SIG

Digestive Health Malaysia Society
Educate • Engage • Empower

TREATMENT ALGORITHMS

for

Inflammatory Bowel Disease

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Treatment Algorithms for Inflammatory Bowel Disease by the Malaysian IBD SIG

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Introduction

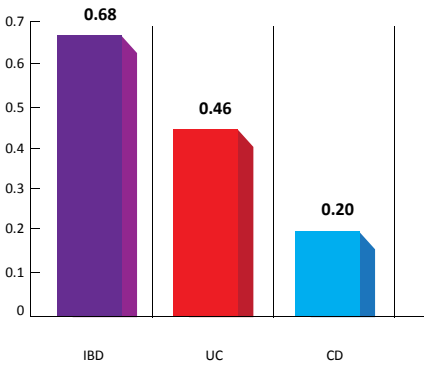
Inflammatory bowel disease (IBD), as its name implies is a chronic inflammatory disease of the gastrointestinal (GI) tract. IBD may be divided further into Crohn's disease (CD) and ulcerative colitis (UC). IBD is still a relatively rare disease in Malaysia, with a mean incidence of 0.69 per 100,000 population.[1] Nevertheless, studies have shown that there has been a steady increase in the incidence of IBD in Malaysia over the last few decades; this has been especially apparent within the last 10 years.[1,2] It is thus important to recognise and diagnose the disease early; the chronic GI inflammation and ulceration, if left unchecked, could lead to further complications that will significantly affect the patient's quality of life as well as incur higher health costs.

It is therefore crucial that immediately after diagnosis, a baseline assessment is made to ascertain the patient's disease status. In general, patients are treated using conventional medications first; biologic therapies and/or surgical intervention will only be introduced later if there is failure of initial treatments. However, for those with moderate to severe disease activity, or if there is presence of complications (e.g. strictures or fistulas) it would then be more prudent to choose a more aggressive treatment approach from the outset. The primary objective of treatment is to induce, and then maintain remission; if there is a disease flare this is then promptly addressed in order to induce remission again as soon as possible. Thus, there is a need to objectively treat-to-target; endpoints such as clinical, biochemical (including fecal calprotectin), endoscopic ("mucosal healing") and even histological parameters should be set at the onset of treatment and reassessed within a specific time frame. The STRIDE programme for example, sets out several endpoints to aim for in the treatment of CD and UC in order to assist in ensuring treatment efficacy.[3]

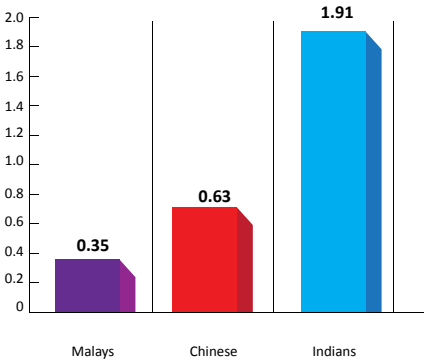
Nevertheless, there are limitations in the treatment of IBD in Malaysia. Firstly, recognition of the disease itself as well as identification of disease severity are key points that should be emphasised. Once diagnosed, appropriate treatment should be initiated. However, unlike Western countries the choices of medications for the treatment of IBD are limited and may be costly. Inappropriate use of corticosteroids for the treatment of disease flares for example may complicate matters; on the other hand, unfamiliarity with biologics restrict the use of this therapeutic modality to only a small number of clinicians. It is thus hoped that with the introduction of the IBD algorithm, clinicians in Malaysia would be more confident in diagnosing and managing this disease.

Incidence and Prevalence of IBD in Malaysia[1]

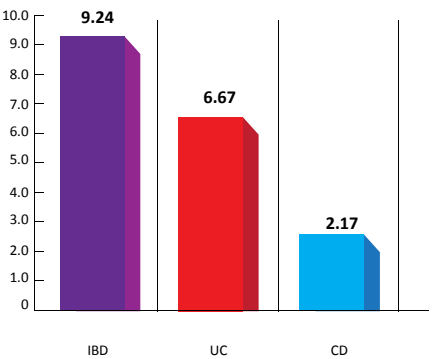
Incidence of IBD, UC and CD in Malaysia (per 100,000 persons)



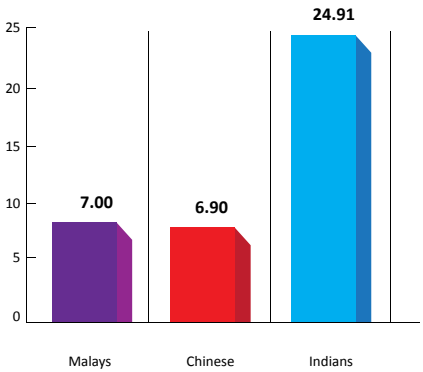
Incidence of IBD, UC and CD according to ethnic group (per 100,000 persons)



Prevalence of IBD, UC and CD in Malaysia (per 100,000 persons)



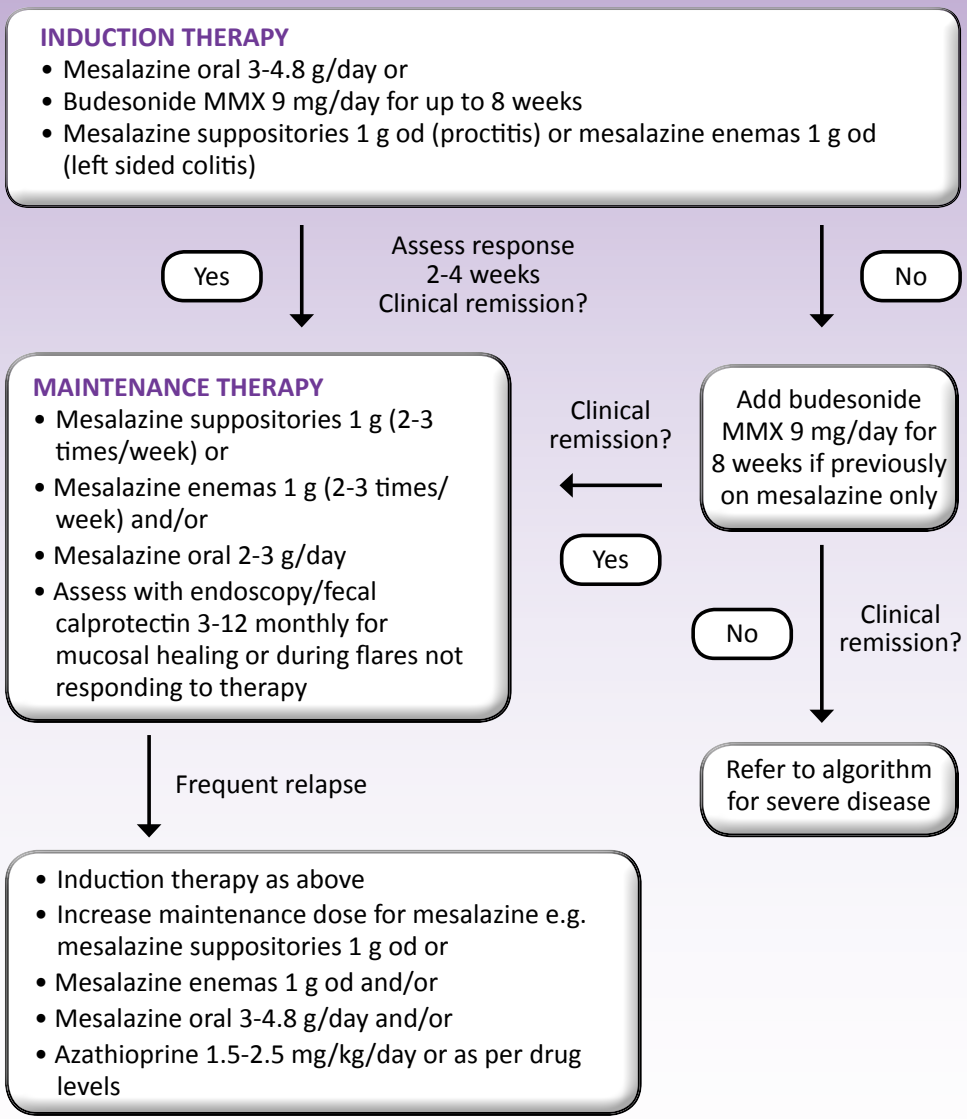
Prevalence of IBD, UC and CD according to ethnic group (per 100,000 persons)



