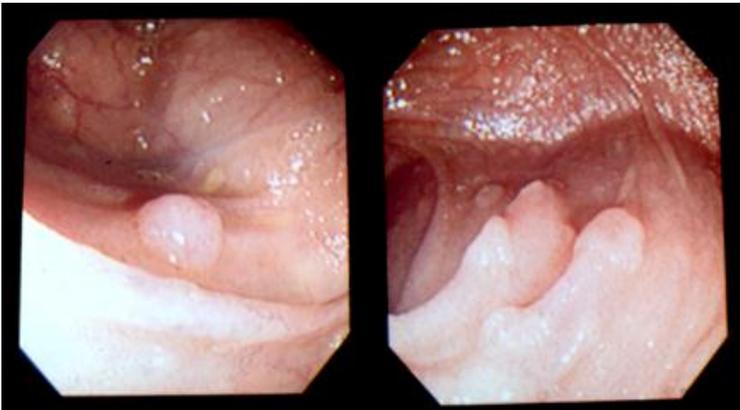
- FAP-Surveillance after ileorectal or ileal pouch anal anastomosis
 - Surveillance endoscopy at 4–6 months interval
 - Biopsy and destruction of all adenomatous lesions
 - Lower-power Nd-YAG laser or argon beam electrocoagulation to be preferred to prevent deep mural injury, responsible for excessive scarring and irregular nodular deformity





- FAP-Risk factors for cancer in rectal stump
 - Large number of rectal polyps at time of colectomy
 - The presence of large size rectal polyps
 - The presence of confluent 'carpet-like' adenomatous growth
 - Presence of colonic cancer at/or prior to colectomy
 - Lack of compliance with follow-up surveillance
 - Increasing chronological age





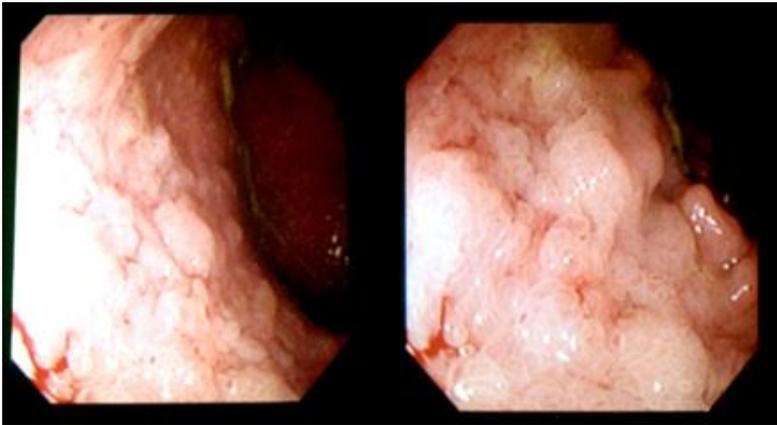
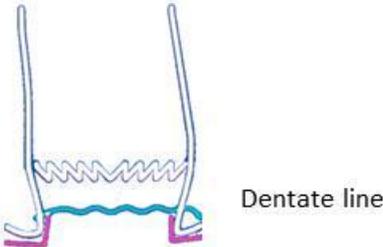
➤ Iliac pouch anal anastomosis

a. Handsewn technique



b. Double stapling technique

0-2.5 cm of rectal columnar epithelium is left behind



IBD-associated cancer

- Who is at risk?
 - Patients with entire colon involvement
 - Duration of colitis for over 8 years
 - Lesser risk with left-sided colitis
 - Risk not related to:
 - severity of initial attack
 - disease activity
 - age at onset

- What is the risk?

IBD Surveillance

- Low-grade dysplasia may be associated with cancer in 19% of cases
 - Low-grade dysplasia may progress to high-grade dysplasia or cancer in 35–50% of cases
- Colectomy instead of enhanced surveillance

- What are the unique features of Colorectal Cancer in Chronic UC?

- Cancer develops at younger age
- Cancer tends to be more advanced at diagnosis
- Cancer tends to be less differentiated
- Cancer tends to be more in the proximal colon
- Cancer is more frequently multiple

- Definition of dysplasia

- An unequivocally neoplastic proliferation
- Essentially equivalent to an adenoma
- Excludes all equivocal or regenerative lesions
- May be the superficial part of a carcinoma
- Often multifocal
- May occasionally be visible to endoscopist

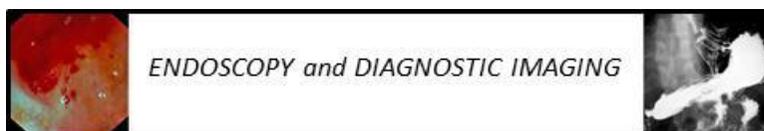
- Definition of IBD- Dysplasia/cancer surveillance (macroscopic classification)

- Flat dysplasia

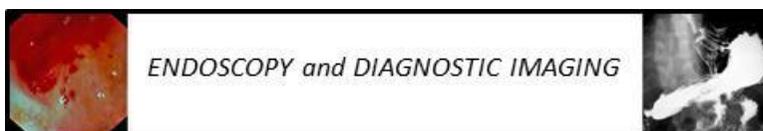
- Endoscopically undetectable
- Endoscopically visible suspicious alterations
 - Discoloration
 - velvety/villous appearance
 - irregular fine nodularity

- Raised dysplasia

- Discrete polypoid lesion or nodular mass



- Irregular plaque-like lesion/wart-like thickening
 - Conglomerate of polypoid lesions in a finite colonic segment
 - Direct special attention to any mass lesion (additional biopsies should be obtained)
 - Dysplasia associated with a lesion or mass (DALM) has a high incidence of cancer
- The problem of DALM (dysplasia-associated lesion or mass)
- Dalms are rather uncommon
 - Difficult/impossible to distinguish from 'ordinary' sessile adenoma
 - Occasionally difficult to distinguish from bizarre pseudopolyps
 - Occasionally difficult to distinguish from early cancer
 - Dalms may be of larger size, irregular shape, conspicuous discoloration and firmer consistency
 - May occur in uninvolved colon
 - May have same significance as (high grade) dysplasia?
 - Distinction between DALM and inflammatory pseudopolyp may be impossible
 - Pointers towards DALM
 - mass lesion over 1 cm in diameter
 - friable
 - firm consistency
 - different coloration than other pseudopolyps
 - surface irregularity
 - lack of exudate cap
 - No need to routinely biopsy pseudopolyps unless:
 - greater than 1 cm in diameter
 - friable
 - different coloration than other pseudopolyps
 - have surface irregularities
- Multiple biopsies of all strictures
- There is no proof that development of cancer can be averted
 - There is no firm proof that cancer mortality is decreased
 - Cancer may develop without the discovery of dysplasia
- The problem of the polypoid lesion
- corresponding to colitis-related raised dysplasia?
 - corresponding to sporadic non-colitis related adenoma?
 - Sporadic pedunculated or small sessile (>1 cm) adenomas, found during surveillance, not accompanied by mucosal dysplasia elsewhere in the colon are considered incidental and not colitis related. Endoscopic removal suffices



- Adenomatous polyps, especially large sessile (<1 cm) lesions, accompanied by dysplasia elsewhere are considered precancerous and colitis-related.
Colectomy is mandatory

Adenomas in IBD

1. No reason why they should not occur, but
2. May be impossible to distinguish from DALM
3. If i) completely excised, ii) adjacent mucosa is not dysplastic; and iii) patient is in adenoma age group (> 50 years), then lesions may be treated by local excision only but careful follow-up is required.

Practice Points: Other biomarkers in surveillance of IBD-associated dysplasia

- Flow cytometry for DNA aneuploidy
- Sucrase/isomaltase immunostaining
- Sialomucins
- Pectin binding
- Carcino embryonic antigen expression
- Endoscopic autofluorescence tissue spectroscopy
- Give the molecular mechanisms of steroid resistance
 - Abnormalities in absorption/metabolism (liver disease)
 - Altered number of GCS receptors or altered numbers of isoforms (α , β , δ)
 - Altered affinity of GCS for GCS receptors
 - Reduced affinity of the GCS receptor ligands to bind DNA
 - Altered expression of transcription factors (AP-1, NF-k B) and/or cytokines (IL-2, IL-4, p38 activated MAP kinase)
 - Genetic factors (primary steroid resistance, MDR-1 [P-glycoprotein 170], HLA class II allele DRB1*0103)

Adapted from: Farrell RJ, and Kelleher D. *J Endocrinol* 2003; 178(3): 339-46.

DIVERTICULAR DISEASE

Practice Pointers:

- Stages of diverticular disease.
 - Stage 0 Development of diverticular disease
 - Stage I Asymptomatic disease
 - Stage II Symptomatic disease
 - Single episode
 - Recurrent
 - Chronic (pain, diarrhea, IBD overlap/SCAD)



- Stage III Complicated
 - Abscess
 - Phlegmon
 - Obstruction
 - Fistulization
 - Bleeding
 - Sepsis
 - Stricture

Abbreviation: SCAD, segmented colitis associated with diverticulum

Printed with permission: Sheth AA, Longo W, and Floch MH. *AJG* 2008;103: pp 1551.

CT/clinical classification of diverticulitis (e.g. Hinchey, Buckley, and EAES).

➤ Hinchey classification (perforated diverticulitis)

CT findings

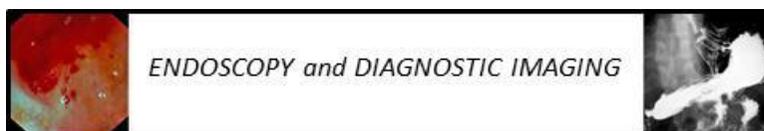
- Stage I – Pericolic abscess or phlegmon
- Stage II – Pelvic, intra-abdominal or retroperitoneal abscess
- Stage III
- Stage IV – Generalized purulent peritonitis
- Generalized fecal peritonitis

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➤ Buckley classification

CT findings

- Mild - Bowel wall thickening, fat stranding
- Moderate - Bowel wall thickening >3 mm, phlegmon or small abscess
- Severe - Bowel wall thickening > 5 mm, frank perforation with subdiaphragmatic free air, abscess > 5 cm



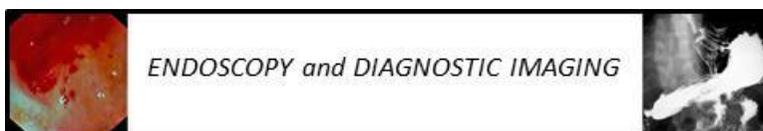
➤ EAES clinical classification

	Clinical description	Recommended diagnostic testing
➤ Grade I ○ Symptomatic, uncomplicated disease	- Fever, crampy abdominal pain	Colonoscopy vs barium enema to rule out malignancy, colitis
➤ Grade II ○ Recurrent, symptomatic disease	- Recurrence of above	CT scan vs barium enema
➤ Grade III ○ Complicated disease	- Abscess - Hemorrhage - Stricture - Fistula - Phlegmon - Purulent and fecal peritonitis - Perforation - Obstruction	CT scan

Abbreviation: EAES, European Association for Endoscopic Surgeons

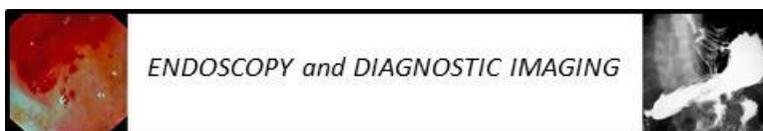
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- Give the differential diagnosis of acute diverticulitis
 - Acute appendicitis - Suspect if RLQ symptoms or non-resolution with medical therapy
 - Crohn disease - Suspect if aphthous ulcers, perianal involvement, or chronic diarrhea
 - Colonic carcinoma - Suspect if weight loss, bleeding. Diagnose with colonic evaluation after acute inflammation resolved
 - Ischemic colitis - Suspect if high-risk patient, bloody diarrhea, or thumbprinting.
 - Pseudomembranous colitis - Suspect with antibiotic use or diarrhea.
- Diagnose with stool toxin



- Complicated ulcer - Suspect if pneumoperitoneum or peritonitis, or with clinical disease history, NSAID use, or dyspepsia
 - Ovarian cyst - Suspect in female patient with unilateral abdominal pain.
 - Abscess, torsion - Diagnose with pelvic or transvaginal ultrasound
 - Ectopic pregnancy - Suspect in female patient of childbearing age.
- Diagnose with pregnancy test and ultrasound
- Give the complications of diverticular disease – Diagnosis and management

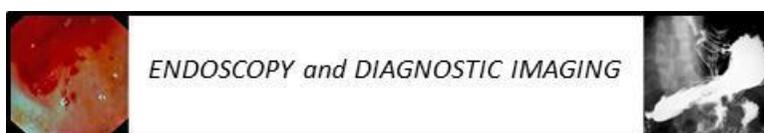
Complication	Symptoms	Findings	Treatment
➤ Diverticulitis	Pain, fever, constipation, diarrhea or both	Palpable tender colon, leukocytosis	Liquid diet, with or without antibiotics or elective surgery
➤ Pericolic abscess	Pain, fever, with or without tenderness or pus in stools	Tender mass, guarding, leukocytosis, soft tissue mass on abdominal films or ultrasound	Nothing by mouth intravenous fluids, antibiotics, early surgery with colostomy
➤ Fistula	Depends on site: dysuria, pneumaturia, fecal discharge	Depends on site: fistulogram, methylene blue	Antibiotics, clear liquids, colostomy and later resection
➤ Perforation	Sudden, severe pain; fever	Septic patient; leukocytosis, free air	Antibiotics; nothing by mouth, venous fluids, immediate surgery
➤ Liver abscess	Right upper quadrant pain, fever, weight loss	Tender liver, tender bowel, or mass, leukocytosis, alkaline phosphatase, lumbosacral scan (filling defect)	Antibiotics, surgical drainage, surgery for bowel disease
➤ Bleeding	Bright red blood, or maroon clots	Blood on rectal exam, sigmoidoscopy, colonoscopy, angiography	Conservative; blood transfusion if needed, with or without surgery

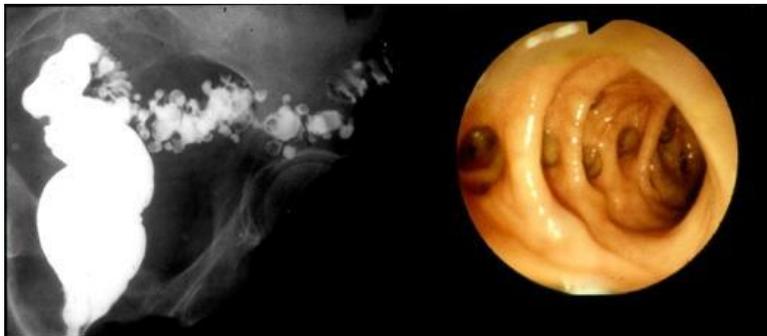


Practice Pointers: Radiologic differentiation between colonic cancer and diverticulitis

	Diverticulitis	Cancer
○ Segment length	Long	Short
○ Mucosa	Intact	Destroyed
○ Contour	Bizarre, "picket fence"	Irregular, Nodular
○ Bowel spasm	Present	Absent
○ Presence of diverticula in remainder of colon	Usual	Occurs
○ Appearance of ends	Tapered or cone	Blunt, shelf, abrupt transition

- Contrasting radiologic features of diverticulitis and Crohn Disease involving the descending and sigmoid colon
- Diverticulitis
 - Short process 3–6 cm in length
 - Diverticula sharply defined & frequently contain fecaliths, but may on occasion simulate abscesses.
 - When a diverticulum perforates, the abscess creates an extramural defect or an arcuate configuration of folds that stretch over the abscess
 - No transverse fissures; folds may be straightened but more commonly have an arcuate configuration
 - A short paracolic tract may be seen occasionally in diverticulitis (usually associated with an extramural defect); on rare occasions a perforation may run parallel to the bowel wall
- Crohn Colitis
 - Long – usually 10 cm or longer
 - Abscesses frequently have a triangular configuration, but may at times be undistinguishable from the coexistent diverticula
 - This is an ulcerating mucosal process; folds are straightened, perpendicular, picket-fence-like & associated with a thick wall & secretions
 - Transverse fissures with marked edema of mucosa produce a step-ladder configuration
 - If a tract is seen, it is long, linear & located in the submucosa or muscular layers





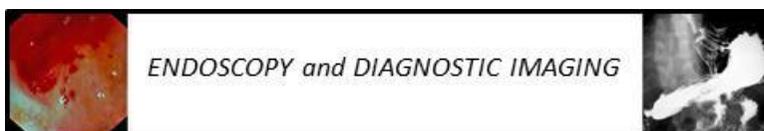
- Prevalence by age:
 - age 40 5%
 - age 60 30%
 - age 85 65%

- Prevalence by gender
 - age <50 males more common
 - age 50–70 slight female increase
 - age >70 females more common

- Diverticular disease in the young (<40 years)
 - 2–5% of diverticular disease <40 years
 - Occurs more in males
 - Obesity is major risk factor
 - Location of diverticula usually in sigmoid and descending colon
 - Surgery necessary in 50% of patients

- Stages of diverticular disease
 - Stage 0 Development of diverticular disease
 - Stage I Asymptomatic disease
 - Stage II Symptomatic disease
 - a. Single episode
 - b. Recurrent
 - c. Chronic (pain, diarrhea, IBD overlap/ SCAD)
 - Stage III Complicated
 - Abscess
 - Phlegmon
 - Obstruction
 - Fistulization
 - Bleeding
 - Sepsis
 - Stricture

Adapted from: Sheth, Anish A., Longo, Walter and Floch, Martin H. *AJG* 2008;103: pp 1551



Diagnostic imaging

- Diverticulitis: complicated diverticular disease
 - CT scanning
 - Presence of diverticulae
 - Thickened colonic wall
 - Stranding of soft tissue (from perforation and extravasation of contrast into pericolonic tissues)
 - Intramural sinus tract
 - Mass / abscess in colonic wall or mesentery
 - Giant sigmoid diverticulum, which develops from enlargement of sinus tract from lumen of diverticulum to the cavity of an abscess
 - Barium studies
 - Presence of diverticulae
 - Thickened colonic wall
 - Mass
 - Overlying mucosa is normal
 - Narrowing of lumen
 - Abscess
 - Penetration / local perforation / walled off abscess (mass effect)
 - Extravasation of barium into the abscess
 - Intramural collection of barium which communicates with colonic lumen (“tracking” of barium)
 - Gas-filled cavity
- Appendicitis
 - Barium studies
 - Filling defect at base of the cecum
 - Non-filling of the appendix (fecolith)
 - Folds
 - Thick
 - Tethered
 - Appendicolith
 - Laminated
 - Calcific densities
 - Sonography (ultrasound)
 - Distention (≥ 6 mm diameter)
 - Fluid-filled appendix
 - Thickened wall (> 2 mm)
 - Appendicolith
 - CT scan
 - Mass
 - Thick wall



- Wall enhancement
 - Distention of appendix (by fluid)
 - Fluid in appendix (stranding attenuation)
 - Soft tissue stranding (fluid in surrounding fat) [periappendical]
 - Appendicolith
 - Periappendiceal fluid (abscess)
 - Types of appendical abscesses
 - Phlegmon
 - Abscess
 - Multicompartmentalized abscess
- Limitations of abdominal sonography
- ↑ abdominal
 - Fat
 - Gas
 - Tenderness

CT and Clinical Classification of Diverticulitis

a) Hinchey classification (perforated diverticulitis)

CT findings

-
- | | |
|-------------|--|
| ○ Stage I | - Pericolic abscess or phlegmon |
| ○ Stage II | - Pelvic, intra-abdominal or retroperitoneal abscess |
| ○ Stage III | - Generalized purulent peritonitis |
| ○ Stage IV | - Generalized fecal peritonitis |

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b) Buckley classification

CT finding

-
- | | |
|------------|--|
| ○ Mild | - Bowel wall thickening, fat stranding |
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| ○ Severe | - Bowel wall thickening > 5 mm, frank perforation with subdiaphragmatic free air, abscess > 5 cm |



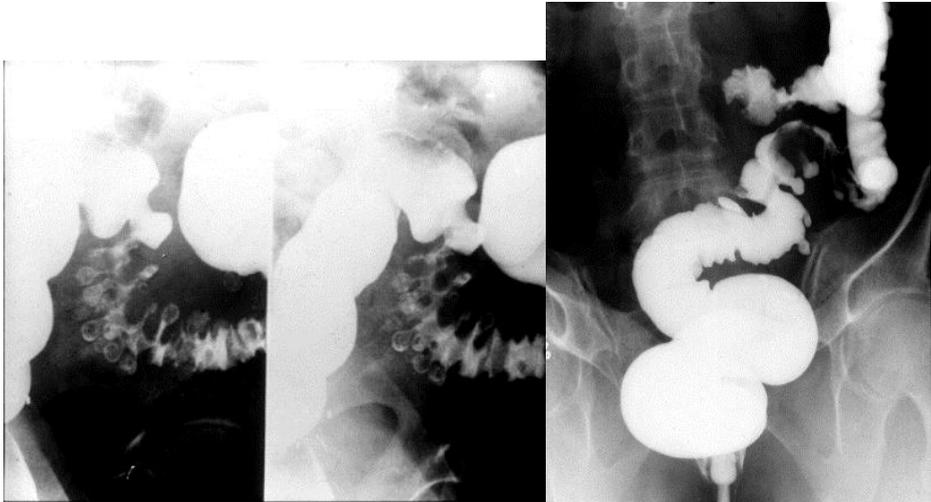
c) EAES clinical classification

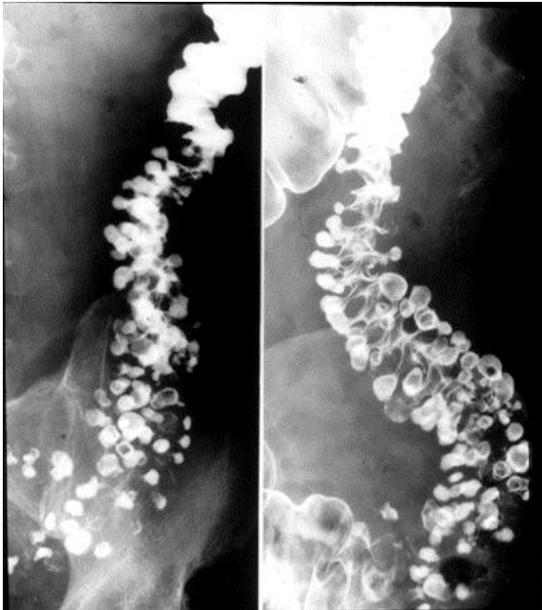
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➤ Grade II <ul style="list-style-type: none"> ○ Recurrent, symptomatic disease 	- Recurrence of above	CT scan vs barium enema
➤ Grade III <ul style="list-style-type: none"> ○ Complicated disease 	- Abscess - Hemorrhage - Stricture - Fistula - Phlegmon - Purulent and fecal peritonitis - Perforation - Obstruction	CT scan

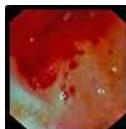
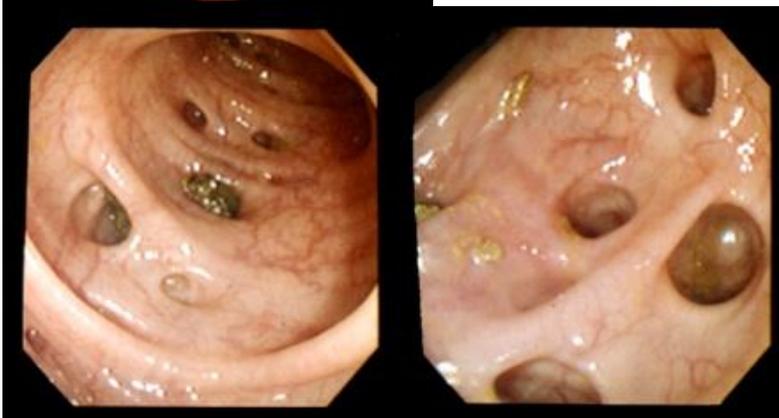
EAES, European Association for Endoscopic Surgeons

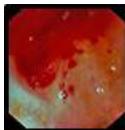
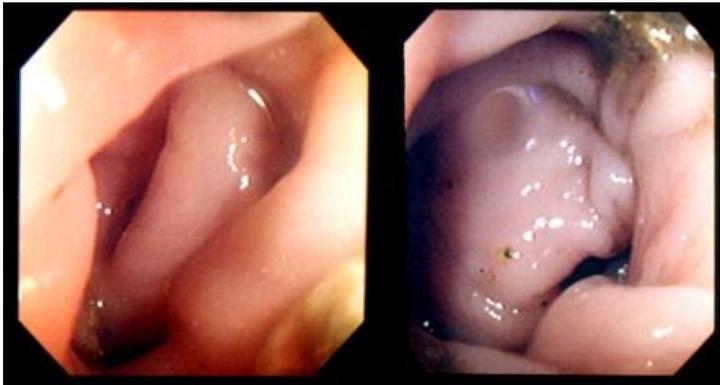
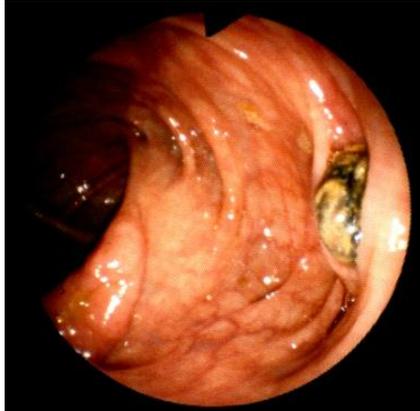
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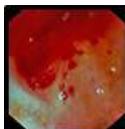
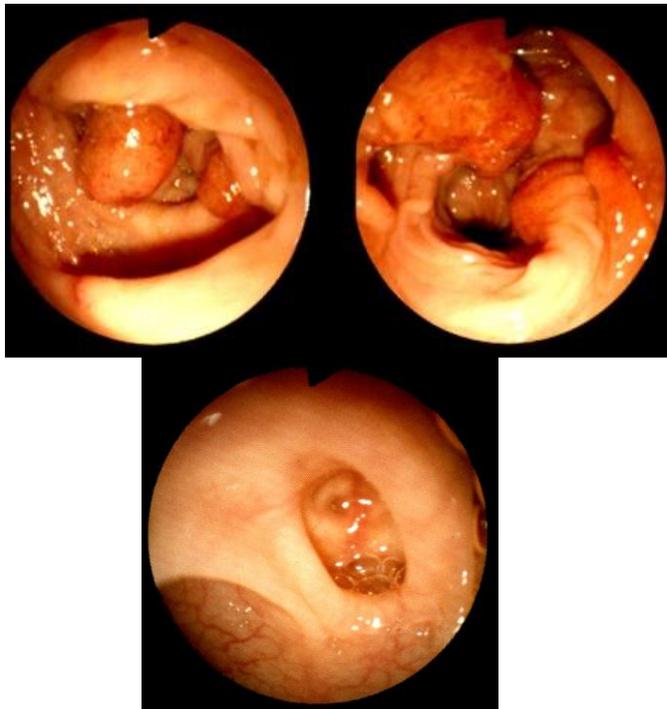
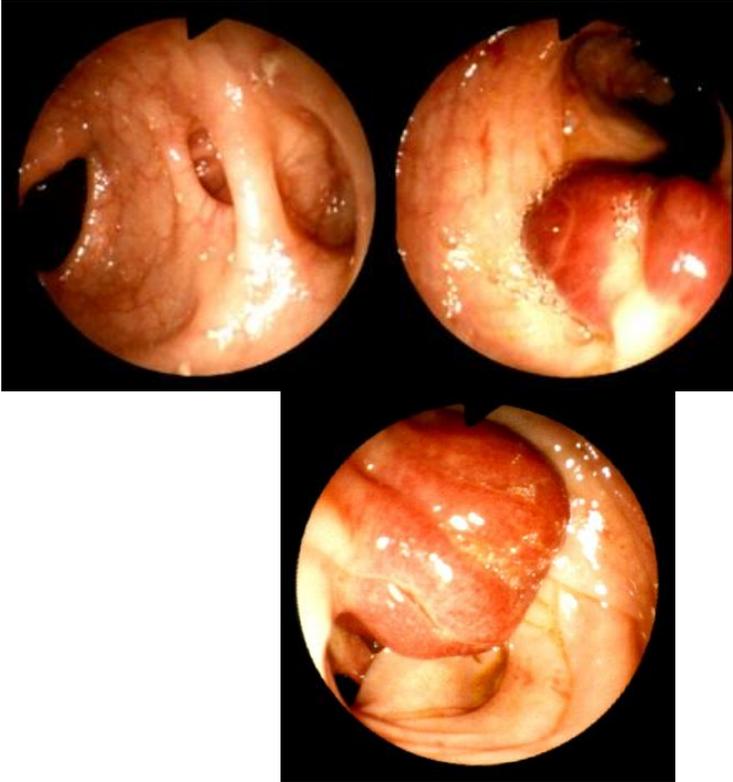


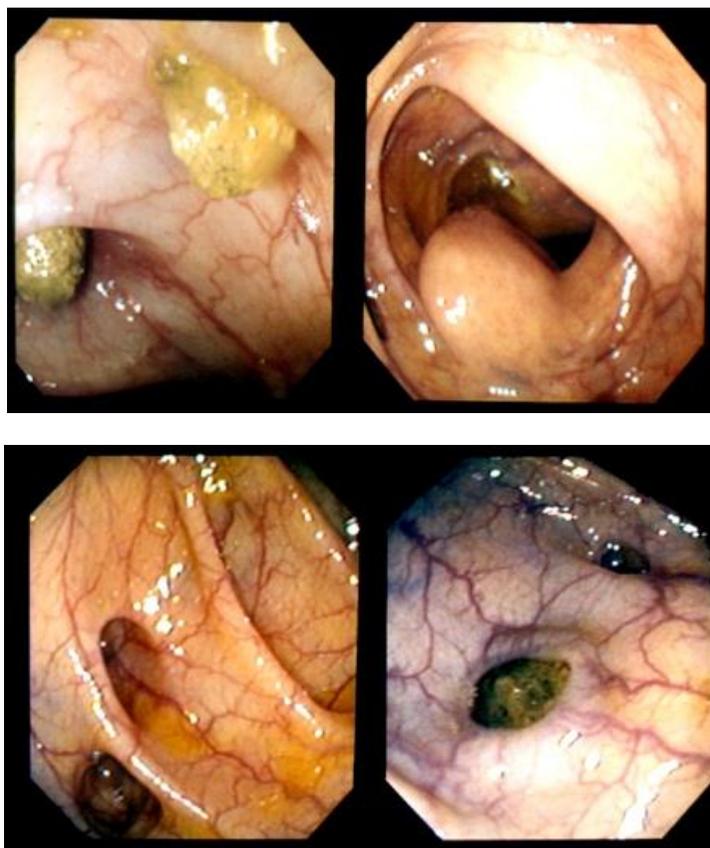






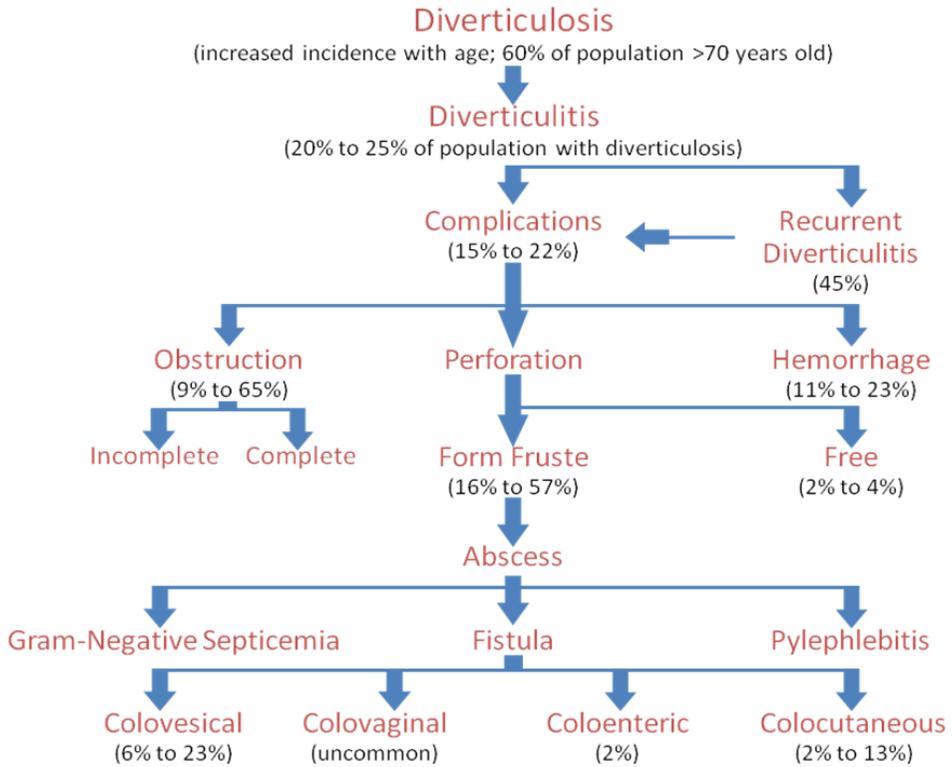




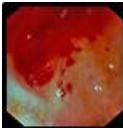
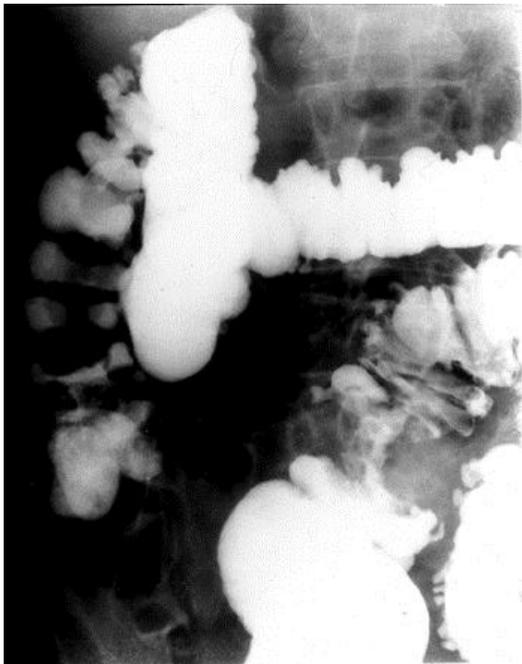


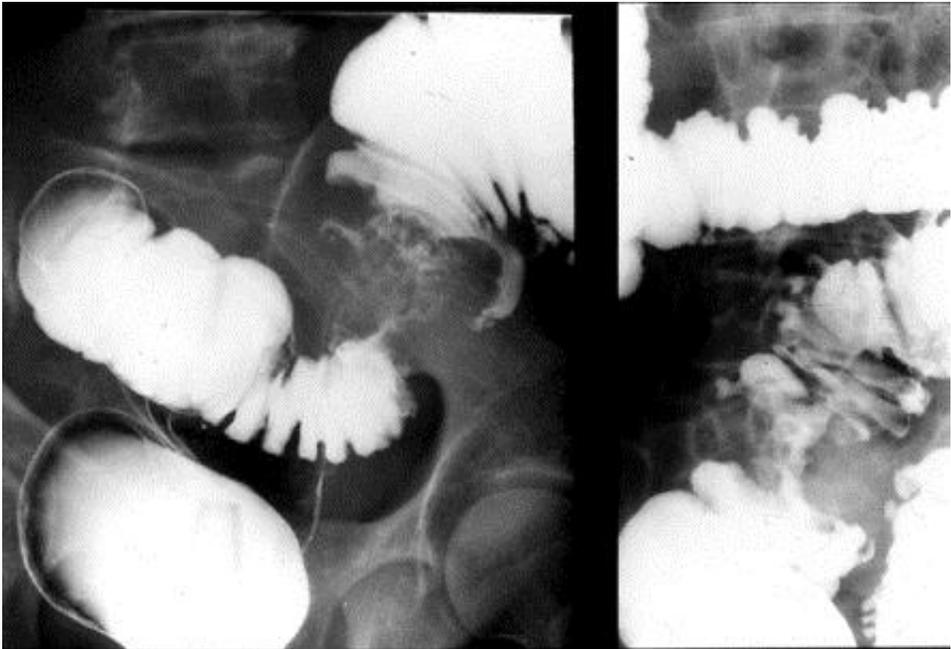
Diverticular Bleeding

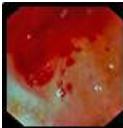
- Asymmetric rupture of vas rectum (vessel draped over diverticulum) towards lumen of diverticulum at its dome on antimesenteric margin. Injurious factors within the colonic lumen produce asymmetric damage to the luminal aspect of the underlying vas rectum resulting in segmental weakness of the artery and predisposition to rupture into the lumen. Rupture is associated with eccentric thickening of intima of vessels with thinning of media near the bleeding point. There is absence of inflammation (diverticulitis)
- The right colon is the source of bleeding in 49–90% of patients (?)
- The source is not identified in 30–40% of cases. Bleeding is usually abrupt, painless and in large volume (33% are massive). Bleeding stops spontaneously in 70–80% of cases
- In those with bleeding, 30% go on to have a 2nd bleed and of those, 50% will have a 3rd bleed

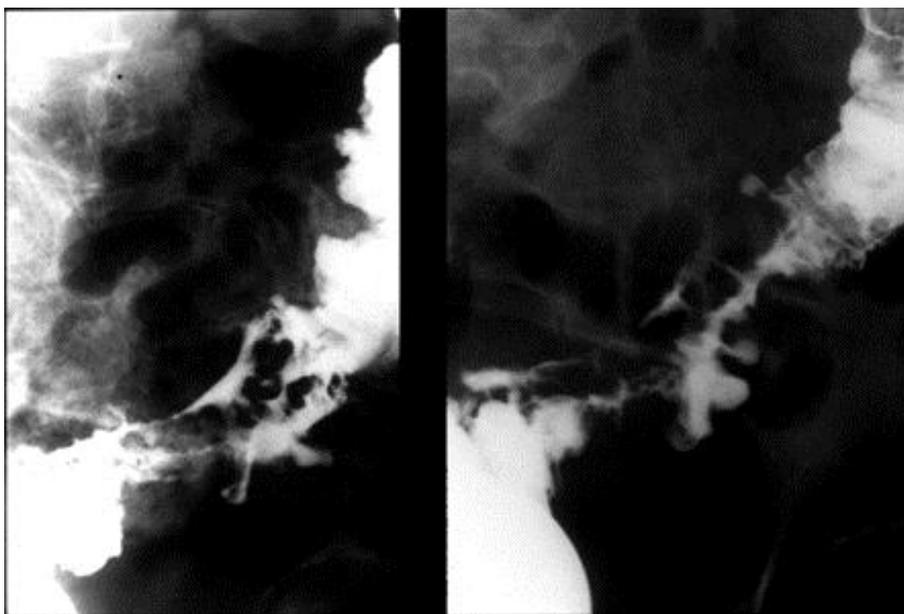






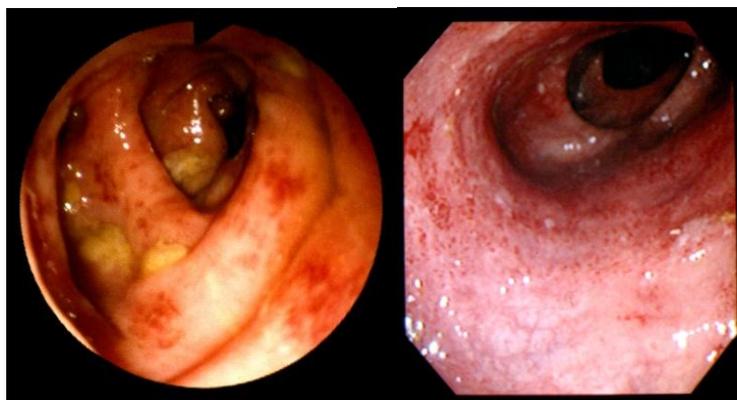


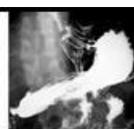
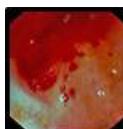
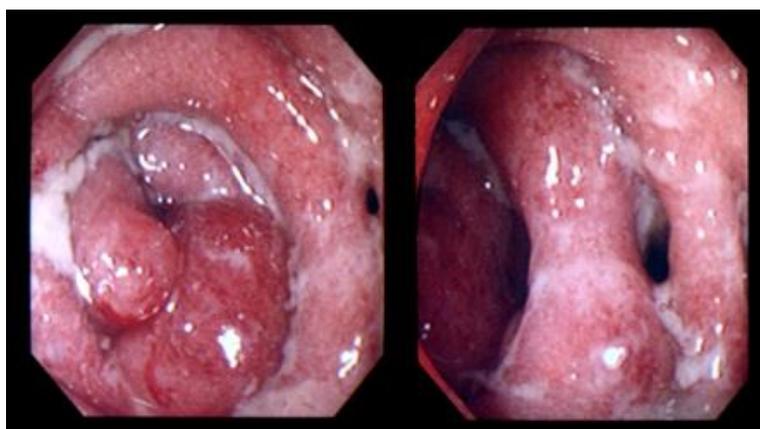
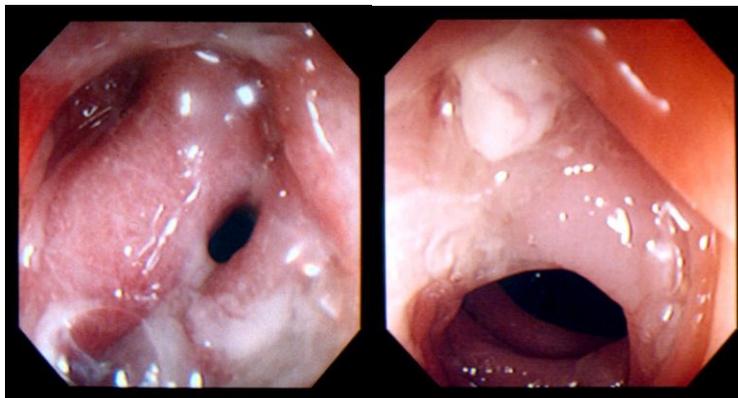


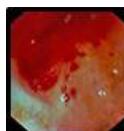
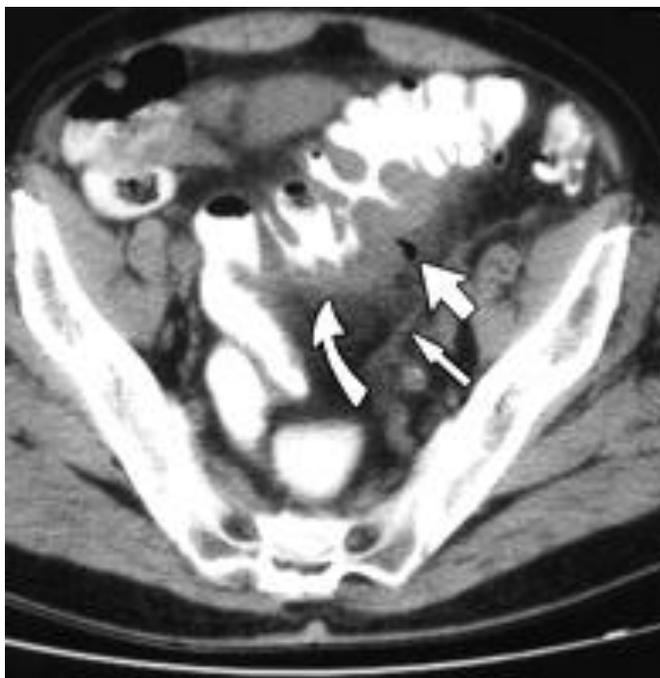


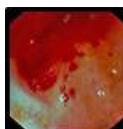
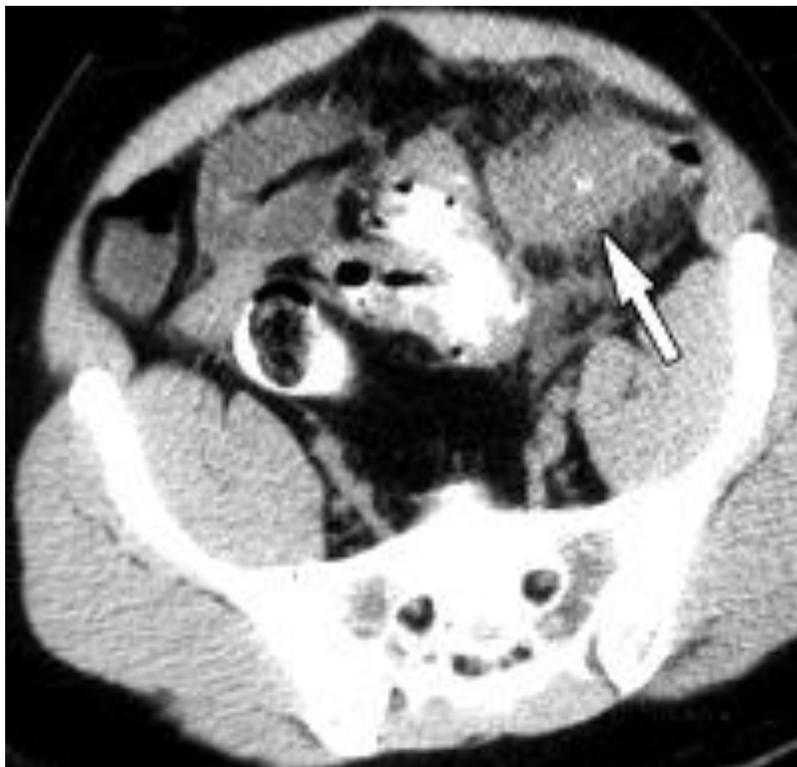
➤ Contrasting radiologic features of diverticulitis and Crohn Disease involving the descending and sigmoid colon

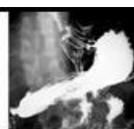
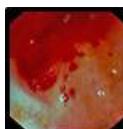
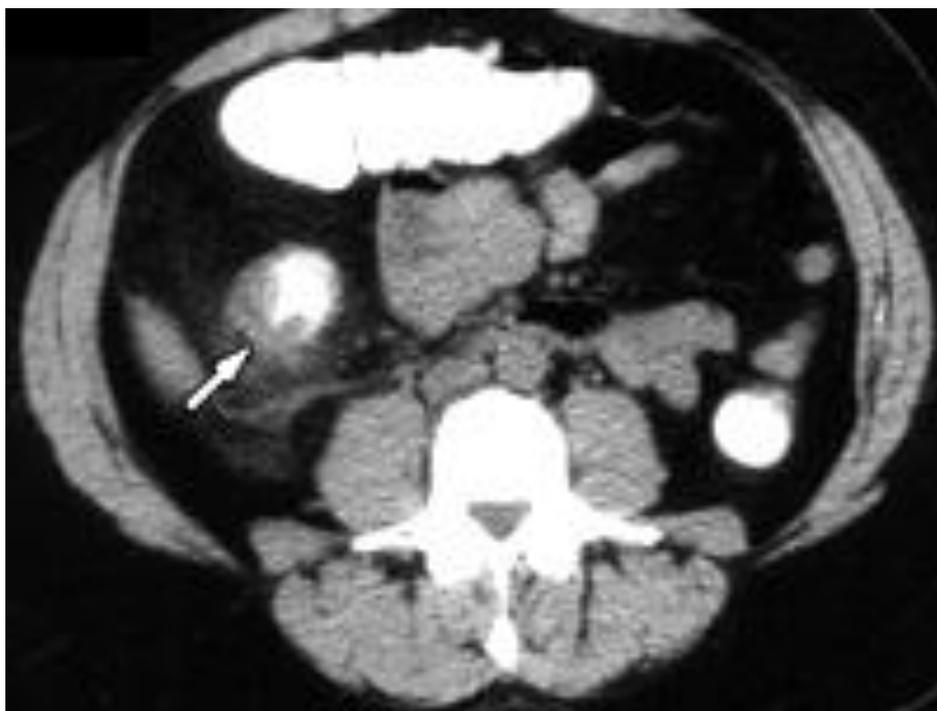
Diverticulitis	Crohn Colitis
<ul style="list-style-type: none"> ○ Short process 3–6 cm in length ○ Diverticula sharply defined & frequently contain fecaliths, but may on occasion simulate abscesses ○ When a diverticulum perforates, the abscess creates an extramural defect or an arcuate configuration of folds that stretch over the abscess ○ No transverse fissures; folds may be straightened but more commonly have an arcuate configuration ○ A short paracolic tract may be seen occasionally in diverticulitis (usually associated with an extramural defect); on rare occasions a perforation may run parallel to the bowel wall 	<ul style="list-style-type: none"> ○ Long – usually 10 cm or longer ○ Abscesses frequently have a triangular configuration, but may at times be undistinguishable from the coexistent diverticula ○ This is an ulcerating mucosal process; folds are straightened, perpendicular, picket-fence-like & associated with a thick wall & secretions ○ Transverse fissures with marked edema of mucosa produce a step-ladder configuration ○ If a tract is seen, it is long, linear & located in the submucosa or muscular layers

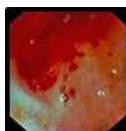






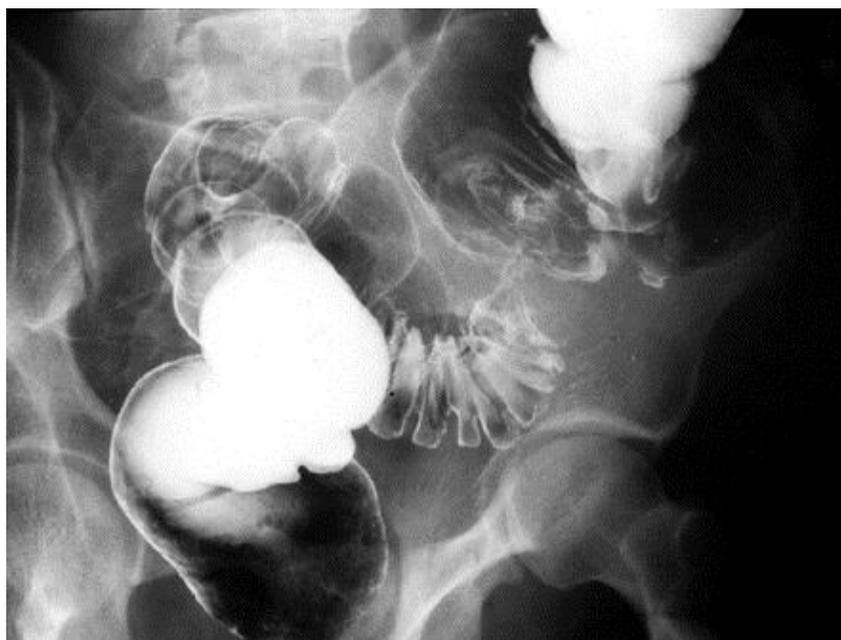


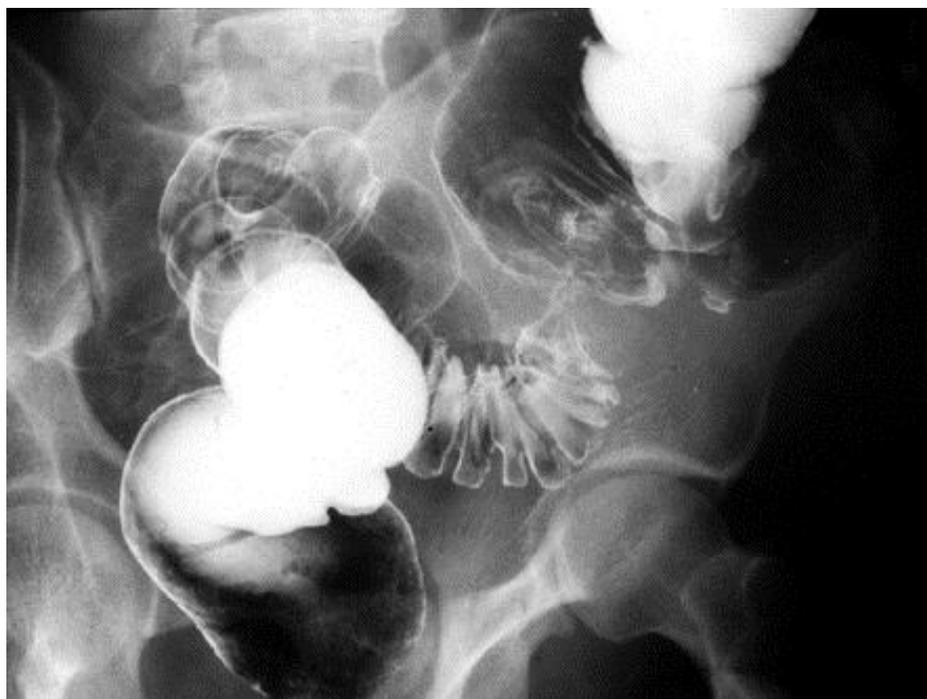
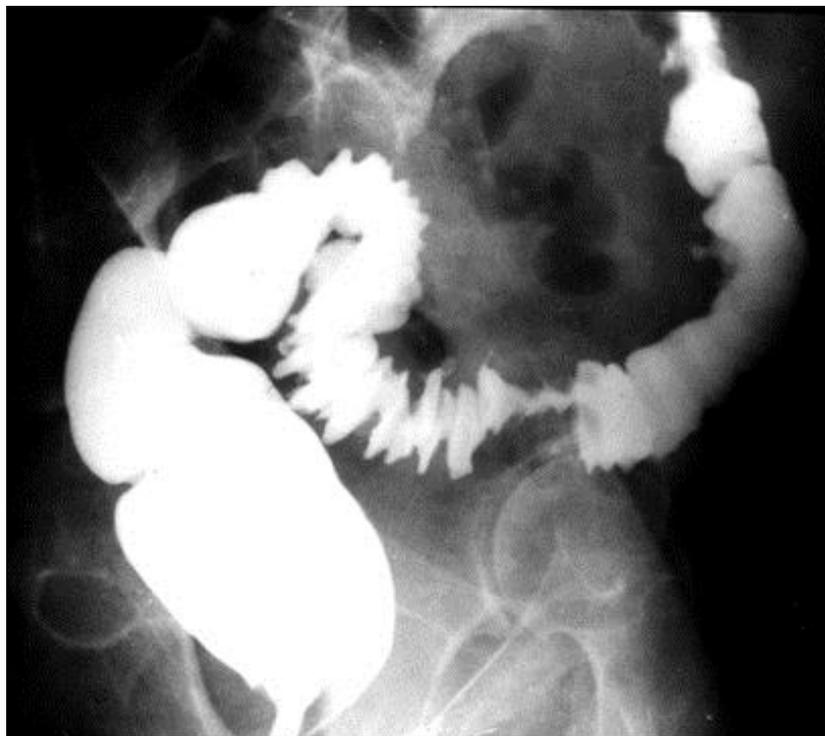


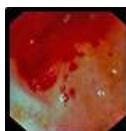
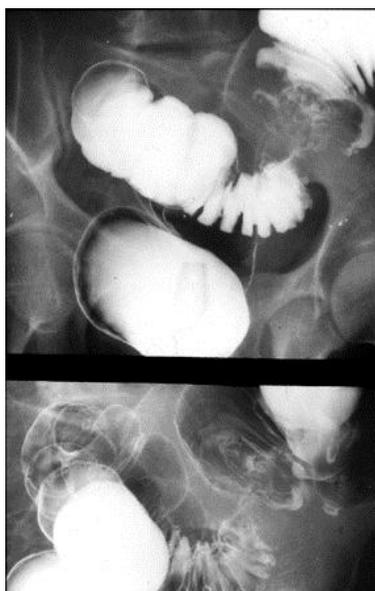
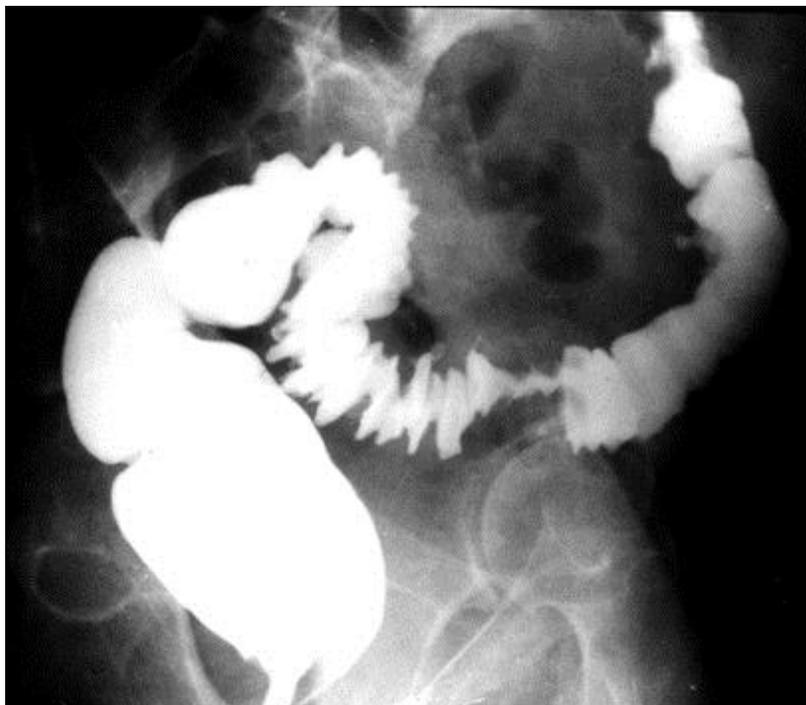


➤ Differential diagnosis of acute diverticulitis

- Acute appendicitis - Suspect if RLQ symptoms or non-resolution with medical therapy
- Crohn disease - Suspect if aphthous ulcers, perianal, or chronic diarrhea involvement
- Colonic carcinoma - Suspect if weight loss, bleeding. Diagnose with colonic evaluation **after** acute inflammation resolved
- Ischemic colitis - Suspect if high-risk patient, bloody diarrhea, or thumbprinting
- Pseudo-membranous colitis - Suspect with antibiotic use or diarrhea. - Diagnose with stool toxin
- Complicated ulcer - Suspect if pneumoperitoneum or peritonitis, or with clinical history, NSAID use, or dyspepsia disease
- Ovarian cyst, abscess, - Suspect in female patient with unilateral pain. - Diagnose with pelvic or transvaginal ultrasound torsion
- Ectopic pregnancy - Suspect in female patient of childbearing age - Diagnose with pregnancy test and ultrasound



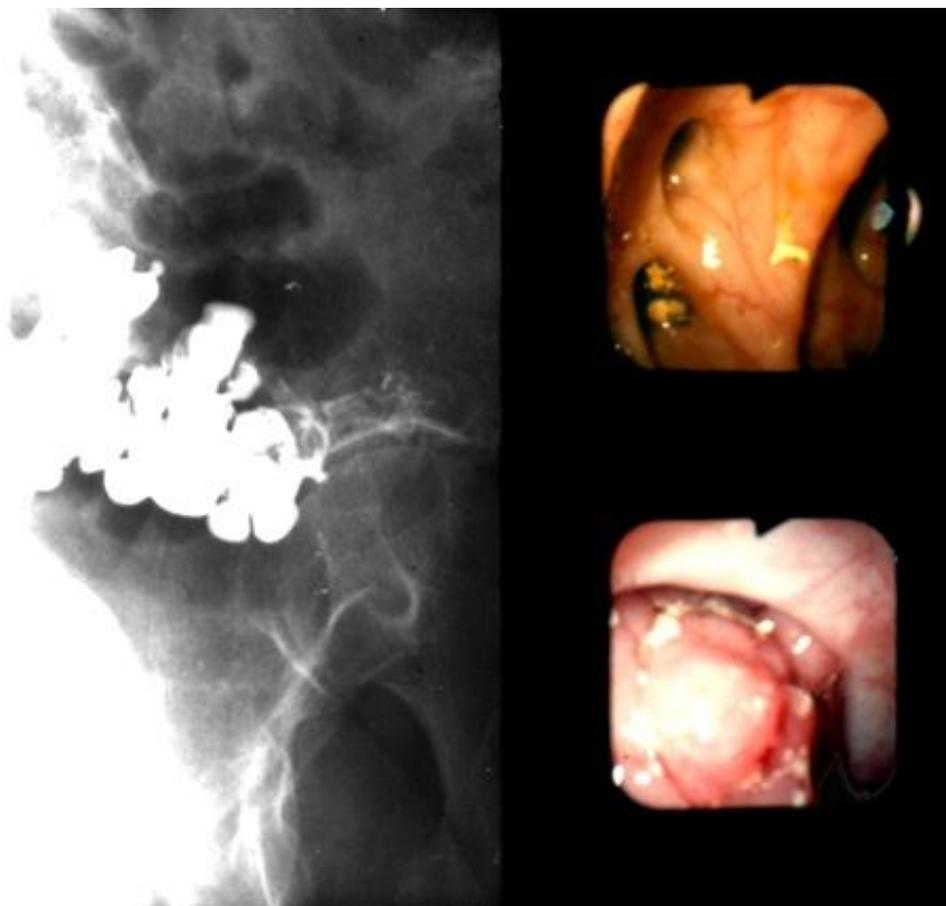






➤ Radiologic differentiation between colonic cancer and diverticulitis

	Diverticulitis	Cancer
○ Segment length	long	Short
○ Mucosa	Intact	Destroyed
○ Contour	Bizarre, "picket fence"	Irregular, nodular
○ Bowel spasm	Present	Absent
○ Presence of diverticula in remain of colon	Usual	Occurs
○ Appearance of ends	Tapered or cone	Blunt, shelf, abrupt transition



- Complications of diverticular disease – diagnosis and management

Complication	Symptoms	Findings	Treatment
➤ Diverticulitis	○ Pain, fever, constipation diarrhea or both	- Palpable tender colon, leukocytosis	▪ Liquid diet, with or without antibiotics or elective surgery
➤ Pericolic abscess	○ Pain, fever, with or without tenderness or pus in stools	- Tender mass, guarding, leukocytosis, soft tissue mass on abdominal films or ultrasound	▪ Nothing by mouth intravenous fluids, antibiotics, early surgery with colostomy

- **Fistula**
 - Depends on site: dysuria, pneumaturia, fecal discharge
 - Depends on site: fistulogram methylene blue
 - Antibiotics, clear liquids, colostomy and later resection

- **Perforation**
 - Sudden, severe pain; fever
 - Septic patient; leukocytosis; free air
 - Antibiotics; nothing by mouth venous fluids, immediate surgery

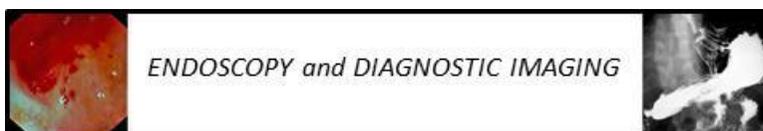
- **Liver abscess**
 - Right upper quadrant pain; fever, weight loss
 - Tender liver, tender bowel or mass, leukocytosis, alkaline phosphatase, lumbosacral scan (filling defect)
 - Antibiotics; surgical drainage, surgery for bowel disease

- **Bleeding**
 - Bright red blood, or maroon or clots
 - Blood on rectal exam, sigmoidoscopy, colonoscopy angiography
 - Conservative; blood transfusion if needed, with or without surgery

- Diverticular Bleeding

Practice Points:

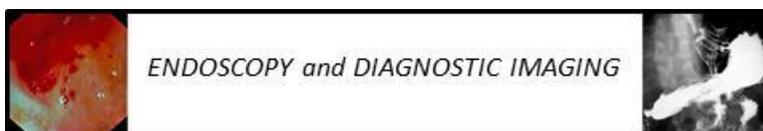
- Asymmetric rupture of vas rectum (vessel draped over diverticulum) towards lumen of diverticulum at its dome on antimesenteric margin. Injurious factors within the colonic lumen produce asymmetric damage to the luminal aspect of the underlying vas rectum resulting in segmental weakness of the artery and predisposition to rupture into the lumen. Rupture is associated with eccentric thickening of intima of vessels with thinning of media near the bleeding point. There is absence of inflammation (diverticulitis)
- The right colon is the source of bleeding in 49–90% of patients (?)
- The source is not identified in 30–40% of cases. Bleeding is usually abrupt, painless and in large volume (33% are massive). Bleeding stops spontaneously in 70–80% of cases



- In those with bleeding, 30% go on to have a 2nd bleed and of those, 50% will have a 3rd bleed
- Selective angiogram
 - Minimum rate needed is 1.0–1.3 mL/minute
 - Therapy
 - vasopressin, somatostatin
 - embolization
 - mark area with methylene blue
- Radioisotope scan
 - Bleeding can be detected at as low as 0.1 mL/minute
 - Technetium 99m labelled sulphur colloid
 - cleared in minutes
 - pools in lumen
 - advantage – short time to complete study
 - labelled RBC
 - longer circulating half life
 - can repeat scans up to 24-36 hours
 - The accuracy of bleeding studies varies widely from 24–91%
- Colonoscopy
 - Emergency colonoscopy for active bleeding
 - Moderate bleeding that has stopped –scope could be done within 12–24 hours
 - Less severe bleeding – outpatient procedure
 - Important to exclude polyp (32%) and carcinoma (19%)

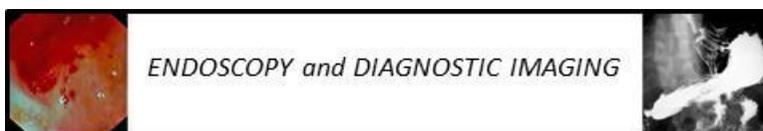
Recent Updates:

- Persons with uncomplicated diverticular disease will have fewer episodes of diverticulitis if given cyclic courses of rifaximin (a poorly absorbed, orally administered antibiotic effective against Gram-positive and negative aerobic and anaerobic bacteria) (Tursi and Papagrigroriadis, APT 2009; 30: 532-546).
- For the person with mild and acute diverticulitis, antibiotic treatment may not be necessary (Hjern et al, Scan. J. Gastro. 2007; 42: 41-47).
- Mesalazine (aka masalamine) is useful to treat painful diverticulitis, and also to maintain its remission, when given alone or in combination with either rifaximin or probiotics (Tursi et al., Int. J. Colorectal Dis., 2009; 24: 49-55; Tursi, 2010; Kruis et al., Gastro. 2007; 132: A-191 (S1187).



