NAMS SYMPOSIUM – SEPT 7 ,2014

DAYANAND MEDICAL COLLEGE & HOSPITAL

सर्वे सन्तु निरामयाः

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LUDHIANA

EMERGENCIES IN IBD

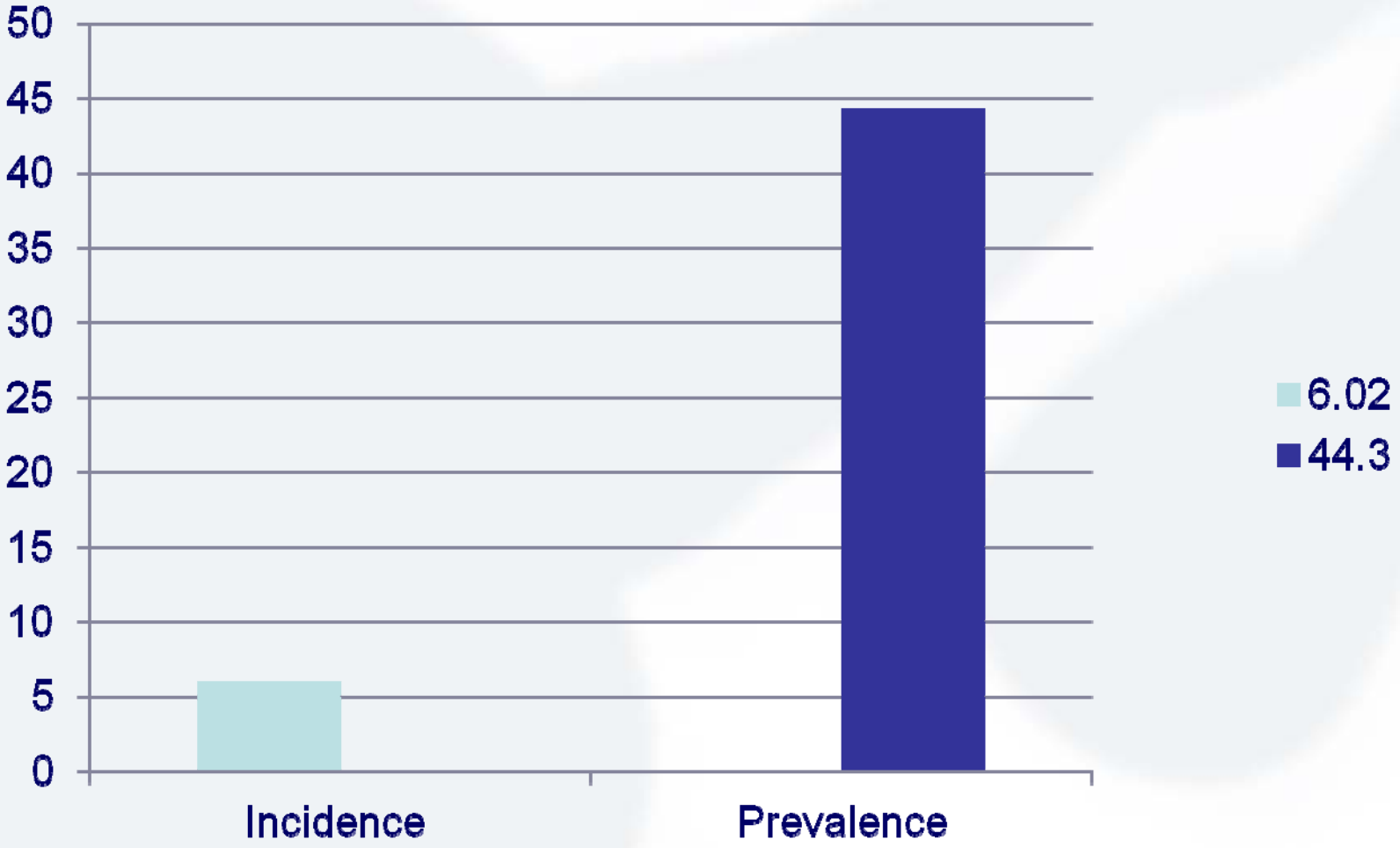
Regional Symposium on Inflammatory Bowel disease
Department of Medicine ,GMCH Chandigarh
NAMS(INDIA)

Prof. Rajoo Singh Chhina
MD,DM,FAMS

IBD

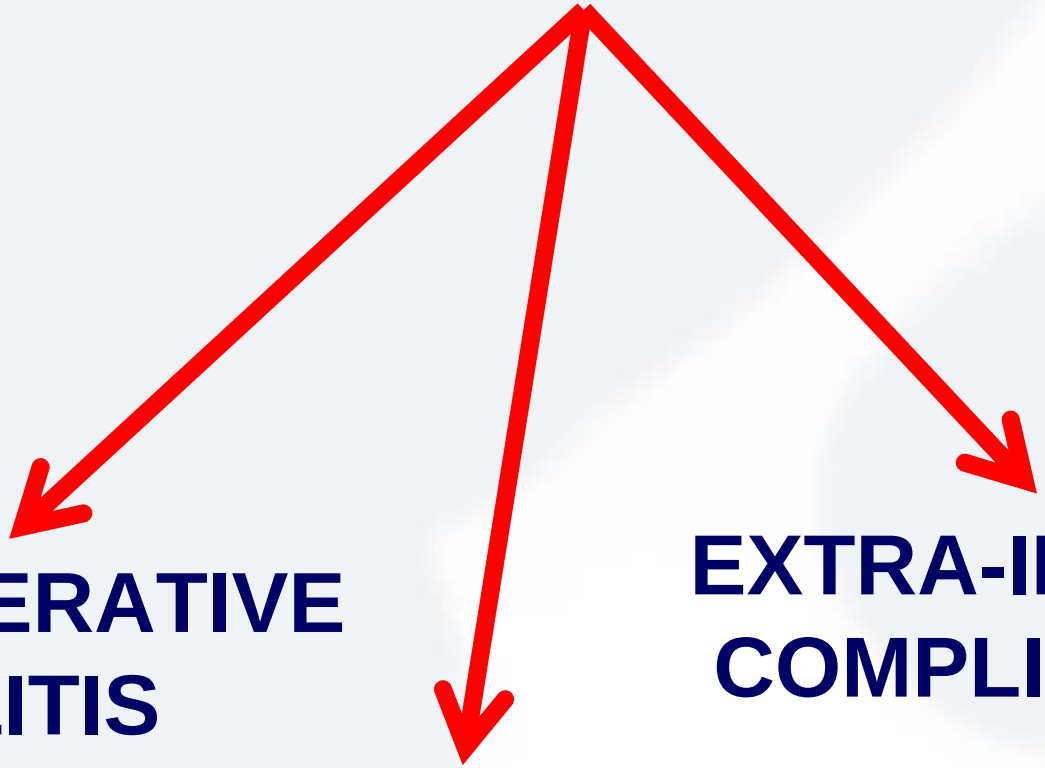
- Chronic inflammatory disease of unknown etiology
- World wide disorder with significant geographical heterogenicity
- Highest prevelance reported from Northern and Western Europe and North America

Incidence and Prevalence of Ulcerative colitis in Punjab



Gut 2003;52:1587–1590

IBD Emergencies



ULCERATIVE COLITIS

CROHNS

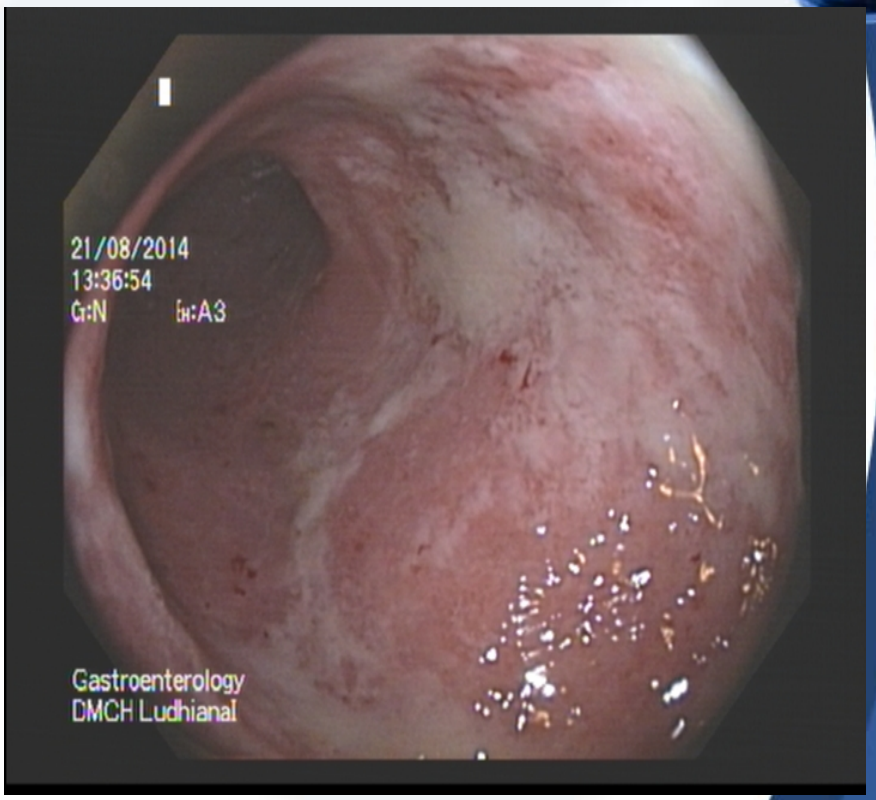
EXTRA-INTESTINAL COMPLICATIONS

IBD Emergencies

- **ASSOCIATED WITH UC**
- ASSOCIATED WITH CROHNS
- EXTRA-INTESTINAL COMPLICATIONS

Ulcerative Colitis –Intestinal Complications

- Fulminant Colitis
- Toxic megacolon
- Lower GI bleed
- Perforation
- Colorectal Cancer

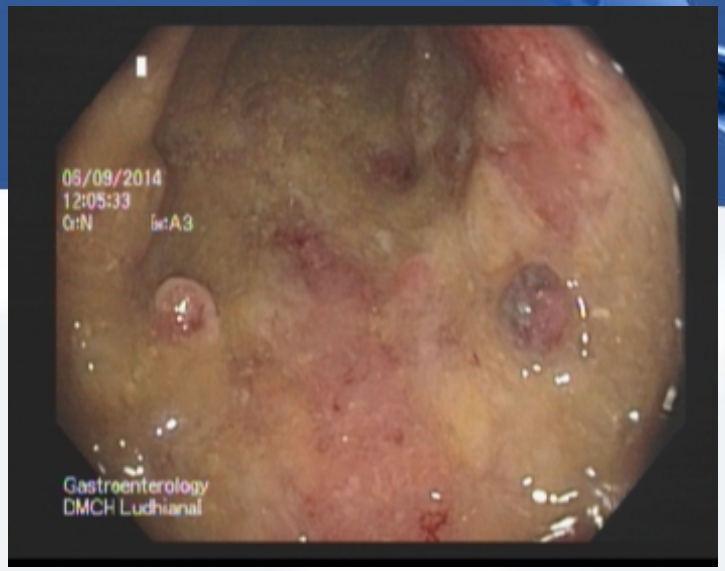


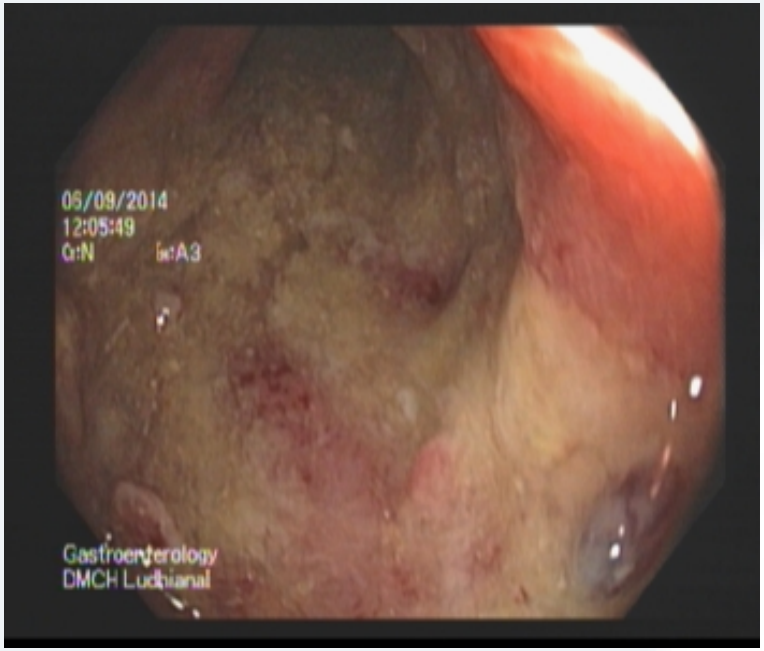
Ulcerative Colitis –Intestinal Complications

- Fulminant Colitis
- Toxic megacolon
- Lower GI bleed
- Perforation
- Colorectal Cancer

Fulminant Colitis

- **15 to 20 percent of UC- episode of fulminant colitis.**





Pancolitis predispose to severe flares

Gut 1996; **38**: 905-910

Suspect – fulminant colitis ?