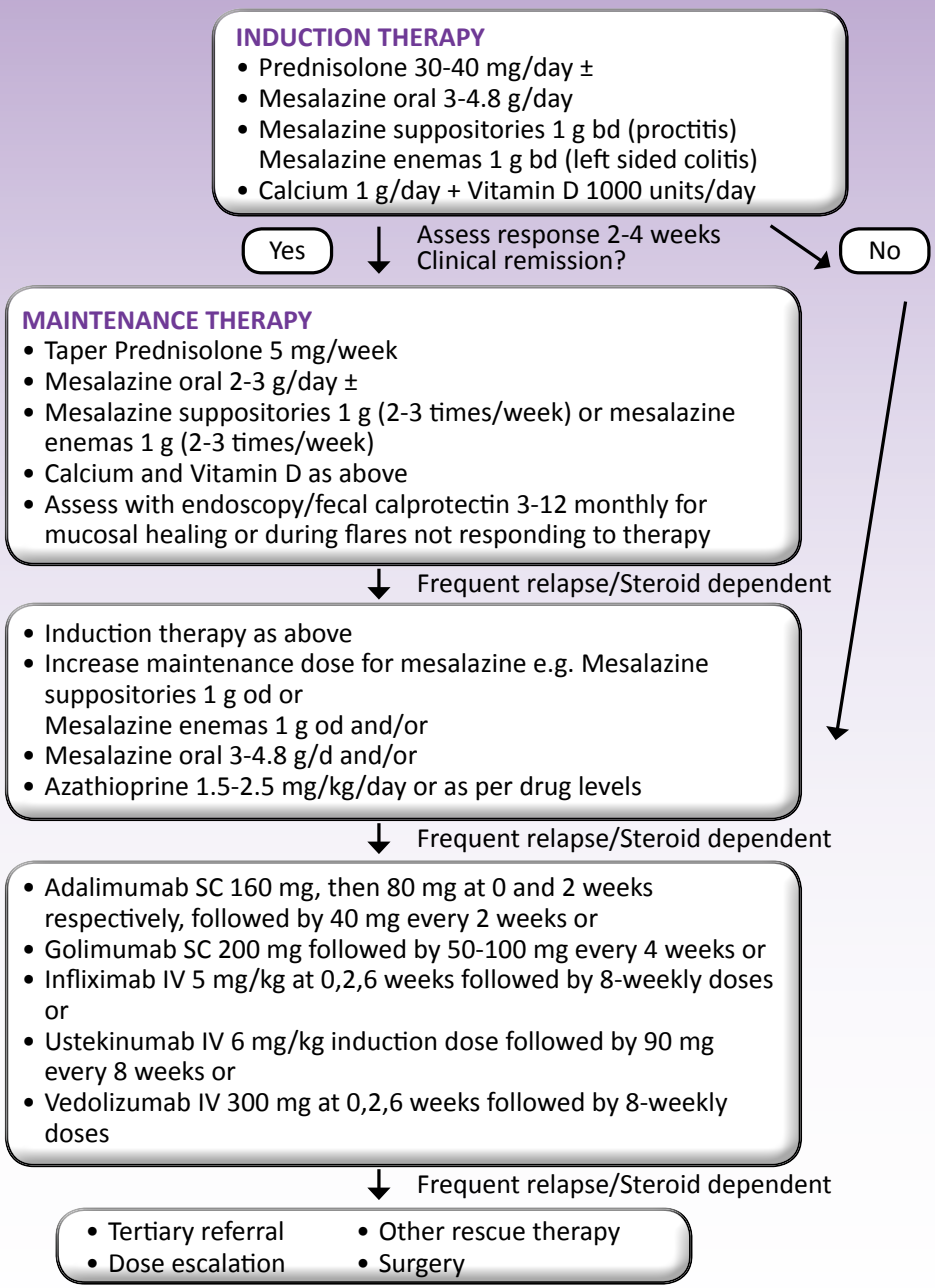
TREATMENT ALGORITHMS: ULCERATIVE COLITIS

Proctitis/Left Sided Colitis

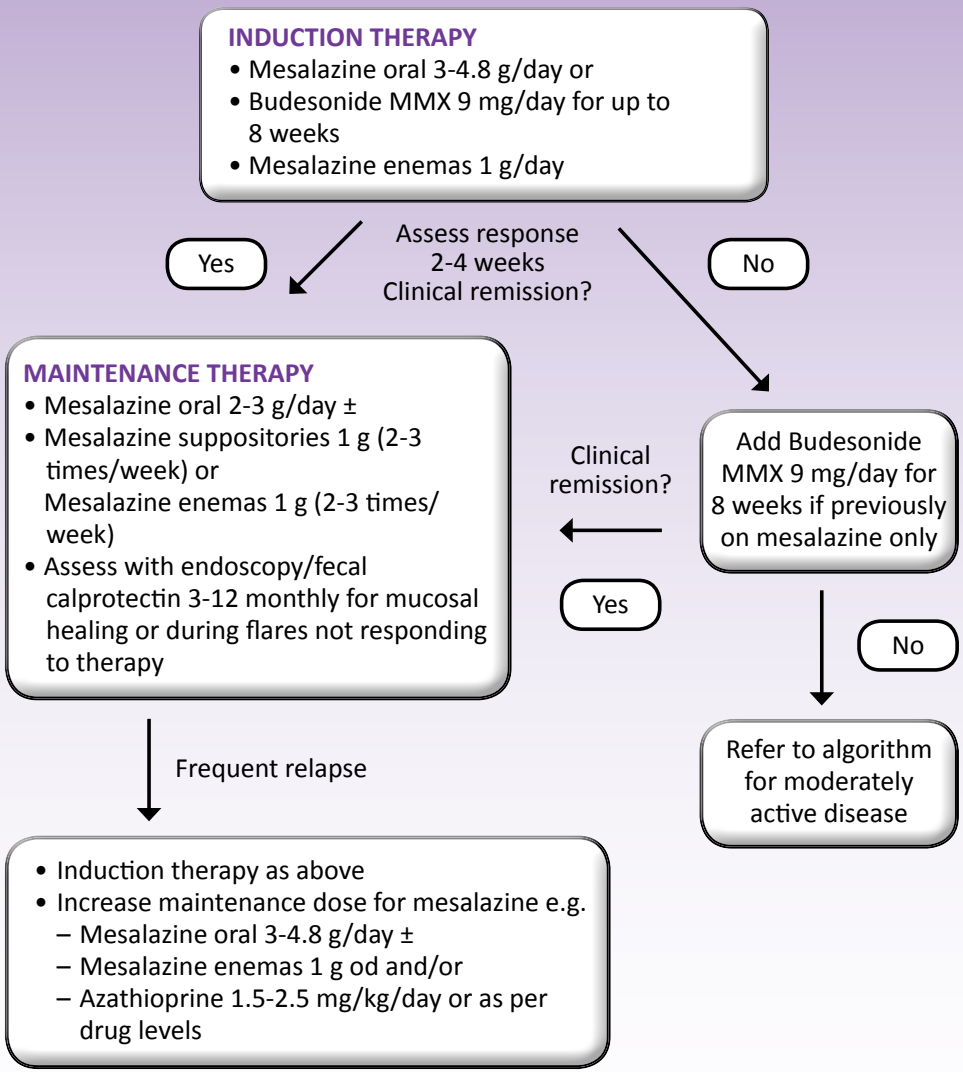
(mild to moderately active disease)



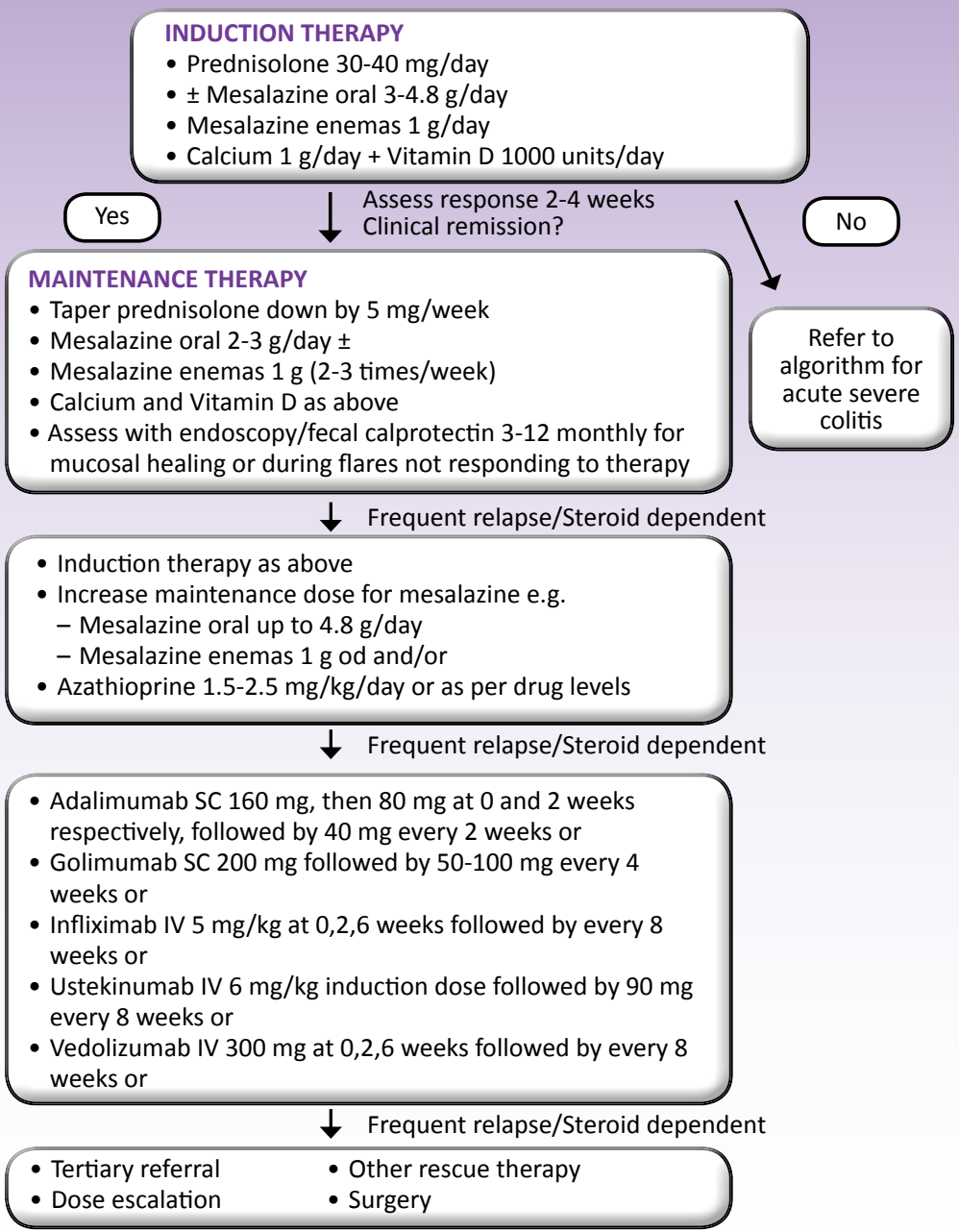
Proctitis / Left Sided Colitis *(severely active disease)*