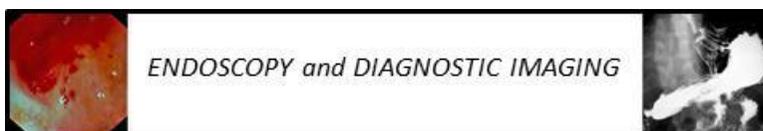
ISCHEMIC BOWEL DISEASE

- Give the causes of acute and chronic mesenteric ischemia.
 - Large artery occlusion
 - atherosclerosis
 - thrombosis
 - embolism
 - aortic aneurysm
 - ligation
 - mesocolon hematoma
 - vasculitis (rheumatoid arthritis, collagen vascular disease)
 - Venous occlusion
 - hypercoagulability and thrombotic states
 - oral contraceptives
 - Increased intraluminal pressure
- Give the clinical presentations of acute and chronic mesenteric ischemia
 - Acute
 - Background clinical picture of underlying disease
 - Acute onset of pain out of proportion to physical exam
 - Rectal bleeding
 - Urge to defecate/diarrhea
 - Abdominal tenderness
 - Confusion, sepsis, hypertension, fever, post prandial pain
 - Rebound guarding
 - Consider risk factors (DM, AF, etc.), including drugs e.g alosetron, tegaserod, cocaine, digitalis
 - IBS – association
 - Chronic
 - Symptoms
 - Post-prandial intestinal angina
 - Fear of eating (sitophobia)
 - Weight loss
 - Nausea and vomiting
 - Signs
 - Abdominal tenderness out of proportion to exam
 - Epigastric bruit
 - Gastric ulceration
 - Gastroparesis
 - Gallbladder dyskinesia



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- Superior mesenteric artery (SMA) embolism (50%)
 - Atrial fibrillation, left ventricle thrombosis, ulcerated aortic plaque
- Superior mesenteric artery thrombosis (15%)
- Non-occlusive mesenteric ischemia (25%)
 - insufficient flow (hypovolemia, cardiac failure, hypotension, digitalis)
 - atheromatous emboli in microcirculation
 - intravascular coagulation in microcirculation
- Medications
 - 5-HT3 antagonist
 - 5-HT4 agonist
 - Cocaine
 - Digitalis
 - Dopamine
- Mesenteric venous thrombus (10%)
 - Hypercoagulable conditions
 - Primary
 - Secondary
 - Cirrhosis, diabetes, hyperlipidemia, IBD, inflammation , intra-abdominal sepsis, paraneoplastic, perforation, postoperative, smoking, trauma
 - Portal hypertension
 - Oral contraceptive agent
 - Perforated viscous
 - Pancreatitis
 - Trauma
 - Inflammatory bowel disease
- Focal segmental ischemia (5%)
 - Mechanical
 - Trauma
 - Radiation
 - Localized small vessel occlusion
 - Cholesterol emboli
 - Strangulated hernias
 - Vasculitis
 - Volvulus
 - Sickle cell disease
- Irritable bowel syndrome (IBS)



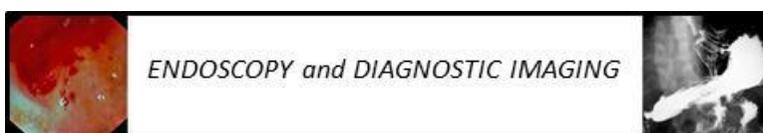
- Chronic mesenteric ischemia
 - Vessel lumen
 - Atherosclerosis and atheroma
 - Diabetes, hyperlipidemia, smoking
 - Vessel wall
 - Celiac artery compression syndrome
 - Fibrovascular dysplasia
 - Mesenteric venous thrombosis
 - Takayasu's arteritis
 - Thromboangiitis obliterans

Abbreviations: IBS, irritable bowel syndrome; SMA, superior mesenteric artery

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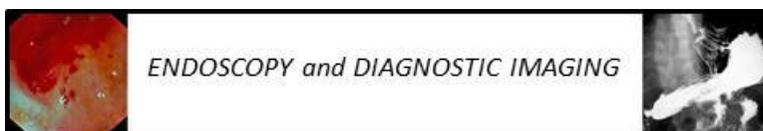
- Give the endoscopic and microscopic pathological changes in acute mesenteric ischemia.
- Colonoscopic
 - Superficial half of colonic mucosa preferentially affected
 - Hemorrhagic streaking
 - Superficial ulceration
 - Deep ulcers
 - UC-like colitis
 - Liquification necrosis
 - Perforation
 - Stricture (reversible, irreversible, sacular stricture)
 - Pneumatosis linearis (colon gangrene ; ddx, HIV disease)
 - Carcinoma (pressure of CRC produces local ischemia)
 - Diverticulosis-associated ischemia
 - Isolated R-colon ischemia (IRCI) may be heralding SMA occlusion
- Mucosal and submucosal hemorrhage
- Microscopic
 - Partial necrosis and ulceration
 - Crypt abscesses
 - Iron-laden macrophages in submucosa
 - Fibrin plugs in capillaries

Abbreviation: IRCI, isolated R-colon ischemia



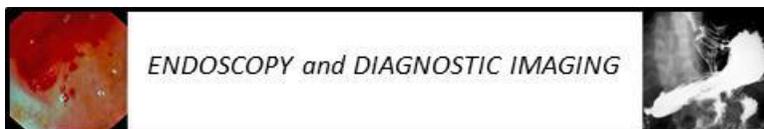
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- Give the investigations and the treatment of acute mesenteric ischemia
- Investigations
 - Colonoscopy or flexible sigmoidoscopy with mucosal biopsy to make initial diagnosis
 - Angiography
 - CT angiography
 - Doppler ultrasound (shows only proximal vessels)
 - Lab – lactic acidosis, ion gap metabolic acidosis, hypercoagulopathy work up, anemia, leucocytosis
 - Abdominal film (3 views)
 - MRI
 - Laparoscopy, if high index of clinical suspicion of infarction
- Treatment
 - Careful ongoing assessment
 - No evidence of peritoneal signs
 - careful clinical observation
 - correction of blood and plasma-volume
 - broad spectrum antibiotics (?)
 - parenteral fluids, electrolytes and nutrition
 - abdominal decompression via nasogastric suction
 - avoidance of corticosteroids
 - Presence of peritoneal signs
 - surgical exploration
 - Absence of clinical improvement after 7–10 days
 - resection of infarcted segment
 - Chronic non-resolving ischemic colitis
 - surgical resection
 - Short or long ischemic stricture without evidence of (sub) obstruction
 - clinical observation with evidence of (sub) obstruction
 - surgical resection
 - Supportive
 - Treat associated, underlying conditions
 - Early surgery with resection for infarction/gangrene/perforation
 - Embolectomy
 - Papaverine
 - Thrombolectomy
 - Broad spectrum antibiotics if micro perforation suspected



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- Give the radiologic, endoscopic and clinical assessment of intestinal ischemia.
- Bowel lumen
 - Caliber
 - Content
 - Transition point if associated obstruction
 - Intraluminal hemorrhage
 - Small bowel feces sign
- Bowel Wall
 - Thickness
 - Homogeneity
 - Enhancement pattern
 - Length of involvement
 - Pneumatosis
- Mesentery
 - Edema
 - Hemorrhage
 - Patency of mesenteric vessels
 - Mesenteric vascular engorgement
 - Ascites
 - Volvulus
 - Intussusception
- X-ray
 - Flat plate
 - Edematous narrowing
 - Distension of gas-filled colon segment
 - Contrast barium enema
 - Severe spasm
 - Thumbprinting
 - Ulceration
 - Structuring
 - Sacculation
- Endoscopy
 - Marked swelling
 - Erythema
 - Intramural hemorrhage



- Slough
 - Ulceration
 - Strictureing
- Clinical evolution
- most often full resolution (transient)
 - rarely gangrene
 - rarely non-resolving ischemic colitis
 - occasionally stricturing

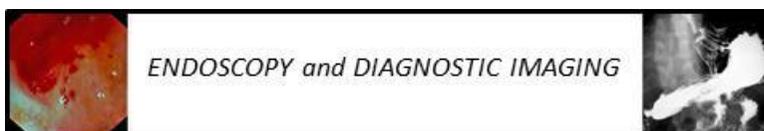
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- Gangrenous ischemic colitis
- Short history, usually of less than 18 hours
 - Severe generalized abdominal pain
 - Diarrhea may be present but rectal bleeding is rather unusual
 - Impressive state of shock and signs of generalized peritonitis predominate
 - Gross congestion and necrotic discoloration of colon at surgery
- Acute (non-gangrenous) transient ischemic colitis
- Short history of left-sided and/or lower abdominal pain
 - Diarrhea mixed with bright red or dark stained blood
 - Mild fever, tachycardia, left-sided abdominal tenderness and guarding
 - Polymorphonuclear leukocytosis

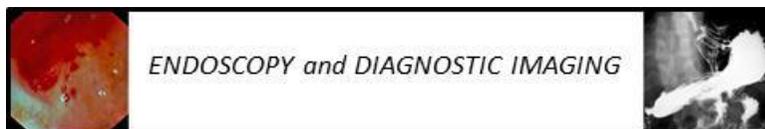
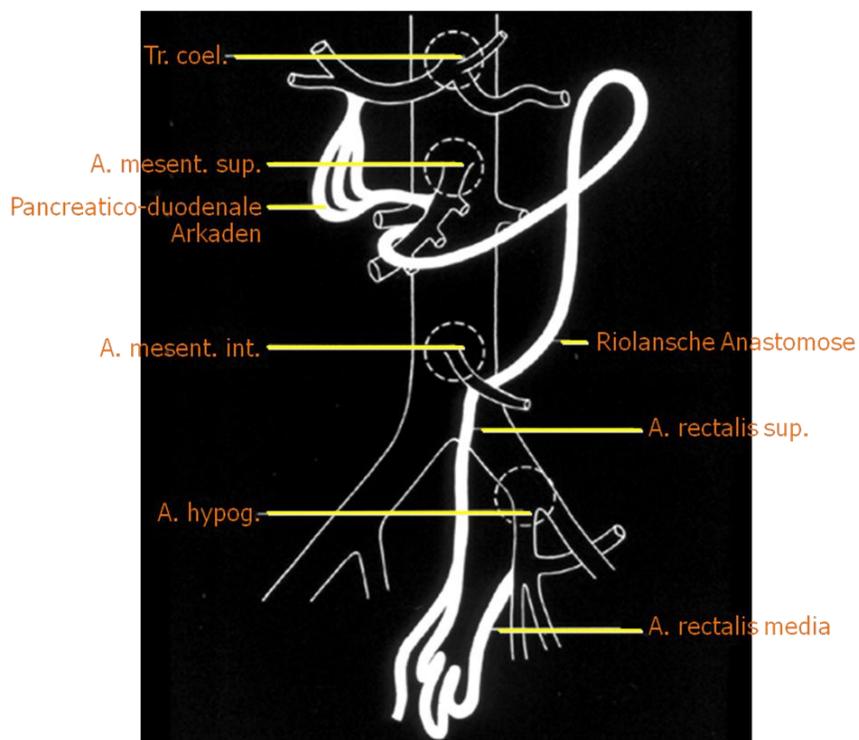
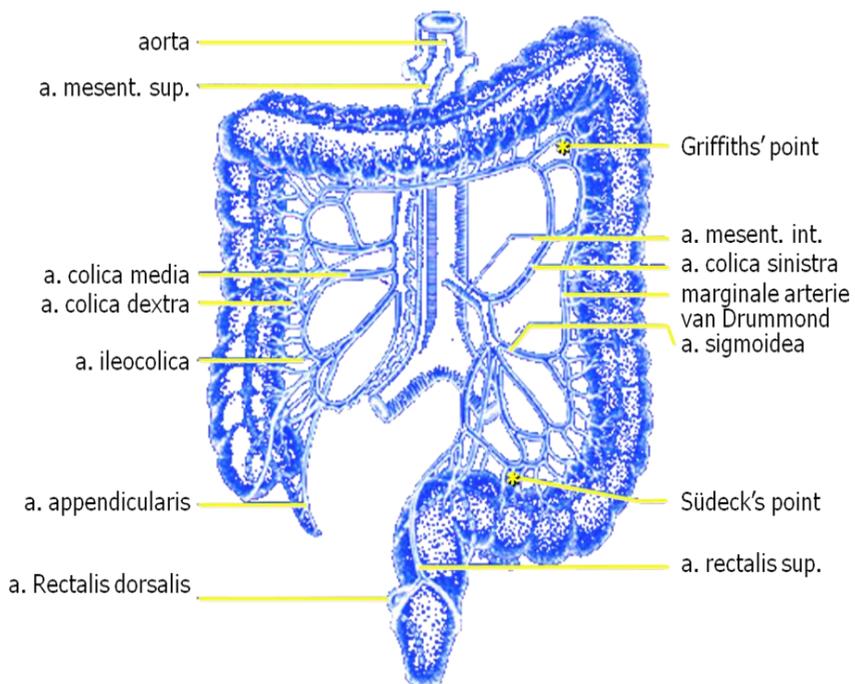
Ischemic colitis

Practice Pointers:

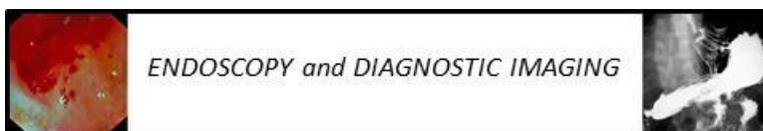
- Acute (non-gangrenous) transient ischemic colitis
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 - Diarrhea mixed with bright red or dark stained blood
 - Mild fever, tachycardia, left-sided abdominal tenderness and guarding
 - Polymorphonuclear leukocytosis
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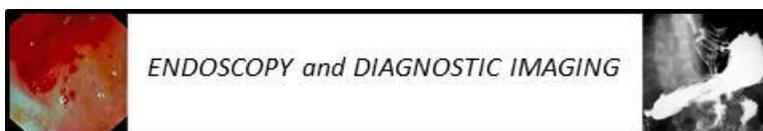
- o Gross congestion and necrotic discoloration of colon at surgery



- Causes of acute and chronic mesenteric ischemia
 - Large artery occlusion
 - atherosclerosis
 - thrombosis
 - embolism
 - aortic aneurysm
 - ligation
 - mesocolon hematoma
 - Non-occlusive state
 - insufficient flow (hypovolemia, cardiac failure, hypotension, digitalis)
 - atheromatous emboli in microcirculation
 - intravascular coagulation in microcirculation
 - vasculitis (rheumatoid arthritis, collagen vascular disease)
 - Venous occlusion
 - hypercoagulability and thrombotic states
 - oral contraceptives
 - Increased intraluminal pressure
 - Superior mesenteric artery (SMA) embolism 50%
 - Atrial fibrillation, left ventricle thrombosis, ulcerated aortic plaque
 - Superior mesenteric artery thrombosis 15%
 - Non-occlusive mesenteric ischemia 25%
 - Vasospasm, shock, congestive cardiac failure, cardiac dysrhythmias
 - Medications
 - 5-HT3 antagonist
 - 5-HT4 agonist
 - Cocaine
 - Digitalis
 - Dopamine
 - Focal segmental ischemia
 - Mechanical
 - Trauma
 - Radiation
 - Localized small vessel occlusion
 - Cholesterol emboli
 - Strangulated hernias
 - Vasculitis
 - Volvulus
 - Sickle cell disease
 - Irritable bowel syndrome (IBS)
- Causes of acute and chronic mesenteric ischemia (cont'd)
 - Mesenteric venous thrombus (10%)
 - Hypercoagulable conditions
 - Primary
 - Secondary
 - Cirrhosis, diabetes, hyperlipidemia, IBD, inflammation, intra-abdominal sepsis, paraneoplastic perforation, postoperative, smoking, trauma



- Portal hypertension
 - Oral contraceptive agent
 - Perforated viscus
 - Pancreatitis
 - Trauma
 - Inflammatory bowel disease
- Chronic mesenteric ischemia
- Vessel lumen
 - Atherosclerosis and atheroma
 - Diabetes, hyperlipidemia, smoking
 - Vessel wall
 - Celiac artery compression syndrome
 - Fibrovascular dysplasia
 - Mesenteric venous thrombosis
 - Takayasu's arteritis
 - Thromboangiitis obliterans
- Clinical presentations of acute and chronic mesenteric ischemia
- Acute
- Background clinical picture of underlying disease
 - Acute onset of pain out of proportion to benign abdominal examination
 - Rectal bleeding
 - Urge to defecate/diarrhea
 - Abdominal tenderness
 - Confusion, sepsis, hypertension, fever, post prandial pain
 - Rebound guarding
 - Consider risk factors (DM, AF, etc.), including drugs e.g alosetron, tegaserod, cocaine, digitalis
 - Association with IBS (irritable bowel syndrome)
- Chronic
- Symptoms
 - Post-prandial intestinal angia
 - Fear of eating (sitophobia)
 - Weight loss
 - Nausea and vomiting
 - Signs
 - Abdominal tenderness out of proportion to benign abdominal examination
 - Epigastric bruit (non-specific)
 - Gastric ulceration
 - Gastroparesis
 - Gallbladder dyskinesia



- Endoscopic and microscopic pathological changes in acute mesenteric ischemia

- Colonoscopic

- Superficial half of colonic mucosa preferentially affected
- Hemorrhagic streaking
- Superficial ulceration
- Deep ulcers
- UC-like colitis
- Subepithelial hemorrhage
- Liquification necrosis
- Perforation
- Stricture (reversible, irreversible, saccular stricture)
- Pneumatosis linearis (colon gangrene ; ddx, HIV disease)
- Carcinoma (pressure of CRC produces local ischemia)
- Diverticulosis-associated ischemia
- Isolated R-colon ischemia (IRCI) may be heralding SMA occlusion

- Microscopic

- Fibrin plugs in capillaries
- Partial necrosis and ulceration
- Crypt abscesses
- Iron-laden macrophages in submucosa

- Investigations for, and the treatment of acute mesenteric ischemia

- Investigations

- Colonoscopy or flexible sigmoidoscopy with mucosal biopsy to make initial diagnosis
- Angiography
- CT angiography
- Doppler ultrasound (shows only proximal vessels)
- Lab – lactic acidosis, ion gap metabolic acidosis, hypercoagulopathy work up, anemia, leucocytosis
- Abdominal film (3 views)
- MRI
- Laparoscopy, if high index of clinical suspicion of infarction

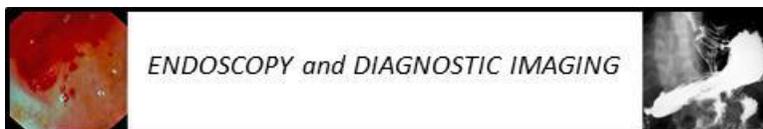
- Treatment

- Supportive
- Treat associated, underlying conditions
- Early surgery with resection for infarction/gangrene/perforation
- Embolectomy
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- Broad spectrum antibiotics if micro perforation suspected

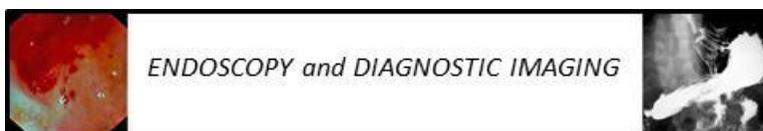
- The radiologic assessment of intestinal ischemia

- Bowel lumen

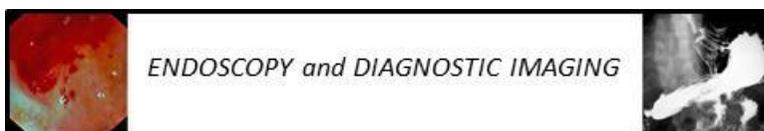
- Caliber
- Content
- Transition point if associated obstruction
- Intraluminal hemorrhage



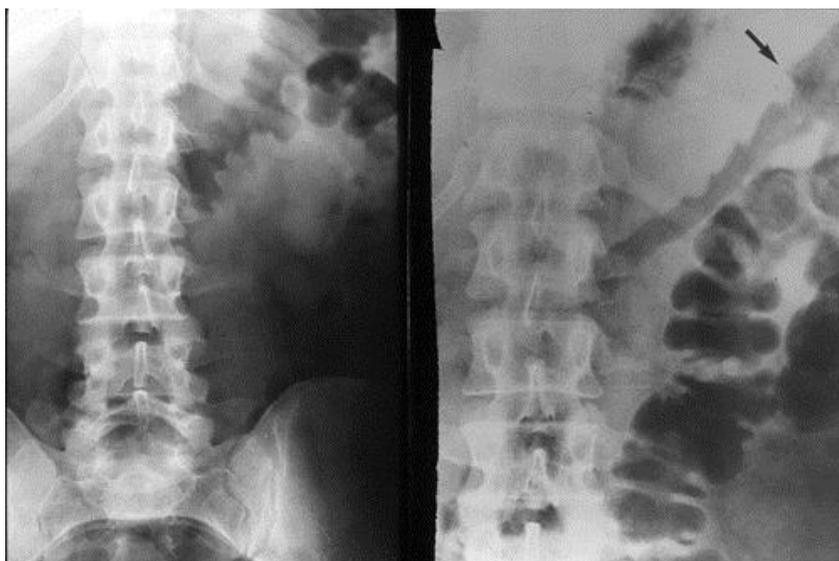
- Small bowel feces sign
- Bowel wall
 - Thickness
 - Homogeneity
 - Enhancement Pattern
 - Length of involvement
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- Mesentery
 - Edema
 - Hemorrhage
 - Patency of mesenteric vessels
 - Mesenteric vascular engorgement
 - Ascites
 - Volvulus
 - Intussusception
- 1. Gangrenous ischemic colitis
 - Short history, usually of less than 18 hours
 - Severe generalized abdominal pain
 - Diarrhea may be present but rectal bleeding is rather unusual
 - Impressive state of shock and signs of generalized peritonitis predominate
 - Gross congestion and necrotic discoloration of colon at surgery
- 2. Acute (non-gangrenous) transient ischemic colitis
 - Short history of left-sided and/or lower abdominal pain
 - Diarrhea mixed with bright red or dark stained blood
 - Mild fever, tachycardia, left-sided abdominal tenderness and guarding
 - Polymorphonuclear leukocytosis
- X-ray
 - flat film: edematous narrowing, distension of gas-filled colon segment
 - contrast enema: severe spasm, thumbprinting, ulceration, stricturing, sacculation depending on timing and severity of damage
- Endoscopy
 - marked swelling, erythema, intramural hemorrhage, slough, ulceration, stricturing
- Evolution
 - most often full resolution (transient)
 - rarely gangrene
 - rarely non-resolving ischemic colitis

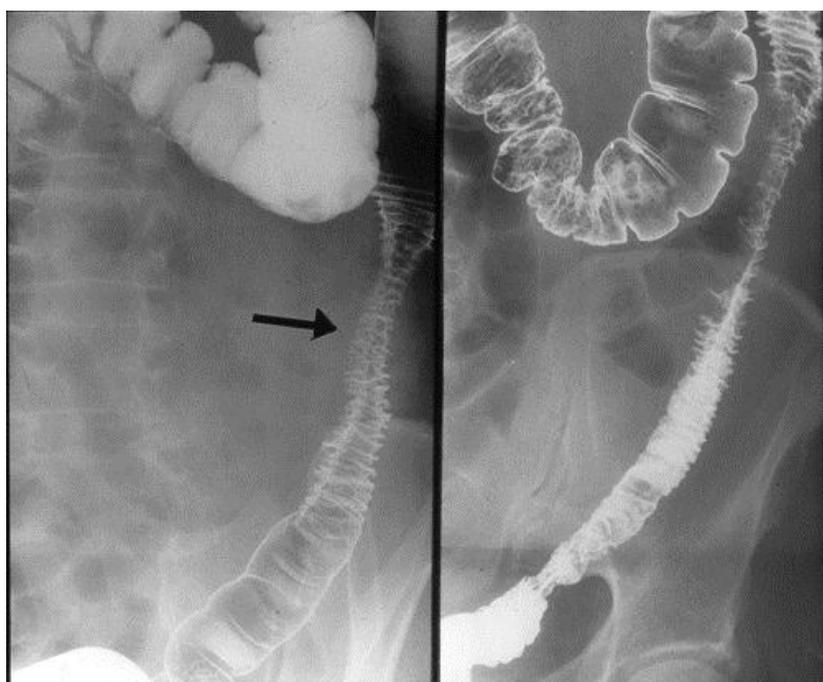
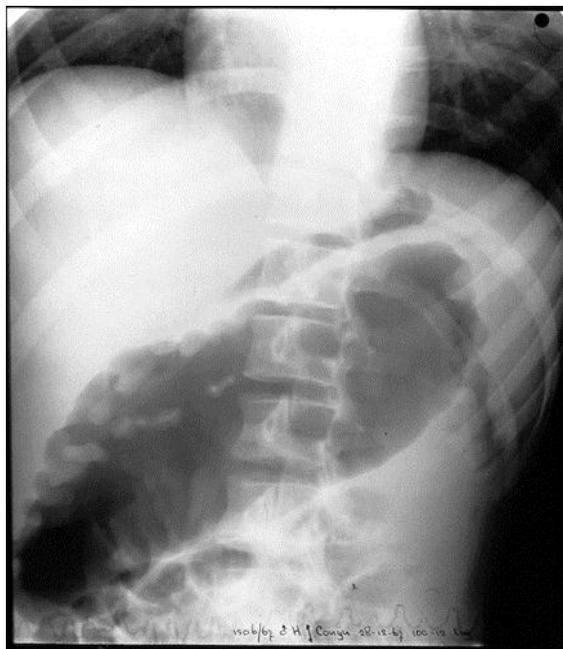


- occasionally stricturing
- Barium Contrast
 - Lumen
 - Narrowed
 - Mucosa
 - Irregular
 - Ulcerated
 - Wall
 - Thickened stricture
 - Short / long
 - Tapered
 - Mucosal pattern lost
 - Irregular contour
 - Transmural necrosis
 - Perforation
- CT scanning
 - Wall thickened
 - Soft tissue stranding
 - Fluid
 - Hemorrhage
 - Gas
 - Pneumatosis coli
 - Mesenteric/ portal veins
 - Filling defect in SMA / SMV (superior mesenteric artery / vein)
- Radiation Colitis
 - Gradual narrowing of lumen
 - Narrow sigmoid colon wall (and sometimes proximal colon)
 - Thick wall (“thumbprinting”)
 - Haustral loss (loss of normal colonic folds)
 - Strictures
- Pseudomembranous Colitis (PMC)
 - Thick haustral markings
 - Diffuse, or local L/R – sided
 - CT
 - Wall: circumferential thickening
 - Pericolonic: soft tissue stranding
- Neutropenic Colitis
 - Typhlitis (inflammation of cecum)
 - Adynamic ileus
 - Wall: thickening
 - Fascia: thickening

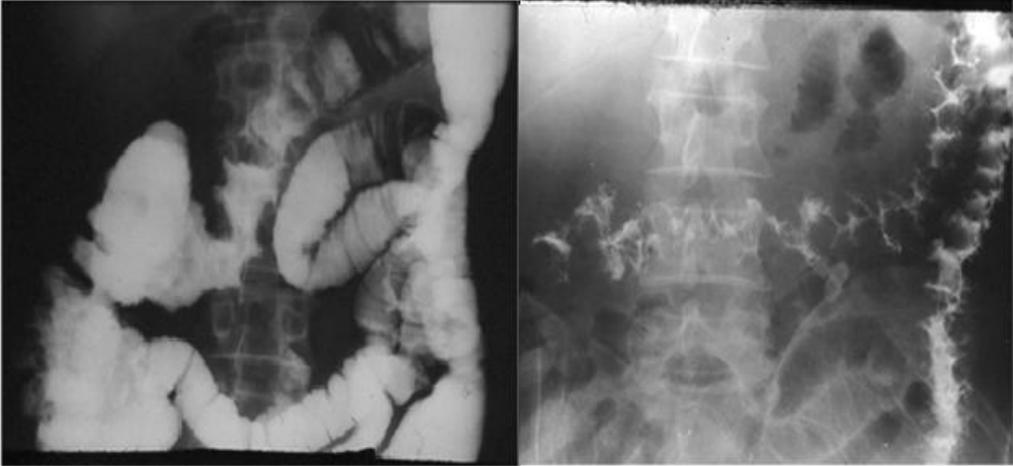
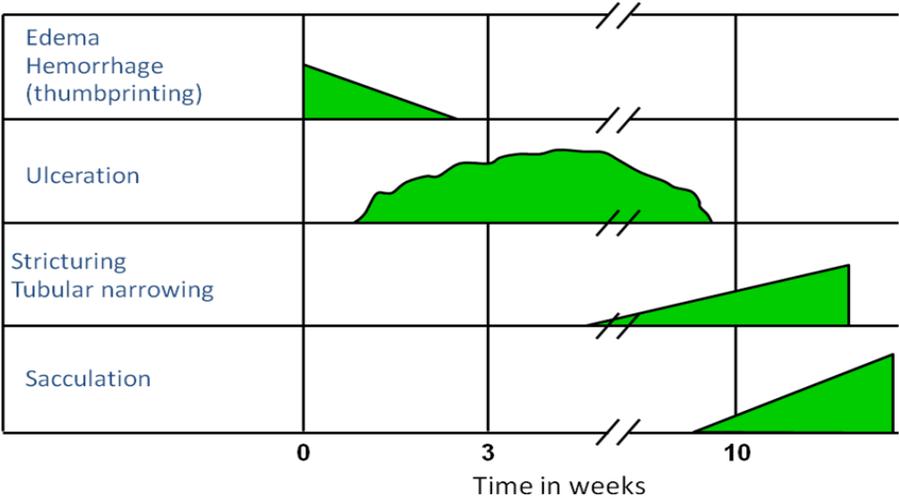


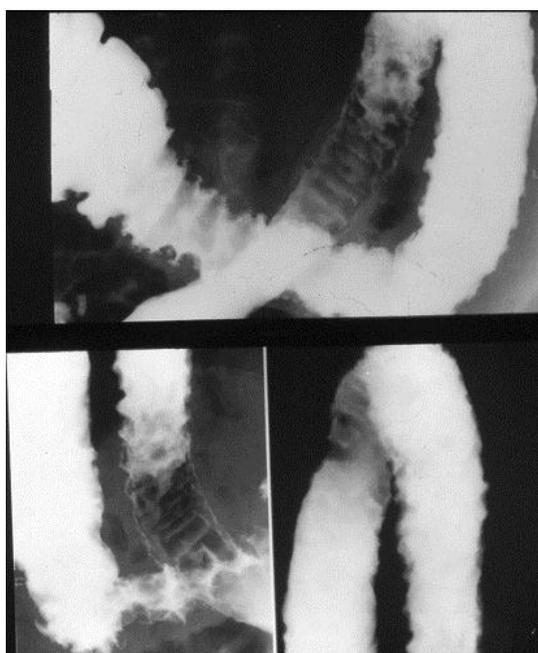
- CT: pericolonic soft tissue stranding

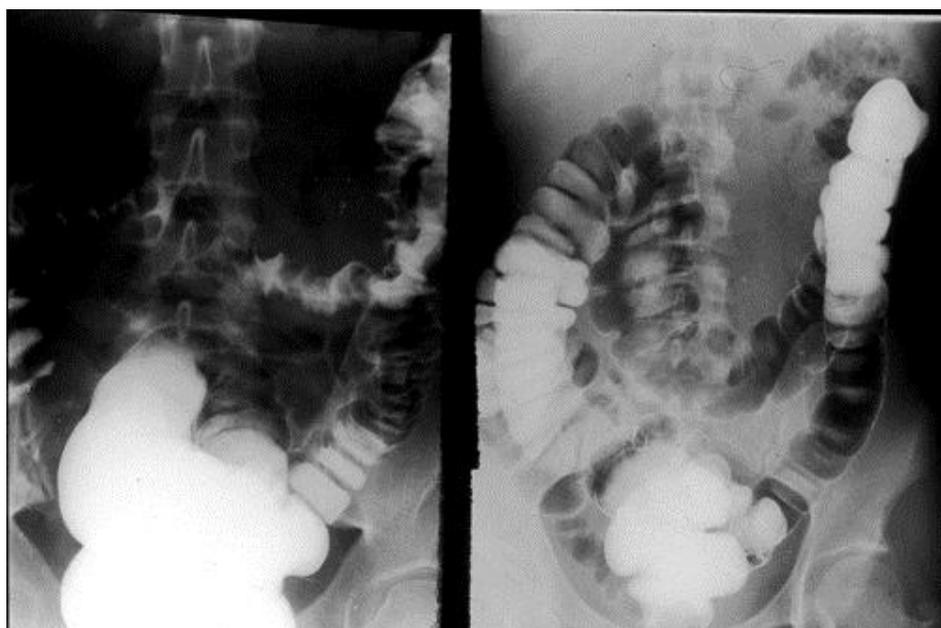
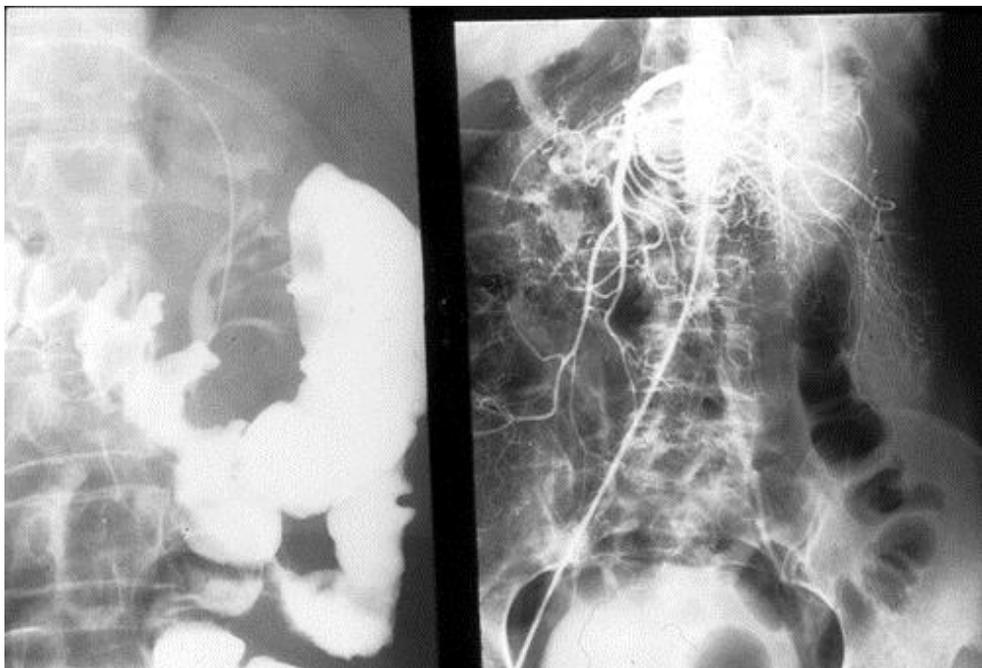


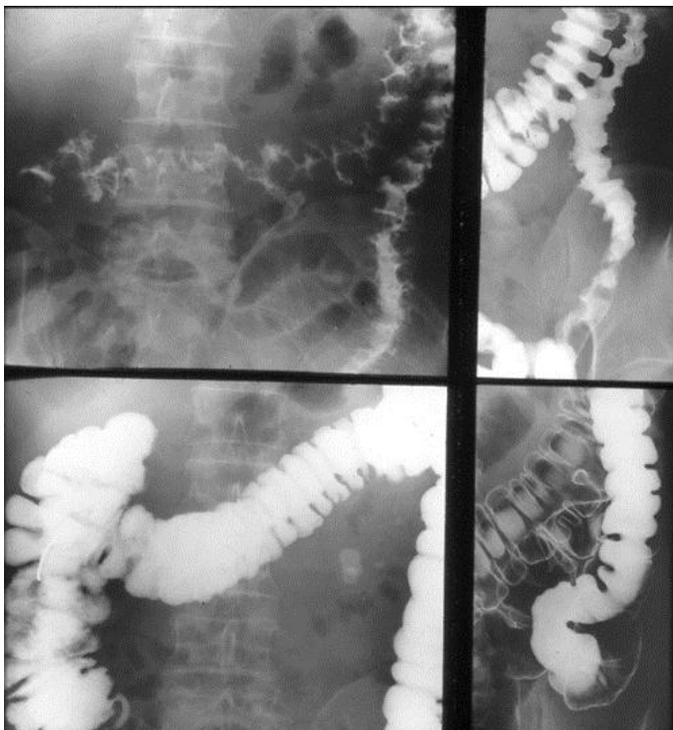


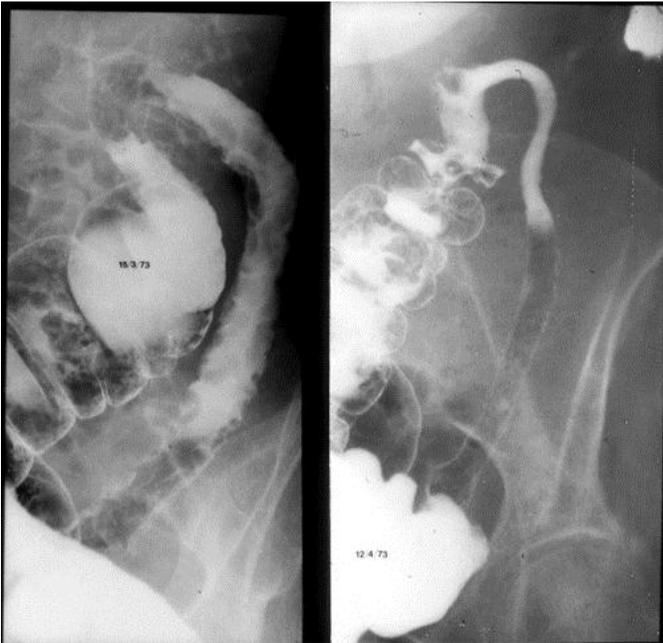
Ischemic Colitis – Radiological Evolution

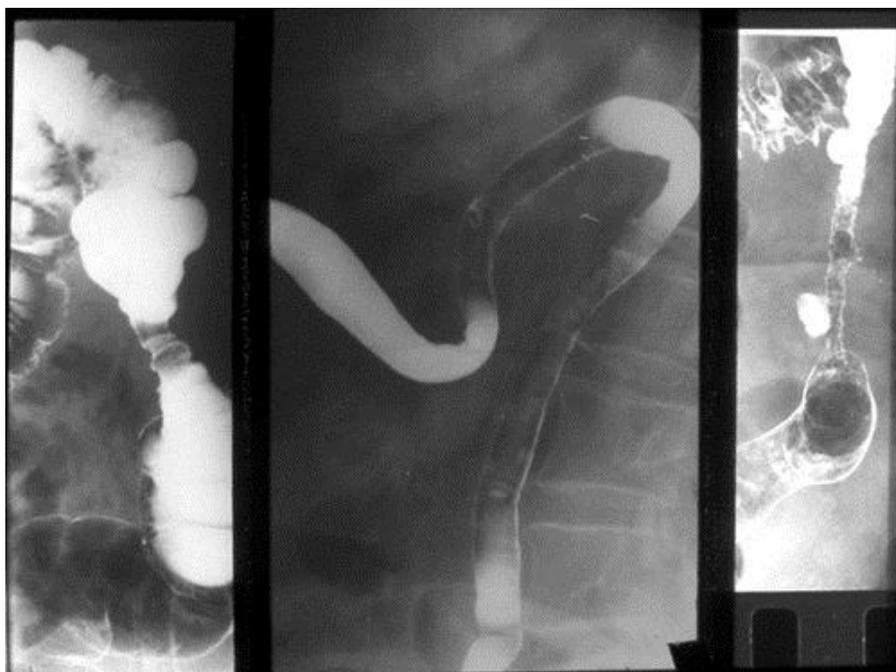
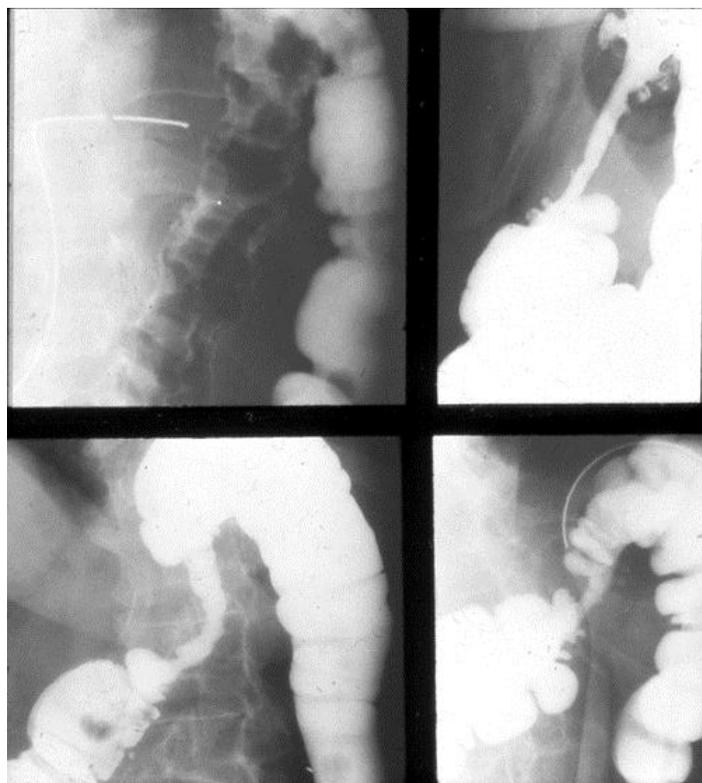


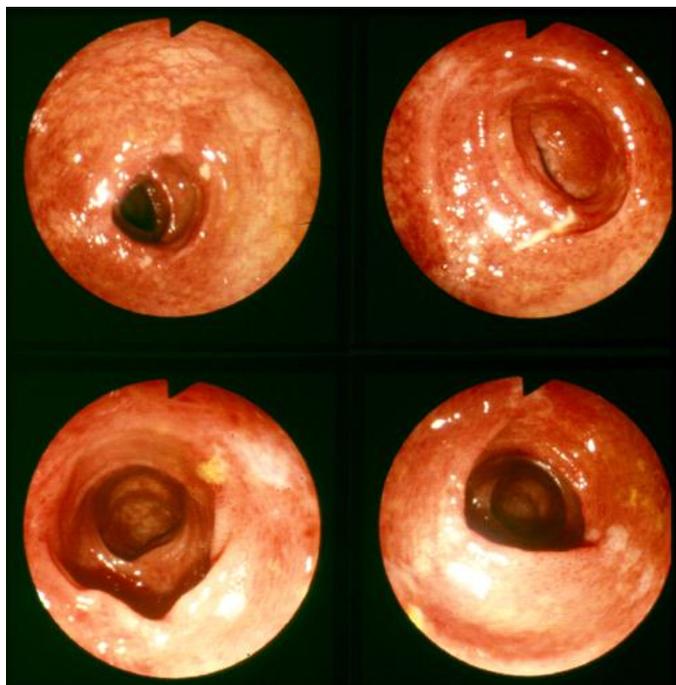
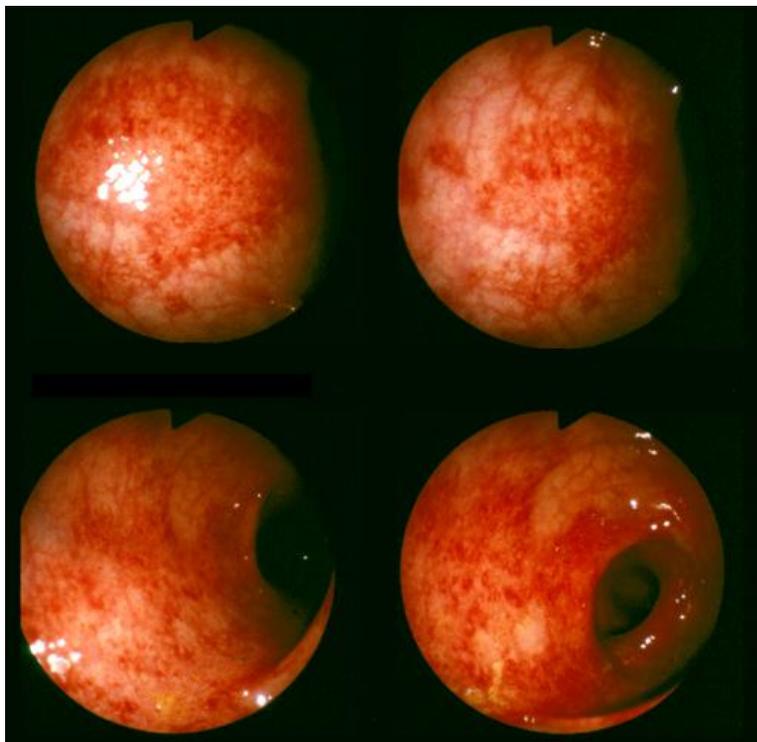


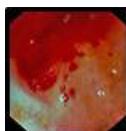
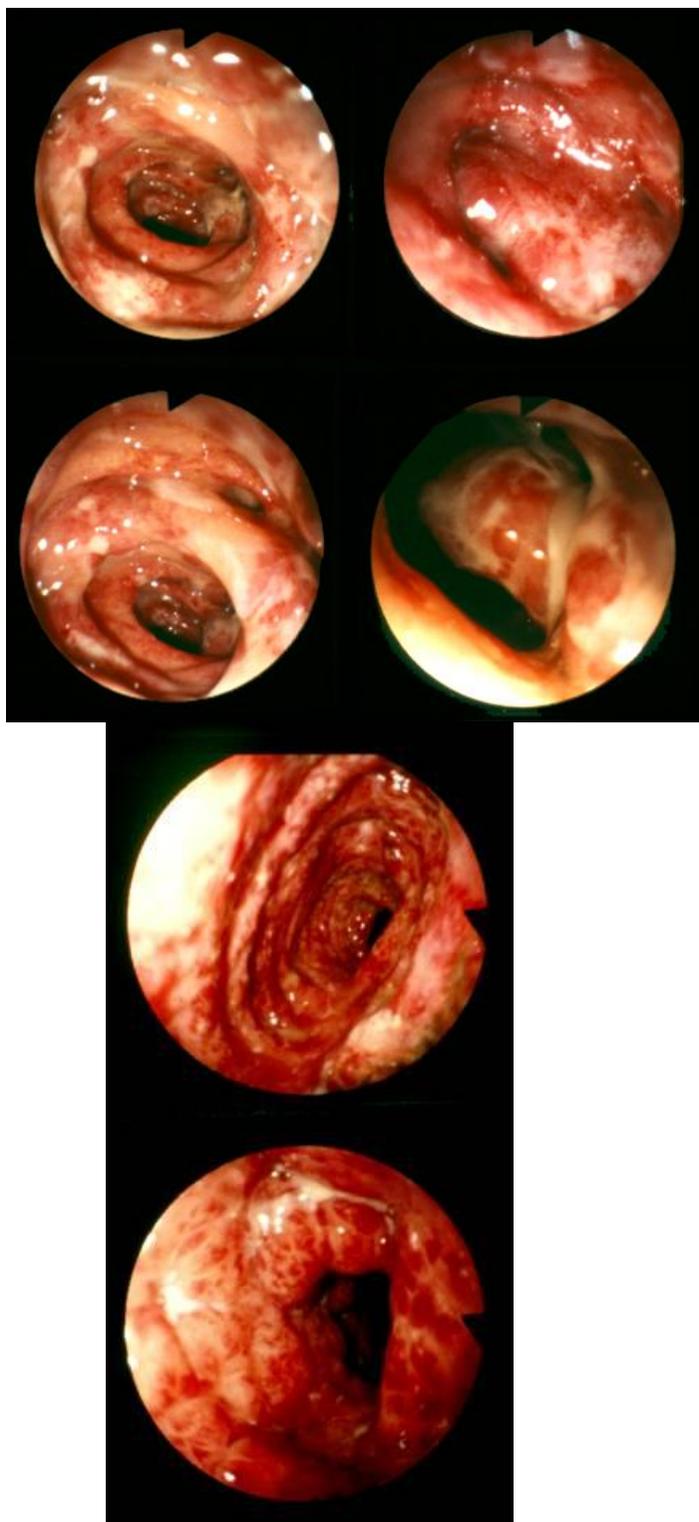


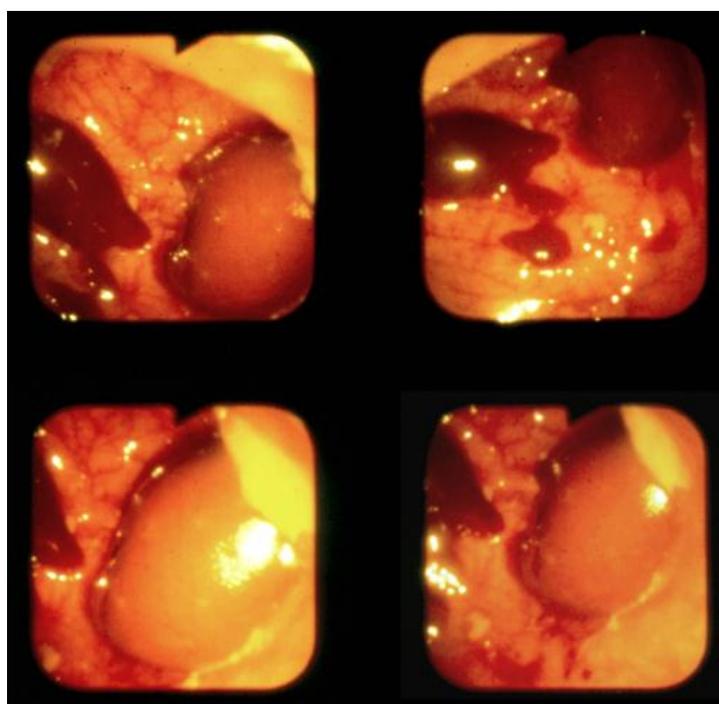
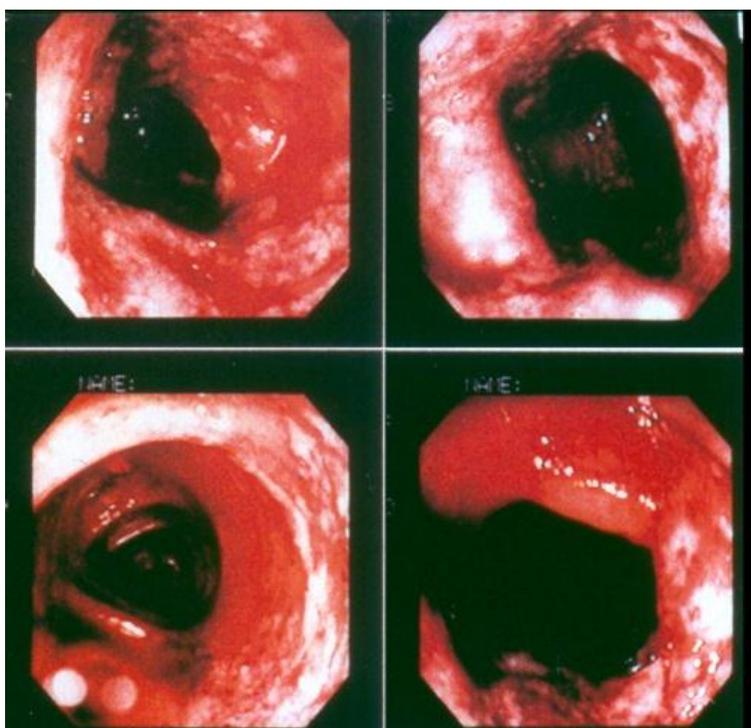


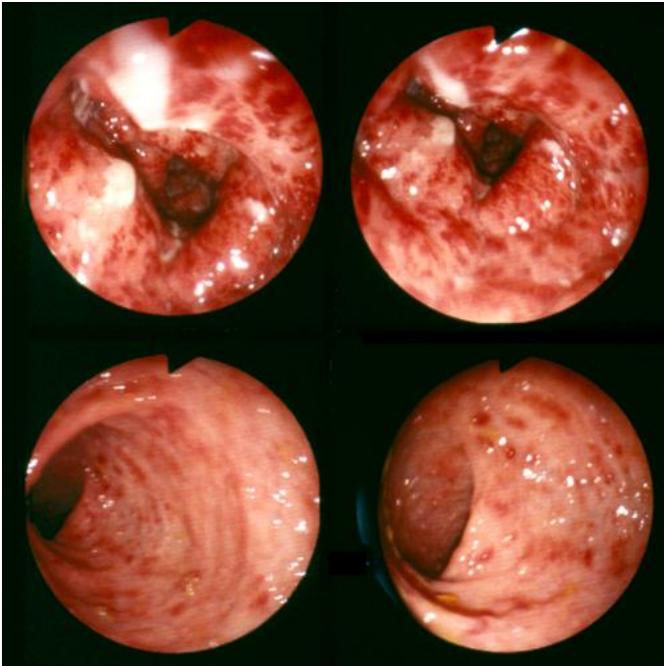
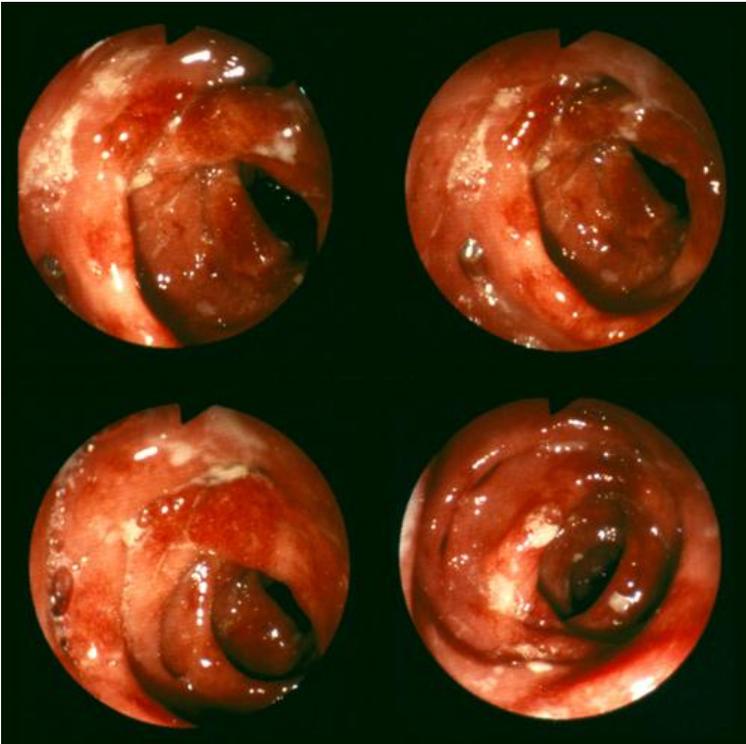