Typical symptoms -UC (ie, bloody diarrhea, rectal urgency tenesmus, and abdominal colic) **+**

Symptoms	Signs
Fever	Tachycardia
Dehydration	Orthostatic hypotension
Mental changes	Fever
Anorexia	Pale and dry mucosal membranes
Weight loss	Abdominal tenderness
	Hypoactive bowel sounds

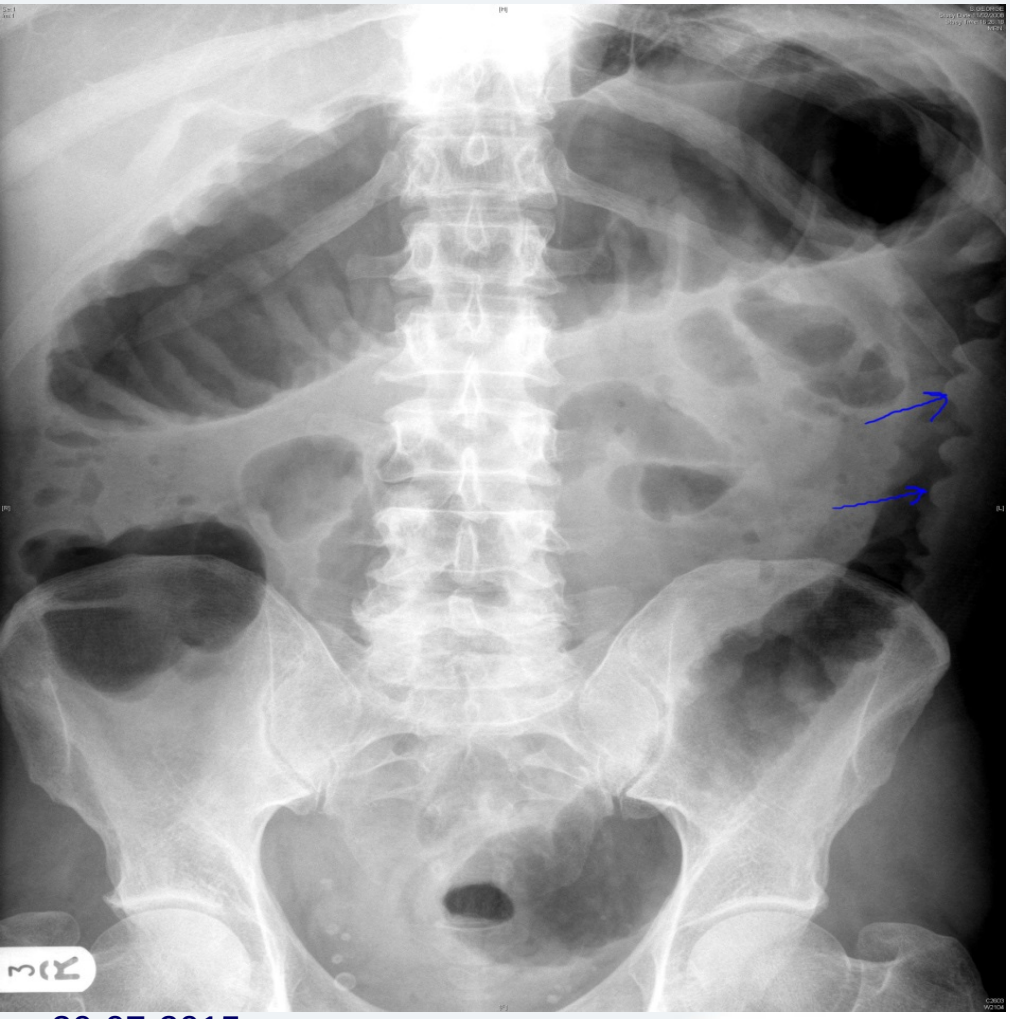
Gastroenterol Clin N Am32 (2003) 1269–1288

Labs -

- Increased TLC(>20,000/mm3)
- Elevated ESR (>40 mm/hr)
- Anemia
- Hypokalemia,Hyponatremia
- Hypoalbuminemia
- Metabolic Alkalosis

Gastroenterol Clin N Am32 (2003) 1269–1288

Abdominal X-Ray

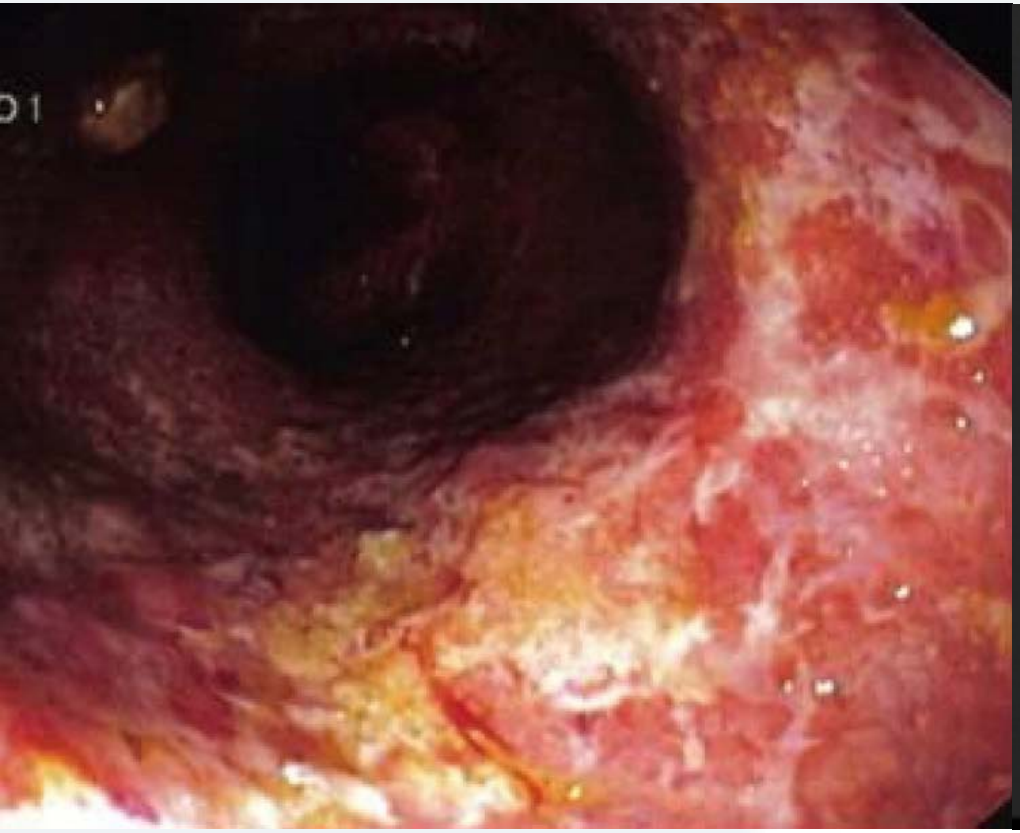


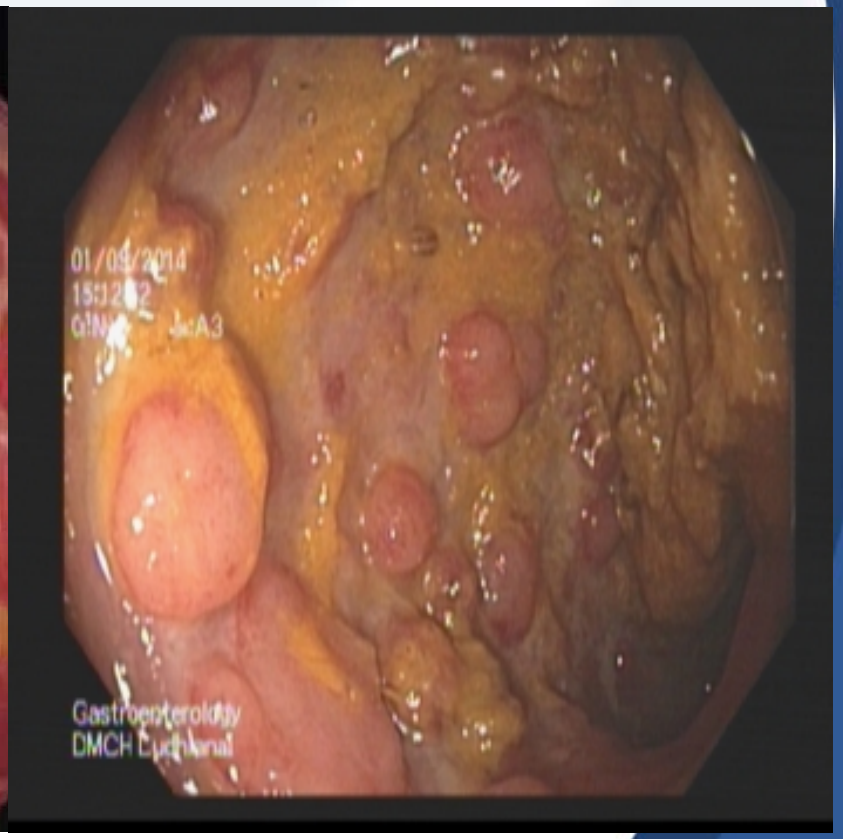
The distance between loops of bowel is increased due to thickening of the bowel wall.

The haustral folds are very thick, leading to a sign known as 'thumbprinting.'

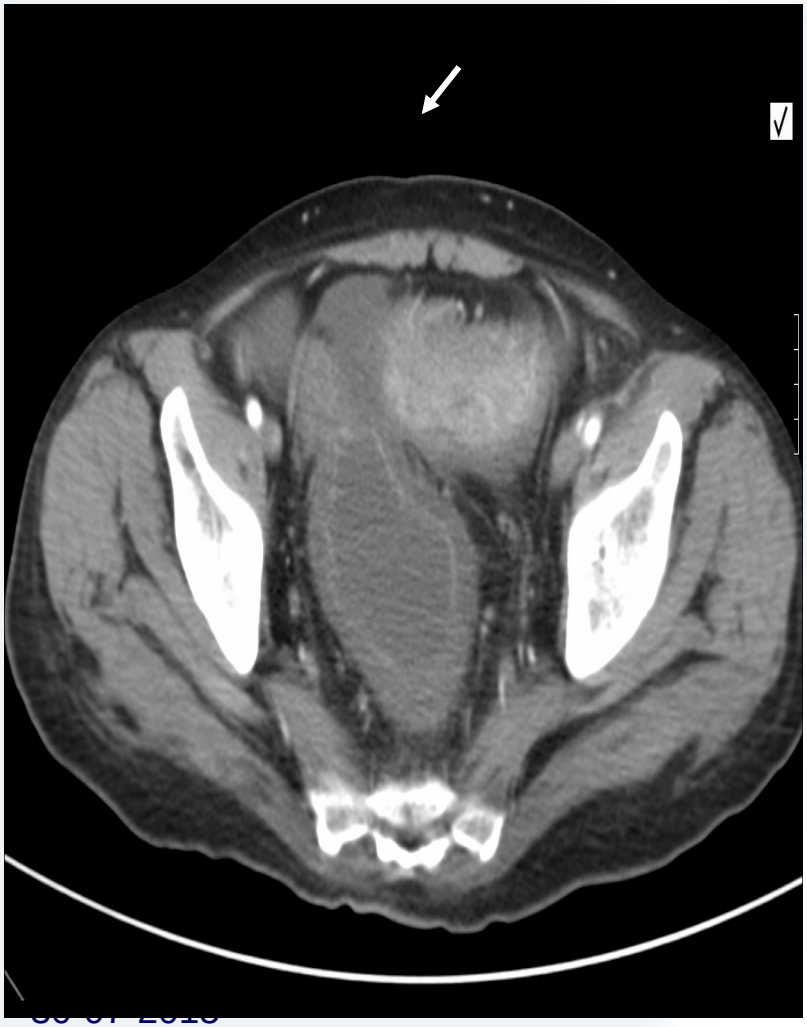
Endoscopy

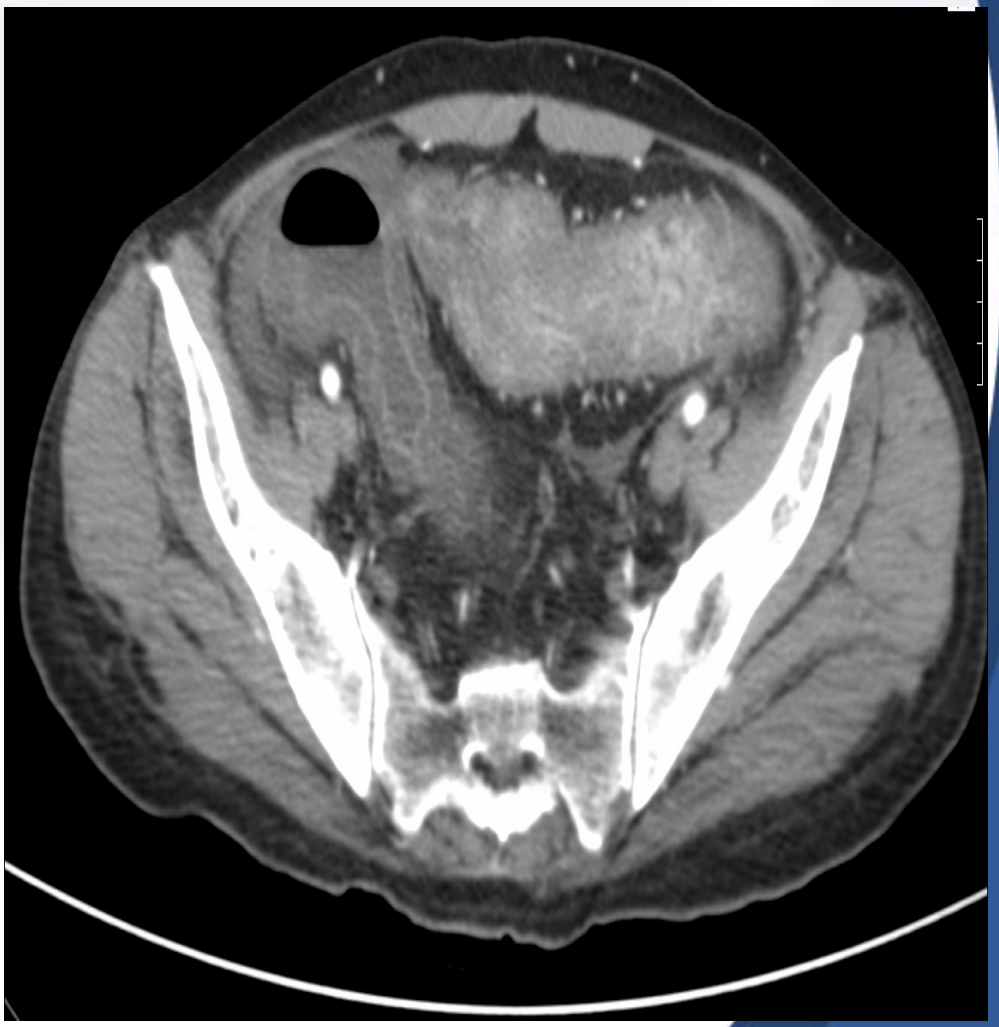
- Sigmoidoscopy with minimal air insufflation





Ulcerative colitis with acute exacerbation





Colonoscopy and Barium studies

CONTRAINDICATED

Gastroenterol Clin N Am 32 (2003) 1269–1288

Differential Diagnosis

- ✓R/o Enteric infections

  Get patient's stool analyzed for salmonella, shigella, campylobacter, Escherichia coli 0157:H7, ova and parasites, and Clostridium difficile.