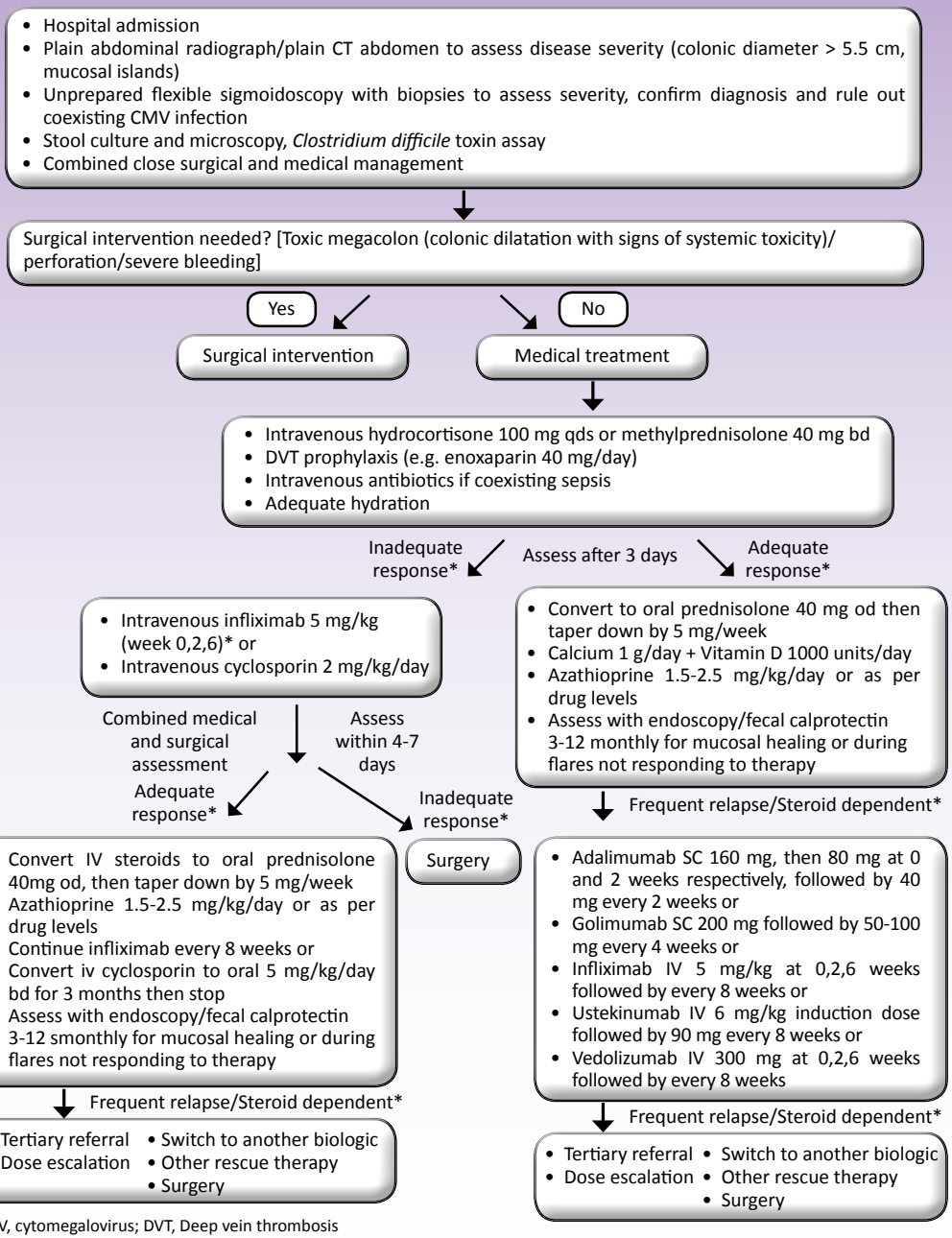
Extensive Colitis *(mildly active disease)*



Extensive Colitis *(moderate to severely active disease)*



Acute Severe Ulcerative Colitis

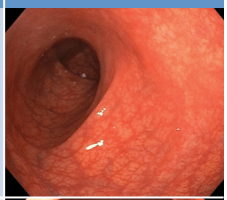
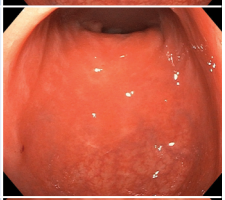
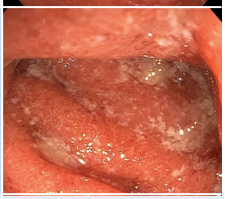


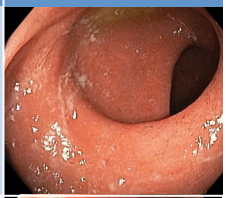
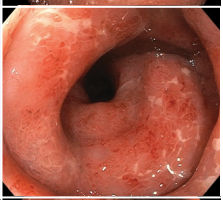
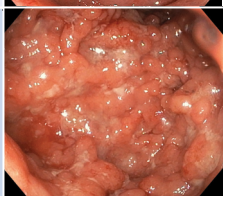
CMV, cytomegalovirus; DVT, Deep vein thrombosis

*Definition as per footnotes section (Page 16)

Truelove and Witts' Criteria[4]			
Variable	**Mild**	**Moderate**	**Severe**
Bloody stool	< 4	4-6	> 6
Pulse	< 90 bpm	≤ 90 bpm	> 90 bpm
Temperature	< 37.5 °C	≤ 37.8 °C	> 37.8 °C
Haemoglobin	> 11.5 g/dL	≥ 10.5 g/dL	< 10.5 g/dL
Erythrocyte sedimentation rate (ESR)	< 20 mm/h	≤ 30 mm/h	> 30 mm/h
C-Reactive Protein (CRP)	Normal	≤ 30 mg/dL	> 30 mg/dL

bpm, beats per minute

Ulcerative Colitis Endoscopic Index of Severity (UCEIS)[5]			
Descriptor	**Likert scale (anchor points)**	**Definition**	
Vascular pattern	Normal (0)	Normal vascular pattern with arborization of capillaries clearly defined, or with blurring or patchy loss of capillary margins	
	Patchy (1)	Patchy obliteration of vascular pattern	
	Obliterated (2)	Complete obliteration of vascular pattern	
Bleeding	None (0)	No visible blood	
	Mucosal (1)	Some spots or streaks of coagulated blood on the surface of the mucosa ahead of the scope, which can be washed away	
	Luminal mild (2)	Some free liquid blood in the lumen	
	Luminal moderately severe (3)	Frank blood in the lumen ahead of endoscope or visible oozing from mucosa after washing intraluminal blood or visible oozing from a hemorrhagic mucosa	

Erosions and ulcers	**None (0)**	**Normal mucosa, no visible erosions or ulcers**	
	Erosions (1)	Tiny (5 mm) defects in the mucosa of a white or yellow color with a flat edge	
	Superficial ulcer (2)	Larger (> 5 mm) defects in the mucosa which are discrete fibrin covered ulcers when compared with erosions but remain superficial	
	Deep ulcer (3)	Deeper excavated defects in the mucosa with slightly raised edge	

Remission (0-1); Mild (2-4); Moderate (5-6), Severe (7-8)
Adapted from: Travis, et al. *Gastroenterology* 2013, 145:987–95.