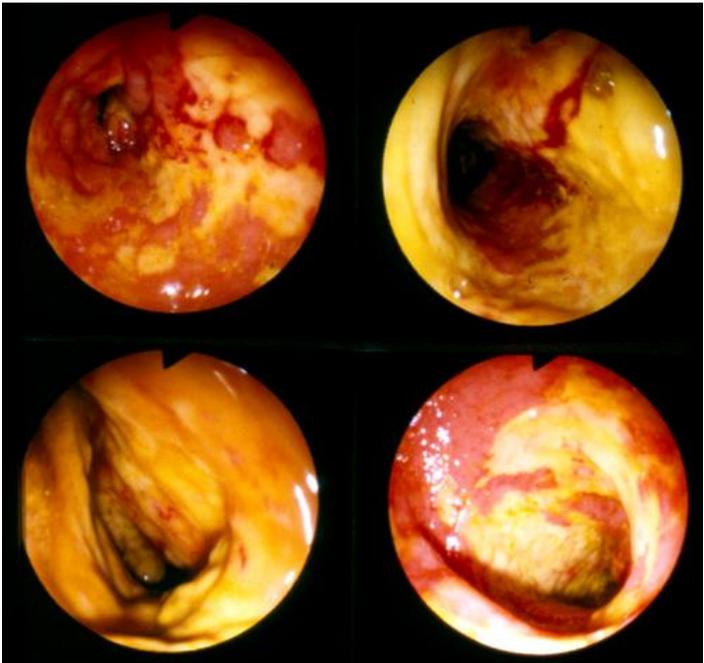
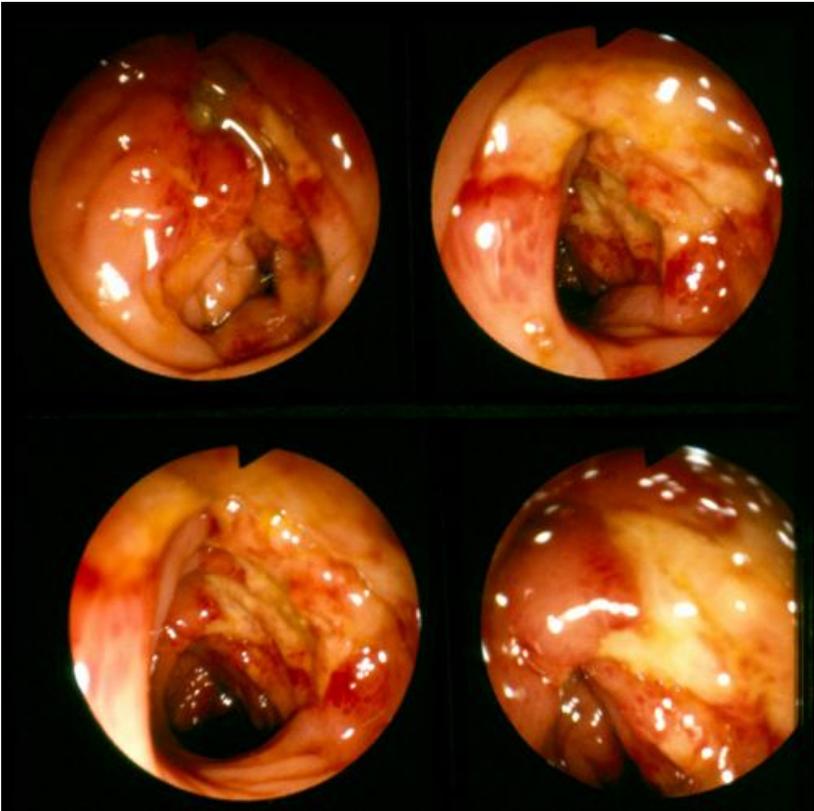


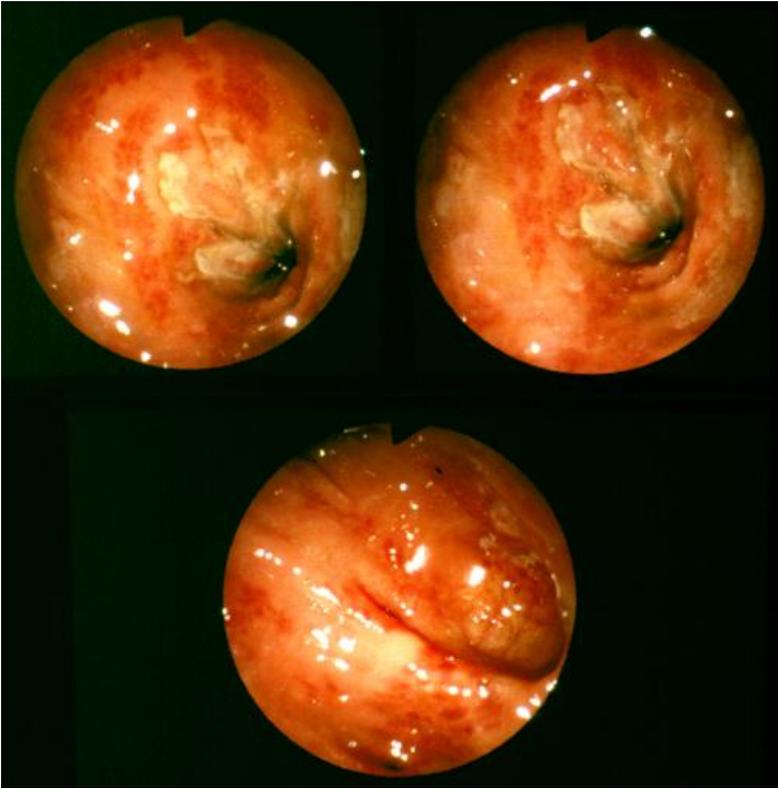
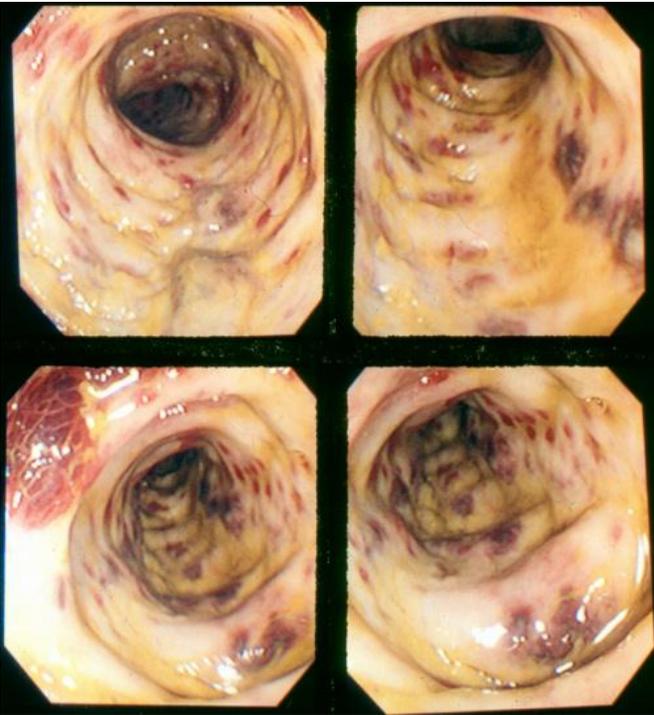


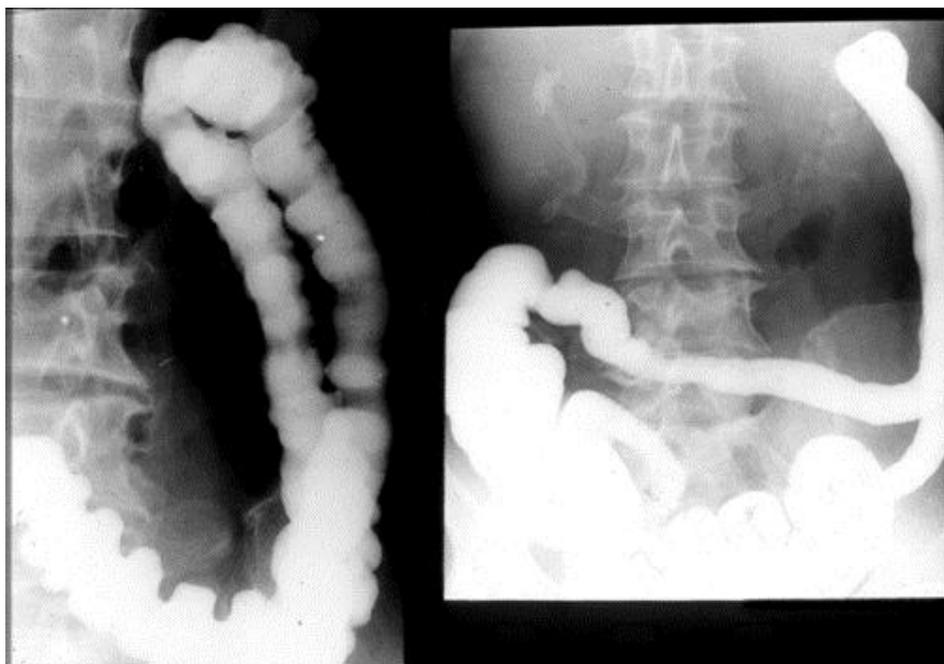


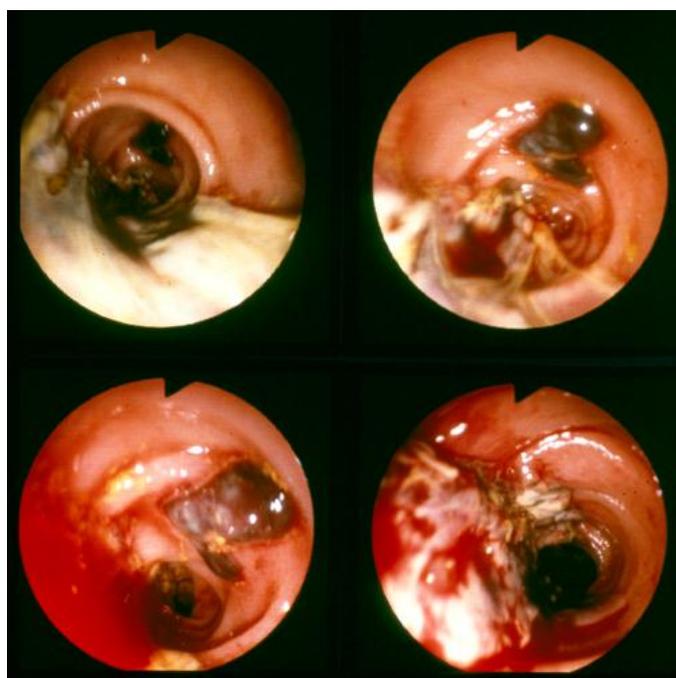


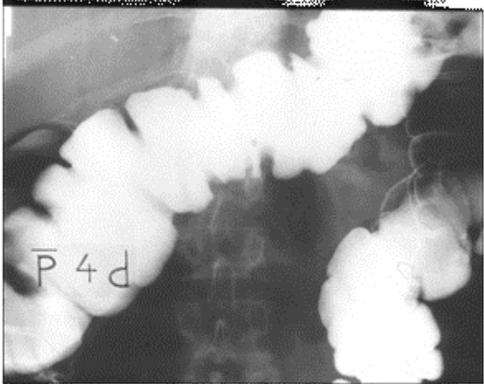
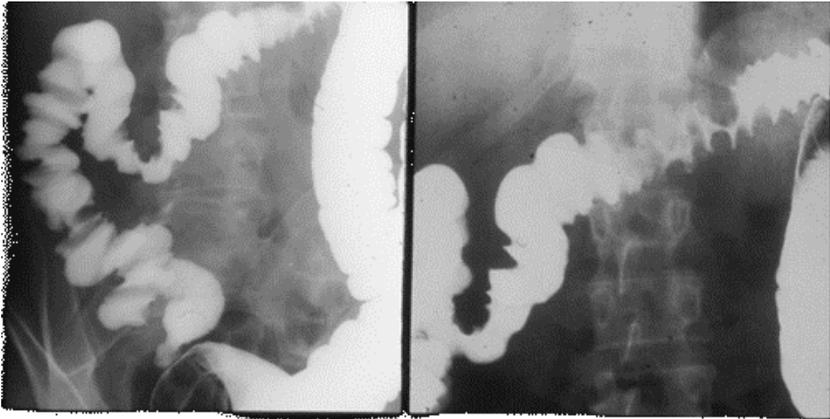








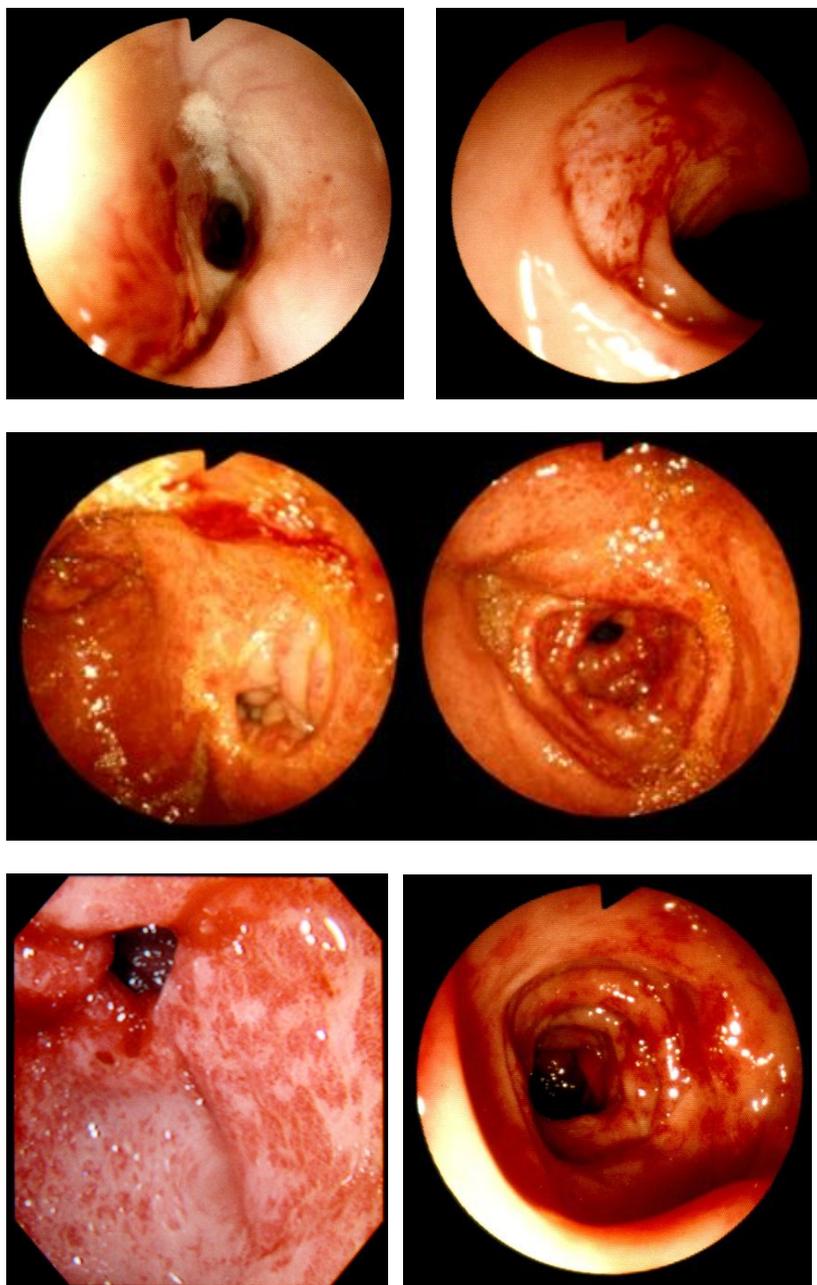


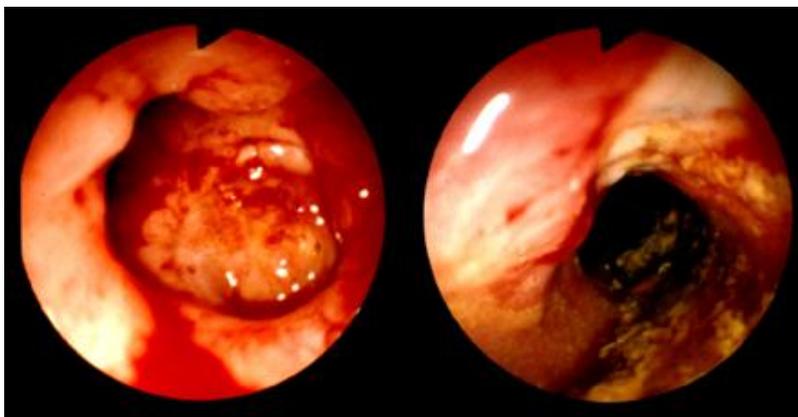
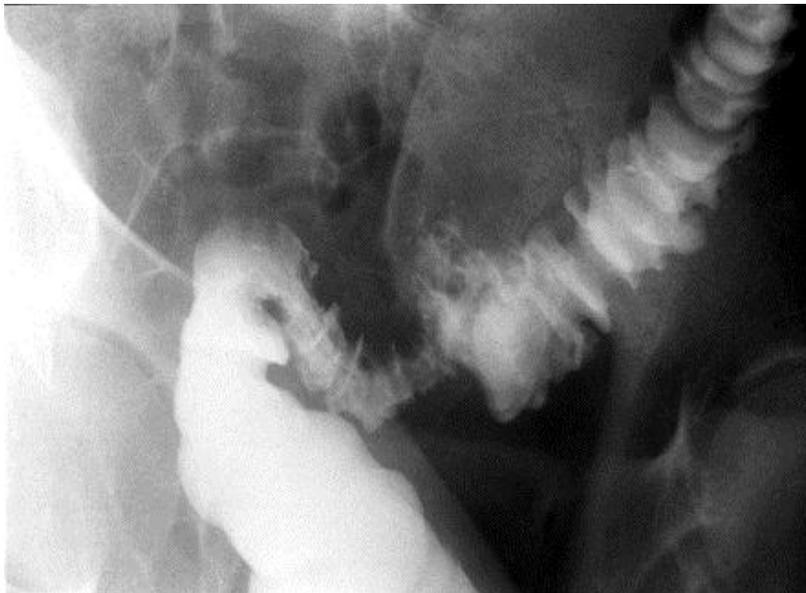


Radiation damage

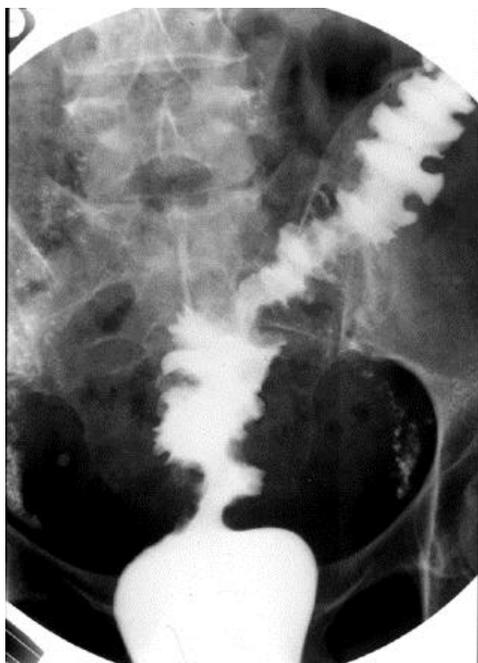
- a. Acute / early radiation damage
 - mucosal necrosis and inflammation
- b. Late / chronic radiation damage
 - Vascular fibrosis and occlusion
 - Fibrotic narrowing
 - Mucosal ulceration / telangiectasia
- Radiotherapy factors
 - The total delivered dose of external irradiation
 - The total treatment time
 - The dose per fraction
 - The dose rate of intracavitary irradiation
 - The combined doses of external and intracavitary irradiation (expressed as Time-Dose-Fractionation (TDF) or Linear-Quadratic (L-Q) number)
- Patient factors
- Age
 - Height and weight
 - Diabetes mellitus
 - Possible cardiovascular disease
- Previous abdominal surgery, especially gynecological operations, cholecystectomy and gastrointestinal surgery



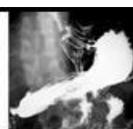
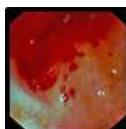
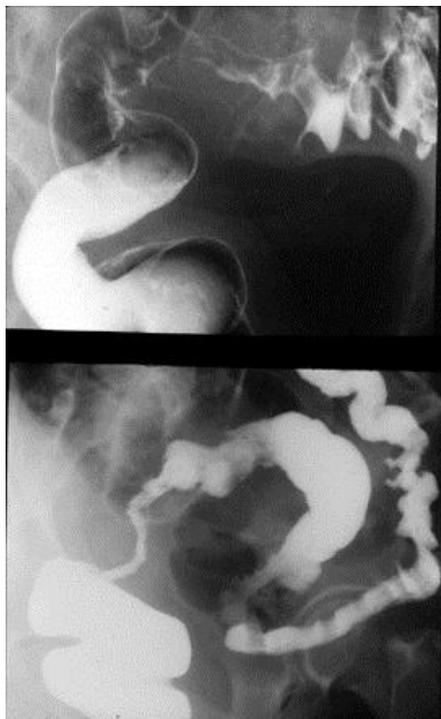




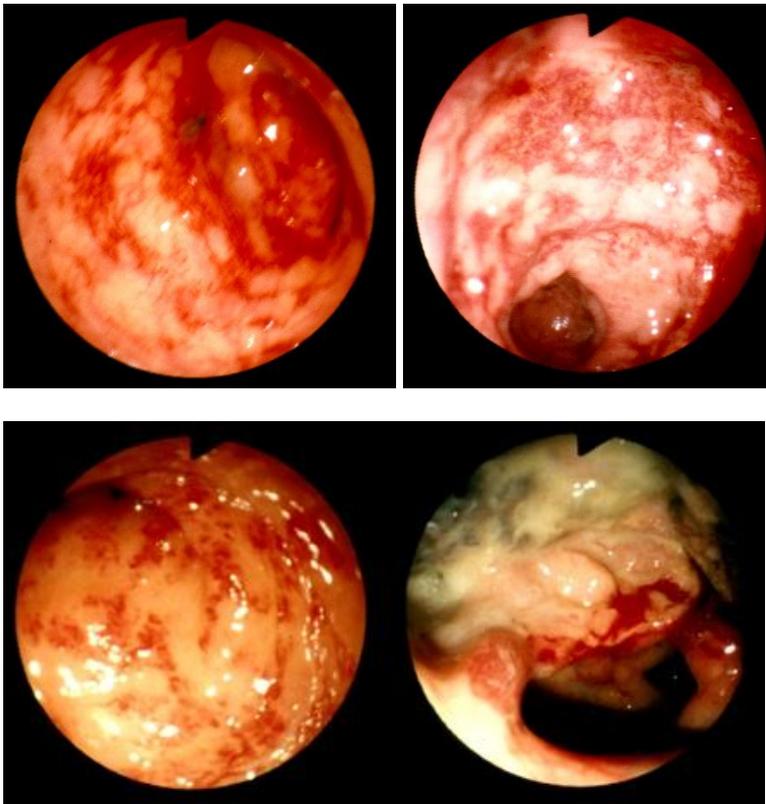
➤ Presenting complaints	%
○ Blood loss	73
○ Diffuse pain	51
○ Diarrhea	44
○ Pain attacks	43
○ Incontinence	33
○ Anal pain	30
○ Constipation	14
○ Both diarrhea & constipation	5







➤ Endoscopic findings (n=110)	%
○ Telangiectasia	51
○ Friable mucosa	30
○ Luminal narrowing	81
○ Solitary ulcer	25
○ Diffuse ulceration	18
○ Fistula	19

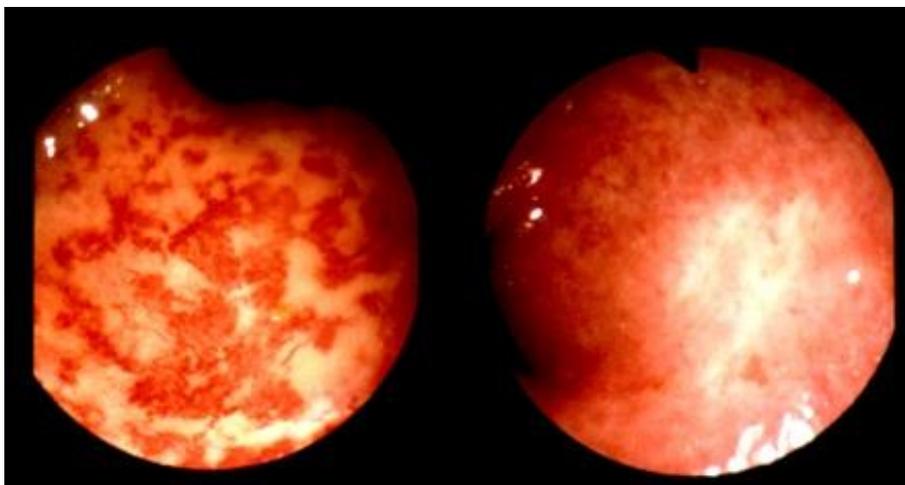




➤ Management of late radiation damage of rectosigmoid colon

○ Bleeding	predn. Enema laser/argon	–	beamer
○ Luminal narrowing	high fiber diet	S	dilatation
○ Ulceration	both hyperbaric	S	oxygen

S= surgery



COLONIC POLYPS AND CANCER

- Give the histological classification of polyps of the Large intestine

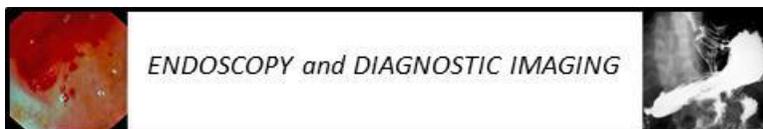
Type	Single or isolated multiple polyps	Polyposis
➤ Neoplastic	○ Adenoma	- Adenomatosis (familial polyposis)
➤ Hamartomas	○ Juvenile polyp, Peutz-Jegher polyp	- Juvenile polyposis, Peutz-Jegher syndrome
➤ Inflammatory	○ Benign lymphoid polyp	- Benign lymphoid polyposis - Inflammatory polyposis (ie in IBD)
➤ Unclassified	○ Metaplastic (hyperplastic polyp)	- Metaplastic polyposis

- Give the risk factors of colorectal cancer*
 - Age over 50 years
 - High-fat, low-fiber diet, smoking
 - Excess caloric intake (BMI > 30, waist circumference > 32-34") or alcohol
 - Personal history of colorectal adenomatous polyps or cancer
 - Chronic inflammatory bowel disease (ulcerative colitis, Crohn colitis)
 - Family history of colorectal adenomatous polyps or cancer
 - Hereditary syndromes
 - Hereditary nonpolyposis colorectal cancer (Lynch Syndrome)
 - Familial Adenomatous Polyposis
 - Gardner syndrome
 - Turcot syndrome
 - Peutz-Jeghers syndrome
 - Familial Juvenile Polyposis

*use when stratifying risk of CRC and need for screening colonoscopy

- Give the risk stratification of CRC

Risk Level	% of CRC	Recommendations for testing
➤ High risk		
○ Familial polyposis	1	Signoidoscopy in teenage years Consider genetic screening Total colectomy if detected
○ HNPCC	5	Colonoscopy in 3 rd /4 th decade at 2-year



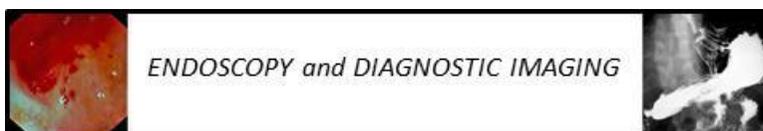
- | | | |
|--|-------|---|
| | | intervals |
| ○ Chronic Ulcerative colitis | <1 | Colonoscopy for universal colitis every 2 years beginning 8-10 years after onset |
| ○ Crohn colitis | | |
| ➤ Moderate Risk | | |
| ○ Familial risk – first degree | 15-20 | Begin screening at an age 10 years younger than age of index case
Consider colonoscopy screening |
| ○ Personal history of breast, uterine, ovarian | <1 | No specific recommendation |
| ➤ Average Risk | | |
| ○ Age > 50 years | 70-75 | Begin screening at age 50 |

Practice Points:

- Familial adenomatous polyposis and hereditary nonpolyposis colon cancer

FAP

- Germline mutation = APC gene
 - Autosomal dominant
 - 100's–1,000's of colonic adenomas
 - Age of Dx=early teens (flex sig w/bx)
 - Tx=colectomy
 - 10% risk duodenal ca
- Median age of onset of CRC in the phenotypes of FAP
- #### Phenotype
- Profuse
 - Intermediate
 - Attenuated (AFAP)
 - MYH (MAP)
 - Age, yrs
 - 39
 - 39-50
 - >50 (R colon)
 - >60 (recessive)
- HNPCC
 - Germline mutation = DNA Mismatch Repair Genes
 - Autosomal dominant
 - Few if any polyps
 - Right-sided colon ca
 - Other ca: uterine, gastric, pancreatic, ovarian, urinary, sm bowel



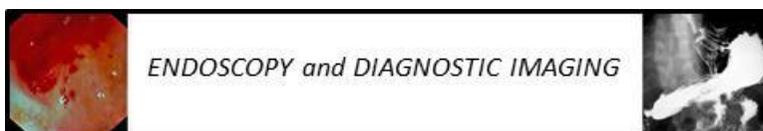
- Early average age of colon cancer Dx:
 - FAP = 39 years of age
 - HNPCC = 44 years of age
- Genetic tests:
 - Should be done w/ genetic counselor
 - FAP=APC protein Truncation Test
 - HNPCC = MSI → MLH1, MSH2
- Controlled trials of fecal occult blood testing in colorectal cancer screening

	Cohort size	Positivity rate %	Predictive value (%) Adenomas and cancers	Dukes A and B cancers (%) screened group	Control group	Mortality reduction (%)
Göteborg, S	27,000	1.9	22	65	33	12
Nottingham, UK	150,000	2.1	53	90	40	15
New York, USA	22,000	1.7	30	65	33	43
Minnesota, USA	48,000	2.4	31	78	35	36
Funen, DK	62,000	1.0	58	81	55	18

- Compliance varies from 35–90%
- <30% of larger polyps and cancers bleed sufficiently to be detected by fecal occult blood testing

CT-Scan staging in rectal malignancy

- Overall tumor detection 65–70%
- Perirectal fat infiltration 50–60%
- Absent perirectal fat infiltration ~80%
- Lymph node involvement ~20%
- Absent lymph node involvement ~100%
- Overall staging accuracy of invasiveness 35–95%



- Determine the absolute risk (AR) of CRC in a 55 year old patient whose father developed proven CRC at age 59, his 50 year old brother had an adenomatous colonic polyp, and a grandmother and an aunt of unknown age had CRC.

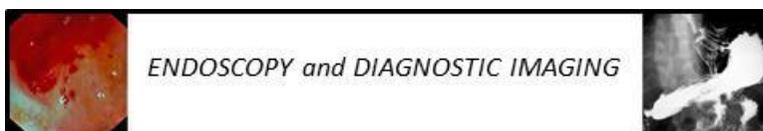
Familial Risk of Colorectal Neoplasia (CRC)	
Familial Setting	RR
○ One first-degree relative with CRC	2.25
○ < 45 yrs	3.87
○ 45 – 59 yrs	2.25
○ > 59 yrs	1.82
○ Two or more first-degree relatives with CRC	4.25
○ Only two first-degree relatives with CRC	3.76
○ One second- or third-degree relative with CRC	1.5
○ Two second-degree relatives with CRC	2.3
○ One first-degree relative with an adenoma < 60 yrs	1.99

Abbreviation: AR, absolute risk; RR, relative risk
 $RR=(2.25 \times 1.99 \times 2.3)= 10.3$; Absolute risk for average risk person, 5%; absolute risk for this person, $RR \times AR= 10.3 \times 5\% = 51.5\%$

Printed with permission: Winawer SJ. *Best Practice & Research Clinical Gastroenterology* 2007; 21(6): pp. 1035.

- Give the recommended follow-up interval for post-polypectomy colonoscopic surveillance.

Finding on screening	Follow-up interval
○ 1-2 tubular adenomas < 1 cm	5-10 yrs
○ 3-10 adenomas, or any adenoma with villous elements, high-grade dysplasia or ≥ 1 cm in size	3 yrs
○ patients with prior advanced adenomas after normal follow-up examination, or only 1-2 small tubular adenomas	< 3 yrs
➤ 10 adenomas (possible familial syndrome)	
○ Large sessile adenoma removed piecemeal	2-6 months to confirm complete

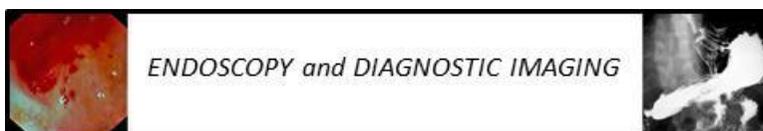


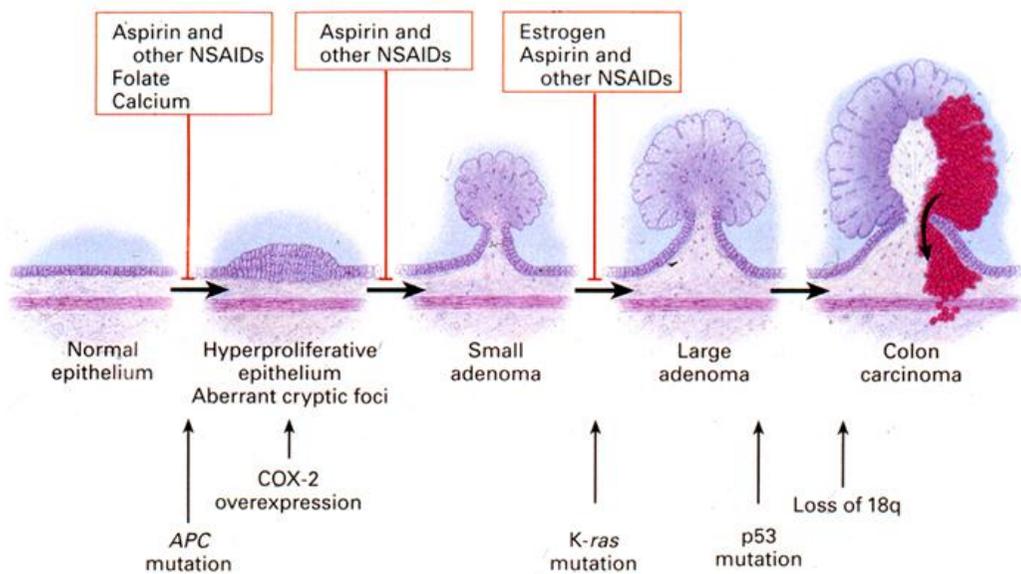
- | | |
|---|--------------------|
| | removal |
| ○ Small distal hyperplastic polyps without adenomas (suspect hyperplastic polyposis syndrome) | 10 yrs |
| ○ Proximal colon hyperplastic polyps | Interval uncertain |

Adapted from: Rex DK. *2008 ACG Annual Postgraduate course book*: pp. 90; and printed with permission: Levin B, et al. *Gastroenterology* 2008;134(5): pg. 1588.

- Give the endoscopic techniques or technical improvements which enhance the colonoscopic sensitivity for CRC screening.
 - Improve performance skills of colonoscopist
 - Improve bowel cleansing
 - Improve insertion
 - Cap-fitted colonoscopy
 - Overtubes
 - Imaging
 - Wide-angle white light colonoscopy
 - Narrow-band imaging
 - Chromoendoscopy
 - Confocal laser microscopy

Sequence of adenoma – CRC progression





- Give the molecular changes involved in the progression of normal colonic epithelium, to adenoma, to CRC, and give the pharmacological or nutritional agents which have been shown to be effective chemoprevention to reduce the risk of development or redevelopment of colorectal adenomas/CRCs.

➤ Drugs

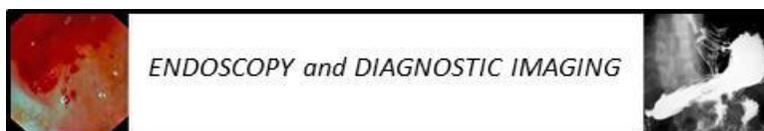
- ASA
- Coxibs
- 5-ASA in IBD
- Hormone replacement therapy (HRT) in post menopausal women

➤ Nutrients

- Selenium
- Calcium (+ vitamin D)
- Non-western diet (low intake of saturated fats in red meat)
- High intake of green leafy vegetables
- Possibly folate, vitamins C, E, B-carotene
- Probably not dietary fiber

➤ Exercise

Adapted from: Arber N, and Levin B. *Gastroenterology* 2008;134(4): 1224-1237; and Meyerhardt JA, et al. *JAMA* 2007;298(7): 754-764.



Colonic polyps and tumours: familial forms

Useful background: Genetic testing is part of the standard management of families with FAP. What are the methods used for genetic testing in FAP to confirm the diagnosis of FAP in suspected cases, and to determine if a person from a family with FAP is a gene carrier.

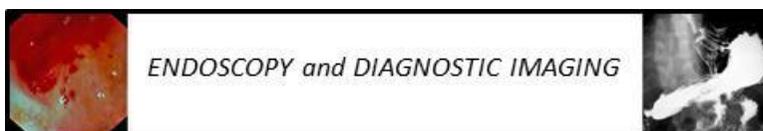
- *In vitro* protein truncation in FAP:
 - Detects the presence of truncating mutations in vitro
 - Detects a mutation in 80% to 90% of affected families known to have FAP
 - Near 100% effective in family members once the presence of a mutation has been found in an affected person

- Gene sequencing
 - Often preceded by single-strand conformational polymorphism (SSCP) or denaturing gradient gel electrophoresis (DGGE) to narrow the area of the gene where sequencing is to be performed
 - Up to 95% effective in finding a disease-causing mutation if it is present
 - Near 100% effective in family members once the presence of a mutation has been found in an affected person

- Linkage testing
 - Used if other methods unsuccessful
 - Two or more affected persons from two generations must be living for DNA to be obtained
 - Effective in >95% of families, with >98% accuracy with present linkage markers.

- Genotype-phenotype correlations:
 - These have not yet been found to be of precise use in the clinical setting
 - The following correlations have been made:
 - CHRPE (congenital hypertrophy of the retinol pigment epithelium): present in families with mutations distal to exon 9 of the APC gene
 - Dense polyposis: present with mutations in the mid portion of exon 15
 - AFAP/AAPC: found with mutation in the extreme proximal or distal end of the gene
 - Osteomas and desmoids (Gardner's syndrome): more commonly found with mutations in the distal portion of exon 15

Abbreviations: DGGE, denaturing gradient gel electrophoresis; SSCP, single-strand conformational polymorphism



Adapted from: Doxey BW, Kuwada SK, Burt RW. *Clin Gastroenterol Hepatol.* 2005;3(7):633-41; and Burt R, Neklason DW. *Gastroenterology* 2005;128(6):1696-716.

FAP-Surveillance after ileorectal or ileal pouch anal anastomosis

- Surveillance endoscopy at 4–6 months interval
- Biopsy and destruction of all adenomatous lesions
- Lower-power Nd-YAG laser or argon beam electrocoagulation to be preferred to prevent deep mural injury, responsible for excessive scarring and irregular nodular deformity

FAP-Risk Factors for Cancer in Rectal Stump

- Large number of rectal polyps at time of colectomy
- The presence of large size rectal polyps
- The presence of confluent 'carpet-like' adenomatous growth
- Presence of colonic cancer at/or prior to colectomy
- Lack of compliance with follow-up surveillance
- Increasing chronological age

• Clinicopathologic Classification of Endocrine Tumors of the Appendix

➤ Well-differentiated tumor (carcinoid)

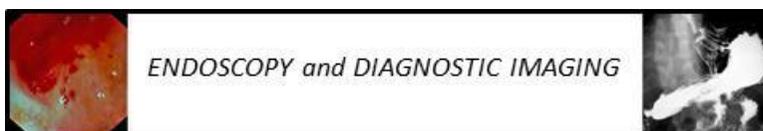
- Benign behaviour: non-functioning, confined to appendiceal wall, non-angioinvasive, < 2 cm in size,
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor
- Uncertain behaviour: non-functioning, confined to subserosa, ≥ 2cm in size or angioinvasive
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor

➤ Well-differentiated endocrine carcinoma (malignant carcinoid)

- Low-grade malignant: invading the mesoappendix or beyond or with metastasis
 - Serotonin-producing carcinoma with or without carcinoid syndrome

➤ Mixed exocrine-endocrine carcinoma

- Low grade malignant:
 - Goblet cell carcinoid





- Clinicopathologic classification of endocrine tumors of the colon and rectum
 - Well-differentiated endocrine tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to mucosa-submucosa, non-angioinvasive, < 2 cm in size,
 - Enteroglucagon-producing tumor
 - Serotonin-producing tumor
 - Uncertain behaviour: non-functioning, confined to mucosa-submucosa, ≥ 2 cm in size or angioinvasive
 - Enteroglucagon-producing tumor
 - Serotonin-producing carcinoma with or without carcinoid syndrome
 - Well-differentiated endocrine carcinoma (malignant carcinoid)
 - Low-grade malignant:
 - Enteroglucagon-producing carcinoma
 - Serotonin-producing carcinoma with or without carcinoid syndrome
 - Mixed exocrine-endocrine carcinoma
 - High grade malignant (small to intermediate cell) carcinoma
 - Mixed exocrine-endocrine carcinoma
 - Moderate to high grade malignant
 - Primary Sites of Origin of 95% of Carcinoid Tumors
 - Appendix: 1/200-300 appendectomies
 - Rectum: 1/2,500 proctoscopies
 - Small intestine: 28/10,000,000 persons

Carcinoids: Tumor size and metastases

- Appendix and rectum
 - <1 cm: never metastases
 - >2 cm: always metastases

- Carcinoid tumor: Rectum

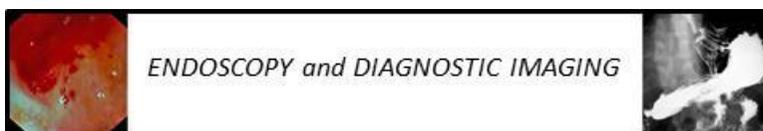
○ Lymphnode metastases	<1 cm	1.7%
○ Lymphnode metastases	1.0-2 cm	10%
○ Lymphnode metastases	>2 cm	80%

- Give the symptoms, risk factors and types of radiation damage to the colon, as well as endoscopic changes.

- Type
 - Acute / early radiation damage
 - mucosal necrosis and inflammation
 - Late / chronic radiation damage
 - Vascular fibrosis and occlusion
 - Fibrotic narrowing
 - Mucosal ulceration / telangiectasia

- Risk factors
 - Radiation factors
 - The total delivered dose of external irradiation
 - The total treatment time
 - The dose per fraction
 - The dose rate of intracavitary irradiation
 - The combined doses of external and intracavitary irradiation (expressed as Time-Dose-Fractionation (TDF) or Linear-Quadratic (L-Q) number)
 - Patient factors
 - Age;
 - Height and weight
 - Diabetes mellitus
 - Possible cardiovascular disease
 - Previous abdominal surgery, (especially gynecological, and gastrointestinal surgery, including cholecystectomy)

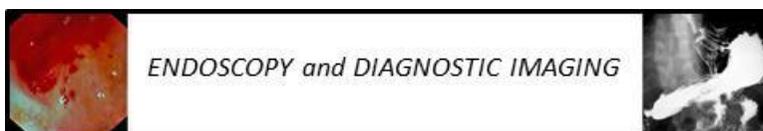
- Symptoms*
 - Blood loss (73%)
 - Diffuse pain (51%)
 - Diarrhea (44%)
 - Pain attacks (43%)
 - Incontinence (33%)
 - Anal pain (30%)



- Constipation (14%)
- Both diarrhea & constipation (5%)
- Endoscopic findings*
 - Telangiectasia (51%)
 - Friable mucosa (30%)
 - Luminal narrowing (81%)
 - Solitary ulcer (25%)
 - Diffuse ulceration (18%)
 - Fistula (19%)
- Angiographic features of angiodysplasia
 - Dilated tortuous slowly emptying intramural veins with prolonged opacification
 - Vascular tuft
 - Early filling vein
 - Dilated feeding artery or arterial feeder to antimesenteric border
 - Intraluminal extravasation

* The numbers in brackets represent the approximate frequency of patients with radiation colopathy who have these symptoms and these endoscopic findings.

Entity Appearance	Age at Clinical Size	Endoscopic Manifestation	
Hemangiomas capillary	Any age	>5.0mm	Nodular
Cavernous the	Any age	Frequently >1.0 cm	Polypoid lesions that protrude into bowel lumen
Blue rubber BLEB conventional	Younger age	Massive; in cm	Polypoid; seen by X-ray
Kaposi grouped, sarcoma	Any age (AIDS)	mm to 1-2 cm	Nodules, or irregular
Idiopathic angiodysplasia the mucosa	Usually over age 60	>3.0 mm	Flattened, not above



<i>Early lesion</i>			
<i>Late lesion</i>	usually over age 60	<5.0 mm	Red puncta, or Irregular patches
Hereditary Hemorrhagic nodular, Telangiectasia	Childhood Epistaxis, GI bleeding	Few mm up to 2-3 cm often after	Multiple, red, pinpoint, or Telangiectatic
(spider)	4-5th decade		
Congenital Arteriovenous Malformation	Any age, but often bleed in adolescence	Variable	Variable, large clots often present

- Clinical features of upper gastrointestinal bleeding in elderly versus younger patients

➤ Similarities

- Presenting manifestations of bleeding: hematemesis (50%); melena (30%); hematemesis and melena (20%)
- Peptic ulcer disease most common etiology
- Safety and efficacy of endoscopic therapy

➤ Differences (in elderly patients)

- Fewer antecedent symptoms (abdominal pain, dyspepsia, heartburn)
- Prior aspirin and NSAID use
- Presence of comorbid conditions
- Higher rates of hospitalization
- Higher rates of rebleeding Higher mortality rate

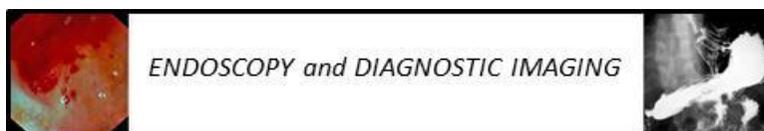
Adapted from: Farrell JJ, and Friedman LS. *Gastroenterol Clin North Am.* 2001;30(2):377-407, viii.

Diagnostic imaging

- Polyps

➤ Barium

- For any adenomatous polyp, the risk for malignancy goes up with increase in size, and a transition from tubulae (to tubulovillus) to villous histological type
- Sessile or pedunculated
- Left side > right of colon (~ 50% rectosigmoid)
- Single or multiple (in 25 to 50 %)
- Homogenous adenoma

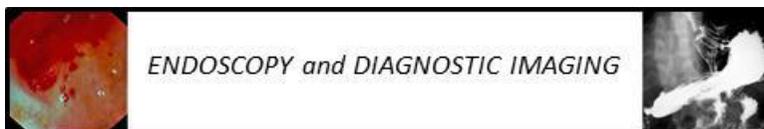


- Small / large
- May be associated with
 - FAP “Gardner syndrome”
 - HNPRC – endometrium, ovary, renal pelvis, stomach, small bowel
- CT colonography (CT C)
 - Mass
 - Irregular shape
 - Flat (RC > LC) / lobulated filling defect (LC > RC)
- Gardner Syndrome
 - Sebaceous cysts
 - Mesenchymal tumors
 - Fibromus
 - Lipofibromas
 - Lipomas
 - Neurofibromas
 - Fibrous tissue tumors
 - Desmoid
 - Keloid
 - Peritoneal adhesions
 - Retroperitoneal fibrosis
 - Mesenteric fibrosis
 - Osteomas
 - Jaw
 - Maxilla
 - Skull

Distinguishing Diagnosis: CT of stool

- Inhomogeneous
- Air / fat attenuation
- Moves

- Villous adenomatous polyp
 - In homogenous
 - Barium interstices (like a “cauliflower”)
- CT
 - Thick wall
 - Irregular thickening
 - Distention
 - Leiomyomas



- Variable size
- Juvenile polyposis syndrome (JPS)
 - Syndrome many polyps
 - Sporadic fewer polyps
 - Varying size
 - Cystic spaces
 - Cystic spaces filled with mucin
 - Increased connective tissue stroma
 - May co-exist with FAP
- Lipoma
 - Smooth surfaced submucosal mass
 - Intraluminal
 - Often > 3 cm
 - Does not displace lumen (because lipoma is pliable)
 - Round / sausage-shaped
 - Often on right-sided
 - Ileocecal valve, when involved large
 - CT
 - Fatty mass
 - Ring of mesenteric fat
 - May show intussusception of colon

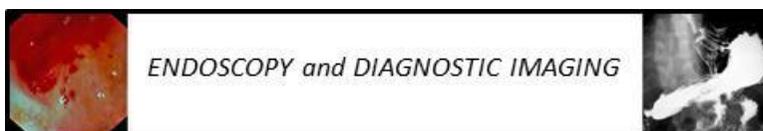
.....
 Distinguishing diagnosis: lipoma vs. serosal metastasis

	Lipoma	serosal metastasis
○ Multiple	-	+
○ Tethering	-	+

.....

- Colorectal Cancer (CRC)

- Barium study
 - Mass
 - Annular mass may resemble a “napkin ring” or an “apple core”
 - Lobulated mass
 - Edge of mass may suddenly stop or produce a “shoulder”
 - May narrow (obstruct) colon
 - Signs of colitis proximal to obstructing CRC mass
 - If ileocecal valve does not open to relieve pressure of obstruction, venous outflow may fall and there may be associated ischemic changes usually < 6 cm in size
 - Synchronous CRC ~ 5%



- Metachronous CRC ~ 5%

➤ CT

- Perforation
 - Fluid / soft tissue mass
- Extraluminal air

	Perforated CRC	Diverticulitis
○ Segment	Short	Long
○ Wall thickening	+	-

➤ CT colonography (CTC)

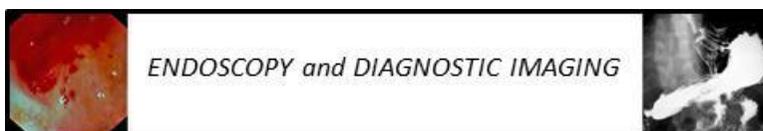
- Mass
- Mass may have irregular surface
- Obstruction
- Fold (haustral) thickening
- Wall
 - Thickening
 - Circumferential wall thickening and perirectal fat
- Caution rectal cancer may look like a region of normal collapse of the colonic wall
- Intussusception
 - Shortened colon
 - Sausage-shaped filling defect
 - Proximal end of filling defect looks like “coiled spring”

➤ CT window settings

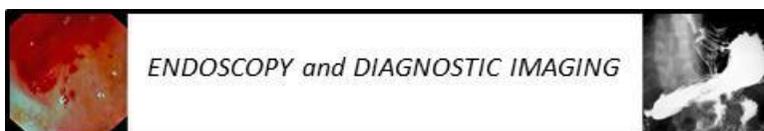
- Soft-tissue cancer
- Lung window polyps

➤ Endoscopic ultrasonography (EUS)

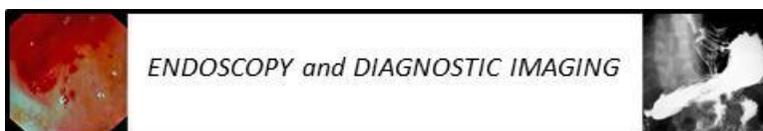
- Inner echogenic €
 - Balloon mucosa
- Hypoechoic (HE)
 - Muscularis mucosa
- Middle E
 - Submucosa
- HE
 - Muscularis propria (MP)
- Outer E
 - Interface of MP
 - Perirectal fat
 - Staging accuracy ~ 90%
 - Sensitive to find recurrent tumor near resection anastomosis
 - Sensitive to distinguish between metastatic inflammatory nodes



- Detecting CRC recurrence
 - Local
 - Barium enema / CTC
 - Lumen
 - Mass
 - Lumen: eccentric narrowing
 - Widened presacral space, with fuzzy margins
 - Lymph adenopathy
 - Extraluminal / distant
 - CT
 - Retroperitoneum
 - Liver
 - Lung
- Metastatic cancer to colon
- Direct extension
 - Mass effect
 - Nodular folds
 - Narrowed lumen
 - Pelvic primary (uterus, ovary, prostate, kidney)
 - Rectum* anterior wall
 - Sigmoid inferior wall
 - * Prostate cancer – mass effect on anterior wall, but may also cause annular narrowing of rectum
 - GI primary
 - Stomach
 - Mass effect
 - Narrowing of colon
 - Tethering of superior portion of transverse colon (TC)
 - Pancreas
 - Mass effect and narrowing of colon
 - Tethering in inferior portion of TC
- Intraperitoneal spread to serosa from malignant ascites
 - Places where flow of intraabdominal fluid is slowed, and malignant ascites seeds the serosa of colon
 - Pouch of Douglas
 - Ileocecal region
 - Superior wall of sigmoid colon
 - Right pariacolic gutter
- Hematogenous spread
 - Breast cancer
 - Metastasis to submucosa of colon
 - Narrowing lack of distensibility of colon (“linitis plastica” appearance)



- Lymphoma
 - Filling defects
 - Multiple
 - Smooth-surfaced
 - Early
 - Focal segment
 - Three types:
 - Polypoid mass
 - May be associated with intussusception
 - Narrowing
 - Dilated segment (aneurysmal); may be associated with ulceration
 - Cecum / rectum
 - Late diffuse segment multiple filling defects
 - Haustra thickening
- CT
 - Bowel wall thickening
 - Focal / diffuse
 - Perforation (~ 25%)
 - May be localized
 - Fluid / gas in lymphomatous mass
- Colitis Cystica Profunda
 - Filling defects limited to colon
 - Multiple
 - Round
 - Mucosal / submucosal
 - Rectum
 - Filled with mucin
 - May sometimes resemble a large villous adenoma / carcinoma
- Post Inflammatory Polyp
 - Filling defects
 - Multiple
 - Round / elongated
 - Long / thin
 - May be branched
 - Focal / diffuse
 - Mass lesion like villous adenoma / carcinoma rarely seen in right colon
- Pseudopolyp
 - Filling defect (stool-filled diverticulum)
 - Round
 - Surrounding ring of barium

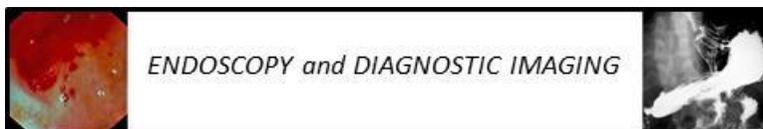


- CT
 - Heterogenous or homogenous
 - Filling defect seen in lumen of diverticulum
 - Defect protrudes into lumen of colon
- CTC not usually useful to distinguish between polyp vs. stool
- Inverted Colonic Diverticulum
 - Caused by incomplete distention of colon
 - Cannot be distinguished from polyp
- Nodular Lymphoid Hyperplasia (NLH)
 - Filling defects
 - Multiple small (< 4 mm diameter)
 - Submucosal
 - Nodular
 - Umblication
 - Entire colon
 - Uniform distribution
 - RC > LC

.....

Distinguishing diagnosis: multiple filling defects

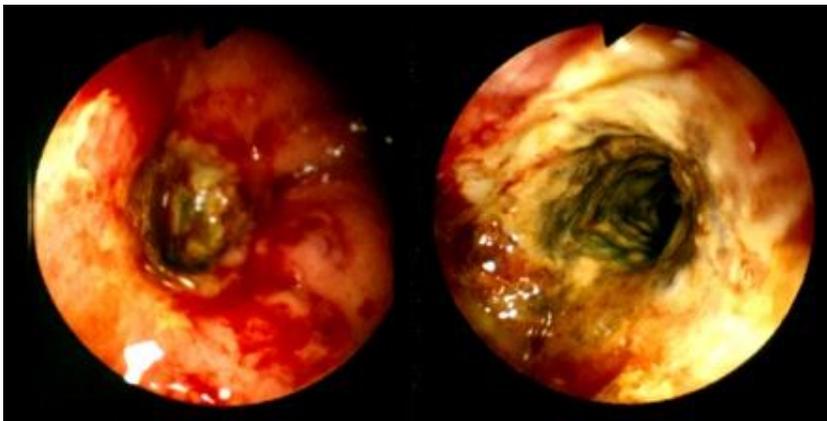
- Polyposis syndrome polyps
 - Larger
 - Variable size
 - Pedunculated
 - Crohn colitis aphthous ulcers
 - Distribution
 - Patchy
 - Segmental
 - Diffuse lymphoma
 - Larger (> 4 mm diameter)
 - Nodules
 - Smooth
 - Round
 - Variable size
 - Retained stool
 - Angular margins
 - Moves
-



LOWER GASTROINTESTINAL BLEEDING

○ Diverticular Disease	30%
○ Cancer/Polyps	18%
○ Colitis	17%
○ Unknown	16%
○ Angiodysplasia	7%
○ Other miscellaneous	8%
○ Post-polypectomy	6%
○ Hemorrhoids/anorectal disorders	4%

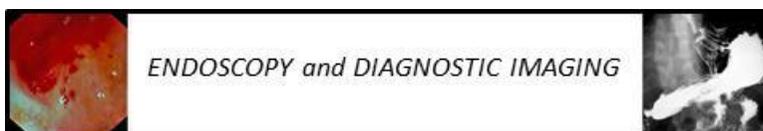
* The numbers in brackets represent the approximate frequency of patients with radiation colopathy who have these symptoms and these endoscopic findings.