- ✓CMV should be excluded by serology and rectal biopsy

Cooper HS Gastroenterology 1977;72:1253–6.

Treatment

- ✓ I/V fluids
- ✓ Electrolytes Replacement
- ✓ Blood transfusion for severe anemia
- ✓ Avoid anti-motility drugs
- ✓ I/V Steroids (Hydrocortisone 300-400 mg/d)

+/- ASA and Antibiotics

Hyde GM, Jewell DP. Aliment Pharmacol Ther 1997;11:419.

Choices available in Steroid Refractory Severe UC

- Medical Rescue therapy
  - Cyclosporine
  - Infliximab
- Surgical
  - Proctocolectomy

Infliximab

- Placebo 14/21 }
- INF 5mg/kg 7/24 } 3 mnths

- Data from the Scandinavian controlled trial, indicates that even a single dose infliximab protects against colectomy at 2 years

Gastroenterology 2007;132-146

Gastroenterology 2005;128:1805-11

Indian J Gastroenterol (January–February 2014) 33(1):31–34
DOI 10.1007/s12664-013-0372-8

ORIGINAL ARTICLE

Infliximab in patients with severe steroid-refractory ulcerative colitis: Indian experience

Ajit Sood · Vandana Midha · Suresh Sharma · Neena Sood · Manu Bansal · Amandeep Thara · Pankaj Khanna

In a recent retrospective study from our institution of 28 patients ,Infliximab achieved clinical response in 24 patients(85.6%) of Severe steroid refractory UC by week 8 and hence avoided urgent colectomy and in 2 years follow up 9/16(56%) did not require colectomy

Cyclosporine

- Data from a single centre controlled trial in 73 patients indicate that **2 mg/kg/day IV cyclosporine is as effective as surgery** for severe attacks of ulcerative colitis

- When results from controlled and non-controlled trials are pooled **76% to 85% of patients will respond to IV cyclosporine and avoid colectomy in the short term**.

CGH 2006:4-760-5

Van et al, Gastroenterology 2003;125:1025e31..

DMC Data

Cyclosporine in the treatment of severe steroid refractory ulcerative colitis: a retrospective analysis of 24 cases.

DMCH data showed that surgery can be avoided in two-thirds of patients with steroid refractory severe UC. drug toxicity and mortality were of significance

Indian J Gastroenterol. 2008 Nov-Dec;27(6):232-5

UNITED EUROPEAN GASTROENTEROLOGY ueg journal

Original Article

United European Gastroenterology Journal
2014, Vol. 2(2) 108–112

DOI: 10.1177/2050640614520865
ueg.sagepub.com
SAGE

Long-term outcome of cyclosporin rescue therapy in acute, steroid-refractory severe ulcerative colitis

Tamás Molnár, Klaudia Farkas, Zoltán Szepes, Ferenc Nagy, Mónika Szűcs, Tibor Nyári, Anita Bálint and Tibor Wittmann

- Recent data suggests that longer the cyclosporin is used , more possible it is to avoid colectomy .

United European Gastroenterology Journal 2014, Vol. 2(2) 108–112

Infliximab Vs Cyclosporine

Int J Colorectal Dis (2013) 28:287–293
DOI 10.1007/s00384-012-1602-8

REVIEW

Infliximab versus cyclosporine as rescue therapy in acute severe steroid-refractory ulcerative colitis: a systematic review and meta-analysis

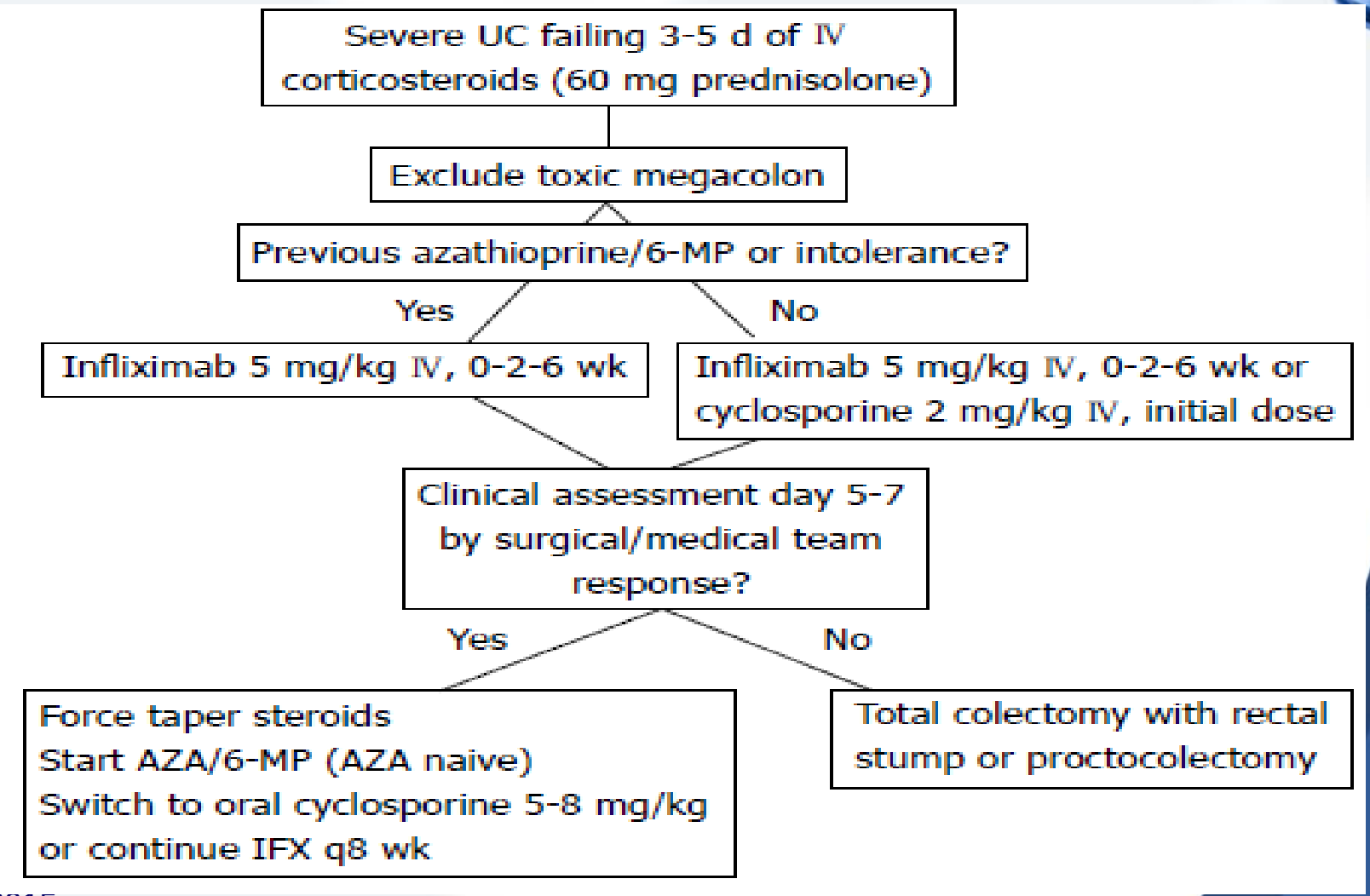
Kah Hoong Chang · John P. Burke · J. Calvin Coffey

Comparable at 3 and 12 mnth in colectomy rates , adverse drug reactions and Post-operative complications.

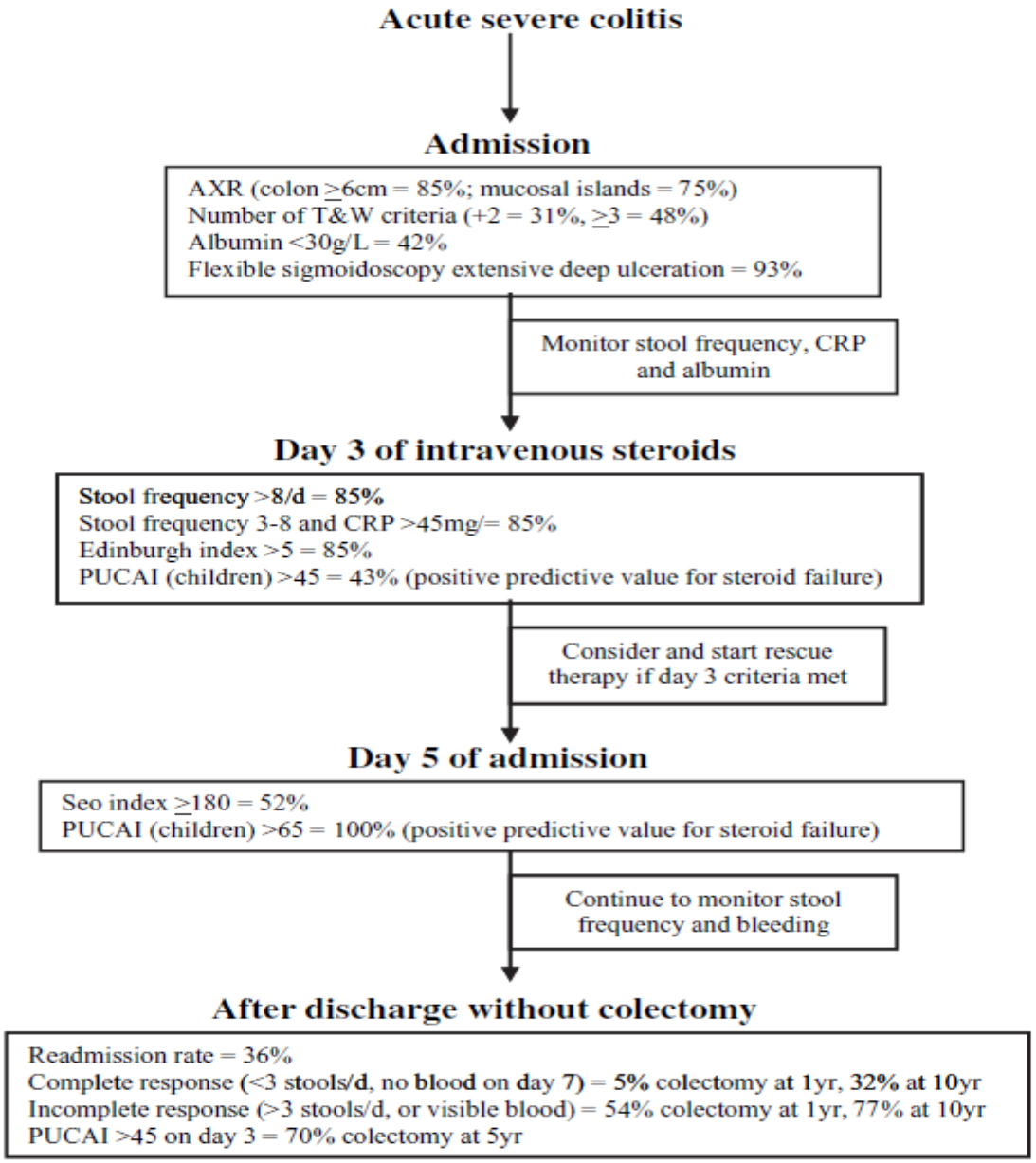
	Cyclosporine-A	Infliximab
Dosing	–IV: 2–4 mg/kg/day, 5 mg/kg orally –Blood level monitoring	IV 5 mg/kg week 0–2–6 and Q 8 weeks maintenance
Efficacy	Evidence from RCT[7 8]	Evidence from RCT[17]
Onset of action	Rapid (4 days)	Rapid
Complications	– Serious infections – Anaphylactic reaction (IV) – Seizures – Nephrotoxicity	– Serious infections – Anaphylactic reaction
Long-term options	Bridge to purine analogue	Induction and maintenance

Gut 2011;**60**:130–133. doi:10.1136/gut.2009.192765

Treatment algorithm for the management of severe steroid refractory ulcerative colitis



Gut 2011;**60**:130—133. doi:10.1136/gut.2009.192765



Gut January 2011 Vol 60 No 1

CLINICAL REVIEW

Toxic Megacolon

Daniel M. Autenrieth, MD, and Daniel C. Baumgart, MD, PhD

- Total or segmental nonobstructive colonic dilatation with systemic toxicity.
- Incidence 1- 5 %