Footnotes

DEFINITIONS:

Flare/relapse – recurrence of symptoms in a patient in clinical remission.

Frequent relapse: ≥ 2 episodes flares/year requiring steroids.

Any definition is arbitrary and calls for clinical judgment. But any further relapse calls for a review of treatment strategy and consideration of multidisciplinary / tertiary level discussion.

Steroid dependent: Relapse of symptoms on steroid tapering.

Acute severe/fulminant ulcerative colitis

Adequate response: ≤ 3 stools/day or 3-8 stools/day with CRP < 45 mg/L

Inadequate response: > 8 stools/day or 3-8 stools/day and CRP > 45 mg/L

Relapse investigation protocol

In patients with flares not responding to therapy, send stools for microscopy and culture as well as *Clostridium difficile* toxin as well as biopsies to look for coexisting CMV colitis.

Endoscopic healing: Consider stepping up therapy regardless of symptoms in patients with inadequate mucosal healing.

Fecal calprotectin < 150 mg/kg may be used as a surrogate marker for mucosal healing.

CMV, cytomegalovirus; CRP, C-reactive Protein

Footnotes

THERAPY:

5-aminosalicylates

- Sulphasalazine (SSZ) can be considered as an alternative to mesalazine but higher risk of side effects (Steven Johnson syndrome, oligospermia) and higher doses less well tolerated.
- SSZ may provide better symptom relief than mesalazine in patients with IBD related arthopathy.
- Mesalazine may cause a paradoxical worsening of symptoms during flare; in the event of this happening, withold treatment and start/continue steroids.
- Another extremely rare but very serious complication is interstitial nephritis.

Thiopurines

- Azathioprine is usually used. Alternatively, 6-mercaptopurine 1-1.5 mg/kg/day, can be used if patient develops nausea.
- Start azathioprine at low dose, typically in increments of 50 mg every 6-8 weeks to a dose of 1.5-2.5 mg/kg/day if no biochemical/hematological abnormalities or side effects.
- FBC & LFT weekly for 4 weeks, then 2 weekly for 4 weeks, at initiation or following dose increase. Once the dose is stable, reduce to 3 monthly.
- Metabolite monitoring 6-TGN and 6-MMP(R) recommended in patients who are intolerant/have significant side effects to the drug or in patients who have frequent relapses despite standard weight-based regime.[8]

	Group 1	Group 2	Group 3	Group 4	Group 5
TDM	Low/absent 6-TGN and Low/absent 6-MMP(R)	Low 6-TGN and Low 6-MMP(R)	Low 6-TGN and High 6-MMP(R)	High 6-TGN and Low 6-MMP(R)	High 6-TGN and High 6-MMP(R)
Risk	Inefficacy (false resistance)	Inefficacy or poor response	Poor response and/or hepatotoxicity	Myelotoxicity	Myelotoxicity and/or hepatotoxicity
Cause	Poor compliance to treatment	Underdosing	Very high TPMT activity i.e. pharmacologic resistance to thiopurines	Deficient TPMT activity	Overdose or refractoriness to thiopurines
Action	Therapeutic patient education	Increase thiopurine dosage	Add allopurinol 100mg/day and decrease thiopurine dosage (25-50% of original dose)	Decrease thiopurine dosage according to TPMT phenotype	Switch to another drug if active disease

FBC, full blood count; LFT, liver function test; TDM, therapeutic drug monitoring; 6-TGN, 6-thioguanine nucleotide; 6-MMP(R), 6-methylmercaptopurine ribonucleotide; TPMT, thiopurine methyltransferase.

- TPMT deficiency which is a common cause of myelotoxity in Caucasians is not common in Asia.
- NUDT15 mutations, on the other hand, is common in Asia but NUDT15 genotyping and its associated metabolites not commercially available at present.

Steroids

- Taper prednisolone therapy as soon as clinical remission achieved, ideally patient should be steroid free within 3 months.
- Always prescribe with calcium/vitamin D supplements as per algorithm.
- If there is recurrence of symptoms during tapering, prednisolone dose may be increased again by 5-10 mg; before re-attempting tapering. Addition of budesonide MMX may be another option to consider.

Rescue therapy in acute severe ulcerative colitis

- Infliximab preferred in thiopurine refractory patients.
- May consider accelerated induction regimen of either two doses of 5 mg/kg with second dose ≤ 7 days after the first, or 10 mg/kg for the first dose with another dose within 2 weeks.
- Sequential use of infliximab followed by cyclosporin or vice versa not recommended.
- Other rescue medications such as tacrolimus and leucocyte apheresis are mainly used in Japan.
- The decision to start rescue therapy is a good time to ask for a surgical opinion by way of contingency planning.

Biologic therapy

- Choice of first line biologics depends on many factors; indication, speed of onset, safety profile, ease of administration, cost/reimbursement and patient preference.
- In terms of indication; preferences include anti-TNFs for perianal fistulizing Crohn's disease, infliximab/vedolizumab for ulcerative colitis, ustekinumab/vedolizumab for patients at high risk of infection including tuberculosis/older adults.
- Infliximab should ideally be given with thiopurines for 6-12 months unless the risk of combination therapy outweighs the benefits (e.g. populations with high risk of infection).
- No evidence of clinical benefit of combination therapy of thiopurines/other immunodulators with the other biologics but may still consider if interruption of scheduled maintenance therapy likely or there is evidence of secondary failure.
- Consider trough levels and anti-drug antibody testing if there is evidence of primary and secondary failure, but need to also rule out other causes of 'failure' such as predominantly fibrostenotic disease and infection.
- May consider stopping biologic therapy with immunomodulator as maintenance if there is evidence of deep remission (clinical and endoscopic remission) at 6-12 months AFTER careful discussion with patient with regards to risk of relapse and potential attenuated response/hypersensitivity on reintroducing therapy after a prolonged drug holiday (particularly anti-TNF). A colonoscopy after 6 months should be carried out to look for signs of early relapse.

	Trough levels	Anti-drug antibody levels	Action
Primary failure	• Normal to high infliximab between 3-7 ug/ml for luminal, 10 ug/ml for fistula • Adalimumab between 4-8 µg/mL	Low	Switch out of class (switching within class can still be considered).
Secondary failure	Low	Low/Absent	Increase dose.
	Low	High	Switch within class (i.e. infliximab to adalimumab and vice versa). Switching out of class is an option.

Pre-biologic and immunosuppressive therapy screening

Latent TB: CXR or CT chest AND Tuberculin skin test (TST) or Interferon-gamma release assays (IGRA) such as QuantiFERON-TB Gold In-Tube (QFT-GIT) and T-SPOT.*TB* test (repeat annually for patients on anti-TNF).

For current or previous chronic Hepatitis B: Hep B sAg, IgG HBcAb.

Patients with positive Hep B sAg must receive prophylactic antiviral therapy 2 weeks before biologic therapy and 6 months after stopping treatment.

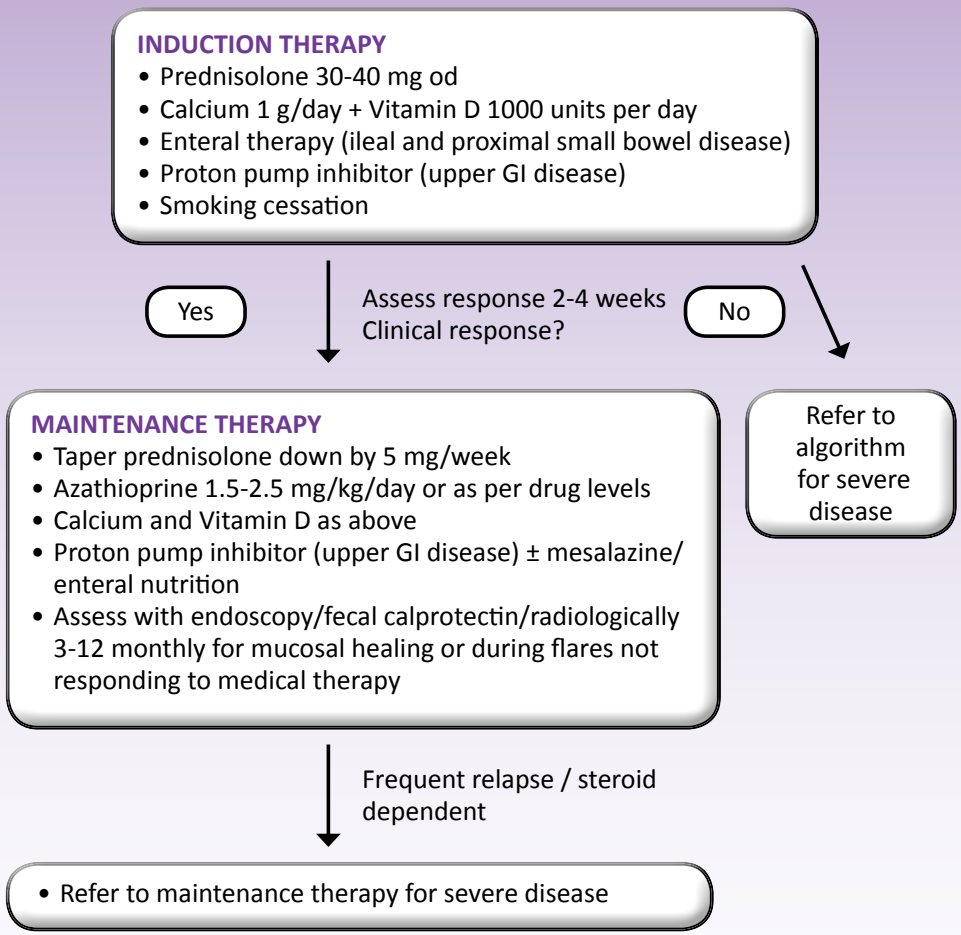
Vaccinations

- Consider all vaccinations especially in the elderly population.
- Main vaccines should include varicella, HPV, influenza, pneumococcal, Hepatitis B.
- Live vaccines should not be given within three weeks before commencing anti-TNF and within three months after last dose.