➤ Causes of hematochezia in adults

Causes	Approximat frequency (%)	Comments
➤ Diverticular disease	30	<ul style="list-style-type: none"> ○ Stops spontaneously in 80% of patients ○ In one series, the need for surgery may be unlikely if < 4 U red cell transfusion given in 24 h, but is required in 60% of patients receiving > 4 U in 24 h
➤ Colonic vascular ectasia*	25	<ul style="list-style-type: none"> ○ Frequency of these lesions vary widely in clinical series ○ Acute bleeding appears to be more frequently due to lesion in proximal colon

- Colitis 10
 - Ischemic colitis often presents with pain and self-limited haematochezia. Colitis is segmental, most often affecting splenic flexure
 - Bleeding may also occur from other types of colitis, such as Crohn disease or ulcerative colitis
 - Bloody diarrhea is most frequent symptom of infectious colitis and inflammatory bowel disease of the colon
 - Colonic neoplasia/ post-polypectomy 10
 - Post – polypectomy bleeding is frequency self-limited, and may occur ≤ 14 days after polypectomy
 - Anorectal causes (including hemorrhoids, varices) 5
 - Anoscopy/proctoscopy should be included in the rectal initial evaluation of these patients
 - Upper gastrointestinal sites (including duodenal/gastric ulcer, esophageal / gastric varices) 5
 - A negative nasogastric aspirate does not exclude this possibility
 - Small bowel sites (including Crohn ileitis, Meckel's diverticula, tumors, vascular ectasia) 10
 - Frequency diagnosed by radiologic studies or enteroscopy after the acute bleeding episode has resolved
 - No site of bleeding is found 5
 - Angiodysplasia,
 - Vascular dysplasia,
 - Vascular ectasia,
 - Hemangioma,
 - Angioma
- *Arteriovenous malformations

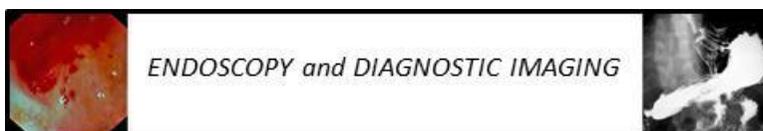


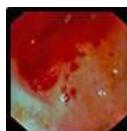
Lower GI Bleeding (LGIB)

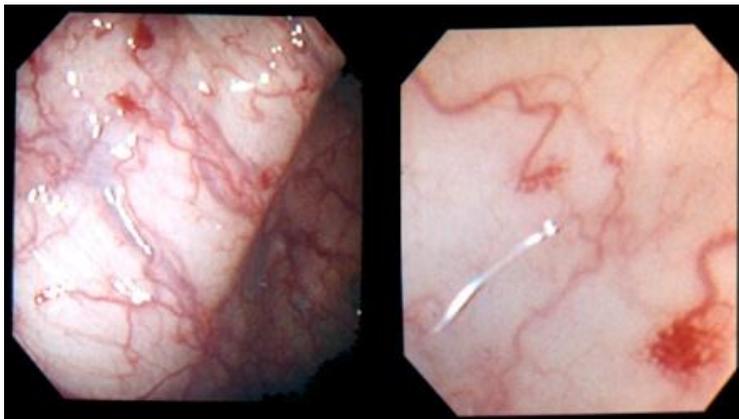
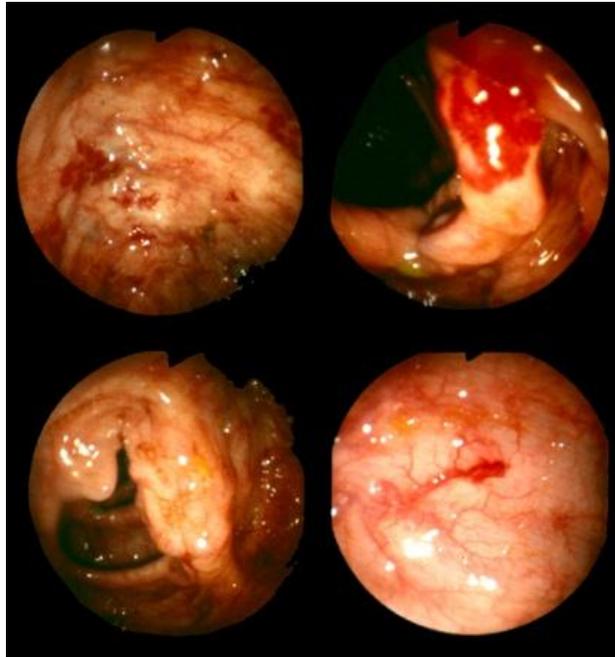
A man who has sex with men (MSM) presents with rectal bleeding, urgency, tenesmus:

Possible diagnoses related to HIV/AIDS

- Infections
 - CMV, HSV, *C. difficile*, *Shigella* sp., campylobacter, entamoeba histolytica
 - Herpes simplex infection involving the distal rectum
 - Infectious ulcerations due to HSV, CMV, tuberculosis, histoplasmosis, HPV, LGV
- Cancer
 - Anorectal carcinomas are more common in homosexual men than in the general population, and the risk increases dramatically with HIV infection
 - CRC – lymphoma, squamous cell carcinoma
 - Kaposi's Sarcoma
 - Lymphoma
 - Perirectal abscesses
- Anal fissure
- Trauma
- Squamous cell Ca, CRC
- Infections
- Idiopathic ulcers
- Perirectal abscess, fistula
- Local diseases
- Bowel diseases
- Investigation
- Anoscopy and sigmoidoscopy with mucosal biopsy and with evaluation of anorectal pus for PMNs gram stain for gonococci
- Tzanck prep, and culture for HSV, VDRL and PCR for *C. trachomatis*. Biopsy should be performed even if visual inspection of the anal canal is normal, since a normal appearance does not exclude high grade dysplasia.







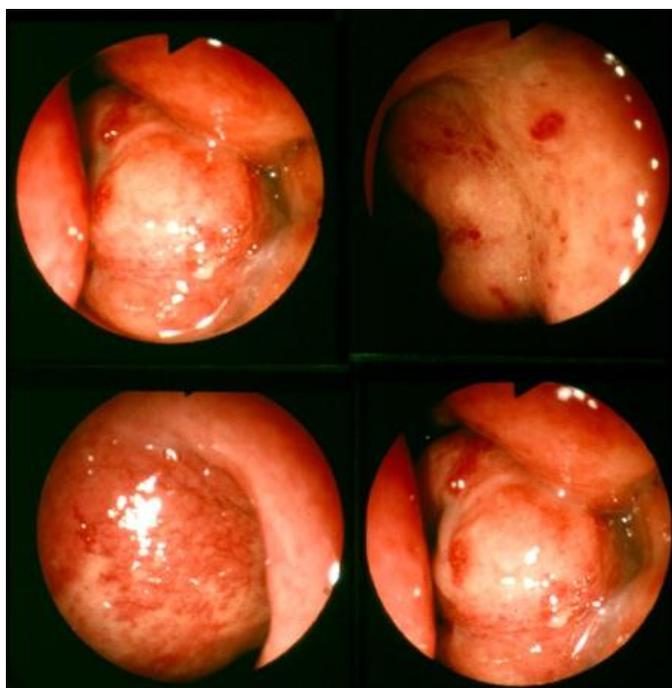
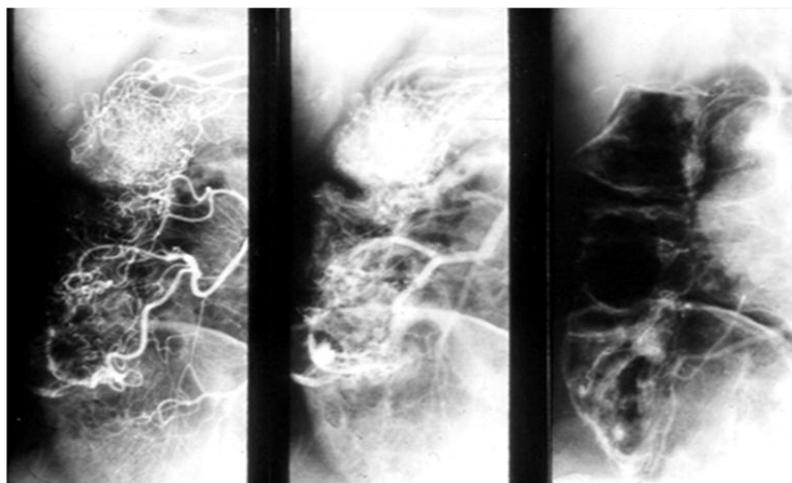
- Angiographic features of angiodysplasia
 - Dilated tortuous slowly emptying intramural veins with prolonged opacification
 - Vascular tuft
 - Early filling vein
 - Dilated feeding artery or arterial feeder to antimesenteric border
 - Intraluminal extravasation

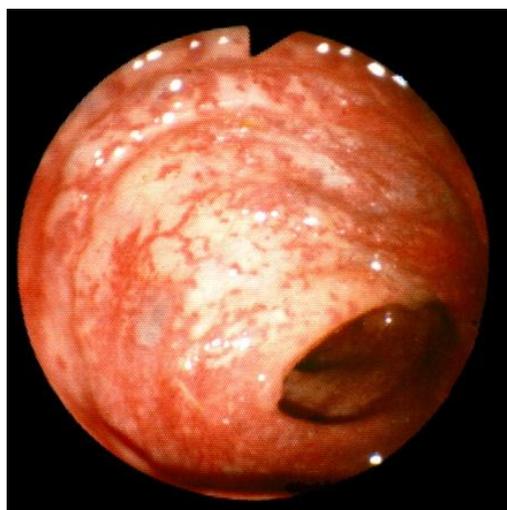
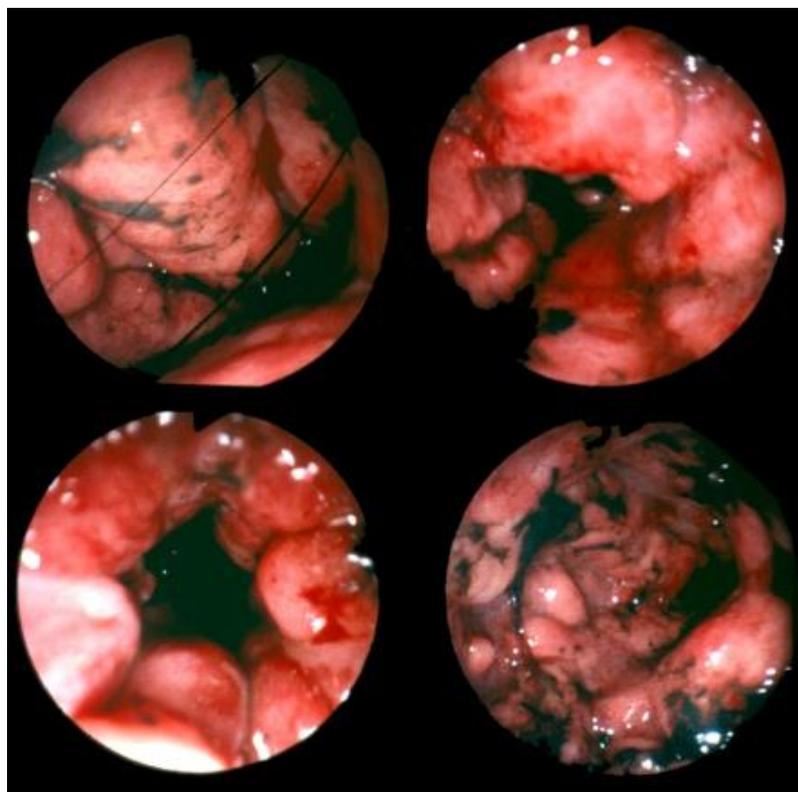
➤ Angiography – Angiodysplasia

clusters
small
arteries

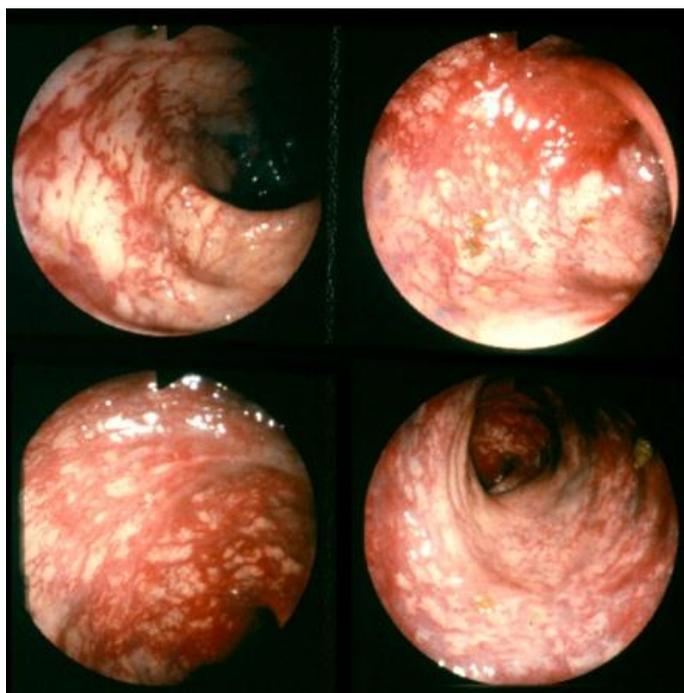
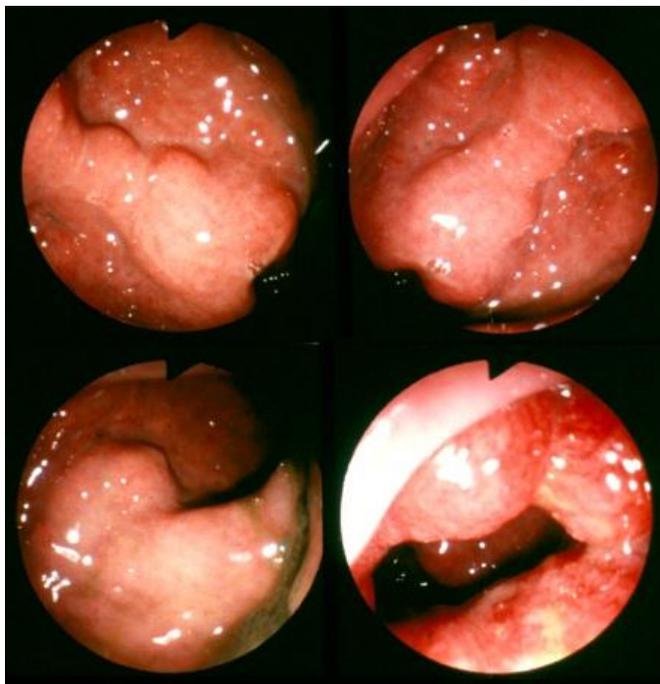
intense
opacification
bowel wall

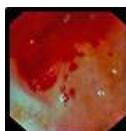
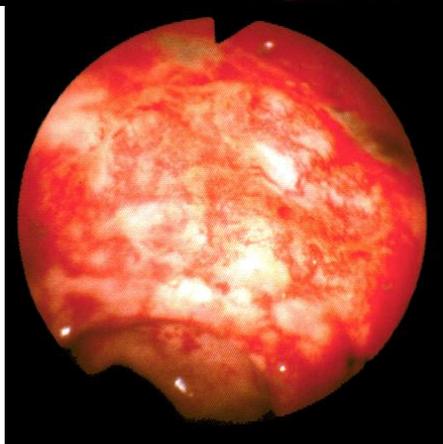
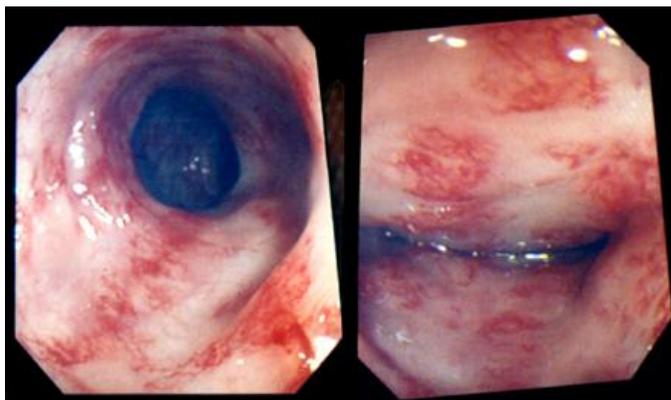
early
venous
filling



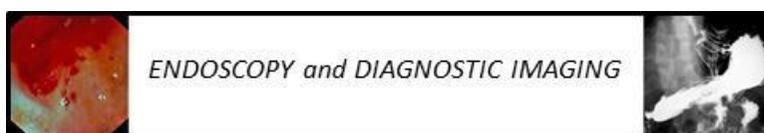


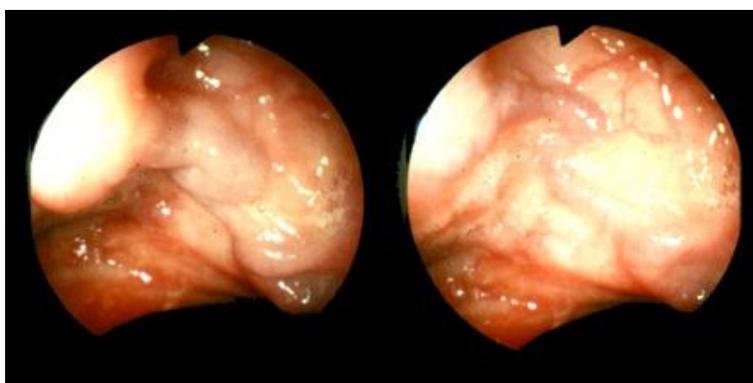
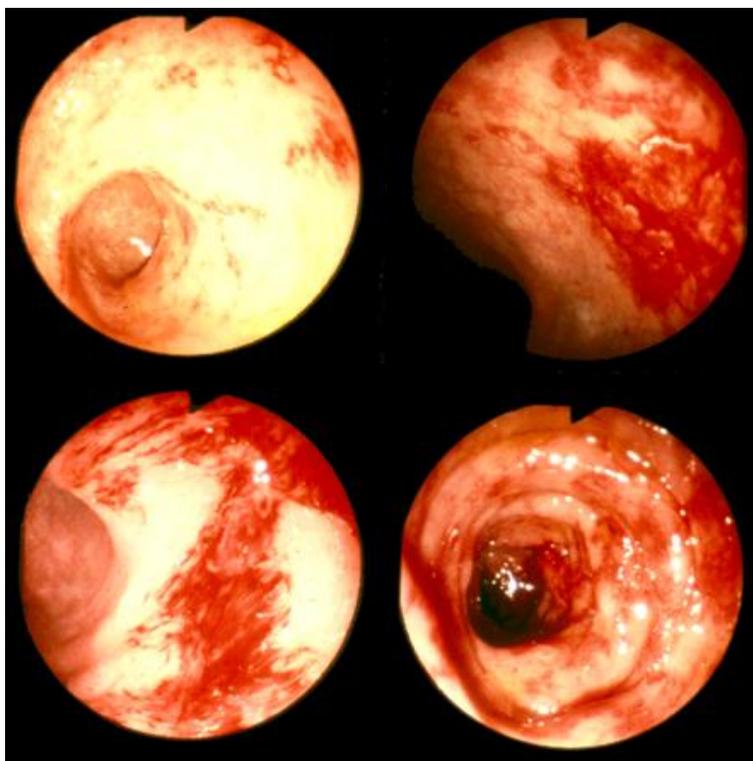


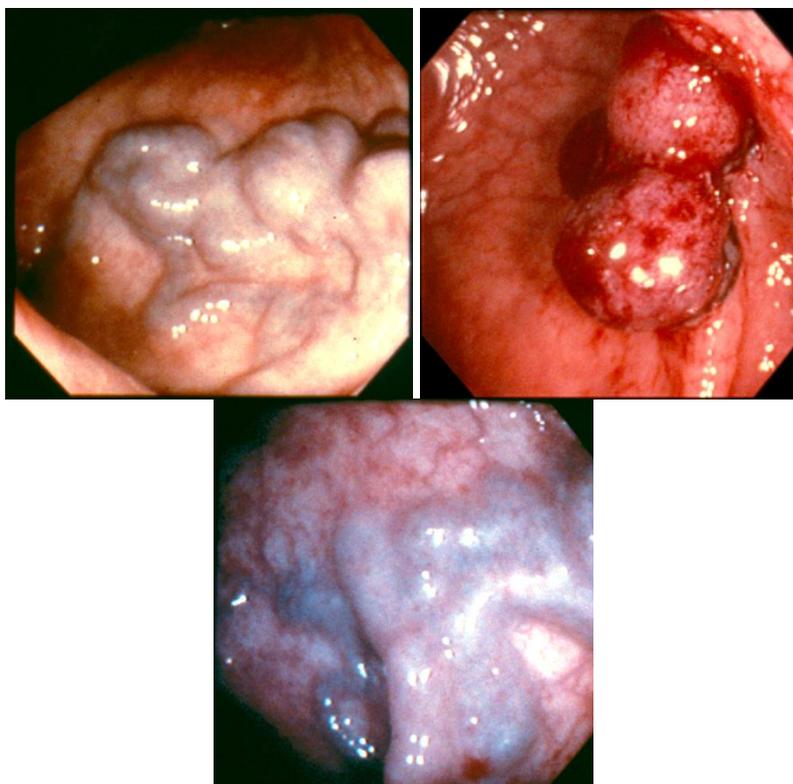
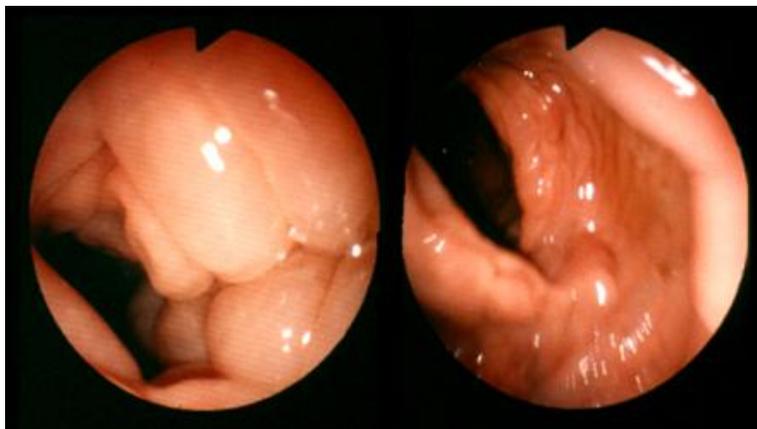




Entity	Age at clinical manifestation	Size	Endoscopic appearance
➤ Hemangiomas capillary	Any age	>5.0 mm	○ Nodular
➤ Cavernous	Any age	Frequently > 1.0 cm	○ Polypoid lesions that protrude into the bowel lumen
➤ Blue rubber BLEB	Younger age	Massive; in cm	○ Polypoid; seen by conventional X-ray
➤ Kaposi sarcoma	Any age (AIDS)	mm to 1-2 cm	○ Nodules, grouped, or irregular
➤ Idiopathic angiodysplasia of the mucosa			
<i>Early lesion</i>	Usually over age 60	>3.0 mm	○ Flattened
<i>Late lesion</i>	Usually over age 60	< 5.0 mm	○ Red puncta, or irregular patches
➤ Hereditary hemorrhagic telangiectasia	Childhood epistaxia, GI bleeding often after 4-5 th decade	Few mm up to 2-3 cm (spider)	○ Multiple, red pinpoint, nodular, or telangiectatic
➤ Congenital Arteriovenous Malformation	Any age, but often bleed in adolescence	Variable	○ Variable, large clots often present







ENDOMETRIOSIS

Practice Pointers:

- Give the postulated pathogenetic sequence of the development of endometriosis, the intestinal localization, and histological characteristics.
 - Serosal implant of endometrial focus
 - Inflammatory response secondary to retained menstruation products
 - Formation of adhesions
 - Extension/invasion of M. Propria
 - Hypertrophy/hyperplasia
 - Fibrosis
 - Extension/invasion of submucosa
 - Hypertrophy of M. mucosae
 - Rarely extension/invasion of mucosa

➤ Intestinal localization

Sigmoid > Rectosigmoid junction > Appendix > Rectum = Cecum

➤ Histological characteristics

- Glandular tubules
- Stromal tissue
- Hemorrhages
- Hemosiderine laden macrophages
- Fibrosis with deposition of hemosiderine and lipid debris
- Hypertrophy/hyperplasia of surrounding smooth muscle

Lipodystrophy Syndrome: Spectrum of Clinical signs

➤ Fat accumulation

- Dorsocervical fat pad enlargement (“Buffalo hump”)
- Increased abdominal girth (visceral adiposity) Breast enlargement
- Multiple symmetric lipomatosis (resembling Madelung disease)

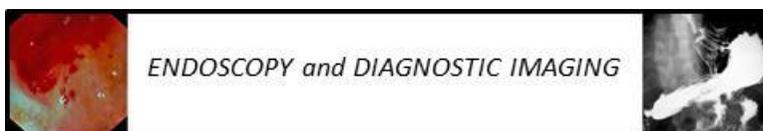
➤ Fat loss

- Peripheral fat wasting / lipodystrophy

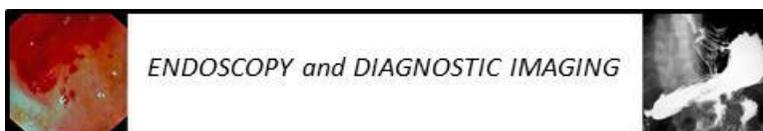
Diagnostic imaging

➤ Endometriosis

- Mass
 - Intramural (submucosal)
 - Extramural (subserosal)
- Mucosa
 - Intact
 - pleated
- Tethered folds



- Sigmoid, inferior surface
- Annular constriction (rare)
- Mucocele of the appendix
 - Filling defect
 - Smooth surface
 - Base of cecum
 - CT
 - Cystic
 - Tubular
 - Wall
 - Thin
 - Calcified
 - Distended
 - Internal contents (eg., stool) causing obstruction
- Definitions: cyst-like intramural collections of air
 - Small bowel
 - Pneumatous intestinalis, pneumatosis cystoidis intestinalis
 - Colon
 - Pneumatosis cystoids coli
- Pneumatosis cystoids coli
 - Air-filled submucosal cysts
 - Cysts do not communicate with lumen
 - Variable size and shape
 - Any intramural position
 - Pneumatosis coli
 - Intramural air cyst linear shape non-dependent position

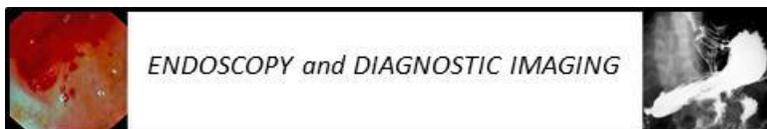


COLON DIAGNOSTIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**



Case 1

30 year old presents with vague lower abdominal discomfort.

Case 2

Patient presents with rectal bleeding after R. hemicolectomy for CRC.

Case 3

Patient presents with LLQ abdominal tenderness and fever.

**Case 4**

69 year old woman presents with rectal bleeding.



Case 5

62 year old woman presents with vague abdominal pain.

Case 6

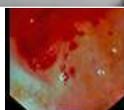
35 year old man with ulcerative colitis presents with abdominal pain and distention.

Case 7

Patient presents with 5 year history of intermittent bloody diarrhea.

Case 8

25 year old male with known Crohn disease presents with abdominal bloating.

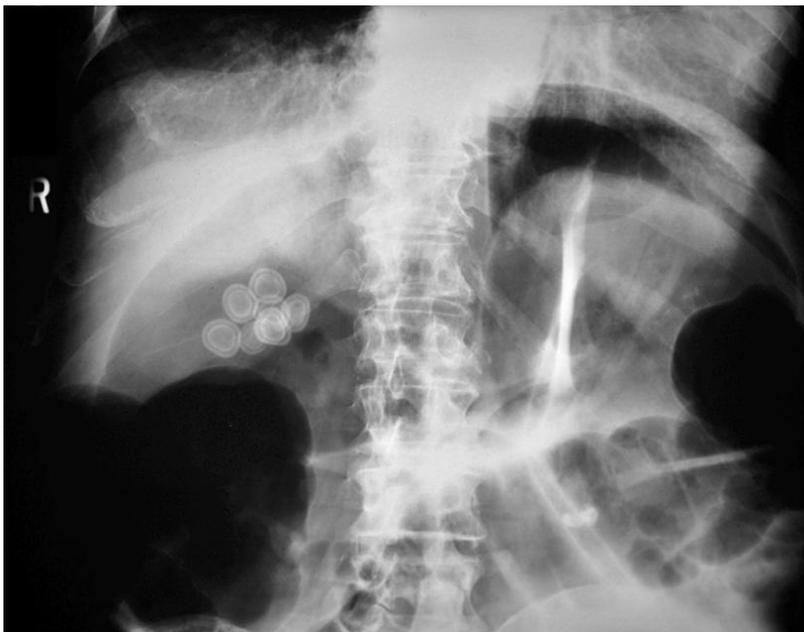


ENDOSCOPY and DIAGNOSTIC IMAGING



Case 9

Patient presents with abdominal discomfort and bloating.

Case 10

92 year old on diuretics for CCF presents with abdominal bloating.

Case 11



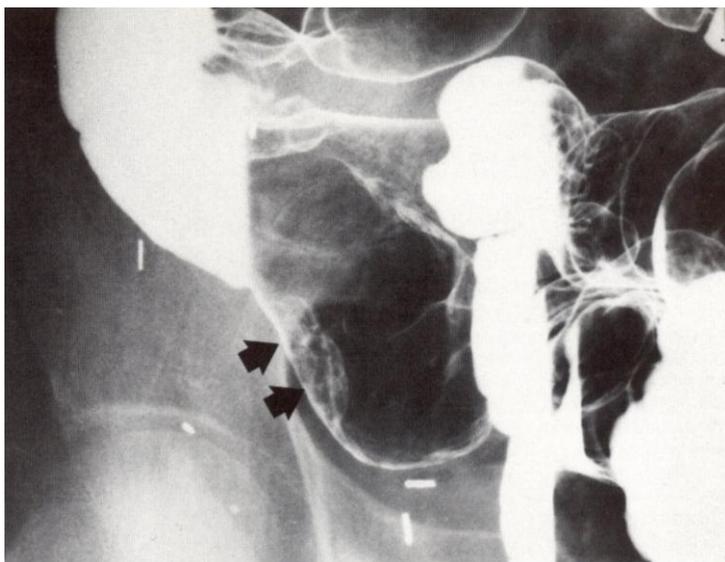
73 year old woman presents with iron deficiency anemia.

Case 12



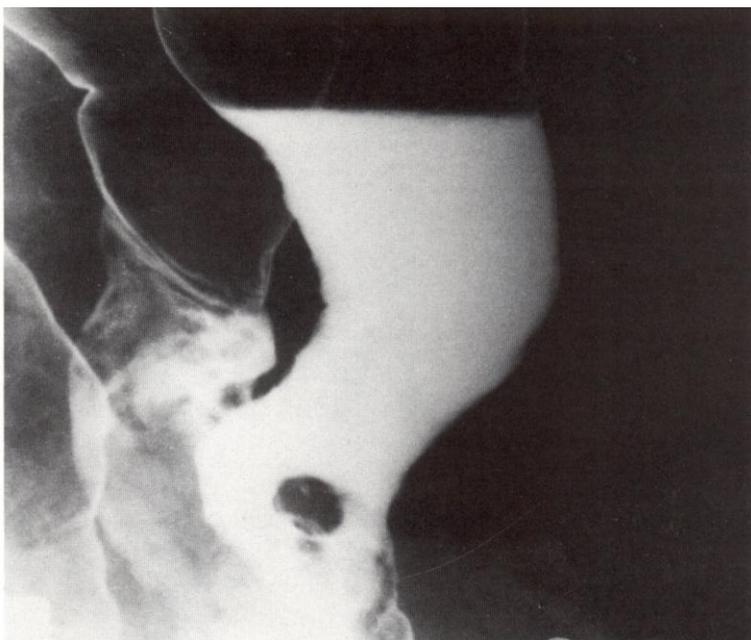
Screening colonoscopy

Case 13

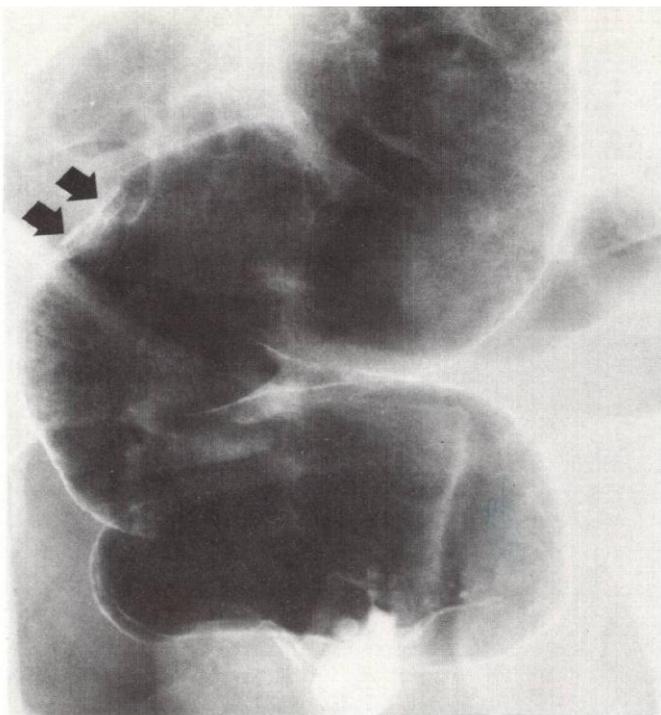


Interval colonoscopy performed for symptoms

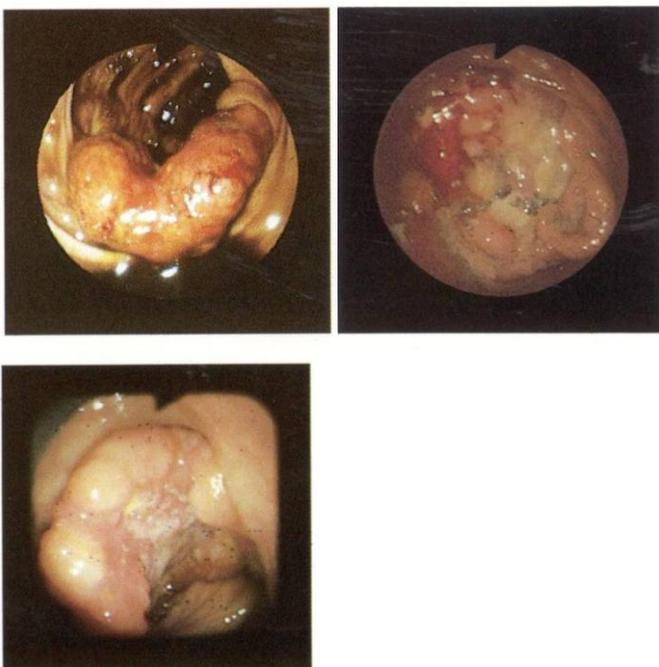
Case 14



FOB positive in 55 year old woman on NSAIDs for OA

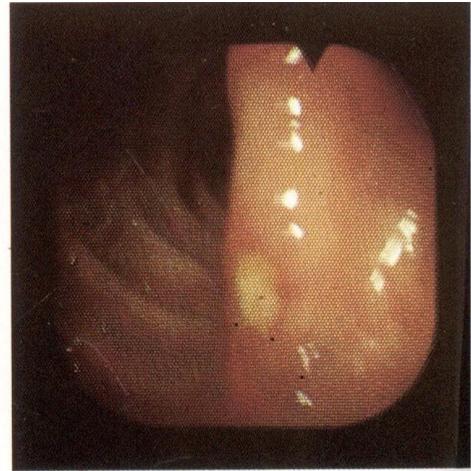
Case 15

A challenging colonoscopy; lesion difficult to visualize (arrows are a big help)



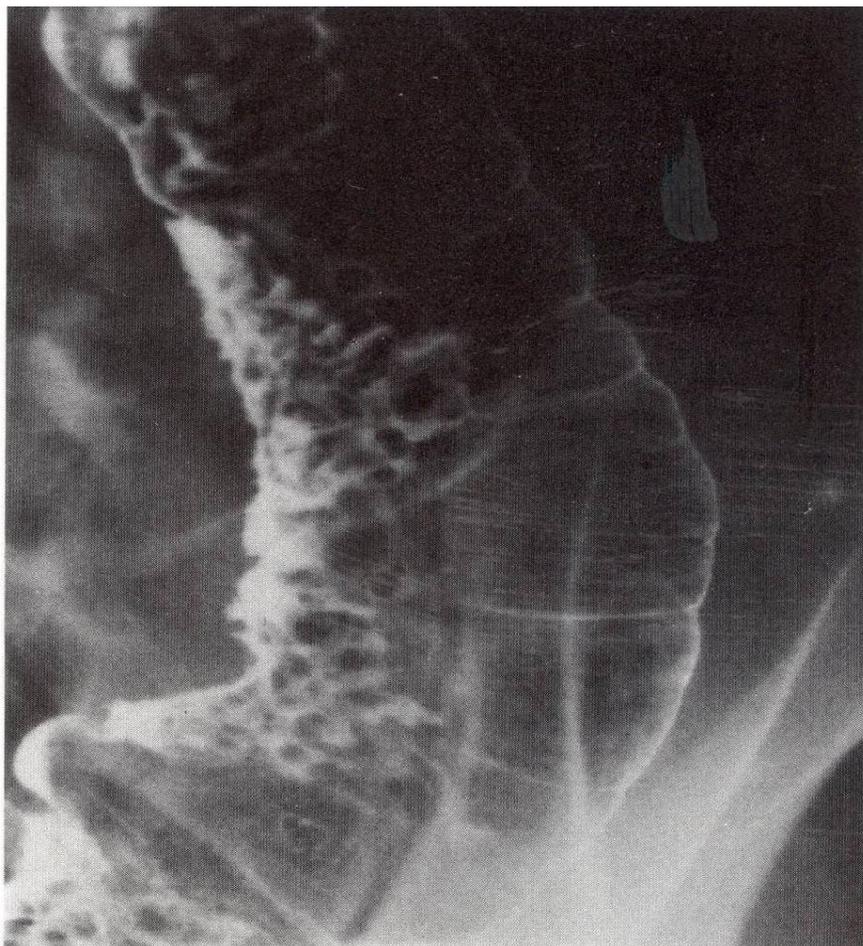
Case 16

35 year old woman with known Crohn disease presents with abdominal pain and altered bowel habit



C

Case 17



Known ileal Crohn disease

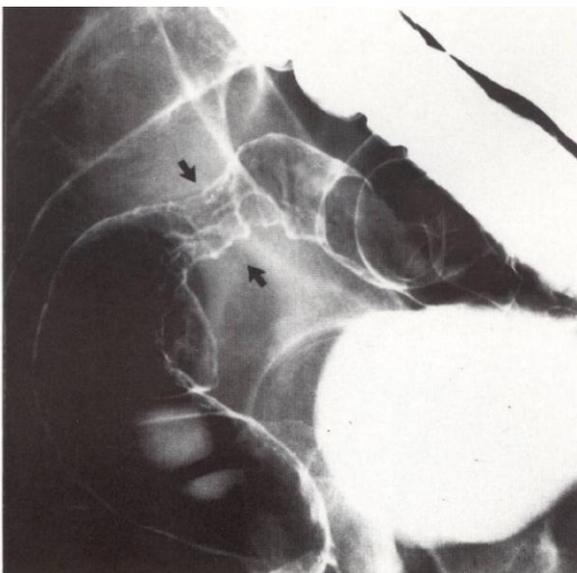


Case 18



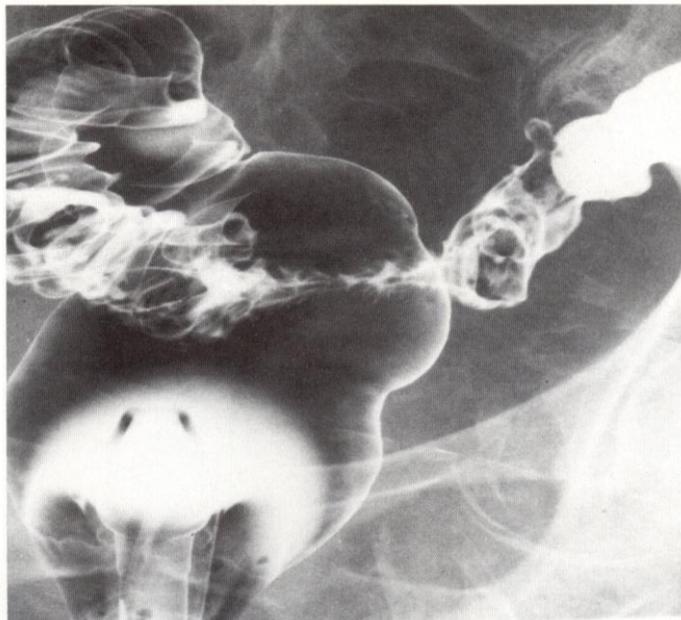
Follow-up colonoscopy arranged

Case 19



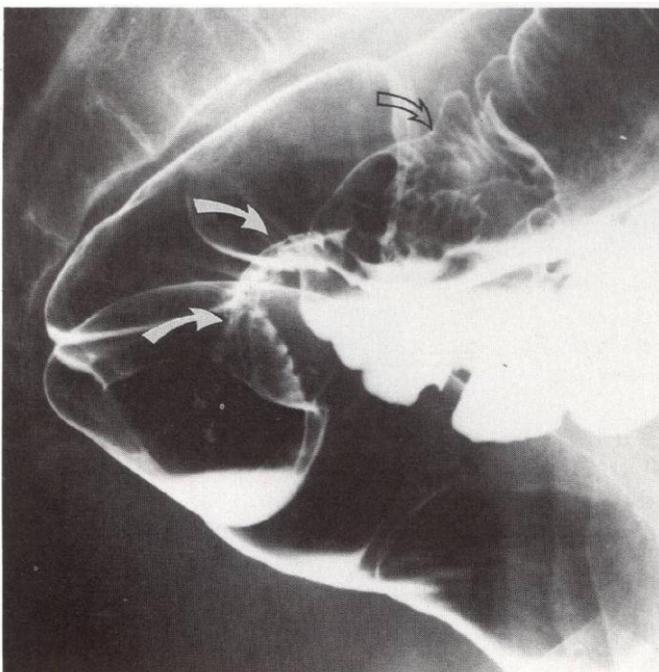
Inability to pass sigmoidoscope

Case 20

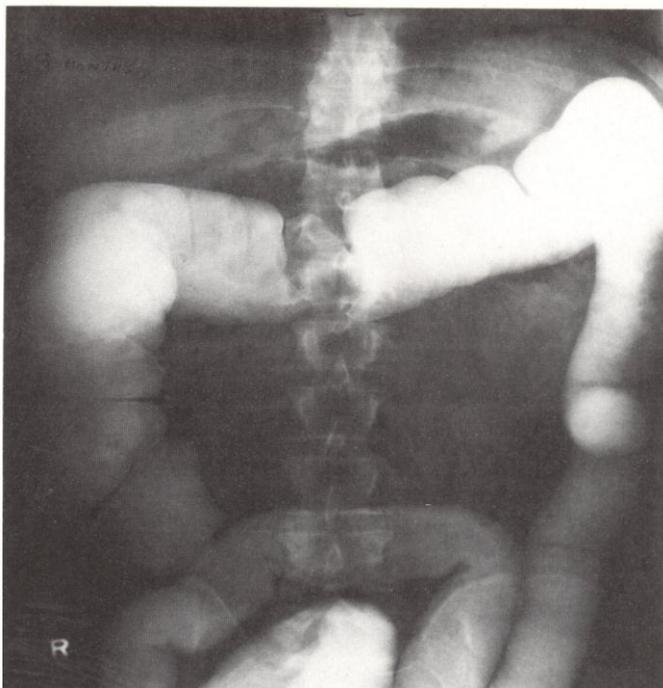


Colorectal cancer screening in patient with known diverticular disease

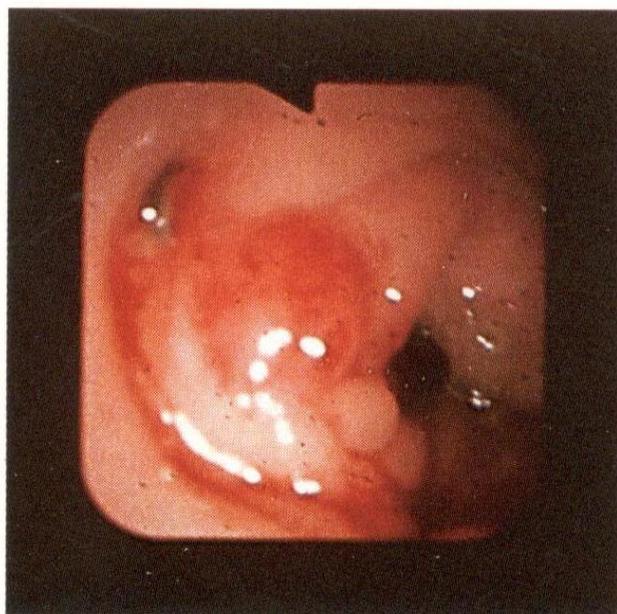
Case 21



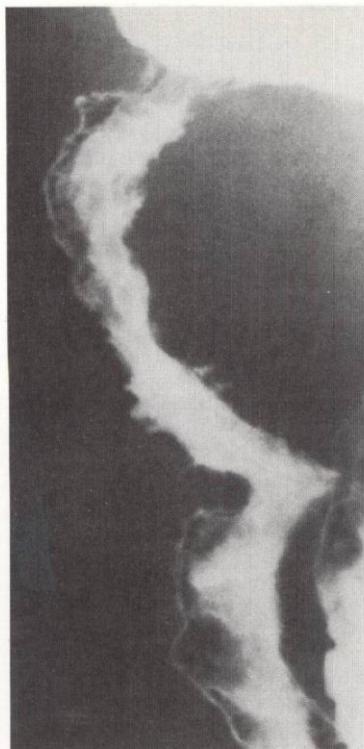
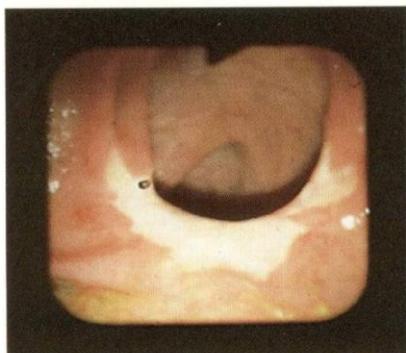
Dyspareunia in young woman with known Crohn disease

Case 22

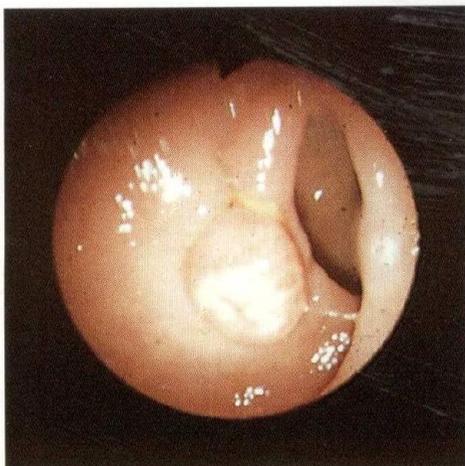
Abdominal symptoms
5 years after previous
colonic surgery in a 70
year old woman



Case 23



Following up a patient with known Crohn disease who is in a research study

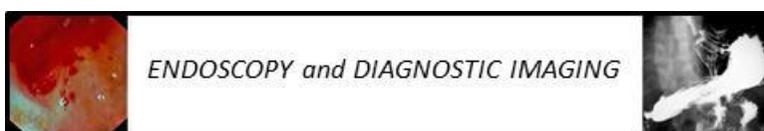


B

Colon Diagnostic Imaging Answers

1. Familial polyposis
2. Metachronous tumour distal to anastomosis
3. Pancolonic diverticulosis
4. Pancolonic polyposis (non-Hodgkins lymphoma)
5. Circumferential tumor of cecum/ascending colon
6. Megacolon
7. Continuous, circumferential UC
8. Filiform inflammatory polyps.
9. Pseudo-obstruction
10. Dilated colon, rectal involvement (pseudo-obstruction); incidental gallstones.
11. Polypoid tumor intussuscepting, with retrograde flow of barium and air; lack of proximal gas suggests this is not an antegrade obstruction.
12. Colonic polyps: Splenic flexure and transverse colon polyps.
13. Cecal lesion: Cecal lesion in profile.
14. Rectal filling defect
15. Cecal lesion: Posterior cecal wall neoplastic lesion.
16. Multiple discrete areas of barium (barium rests) from colonic Crohn disease. Differential: Crohn colitis, amebiasis, HSV, Behcet's disease, Yersinia infection, TB.
17. Multiple, discrete, asymmetric areas of (barium rests) filling from colonic Crohn disease.
18. Double contrast barium enema, localized area of colonic lumen, suggestive of "apple-core" colon cancer.
19. Narrowing of rectosigmoid area on double-contrast barium enema, with intact mucosal pattern, suggestive of extrinsic lesion such as from pelvic malignancy.
20. Narrowing of colonic lumen : Intact mucosa of area of narrowing with associated diverticular disease seen on double contrast barium enema.
21. Endometriosis of colon: Long linear indentations of colonic mucosa.
22. Post-surgical filling defect: Recurrent carcinoma at colonic anastomosis.
23. Post-resection for Crohn disease

Please compare your findings with those described in the previous material.



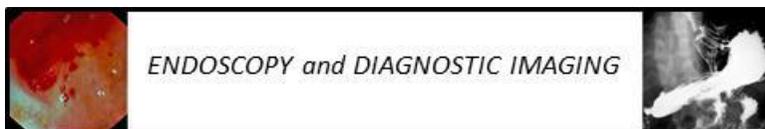
COLON ENDOSCOPIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

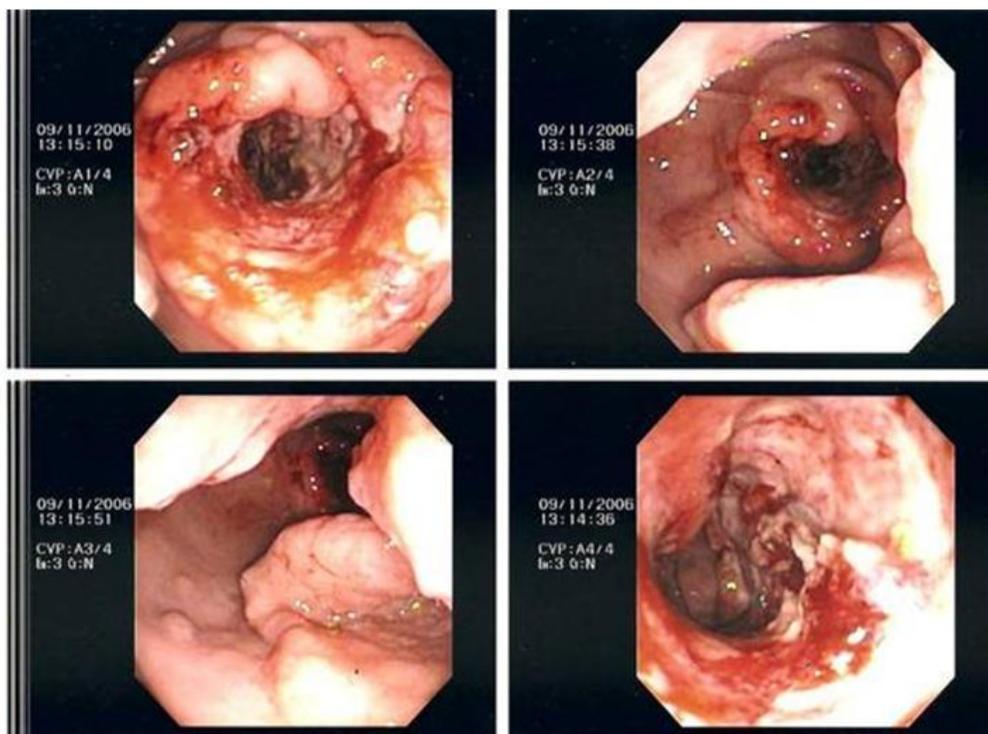
*Provided through the courtesy of Dr. C. Noel Williams, Dalhousie University
and University of Alberta, and Dr. Edgar Jaramillo, Center of
Gastrointestinal Disease, Ersta Hospital, Stockholm, Sweden*



Colonoscopy

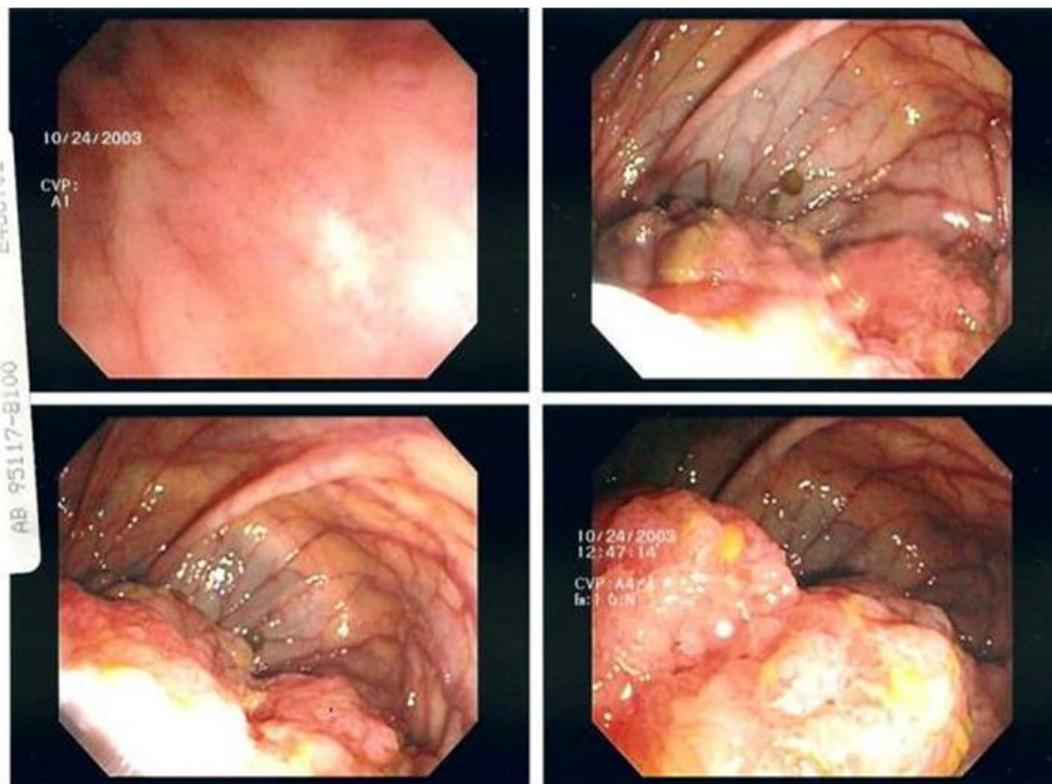
Case 1

A 58 year old man presents for a screening colonoscopy because his 10 year younger brother has recently had colon cancer. Please describe the endoscopic findings, and outline your advice to the patient and his family.



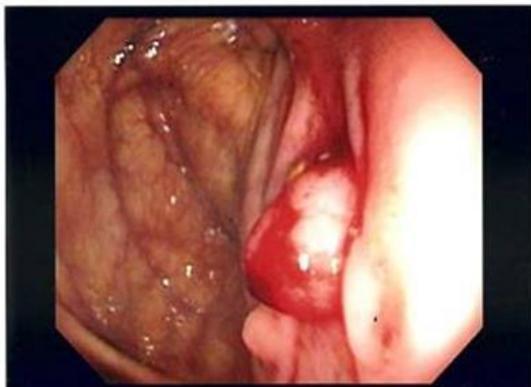
Case 2

A 64 year old woman is found to have an asymptomatic elevation in her alkaline phosphatase and GGT, with a low serum K⁺ and albumin concentration. Please describe the colonoscopic findings, and provide a differential diagnosis of the likely pathology.



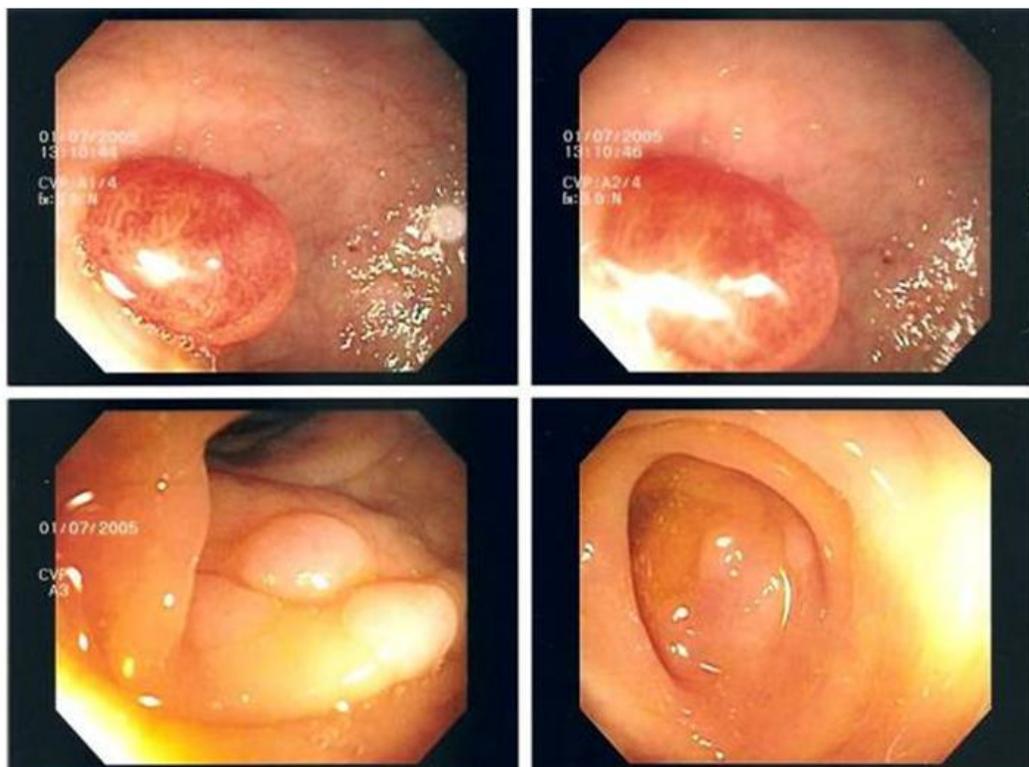
Case 3

A 63 year old male had an adenomatous polyp removed 3 years ago. Surveillance colonoscopy is now performed. Please describe the endoscopic findings, give the differential diagnosis and outline the endoscopic management for each of the lesions.



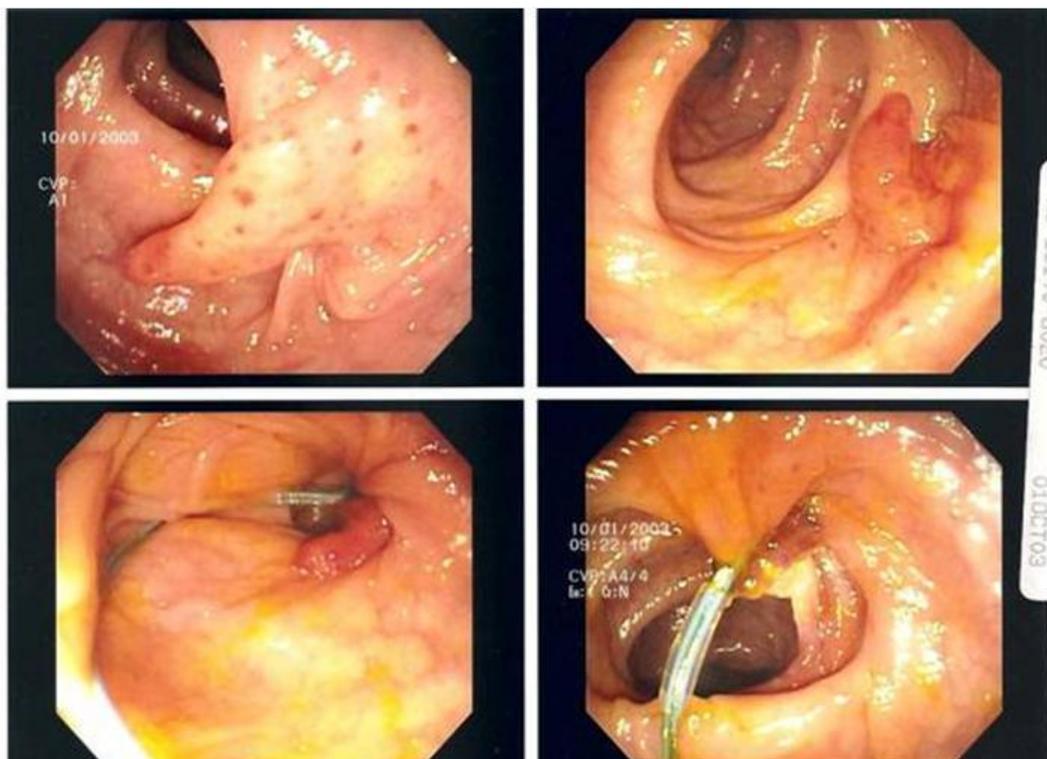
Case 4

A 62 year old man presents with rectal bleeding. Please describe the colonoscopic findings, a differential of the pathology, and the management.



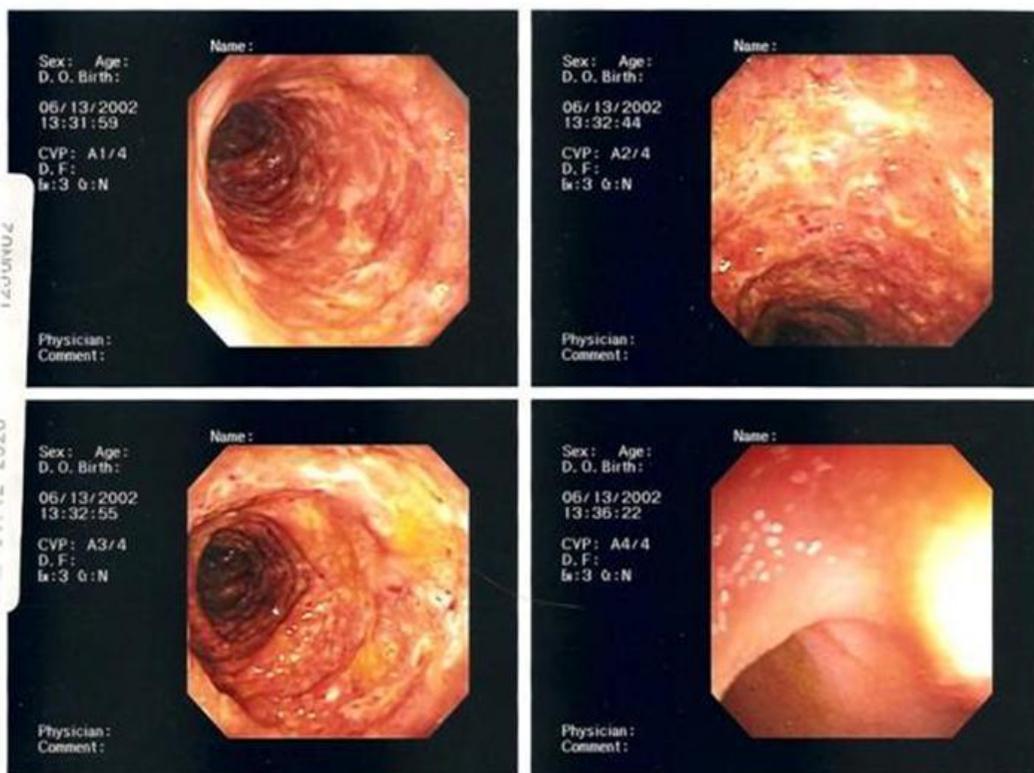
Case 5

A 59 year old woman presents with fatigue and iron deficiency anemia. Please describe the colonoscopic lesion and outline the management.