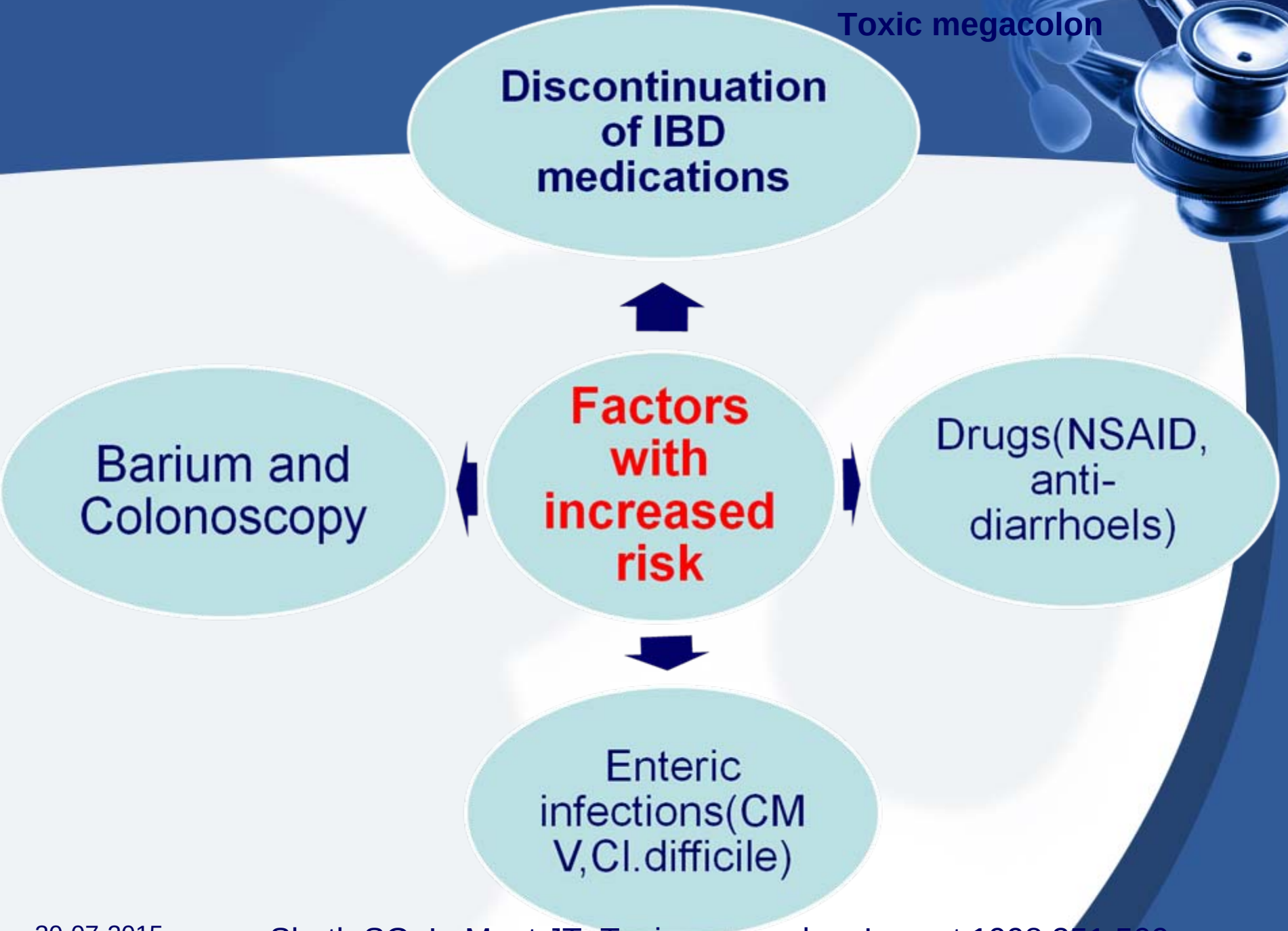
In a prospective study toxic megacolon was reported in 7.9% of patients admitted with UC.

- Mortality rates declined to 0-2 % from 27 % in 1976

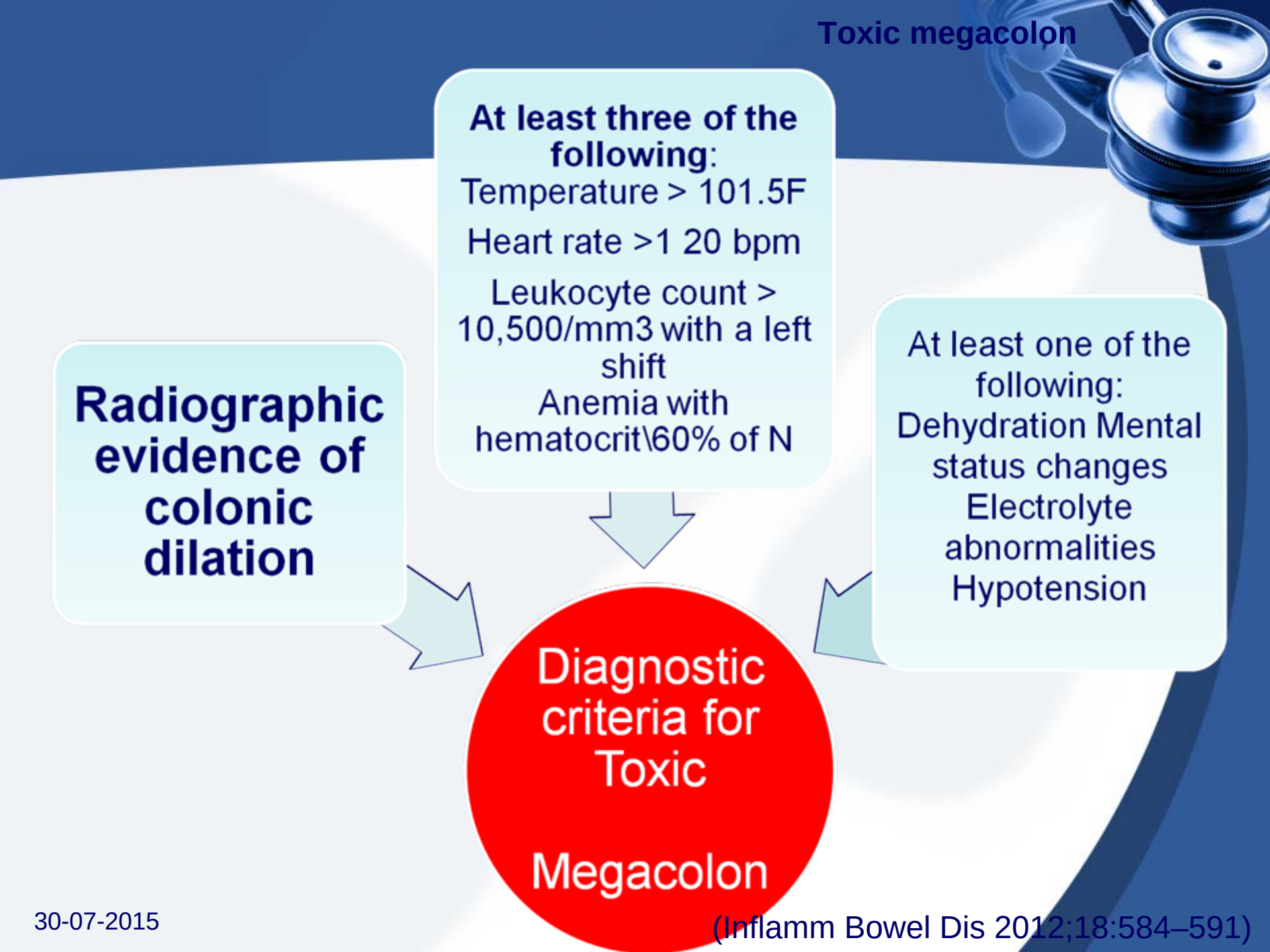
(Inflamm Bowel Dis 2012;18:584–591)

- ***Patients with IBD are at highest risk of developing toxic megacolon at an early stage of disease: up to 30% of patients present within 3 months of diagnosis***

Sheth SG, LaMont JT. Toxic megacolon. Lancet. 1998;351:509–513.

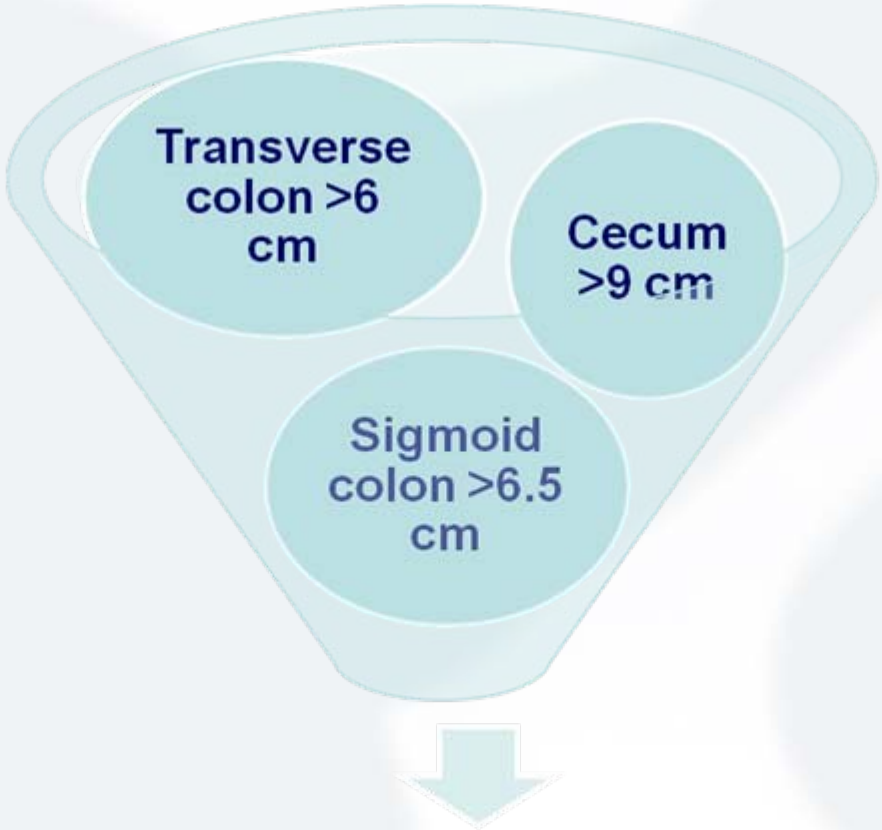


Sheth SG, LaMont JT. Toxic megacolon. Lancet 1998;351:509



(Inflamm Bowel Dis 2012;18:584–591)

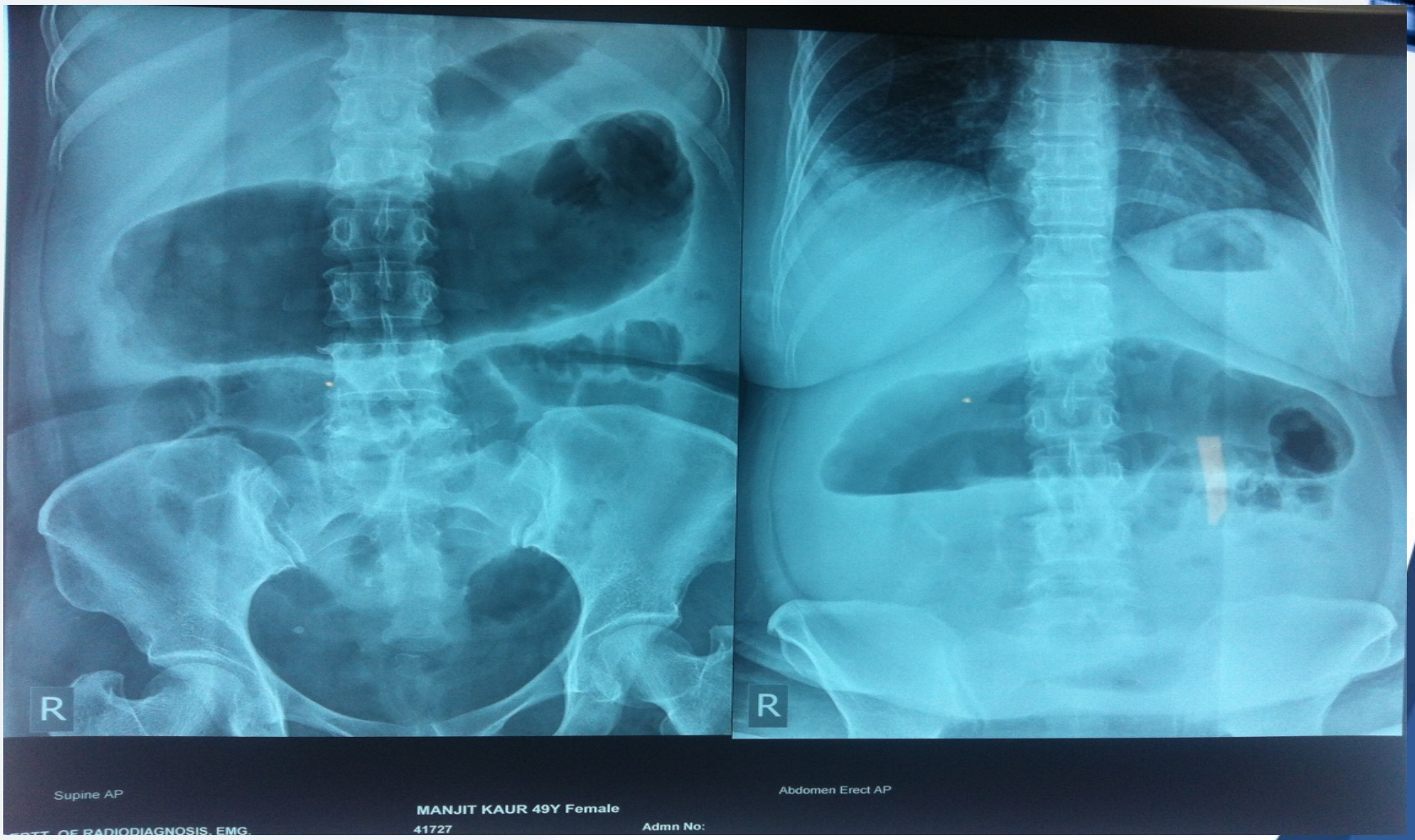
Colonic dialatation



Megacolon

(Inflamm Bowel Dis 2012;18:584–591)