TREATMENT ALGORITHMS: CROHN'S DISEASE

Crohn's Disease (Luminal)

(mild to moderately active disease)



Crohn's Disease (Luminal) *(severely active disease)*

- Hospital admission
- Exclude surgical abdomen (bowel obstruction, perforation)
- Assess extent of disease (CT/MRI enterography if suspected small bowel involvement)

↓

INDUCTION THERAPY

- Intravenous hydrocortisone 100 mg qds/methylprednisolone 40 mg bd or
- Adalimumab SC 160 mg, then 80 mg at 0 and 2 weeks respectively, followed by 40 mg every 2 weeks or
- Infliximab IV 5 mg or 10 mg/kg at 0,2,6 weeks or
- Ustekinumab IV 6 mg/kg or
- Vedolizumab IV 300 mg at 0,2,6 weeks
- Enteral nutrition and/or parenteral nutrition in extensive small bowel disease/fistulae
- Proton pump inhibitor in upper GI disease
- DVT prophylaxis e.g. enoxaparin 40 mg od
- Intravenous antibiotics if coexisting sepsis

Assess 5-7 days
Adequate response*?

Yes ↙ ↘ No

MAINTENANCE THERAPY

- Convert to oral prednisolone 30-40 mg od then taper 5 mg/week or
- Adalimumab SC 40 mg every 2 weeks or
- Infflliximab IV 5 mg/kg 8 weekly or
- Ustekinumab SC 90 mg every 8 weeks or
- Vedolizumab IV 300 mg every 8 weeks or
- Azathioprine 1.5-2.5 mg/kg/day or as per drug levels
- Smoking cessation
- Calcium 1 g/day + Vitamin D 1000 units per day
- Proton pump inhibitor (upper GI disease)
- ± mesalazine/enteral nutrition
- Assess with endoscopy/fecal calprotectin for mucosal healing every 3-12 monthly or during flares not responding to medical therapy.

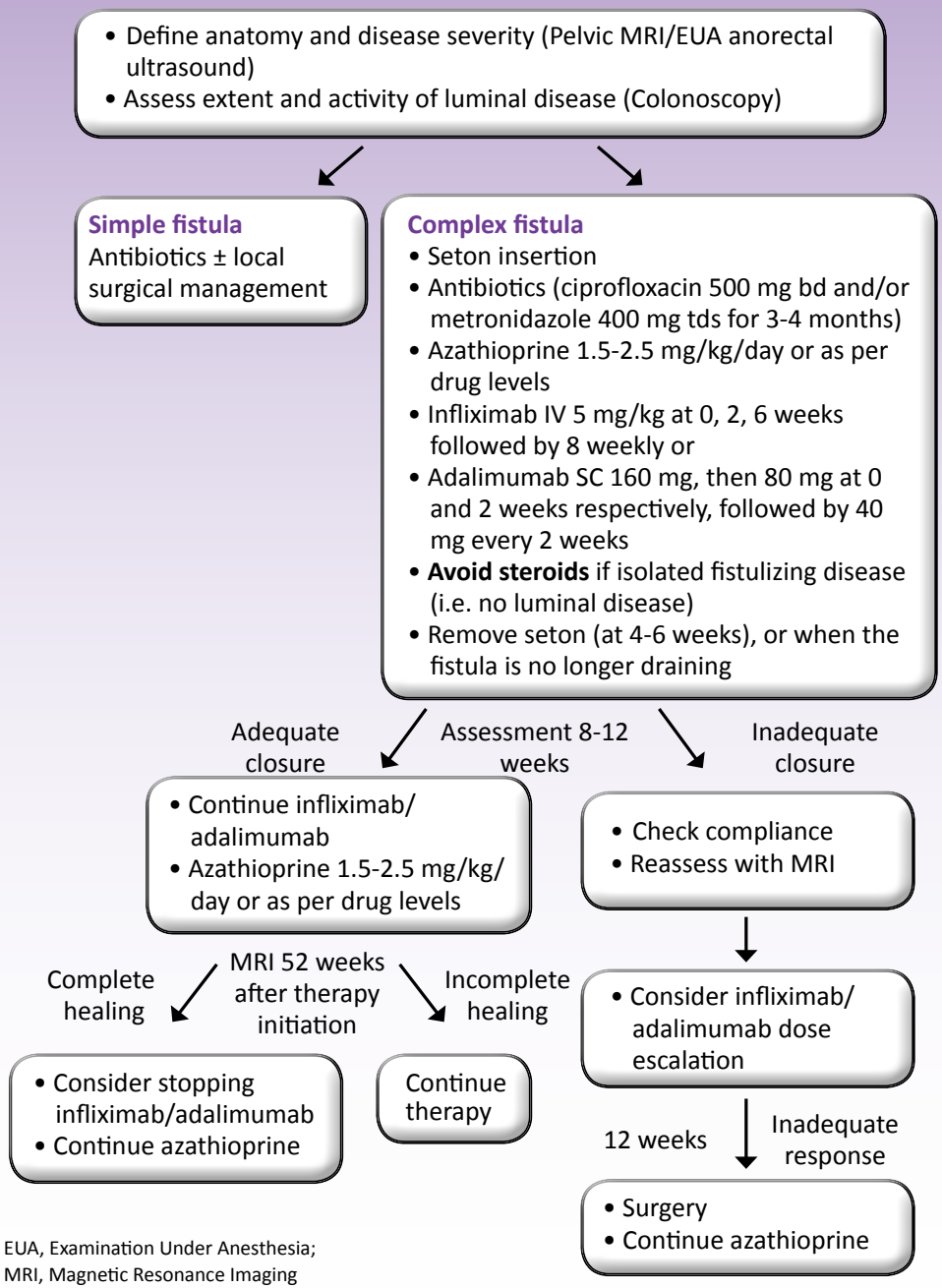
- Switch to infliximab if on steroids
- Tertiary referral
- Surgery

↓ Frequent relapse/steroid dependent*

- Tertiary referral
- Dose escalation
- Other rescue therapy
- Surgery

*Definition as per footnotes section (Page 30)