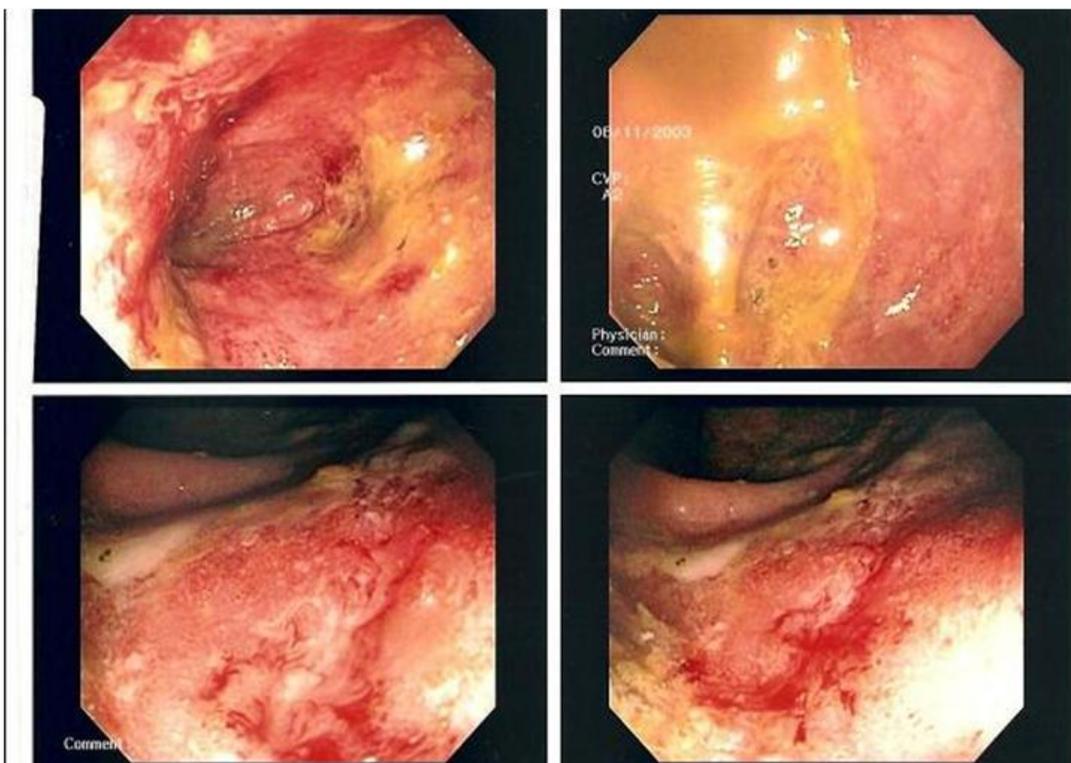
Case 6

A 44 year old man has a 12 year history of pancolitis (uc), treated with maintenance 5-ASA. He presents with rectal bleeding, and the colonoscopic findings are limited to the left colon. Please describe the endoscopic findings, and outline the management.



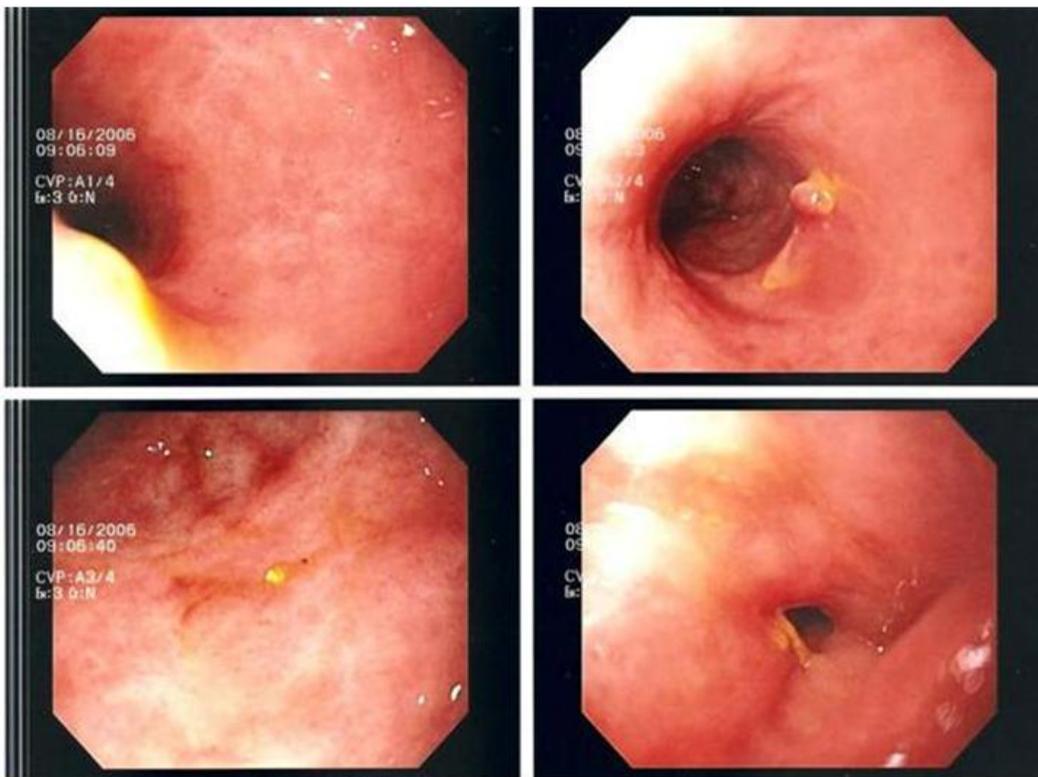
Case 7

A 33 year old man presents with a one week history of bloody diarrhea. Please describe the colonoscopic findings, and the anticipated biopsy findings.



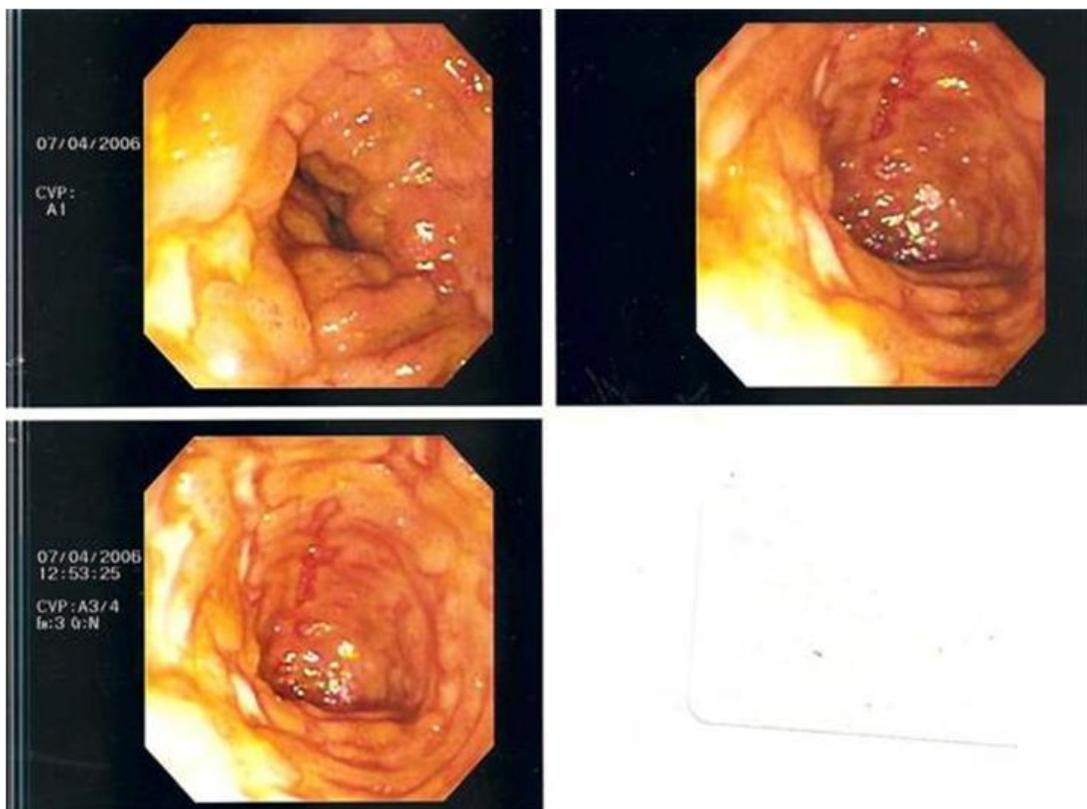
Case 8

A 72 year old man with pain and rectal bleeding is recently troubled by increasing of "colitis" symptoms of 15 years duration. Please describe the endoscopic findings and management.



Case 9

46 year old woman, diagnosed with, 2 years ago, a R. hemi' presented with symptoms of small bowel obstruction. Please describe the endoscopic findings and management.



Case 10

64 year old woman, R. hemi-CD, now presents with symptoms of small bowel obstruction despite entocort, 5-ASA, cipro, alendronate. Please describe the endoscopic findings and management.



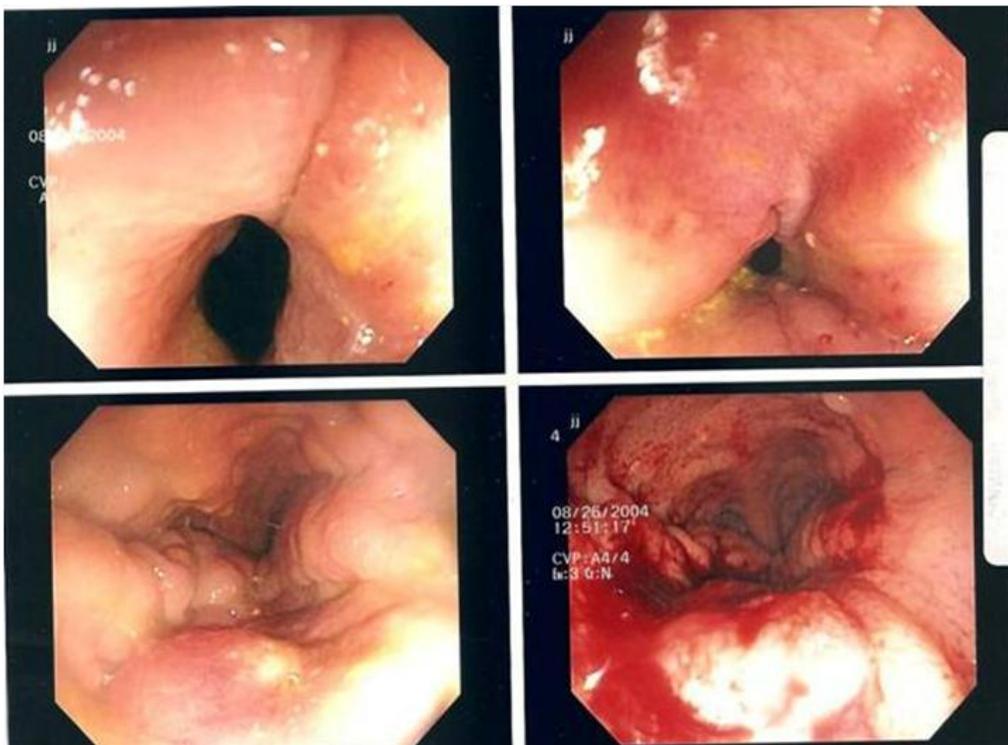
Case 11

28 year old man, 3 days bloody diarrhea following restaurant burger. No fever. Please describe the endoscopic findings, and give a differential diagnosis and management.



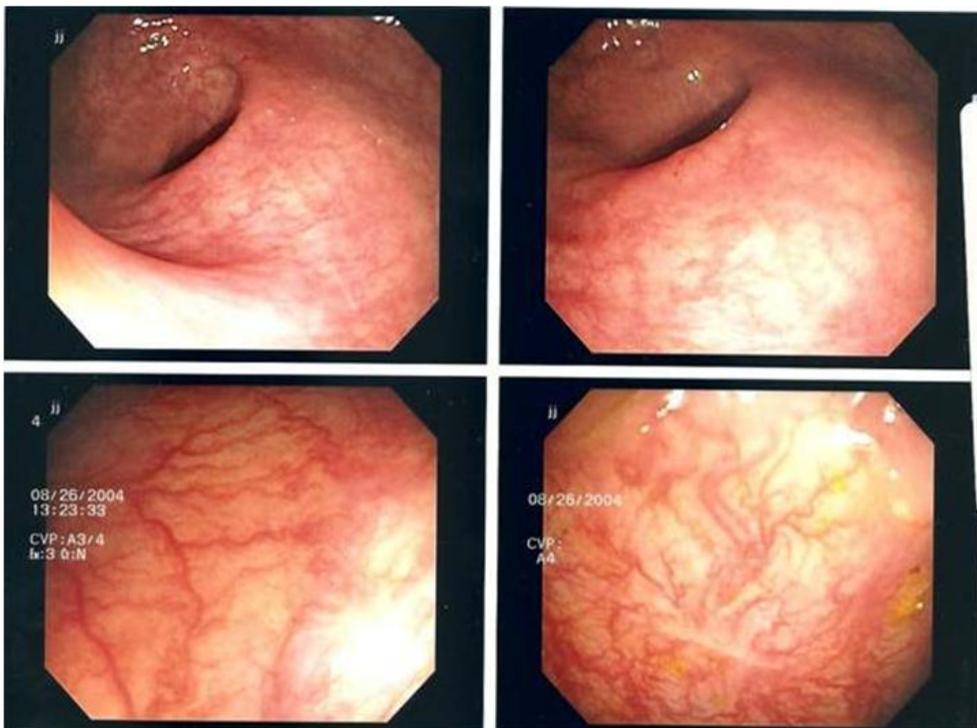
Case 12

72 year old man with rectal bleed, pernil pain for 2 months, loss of 10 pounds, smaller calibre stools, prostatism worse over 6 months, DRE nodule on prostate, poor air distensibility to 20cm. Please describe the findings and management.



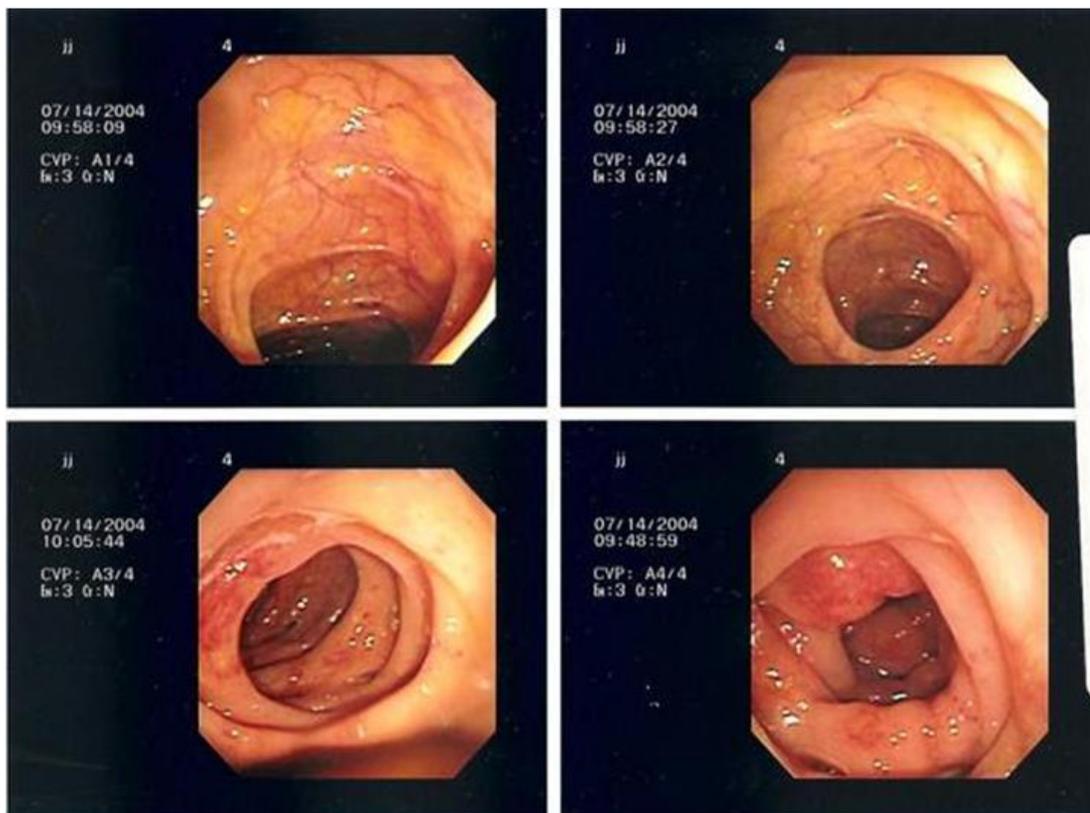
Case 13

64 year old woman, 6 months watery diarrhea. Please describe the endoscopic findings and the management.



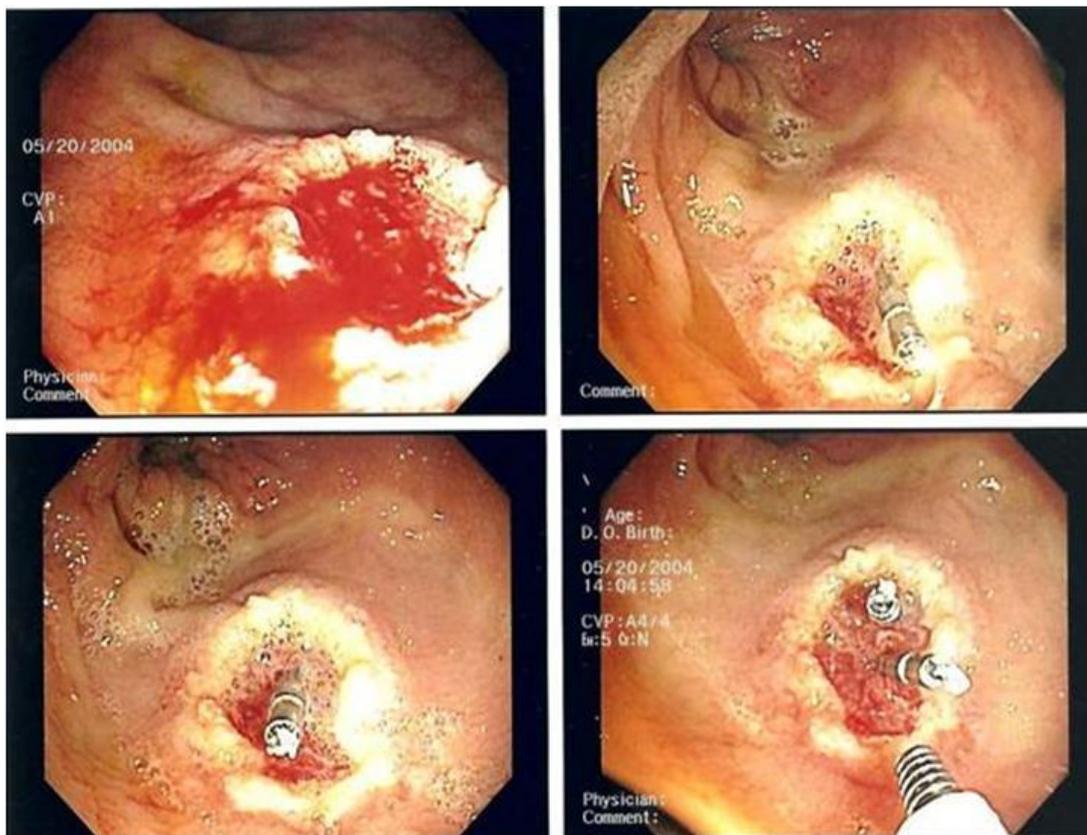
Case 14

67 year old man, with recurrent L-GIB colon. Please describe the endoscopic findings and management.



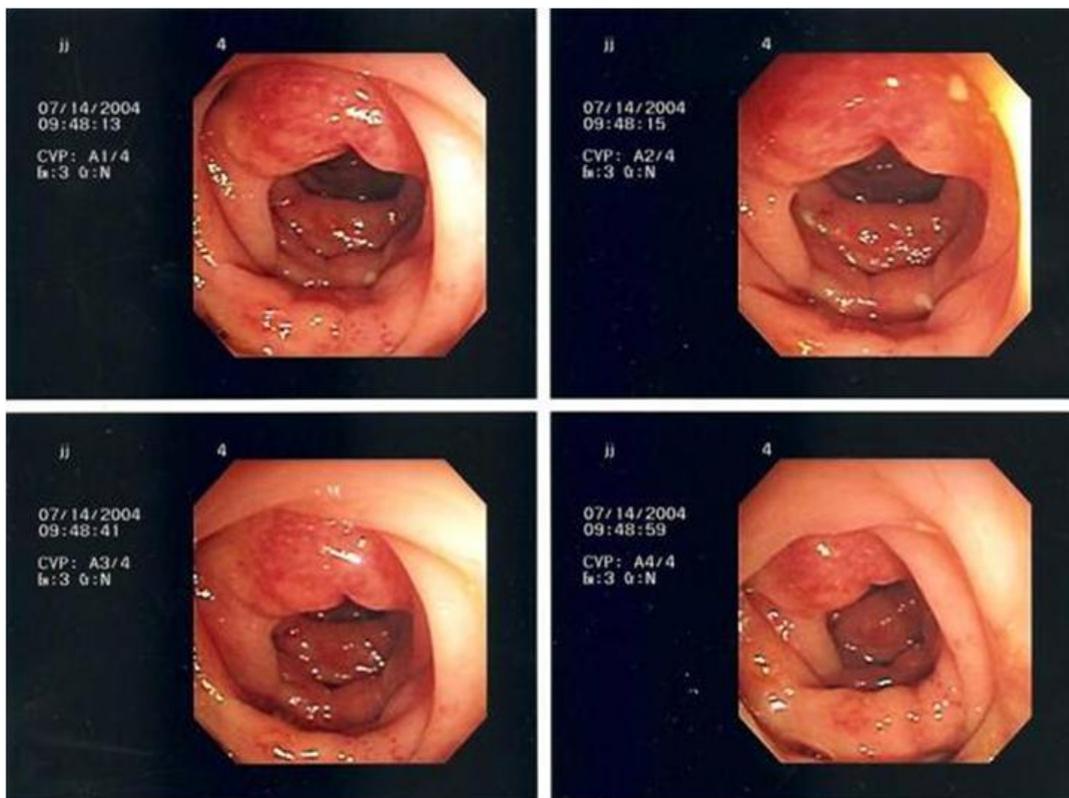
Case 15

89 year old woman, 4 years ago polyp, biopsy, intermittent rectal bleed now.
Please describe the endoscopic findings and management.



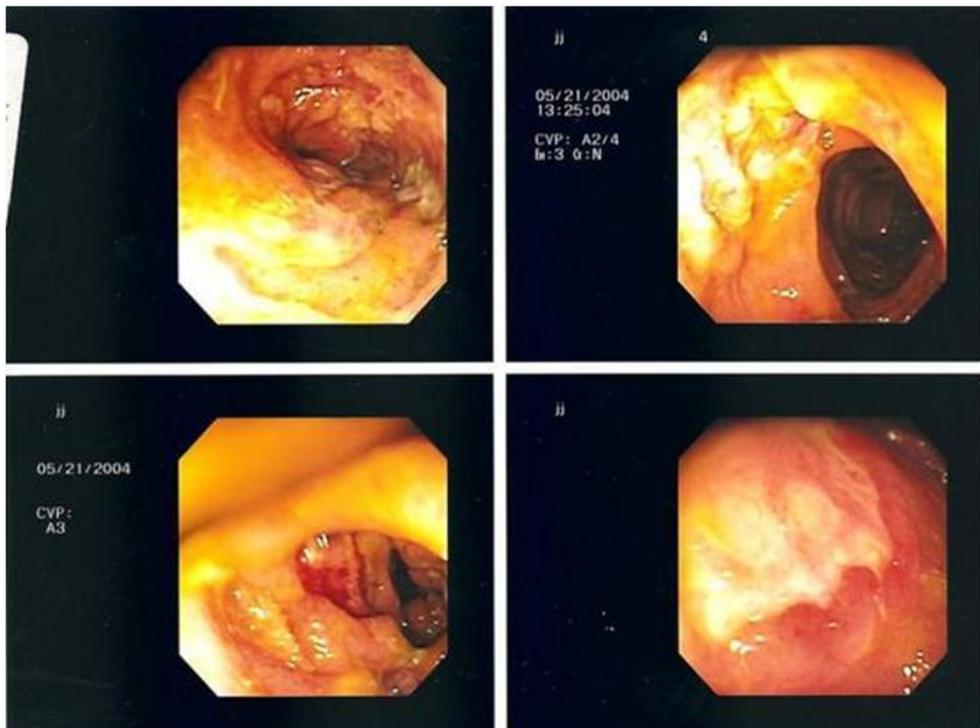
Case 16

66 year old man, L.GIB, anemia, CT-h.flexure thickening. Please describe the endoscopic findings and management.



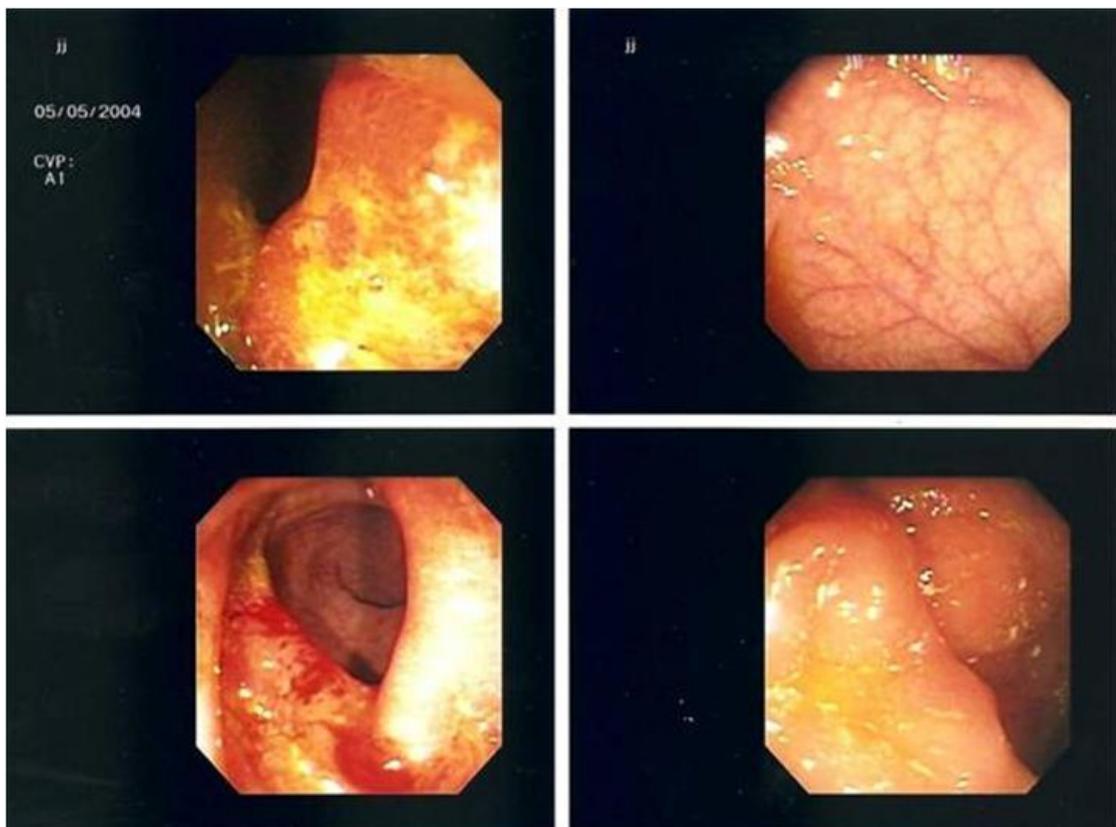
Case 17

A 66 year old woman, chronic bloody diarrhea, R.A. on NSAIDs, EGD (normal). Please describe the endoscopic findings and management.



Case 18

26 year old man with 3 weeks bloody diarrhea. Please describe the endoscopic findings and management.

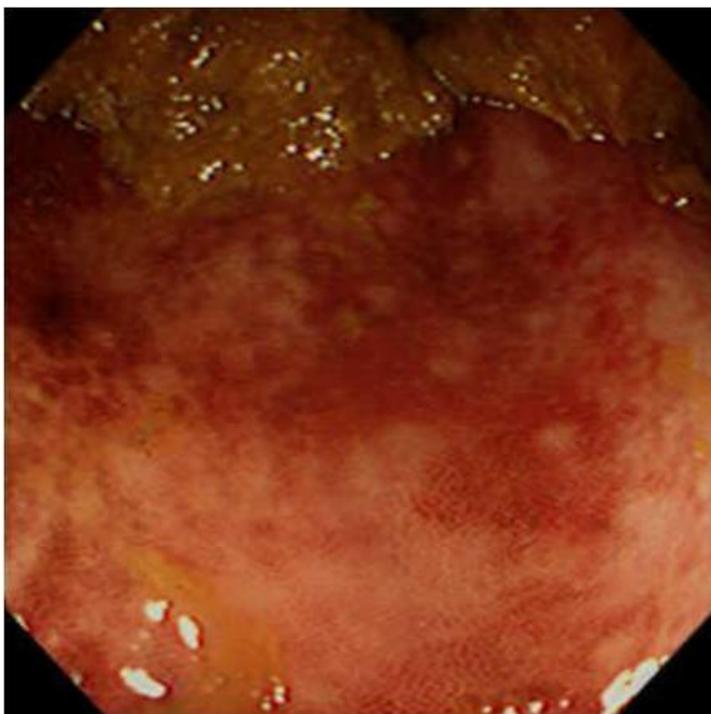


Case 19

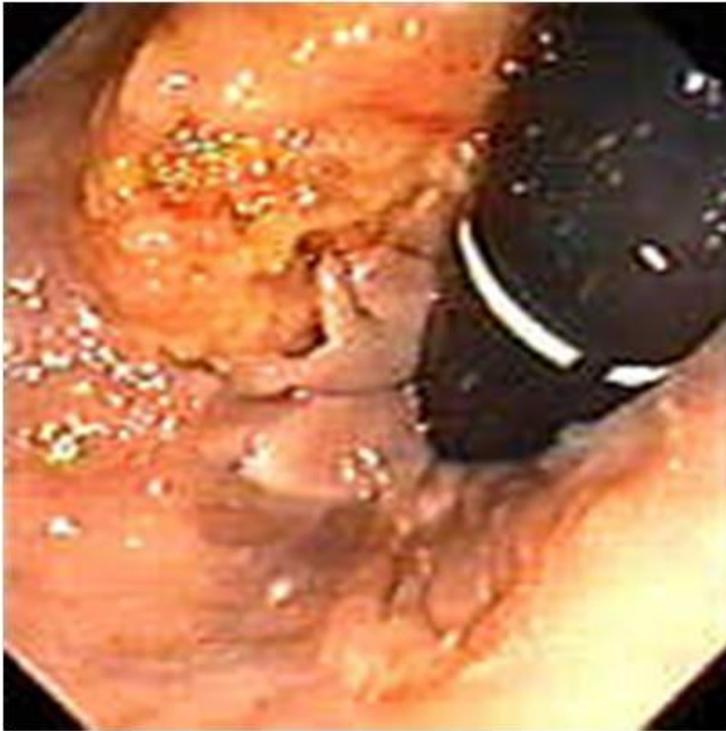


Hematochezia in an octogenerian

Case 20



Diarrhea after a visit to the farm

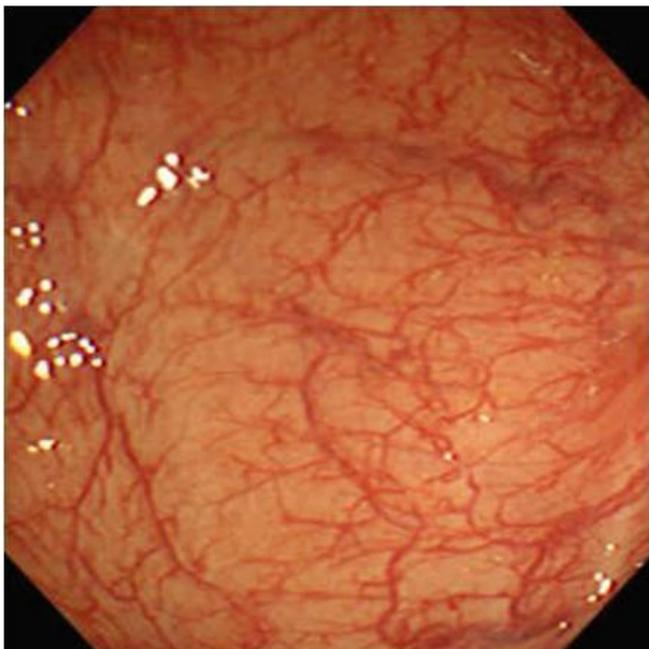
Case 21

Abnormal digital
rectal
examination in
person who is
HIV positive

Case 22

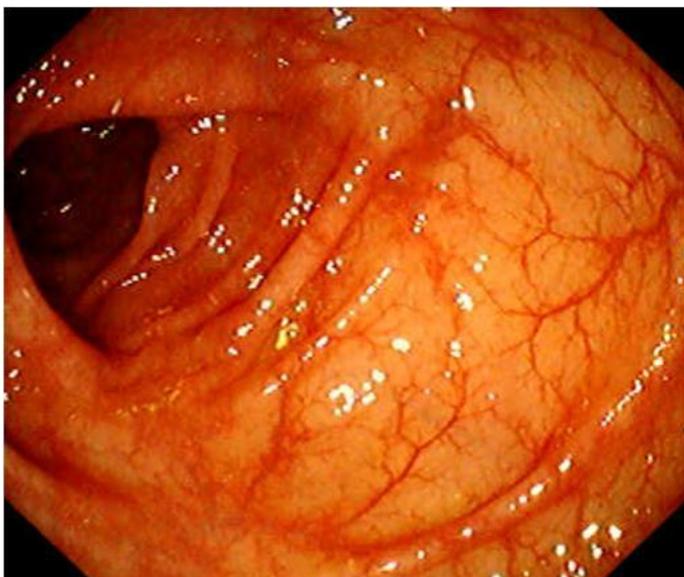
Watery diarrhea 5 days
after an oral antibiotic

Case 23



Watery diarrhea in middle-aged woman

Case 24



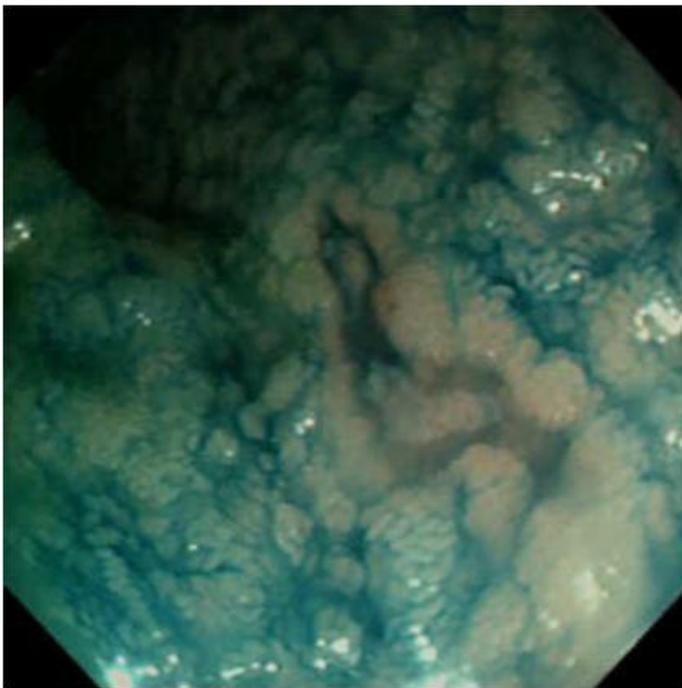
Same patient and procedure as above

Case 25

Tenesmas in
70 year old
male
following
radiation
therapy for
prostate
cancer

Case 26

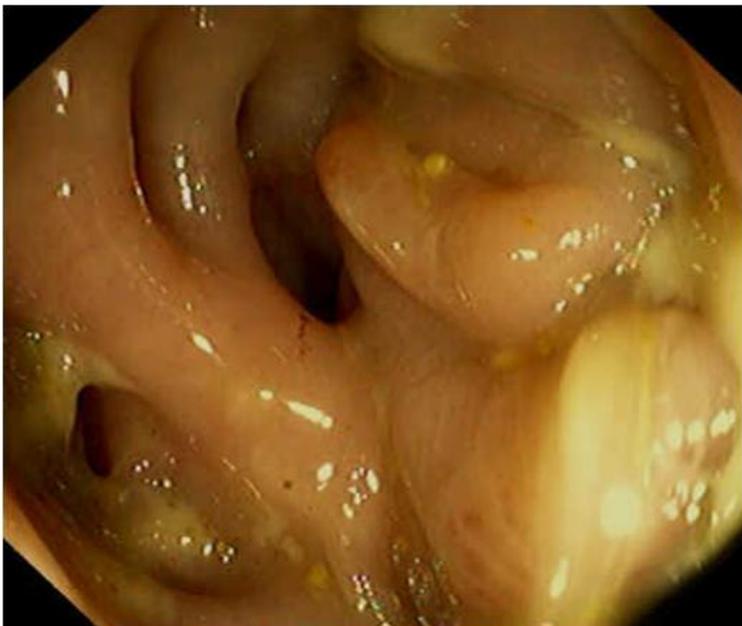
75 year old man on
digitalis for
congestive heart
failure develops
rectal bleeding

Case 27

Rectal bleeding in 25 year old man with ankylosing spondylitis

Case 28

Colonoscopy performed on 40 year old man with 15 yer history of "colitis"

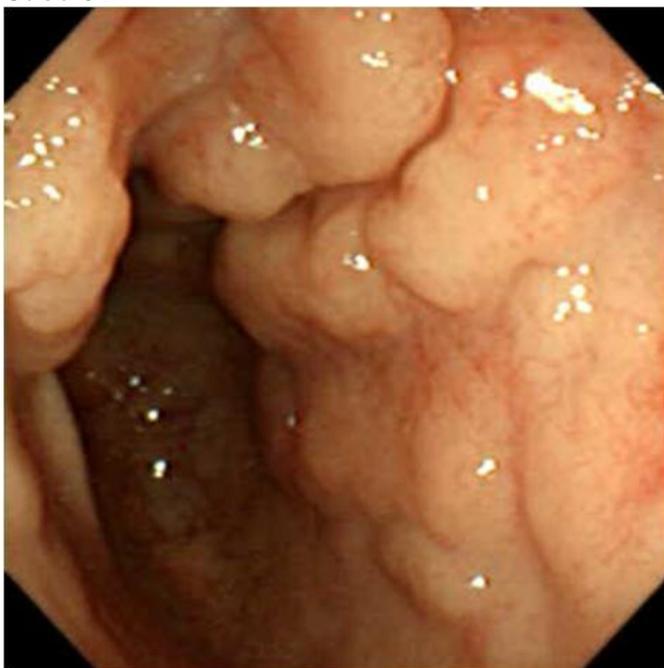
Case 29

Abdominal pain,
altered bowel
habit and fever
in a 75 year old
man

Case 30

Incidental finding
on screening
colonoscopy

Case 31

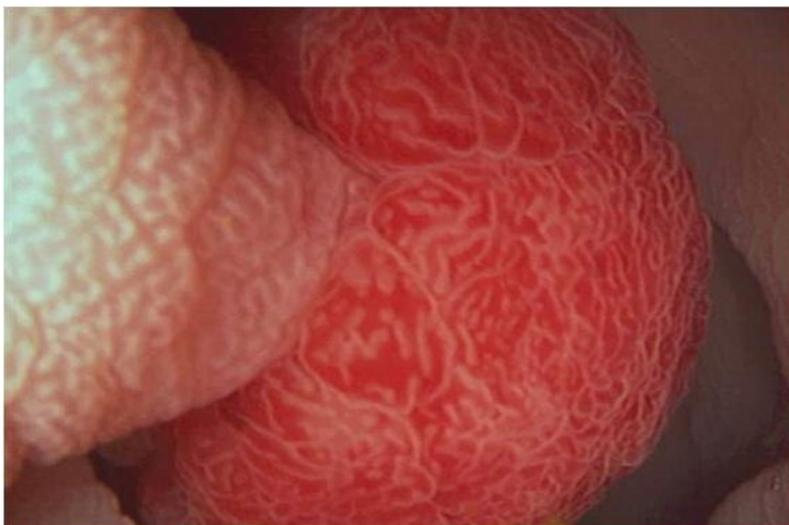


Filling defects seen on air contrast barium enema

Case 32



History of chronic constipation

Case 33

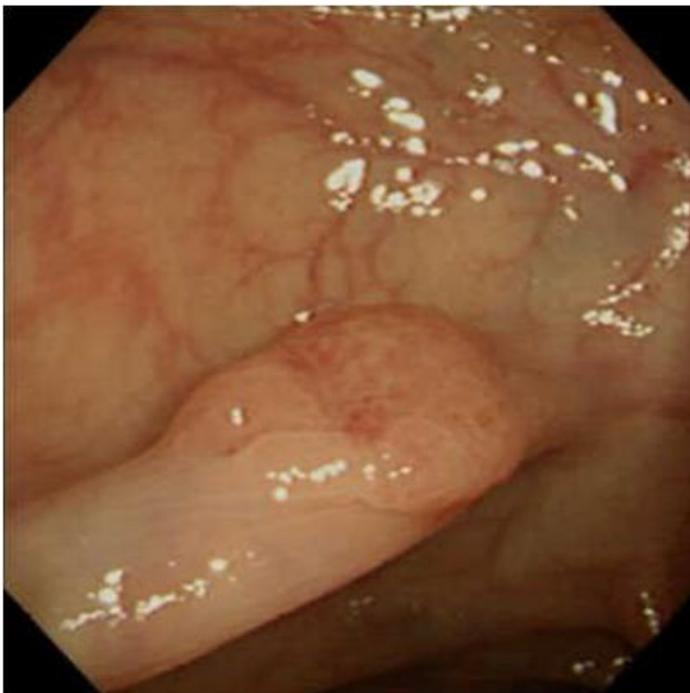
Inspection of colonic mucosa before taking mn Hiple biopsies

Case 34

More filling defects seen on air contrast barium enema

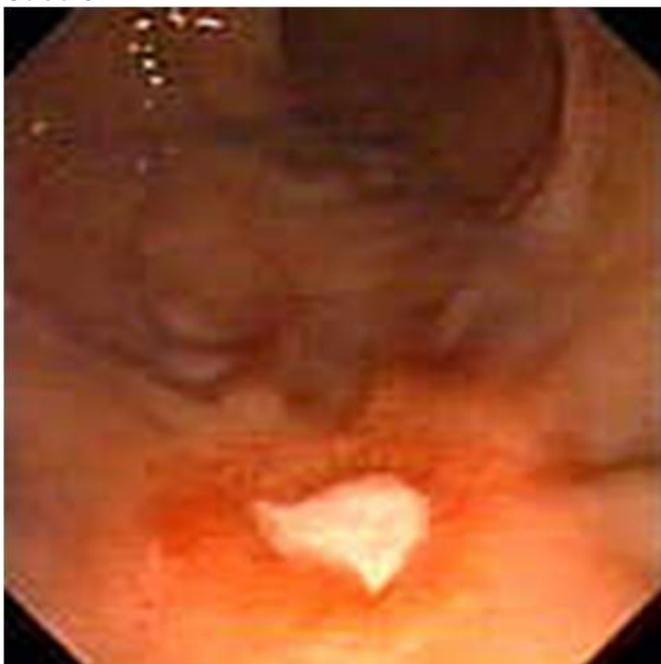
Case 35

Give the recommendations for colonoscopic surveillance in this patient

Case 36

Give the recommendations for colonoscopic surveillance in this patient

Case 37

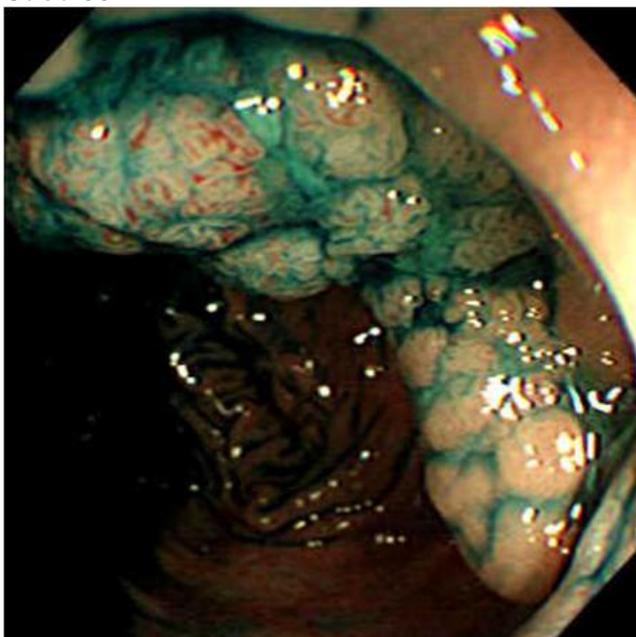


Tenesmus, straining at stool

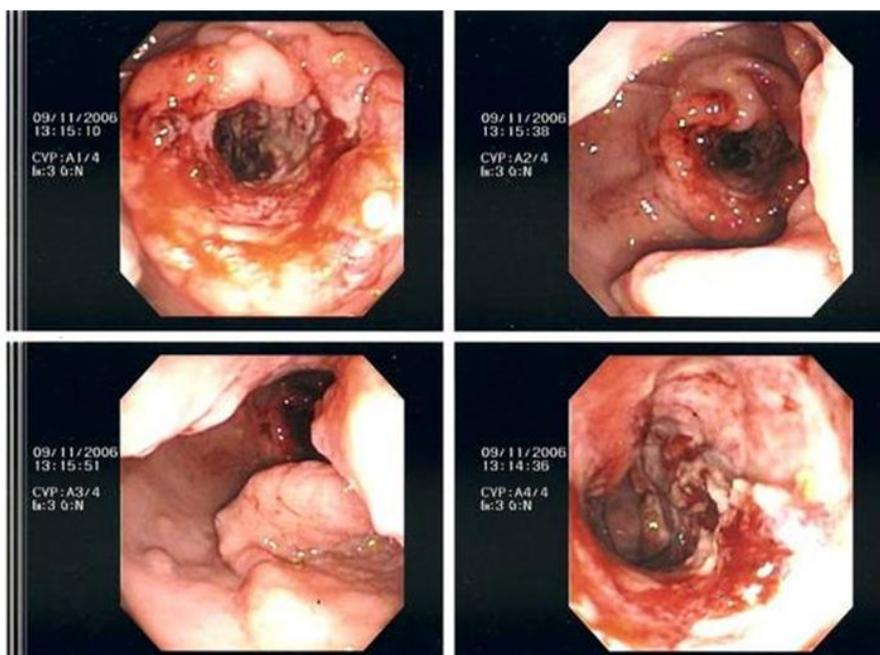
Case 38



Acute onset of bloody diarrhea in an 18 year old lady

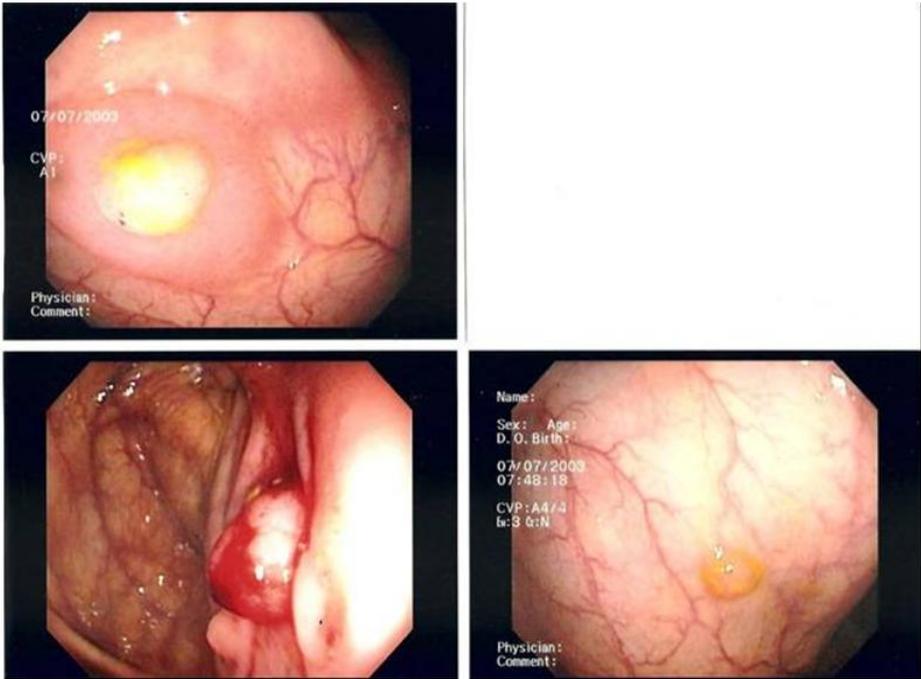
Case 39

Patient presents with weakness and hypokalemia

Case 40

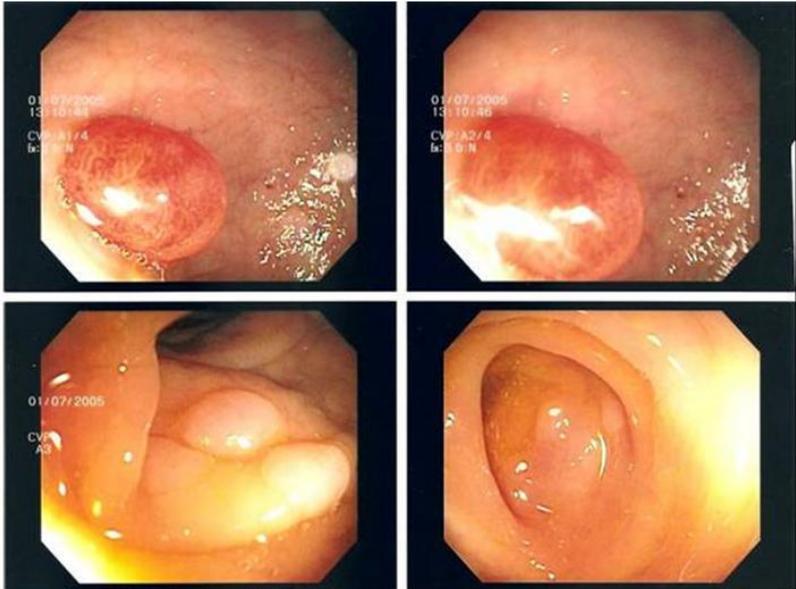
Give the recommendations for the endoscopic following of this patient.

Case 41



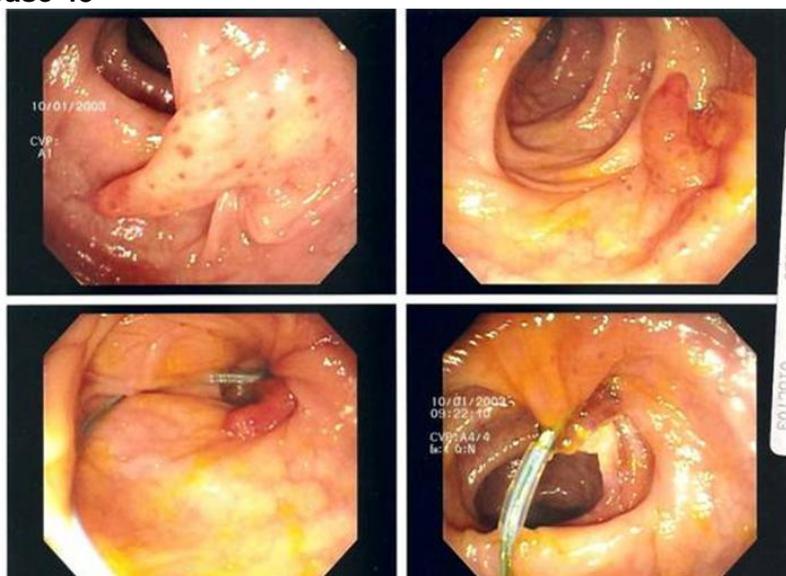
Multiple findings 5 years after previous polypectomy for a tubular adenoma

Case 42



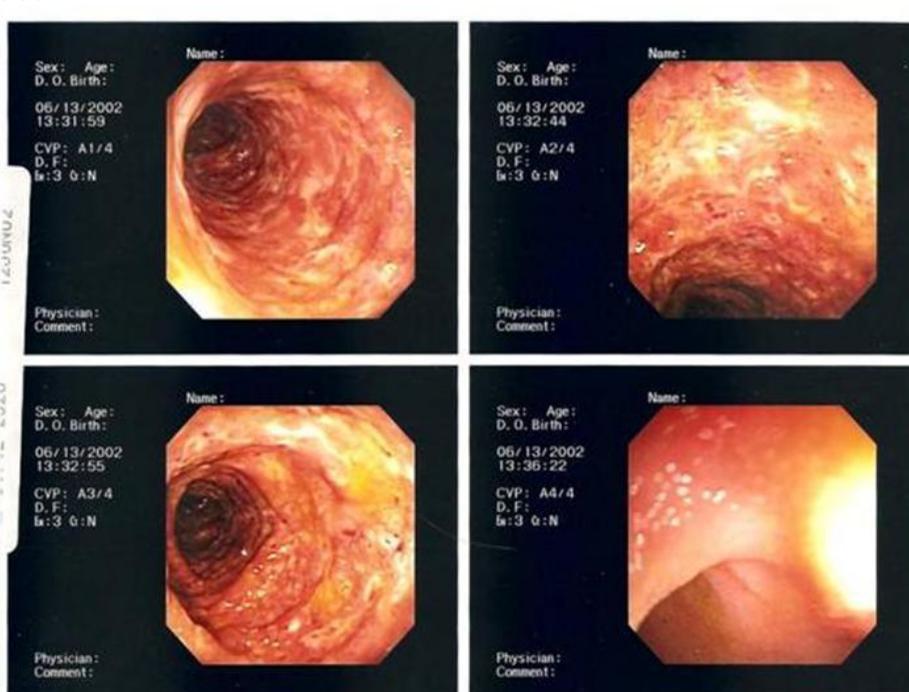
Screening colonoscopy

Case 43

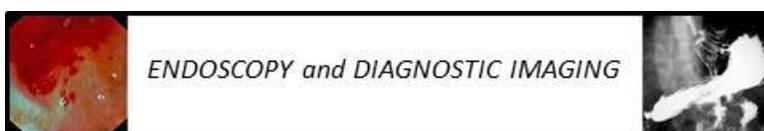


Classic iron deficiency anemia

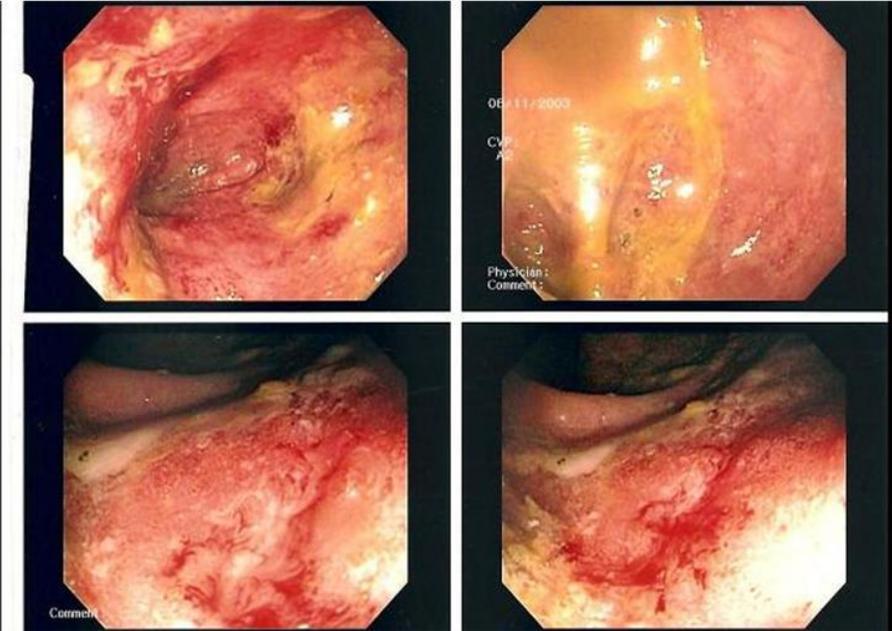
Case 44



Acute onset of blood per rectum; 4 days previously

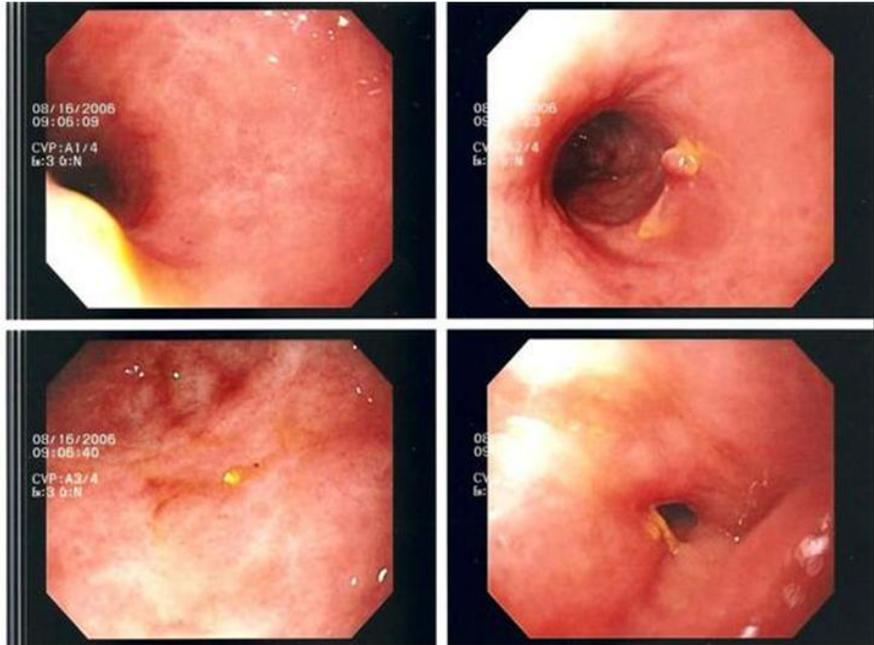


Case 45

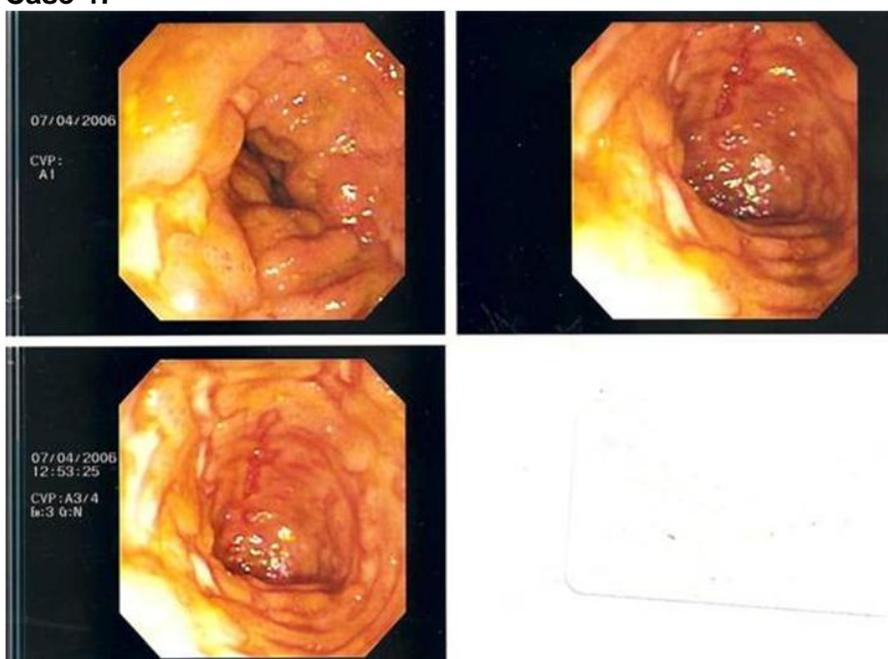


What is the likely cause (s) of this pattern in a 25 year old who presents with rectal bleeding?