Abdominal X-ray



Labs:

- Anemia
- Increased TLC with left ward shift
- Hypokalemia,Hypophosphatemia
- Hypocalcemia,hypomagnesemia
- Hypoalbuminemia
- Increased ESR,CRP

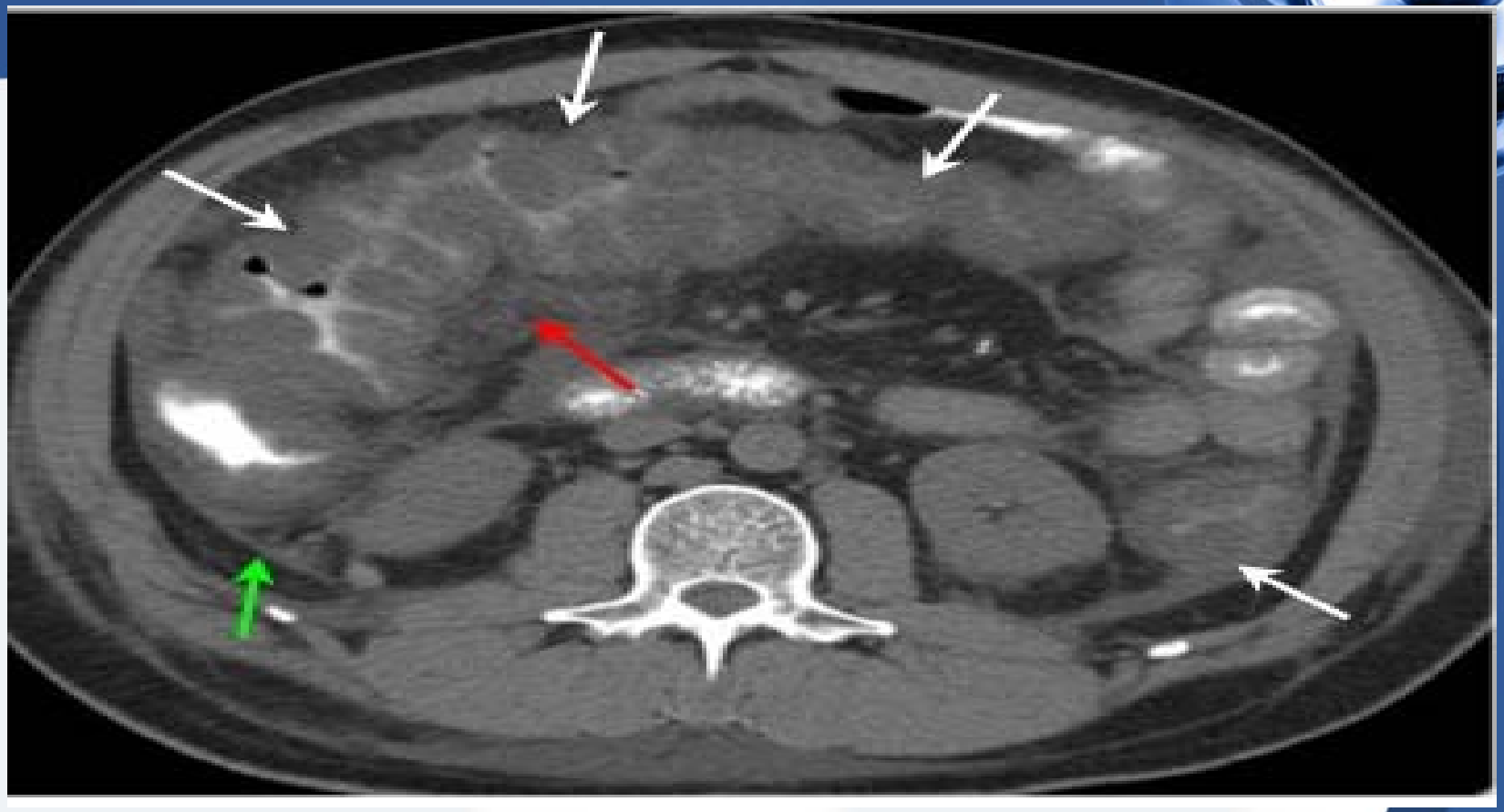
- Enteric infection should be ruled out

- ***In one series, cytomegalovirus was found in the resected colon of 6 out of 46 patients with UC and of the six who had cytomegalovirus, five had a toxic megacolon***

Orloff J, Saito R, Lasky S, et al Am J Gastroenterol 1989;84:794–7.

Imaging

Toxic megacolon



I. **Diffuse colonic thickening**
II. **Accordion Sign(thickened haustra with alternating bands of high and low density)**

I. **Target Sign**
II. **Peri-colic stranding**

Clin Imaging. 2001;25:349–354 Imbriaco M, Balthazar EJ. Toxic megacolon

Management

Medical management

- Correct Electrolytes,dehydration and Anemia
- Avoid Anti-motility drugs
- Bowel Rest
- Repositioning techniques
- Prophlaxis of Deep Venous thrombosis

(Inflamm Bowel Dis 2012;18:584–591)

Role of Steroids

- Hydrocortisone 400 mg/day or Methylprednisolone 60 mg/day for 5 days is the recommended regimen
- No benefit in higher dose or extension of therapy.

- Failure rate of intravenous steroids in patients with severe colitis is 20%–40%

Inflamm Bowel Dis 2012;18:584–591

Other Therapies

- No data support a benefit of oral aminosalicylates.

- ***Though used by some in the setting of severe UC, there are no controlled studies investigating the use of cyclosporin A or the monoclonal antibody infliximab in toxic megacolon.***

(Inflamm Bowel Dis 2012;18:584–591)

Studies

Surgery

Grant showed that 47% of patientswith severe UC undergo surgical resection even after initially successful medical treatment

In a study by Katzka et al 19 patients treated conservatively with steroids and antibiotic improved clinically with75% did not require colectomy in longterm

Medical

Inflamm Bowel Dis 2012;18:584–591

Definite Role of Surgery

- Mainstay of therapy in

➢ Medically unresponsive patients.
➢ Perforation
➢ Uncontrollable bleeding
➢ Clinical deterioration

- ***Colectomy with ileostomy followed by restorative proctocolectomy with IPAA anastomosis later***

Ausch C, Madoff RD, Gnant M, et al. Colorectal Dis. 2006;8:195–201

INTERNAL MEDICINE

CASE REPORT

Oral Tacrolimus for Megacolon in Patients with Severe Ulcerative Colitis

Ken Narabayashi, Takuya Inoue, Taisuke Sakanaka, Munetaka Iguchi, Kaori Fujiwara, Naoki Yorifuji, Kazuki Kakimoto, Sadaharu Nouda, Toshihiko Okada, Kumi Ishida, Yosuke Abe, Daisuke Masuda, Toshihisa Takeuchi, Shinya Fukunishi, Eiji Umegaki and Kazuhide Higuchi

(Intern Med 53: 1755-1758, 2014)

LGI bleed

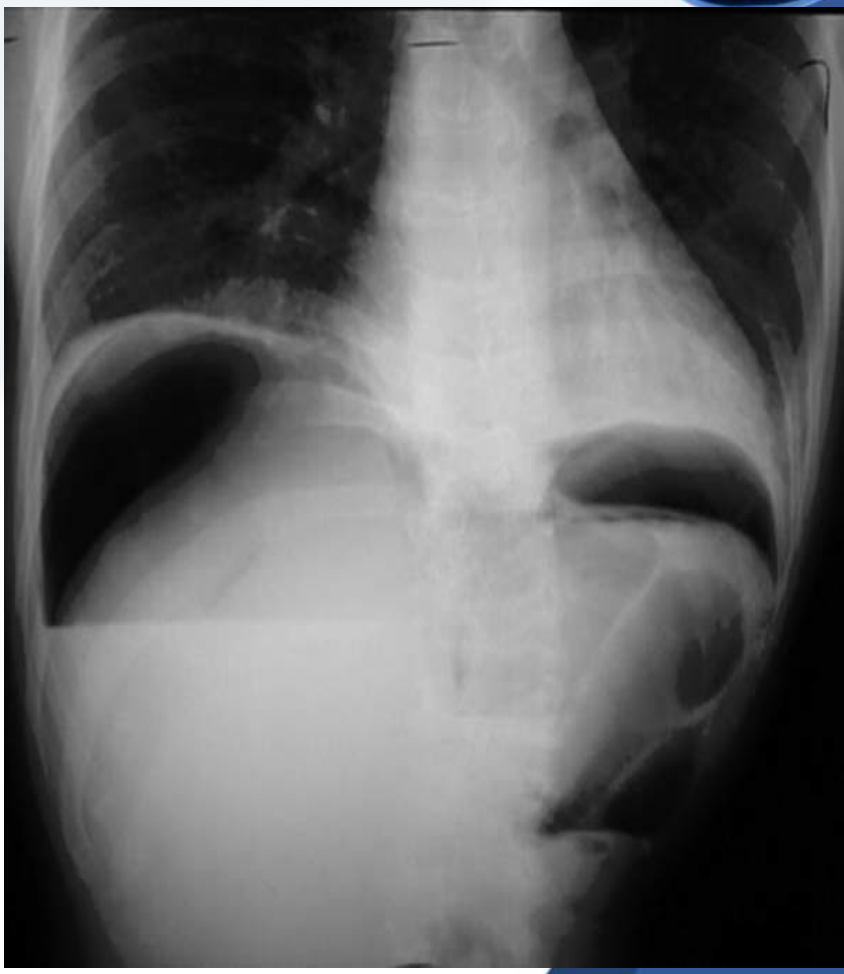
- Massive life threatening LGI bleed uncommon -6%
- Endoscopic management not possible due to diffuse nature of colonic inflammation
- Surgery usually curative for UC
- Colectomy significantly decreases the chance of rebleeding and has a better outcome than in those treated medically even for Crohns

Robert JR, Sachar DB, Greenstein J. Ann Surg 1991;213:207–11.

Perforation

- Rare – 1 %
- MC segment at risk – Sigmoid Colon
- Classical presentation of Peritonitis –Absent
- Hepatic Dullnes –

  CHECK DAILY IN UC
- Mortality >50 %



Sleisenger and Fordtran's Gastrointestinal and Liver Disease 2010

Perforation

Risk with Colonoscopy

Disease related

- Female sex
- Advance age
- Severe colitis
- Use of corticosteroids
- Presence of co-morbidites
- Stricture dilation

Technique related

- Lack of Proper training
- Poor coordination
- Excessive air insufflation and endoscopic looping
- Lack of well defined anatomy prior to stricture dilatation.
- Balloon inflated too rapidly for dialatation

Risk factors for perforation in Endoscopic dilation of Strictures

Study	Reported Risk Factors
Couckuyt (1995)[56]	Ileosigmoidal/ileorectal strictures, balloon size, anesthesia
Thomas-Gibson (2003)[61]	De novo strictures
Nomura (2006)[77]	Balloon size, de novo strictures
Singh (2005)[57]	Inflamed area, angulation, multiple dilations, passage of endoscope immediately after dilation
Ferlitsch (2006)[78]	Fistulae, passage of endoscope immediately after dilation
Foster (2008)[18]	Complex anastomotic strictures
Stienecker (2009)[81]	Multiple dilations
Shen (2011)[63]*	Multiple dilations, angulation

*Dilation of ileal pouch strictures.

Management

- **SURGERY**

IBD Emergencies

- ASSOCIATED WITH UC
- ASSOCIATED WITH CROHNS
- **EXTRA-INTESTINAL COMPLICATIONS**

Extra-Intestinal manisfestation

Thromboembolic

Deep vein thrombosis
Thrombophlebitis
Pulmonary embolus
Portal vein thrombosis or hepatic vein thrombosis

Cerebral vascular thrombosis

Carotid thromboembolism
Retinal venous thrombosis
Gonadal vein thrombosis
Mesenteric venous thrombosis

Ocular

Episcleritis

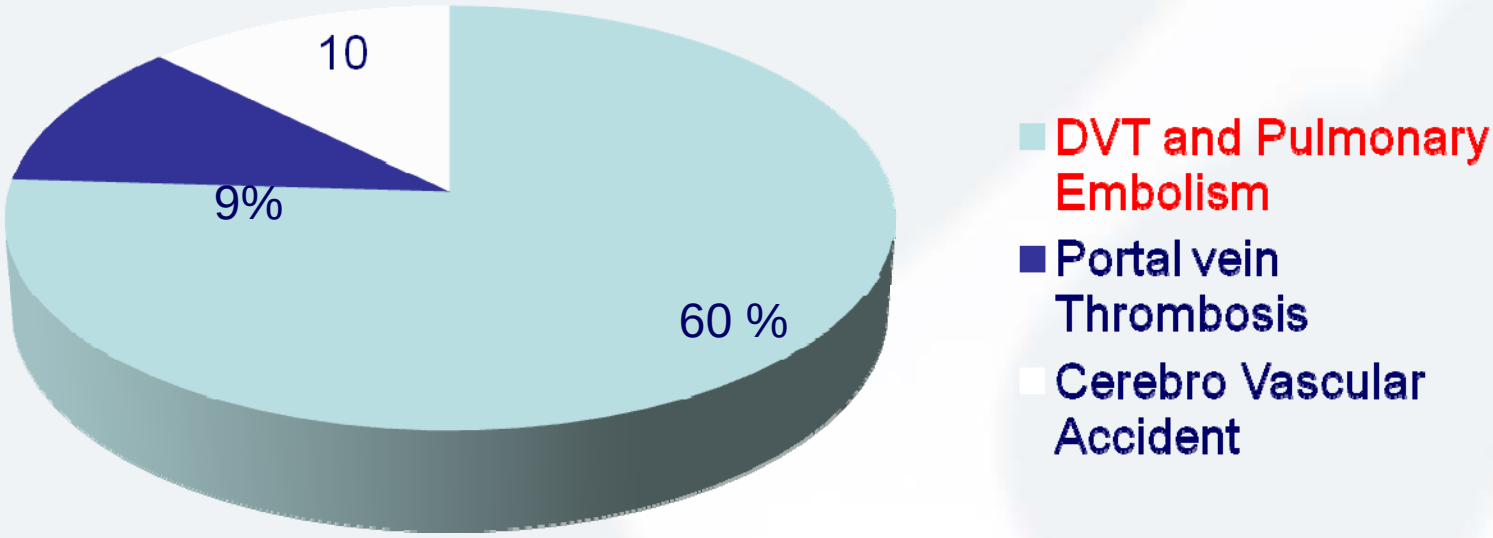
Uveitis (may lead to blindness)

Subcapsular cataracts (complication of corticosteroids)

Hepatobiliary

Primary sclerosing cholangitis
Pericholangitis
Cholelithiasis
Hepatitis

Incidence



Am J Gastroenterol 2011;106:713–718.