Crohn's Disease *(active perianal fistulizing disease)*



EUA, Examination Under Anesthesia;
MRI, Magnetic Resonance Imaging

Crohn's Disease *(postoperative recurrence)*

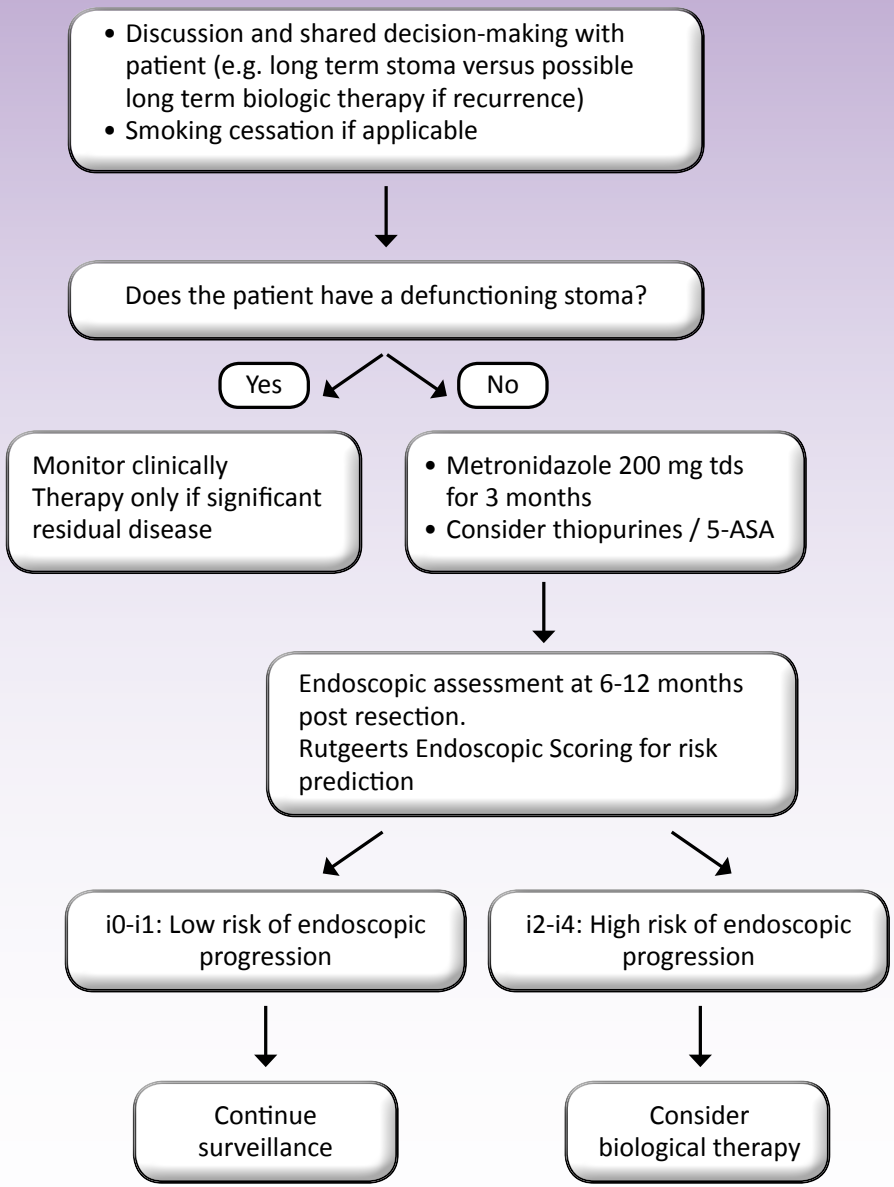
INTRODUCTION:

- The rates of postoperative recurrence (POR) varies:
  - Endoscopic recurrence in the first postoperative year is reported in 35-85% of cases, with 10-38% of patients being symptomatic.
  - By the third year, the rates are 85-100% and 34-86% respectively.

Risk Factors for Postoperative Recurrence in Crohn's Disease

Risk factors	Odds Ratio
Established Increased Risk	
Smoking	2.0
Penetrating disease behavior	1.5
Prior intestinal resection	1.8 – 2.6
Perianal disease	1.6
Extensive small bowel resection (>50cm)	1.4
Possible Increased Risk	
Myenteric plexitis	1.9
Inconclusive Risk	
NOD2/CARD15 mutation	–
Presence of granulomas	–
Young age at disease onset	–
Location of disease	–

Postoperative Management of Crohn's Disease



Harvey Bradshaw Index (HBI)

Indices	Score
General well-being (Yesterday) (0 = very well, 1 = slightly below average, 2 = poor, 3 = very poor, 4 = terrible)	
Abdominal pain (Yesterday) (0 = none, 1 = mild, 2 = moderate, 3 = severe)	
Number of liquid stools per day (Yesterday)	
Abdominal mass (0 = none, 1 = dubious, 2 = definite, 3 = tender)	
Complications (1 point for each) – Arthralgia – Uveitis – Erythema Nodosum – Aphthous Ulcers – Pyoderma Gangrenosum – Anal Fissure – New Fistula – Abscess	

Disease activity - Luminal

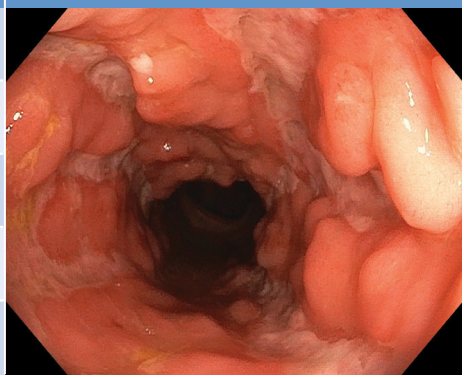
Mild disease: HBI 5-7
Moderate disease: HBI 8-16
Severe disease: HBI > 16
Clinical remission is HBI < 5

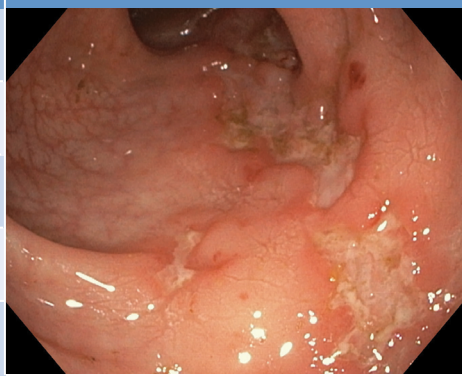
Simple Endoscopic Score for Crohn's Disease *(SES-CD)*[11]

Descriptor	Score	Terminal Ileum	Right Colon	Transverse Colon	Descending Colon	Rectum	Total Score
Ulcer size	None (0) Aphthous ulcers, 0.1-0.5 cm (1) Large ulcers, 0.5-2 cm (2) Very large ulcers, > 2 cm (3)						
Ulcerated surface	0% (0) < 10% (1) 10-30% (2) > 30% (3)						
Affected surface (ulcerated surface, inflammation and other abnormal areas)	0% (0) < 50% (1) 50-75% (2) > 75% (3)						
Narrowings	None (0) Single, can be passed (1) Multiple, can be passed (2) Cannot be passed (3)						
*Remark: Segments not explored is recorded as 0						Grand total : (SES-CD)	

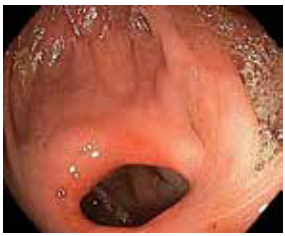
Inactive disease: SES-CD ≤ 2
Mild disease: SES-CD = 3-6
Moderate disease: SES-CD = 7-15
Severe disease: SES-CD ≥ 16

Example of SES-CD Calculation

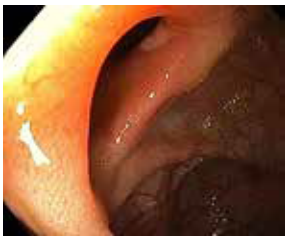
Descending colon	
Very large ulcers, > 2cm = 3	
Ulcerated surface > 30% = 3	
Affected surface 50-75% =2	
Narrowings None = 0	
Total score in left colon 8	

Descending colon	
Very large ulcers, 0.5-2cm = 2	
Ulcerated surface 10-30% = 1	
Affected surface < 50% = 1	
Narrowings None = 0	
Total score in descending colon = 4	

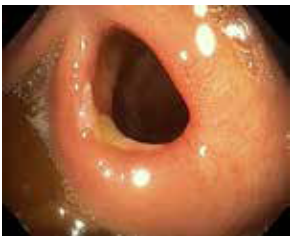
Rutgeerts Endoscopic Scoring System[12]	
Endoscopic	**Score Definition**
i0	No aphthous ulcers
i1	≤ 5 aphthous ulcers
i2	> 5 aphthous ulcers with normal intervening mucosa, skip areas of large lesions or lesions confined to ileocolonic anastomosis
i3	Diffuse aphthous ileitis with diffusely inflamed mucosa
i4	Diffuse inflammation with large ulcers, nodules and/or narrowing



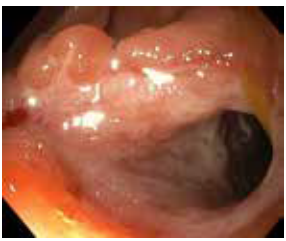
i0



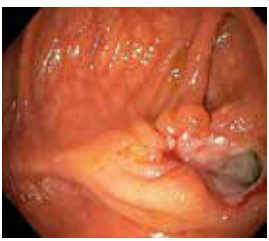
i1



i2



i3



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Footnotes

DEFINITIONS:

Disease activity - Luminal

Clinical remission is Harvey Bradshaw Index < 5

Flares: recurrence of symptoms in a patient in clinical remission.

Frequent relapse: ≥ 2 episodes flares/year requiring steroids.

Any definition is arbitrary and calls for clinical judgment. But any further relapse calls for a review of treatment strategy and consideration of multidisciplinary/tertiary level discussion.

Adequate response: A ≥ 3 point decrease in HBI score from baseline.

Steroid dependent: Relapse of symptoms on steroid tapering.

Fistula

Simple - superficial/low, without signs of abscess formation or anorectal stricture.

Complex - high/multiple openings with abscesses; rectovaginal fistula; anorectal stricture with rectal inflammation.

Adequate response - Closure of fistula based on clinical symptoms and external examination.

Endoscopic Assessment

Mucosal healing - Although no clear definition exists, generally defined as absence or almost complete absence of ulcers and erosions.

Stepping up therapy to achieve mucosal healing should be considered in all patients with Crohn's disease regardless of symptoms to avoid long term complications and surgery.

