# Welcome to the IBD Nurse Fellowship Program!

The program consists of 13 modules:

Module 1 – Ulcerative Colitis
Module 2 – Crohn's Disease
Module 3 – Ulcerative Colitis vs. Crohn's Disease
Module 4 – Management of Ulcerative Colitis
Module 5 – Management of Crohn's Disease
Module 6 – IBD and Surgery
Module 7 – Medication Adherence in IBD
Module 8 – Health Promotion and Maintenance in IBD
Module 9 – Nutrition and IBD
Module 10 – Extra-intestinal Manifestations of IBD
Module 11 – Anemia in IBD
Module 12 – Fatigue in IBD
Module 13 – Anxiety and Depression in IBD

Each module is divided into sections, all of which are listed in the Table of Contents. The Table of Contents allows you to click on the page numbers to navigate to each section. Each page has a Home Button on the bottom right-hand corner that will take you back to the Table of Contents.

The learning objectives are at the beginning and end of each module. Before completing the module, you will have the opportunity to take a self-directed quiz, which will test your knowledge on several of the key concepts and takeaways from the module. It is recommended that you take the quiz and accomplish all of the learning objectives before moving on to the next module.

This program is supported through an educational grant from janssen

IBD nurse fellowship PROGRAM

csgna
Canadian Society of Gastroenterology Nurses & Associates
Société canadienne des infirmières et infirmiers en gastroentérologie et travailleurs associés

CANIBD
Canadian Nurses IBD Group

# Module 5

## Management of Crohn's disease

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# Table of contents



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# Learning objectives

After completing Module 5 you will be able to:

- Summarize the treatment goals of Crohn's disease
- Assess disease activity and diagnose and grade disease severity using the Symptomatic Assessment Questionnaire
- Describe the current pharmacotherapy options for Crohn's disease
- Advise on treatment strategies based on disease severity using the treatment algorithms for Crohn's disease

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# Section 1

## Goals of treatment

# Goals of treatment

Timely entry to remission

Maintain symptomatic control

Minimize short and long term toxicity of therapy

Delay or reduce likelihood of recurrence after surgery

Optimize quality of life

Feldman M *et al.*, 2016.

# A few key points to remember…

- Many of the therapies used in Crohn's disease are also used in ulcerative colitis
- Practice guidelines are categorized according to severity of the disease; subdivided into acute and maintenance phases
- Therapies that induce remission do not necessary mean it can be used as maintenance therapies

# Section 2

## Clinical assessment

# Before therapy is initiated, disease activity should first be determined

- **Crohn's Disease Activity Index (CDAI)** looks at:
  - Number of stools per day
  - Extent of abdominal pain
  - General sense of well being
  - Presence of extra-intestinal manifestations (EIMs)
  - Presence of abdominal masses
  - Hematocrit
  - Taking Lomotil or opiates for diarrhea
  - Body weight
  - Height also determined in paediatrics with Pediatric Crohn's Disease Activity Index (PCDAI)

Feldman M *et al.*, 2016. Best *et al*. 1976.

# Working definitions of clinical disease activity

## Mild-to-moderate

- Ambulatory patient
- Tolerates an oral diet
- Absence of:
  - Dehydration
  - Toxicity (eg. febrile)
  - Abdominal tenderness, with or without mass
  - Obstruction

Engstrom and Goosenberg, 2007.

# Working definitions of clinical disease activity

## Moderate-to-severe

- Failure to responded to treatment of mild-to-moderate disease
- More distinguished symptoms, such as:
  - Fever
  - Weight loss >10%
- Abdominal pain or tenderness, without rebound
- Nausea and vomiting, without obstruction
- Significant anemia

Engstrom and Goosenberg, 2007.

# Working definitions of clinical disease activity

## Severe-to-fulminant

- Persistent symptoms despite outpatient use of corticosteroids
- Increasing significant symptoms:
  - High fever
  - Persistent vomiting
  - Evidence of intestinal obstruction
  - Rebound tenderness
  - Cachexia
  - Presence of abscess

Engstrom and Goosenberg, 2007.