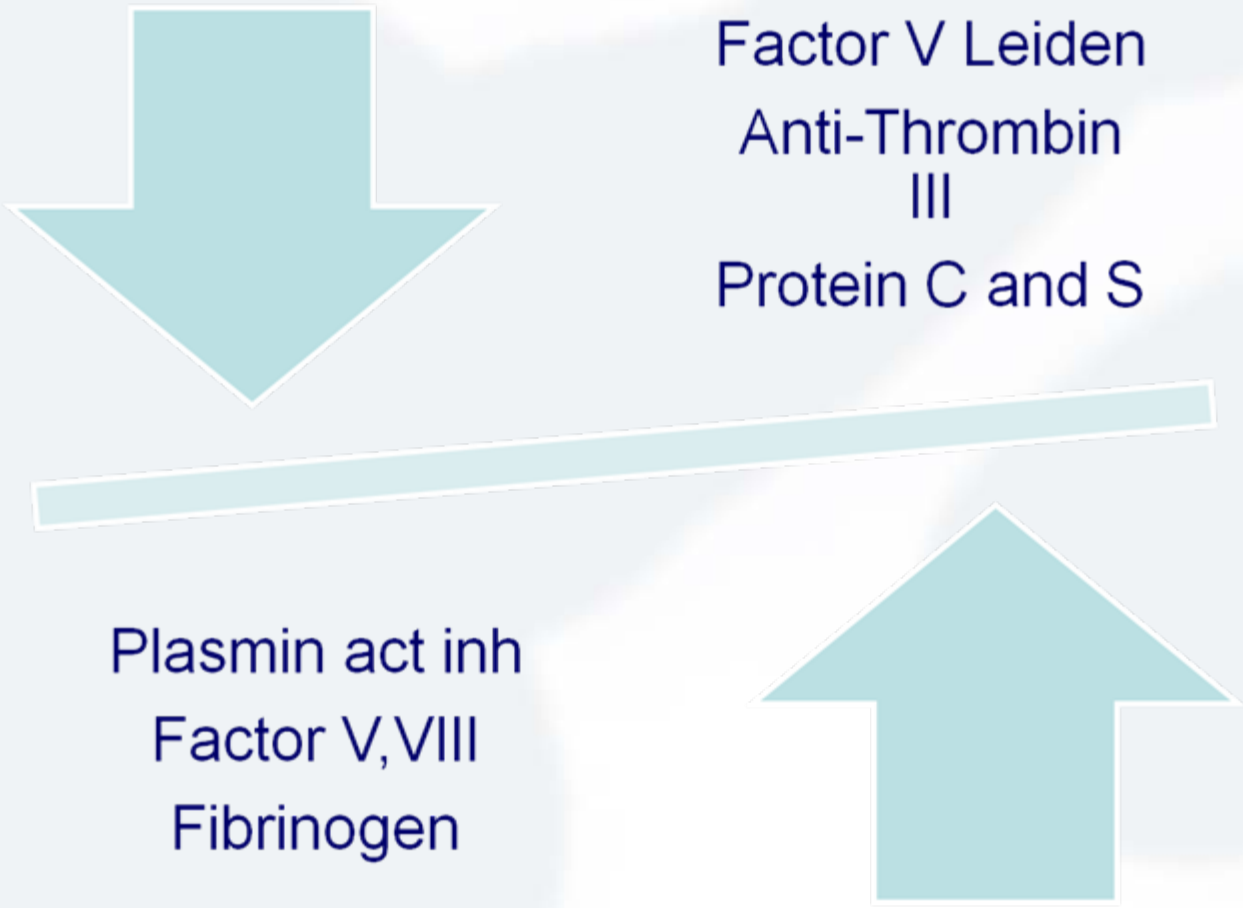
Thromboembolic Complication

The incidence for thrombotic complications in IBD has been reported as low as 1% to 6% in one study and as high as 39% in a postmortem study

One study found that 60% of patients with active inflammatory disease had a hypercoagulable state compared with 15% with inactive disease .

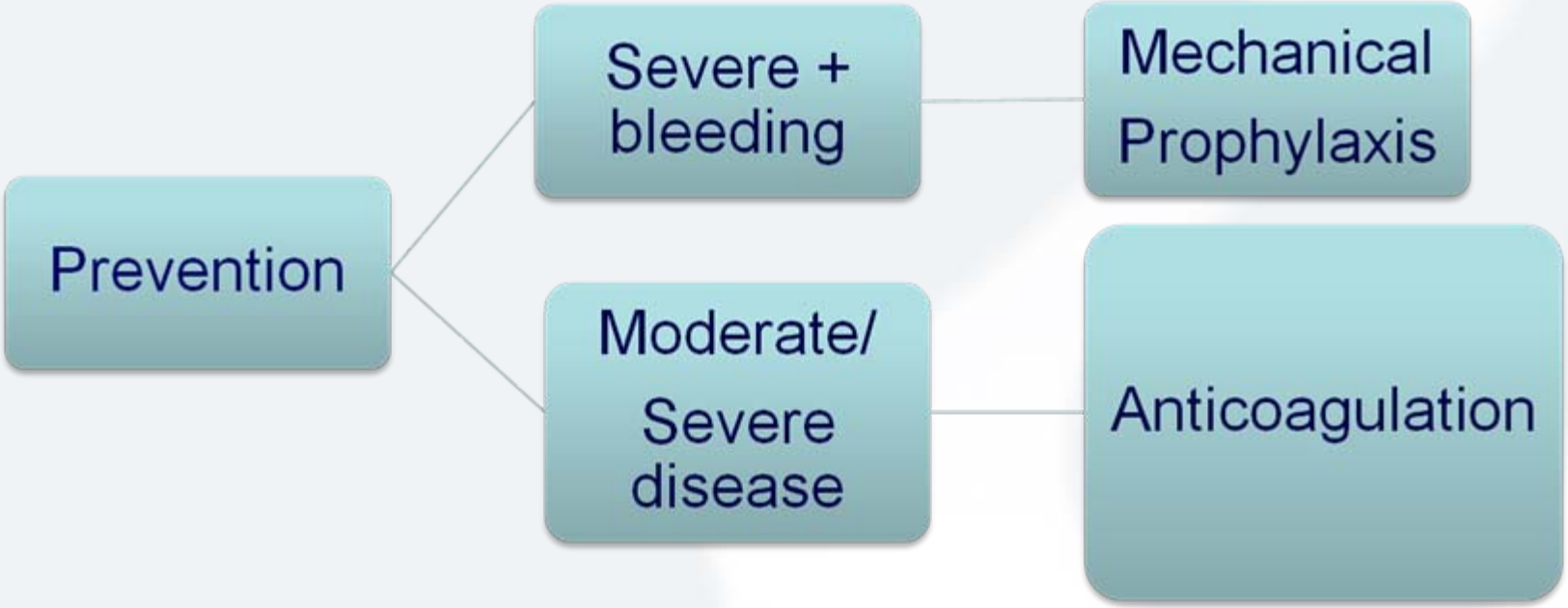
Grainge MJ Lancet 2010 ;375:657-663
Lim A Gastroenterology 2011 ;140(suppl);S428

Coagulation abnormalities



Solem CA, Loftus EV, Tremaine WJ, et al. Am J Gastroenterol 2004;99:97–101.

PREVENTION



Gastroenterology 2014;46:835-848

Guidelines

VTE –

Active disease-Anticoagulation to continue until IBD in remission for atleast 3 mnths

Inactive disease-

Life long Anti-coagulation

Gastroenterology 2014;46:835-848

Recurrent pulmonary emboli from thrombosis of the ileofemoral veins and massive colonic bleeding during anticoagulation require vena caval interruption with or without colectomy.

Panes J, Esteve M, Cabre E, et al Gastroenterology 2000;119:903–8.

IBD Complications

- ASSOCIATED WITH UC
- **ASSOCIATED WITH CROHNS**
- EXTRA-INTESTINAL COMPLICATIONS

Complications Associated with Crohns

- Abscess-Intra-abdominal and Peri-anal
- Intestinal Obstruction
- Fistula
- Fissure
- Bile Acid Diarrhoea
- Bacterial Overgrowth
- Malabsorption and Malnutrition

Complications Associated with Crohns

- Abscess-Intra-abdominal and Peri-anal
- Intestinal Obstruction
- Fistula
- Fissure
- Bile Acid Diarrhoea
- Bacterial Overgrowth
- Malabsorption and Malnutrition

Abscess

- Abdominal or perirectal abscesses associated with perforating or fistulizing crohns disease

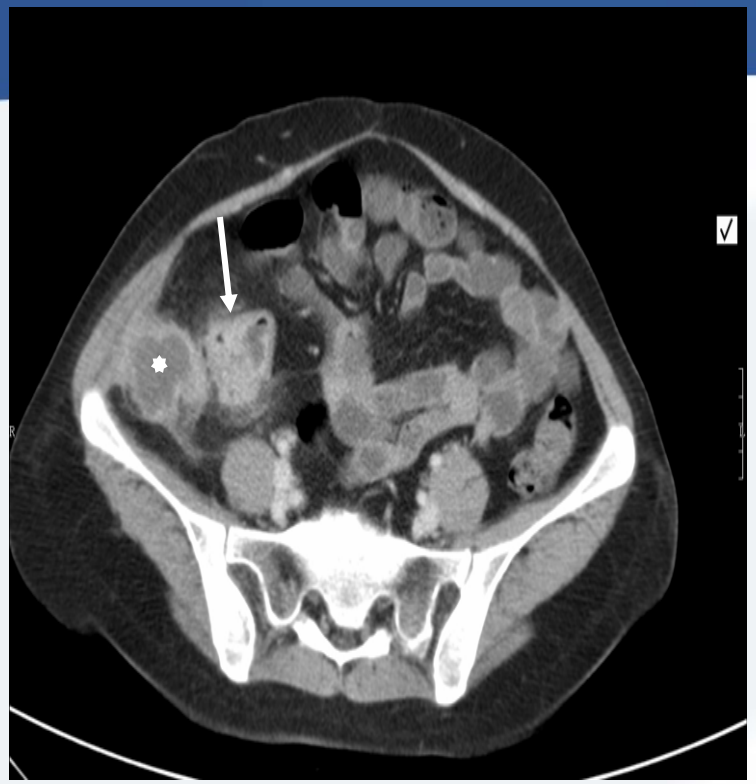
- Prevelance -25%

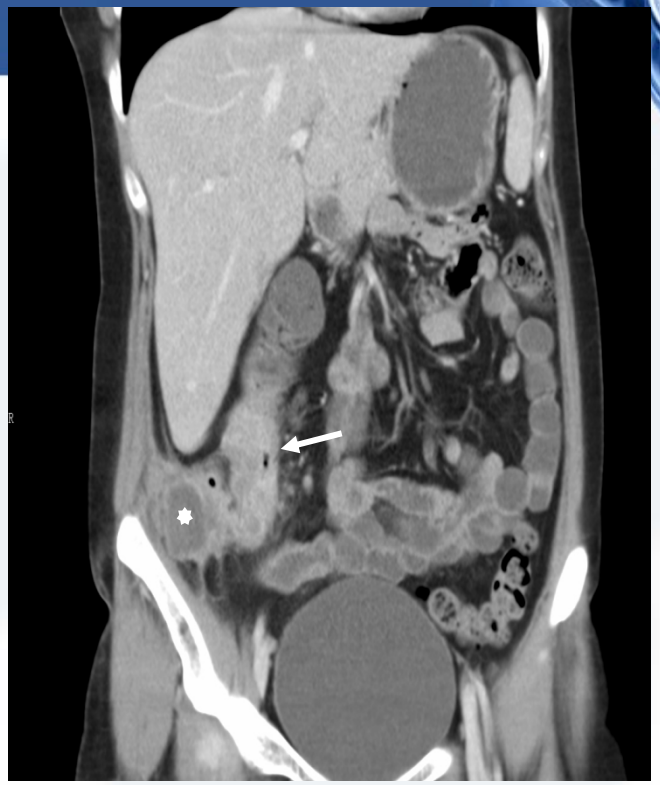
Ribeiro MB, Greenstein AJ, Yamazaki Y, et al.
Gastroenterol Clin N Am 32 (2003) 1269–1288

	Intra abdominal	Peri anal
Symptoms and Signs	Abdominal pain and Fever Toxic appearance Tenderness on abdominal Examination	Fever Severe anal pain Erythema and Induration of the skin overlying the perianal space
Diagnosis	Elevated WBC Abdominal and pelvic CT scan (deep pelvic cuts if iliopsoas abscess Suspected	Digital rectal Examination Pelvic CT scan or MRI Endorectal Ultrasonography Examination under anesthesia
Treatment	Antibiotics Percutaneous drainage by US or CT guidance Surgery: primary resection and anastomosis if abscess amenable to radiologic drainage, otherwise surgical drainage, resection, and temporary ileostomy	Antibiotics-Ciprofloxacin and metronidazole Surgery: Local incision and drainage Examination under anesthesia with catheter or seton placement Medical therapy for fistula once abscess drained: Azathioprine/ 6MP Infliximab