Fecal calprotectin < 150 mg/kg may be used as a surrogate marker for mucosal healing.

Footnotes

Enteral nutrition

Polymeric formula (e.g. Ensure) or dipeptide based formula (e.g. Peptamen) 30 kcal/kg/day can be used as exclusive enteral nutrition for 4-6 weeks or as a supplement to normal diet.

5-aminosalicylates

- Limited evidence for 5-aminosalicylates except for in mild colonic disease.

Thiopurines/Methotrexate

- Azathioprine is usually used. Alternatively, 6-mercaptopurine 1-1.5 mg/kg/day, can be used if patient develops nausea.
- Start azathioprine at low dose, typically in increments of 50 mg every 6-8 weeks to a dose of 1.5-2.5 mg/kg/day if no biochemical/hematological abnormalities or side effects.
- FBC & LFT weekly for 4 weeks followed by 2 weekly for 4 weeks, at initiation or following dose increase. Once the dose is stable, reduce monitoring to 3 monthly.
- Metabolite monitoring of 6-TGN and 6-MMP(R) recommended in patients who are intolerant/have significant side effects to the drug or in patients who have frequent relapses despite standard weight-based regime.

	Group 1	Group 2	Group 3	Group 4	Group 5
TDM	Low/absent 6-TGN and Low/absent 6-MMP (R)	Low 6-TGN and Low 6-MMP(R)	Low 6-TGN and High 6-MMP(R)	High 6-TGN and Low 6-MMP(R)	High 6-TGN and High 6-MMP(R)
Risk	Inefficacy (false resistance)	Inefficacy or poor response	Poor response and/or hepatotoxicity	Myelotoxicity	Myelotoxicity and/or hepatotoxicity
Cause	Poor compliance to treatment	Underdosing	Very high TPMT activity i.e. pharmacologic resistance to thiopurines	Deficient TPMT activity	Overdose or refractoriness to thiopurines
Action	Therapeutic patient education	Increase thiopurine dosage	Add allopurinol 100mg/day and decrease thiopurine dosage (25-50% of original dose)	Decrease thiopurine dosage according to TPMT phenotype	Switch to another drug if active disease

FBC, full blood count; LFT, liver function test; TDM, therapeutic drug monitoring; 6-TGN, 6-thioguanine nucleotide; 6-MMP(R), 6-methylmercaptopurine ribonucleotide; TPMT, thiopurine methyltransferase.

- TPMT deficiency which is a common cause of myelotoxity in Caucasians is not common in Asia.
- NUDT15 mutations, on the other hand, is common in Asia but NUDT15 genotyping and its associated metabolites not commercially available at present.
- Methotrexate can be considered as an alternative choice to thiopurines and may be preferred in EBV negative young adults/children.
  Methotrexate can be given as a loading dose 25 mg/week subcutaneously or intramuscularly for 12-16 weeks with oral folic acid 5 mg stat on Day 3 after administration. This is followed by maintenance of 15 mg/week either orally or SC/IM. Another alternative is to start at 15 mg/week orally without loading and titrate up to 25 mg/week. Blood monitoring similar as for thiopurines.
- Methotrexate is **ABSOLUTELY CONTRAINDICATED** in pregnancy.

Biologic therapy

- Choice of first line biologics depends on many factors; indication, speed of onset, safety profile, ease of administration, cost/reimbursement and patient preference.
- In terms of indication; preferences include anti-TNFs for perianal fistulizing Crohn's disease, infliximab/vedolizumab for ulcerative colitis, ustekinumab/vedolizumab for patients at high risk of infection including tuberculosis/older adults.
- Infliximab should ideally be given with thiopurines for 6-12 months unless the risk of combination therapy outweighs the benefits (e.g. populations with high risk of infection).
- No evidence of clinical benefit of combination therapy of thiopurines/other immunodulators with the other biologics but may still consider if interruption of scheduled maintenance therapy likely or there is evidence of secondary failure.
- Consider trough levels and anti-drug antibody testing if there is evidence of primary and secondary failure, but need to also rule out other causes of 'failure' such as predominantly fibrostenotic disease and infection.
- May consider stopping biologic therapy with immunomodulator as maintenance if there is evidence of deep remission (clinical and endoscopic remission) at 6-12 months AFTER careful discussion with patient with regards to risk of relapse and potential attenuated response/hypersensitivity on reintroducing therapy after a prolonged drug holiday (particularly anti-TNF). A colonoscopy after 6 months should be carried out to look for signs of early relapse.

EBV, Epstein Barr Virus

	Trough levels	Anti-drug antibody levels	Action
Primary failure	• Normal to high infliximab between 3-7 ug/ml for luminal, 10 ug/ml for fistula • Adalimumab between 4-8 µg/mL	Low	Switch out of class (switching within class can still be considered).
Secondary failure	Low	Low/Absent	Increase dose.
	Low	High	Switch within class (i.e. infliximab to adalimumab and vice versa). Switching out of class is an option.

Pre-biologic and immunosuppressive therapy screening

Latent TB: CXR or CT chest AND Tuberculin skin test (TST) or Interferon-gamma release assays (IGRA) such as QuantiFERON-TB Gold In-Tube (QFT-GIT) and T-SPOT.*TB* test (repeat annually for patients on anti-TNF).

For current or previous chronic Hepatitis B: Hep B sAg, IgG HBcAb.

Patients with positive Hep B sAg must receive prophylactic antiviral therapy 2 weeks before biologic therapy and 6 months after stopping treatment.

Vaccinations

- Consider all vaccinations especially in the elderly population.
- Main vaccines should include varicella, HPV, influenza, pneumococcal, Hepatitis B.
- Live vaccines should not be given within three weeks before commencing anti-TNF and within three months after last dose.

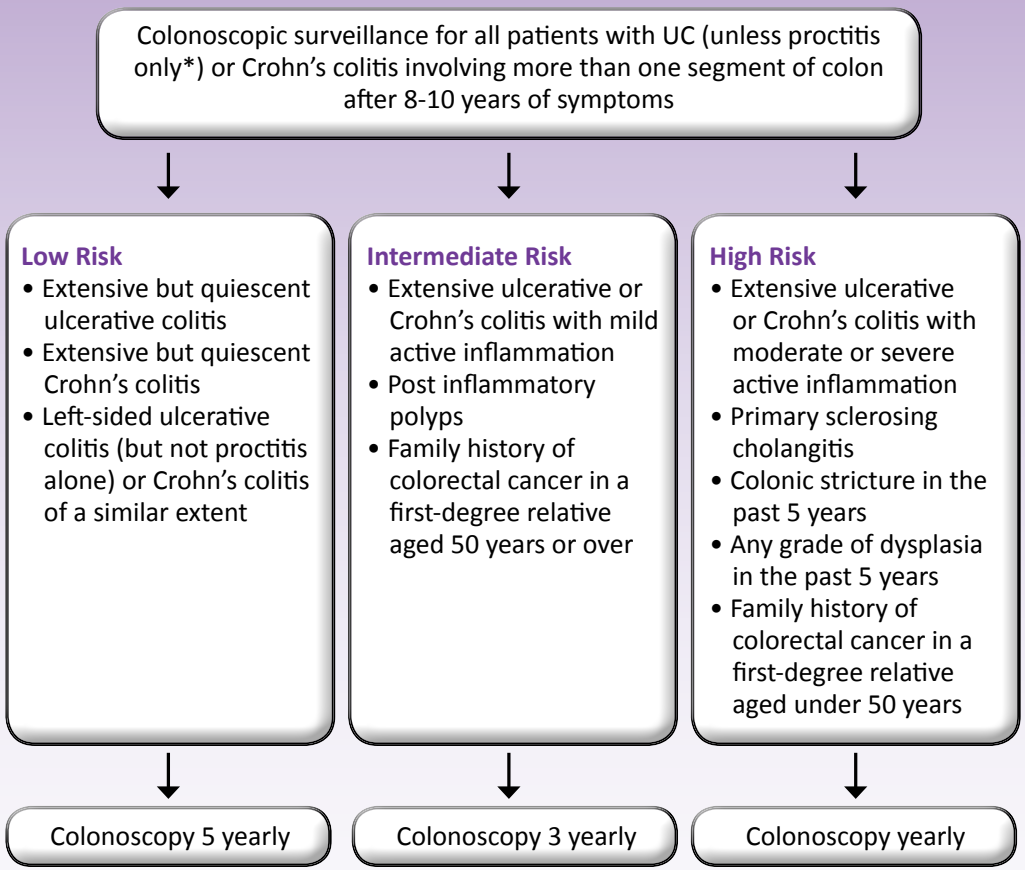
PERIOPERATIVE MANAGEMENT OF BIOLOGICS AND IMMUNOMODULATORS

Perioperative Management of Biologics and Immunomodulators[13]