# Working definitions of clinical disease activity

## Remission

- Asymptomatic; no inflammatory sequelae, such as fistulae or abscesses, with improving inflammatory markers
- Responds to medical intervention
- Surgical intervention completion without gross residual disease
- Ability to stop use of corticosteroids

Engstrom and Goosenberg, 2007.

# Symptomatic Assessment Questionnaire

| Symptoms | Questions to consider |
|---|---|
| Onset date of symptoms | • When did the symptoms start?<br>• When did the symptoms escalate? |
| Abdominal pain and/or cramping | • Character of pain or discomfort—is it stabbing, dull, aching, cramping, other?<br>• Severity of pain or discomfort—rating out of 10 (0= no pain, 10= worst imaginable)<br>• Timing of pain or discomfort—constant, prior to or after eating, prior to defecation, intermittent, nocturnal, other?<br>• Trigger(s) of pain or discomfort—eating, activity, lying down, needing to have bowel movement, other, no identifiable trigger?<br>• Alleviator(s) of pain or discomfort—defecation, not eating, avoiding activity, medication, heat, other, no identifiable alleviator? |
| Bowel movements | • Number of current bowel movements in 24 hour period? How many of these are nocturnal?<br>• As comparator: what is baseline number of bowel movements in 24 hours when feeling well and IBD is well-controlled?<br>• Consistency of stool—formed, soft, semi-formed, loose, very loose, liquid?<br>• Color of stool—brown, yellow, green, black, other?<br>• Pattern of bowel movements—immediately upon waking, waking at night, clustered, following meals, other?<br>• Presence of blood—pure blood with no stool, mixed into stool, dripping into toilet, on toilet paper with wiping, other, none?<br>• Amount of blood—with every bowel movement, small consistent amounts, intermittent, rare, other?<br>• Color of blood—bright red, dark red, maroon, black, clots present, other?<br>• Urgency and/or incontinence—mild urgency, need to hurry, fecal incontinence, other?<br>• Tenesmus—any feeling of incomplete emptying after having bowel movement? |
| Fever and nights sweats | • Documented fever?<br>• Timing of fever—consistent throughout day, upon waking, at bedtime or during night, inconsistent, other?<br>• Night sweats—drenching night sweats necessitating change of linens and pajamas, mild night sweats, every night, intermittent? |

# Symptomatic Assessment Questionnaire

| Symptoms | Questions to consider |
|---|---|
| Nausea and vomiting | • Timing of nausea—constant, intermittent, nocturnal, before eating, after eating, other?<br>• Vomiting—number of vomiting episodes in 24 hours<br>• Character of emesis—bile, undigested food, fecal, coffee grounds, other?<br>• Associated bloating?<br>• Triggers(s) of nausea and/or vomiting—eating, activity, pain, having bowel movement, other, no identifiable trigger?<br>• Alleviator(s) of nausea and/or vomiting—defecation, not eating, avoiding activity, medication, other, no identifiable alleviator? |
| Appetite and changes in weight | • Appetite—change in appetite, anorexia, other?<br>• Change in weight—documented weight loss (how many kilograms or pounds in what time period), documented weight gain (how many kilograms or pounds in what time period)?<br>• Food intake- avoidance of food, change in diet (i.e., liquids only, soft foods, bland foods, other)? |
| Fatigue, sleep and stressors | • Fatigue- present but manageable, present and affecting quality of life or ability to complete activities of daily living, other?<br>• Sleep- waking at night, requiring more sleep than usual, waking up feeling tired, insomnia, other?<br>• Stressors- personal, family, other relationships, occupational, financial, other? |
| Perianal symptoms | • Any symptoms suggestive of perianal abscess or fistula—perianal pain, perianal swelling, sensation of sitting on lump or egg, perianal drainage (purulent, sanguineous, serosanguinous, yellow, clear, malodorous)? |