Gastroenterol Clin N Am 32 (2003) 1269–1288

Crohn’s Disease with perforation and abscess formation





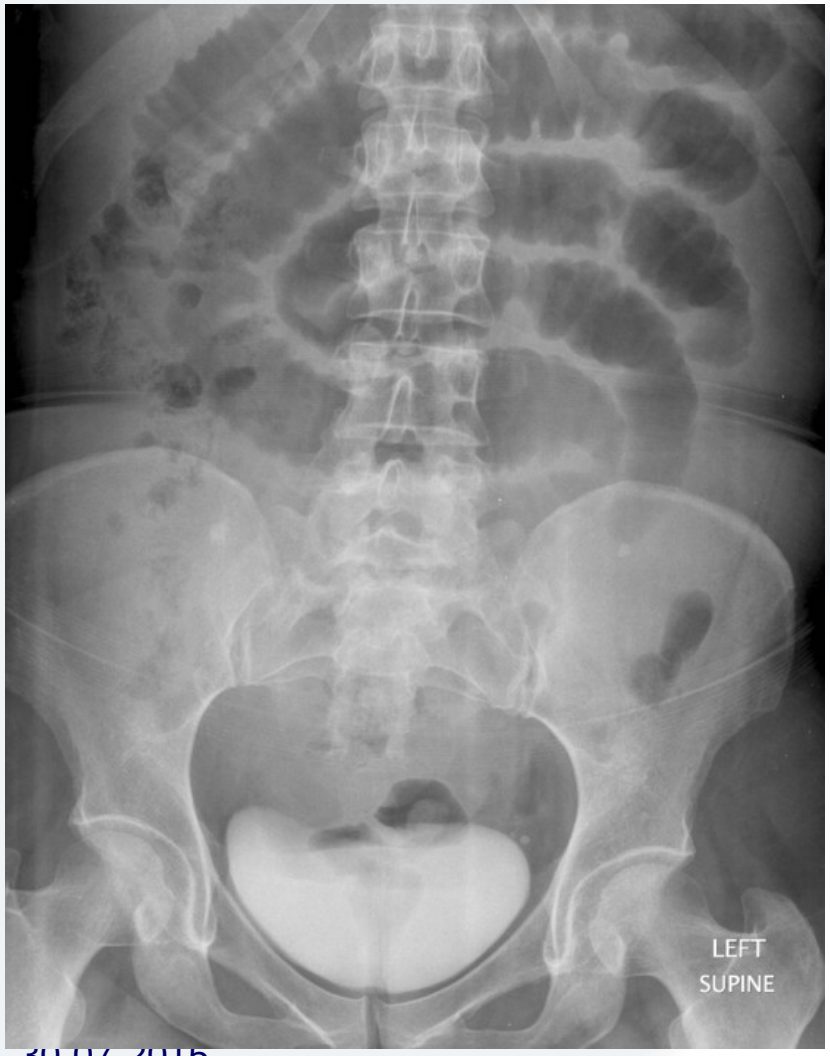
Axial and coronal contrast enhanced CT images reveal : Enhancing wall thickening involving the caecum and ascending colon (white arrow) with associated peripherally enhancing collection (asterisk) adjacent to it in the right iliac fossa secondary to perforation. Histopathology : Crohn’s disease.

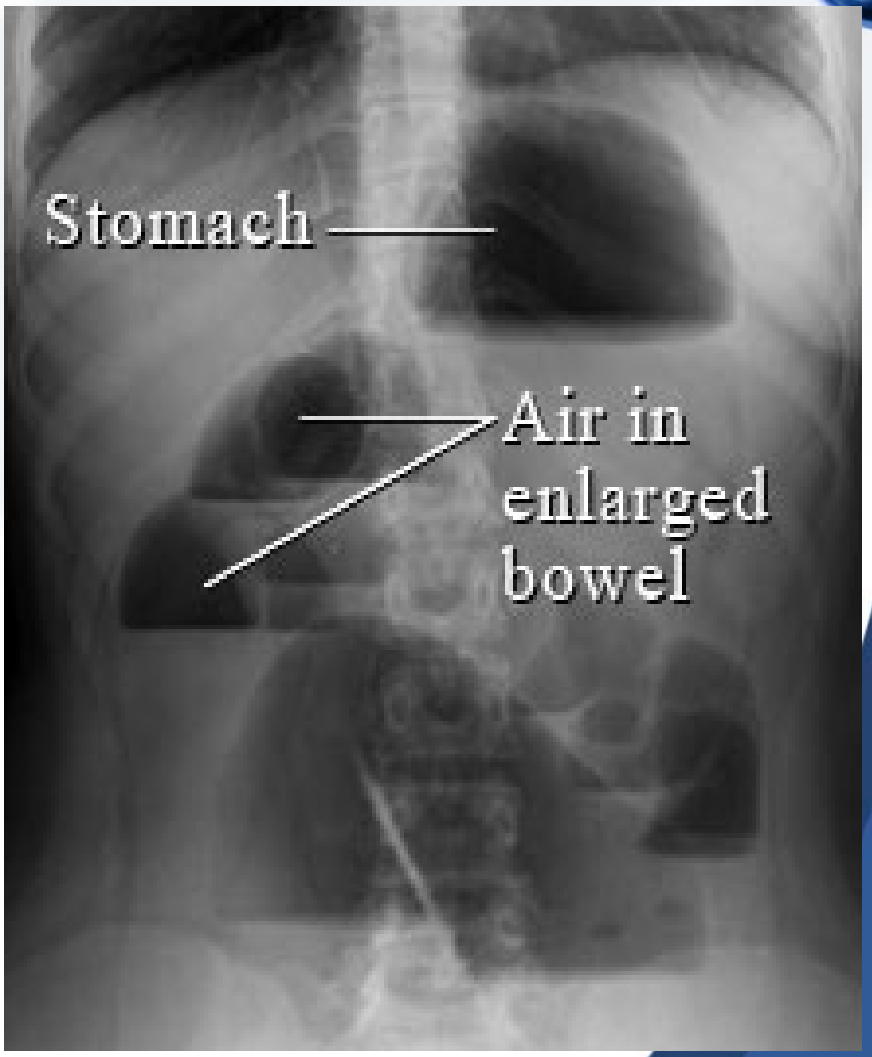
Instestinal Obstruction

- Inflammatory or fibro-stenotic narrowing of the intestine
- Most common location is Terminal ileum
- Gastroduodenal involvement is less common.

Nugent FW, RichmondM, Park SK. Gut 1977;18:115–20.

Radiology





Small Bowel Obstruction

Clinical Features

Abdominal pain
Bloating and distension
Borborygmi
Nausea ,vomiting
Weight loss

Diagnosis

Abdominal X-ray

Small bowel dialatation
Air fluid levels

BMFT

Luminal Stricture
Small bowel dilation

Management

Bowel rest
Nasogastric Decompression
I/V fluids
Anti-inflammatory Medication

Fibrostenotic Obstruction

Surgical Resection
Stricturoplasty
Endoscopic Balloon Dialation

Gastrointest Endosc Clin N Am 2002;12:621–33.

Gastroduodenal Obstruction

Clinical features

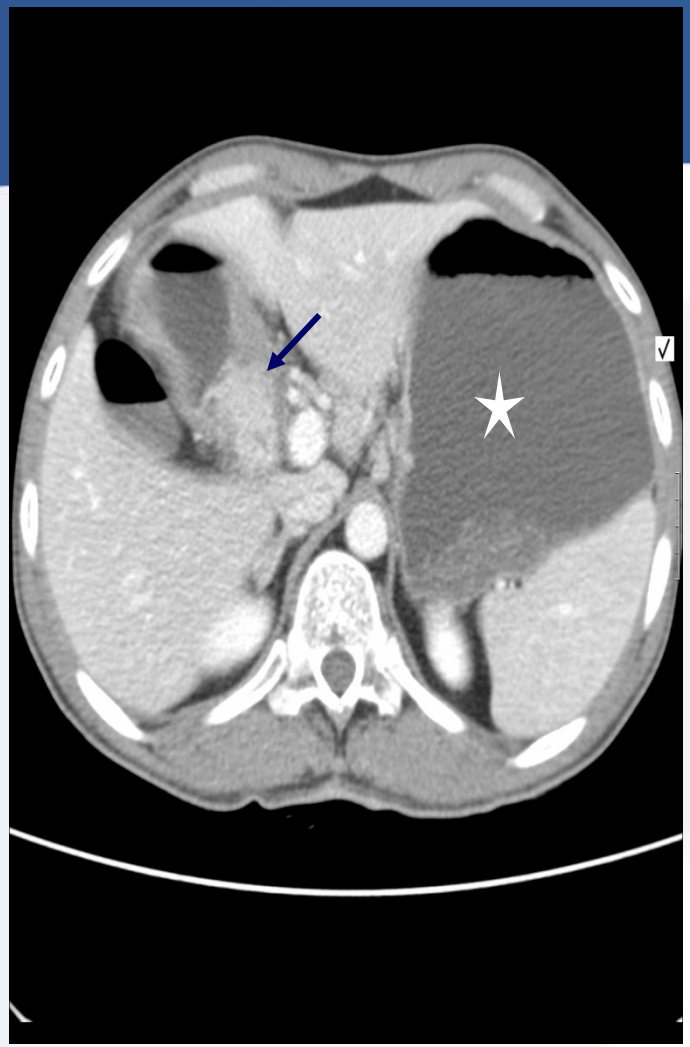
- Early satiety
- Vomiting After meals
- Abdominal pain

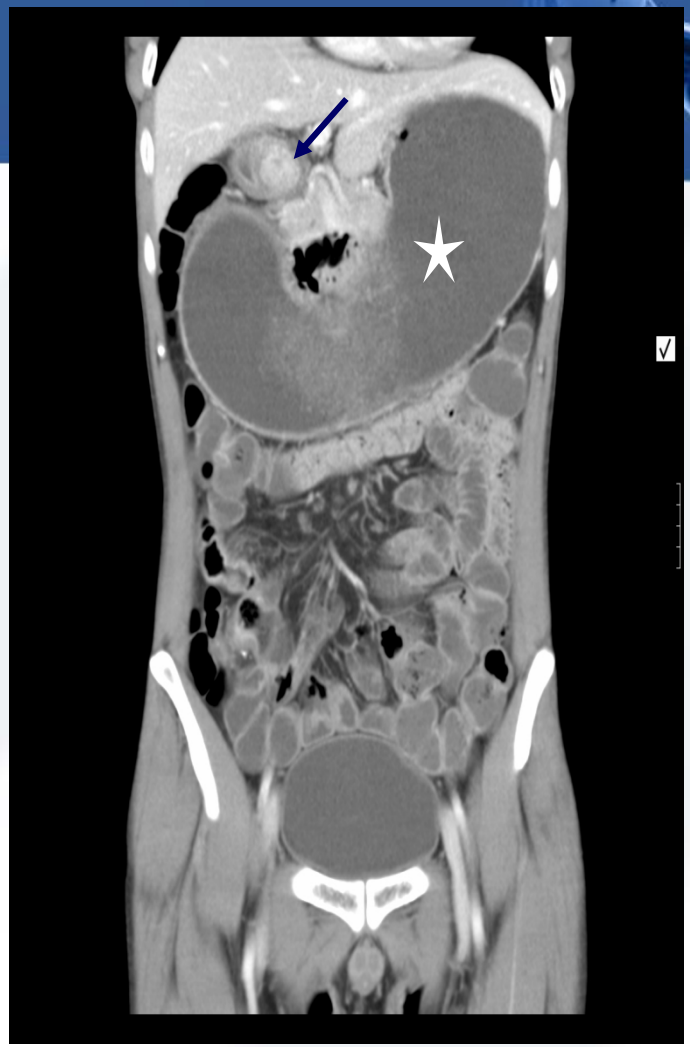
Diagnosis

- Dialated Stomach on X-ray Abdomen
- UGI endoscopy showing pyloric obstruction

Gastrointest Endosc Clin N Am 2002;12:621–33.

Crohn’s disease with gastric outlet obstruction.





37 year old male with features of gstric outlet obstruction : Axial and Coronal CT images reveal dilated stomach (asterisk) with narrowed , thickened pylorus and first part of duodenum. Histopathology : Crohn’s disease.

Management

- Endoscopic balloon dialatation of Pyloric Stricture
- PPI
- Treatment of Active Crohns
- Surgery for refractory disease

Gastrointest Endosc Clin N Am 2002;12:621–33

Ocular

Episcleritis

3-4 %of IBD pts

Mild burning and Itching with no pain

Treat IBD Topical Steroids may help

Uveitis

0.5-3 % Ass with HLA-B27

Pain, photophobia, headache visual blurring

Topical /Systemic Steroids

Hamilton, Ontario: BC Decker; 2001. p. 275–7.

Cataract

One study reported that cataracts developed in 25% of patients receiving 15 mg of prednisone for 1 year

Levine SB, Leopold IH WB Saunders; 1975.

IBD patients who have received chronic corticosteroids should have routine (annual) slit lamp examinations.