Case 46



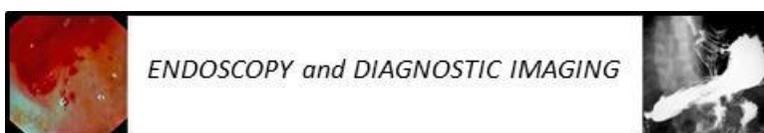
10 year history of UC

Case 47

Pouchitis-like symptoms after colonic resection, not responding to probiotics

Case 48

Endoscopic treatment for constipation

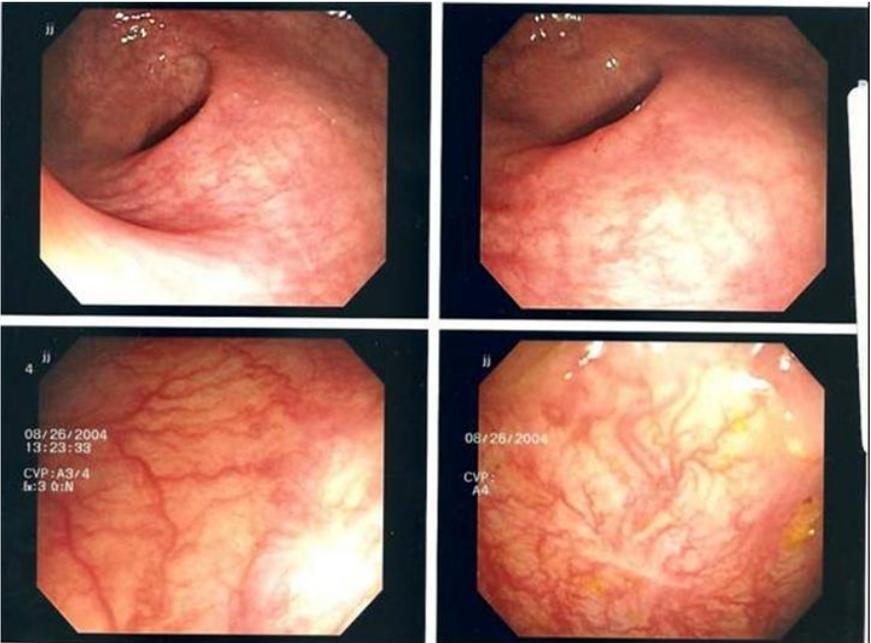


Case 49



Rectal bleeding

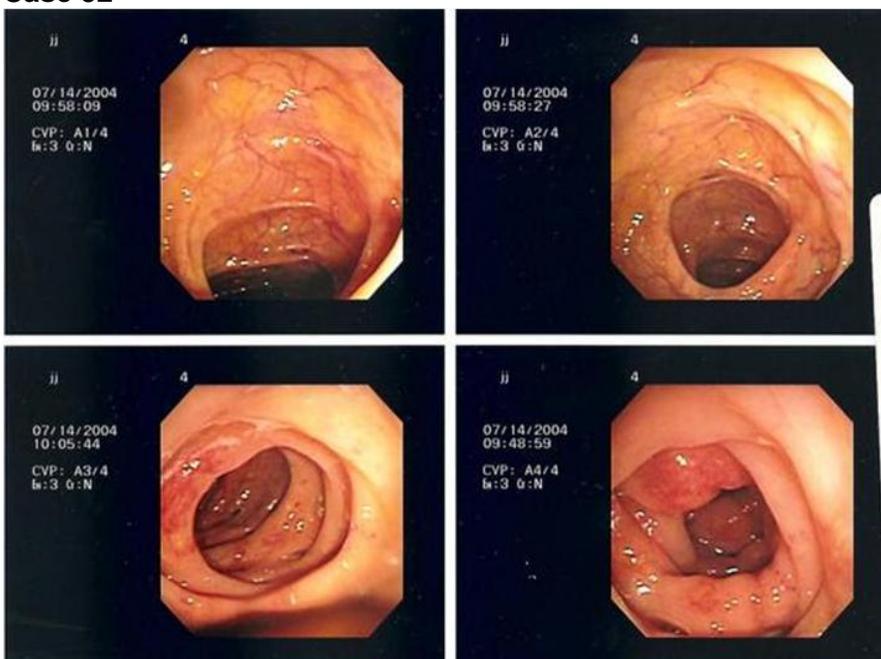
Case 50



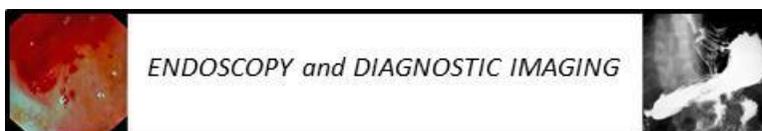
Findings on screening colonoscopy

Case 51

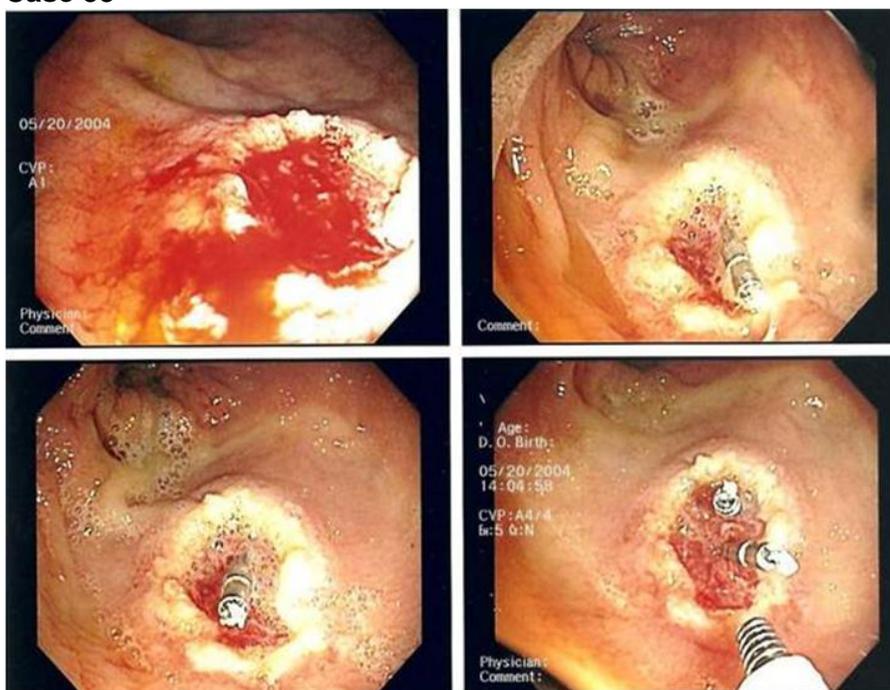
Screening colonoscopy in 50 year old, whose brother had colorectal cancer at age 56

Case 52

68 year old man with rectal bleeding after hypotension

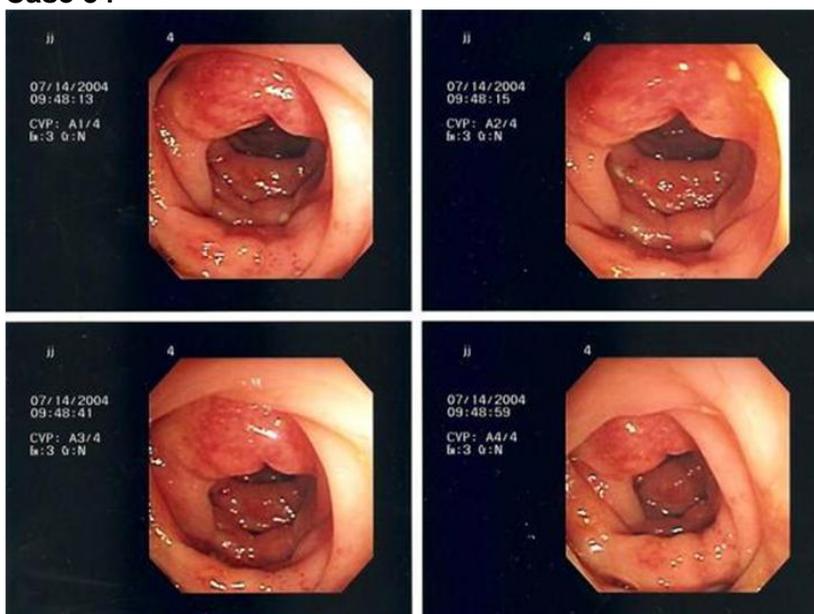


Case 53

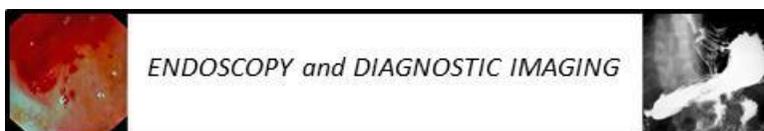


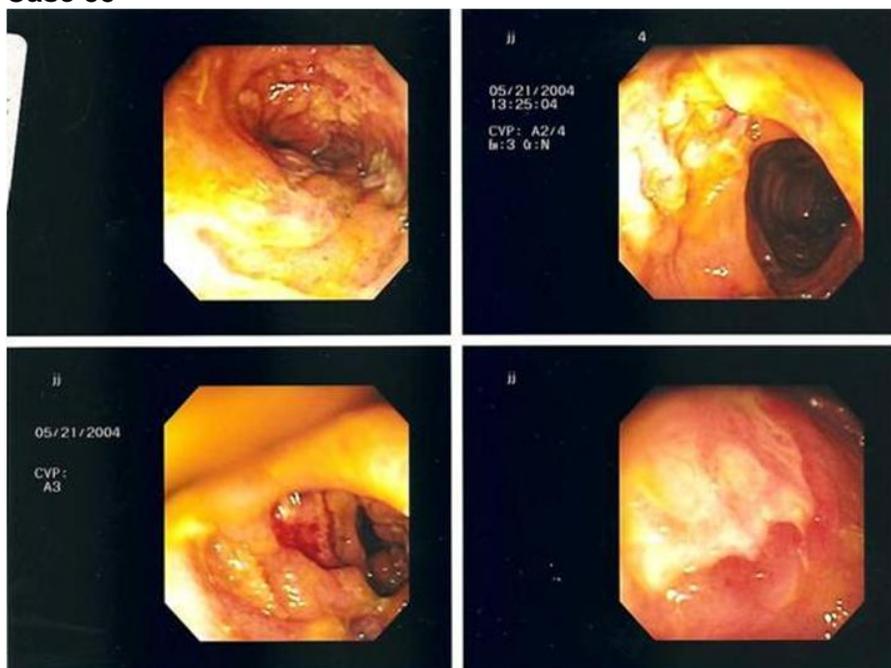
Rectal bleeding after polypectomy

Case 54

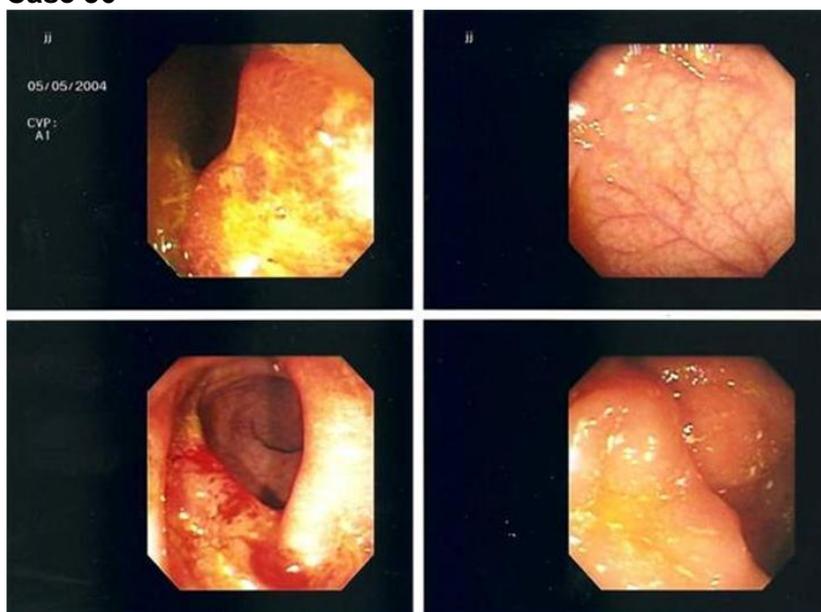


Rectal bleeding

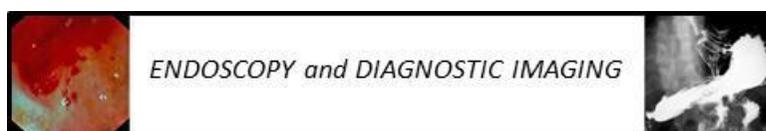


Case 55

35 year old male patient offered colonoscopy after failed IBS therapy

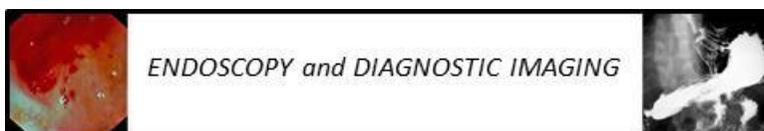
Case 56

Rectal bleeding

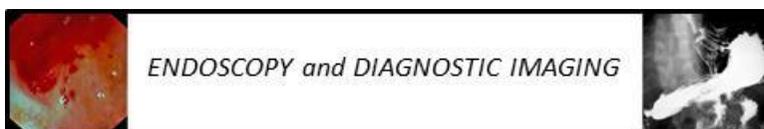


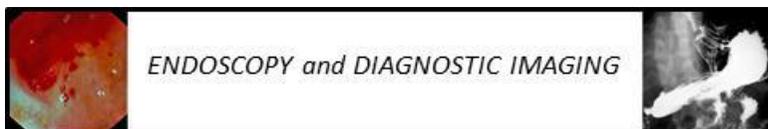
Endoscopy case answers

1. Colorectal cancer
2. Colonic villous adenoma
3. Hyperplastic polyp
4. Serrated hyperplastic polyp
5. Adenomatous polyp on long stalk
6. Proctosigmoiditis
7. Infectious colitis
8. UC/CD/NSAID colitis? Adenomatous polyp, ?DALM
9. Anastomosis – ulceration, but no stricture.
10. Stricture, balloon dilation
11. Patchy redness in R/sig.colon, then diffuse to splenic flexure. TC, AC, cecum, TI-normal
12. Colonic mass
13. Transverse colon, tortuous blood vessels, scar
14. Abn. AC colon, 25 cm thick folds, loss of vessel pattern, petechiae, red folds, ? ischemia.
15. Adenoma 3 cm, removed – bleeding: injection, clips.
16. Rectal mucosa, petechiae, reddening, swollen folds, loss of vessel pattern.
17. Multiple different sized, aphthons ulcers, normal intervening mucosa, ileal ulceration.
18. Proctitis, sharp demarcation at 10 cm, diffuse swollen, friable.
19. Angiodysplasia of colon
20. Campylobacter of colon
21. Anal cancer
22. Antibiotic-associated colitis
23. Collagenous colitis
24. Lymphocytic colitis
25. Radiation colitis
26. Ischemic colitis
27. Crohn disease of colon
28. DALM in colitis
29. Diverticulitis
30. Colonic lymphoid hyperplasia
31. Colonic lymphoma
32. Melanosis coli
33. Colonic pit pattern
34. Colonic pneumatosis cystoides
35. Colonic hyperplastic polyp
36. Colonic serrated adenomas
37. Ulcer rectal solitary
38. Ulcerative colitis
39. Villous adenoma
40. Colorectal cancer



41. Colonic villous adenoma
42. Lipoma, leiomyoma and polyp resection
43. Serrated hyperplastic polyp
44. Adenomatous polyp on long stalk; HAT
45. Proctosigmoiditis
46. Infectious colitis
47. Adenomatous polyp, or DALM?
48. Anastomosis-ulceration, but no stricture
49. Stricture, balloon dilation
50. Colonic mass
51. Patchy redness in rectum and sigmoid colon, then diffuse to splenic flexure. TC, AC, cecum, TI-normal
52. Transverse colon, tortuous blood vessels, scar
53. Abn. ascending colon, thick folds, loss of vessel pattern, petechiae, red folds, ischemia
54. Adenoma 3 cm, removed-bleeding: injection, clips
55. Rectal mucosa, petechiae, reddening, swollen folds, loss of vessel pattern
56. Multiple different sized, aphthous ulcers, normal intervening mucosa, ileal ulceration





HEPATOBIILIARY DISORDERS

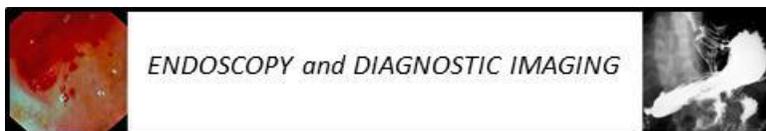
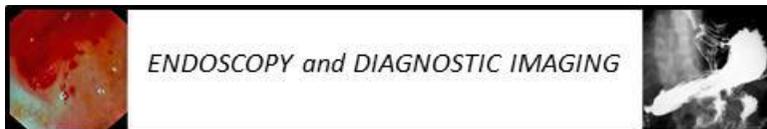


Table of Contents

	Page
Fatty liver disease	342
Cholestasis	343
Portal hypertension	348
Diagnostic imaging	379



LIVER

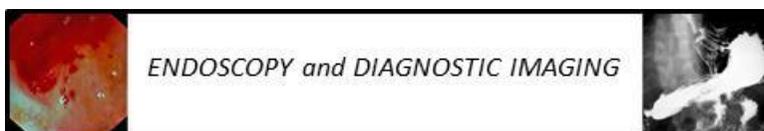
“Sharpening Knowledge to Enhance Clinical Skills”

FATTY LIVER DISEASE

- The molecular mechanisms of fat accumulation in the liver, and the development of non-alcoholic fatty liver disease (NAFLD)/ non-alcoholic steatohepatitis (NASH).
 - Hepatic steatosis
 - ↑ dietary fat or delivery of fat to the liver
 - ↑ carbohydrate transport to the liver, with formation of fatty acids (↑ lipogenesis)
 - Bacterial flora
 - Oxidative stress
 - ↑ peripheral insulin resistance (↑ leptin, ↓adiponectin ;↑insulin, ↑TNF α)
 - ↑ mitochondrial synthesis of FA's
 - ↑ fat synthesis (increased insulin activates SREBP-1, the sterol regulatory element binding protein 1-c, and increase CHREBP, the carbohydrate regulatory element binding protein)
 - ↓ transport of FA's out of the liver (↓ β -oxygenation), ↓Apo B-100
 - Hepatocyte injury and inflammation
 - ↑Oxidative stress
 - ↑Lipotoxicity
 - ↑ DRs (death receptor)
 - ↑ apoptosis
 - ↓ DNGA (transcriptional sensitizer)
 - Hepatic fibrosis
 - Stellate cell activation

Adapted from: Pellicoro A, and Faber KN. *APT* 2007; 26 (2): pg. 149-160.

- Inherited iron overload
 - HFE-related hereditary hemochromatosis
 - C282Y/C282Y
 - C282Y/H63D
 - Other HFE mutations
 - Non-HFE related mutations
 - Neonatal hemochromatosis

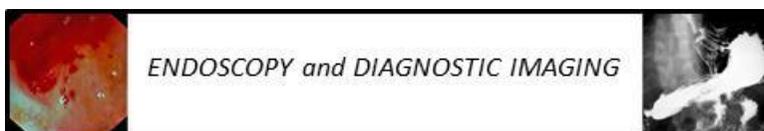


- Juvenile hemochromatosis
- Hemojuvelin (HJV)
- Transferrin receptor-2 (TfR-2)
- Atransferrinemia
- Ferroportin (SLC40A1)
- Hpcidin (HAMP)
- Acquired iron overload.
 - Hematological disorders
 - Iron-loading anemias
 - thalassemia major
 - sideroblastic anemia
 - chronic hemolytic anemia
 - ineffective erythropoiesis
 - Chronic liver disease (end stage, cirrhosis)
 - HCV, HBV
 - HCV porphyria, (porphyria tarda)
 - Alcoholic liver disease
 - NAFLD/NASH
 - Porta-caval shunt
 - Increased iron intake
 - Dietary iron overload (African iron syndrome)
 - Parenteral iron overload
 - Longterm hemodialysis
 - Multiple blood transfusions (for example, for chronic hemolytic anemia)
 - Acerloplasminemia

Adapted from: Nairz M, and Weiss G. *Wien Klin Wochenschr* 2006;118(15-16):442-62.

CHOLESTASIS

- The major intrahepatic and extrahepatic causes of cholestasis leading to jaundice.
- Intrahepatic
 - Drugs
 - Alcoholic hepatitis ± cirrhosis
 - PBC
 - Viral hepatitis
 - Chronic hepatitis ± cirrhosis
 - Cholestasis of pregnancy
 - Sepsis
 - TPN



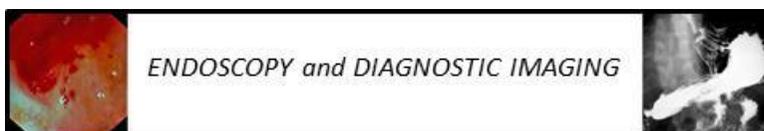
- Extrahepatic
 - Common bile duct stone(s)
 - Pancreatic/periampullary cancer
 - Benign biliary stricture
 - PSC, SSC (secondary sclerosing cholangitis)
 - Bile duct carcinoma
 - Benign pancreatic disease
 - Extrinsic duct compression

Adapted from: Heathcote J. *First Principles of Gastroenterology* 2005. pg. 590.

- The mechanisms of action of different types of drugs used for the treatment of pruritus in patients with cholestatic liver disease.
 - Decrease degree of cholestasis: UDCA
 - Non-absorbable anion exchange resins: cholestyramine
 - Changes in opioidergic neurotransmission : naloxone, naltrexone
 - Hepatic enzyme (cP452) inducers: rifampicin, metronidazole, phenobarbitol
 - Cannabinoid agonist
 - Serotonin antagonists: ondansetron
 - Changes in threshold to experience nociception: dronabinol
 - Antidepressants (SSRIs)
 - Sedation (antihistamines)
 - Invasive procedures: plasmapheresis, MARS (extracorporeal albumin dialysis), biliary drainage
 - IV propofol
 - Gabaergic changes: gabapentin
 - UV light
 - Liver transplantation – removes cause of cholestasis

Adapted from: Kremer AE, et al. *Drugs* 2008;68(15):2163-82.

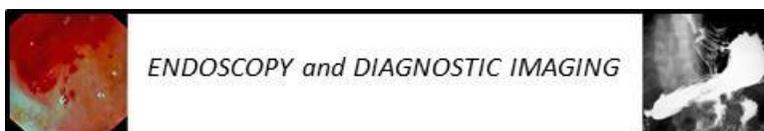
- The causes of post-operative jaundice, associated first with hepatocellular Injury (predominant serum ALT elevation with or without hyperbilirubinemia), and secondly with cholestatic jaundice (elevated serum alkaline phosphatase, GGT, direct hyperbilirubinemia).
 - Hepatocellular Injury (predominant serum ALT elevation with or without hyperbilirubinemia)
 - Inhalational anesthetics-halothane, others
 - Ischemic hepatitis (shock liver)
 - Hepatic artery thrombosis



- Other drugs-antihypertensives (eg: labetalol), heparin
 - Acute post-transfusion hepatitis
 - Unrecognized previous chronic liver disease-NASH, HCV etc
 - Hepatic allograft rejection
- Cholestatic Jaundice (elevated serum alkaline phosphatase, GGT, direct hyperbilirubinemia)
- Benign postoperative cholestasis
 - Cardiac bypass of prolonged duration
 - Sepsis
 - Acalculous cholecystitis
 - Common bile duct obstruction-gallstones, pancreatitis
 - Cholangitis
 - Bile duct injury-post-cholecystectomy, post-liver transplantation
 - Microlithiasis (biliary sludge)
 - Prolonged total parenteral nutrition
 - Hemobilia
 - Drugs-amoxicillin-clavulanate, chlorpromazine, erythromycin, teletromycin, trimethoprim-sulfamethoxazole, warfarin, others
- Indirect hyperbilirubinemia (serum alkaline phosphatase and ALT often normal)
- Multiple blood transfusions
 - Resorbing hematoma
 - Hemolytic anemia

Adapted from: Stevens WE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1856.

- The causes of postoperative jaundice .
- Increased bilirubin production (indirect hyperbilirubinemia; SAP/ALT often normal)
- Destruction of transfused erythrocytes
 - Hemolysis secondary to pre-existing hemolytic conditions (eg: G6PD deficiency, hemoglobinopathies)
 - Hemolysis secondary to mechanical heart valve prostheses
 - Reabsorption of hematomas
 - Multiple blood transfusions
- Hepatocellular Injury
- Ischemic hepatitis ("shock liver")
 - Hepatic artery thrombosis
 - Hepatic allograft rejection
 - Drug- or anesthetic-induced hepatotoxicity
 - Viral hepatitis



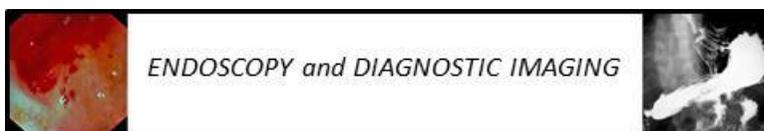
- Intrahepatic cholestasis (↑ SAP; GGT; direct hyperbilirubinemia)
 - Sepsis, bacterial abscess
 - Drug-induced cholestasis
 - Total parenteral nutrition
 - Benign postoperative cholestasis
 - Prolonged cardiac bypass
- Extrahepatic biliary obstruction
 - Bile duct ligation/injury
 - Choledocholithiasis
 - Acalculous cholecystitis
 - Post cholecystectomy, post liver transplantation
 - Microlithias (biliary sludge)
 - Postoperative pancreatitis
 - Extrinsic compression of common bile duct or common hepatic duct
 - Hemobilia
- Pre-existing Abnormalities in Bilirubin Metabolism/Excretion
 - Chronic liver disease
 - Gilbert's syndrome

Adapted from: Faust TW, and Reddy KR. *Clin Liver Dis* 2004;8(1):151-66.

- The factors contributing to physiological jaundice in the neonate.
 - Absence of placental bilirubin metabolism
 - Reduced hepatic blood flow via ductus venosus shunting
 - Decreased red blood cell survival
 - Proportionally increased red blood cell mass
 - Reduced enteric bacterial flora
 - Presence of intestinal β -glucuronidase
 - Immature liver function
 - Delayed oral feeding

Hepatic Fibrosis

- The pathophysiological factors responsible for the development of hepatic fibrosis.
 - Extracellular matrix proteins (EMP)
 - Hepatic stellate cells (HSC)
 - Activation of HSC to form myofibroblasts
 - Other mesenchymal cell populations and bone marrow-derived cells



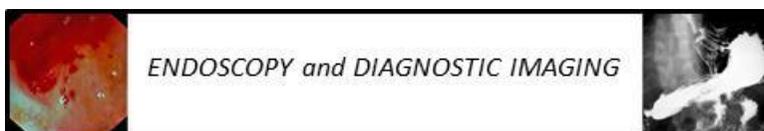
- Hepatocyte growth factor
- TGFB
- Renin-angiotensin system (RAS)
- Angiotensin-converting enzyme (ACE)
- Angiotensin I and II receptors
- Endotoxin, lipopolysaccharide (LPS)
- Toll-like receptor (TLR4)
- Angiogenesis
 - Vascular endothelial growth factor (VEGF)
 - Angioporetin 1, 2

Adapted from: Jiao J, et al. *Curr Opin Gastroenterol* 2009;25(3):223-9.

Enterohepatic Circulation of Bile Salts

- The hepatocyte and ileal enterocytes transporters responsible for the enterohepatic circulation of bile salts.
 - Hepatocyte
 - Blood side (sinusoidal /BLM)
 - NTCP/SLC10A1 (sodium-taurocholate cotransporting polypeptide)
 - Na⁺/K⁺-ATPase
 - OATPs/SLCO1 (organic anion transporting peptides)
 - Bile side
 - BSEP/ABCB11 (bile salt export pump)
 - MRP₃/ABCC₃ and MRP₄/ABCC₄ (multidrug resistance-associated proteins 3 and 4)
 - OST2/B (organic solute transporter alpha-beta)
 - Enterocyte
 - Lumen side (BBM)
 - ASBT/SLC10A₂ (apical Na⁺- dependent bile salt transporter)
 - OST2/B (organic solute transporter alpha-beta)

Adapted from: Dawson PA. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1374.



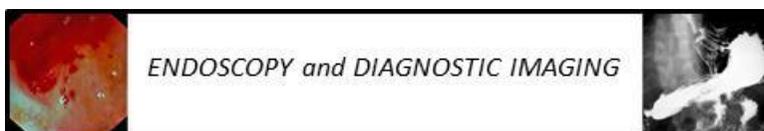
Useful background: Give 4 proteins involved in the hepatic transport, metabolism and signaling of secretion of bile; indicate the diseases associated with defects in these proteins, and the potential implications for therapy of ductopenia (VBDS, vanishing bile duct syndrome).

- FXR agonists (for cholestasis and NAFLD)
- Nuclear receptor (PXR CAR) stimulation to activate cytochromes
- Stimulate phospholipid export pumps (Mdr3[Abcb4])
- Statins (\uparrow PPAR α)
- Replace toxic CDCA with KDCA (NOX3-rich choleresis, but high doses cause bile infarcts and \uparrow mortality) or modified KDCA (Norkoca), resistant to taurine conjugation
- VCAM reduction by NARKDCA (silence the active phenotypes so there is less vascularisation – bile ducts both cause duct damage, and are themselves damaged)
- AKT, mTOR, Rps6 stimulation

Adapted from: Francis GA, et al. *Annu Rev Physiol* 2003;65:261-311. Epub 2002 May 1.

PORTAL HYPERTENSION

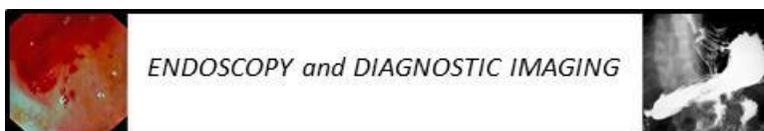
- The constituents of the portal vasodilatory and vasoconstrictory systems.
 - Vasodilator systems
 - Adenosine
 - Adrenomedullin
 - Arterial natriuretic peptide (ANP)
 - Bradykinin
 - Brain natriuretic peptide (BNP)
 - Calcitonin gene-related peptide (CGRP)
 - Carbon monoxide (CO)
 - Endocannabinoids
 - Endothelin-3 (ET-3)
 - Endotoxin
 - Enkephalins
 - Glucagon
 - Histamine
 - Hydrogen sulphide
 - Interleukins
 - Natriuretic peptide of type C (CNP)
 - Nitric oxide (NO)
 - Prostacyclin (PGI₂)
 - Substance P



- Tumor necrosis factor- α (TNF- α)
- Vasoactive intestinal polypeptide (VIP)
- Vasoconstrictor systems
 - Angiotensin II
 - Adrenaline and noradrenaline
 - Sympathetic nervous system (SNS)
 - Endothelin-1 (ET-1)
 - Neuropeptide Y
 - Renin-angiotensin-aldosterone system (RAAS)/
 - Vasopressin (ADH)

Printed with permission: Møller S, and Henriksen JH. *GUT* 2008; 58: pg. 271.

- The circulatory changes in specific vascular beds in cirrhosis.
 - Systemic circulation
 - Plasma volume \uparrow
 - Total blood volume \uparrow
 - Non-central blood volume \uparrow
 - Central and arterial blood volume \downarrow (\rightarrow)
 - Arterial blood pressure \downarrow (\rightarrow)
 - Systemic vascular resistance \downarrow
 - Cutaneous and skeletal muscle circulation
 - Skeletal muscular blood flow* $\uparrow \rightarrow \downarrow$
 - Cutaneous blood flow* $\uparrow \rightarrow \downarrow$
 - Heart
 - Heart rate \uparrow
 - Cardiac output \uparrow
 - Left atrial volume \uparrow
 - Left ventricular volume \rightarrow (\uparrow)
 - Right atrial volume $\rightarrow \uparrow \downarrow$
 - Right atrial pressure $\rightarrow \uparrow$
 - Right ventricular end-diastolic pressure \rightarrow
 - Pulmonary artery pressure $\rightarrow \uparrow$
 - Pulmonary capillary wedge pressure \rightarrow
 - Left ventricular end-diastolic pressure \rightarrow
 - Total vascular compliance \uparrow
 - Arterial compliance \uparrow
 - Hepatic and splanchnic circulation
 - Hepatic blood flow† $\downarrow \rightarrow (\uparrow)$



- Hepatic venous pressure gradient ↑
- Postsinusoidal resistance ↑
- Renal circulation
 - Renal blood flow ↓
 - Glomerular filtration rate (↑) ↓ →
- Cerebral circulation
 - Cerebral blood flow ↓ →
- Pulmonary circulation
 - Pulmonary blood flow ↑
 - Pulmonary vascular resistance ↓ (↑‡)
 - Pulmonary blood volume ↓
 - Pulmonary transit time ↓

↑→↓ denote: increased, unchanged and decreased, respectively. Arrows in parentheses describe early/less typical changes.

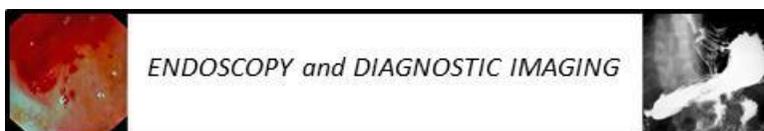
*Available data are highly dependent on the applied technique

†Changes in intrahepatic blood flow due to variable co-determination of portosystemic shunts

‡Increased in portopulmonary hypertension

Printed with permission: Møller S, and Henriksen JH. *GUT* 2008; 58: pg. 269.

- The patient-related 5 laboratory-related predictors of progression of NAFLD to NASH.
 - Patient
 - Age > 45 years
 - Ethnicity (Hispanic, Asian >White >Black)
 - Female
 - Type II diabetes mellitus
 - BMI > 35 (especially visceral obesity)
 - Insulin resistance
 - Hypertension
 - Metabolic syndrome (insulin resistance), even in young, non-obese persons
 - Stigmata of portal hypertension
 - Laboratory
 - ↑ ALT > 2x ULN
 - ↑AST:ALT >1 [suggests fibrosis]
 - ↑ Triglycerides >1.5
 - ↑ INR

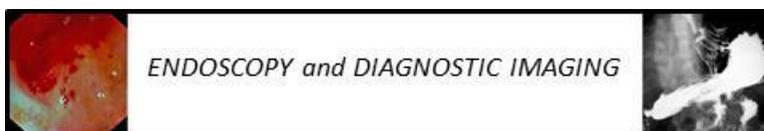


- ↑ Bilirubin
 - ↓ Platelets
 - ↓ Albumin
 - Indexes of insulin resistance (HOMA, QUICKI, OGIS)
 - ↑ Elevated ferritin levels
 - ↑ Hyaluronic acid*
 - Anti-MDA antibodies*
- Imaging biopsy
- Fibroscan
 - Severe steatosis (macro steatosis, centrilobular)
 - Stainable iron
 - Signs of cirrhosis
- * useful if normal

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HOMA, homeostatic model assessment; MDA, malondialdehyde; OGIS, oral glucose insulin sensitivity index; QUICKI, quantitative insulin-sensitivity check index; ULN, upper limit of normal.

Adapted from: Pinzani, et al. *Nature Clinical Practice Gastroenterology & Hepatology*, 2008; 5(2): pg 102. and from Reid et al., *Gastrointestinal and Liver Disease*, 2010, pg 1408

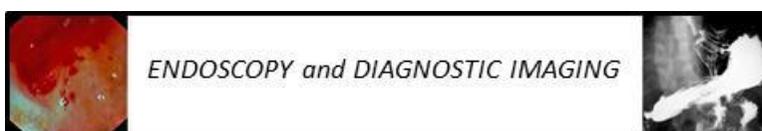
- The liver biopsy criteria for NASH.
- Present in all or most cases
- Diffuse or centrilobular steatosis, predominantly macrovesicular degree may correlate with BMI
 - parenchymal inflammation (+/- focal necrosis), neutrophils, macronuclear cells
 - Lobular necrosis
- Features observed with varying frequency
- Ballooning hepatocyte degeneration
 - Pericellular fibrosis (chicken wire fibrosis) – perivenular* (zone 3), perisinusoidal on periportal (37%-84%)
 - Mallory bodies
 - NAFLD Activity Score
 - Cirrhosis (7%-16% on index biopsy)
 - Glycogenated nuclei
 - Lipogranulomas
 - Stainable iron



Adapted from: Reid AE. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1796 and 2010, pg 1407

- A detailed grading and staging of the biopsy lesions of NASH.
 - Grade I. Mild
 - Steatosis: predominantly macrovesicular, involves <33% or up to 66% of the lobules; increased BMI may correlate with BMI
 - Ballooning: occasionally observed; zone 3 hepatocytes
 - Lobular inflammation: scattered and mild acute (polymorphs) and chronic (mononuclear cells) inflammation
 - Portal inflammation: none or mild
 - Grade 2. Moderate
 - Steatosis: any degree and usually mixed macrovesicular and microvesicular
 - Ballooning: present in zone 3
 - Lobular inflammation: polymorphs may be noted associated with ballooned hepatocytes, pericellular fibrosis; mild chronic inflammation may be seen
 - Portal inflammation: Mild to moderate
 - Grade 3. Severe
 - Steatosis: typically >66% (panacinar): commonly mixed steatosis
 - Lobular inflammation: scattered acute and chronic inflammation; polymorphs may appear concentrated in zone 3 areas of ballooning and perisinusoidal fibrosis
 - Portal inflammation: Mild to moderate
 - Staging (fibrosis)
 - Stage 1: zone 3 perivenular perisinusoidal fibrosis, focal or extensive
 - Stage 2: as above plus focal or extensive periportal fibrosis
 - Stage 3: bridging fibrosis, focal or extensive
 - Stage 4: cirrhosis

Printed with permission: Cortez-Pinto H, and Camilo ME. *Best Practice & Research Clinical Gastroenterology* 2004;18(6): pg 1097.



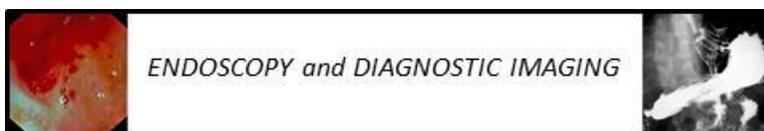
Autoimmune Hepatitis (AIH)

- Give 4 forms or types of AIH
 - I (f, 50) ANA+ ASM+ IgG↑
 - II (children) ALKMI+
 - III (M, 30) ASLA/LP+
 - Overlap syndrome AMA-neg. PBC, PSC, AMA-

Adapted from: Czaja AJ. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1872-1875 and 2010, pg 1467

- The clinical presentations of AIH.
 - Acute hepatitis
 - Fulminant hepatitis
 - Asymptomatic chronic hepatitis +/- cirrhosis
 - Symptomatic chronic hepatitis +/- cirrhosis
 - "Burned out" decompensated cirrhosis +/-
 - *De novo* or recurrent AIH after liver transplantation
 - AIH with overlapping PBC/PSC/AMA-neg PBC
- The established or likely factors that are associated with progression of HCV.
 - Established
 - Age at infection (>40 yrs)
 - Gender (Male)
 - Race (Caucasian)
 - Immunosuppression (HIV coinfection, agammaglobulinemia, organ transplantation)
 - Genotype, no association
 - Level of viremia, no association
 - Alcohol (>50 g/day)
 - Likely
 - HBV coinfection
 - NASH/obesity/diabetes (hepatic steatosis)
 - Schistosomiasis
 - Smoking
 - Iron overload
 - Elevated serum ALT levels (elevated)
 - Histology - Moderate to marked necroinflammation

Adapted from: Berenguer M, and Wright TL. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1696; 2010, pg 1325



- The adverse effects of the use of interferon to treat HBV

- Early

- Flu-like illness; headaches, nausea
- Tenderness at site of infection

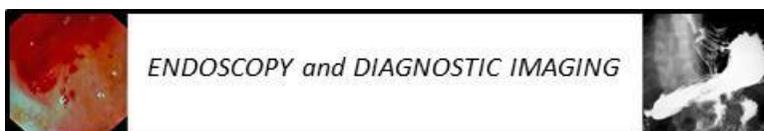
- Late

- Fatigue
- Muscle aches
- ↑retinopathy m'DM
- Irritability Anxiety and depression
- Weight loss
- Diarrhea
- Alopecia
- Bone-marrow suppression
- Bacterial Infections
- Autoimmune autoantibodies
- Optic tract neuropathy
- Anorexia
- Worsening thyroid disease
- CNS (neuropsychiatric)
- Bone marrow
- HCV?
- Child pregnancy
- Eyes
- Head/neck
- Lichen planus worsens
- IBD worsens
- Autoimmune diseases worsen
- Class C for pregnancy

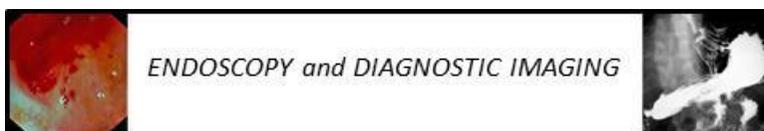
Adapted from: Grover PT, and Bain V. *First Principles of Gastroenterology* 2005: 547-563.

Blood vessels

- The presentation, etiology, diagnostic imaging and histological changes, as well as management of hepatic vein occlusion (Budd-Chiari syndrome).
- Presentation
 - Abdominal pain
 - Hepatomegaly
 - Ascites

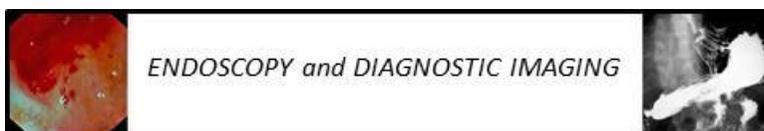


- Etiology
 - Hypercoagulable states
 - Inherited
 - Factor V Leiden mutation
 - Prothrombin mutation
 - Antithrombin deficiency
 - Protein C deficiency
 - Protein S deficiency
 - Acquired
 - Myeloproliferative disorders
 - Cancer
 - Pregnancy
 - Oral contraceptive use
 - Paroxysmal nocturnal hemoglobinuria
 - Antiphospholipid syndrome
 - Tumor invasion
 - Hepatocellular carcinoma
 - Renal cell carcinoma
 - Adrenal carcinoma
 - Miscellaneous
 - Aspergillosis
 - Behçet's syndrome
 - Inferior vena cava webs
 - Trauma
 - Inflammatory bowel disease
 - Dacarbazine therapy
 - Idiopathic
- Diagnostic imaging/histology
 - MRI (contrast enhanced)
 - Doppler ultrasound
 - Liver biopsy (zone 3 congestion)
- Management
 - Cause
 - Anticoagulants, thrombolysis, venesection
 - Cytotoxic drugs
 - Surgical
 - Porta-caval shunt
 - TIPS
 - Liver transplantation



Adapted from: Stevens WE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1756.; and printed with permission: Kamath PS. *Clinic Gastroenterology and Hepatology Board Review* 2008: pg. 343; 2010, pg 1372.

- The causes of portal vein thrombosis.
 - Hypercoagulable states
 - Antiphospholipid syndrome
 - Antithrombin deficiency
 - Factor V Leiden mutation
 - Methylenetetrahydrofolate reductase mutation TT677
 - Myeloproliferative disorders
 - Nephrotic syndrome
 - Oral contraceptives
 - Paroxysmal nocturnal hemoglobinuria
 - Polycythemia rubra vera
 - Pregnancy
 - Prothrombin mutation G20210A
 - Protein C deficiency
 - Protein S deficiency
 - Sickle cell disease
 - Impaired portal vein flow
 - Budd-Chiari syndrome
 - Cirrhosis
 - Nodular regenerative hyperplasia
 - Sinusoidal obstruction syndrome
 - Inflammatory diseases
 - Behçet's syndrome
 - Inflammatory bowel disease
 - Pancreatitis
 - Infections
 - Appendicitis
 - Cholangitis
 - Cholecystitis
 - Diverticulitis
 - Liver abscess
 - Cancer
 - Pancreas
 - Cholangiocarcinoma
 - HCC
 - Bladder cancer



- Intra-abdominal procedures
 - Alcohol injection
 - Colectomy
 - Endoscopic sclerotherapy
 - Fundoplication
 - Gastric banding
 - Hepatic chemoembolization
 - Hepatobiliary surgery
 - Islet cell injection
 - Liver transplantation
 - Peritoneal dialysis
 - Radiofrequency ablation of hepatic tumor (s)
 - Splenectomy
 - TIPS procedure
 - Umbilical vein catheterization

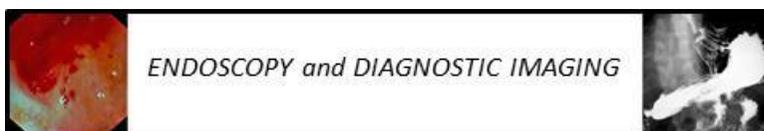
Adapted from: Stevens WE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1762; 2010: pg 1378.

HE; Hepatic encephalopathy (aka PSE, portosystemic encephalopathy)

A semi-quantitative grading of the mental state of persons with PE.

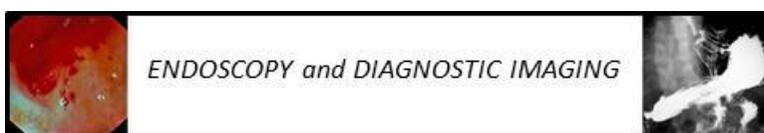
Grade	Criteria
○ 0 (MHE, sub clinical HE)	Impaired mental tasks (psychomotor speed, visual perception, attention)
○ I	Trivial lack of awareness; euphoria or anxiety; shortened attention span; impaired performance of addition; sleep-wake disorder; tremor
○ II	Lethargy or apathy; minimal disorientation of time or place; subtle personality changes; inappropriate behavior; impaired performance of subtraction
○ III	Somnolence to semi-stupor, but responsive to verbal stimuli; confusion, gross disorientation
○ IV	Coma (unresponsiveness to verbal or noxious stimuli)

Adapted from: Fitz GJ. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006 pg. 1966; 2010, pg 1545



- Risk factors for developing HCC (hepatocellular cancer).
 - Patient
 - Africans > 20 years (HBV)
 - Asian males > 40 years (HBV)
 - Asian females > 50 years (HBV)
 - FH of HCC
 - Dietary aflatoxin exposure
 - Obesity
 - Tobacco, marijuana smoking
 - Oral contraceptives
 - Without cirrhosis
 - Chronic HBV infection (even without cirrhosis)
 - Chronic HCV infection (Japan; all others, HCV cirrhosis)
 - Hepatic adenoma
 - Hemochromatosis
 - Aflatoxin B1
 - Congenital/familial
 - Previously resected HCC
 - Cirrhosis
 - HCV
 - HCV +ALD + obesity (accelerated)
 - ETOH
 - Hemochromatosis- dietary Fe overload in persons of African ancestry; hereditary hemochromatosis
 - PBC
 - alpha-1-antitrypsin deficiency
 - NASH
 - autoimmune hepatitis
 - Wilson's disease
 - Type 1 hereditary tyrosinemia
 - Type 1 and type 2 glycogen storage disease
 - Hypercitruinemia
 - Ataxia-telangiectasia

Adapted from: Gores GJ. *AGA Institute Post Graduate course book* 2006. pg. 257.; and Kew MC. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006: pg.2014; 2010: pg. 1575



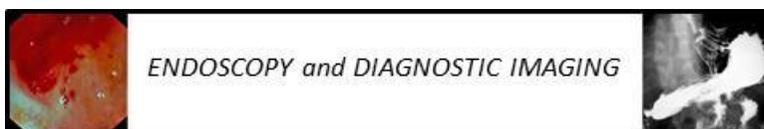
- The most common primary liver diseases representing indications for liver transplantation.
 - Chronic HCV
 - Alcoholic liver disease (ALD)
 - Cryptogenic cirrhosis (NASH)
 - PSC
 - PBC
 - Chronic HBV
 - ALD + HCV
 - Hepatoma
 - AIH
 - α_1 AT deficiency
 - Drug induced liver disease
 - Hemochromatosis, Budd-Chiari syndrome, Wilson's disease

Adapted from: Martin P, and Rosen HR. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 2037; 2010; pg 1594

- The protocol for evaluation of potential living-related liver donors.

- | | |
|---------|--|
| Stage 1 | <ul style="list-style-type: none"> ○ Complete history and physical examination ○ Laboratory blood tests: liver biochemical test, blood chemistry, hematology, coagulation profile, urinalysis, alpha-fetoprotein, carcinoembryonic antigen, and serologic tests for hepatitis A, B, and C, cytomegalovirus, Epstein-Barr virus, and human immunodeficiency virus ○ Imaging studies: abdominal ultrasound examination, chest x-ray |
| Stage 2 | <ul style="list-style-type: none"> ○ Complete psychiatric and social evaluation ○ Imaging studies: computed tomography scan of the abdomen |
| Stage 3 | <ul style="list-style-type: none"> ○ Other studies: pulmonary function tests, echocardiography ○ Histology: liver biopsy ○ Imaging studies: celiac and superior mesenteric angiography with portal phase |
| Stage 4 | <ul style="list-style-type: none"> ○ Imaging studies: magnetic resonance cholangiogram <p>Informed consent</p> |

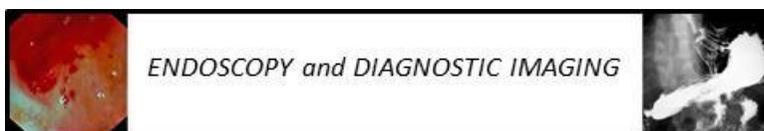
Printed with permission: Ghobrial RM, et al. *Clin Liver Dis* 2000; 4: pg. 553. Cholangiocarcinoma is the second most common hepatic tumor.



- The causes, locations and imaging characteristics of cholangiocarcinoma.
 - Etiologies
 - PSC
 - Caroli's
 - Choledochal cyst
 - Thoratrast
 - Locations
 - Hepatic bifurcation (Klatskin tumor)
 - Distal CBD
 - Intrahepatic (5-15%)
 - Imaging
 - Variable fibrosis and necrosis
 - Atrophy
 - Capsular retraction
 - Biliary duct dilation
 - Hypovascular (progressive, delayed hyperenhancement)

Recent Updates:

- Hepatocellular Cancer (HCC)
 - Hepatic nodules smaller than 2 cm in diameter may still contain a focus of HCC. Imaging techniques may show hypervascularization in the arterial phase, followed by washout in the venous phase, suggestive of malignancy. Non-invasive criteria have been established by American and European groups (AASLD and EASL), and provide a similar sensitivity of about 80% in making a diagnosis of what turns out to be HCC. The most sensitive and specific imaging technique for the diagnosis of HCC is Gad-MR (gadolinium magnetic resonance). Other methods include contrast-enhanced ultrasonography, helical-computed tomography, and superparamagnetic iron oxide magnetic resonance (Lesni et al., AJC 2010; 105: 599-609).
- Post Liver Transplantation Steatosis
 - Steatosis occurs in as many as a third of persons following a liver transplantation (LT), with a histological diagnosis of NASH occurring in about 10% of these persons. Multivariate analysis has shown that seven factors predict the risk for post-LT steatosis: post-LT obesity, diabetes mellitus, hyperlipidemia, arterial hypertension, a tacrolimus-based immunosuppression regimen, and alcoholic cirrhosis as the primary indication for LT (Dumortier et al., AJG 2010; 105: 613-620). The more of these risk factors that are present, the higher their rate



for steatosis: for example; 3 factors, 30% risk; 4-66%; 5-82%; 6 risk factors, 100% ped LT steatosis.

SO YOU WANT TO BE A HEPATOLOGIST!