# Symptomatic Assessment Questionnaire

| Symptoms | Questions to consider |
|---|---|
| Extra-intestinal manifestations | • Any arthralgias and/or myalgias—which joints or muscles affected, migratory versus specific joints, description and severity of pain, timing of arthralgia or myalgia (after biologic therapy administration, towards end of biologic therapy dosing cycle, constant, intermittent, other), joint swelling, impact on quality of life and/or activities of daily living, treatments used and outcome (i.e., medication, heat, rest, other, no reliever identified)?<br>• Any symptoms affecting the eyes—pain, photophobia, redness, dryness, other?<br>• Any symptoms affecting the skin—new rash or worsening of existing rash, new lesions, distribution of rash or lesions, new onset or worsening of existing psoriasis, treatments used and outcome? |
| Risk factors for gastroenteritis | • Recent antibiotic use?<br>• Recent travel? If yes, where?<br>• Any contact with sick individuals with GI symptoms?<br>• Recent meal at commercial eating establishment, cafeteria/dining hall, vending machine or external event where you did not prepare the food? |
| Current medications | • Obtain list of name and dosage of all prescribed medications, over-the-counter products, vitamins, herbals, supplements<br>• Any prescribed medications, over-the-counter products, vitamins, herbals, supplements recently started? If yes, start date?<br>• If patient on tapering course of prednisone or budesonide: did symptoms start at particular dose of prednisone or budesonide when tapering?<br>• If patient on biologic therapy: when is next biologic therapy infusion or injection scheduled, does patient get breakthrough symptoms before biologic therapy cycle is completed (i.e., prior to next infusion or injection)? |

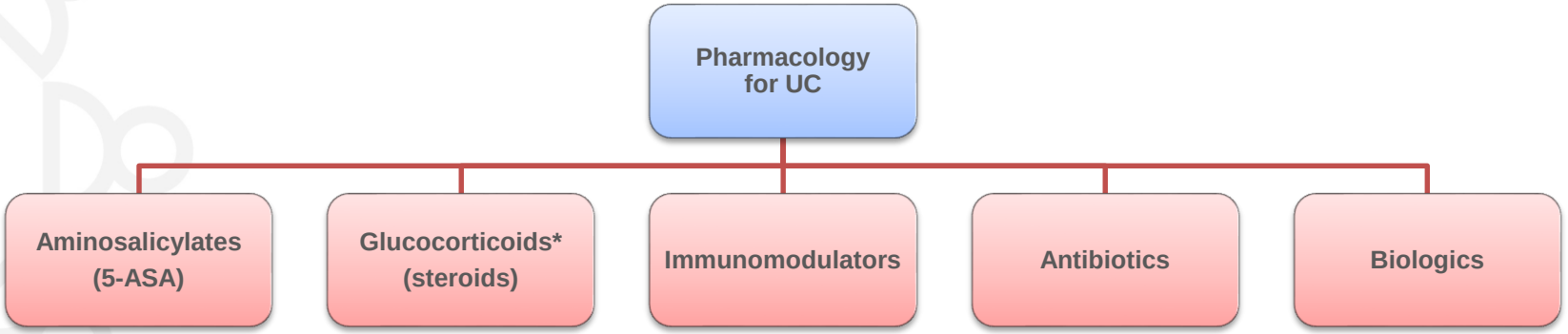
# Section 3

## Pharmacotherapy

# Pharmacology for Crohn's disease

## Overview

- Many medications are prescribed to control inflammation
- There are five types, or classes, of these medications:




- Generics are available for older medications, however certain brand names will be called out in the following pages where relevant
  - To learn more about specific products, please refer to the Health Canada Drugs and Health products database (http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp)

*This class may also be called "corticosteroids," which includes glucocorticoids.

CCC-Biologic therapy, 2015; CCC-Prescription health brochure, 2015; Feldman M *et al.,* 2016.; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Aminosalicylates

| Definition | Examples | Used for | How it works |
|---|---|---|---|
| • Products that include 5-aminosalicylic acid (5-ASA) | • Sulfasalazine (Salazopyrin®)<br>• Mesalamines (5-ASA) (Pentasa®) | • Mild to moderate Crohn's disease and maintenance of Crohn's disease in remission<br>• Particularly used when Crohn's disease affects the colon | • Limits the production of chemicals that trigger inflammation |