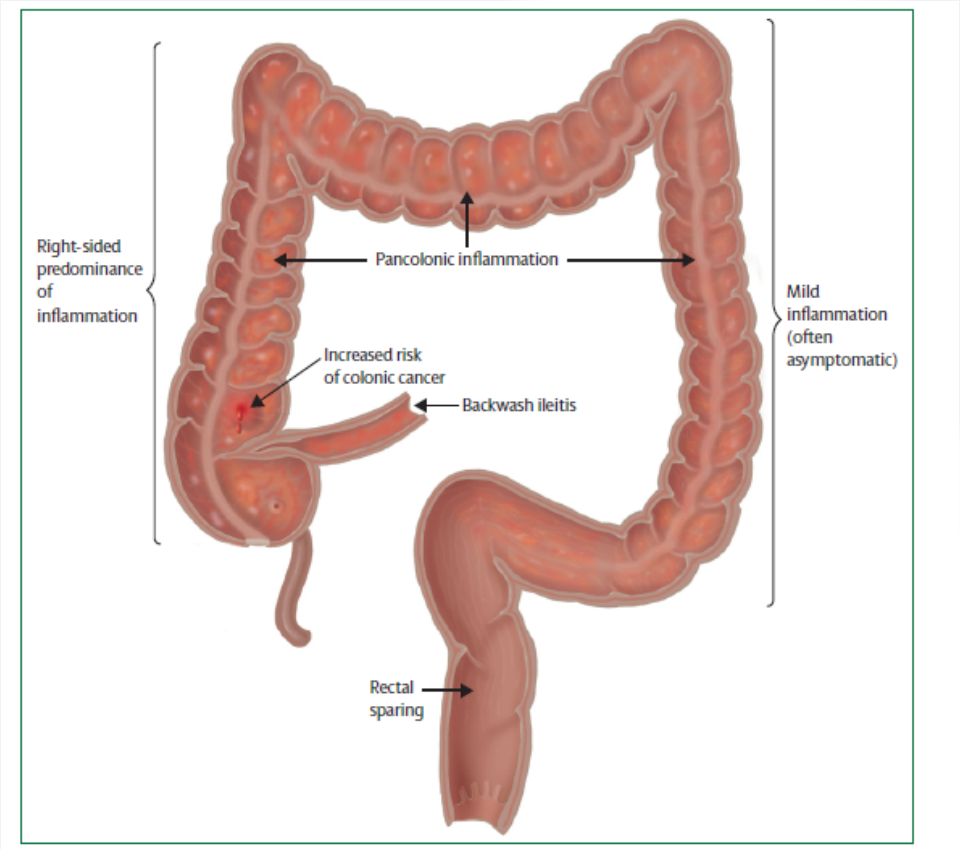
Gastroenterol Clin N Am 32 (2003) 1269–1288

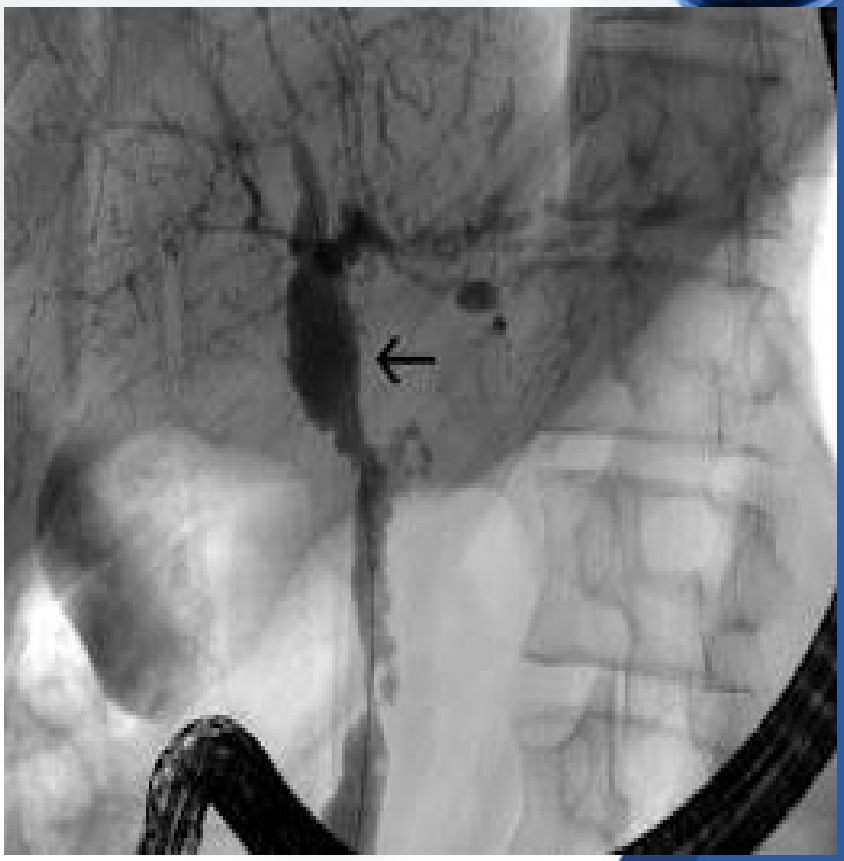
IBD and PSC

- PSC has been diagnosed in between 2.4% and 7.5% of patients with UC and was found in 3.4% among a large group of 262 CD patients
- **Conversely prevalence of IBD in PSC :60%-80%.**
- The most frequent type of IBD in PSC is
  - -UC(48%-86%)
  - -Up to 13% have Crohn disease (CD) which usually involves the colon.

Semin Liver Dis 1991;11:31- 39.

Characteristics of IBD unique to PSC





Gut 2005;54:91- 96

PSC and IBD

- ✓ *The course of PSC is variable and does not parallel the natural course of IBD .*
- ✓ *The median time from diagnosis of PSC to either death or liver transplantation is approximately 12 years.*
- ✓ *Patients who are asymptomatic and have normal serum bilirubin at diagnosis have a longer survival time than symptomatic patients.*

Gastroenterology 1989;96:790–4.

Complication

- M.C Emergent Complication :Bacterial cholangitis
- Etiology: Choledocholithiasis or Biliary stricture
- Management

➢ ***Broad –Spectrum Antibiotics***

➢ ***Endoscopic balloon Dialation /Stenting of dominant stricture***

➢ ***For small stones /debris Sphincterotomy is sufficient***

Gut 2005;54:91- 96

- THKS….

Diagnostic criteria for Toxic Megacolon

1. **Radiographic evidence of colonic dilation**

2. **At least three of the following**:

- Temperature > 101.5F
- Heart rate > 20 bpm
- Leukocyte count > 10,500/mm3 with a left shift
- Anemia with hematocrit\60% of N

3. At least one of the following:

- Dehydration
- Mental status changes
- Electrolyte abnormalities
- Hypotension

Severity of disease

- **True love and Witts criteria**
- Mild
  - <4 stools/day with or without only small amounts of blood
  - No fever
  - No tachycardia
  - Mild anemia
  - ESR< 30 mm/HR
- Moderate
  - Intermediate between mild and severe
- Severe
  - > 6 stools/day, with blood
  - Fever >37.5° C
  - Heart rate > 90 beats/min
  - Anemia with Hb< 75 % of normal
  - ESR> 3O mm/hr

UCDAI

- **Stool Frequency**
  - 0 Normal
  - 1 1-2 stools/day > normal
  - 2 3-4 stools/day > normal
  - 3 > 4 stools/day > normal
- **Rectal bleeding**
  - 0 None
  - 1 Streaks of blood
  - 2 Obvious blood
  - 3 Mostly blood

Mucosal Appearance

- 0 Normal
- 1 Mild friability
- 2 Moderate friability
- 3 Exudation , spontaneous bleeding

Physician Global assessment

- 0 Normal
- 1 Mild
- 2 Moderate
- 3 Severe

>10-Severe disease

Infliximab VS Cyclosporine

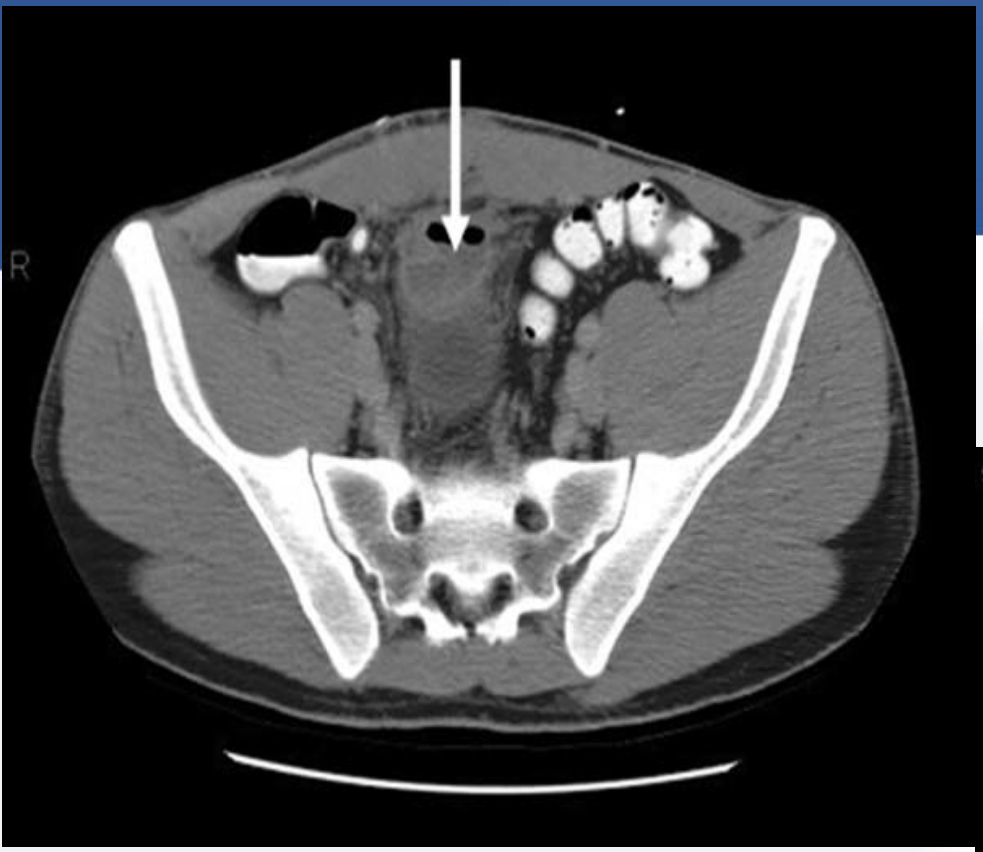
- Preliminary results from a randomized controlled trial that compared the effects of cyclosporine and infliximab in 110 patients showed no difference in short-term (7- and 90-day) efficacy.

J Crohns Colitis 2011;5:S8.

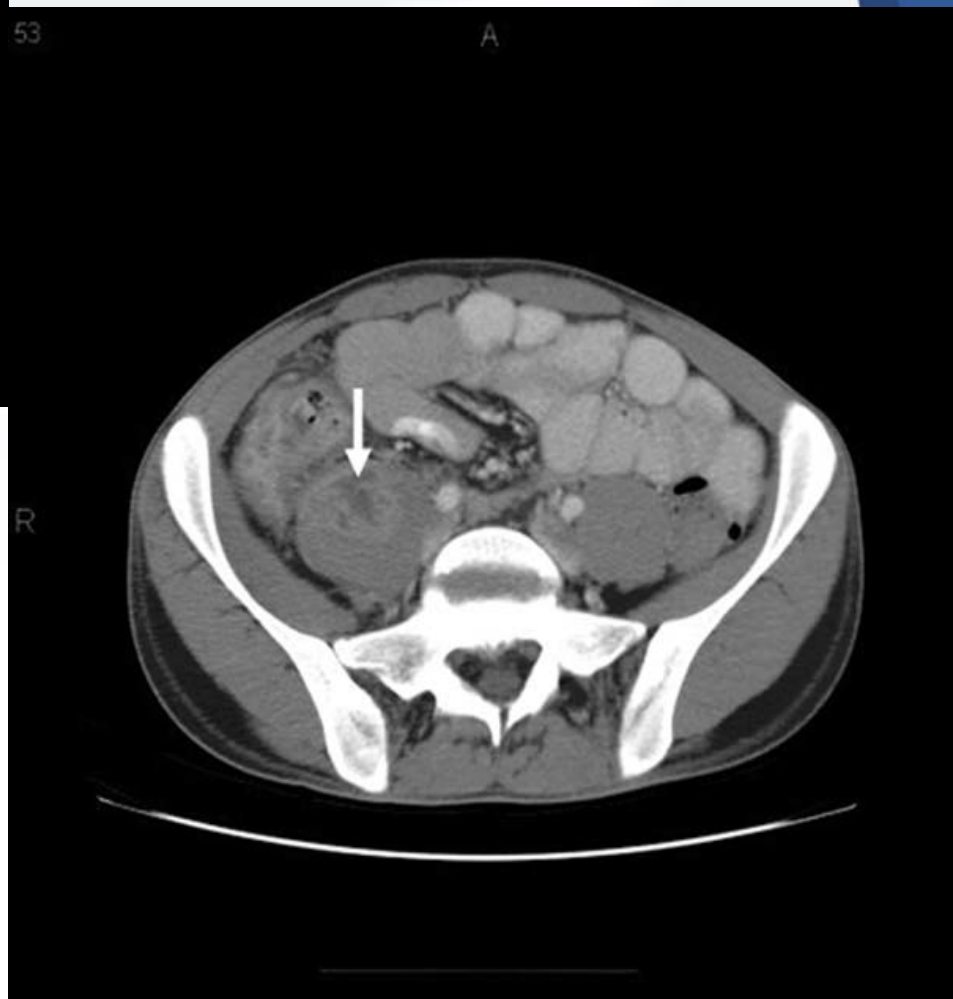
DMC DATA

- In a recent retrospective study from our institution of 28 patients ,Infliximab achieved clinical response in 24 patients(85.6%) of Severe steroid refractory UC by week 8 and hence avoided urgent colectomy and in 2 years follow 9/16(56%) did not require colectomy

Indian J Gastroenterol (January–February 2014) 33(1):31–34



Abscess emanating from diseased ileum



Ilipsoas Abscess