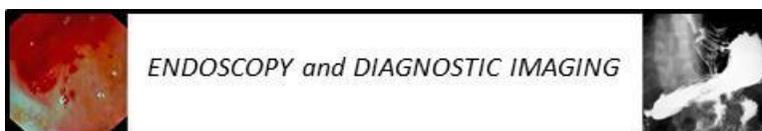
- Q. Bariatric surgery may improve NASH; how useful is dieting for persons with NASH?
- A. There is an inverse linear relationship between increasing weight loss and a decline in NAS (NAFLD activity score; even just a 5% loss of body weight has a clinically meaningful decline in NAS)

Diagnostic imaging

- Diffuse Disease
 - Cirrhosis
 - Fatty infiltration
 - Iron overload
 - Glycogen storage disease
 - Budd-chiari syndrome
 - Amiodarome-induced disease
 - Radiation-induced disease

MRI	Signal intensity	
	Low	High
○ T ₁	+	
○ T ₁ Fe		+
○ T ₂		+
○ T ₂ Cu/Fat	+	

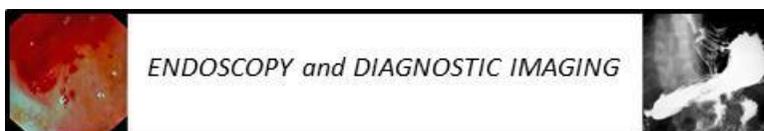
- Cirrhosis
- CT
 - Small liver nodules (≤ 3 mm)
 - Heterogeneous
 - Nodules
 - Multiple
 - Small / large
 - Low-density (R.lobe atrophy; left and candate lobes – hypertrophy)
 - Lobe L > R
 - Confluent hepatic fibrosis – nedge –shape area from porta hepatitis to capsule
 - Low-intensity on T₁ high – intensity on T₂ MRI
 - No venous invasion



- Does not change size over time
- Spleen – enlarged
- Esophageal varices
- Recanalized “umbilical veins” (enlarged collateral vein (i.e., a paraumbilical vein; when large, are called “cap” and nodusae)
- MRI T₁
 - Weighted, unchanged
 - Multiple
 - Nodules
 - Small / large
 - Low-signal intensity on T₁
 - Varying signal intensity
 - High signal intensity on T₁
 - Nodule contains fat / copper
- MRI T₂
 - Weighted, unenhanced
 - High signal intensity mass

T₁ – weighted low-signal intensity appear high-signal intensity on T₂ (T₁ – low-signal, dark; T₂ – high-signal, white) when T₂ is low-signal intensity (is normally high-signal intensity)

- Cardiac Cirrhosis (C6.5)
 - Enlarged liver
 - Mottled (like B.C.S)
 - Enlarged IVC, hepatic vein
 - Ascites
 - Doppler ultrasound:
 - Reduced-continuous flow
 - Increased-Pul satility
- Fatty Liver (C6.6, 7, 8)
 - Diffuse / focal
- MRI
 - T₁ – weighted
 - In-phase - ↑ signal intensity (low attenuation) dark
 - Out-of-phase - ↓ signal intensity (high attenuation) light
 - T₂ – normal
- CT
 - ↓ attenuation
- Ultrasound
 - ↑ echogenic



- Hemochromatosis
 - T₂ – weighted MRI liver: diffuse, low-signal intensity (↑ attenuation)
 - If focal, high-signal intensity, possible HCC
 - Spleen: high-signal intensity
 - Hemochromatosis
 - Heart (but not spleen or bone marrow) Fe in liver, spleen, bone marrow

- Budd – Chiari Syndrome
 - CT
 - Liver-heterogeneous diffuse, enhancement (hyperattenuation) of hepatic parenchyma
 - Hepatomegaly
 - Ascites
 - Chronic B-CS: parts of liver:
 - Peripheral – atrophy
 - Candidate lobe, hypertrophy
 - Portal vein thrombosis
 - Compression of IVC
 - Thombus (↑ density)

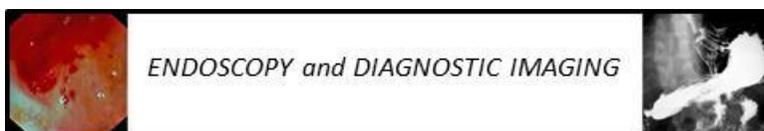
 - Wedge hepatic venogram
 - “spider-web” pattern of intrahepatic collaterals (pathognomonic for sublobular venous occlusion)

 - Primary B-CS – membranous obstruction of hepatic veins

 - 2° B-CS – obstruction of
 - Central and sublobular venous flow to liver, or
 - Obstruction of major hepatic veins

- Radiation – associated liver injury
 - Ultrasound: irradiation zone ↓echogenicity (edema / fat)
 - CT: ↓ attenuation (white)
 - MRI:
 - T₁ – weighted images, low-signal intensity
 - T₂ – weighted images, high – signal intensity

 - Hepatic Cysts
 - Simple
 - Polycystic
 - Hemorrhagic
 - Von Meyenbury complexes
 - Peri biliary



➤ Liver Cyst (C6.16)

Definition: Liver cyst – an epithelial-lined, fluid-filled space

➤ Ultrasound

- Cysts
- Anechoic (dark)
- Thin-walled
- Well-circumscribed
- Posterior acoustic enhancement
- Superior test to CT for cysts

➤ CT

- Low-attenuation lesions (no enhancement, dark)

➤ MRI-unenhanced

- T₂-weighted (white)

• Polycystic Disease, autosomal

➤ Dominant some cysts may be hemorrhagic

- Multiple cysts
- Cysts in kidney, liver, pancreas, spleen, bile ducts, heart
 - Peribiliary cysts
 - Mitral valve prolapsed
 - Bicuspid aortic valve
 - Aortic aneurysms
 - Aortic dissections
- CNS
 - Berry aneurysms
- Doppler ultrasound
 - No blood flow
- No fibrosis
- Large cysts may compress portal / vein (→ portal hypertension)

➤ Recessive

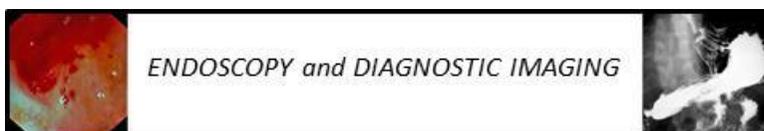
- Cysts may be associated with fibrosis

• Hemorrhagic Cyst

➤ Ultrasound

- Complex cystic masses
- Internal echos (cystic mass plus solid blood clots)
- No internal blood flow

➤ CT



- ↑ attenuation (fluid density masses)
- As enhancing rim

Distinguishing Diagnosis: cyst vs. cystic tumor

	Cyst	Cystic Tumor
○ CT: enhancing rim	-	+
○ Doppler: internal blood flow	-	+

• Von Meyen Burg Complex

Definition: Von Meyen Burg complexes (biliary hamartomas) – cluster of proliferating bile ducts within a fibrous stroma

➤ Ultrasound

- Small
- Hypochoic if cholesterol is proliferating bile ducts

➤ CT

- Small
- Low-attenuation (dark)

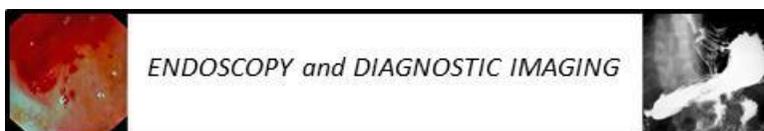
➤ MRI

- T₂ – weighted images no little enhancement

• Peribiliary Cysts

➤ MRCP

- Cysts
 - Around bile ducts
 - Whitish
 - Discrete
 - Clusters
 - Strings
- Intra- / extrahepatic bile ducts – normal
- Associations
 - Cirrhosis
 - Portal hypertension
 - Cholangitis
 - Hepatic transplantation
 - Autosomal dominant polycystic kidney disease



➤ Hepatic Abscesses

- Pyogenic
- Amebic
- Echino coccal
- Candidiasis

• Pyogenic Hepatic Abscess

➤ CT

- Solitary or multiple (cluster of masses)
- Masses often communicate
- Low-attenuation (dark) (“water density”, water-attenuation)
- High-attenuation rings / rim (light)

• Amebic Hepatic Abscess

➤ CT

- Large mass
- Single (unilobular)
- Right lobe
- Low-attenuation. “water density” (dark)
- Low-attenuation (low density) (dark)

• Echinococcal Hepatic Abscess

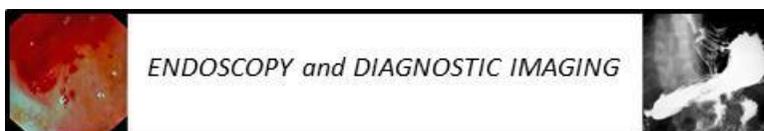
➤ CT

- Small cysts within large multilobulated mass
- Unilocular
- Low-attenuation (low-density) (dark)
- Walls of variable density
- Ring of calcification (high-attenuation, high density; white)

• Candidiasis of Liver

➤ Ultrasound

- Masses
 - Small
 - Multiple
 - Low-attenuation
- “Bull’s eye” pattern (hyperechoic centre, hypoechoic rim)
- “wheel-within-a wheel” patters hypoechoic centre, hyperechoic rim surrounded by hypoechoic rim
- Hypoechoic liver (fibrosis)
- Echogenic liver
 - Scar formation



- CT
 - Masses
 - Small
 - Multiple
 - Hypoattenuating
 - Calcification, scattered
 - Periportal ↑ attenuation (fibrosis)

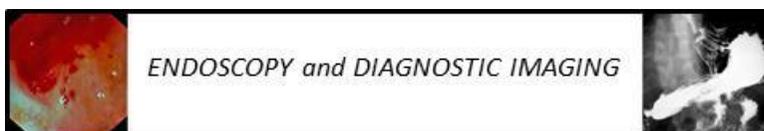
Benign Liver Tumors

- Hemangioma
- Focal nodular hyperplasia (FNH)
- Hepatic adenoma
- Biliary cystadenoma
- Angiomyolipoma
- Cyst

- Hepatic Hemangioma

Definition: Hemangioma-vascular channels of varying size arising from vascular endothelial cells in fibrous septae

- CT
 - Masses
 - Single (2/3) or multiple
 - Small (< 4 cm)
 - When > 4 cm, called “giant cavernous hemangioma”
 - Globular
 - Peripheral
 - Low-attenuation (dark)
 - Peripheral nodular enhancement (high attenuation; white)* on early phase of contrast enhancement
 - Progressive centripetal fill-in** of peripheral enhancement after 5 to 30 min pathognomic
 - Central area of fibrosis in larger tumor masses
 - Central enhancement
 - Early enhancement
 - Diffuse
 - Rapid washout
- MRI
 - T₁-weighted sequence – low-signal intensity (dark)
 - T₂-weighted sequence (suppresses signal from fat)
 - High signal intensity (white)
- Gadolinium scan



- Peripheral nodular enhancement
 - Delayed filling (1 to 2 hours)
 - Progressive centripetal fill-in
- Ultrasound
- Mass
 - Homogeneous (in 2/3)
 - Hyperechoic (white; from numerous vascular channels)
 - Doppler ultrasound not helpful because of low flow in hemangioma
 - No hypoechoic halo (as is seen in echogenic tumor metastases)

Distinguishing diagnosis: Hemangioma vs Vascular tumor

	Hemangioma	Vascular tumor
Ultrasound		
Mass hyperchoic	+	+
Hypogenic halo	-	+
RBC scan		
Uptake early	-	+
Uptake late	+	

• Giant Cavernous Hemangioma

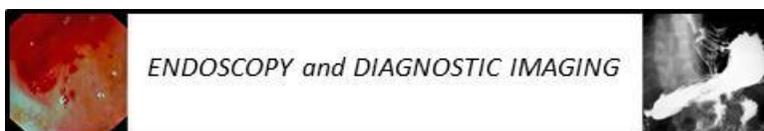
- Associated with
- Rupture
 - Bleeding
 - Thrombocytopenia
 - Intrahepatic consumptive coagulopathy
 - Biliary obstruction
 - Budd – Chiari Syndrome

• Focal Nodular Hyperplasia (FNH)

Definition: Focal nodular hyperplasia (FNH) – “a solid mass of abnormally arranged hepatocytes, bile ducts and Kupffer cells” (hemartoma)

➤ CT

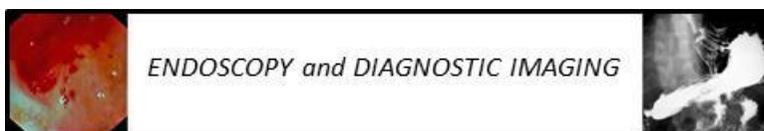
- Mass
- Unenhanced, very difficult to see (“stealth”)
- Solitary (80%)
- Homogeneous enhancement during arterial phase
- Central stellate scar
- No capsule



- Peripheral enhancement (large peripheral veins)
 - Fibrous septa which divides tumor into lobules
- Ultrasound
- Difficult to see (isoechoic)
 - Central scar, hypoechoic
 - Subtle changes in contour
 - Subtle displacement of normal vessels
 - Hypervascular centrally
- MRI
- T₁-weighted
 - Isointense mass, hypotense/low-signal intensity (white/dark)
 - T₂-weighted
 - Central stellate scar, hyperintense (white)
 - Mass, isotense / hypotense
 - Post-gadolinium
 - Arterial-phase
 - Mass
 - Homogeneous arterial enhancement
 - Central stellate scar
 - Hypointense
 - Central to peripheral septations (lobulation, segmentation)
 - Portal venous phase
 - Isotense
 - Homogenous enhancement in arterial phase of MRI enhancement, with no late-enhancing capsule
- Sulphur colloid scintigraphy
- Uptake of tracer into Kupffer (RE, reticuloendothelial) cells equal to or greater than that of normal surrounding liver-pathognomic for FNH
 - When FNH is multiple (20%), then in 25% of the multiple FNH, there are hepatic hemangiomas

Distinguishing diagnosis: FNH, Adenoma, Fibrolamellar HCC

	FNH	Hepatic adenoma	Fibrolamellar HCC
Enhancement	Homogenous	Heterogeneous	Homogeneous
Central stellate scar	+	-	+
Adenopathy, invasion of vessels	-	-	+



- Hepatic Adenoma

- CT
 - Contrast enhanced
 - Mass
 - Large
 - Solitary
 - Heterogeneously enhancement
 - Multiple compartments
 - Capsule
 - Unenhanced
 - High attenuation mass
 - “whorled” appearance: hemorrhage into adenoma
- MRI
 - T₁ weighted
 - Increased signal intensity (dark)
 - T₂ weighted
 - Heterogeneous
 - High-intensity

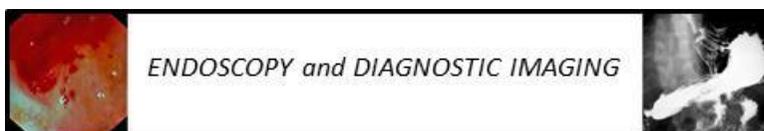
Note: cannot be reliably distinguish between metastases and hepatoma
HCC

Subcapsular hemorrhage (unenhanced CT, high attenuation mass with
“whorled” appearance suggests bleeding into hepatoma

- Biliary Cystadenoma

Definition: Cystic tumors formed from bile duct precursors, lined by mucin-secreting columnar epithelium

- CT, contrast-enhanced
 - Cystic mass
 - Large
 - Multilocular (septations)
 - Thick capsule
 - No
 - Wall calcification
 - RIM of hyperenhancement
 - Difficult to distinguish from cystadenocarcinoma
 - Mural nodules
 - Septae
 - Thick
 - Irregular
 - Enhancing cystic HCC does not have attenuation / enhancing septations



- Hepatic Angiomyolipomas

- Ultrasound

- Hyperechoic mass
- Single / multiple

- CT, contrast-enhanced

- Focal hyperenhancement (fat; must have in mass to make diagnosis)

Note: Difficult to distinguish from HCC or metastatic liposarcoma (also may contain fat)

- Hepatocellular Cancer (HCC)

- Early

- Advanced

- Focal
- Multifocal
- Diffuse
- Cystic

- Complications

- PV/HV thrombosis (angioinvasion)
- CT, contrast enhanced, arterial phase
 - Hyperattenuating (white) thrombus
- Shunting, intratumoral
- Iron overload
- Thorium dioxide exposure
- Multiple discrete cystic / solid regions
- Cystic / solid regions are central or peripheral

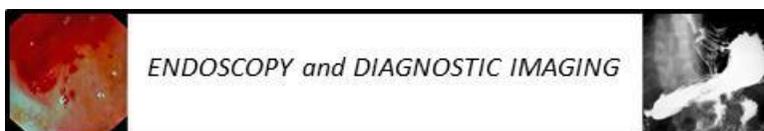
- Diffuse HCC

- Contrast-enhanced CT

- Arterial phase
 - Masses
 - Multiple
 - Fuzzy (not clearly defined)
 - Nodular
 - Enhancing (white)
- Portal-venous/delay phase
 - Poor visualization

- Fibrolamellar HCC

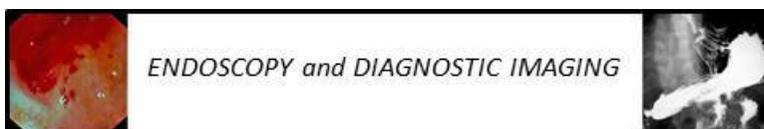
- CT, contract enhanced



- Mass
- Well-circumscribed
- Central scar
- Calcification
- No underlying cirrhosis

Malignant Liver Masses

- Hepatoceelualr carcinoma (HCC)
- Intrahepatic Cholangiocarcinoma
- Biliary cystadenocacinoma
- Lymphoma
- Epitheloid Hemangioendothelioma
- Angiosarcoma
- Metastases
- MRCP
 - Hyperintense mass
 - Multiple dilated ducts
- Hepatocellular Cancer
 - Types
 - Focal
 - Capsule
 - Transient hepatic attenuation defects (THAD) (mass contains both hyper- and hypoattenuating areas; may also see a triangle-shaped area of hyperattenuation)
 - Mosaic appearance
 - Multifocal (multicompartmentalized, mosaic)
 - Multiple discrete cystic / solid regions are central or peripheral
 - MRI
 - T₁ – weighted
 - Hyper intense mass (white)
 - When HCC contains fat, MRI detects mass
 - Low-intensity internal focaus (dark; nodule within a nodule)
 - Capsule
 - Low-intensing T₂-weighted
 - Isointense / hypointense mass
 - High-intensity internal focus (white)
 - Dynamic contrast-enhanced
 - High-intensity internal focus (white) becomes hyperenhancing (white)
 - Delayed contrast-enhanced internal focus becomes isointense
 - High intensity T₁ – weighted MRI images



- HCC or dysplastic nodule
- High intensity T₂-weighted
 - Dysplastic nodule isotense
 - HCC hyperintense

Distinguishing Diagnosis: HCC vs Dysplastic Nodule

	HCC	Dysplastic nodule
○ High-intensity-weighted mass	+	+
○ High intensity mass	+	- (remains isointense)

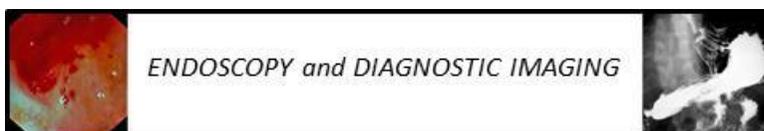
- CT, contrast-enhanced , hypoattenuating mass if HCC contains blood / necrosis
- Arterial phase
 - Hyperenhancing (hyperattenuating) mass (white)
 - Slowly hypoenhancing (hypoattenuating) capsule
 - Portal-venous phase (“washout”); AV shunting)
 - Hyperenhancing disappears
 - Arterial phase hypoattenuating
 - Capsule becomes hyperattenuating on portal-venous phase (late)
 - Dysplastic hepatic nodules also enhance in arterial phase; use MRI to distinguish HCC from dysplastic nodule

Distinguishing Diagnosis: HCC, Lipoma and Hematoma

	HCC	Lipoma	Hematoma
○ T ₁ / ₂ – weighted hyperintense mass	+	-	
○ Capsule	+	-	-

Distinguishing Diagnosis: HCC vs hepatic metastases

	HCC	Metastases
○ Multifocal	+	+
○ Dominant lesion	+	-
○ Hyperattenuation on early phase contrast enhancement	+	-



- Intrahepatic Cholangiocarcinoma (IHC)

- Infiltrating or polypoid mass
- Lobular atrophy hepatic segment
- Metastases
 - Regional nodes
 - Poracaval area
 - Peri pancreatic regions

- MRI

- T₁ – weighted
 - Polypoid mass in bile duct lumen
 - Non-specific changes
 - Hypointense (low signal intensity)
 - Bile duct thickening
 - Mass may surround PV/HA
 - Lobular atrophy
- T₂ – weighted
 - High signal intensity
 - Heterogeneous
 - Duct obstruction
- Mucin
 - Elongated
 - Filling defect

- CT

- MRCP is best exam for IHC
- Hypoattenuating / isoattenuating
- Delayed – hyperattenuating (from fibrosis [desmoplastic] reaction)

.....

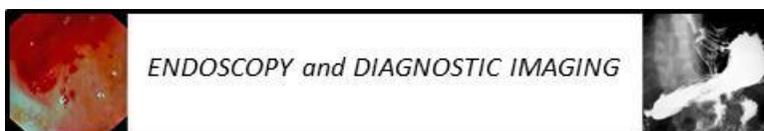
Distinguishing Diagnosis: Intrahepatic cholangiocarcinoma (IHC)

- HCC – hypervascular
 - Cystadenomas – cystic, lobular (septated)
 - Metastasis – cannot be distinguished from IHC
-

- Biliary Cystadenocarcinoma

- Contrast enhanced CT

- Cystic mass
- Multiloculated
 - Septae
 - Thick

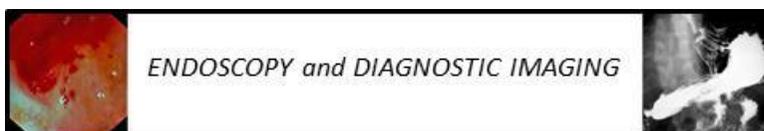


- Nodular
- Enhancing
- Calcification, coarse
- With/without ovarian stroma

Distinguishing diagnosis with biliary cystadenocarcinoma

- Echinococcal cysts
 - Thin septae (not thick)
 - “daughter” cyst
 - Calcifications, fine

- Epithelioid Hemangioendothelioma
- Contrast-enhanced CT
 - Masses
 - Multiple
 - Confluent
 - Hypoattenuation (dark)
 - Peripheral
 - Capsule retraction
- Angiosarcoma
- Unenhanced CT
 - High attenuation (white)
 - Heterogeneous
- Useful Background: Angiosarcoma may be associated with
 - HCC
 - Cholangiocarcinoma
 - Lung cancer
 - Peritoneal tumors
- Hepatic Metastases
- Contrast – enhanced CT (portal-venous phase)
 - Hypovascular
 - Masses
 - Multiple
 - Hypoattenuating (dark)
 - Calcified
 - Site
 - Colon – large, calcified



- Stomach, small bowel – less calcification
 - Breast, lung – small diffuse / infiltrative
- Hypervascular (CT, arterial phase)
- Types
 - Neuroendocrine
 - Melanoma
 - Choliocarcinoma
 - Breast
 - Thyroid
 - Kidney

➤ Ultrasound

- Mass – hyperchoic (white)
- Halo – hypoechoic (dark)
- Arterial phase hyperenhancing cystic
- Portovenous phase hyper → isoattenuating

Useful background: Hypoechoic halos

- Metastases
- HCC
hepatic adenoma
- Atypical FNH

• Pseudocirrhosis

From Chemotherapy for breast cancer

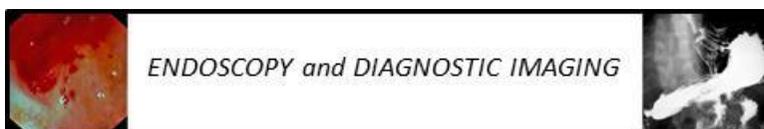
➤ Contrast enhanced CT

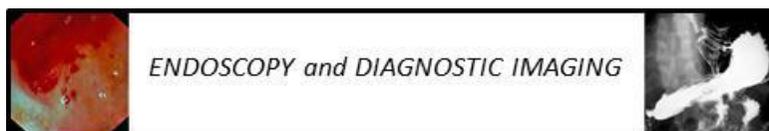
- Focal masses
- Shrunken liver
- Nodular liver
- Large caudate lobe
- Capsule retraction (metastases)

• Periportal Fibrosis

➤ Contrast-enhanced CT (porto-venous phase) portal tracts

- Hyperenhancement (white)
- Thickening
- Linear branching in liver parenchyma
- Cause (granulomatous disease)
 - Infection e.g.,
 - Schistosomiasis
 - Mycobacterial
 - Brucellosis
 - Immune





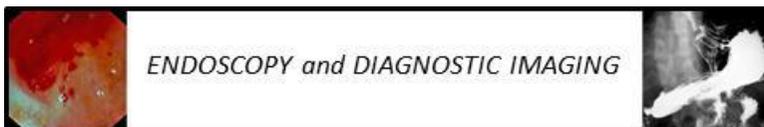
HEPATOBILIARY DIAGNOSTIC IMAGING

CLINICAL SKILLS

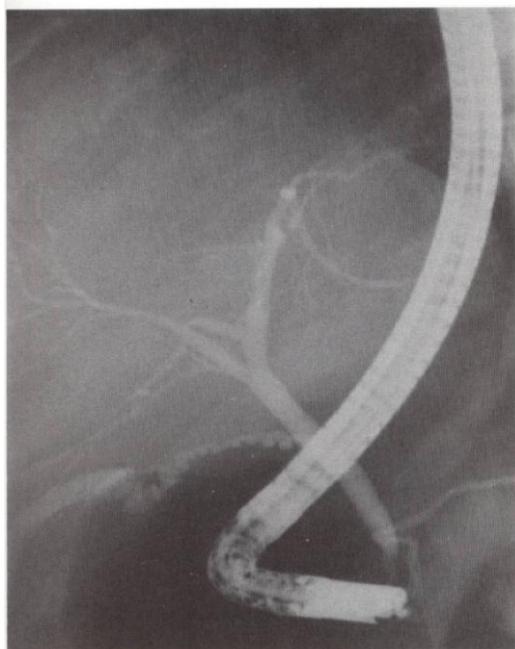
Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

All patients in the following cases had symptoms justifying imaging of the hepatobiliary tree, but the details of all of the cases are not provided so as not to confuse the interpretation of the films.



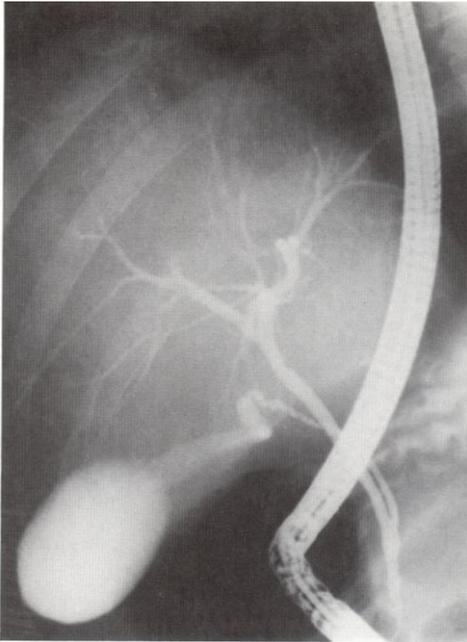
Case 1



Case 2



Case 3



Case 4

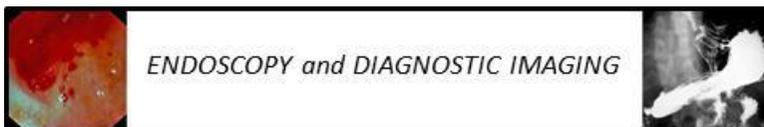


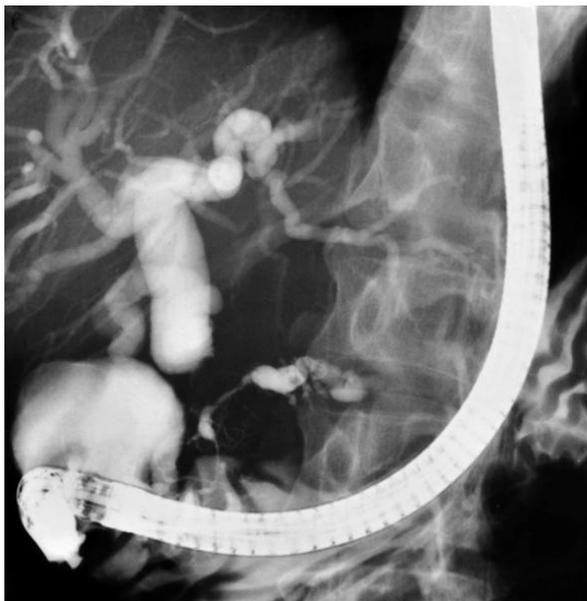
Case 5

81 year old woman presents with jaundice.

Case 6

40 year old woman presents with vague abdominal discomfort 3 months after open cholecystectomy.

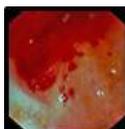


Case 7

70 year old man presents with abdominal discomfort and weight loss.

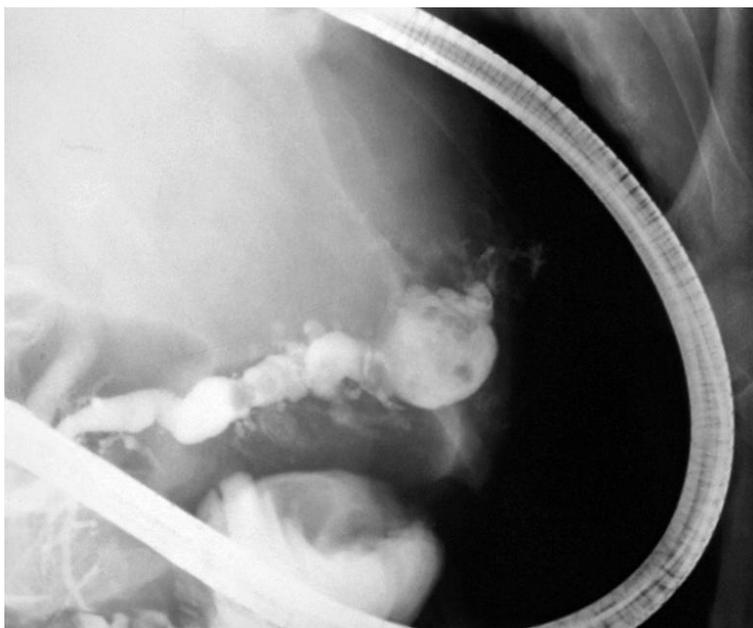
Case 8

30 year old male presents with pruritus.

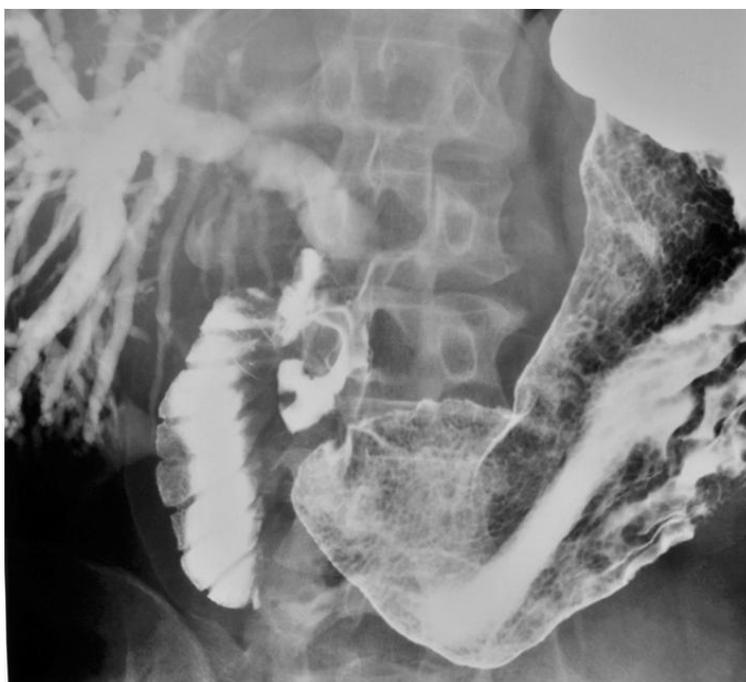


ENDOSCOPY and DIAGNOSTIC IMAGING



Case 9

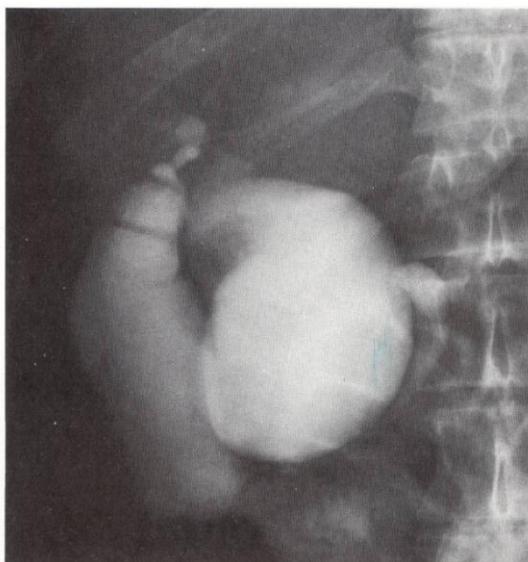
65 year old woman presents with recurrent abdominal pain, and recent onset of distention.

Case 10

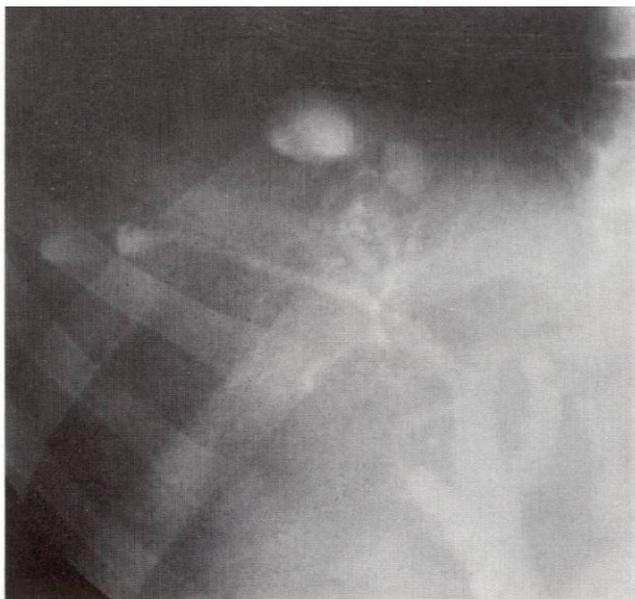
54 year old male presents with painless jaundice.

Case 11

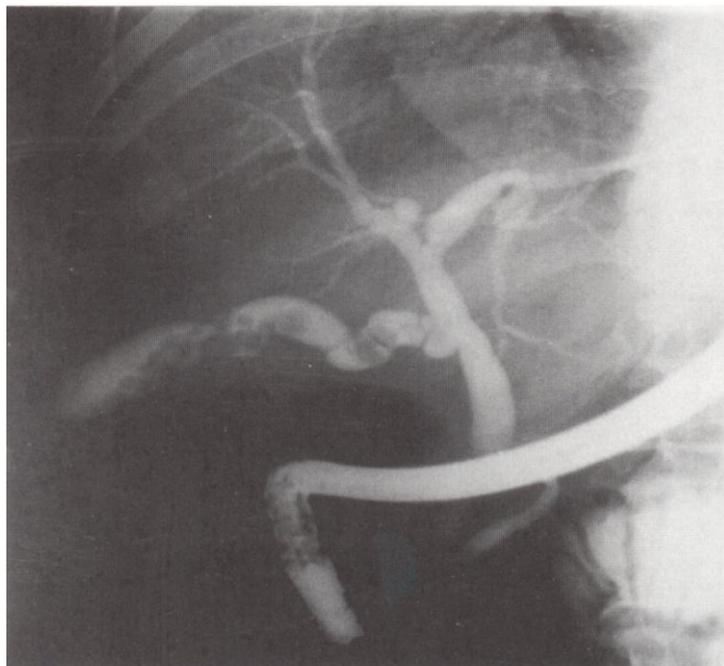
40 year old diabetic male presents with abdominal pain.

Case 12

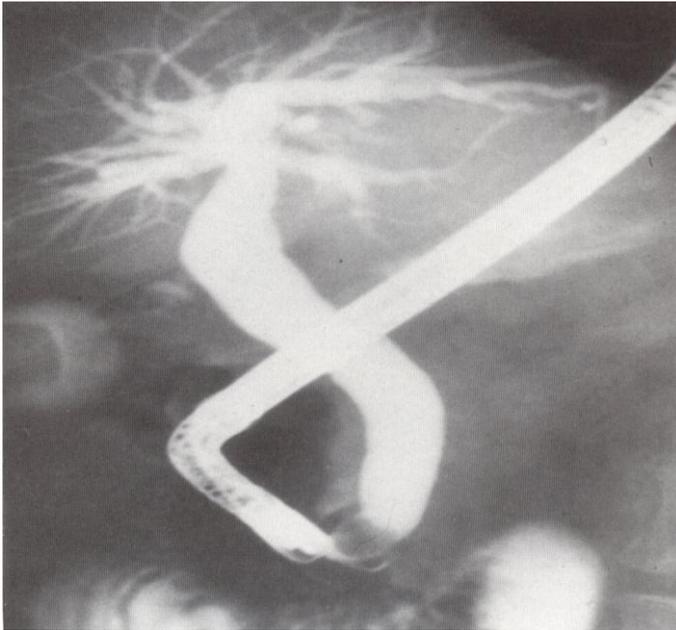
Case 13



Case 14



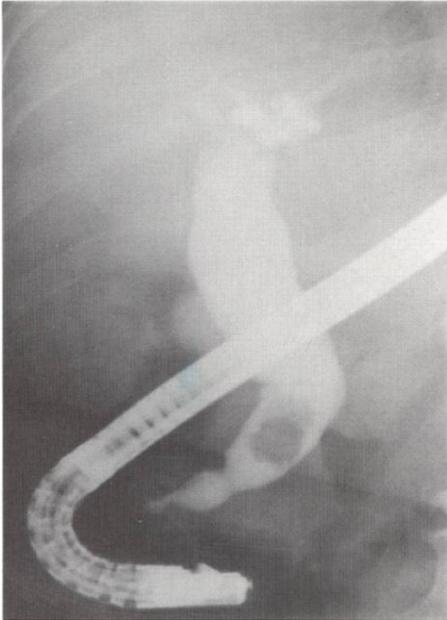
Case 15



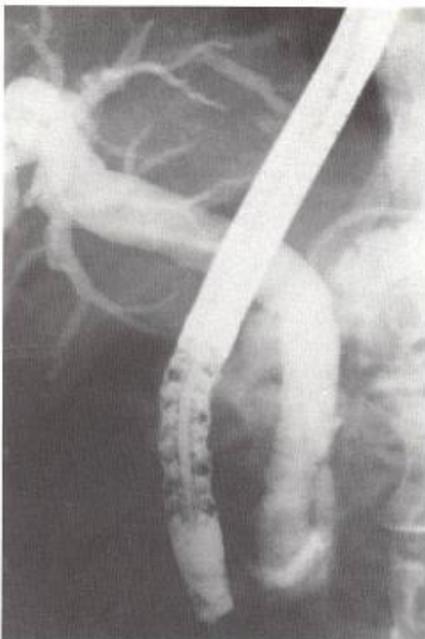
Case 16



Case 17



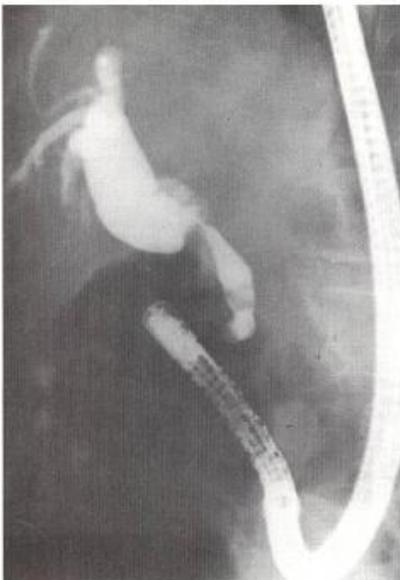
Case 18



Case 19



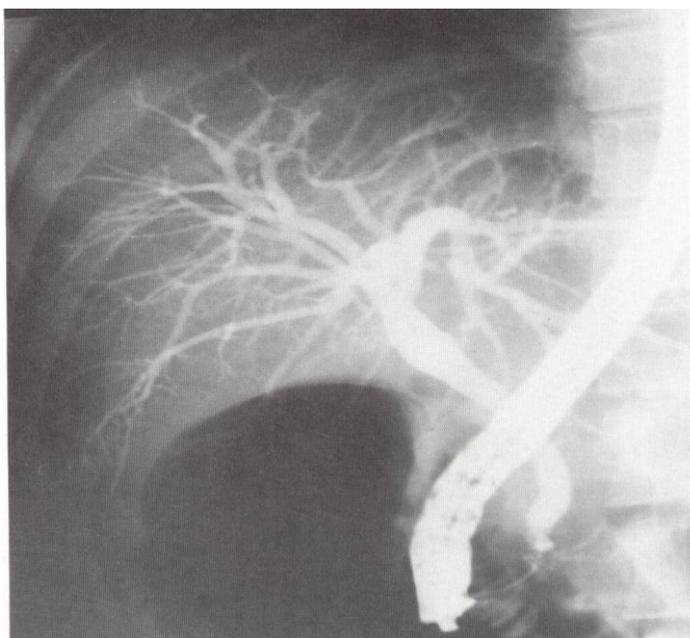
Case 20



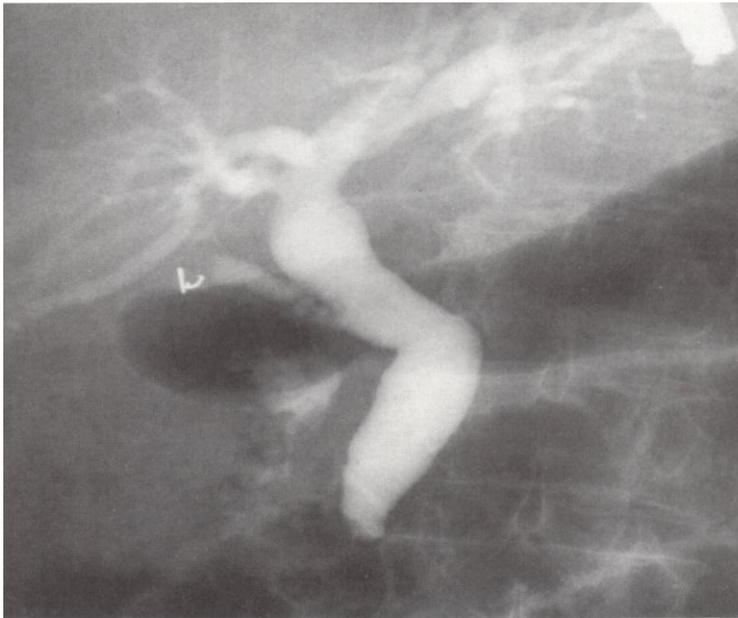
Case 21



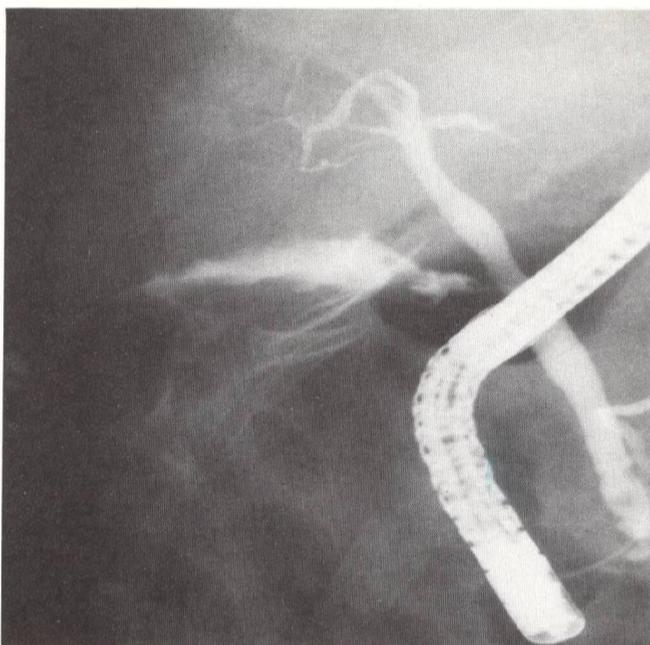
Case 22



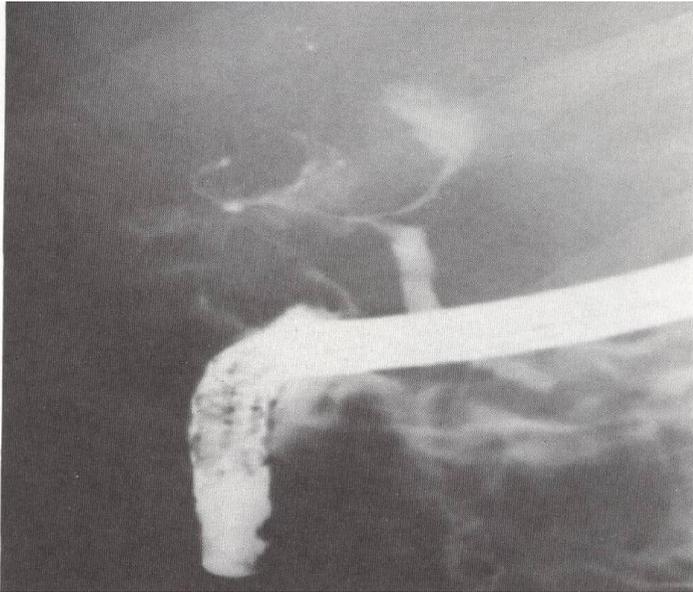
Case 23



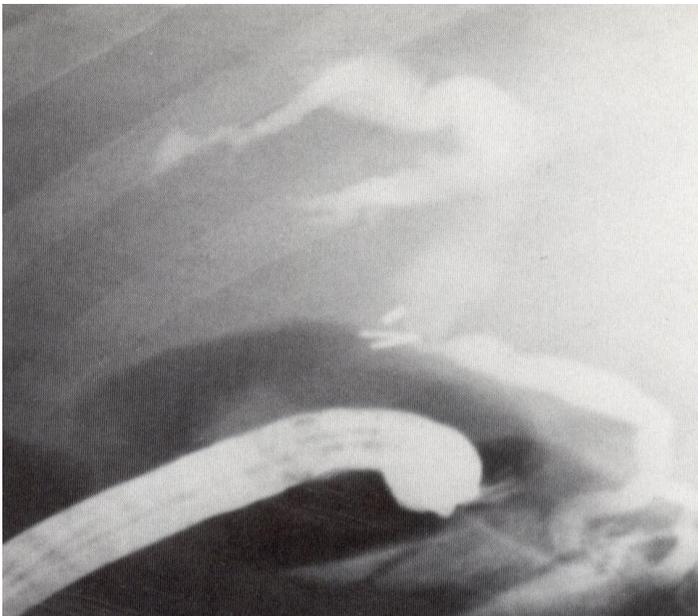
Case 24



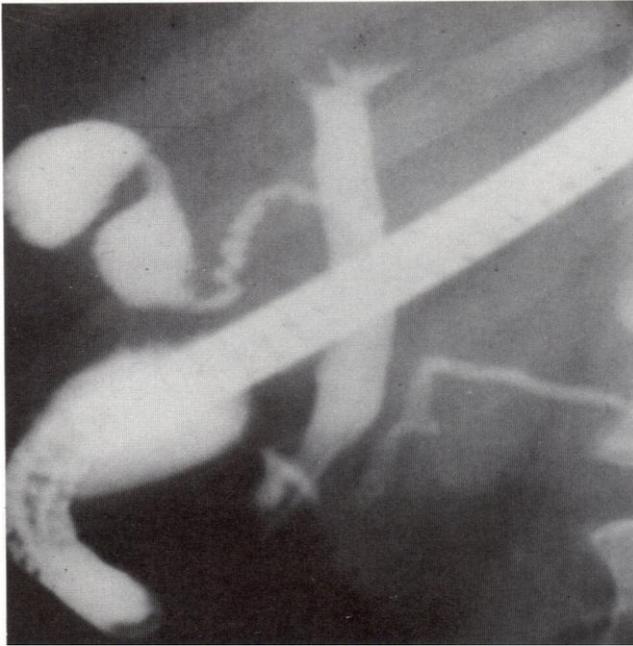
Case 25



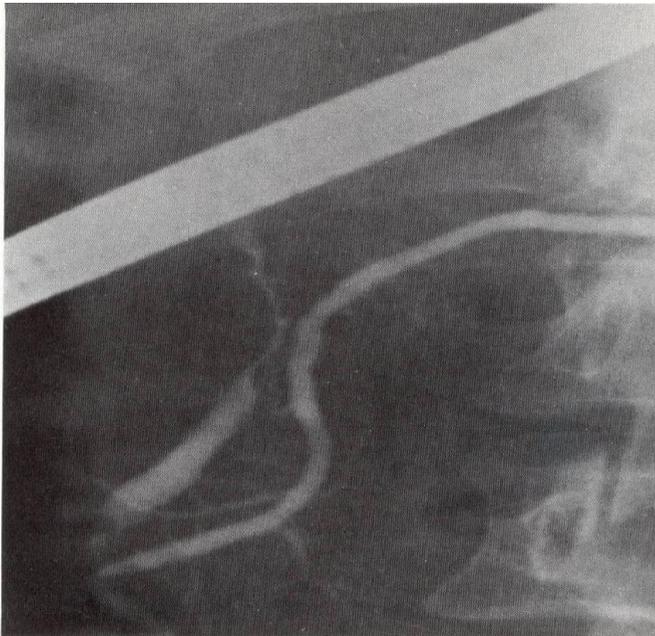
Case 26



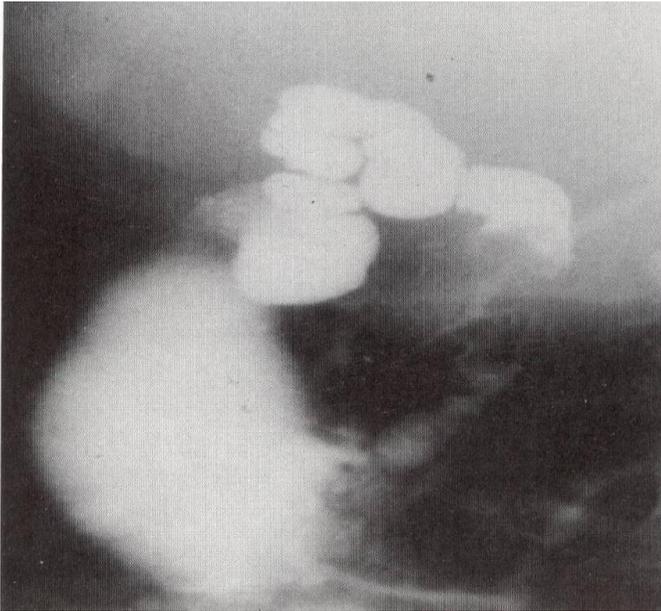
Case 27



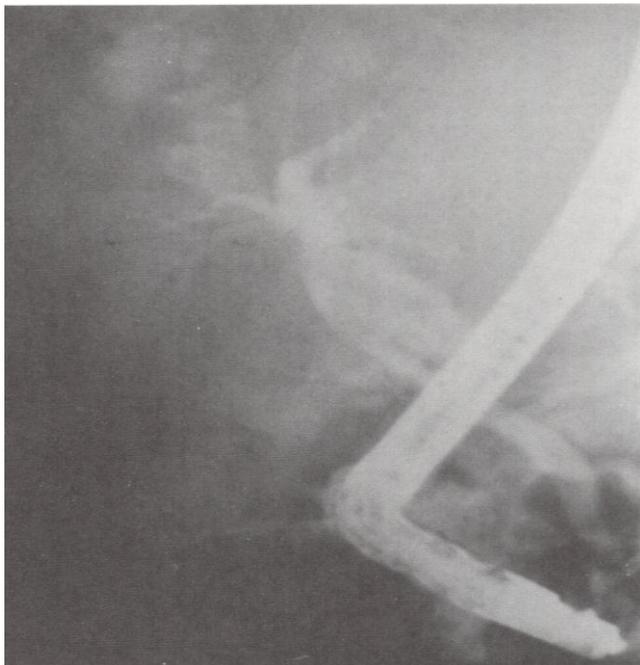
Case 28



Case 29



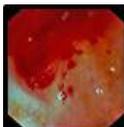
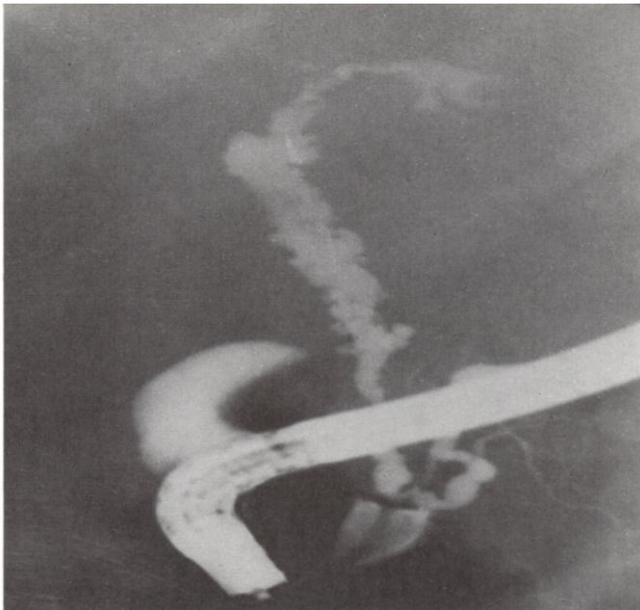
Case 30



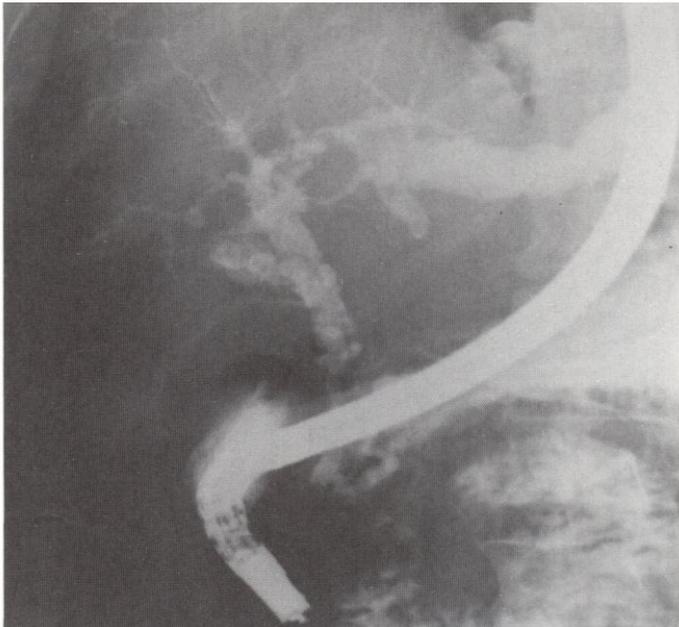
Case 31



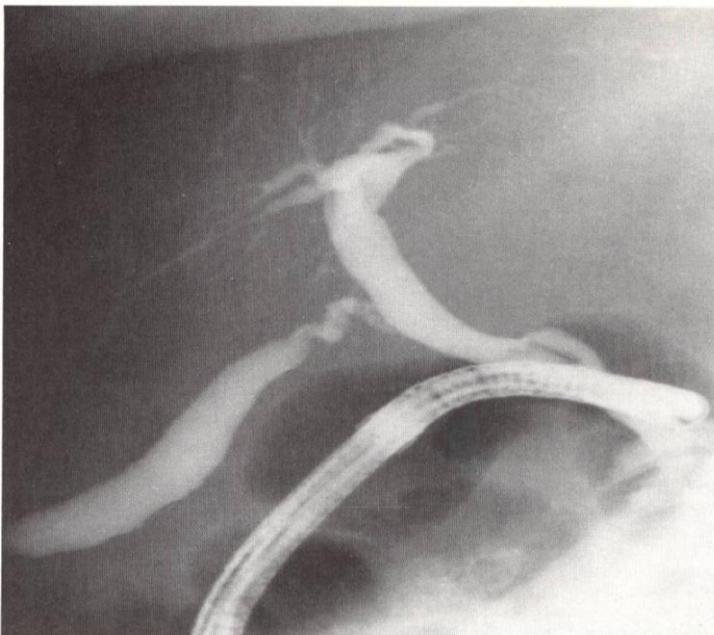
Case 32



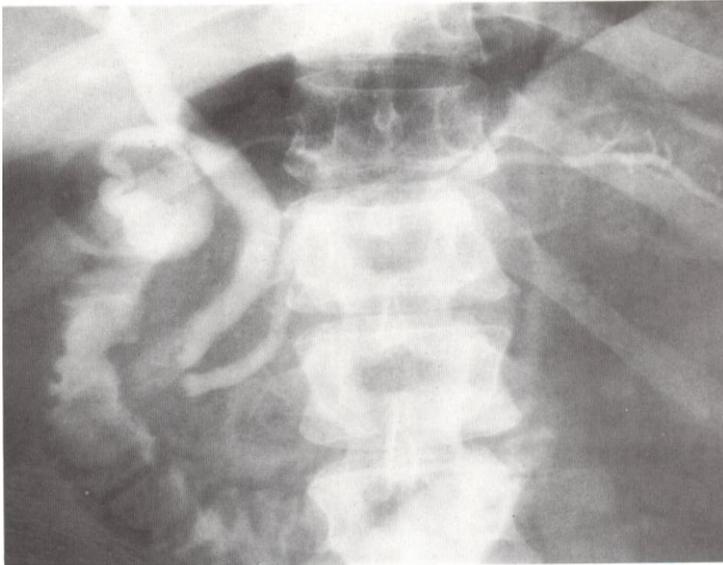
Case 33



Case 34



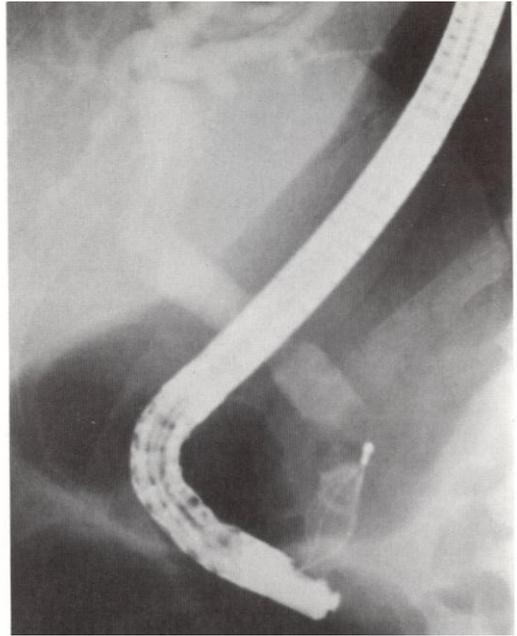
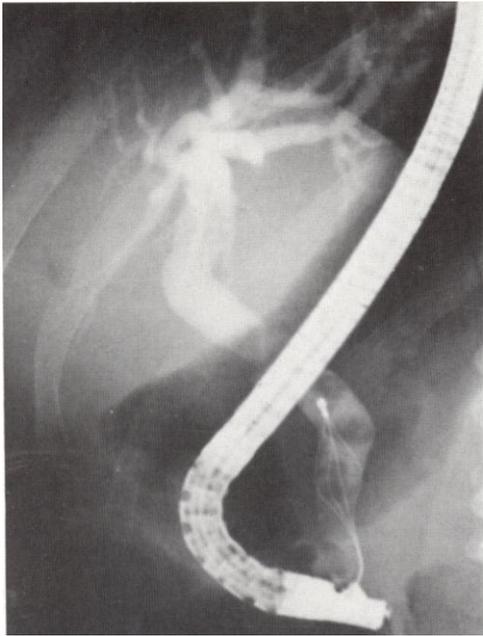
Case 35



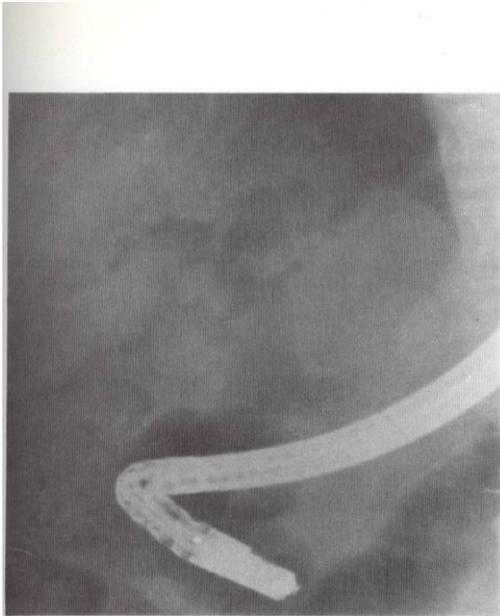
Case 36



Case 37



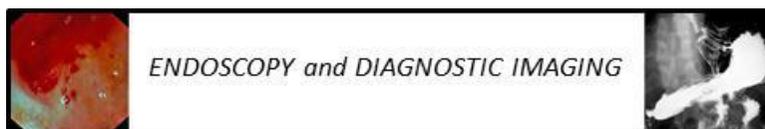
Case 38



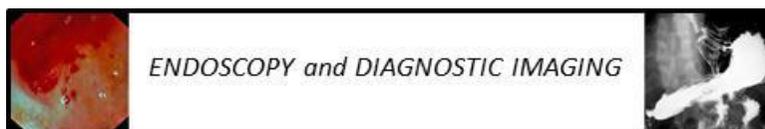
B

Hepatobiliary Diagnostic Imaging Answers

1. Normal biliary system: Endoscope ~10 mm, the ULN for common bile duct. Note cystic duct and gallbladder.
2. Normal biliary system
3. Normal biliary system
4. Normal biliary system
5. Choledocholithiasis
6. Abdominal film, hemato-bilia
7. ERCP and narrowed distal CBD and pancreatic duct ("double duct" sign, pancreatic carcinoma)
8. Sclerosing cholangitis
9. Ectasia of main pancreatic duct, pseudocyst in tail of pancreas displacing gas-filled stomach forward (as seen on lateral view) (pancreatitis)
10. PTC plus upper GI series; long segment of tapered narrowing of supraduodenal CBD to ampulla (pancreatic cancer infiltrating CBD)
11. Air in wall and lumen of gallbladder (emphysematous cholecystitis)
12. Choledochal cyst: Cystic Duct and Gallbladder on left, large choledochal cyst in centre which is filled with contrast from the right pancreatobiliary duct
13. Intrahepatic cysts: Caroli's disease, congenital intrahepatic cystic dilation: multiple intrahepatic cysts connecting to biliary radicles. Distinguish from polycystic liver disease where the intrahepatic cysts do not connect to the biliary radicles.
14. Filling defects in the biliary system: Multiple radiolucent stones in gallbladder and cystic duct. SCH
15. Filling defects in the biliary system: Single large radiolucent stone in distal common bile duct, with dilated extrahepatic and intrahepatic ducts.
16. Filling defects in the biliary system: Impacted radiolucent common bile duct (CBD) stone with dilation of CBD and cystic duct; non-filling of gallbladder may be from an unseen impacted stone, or previous cholecystectomy.
17. Filling defects in the biliary system: Stone in CBD with area of narrowing, from spasm or fibrosis.

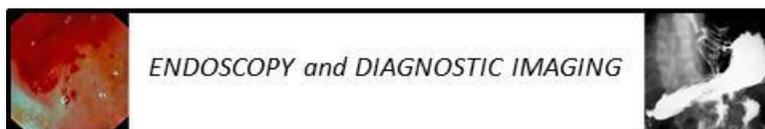


18. Dilated common bile duct: Dilated intra- and extrahepatic bile ducts, with no stone seen until after sphincterotomy (right-side panel).
19. Dilated common bile duct: Dilated intra- and extrahepatic bile ducts, with no stone seen until after sphincterotomy (right-side panel).
20. Filling defects in the biliary system: Billroth II partial gastrectomy (unusual configuration of ERCP in afferent loop) with radiolucent stone in CBD, area of narrowing, and dilated common hepatic duct above narrowing.
21. Filling defects in the biliary system: Same patient, with later filling of gallbladder showing multiple radiolucent stones.
22. Post-cholecystectomy ERCP: Normal post-cholecystectomy dilation of CBD and CHD
23. Post-cholecystectomy ERCP: Normal post-cholecystectomy dilation of CBD and CHD, after removal of choledocholithiasis at time of cholecystectomy. Note cystic duct stamp.
24. Postoperative leak from CBD: Leakage from stump of cystic duct post cholecystectomy
25. Postoperative abscess and biliary structure: Narrowing of left hepatic duct and proximal dilation, plus biliary leak post cholecystectomy, with right hepatic duct leading to abscess cavity.
26. CBD narrowing: Cholecystectomy, clips on cystic duct, clip on CBD.
27. Cholangiocarcinoma: Obstruction at confluence of CHD and the right and left hepatic ducts (Klatskin tumour).
28. Cholangiocarcinoma: Long narrowing of CBD (normal pancreatic duct), with a wide differential diagnosis.
29. Cholangiocarcinoma: Enlarged gallbladder, dilated cystic duct with cholangiocarcinoma of cystic duct.
30. Hepatic abscess: Large abscesses at hilum of and within liver.
31. Biliary tract stone: Multiple stones in gallbladder and above left hepatic duct narrowing.
32. Sclerosing cholangitis: Multiple areas of narrowing and dilation of both extrahepatic (CBD, CHD) and intrahepatic (left hepatic) ducts. Differentiate from multifocal cholangiocarcinoma (which only rarely is both extra- and intrahepatic).
33. Sclerosing cholangitis: Irregular (narrowing and dilation) of CBD, CHD, intrahepatic duct, and sacculaton of left hepatic duct. No stones in gallbladder.



34. Narrowing of intrahepatic ducts: Smooth narrowing of R/L hepatic duct from shrunken, cirrhotic liver, giving a “pruned tree” appearance. Long narrow gallbladder without stones.
35. Narrowing of both common bile duct and pancreatic duct: Blockage of CBD and pancreatic duct (PD) (“Double-duct” sign) without duct dilation. The CBD and PD are separated as they enter the duodenal lumen, giving the appearance of a filling defect.
36. Obstruction of both common bile duct and pancreatic duct: Dilation of both CBD and PD (“Double-duct” sign), with blockage of ducts and papillary carcinoma.
37. ERCP: choledocholithiasis: Insertion of basket catheter post sphincterotomy.
38. After sphincterotomy: Choledocholithiasis, sphincterotomy, balloon extraction of stones; follow-up ERCP shows an air cholangiogram, possible missed CBD stones.

Please compare your findings with those described in the previous material.



Index

Note: Page references to Parts One and Two of the text are preceded by **I:** and **II:** respectively. *Italicized* page references indicate images.