	Data	Preoperative	Postoperative
Steroids	Increased risk of postoperative complications if 20 mg of prednisolone or equivalent taken over a period of 3 weeks	Slow tapering by 5 mg/week	No data
Thiopurines	Controversial but some data suggests slightly increased risk of postoperative sepsis	Continue but may consider stopping if benefit of continuing not clear	May resume after 1-3 days if indicated (e.g. postoperative prophylaxis although this remains controversial)
Methotrexate	Minimal data	Surgery 1 week after last dose but consider stopping if benefit of continuing not clear	May resume after 1-2 weeks
Anti-TNFs	Generally safe but some data shows higher postoperative septic complications after abdominal surgery for Crohn's disease	**Elective:** Discontinue at least 4 weeks before surgery for infliximab and 2 weeks before surgery for adalimumab **Emergency:** Discontinue as soon as surgery planned	Resume no earlier than 2 weeks post operatively if strong indication (e.g. high risk of recurrence, residual disease)
Vedolizumab	Limited data	Elective: Discontinue at least 4-8 weeks before surgery Emergency: Discontinue as soon as surgery planned	Resume no earlier than 2-4 weeks post operatively if strong indication

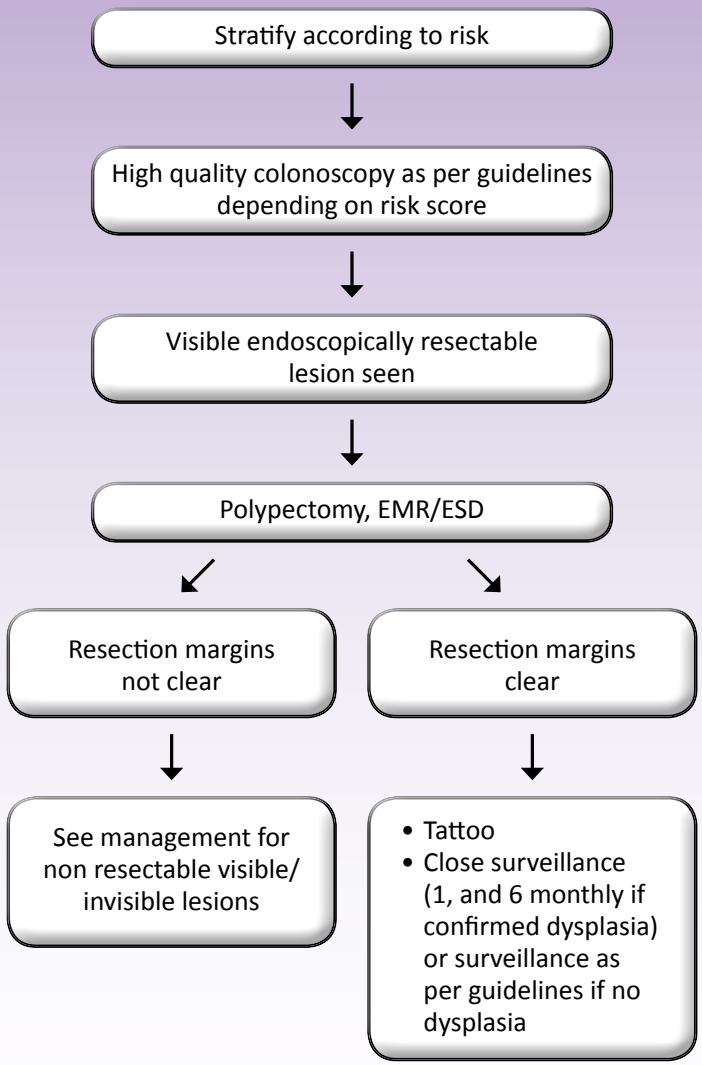
SURVEILLANCE AND MANAGEMENT OF DYSPLASIA

Guidelines for Dysplasia Surveillance in IBD[14]



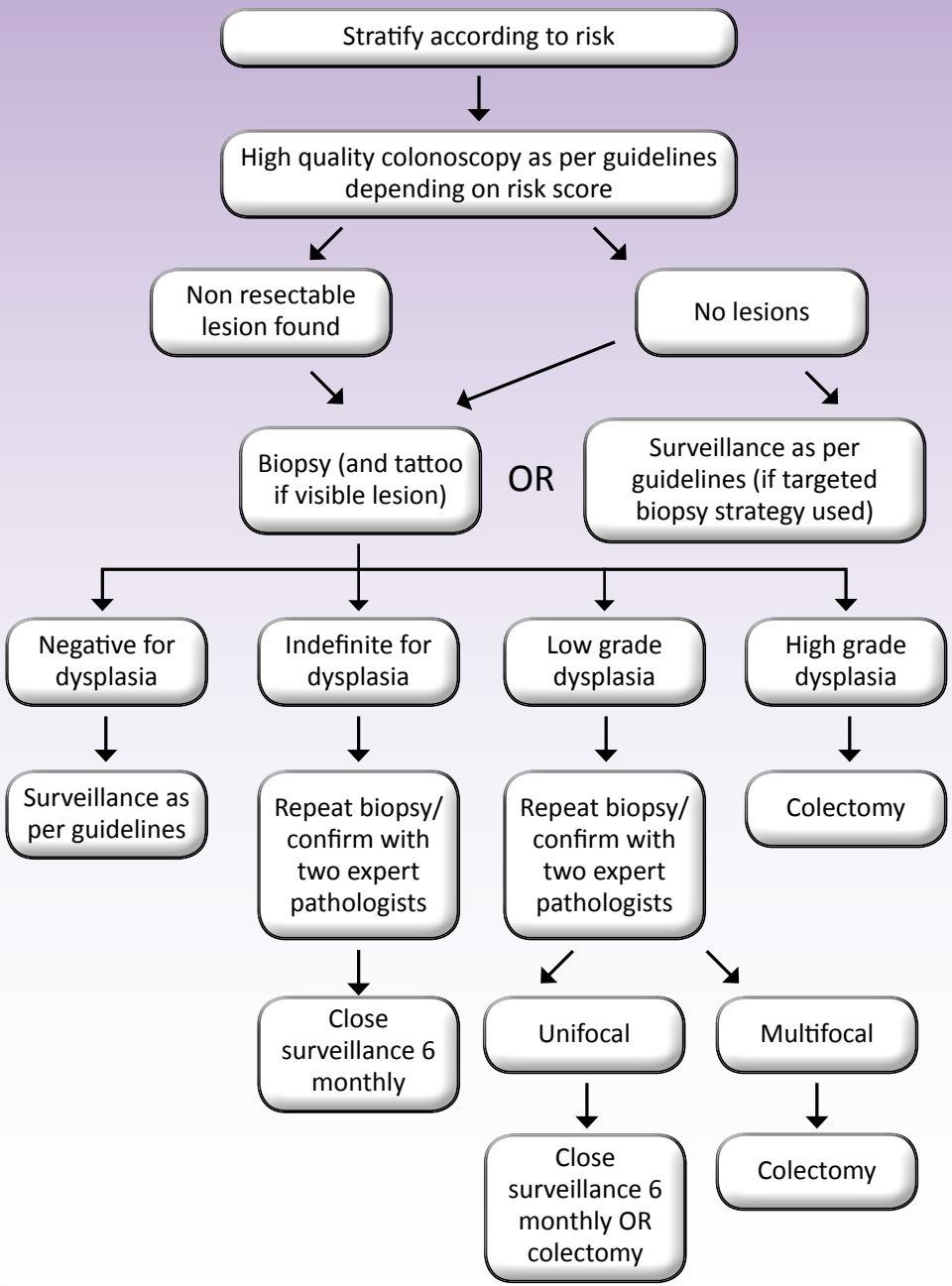
* Patients who had previously documented left sided/extensive colitis but proctitis only during reassessment should also undergo surveillance

Management of Resectable Dysplastic Lesions[15]



EMR, Endoscopic Mucosal Resection; ESD, Endoscopic Submucosal Dissection

Management of Visible Non-resectable or Invisible Dysplastic Lesions



Appendix

Technique for colonosocopy:

- Ensure good bowel preparation
- Surveillance should not be carried out during flares
- High definition white light and chromoendoscopy (image enhanced endoscopy) should be used
- Characterization of visible lesions as per SCENIC guidelines*[9]
- ***Targeted*** (after careful examination using image enhanced techniques) rather than random biopsies preferred although obtaining random biopsies remains an option
- Post inflammatory polyps or 'pseudopolyps' (although a marker for severe disease) have no malignant potential and should not be biopsied or removed unless there are suspicious features

Endoscopic resection of lesions:

- ESD/EMR should be performed in expert centres only and referral should be made to these centres if available. Biopsy and colectomy if confirmed dysplasia remains an option.

* SCENIC, Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients.

ESD, Endoscopic Submucosal Dissection; EMR, Endoscopic Mucosal Resection

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The algorithms are intended as a treatment guide for standard adult patients with IBD. They MAY NOT be suitable/contraindicated for special groups (e.g. children, pregnant/breastfeeding women, older adult patients). In these situations, tertiary referral or expert opinion is advised.

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