A

Abscess

- in acute pancreatitis, **I:**334
- appendiceal, **II:**186
- in barium studies, **II:**185
- Crohn disease and, **I:**289
- crypt, **I:**289, **II:**79, 82, 92, 216, 223
- in diverticular disease, **II:**180–182
- liver, **II:**182, 212, 395
- pancreatic, **I:**334, 348, 350, 356, 399, 400
 - barium study, **I:**351
 - CT scan, **I:**351, 376
- pancreatic cancer and, **I:**358
- pericolonic, **II:**180, 182, 186, 211
- pericolonic, **II:**70
- perirectal, **II:**271
- postoperative, **II:**393
- retroperitoneal, **II:**186

Acanthosis nigricans, **I:**10

Achalasia, **I:**24, 28

- food retention and, **I:**69
- idiopathic, **I:**44
- manometry, **I:**111–114
- secondary, **I:**43
- therapy for, **I:**42

Acute colonic pseudo-obstruction, **II:**31–32, 42

Adenocarcinoma, **I:**219, 294, 295

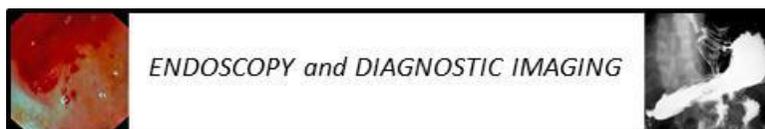
- lymphoma vs., **I:**221

Adenoma, **II:**315

- colonic serrated, **II:**327
- colonic villous, **II:**302
- dysplasia-associated lesion or mass vs., **II:**138, 308, 332
- giant villous, **II:**149
- hepatic, **II:**371
- inflammatory bowel disease and, **II:**138, 179
- villous, **II:**149, 150, 263, 302, 329

Adenomatous polyp, **II:**332

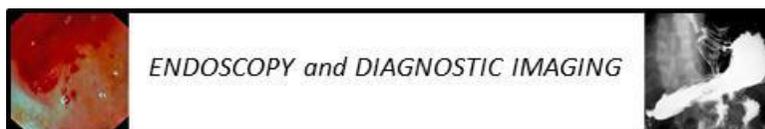
- on long stalk, **II:**331



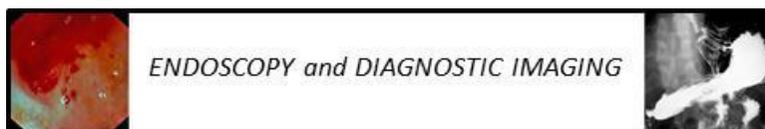
- Alpha adrenergic antagonists, **I**:28
- American College of Gastroenterology, EGD surveillance recommendations, **I**:32
- Ampullary carcinoma, **I**:293
- Anal cancer, **II**:320
- Anastomosis, **II**:176
- colorectal cancer and, **II**:265, 297
 - metachronous tumour distal to, **II**:285
 - ulceration and, **II**:309, 333
- Angiodysplasia, **II**:261, 319
- angiographic features, **II**:273, 273–278, 319
- Angiodysplasias, **I**:258
- Angioma, spider, **I**:11
- Angiomyolipomas, hepatic, **II**:372
- Angiosarcoma, **II**:373, 376
- Angular cheilosis, **I**:6
- Ankylosing spondylitis, **II**:108–109, 323
- Annular pancreas, **I**:395
- Anterior uveitis, **I**:9
- Anti-apoptosis genes, **I**:31
- Anti-senescence markers, **I**:31
- Anticholinergics, **I**:28, 34, 348
- Antral erosions, **I**:252
- Aortoenteric fistula, **I**:293
- Aphthous stomatitis, **II**:114, 114, 115
- Aphthous ulcers, **II**:317, 337
- Appendicitis
- barium studies in, **II**:185
 - CT scan in, **II**:185–186
 - ultrasound in, **II**:185
- Appendix, endocrine tumours of, **II**:258
- Argon plasma coagulation (APC), **I**:32
- Ascending colon, abnormal, **II**:335
- Ascites, **I**:28, 128
- abdominal, **I**:15

B

- B₁₂ deficiency, **I**:122
- Balloon dilation, of stricture, **II**:310, 333
- Balthazar score, **I**:339
- Bariatric procedures, **I**:28, 121–124
- bone disease and, **I**:123
 - complications of, **I**:121–122
 - diarrhea and, **I**:122–123

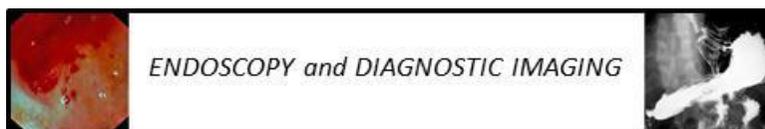


- iron deficiency and, **I**:122
- peptic ulceration and, **I**:123
- Barium studies
 - in appendicitis, **II**:185
 - in colorectal cancer, **II**:264–265
 - in diverticulitis, **II**:185
 - filling defects in, **II**:185
 - in inflammatory bowel disease, **II**:68
 - polyps and, **II**:262–263
 - in ulcerative colitis, **II**:95, 95–107
- Barrett's epithelium. *See* Barrett's esophagus
- Barrett's esophagus, **I**:30, 74
 - diagnostic imaging in, **I**:51
 - dysplasia associated with, detection of, **I**:31
 - EGD surveillance of, **I**:32
 - endoscopic therapies for, **I**:32
 - histological changes in, **I**:31
 - recommendation for endoscopic surveillance, **I**:31
- Barrett's ulcer, **I**:74
- Beau lines, **I**:18
- Behçet's syndrome, **I**:8
- Benign liver tumours, **II**:368
- Bile duct, **I**:380–384
 - common, **I**:355, 362
 - obstruction, **I**:374
- Bile gastritis, **I**:257
- Biliary cystadenocarcinoma, **II**:375–376
- Biliary cystadenoma, **II**:372
- Biliary sludge, **I**:346, 383, 384, 387
- Biliary system, normal, **II**:381, 382
- Biliary tract stone, **II**:396
- Biliopancreatic diversion, **I**:121
- Billroth I, **I**:255, 257, 258
- Billroth II, **I**:122–123, 267, **II**:390
- Black tongue, **I**:6
- Bleeding
 - diverticular, **II**:193, 212–213
 - gastric, **I**:191, 262, 263
 - gastrointestinal. *See* Gastrointestinal bleeding
 - rectal. *See* Rectum, bleeding from
- Blue rubber bleb nevus syndrome, **I**:11
- Botox injections, **I**:28
- Brunner gland hyperplasia, **I**:294, 295

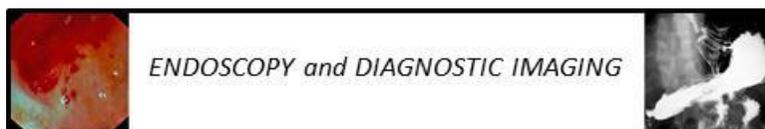


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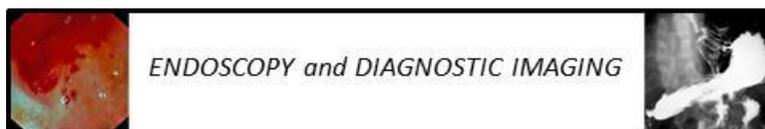
- Calcinosis crest syndrome, **I**: 19
- Calcium channel blockers, **I**:28
- Campylobacter* infection, **II**: 320
- Cancer. *See also* Carcinoma
 anal, **II**:320
 of colon. *See* Colon cancer
 colorectal. *See* Colorectal cancer
 esophageal, **I**:54, 55
 hepatocellular, **II**:372–373
 diffuse, **II**:372
 fibrolamellar, **II**:372–373
 of pancreas. *See* Pancreatic cancer
 rectal stump, risk factors for, **II**:175
 of stomach. *See* Gastric cancer
- Candidiasis, **I**:37, 51, 75, 259
 hepatic, **II**:367
- Canker sores, **I**:6
- Carcinoid syndrome, **I**:281, 283
- Carcinoid tumour, **I**:255, 279, 282–283, 299, **II**:258, 260
 appendiceal, **I**:281
 clinicopathologic classification of, **I**:282–283
 colonic, **I**:280–281
 duodenal and upper jejunal, **I**:283
 filling defects in, **I**:299
 lower jejunal and ileal, **I**:280
 malignant, **II**:258
 rectal, **I**:280–281, **II**:260
 size and metastases of, **II**:260
- Carcinoma. *See also* Cancer
 cholangiocarcinoma, **II**:394, 395
 duodenal, **I**:320
 polypoid esophageal, **I**:66
- Caroli disease, **I**:384
- Carotenemia, **I**: 16
- CBD. *See* Common bile duct (CBD)
- CD. *See* Crohn disease (CD)
- Cecum, **II**: 143
 lesion in, **II**:291, 292
 tumour in, **II**:287
- Celiac disease, **I**:274–276, 293, 294, 320
 grading of, **I**:275
 lymphoma and, **I**:276
 villous atrophy in, **I**:276



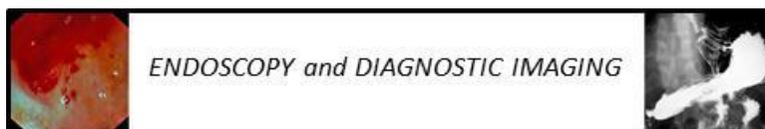
- Cheilosis, angular, **I**:6
- Cholangiocarcinoma, **II**:394, 395
- Cholangiohepatitis, **I**:382
- Cholecystectomy, **II**:393
 biliary leak following, **II**:392, 393
- Cholecystitis
 acalculous, **I**:385
 acute, **I**:384–386
 chronic, **I**:386, 388, 389
 serum enzymes and, **I**:340
 gangrenous, **I**:385
- Cholecystitis, emphysematous, **II**:386
- Choledochal cyst, **II**:386
- Choledocholithiasis, **II**:383, 399
- Cholescintigram, **I**:385
- Cholestasis, **II**:344–349
- Chronic intestinal pseudo-obstruction (CIPO), **II**:28–42
 radiological findings in, **II**:34–36
- Cirrhosis, **II**:365
- Colectomy, total, **II**:146
- Colitis
 acute vs. chronic, **II**:75
 antibiotic-associated, **II**:320
 biopsy features in, **II**:80
 collagenous, **II**:321
 Crohn, **II**:201
 dysplasia-associated lesion or mass in, **II**:323
 hematochezia and, **II**:11, 270
 infectious, **II**:81, 307
 ischemic, **II**:322
 lymphocytic, **II**:321
 radiation and, **II**:322
 steroid resistance and, **II**:80
 of undetermined etiology, **II**:308
- Colitis cystica profunda, **II**:267
- Colon, **I**:351, **II**:311
 abnormal ascending, **II**:314
 angiodysplasia of, **II**:319
 Campylobacter infection of, **II**:320
 clinical cases involving, **I**:408–409
 dilated, rectal involvement and, **II**:289
 endocrine tumours and, **II**:259–260
 endometriosis of, **II**:296
 gallstone erosion and, **I**:302



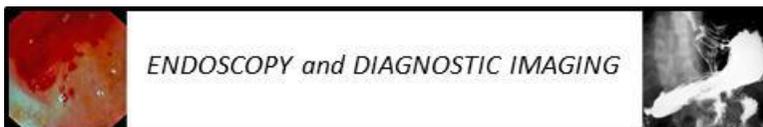
- metastases to, **I**:134, 301
- metastatic cancer to, **II**:266–268
- narrowing of, **II**:296
- radiation damage to, **II**:260–261
- transverse, **II**:313
 - clinical stomal cancer and, **I**:125
 - tortuous blood vessels of, **II**:335
- Colon cancer, **I**:208, 292
 - apple-core, **II**:295
 - diverticulitis vs., radiologic difference between, **II**:156, 183, 210
 - hereditary nonpolyposis, **II**:152, 252
 - polyps and, **II**:149–150, 167
 - radiologic difference between diverticulitis and, **II**:156, 183, 210
 - recurrent, **II**:297
- Colonic adenoma
 - serrated, **II**:327
 - villous, **II**:302
- Colonic diverticulum
 - inverted, **II**:268
 - scleroderma and, **II**:37
- Colonic hyperplastic polyp, **II**:327
- Colonic lymphoid hyperplasia, **II**:324
- Colonic lymphoma, **II**:325
- Colonic mass, **II**:312, 334
- Colonic pit pattern, **II**:326
- Colonic pneumatosis cystoides, **II**:326
- Colonic polyps, **II**:251–268, 290
 - cancer and, **II**:149–150, 167
 - histological classification of, **II**:150
- Colonic vascular ectasia, **II**:269
- Colonography, **II**:263, 265
- Colonoscopy, **II**:44, 52
 - cecal, **II**:143
 - for etiology of constipation, **II**:44, 52
 - screening, **II**:154, 168, 169
 - surveillance, **II**:139
 - post-polypectomy, **II**:168
- Colorectal cancer, **II**:301, 329
 - barium studies in, **II**:264–265
 - chemoprevention for, **II**:169
 - diagnostic imaging in, **II**:264–266
 - endoscopic ultrasonography in, **II**:265
 - familial risk in, **II**:167, 254–255
 - normal colonic epithelium to, **II**:256



- recurrence of, **II**:266
- risk factors for, **II**:151–152
- risk stratification in, **II**:153, 251–253
- screening for, **II**:154, 255
- Common bile duct (CBD)
 - dilated, **II**:389, 390
 - narrowing of, **II**:384, 385, 393, 398
 - postoperative leak from, **II**:392
 - stone in, **II**:389
- Computed tomography (CT), **I**:56
 - abdominal, **I**:131
 - adenocarcinoma, **I**:300
 - angiography, **I**:191
 - angiosarcoma, **II**:376
 - appendicitis, **II**:185–186
 - benign liver tumours, **II**:368
 - biliary cystadenoma, **II**:371
 - carcinoid tumour, **I**:299
 - colorectal cancer, **II**:265
 - contrast-enhanced. *See* Contrast-enhanced computed tomography (CT)
 - Crohn disease, **I**:285
 - fibrovascular tumour, **I**:57
 - filling defects, **I**:294
 - focal nodular hyperplasia, **II**:369–370
 - gastric bleeding, **I**:191
 - gastric cancer, **I**:220
 - gastroesophageal reflux disease, **I**:56
 - gastrointestinal stromal tumour, **I**:297
 - hepatic adenoma, **II**:371
 - hypoproteinemia, **I**:306
 - intrahepatic cholangiocarcinoma, **II**:375
 - lipoma, **I**:298
 - lymphadenopathy, **I**:221, 307
 - lymphoma, **I**:300
 - metastatic cancer to colon, **II**:267, 268
 - MRI and, **I**:191
 - pancreatic adenocarcinoma, **I**:370
 - pancreatitis, **I**:354
 - pericolonic soft tissue stranding, **II**:226, 227
 - polyps, **II**:263
 - small bowel obstruction, **I**:303
 - spiral, **I**:366
 - in ulcerative colitis, **II**:263
 - volvulus, **I**:303



- Zollinger-Ellison syndrome, **I**:125
- Constipation, **II**:43–48
 causes of, **II**:43–45, 51
 diagnostic imaging in, **II**:46
 filling defects, diseases associated with, **II**:48
 following colectomy, **II**:54
 obstruction, **II**:46–48
 in pregnancy, **II**:45–46
- Contrast-enhanced computed tomography (CT)
 biliary cystadenocarcinoma, **II**:375–376
 epitheloid hemangioendothelioma, **II**:376
 hepatic metastases, **II**:376–377
 hepatocellular cancer, **II**:372–374
 pancreatic disease, **I**:346, 349, 351, 371
 periportal fibrosis, **II**:377
 pseudocirrhosis, **II**:377
- Corkscrew esophagus, **I**:64
- Crohn disease (CD), **I**:4, 285–291, 293, 294, 321, **II**:293, 294
 abscess and, **I**:289
 anal fissures and, **I**:286
 aphthoid lesions in, **II**:85
 causes of, **I**:290
 characteristics of, **II**:76
 classification of, **I**:285
 colonic, **II**:323
 cytokines and, **I**:286
 diagnosis of, **I**:285, 290
 diarrhea in, **I**:288
 causes of, **II**:79
 differential diagnosis of, **I**:290, **II**:92, 107
 endoscopic features of, **II**:91–92
 fistulae and, **I**:52, 317
 index of activity for, **II**:79
 intestinal tuberculosis vs., **II**:75
 nuclear factor kappa B and, **I**:287
 perianal, **I**:286, **II**:120, 121, 121–122
 post-resection for, **II**:298
 predictors of future severe, **II**:72–73
 sites of involvement for, **II**:78
 surgery for, **I**:289–290
 TNF-alpha and, **I**:286–287
 treatments for, **I**:285–286, 289–290
 ulcerative colitis vs., **II**:71
- Cryotherapy, **I**:32



Crypt abscesses, **I**:289, **II**:79, 82, 92, 216, 223

CT. See Computed tomography (CT)

Cullen's sign, **I**: 13

Cyst

choledochal, **II**:386

hemorrhagic, **II**:365

hepatic, **II**:365

intrahepatic, **II**:387

polycystic liver disease vs., **II**:387

pseudocyst, pancreatic, **I**:398

Cystadenocarcinoma, biliary, **II**:375–376

Cystadenoma, **II**:371, 372

Cystic fibrosis, **I**:294, 379–384

pancreatic cancer and, **I**:364, 365

pancreatitis and, **I**:350, 358

Cytomegalovirus (CMV) esophagitis, **I**:52

D

DALM. See Dysplasia associated lesion or mass (DALM)

Defecation, **II**:3–10

Dermatitis herpetiformis, **I**: 12

Dermatomyositis, **I**: 10

Diarrhea, **I**:291–311

bariatric surgery and, **I**:122–123

in Crohn disease, **I**:288

causes of, **II**:79

drugs associated with, **I**:291

pancreatitis and, **I**:288

protein-losing enteropathies, **I**:292–293

Dieulafoy's lesion, **I**:260

Diverticular bleeding, **II**:193, 212–213

Diverticular disease, **II**:179–213

clinical classification of, **II**:181

complications of, **II**:211–212

CT findings in, **II**:180

hematochezia and, **II**:11, 269

Diverticulitis, **II**:195, 201, 207, 324

barium studies in, **II**:185

colon cancer vs., radiologic difference between, **II**:156, 183, 210

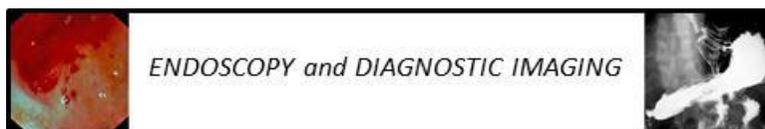
CT findings in, **II**:185

classification of, **II**:186

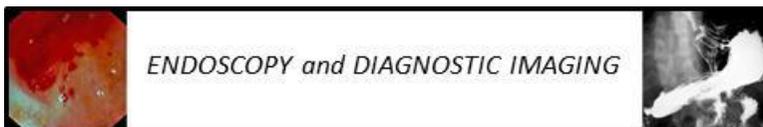
diagnostic imaging in, **II**:195

Diverticulosis, **I**:310, **II**:195

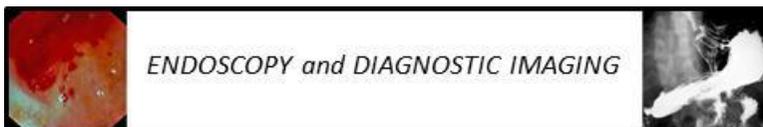
jejunal and ileal, **I**:314



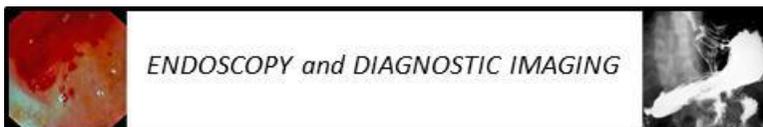
- pancolonic, **II**:286
- Diverticulum, **I**:293, 296, **II**:193
 - colonic
 - inverted, **II**:268
 - scleroderma and, **II**:37
 - food particles in, **I**:315
 - giant sigmoid, **II**:185
 - Killian-Jamieson, **I**:59, 60
 - Meckel, **I**:310
 - segmented colitis associated with, **II**:179
 - small bowel, **I**:321
 - Zenker's, **I**:59, 60, 65, 75
- DNA aneuploidy, **I**:31
- Double duct sign, **II**:384, 398
- Duct of Santorini, filling of, **I**:394
- Duodenal bulb, deformed, **I**:244
- Duodenum
 - carcinoma of, **I**:320
 - diverticulum in, food particles in, **I**:315
 - filling defect in, **I**:247
 - narrowing of, **I**:244
 - ulcer of, **I**:245
 - healed, **I**:246
- Dupuytren's contracture, **I**:17
- Dysmotility
 - colonic, **II**:25
 - gastric, **I**:125–134
 - diagnostic imaging in, **I**:133–134
- Dyspepsia, **I**:151–154
- Dysphagia, **I**:23–24
 - achalasia, **I**:24
 - benign stricture in, **I**:23–24
 - defined, **I**:24
 - differential diagnosis of, **I**:57–58
 - diffuse esophageal spasm and, **I**:24
 - dilation for, **I**:23
 - esophageal, **I**:23
 - esophageal bougie dilation for, **I**:23
 - grading of, **I**:23
 - malignant stricture of, **I**:24
 - pre-esophageal oropharyngeal, **I**:23
 - with solids, **I**:24
- Dysplasia, ulcerative colitis and, **II**:124–128, 131–136
- Dysplasia-associated lesion or mass (DALM), **II**:138



- adenoma vs., **II**:138, 308, 332
 - cancer and, **II**:138, 178
 - in colitis, **II**:323
 - colonoscopic examination of, **II**:138
 - inflammatory pseudopolyp vs., **II**:137, 179
 - problems of, **II**:131, 178
- E**
- Ectasia
 - colonic vascular, **II**:269
 - of pancreatic duct, **II**:385
 - Ectopic gastric mucosa, **I**:59
 - Ectopic pregnancy, **II**:182, 207
 - EGD. See Esophageal gastroduodenoscopy (EGD)
 - EMR (endoscopic mucosal resection), **I**:32
 - Endocrine tumours, **II**:258, 259–260
 - Endometriosis, **II**:282–283
 - Endoscopic hemostatic therapy, **I**:177
 - Endoscopic mucosal resection (EMR), **I**:32
 - Endoscopic retrograde cholangiopancreatography (ERCP), **II**:391
 - choledocholithiasis, **II**:399
 - post-cholecystectomy, **II**:391, 392
 - Endoscopy
 - assessing esophageal damage with, **I**:29
 - capsule, **I**:29
 - of colorectal cancer, **II**:265
 - high resolution, **I**:33
 - of intestinal ischemia, **II**:218, 224
 - of mesenteric ischemia, **II**:223
 - radiation damage and, **II**:249, 261
 - surveillance and, **II**:174, 258
 - of ulcerative colitis, **II**:68, 70, 79, 91–92
 - ultrasound and, **II**:265
 - upper GI tract, **I**:48
 - video, **I**:27
 - Enzyme therapy, pancreatic, **I**:330–334
 - Eosinophilic gastrointestinal disorders, **I**:48–51, 141–145
 - Epitheloid hemangioendothelioma, **II**:376
 - ERCP. See Endoscopic retrograde cholangiopancreatography (ERCP)
 - Erythema, palmar, **I**:17
 - Erythema nodosum, **I**:14, **II**:110, 111, 117
 - Esophageal bougie, **I**:23
 - Esophageal cancer, **I**:54, 55
 - Esophageal gastroduodenoscopy (EGD), **I**:131, 138, 211



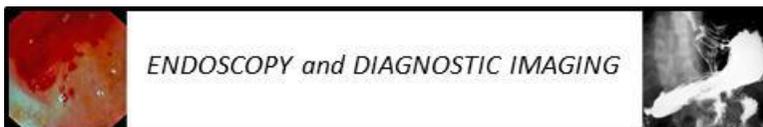
- changes in eosinophilic esophagitis seen with, I:50
- in dyspepsia, I:152
- false negative results in, I:151
- optical white light, I:29
- for pancreatitis management, I:349
- recommendations for surveillance with, I:32, 210
- second-look, I:176
- Esophageal manometry. See Manometry
- Esophageal motility disorders, I:40–52
 - cause of short luminal narrowing in, I:48
 - classification of, I:40–41
 - diagnostic criteria for, I:45–46
 - diagnostic imaging, I:51–52
 - endoscopic and diagnostic imaging of, I:47
- Esophageal stricture, I:70
 - in GERD, I:28
 - non-GERD
 - etiologies of, I:38–39
 - recent updates, I:35–37
 - therapy for, I:39
- Esophageal tumours, I:52–61
 - diagnostic imaging, I:56–61
 - endoscopic imaging modalities for detecting, I:55–56
 - epithelial, I:52–53
 - nonepithelial, I:52–53
- Esophageal ulcers, giant, I:51–52
- Esophageal varices, I:67, 253
 - portal hypertension gastropathy and, I:192–195
- Esophagectomy, I:32
- Esophagitis
 - candidal, I:51, 75
 - Crohn, I:52
 - cytomegalovirus, I:52
 - diagnostic imaging, I:51
 - eosinophilic, I:50–51
 - herpes simplex virus, I:51
 - medication-induced, I:52
 - radiation, I:76
 - viral, I:51, 52, 76
- Esophago-gastro-duodenoscopy, I:261
- Esophago-jejunostomy, I:261
- Esophagus, I:23–117
 - clinical cases involving, I:405
 - corkscrew, I:64



diagnostic imaging in, **I**:63–71
 dysphagia, **I**:23–24. *See also* Dysphagia
 endoscopic imaging in, **I**:73–82
 filling defects on barium swallow, **I**:53–54
 gastroesophageal reflux disease and, **I**:24–39
 manometry, **I**:83–117
 motility disorders of, **I**:40–52
 nutcracker, **I**:103–105
 tumours, **I**:52–61

F

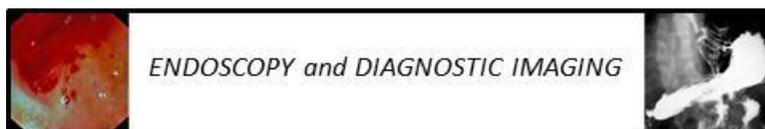
Familial adenomatous polyposis (FAP), **II**:152, 263, 285
 hereditary nonpolyposis colon cancer and, **II**:152, 252
 juvenile polyposis syndrome and, **II**:264
 risk factors for cancer in rectal stump, **II**:175, 258
 surveillance, **II**:174, 258
 FAPS (functional abdominal pain syndrome), **II**:27
 Fatty liver disease, **II**:343–344
 Fecal continence, **II**:8–10
 Fecal incontinence, **II**:5
 Fibrosis, periportal, **II**:377
 Filiform inflammatory polyps, **II**:288
 Filling defects, **II**:48
 in barium studies, **II**:185
 in CT colonoscopy, **II**:263, 265
 diagnostic imaging of
 appendicitis, **II**:185
 bile reflux gastritis, **I**:125
 candidal esophagitis, **I**:51
 caustic stricture, **I**:134
 colorectal cancer, **II**:265
 constipation-related diseases, **II**:48
 diffuse hemangiomas, **I**:298
 esophageal varices, **I**:59, 71
 esophagus, **I**:59
 gastric polyps, **I**:207–209
 gastric varices, **I**:222
 gastrointestinal stromal tumour, **I**:297
 hematoma, **I**:296–297
 herpes simplex virus esophagitis, **I**:51
 inflammatory bowel disease, **I**:293–295, 297, 298
 intrahepatic cholangiocarcinoma, **II**:375
 jejuno gastric intussusceptions, **I**:124
 lipoma, **I**:298



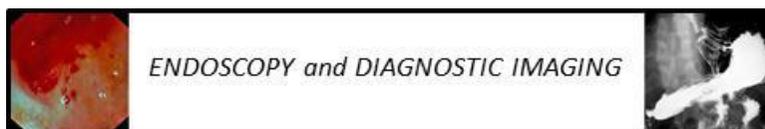
liver abscess, **II**:212
 Meckel diverticulum, **I**:310
 mucocele of appendix, **II**:283
 polyps, **II**:263
 pseudocalculus, **I**:383
 pseudopolyp, **II**:267–268
 rectum, **II**:291
 stomal cancer, **I**:125
 superior mesenteric artery and vein, **II**:225
 duodenal, **I**:247, 295
 intraluminal, **I**:59, 134, 297, 298, 381
 inversion, **I**:310
 in MRI results, **II**:185
 non-neoplastic gastric, **I**:221–222
 post-surgical, **II**:297
 serpiginous, **I**:59
 subserosal, **I**:297
 swallow, **I**:53
 tubular, **I**:124
 Fistula, **I**:284–285
 aortoenteric, **I**:293
 Crohn disease, **I**:52, 316
 non-Hodgkin's lymphoma and, **I**:299
 pancreatitis and, **I**:340
 Flocculation, **I**:314
 Focal nodular hyperplasia, **II**:369–370
 Forrest I non-variceal upper GI bleeding, **I**:182
 Functional abdominal pain syndrome (FAPS), **II**:27
 Fundic gland polyps, **I**:200, 250, 262
 Fundoplication, **I**:77

G

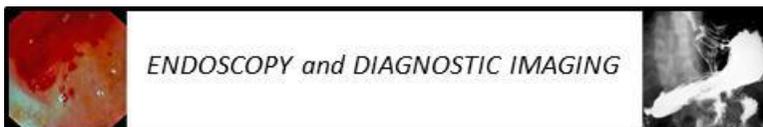
G cell hyperplasia, **I**:28
 Gadolinium scan, **II**:368–369
 Gallbladder, **I**:377, 384–389
 filling defect, **I**:132, 369, 383, 387
 motility, **I**:233, 332
 polyps, **I**:387
 porcelain, **I**:386
 Gallstones, **I**:386–390, **II**:388, 391
 Gardner syndrome, **II**:263
 Gastrectomy, **I**:28
 Gastric atrophy, **I**:264
 Gastric banding, **I**:121



- Gastric bleeding, **I**:191, 262, 263
- Gastric bypass, **I**:121
- Gastric cancer, **I**:201–233, 222–226, 254, 259
 - development of, risk factors associated with, **I**:211
 - diagnostic imaging in, **I**:219–231, 227, 228
 - early, **I**:260
 - fistulae and, **I**:210, 228
 - gastric stump, **I**:217
 - diagnostic imaging of, **I**:229–231
 - intestinal vs. diffuse type, **I**:216
 - Laurén classification of, **I**:218
 - macroscopic types of, **I**:212
 - metastatic, **I**:220
 - mortality and, **I**:217–218
 - palliation of, **I**:216
 - pathological conditions associated with, **I**:218
 - presentations of, **I**:210
 - prevention of, **I**:215–216, 218
 - sites for metastasis of, **I**:217
 - survival rate in, **I**:218
- Gastric dilation, **I**:240
- Gastric dysmotility, **I**:125–134
 - diagnostic imaging in, **I**:133–134
- Gastric folds, **I**:242
- Gastric fundic polyps, **I**:200, 250
- Gastric lymphoma, **I**:233–237, 234, 235, 265, 322
- Gastric polyps, **I**:196–197, 198–201, 256, 264
 - benign, **I**:204–206
 - classification of, **I**:196, 197
 - diagnostic imaging of, **I**:207–209
 - distribution of, **I**:196
 - fundic, **I**:200, 250
 - types of, **I**:201–203
- Gastric stricture, **I**:65
- Gastric stump cancer, **I**:217
 - diagnostic imaging of, **I**:229–231
- Gastric surgery, **I**:121–125
 - bariatric, **I**:121–123
 - complications of, **I**:121–122
 - diagnostic imaging for, **I**:124–125
- Gastric ulcer, **I**:187, 243
 - penetrating giant, **I**:241
 - visible vessel, **I**:187–190
- Gastric varices, **I**:251, 253



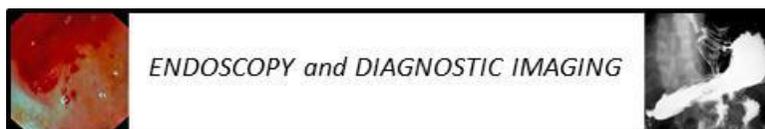
- Gastritis, I:135–150, 322
 causes of, I:135
 diagnostic imaging of, I:145–150
 enterogastric reflux and, I:138–141
 eosinophilic, I:141–145
 phlegmonous, I:137, 149, 171
 types of, I:136–145
- Gastroesophageal polyp, inflammatory, I:58
- Gastroesophageal reflux disease (GERD), I:24–39
 acid and, I:26
 damaging factors, I:25
 test to assess, I:29
 diagnostic imaging, I:51
 endoscopic grading, I:27
 epithelial resistance factors, I:26
 epithelial defense, I:26
 post-epithelial defense, I:26
 pre-epithelial defense, I:26
 erosions of, I:31
 esophageal function in, I:29
 esophageal strictures in, I:28
 esophagitis associated with, I:27
 classification system for endoscopic assessment of, I:27
 heartburn and, I:26
 lifestyle modifications for, I:34
 motility disorders and, I:24–25
 motor abnormalities in, I:28
 non-dietary causes of, I:28
 non-erosive, I:25
 classification of, I:35
 endoscopic assessment of changes in, I:33–34
 pathophysiology of, I:30
 practice pointers for, I:25–28
 reactive epithelial changes in, I:30
 recurrence, predictors of, I:28
 resistance factors in, I:25
 surgery for, I:29–30
 tests to assess, I:29
 therapy for, I:30
- Gastrointestinal barrier, I:273–274
- Gastrointestinal bleeding, II:262, 334, 336, 337
 fistulae and, I:179
 Forrest I non-variceal upper, I:182
 lower, I:179–191, II:269–281



- non-variceal upper, **I**:172–179, 182–187
- risk factors for, **I**:180
- upper, **I**:179–191, 262, 263
 - relative frequency of, **I**:179
- Gastrointestinal (GI) tract
 - bleeding in. See Gastrointestinal bleeding
 - diseases of, extra-intestinal changes in, **I**:3–20
 - tumours of, **I**:277–283
- Gastrointestinal stromal tumour (GIST), **I**:58, 293, 294, 297–299
 - malignant, **I**:208, 278
- Gastroparesis, **I**:28, 125–134
- Gastropathy
 - alcoholic, **I**:334
 - NSAID-induced, **I**:266
 - pancreatitis and, **I**:334
 - stress-related mucosal, **I**:334
- Gastroplasty, **I**:121
- Gastroprotection, **I**:167–172
- GERD. See Gastroesophageal reflux disease (GERD)
- Giant cavernous hemangioma, **II**:369
- Giant ulcer
 - esophageal, **I**:51–52
 - gastric penetrating, **I**:241
- Giant villous adenoma, **II**:149
- GIST. See Gastrointestinal stromal tumour (GIST)
- Glasgow score, **I**:338
- Glossitis, **I**:7
- Gluten enteropathy. See Celiac disease
- Grey Turner's sign, **I**:13
- Gut endocrine tumours, **I**:131–132

H

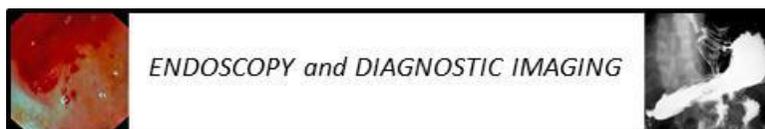
- Hamartomas, **I**:298
- Heartburn, **I**:26
- Helicobacter pylori* infection, **I**:155–161
 - gastritis, **I**:162, 162–164, 163
- Hemangioendothelioma, epitheloid, **II**:376
- Hemangioma, **I**:78, 298, **II**:368, 369
- Hematemesis, **II**:383
- Hematochezia, **II**:269, 319
 - causes of, **II**:11, 269–271
 - small bowel sites for, **II**:270
- Hematoma, **I**:77, 294
- Hemochromatosis, **I**:16



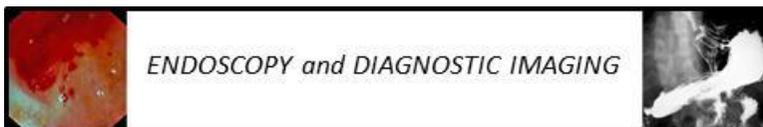
- Hemorrhagic cyst, **II**:365
- Hemorrhoids, **II**:12–13
 - hematochezia and, **II**:11, 270
- Hepatic abscess, **II**:182, 212, 395
- Hepatic adenoma, **II**:371
- Hepatic angiomyolipomas, **II**:372
- Hepatic candidiasis, **II**:367
- Hepatic encephalopathy, **II**:358–378
- Hepatic hemangioma, **II**:369
- Hepatic metastases, **II**:376–377
- Hepatocellular cancer, **II**:372–373
 - diffuse, **II**:372
 - fibrolamellar, **II**:372–373
- Hereditary nonpolyposis colon cancer, **II**:152, 252
- Hernia
 - diagnostic imaging of, **I**:60–61
 - hiatal, **I**:28, 64, 67
 - manometry in, **I**:88–91
 - paraesophageal, **I**:79
- Heterotopic gastric mucosa, **I**:78
- Hiatal hernia, **I**:28, 64, 67
 - manometry in, **I**:88–91
- Hyperplasia, **II**:303, 304
 - Brunner gland, **I**:294
 - colonic lymphoid, **II**:324
 - focal nodular, **II**:370
 - nodular lymphoid, **II**:268
- Hyperplastic polyp, **II**:303
 - serrated, **II**:304
- Hypertension. See Portal hypertension

I

- IBD. See Inflammatory bowel disease (IBD)
- IBS. See Irritable bowel syndrome (IBS)
- Ileal lymphoid hyperplasia, **I**:322
- Ileum, narrowing of neo-terminal of, **I**:316
- Iliac pouch anal anastomosis, **II**:176
- Immobility, **I**:28
- Incoordinate pharyngo-esophageal sphincter, **I**:115–117
- Infectious colitis, **II**:81, 307, 332
- Inflammatory bowel disease (IBD), **I**:49, **II**:77–122
 - adenomas and, **II**:138, 179
 - ankylosing spondylitis and, **II**:108–109
 - aphthous stomatitis and, **II**:114, 114, 115



- barium studies in, **II**:68
- cancer surveillance in, **II**:129–131, 137, 140, 140, 177–179
- diagnostic imaging in, **I**:293–311
- erythema nodosum and, **II**:110, 111, 117
- extraintestinal complications of, **II**:108
- extraintestinal manifestations of, **II**:107–108, 110
- lactase deficiency and, **I**:292
- malnutrition and, **I**:289, **II**:79
- presentation of, **II**:78
- primary sclerosing cholangitis and, **II**:116
- pyoderma gangrenosum and, **II**:112, 112, 113, 114, 118
- scleritis and, **II**:119
- sclerosing cholangitis and, **II**:116, 119
- spondyloarthropathy and, **II**:109, 110
- steroid resistance and, **II**:80
- uveitis and, **II**:116, 116, 118
- Insulinoma, **I**:368
- Intestinal ischemia, **II**:218, 224
- Intestinal pseudo-obstruction, secondary, **II**:45
- Intrahepatic cholangiocarcinoma, **II**:375
- Intrahepatic cysts, **II**:387
 - polycystic liver disease vs., **II**:387
- Intrahepatic ducts, narrowing, **II**:397
- Inverted colonic diverticulum, **II**:268
- Iron deficiency, **I**:122
- Irritable bowel syndrome (IBS), **II**:25–28, 215
 - constipation-predominant, **II**:49, 50
 - ischemic bowel disease and, **II**:214, 215, 221, 222
 - pathogenesis of, **II**:27
 - Rome III criteria for, **II**:26
 - smooth muscle irritability and, **II**:25
 - stress and, **II**:25–26
 - treatment of, **II**:27
 - visceral sensitivity and, **II**:25
- Ischemia
 - intestinal, **II**:218, 224
 - mesenteric. *See* Mesenteric ischemia
- Ischemic bowel disease, **II**:214–250
 - irritable bowel syndrome and, **II**:214, 215, 221, 222
- Ischemic colitis, **II**:219–242
 - barium studies in, **II**:225
 - radiological evaluation of, **II**:228, 228–242



J

Juvenile polyposis syndrome, **II**:264

K

Ki67 proliferation, **I**:31

Killian-Jamieson diverticulum, **I**:59, 60

Klatskin tumour, **II**:394, 395

L

Laxatives, **II**:49–69

classification of, **II**:49

Leaky gut, **I**:292

Leiomyoma, **I**:278, **II**:330

Leiomyosarcoma, **I**:278

Leukocytoclastic vasculitis, **I**:12

Linitis plastica, **I**:68, 240

Lipoma, **I**:293, 298, **II**:264, 330

distinguishing diagnosis in, **II**:374

serosal metastases vs., **II**:264

Liver. *See also* Hepatic *entries*

abscess of, **II**:182, 212, 395

cyst of, **II**:365

malignant masses in, **II**:373–378

in polycystic disease, **II**:387

tumours of, benign, **II**:368

Lower gastrointestinal bleeding, **I**:179–191, **II**:269–281

Lymphoma, **I**:294, **II**:13, 48, 107, 267

adenocarcinoma vs., **I**:221

cancer and, **II**:271

celiac disease and, **I**:276

colonic, **II**:325

diagnostic imaging in, **I**:56, 58

diffuse, **II**:268

esophageal, **I**:47, 52, 53

gastric, **I**:233–237, 234, 235, 265, 322

non-Hodgkin's, **II**:286

fistulae and, **I**:299

M

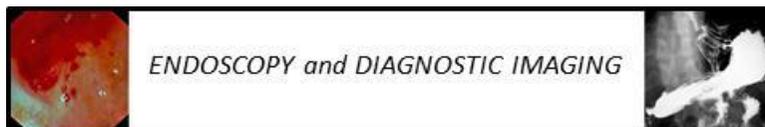
Macroglossia, **I**:7

Magnetic resonance imaging (MRI)

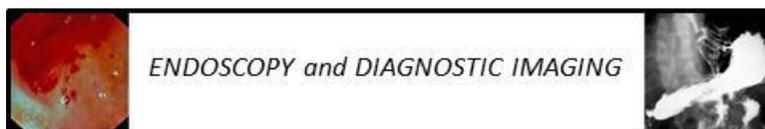
abdominal, **I**:131

autoimmune pancreatitis, **I**:353, 354

benign liver tumours, **II**:368



- Caroli disease, **I**:384
- cholangiocarcinoma, **I**:381
- enteropathy, **I**:290
- fecal incontinence, **II**:5
- filling defects in, **II**:185
- focal nodular hyperplasia, **II**:370
- gastric bleeding, **I**:191
- hepatic adenoma, **II**:371
- hepatocellular cancer, **II**:374
- intrahepatic cholangiocarcinoma, **II**:375
- oriental cholangiohepatitis, **I**:382
- pancreatic neuroendocrine tumour, **I**:329
- pancreatic tumours, **I**:372, 375
- pelvic, **I**:191
- Malignant liver masses, **II**:373–378
- Manometry, **I**:83–117
 - achalasia, **I**:111–114
 - diffuse esophageal spasm, **I**:99–102
 - hiatal hernia, **I**:88–91
 - high resolution, advantages of, **I**:41
 - incoordinate pharyngo-esophageal sphincter, **I**:115–117
 - normal study, **I**:84–87
 - nutcracker esophagus, **I**:103–105
 - pre- and post-fundo mechanical obstruction, **I**:92–98
 - scleroderma pattern, **I**:108–110
 - symptomatic wave with chest pain, **I**:106–107
- Mastocytosis, **II**:38
- Megacolon, **II**:45–46, 287
 - cause of, **II**:54
 - ulcerative colitis and, **II**:69
- Melanosis coli, **II**:325
- Mesenteric ischemia
 - acute
 - clinical presentation of, **II**:222–223
 - pathological changes in, endoscopic and microscopic, **II**:223
 - treatment for, **II**:223
 - causes, **II**:221–222
 - chronic, clinical presentation of, **II**:222–223
 - radiologic assessment of, **II**:223–225
- Mirizzi syndrome, **I**:383
- Motility disorders, **II**:13–25, 376. *See also* Dysmotility
 - esophageal. *See* Esophageal motility disorders
 - in gastroesophageal reflux disease, **I**:24–25
- MRI. *See* Magnetic resonance imaging (MRI)



Mucosa, ectopic gastric, **I:59**
 Multiple endocrine neoplasia (MEN), type I, **I:215**
 Myenteric plexus, disorders of, **II:24–25**
 Myotomy, **I:28**

N

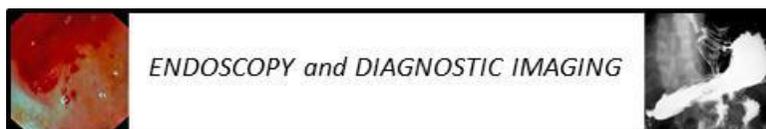
Nail pitting-psoriasis, **I:19**
 Neuroendocrine tumours, pancreatic, **I:328–329**
 Neurofibromatosis, **I:278–279**
 Neurotrophins, **II:24**
 Nissen fundoplication, **I:39**
 Nitrates, **I:28**
 Nodular lymphoid hyperplasia, **II:268**
 Non-Hodgkin's lymphoma, **II:286**
 fistulae and, **I:299**
 Non-neoplastic gastric filling defects, **I:221**
 Non-variceal upper GI bleeding, **I:172–179, 182–187**
 Nonsteroidal anti-inflammatory drugs (NSAIDs), **I:164–166**
 gastropathy associated with, **I:266**
 Nuclear factor kappa B, **I:287**
 Nutcracker esophagus, **I:103–105**

O

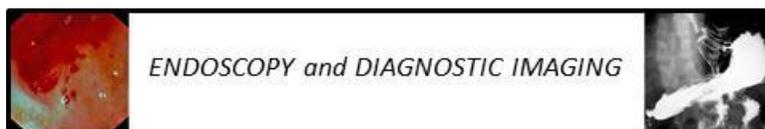
Obesity, **I:28**
 Odynophagia, **I:57**
 Ogilvie's syndrome, **II:31–32, 42**
 Oncogenes, **I:31**
 Osler Weber Rendu disease, **I:5**

P

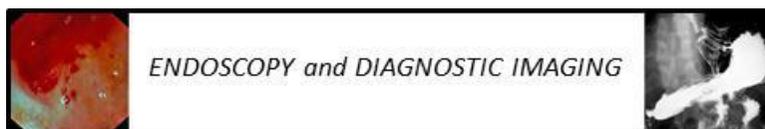
Palmar erythema, **I:17**
 Pancolonic diverticulosis, **II:286**
 Pancolonic polyposis, **II:286**
 Pancreas, annular, **I:395**
 Pancreas divisum, **I:394, 395**
 Pancreatic abscess, **I:334, 348, 350, 356, 399, 400**
 barium study of, **I:351**
 CT scan of, **I:351, 376**
 Pancreatic cancer, **I:358–379, 402, II:384**
 abscess and, **I:358**
 cystic fibrosis and, **I:364, 365**
 diagnostic imaging in, **I:370–379**
 genetic predisposition to, **I:363**
 infiltrating common bile duct and, **II:385**



- risk factors for, **I:363–365**
- screening for, **I:365**
- staging of, **I:370**
- Pancreatic duct, **I:392, 393**
 - calculi in, **I:398**
 - drainage of, **I:399**
 - ectasia of, **II:385**
 - leaking, **I:400**
 - narrowing of, **I:393, 401, 402, II:398**
- Pancreatic enzyme therapy, **I:330–334**
- Pancreatic pseudocysts, **I:398**
- Pancreatic tumorigenesis, **I:390**
- Pancreatitis, **I:222, 253, 293, 294, 296**
 - acute, **I:334–343**
 - abscess in, **I:334**
 - causes of, **I:334**
 - complications of, **I:334, 340**
 - diagnostic imaging of, **I:341–343**
 - drug-related, **I:340–341**
 - fistulae and, **I:340**
 - Grey Turner's sign in, **I:13**
 - prognostic scores for, **I:339**
 - autoimmune, **I:352–358**
 - chronic, **I:327–328, 343–352, 396, 397, 401**
 - pain in, management of, **I:348**
 - cystic fibrosis and, **I:350, 358**
 - diarrhea and, **I:288**
 - eosinophilic, **I:143**
 - familial, **I:350**
 - minimal change, **I:396**
 - polyps and, **I:206**
 - PPI therapy and, **I:38**
- Paraesophageal hernia, **I:79**
- PDT (photodynamic therapy), **I:32**
- Peptic stricture, **I:79**
- Peptic ulcer disease, **I:151–172, 293, 294**
 - bariatric surgery and, **I:123**
 - dyspepsia and, **I:151**
- Perianal disease, **II:10–13**
- Periportal fibrosis, **II:377**
- Peutz-Jegher's syndrome, **I:5, 298**
- Pharyngeal pouch, **I:69**
- Pharyngo-esophageal sphincter (PE), incoordinate, **I:115–117**
- Photodynamic therapy (PDT), **I:32**



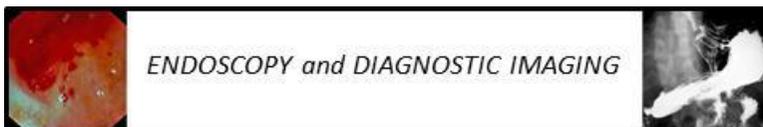
- Phytobezoar, **I**:267
- Pneumatosis cystoides, colonic, **II**:326
- Polycystic liver disease vs. intrahepatic cysts, **II**:387
- Polyp
- adenomatous, on long stalk, **II**:305, 331
 - barium studies, **II**:262–263
 - colonic, **II**:251–268, 290
 - cancer and, **II**:149–150, 167
 - histological classification of, **II**:150
 - CT imaging of, **II**:263
 - diagnostic imaging in, **II**:262–264
 - filiform inflammatory, **II**:288
 - gallbladder, **I**:387
 - gastric, **I**:196–197, 198–201, 256, 264
 - benign, **I**:204–206
 - classification of, **I**:196, 197
 - diagnostic imaging of, **I**:207–209
 - distribution of, **I**:196
 - fundic, **I**:200, 250
 - types of, **I**:201–203
 - gastroesophageal, inflammatory, **I**:58
 - histological classification of, **II**:251
 - hyperplastic, **II**:303
 - pancreatitis and, **I**:206
 - postinflammatory, **II**:267
 - resection of, **II**:330
 - serrated hyperplastic, **II**:330
 - sessile, **I**:322
 - villous adenomatous, **II**:263
- Polypectomy, hematochezia and, **II**:270
- Polypoid esophageal carcinoma, **I**:66
- Polypoid tumour intussusception, **II**:290
- Polyposis
- familial, **II**:285
 - pancolonic, **II**:286
- Polyposis syndrome, **II**:48, 268
- hyperplastic, **II**:168, 169
 - juvenile, **II**:264
- Porcelain gallbladder, **I**:386
- Portal hypertension, **II**:349–358
- gastropathy associated with, **I**:192–195
- Portal hypertensive gastropathy, **I**:150, 195, 268
- Post-surgical filling defect, **II**:297
- Post-transplantation lymph proliferative disorder, **I**:81



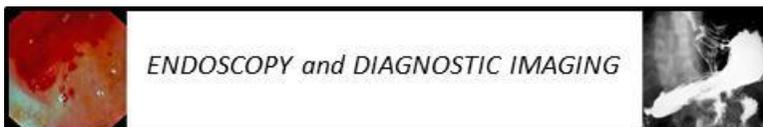
- Pouchitis, **II**:146–148, 333
 Pregnancy, **I**:28
 ectopic, **II**:182, 207
 Prepyloric ulcer, **I**:241
 Primary sclerosing cholangitis, **II**:116
 Proctitis, **II**:318
 Proctocolectomy, with permanent ileostomy, **II**:146
 Proctosigmoiditis, **II**:306, 331
 Proton pump inhibitor (PPI), **I**:30
 acid rebound with, **I**:36
 alcohol metabolism and, **I**:36
 anaphylaxis and, **I**:38
 bacterial colonization and, **I**:38
 bacterial overgrowth and, **I**:37
 calcium malabsorption and, **I**:37
 candidal infection and, **I**:37
 drug interactions and, **I**:38
 enteral infection and, **I**:36
 gastric mucosa and, **I**:36
 H. pylori gastritis and, **I**:37
 hypergastrinemia-induced carcinoid tumours and, **I**:37
 intragastric therapy and, **I**:35–36
 iron malabsorption and, **I**:37
 long-term, **I**:35
 nephritis and, **I**:38
 nocturnal acid breakthrough and, **I**:36
 pancreatitis and, **I**:38
 pneumonia and, **I**:38
 polyp formation and, **I**:37
 potential risks of, **I**:37–38
 pregnancy and, **I**:38
 vitamin B₁₂ malabsorption and, **I**:37
 Pseudo-obstruction, **II**:289
 Pseudocirrhosis, **II**:377
 Pseudocysts, pancreatic, **I**:398
 Pseudopolyp, **II**:267
 inflammatory, **II**:137, 179
 Psoriatic nails, **I**:19
 Pyloric torus defect, **I**:297
 Pyoderma gangrenosum, **I**:14, **II**:112, 112, 113, 114, 118

R

- Radiation damage, **II**:243, 243–248
 endoscopic findings of, **II**:249, 261



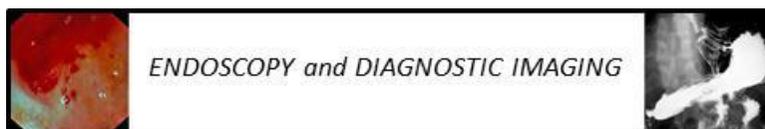
- management of, **II**:250
 - risk factors for, **II**:260
 - symptoms of, **II**:260–261
 - types of, **II**:260
 - Radiofrequency ablation (RF), **I**:32
 - Ram's horn deformity, **I**:134
 - Ranson score, **I**:338
 - Rectal stump, risk factors for cancer in, **II**:175, 258
 - Rectosigmoid, narrowing of, **II**:295
 - Rectum
 - bleeding from, **II**:334, 336, 337
 - following polypectomy, **II**:336
 - endocrine tumours, **II**:259–260
 - filling defect, **II**:291
 - malignancy in, CT scan staging of, **II**:159
 - mucosa, **II**:316
 - patchy redness in, **II**:334
 - stump cancer, risk factors for, **II**:175
 - villous adenoma of, **II**:150
 - RF. See Radiofrequency ablation (RF)
- S**
- Santorini, duct of, **I**:394
 - Scalloping, **I**:322
 - Scintigraphy
 - cholescintigram, **I**:385
 - sulphur colloid, **II**:370
 - Scleroderma, **I**:3, 28, 66, **II**:37
 - colonic diverticuli and, **II**:37
 - Sclerosing cholangitis, **II**:119, 384, 396, 397
 - Sclerosis, systemic, **I**:68
 - Secondary intestinal pseudo-obstruction, **II**:45
 - Serrated hyperplastic polyp, **II**:330
 - Sessile polyp, **I**:322
 - Sigmoid colon, patchy redness in, **II**:334
 - Sjögren syndrome, **I**:28
 - Skin pigmentation, **I**:16
 - Sludge, biliary, **I**:346, 383, 384
 - SMA (superior mesenteric artery) syndrome, **I**:294, 295
 - Small bowel obstruction, **I**:315
 - Small intestine, **I**:273–323
 - clinical cases involving, **I**:407
 - diagnostic imaging, **I**:314–317
 - endoscopic imaging, **I**:320–323



- Smoking, **I**:28
- Sphincterotomy, **II**:389, 390
- Spider angioma, **I**:11
- Spondyloarthropathy, **II**:109, 110
- Stomach, **I**:119–269. *See also* Gastric *entries*
 cancer of. *See* Gastric cancer
 clinical cases involving, **I**:406
 diagnostic imaging of, **I**:240–248
 endoscopic imaging of, **I**:249–269
 intestinal metaplasia in, **I**:265
 metastasis to, **I**:266
 watermelon, **I**:268
- Stomal ulcer, **I**:267
- Stomatitis, aphthous, **II**:114, 114, 115
- Stricture
 balloon dilation of, **II**:310, 333
 in dysphagia
 benign in, **I**:23–24
 malignant, **I**:24
 esophageal. *See* Esophageal stricture
 gastric, **I**:65
 peptic, **I**:79
- Submucosal tumour, **I**:80
- Sulphur colloid scintigraphy, **II**:370
- Superior mesenteric artery syndrome (SMA syndrome), **I**:294, 295

T

- Telomerase, **I**:31
- Theophylline, **I**:28
- TNF-alpha (tumor necrosis factor-alpha), **I**:286–287
- Transient LES relaxations (TLESR), **I**:34
 pharmacological blockade of, **I**:34
 physiology of, **I**:34
 stimuli for, **I**:34
- Tumorigenesis, pancreatic, **I**:390
- Tumour, **I**:277
 carcinoid, **I**:255, 299, **II**:258, 260
 malignant, **II**:258
 rectal, **II**:260
 size and metastases, **II**:260
 endocrine, **I**:282–283
 appendiceal, **II**:258
 colonic, **II**:259–260
 rectal, **II**:260



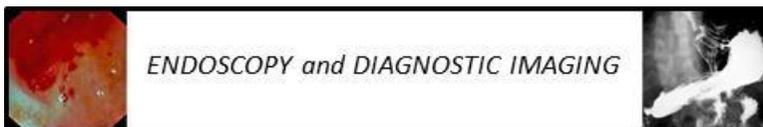
Klatskin, **II**:394–395
 liver, benign, **II**:368
 pancreatic, **I**:369, 372
 Tumour necrosis factor-alpha (TNF-alpha), **I**:286–287
 Tumour suppressor genes, **I**:31

U

UC. See Ulcerative colitis (UC)

Ulcer

aphthous, **II**:317, 337
 Barrett's, **I**:74
 Barrett's ulcer, **I**:74
 duodenal, **I**:245, 246
 esophageal, **I**:51–52
 gastric, **I**:187–190, 241, 243
H. pylori associated, **I**:251
 prepyloric, **I**:241
 solitary, **II**:249, 251
 rectal, **II**:328
 stomal, **I**:267
 Ulcerative colitis (UC), **I**:288, **II**:328
 acute self-limiting vs. chronic idiopathic colitis, **I**:289
 barium enema results in, **II**:95, 95–107
 cancer and, **II**:77–122
 characteristics of, **II**:76
 clinical presentation of, **I**:287
 colonoscopic surveillance in, **II**:124–128, 131–136
 correlation between endoscopic findings and histology in, **II**:136
 shortcomings of, **II**:139
 conditions mimicking, **II**:81
 continuous and circumferential, **II**:288
 Crohn disease vs., **II**:71
 differential diagnosis of, **II**:91–92, 107
 dysplasia and, **II**:124–128, 131–136
 endoscopy in, **II**:70, 79, 91–92
 megacolon and, **II**:69
 severity assessment in, **II**:77
 vasculature in, **II**:82
 Ultrasound, **I**:376, 382
 abdominal, **I**:131, 290, 346, 349, **II**:360
 appendicitis, **II**:185
 benign liver tumour, **II**:369
 Chiari syndrome, **II**:364
 cirrhosis, **II**:365



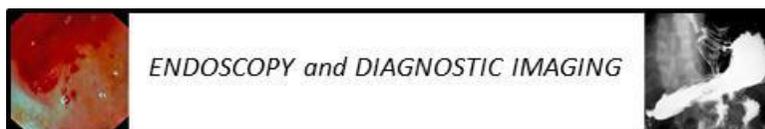
contrast enhanced CT, **I**:385, 388
 Crohn disease, **I**:285
 in distinguishing diagnoses, **I**:373
 diverticular disease, **II**:182, 211
 diverticulitis, **II**:207
 Doppler, **I**:290, 366, **II**:217, 223, 356, 363, 365, 369
 ectopic pregnancy, **II**:182, 207
 focal nodular hyperplasia, **II**:370
 gallbladder, **I**:387–389
 hemorrhagic cyst, **II**:365
 hepatic angiomyolipoma, **II**:372
 hepatic angiomyolipomas, **II**:372
 hepatic candidiasis, **II**:367
 hepatic cyst, **II**:365
 hepatic hemangioma, **II**:369
 hepatic metastases, **II**:377
 intraoperative, **I**:366, 372
 limitations, **II**:186
 metastases to pancreas, **I**:375
 pancreatic adenocarcinoma, **I**:370, 371
 pancreatic tumour, **I**:372
 pancreatitis, **I**:342–343, 349
 pelvic, **I**:285, **II**:182
 transvaginal, **II**:182
 Von Meyenburg complex, **II**:366
 Urea breath test, **I**:160–161
 Uveitis, **I**:9, **II**:116, 116, 118

V

Vagotomy, **I**:28
 Varices, **I**:59
 esophageal, **I**:67, 192–195, 253
 gastric, **I**:251, 253
 Vasculitis, leukocytoclastic, **I**:12
 Villous adenoma, **II**:150, 263, 329
 Villous adenomatous polyp, **II**:263
 Villous atrophy, **I**:276
 Von Meyenburg complex, **II**:366

W

Watermelon stomach, **I**:268
 Whipple disease, **I**:294
 White nails, **I**:18



X

Xanthelasmata, **I**:9

Y

YAG laser, **I**:32

Z

Zenker's diverticulum, **I**:59, 60, 65, 75Zollinger-Ellison syndrome, **I**:28, 293, 294bariatric procedures and, **I**:123mechanisms of malabsorption in, **I**:133presenting features, **I**:123–124