CCC-Prescription health brochure, 2014; Feldman M *et al.,* 2016; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Glucocorticoids (steroids)

| Definition | Examples | Used for | How it works |
|---|---|---|---|
| • Steroids that are derived from cortisol (a hormone produced by the adrenal glands) | • Prednisone<br>• Hydrocortisone<br>• Betamethasone<br>• Budesonide<br>• Methylprednisolone | • Induction therapy but not maintenance and relapse-prevention therapy due to clinically significant short- and long-term adverse effects<br>• Moderate to severe attacks | • Supresses inflammation in the body and decreases the activity of the immune system throughout the body |

CCC-Prescription health brochure, 2014; Feldman M *et al.,* 2016; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Immunomodulators

| Definition | Examples | Used for | How it works |
|---|---|---|---|
| • Medication that alters how the body mounts an inflammatory response | • Thiopurines, such as: 6-Mercaptopurine (Purinethol®) and azathioprine (Imuran®)<br>• Methotrexate<br>• Cyclosporin(e) | • Patients who have not met their treatment goals with aminosalicylates and steroids<br>• 6-Mercaptopurine, azathioprine. and Methotrexate:<br>  ○ Long-term treatment and remission<br>  ○ Helping patients reduce the use of steroids (steroid-sparing agents)<br>• Cyclosporin(e):<br>  ○ Severe flare-ups in hospitalized patients | • Suppresses immune responses throughout the entire body |

CCC-Prescription health brochure, 2014; Feldman M *et al.,* 2016; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Antibiotics

| Definition | Examples | Used for | How it works |
|---|---|---|---|
| • Medications that treat bacterial infections | • Metronidazole<br>• Ciprofloxacin<br>• Amoxicillin/ clavulanic acid | • Preventing or controlling infection<br>• May be used as a primary therapy | • Treat infection, such as abscesses, and are helpful with fistulas |

CCC-Prescription health brochure, 2014; Feldman M *et al.,* 2016; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Biologics

| Definition | Examples | Used for | How it works |
|---|---|---|---|
| • Drug that is derived from living cells, which tend to have large, complex molecular structures in comparison with "small molecule" drugs<br>• In CD, this includes:<br>  ○ Anti-TNF blockers | **Anti-TNF blockers:**<br>• Adalimumab (Humira®)<br>• Infliximab (Remicade®)<br>**$\alpha_4\beta_7$ integrin blockers:**<br>• Vedolizumab (Entyvio®)*<br>*Not yet approved for treatment of CD in Canada, although it is approved in the US (by the FDA) and in Europe (by the EMA) for this indication | • Patients with moderate to severe CD who have not responded adequately to conventional therapies<br>• May not be suitable for all patients and have been associated with infection, and an increased risk of developing certain cancer types | **Anti-TNF blockers:**<br>• One of the signals involved in causing inflammation in people with CD is called tumour necrosis factor alpha, or TNF-alpha<br>• Biologic medications that block those signals are known as anti-TNF blockers<br>**$\alpha_4\beta_7$ integrin blockers:**<br>• These biologic medications attempt to block the movement of some inflammatory cells to areas of inflammation in the gut, allowing the affected colon to heal |

CCC-Biologic therapy, 2015; CCC-Prescription health brochure, 2014.; Entyvio® (vedolizumab) [US Prescribing Information], Apr 2014; Entyvio® (vedolizumab) [European Public Assessment Report (EPAR)—Product Information] Sept 2015; Feldman M *et al.,* 2016; Health Canada, Drugs and Health Products database (and associative product monographs); Mayo Clinic-Crohn's, 2014.

# Pharmacotherapy

## Biologics: dosing

| REMICADE® | HUMIRA® |
|---|---|
| **6** infusions per maintenance year[1] | **26** subcutaneous injections per maintenance year[2] |
|  |  |
| **Dosing:** *Induction* — 5mg/kg at weeks 0, 2, 6; *Maintenance* — 5 mg/kg every 8 weeks thereafter | **Dosing:** *Induction* — 160 mg at week 0 followed by 80 mg at week 2; *Maintenance* — 40 mg every other week beginning at week 4 |

Please note that ENTYVIO™ (vedolizumab) is not indicated for the treatment of CD in Canada.

REMICADE® (infliximab) product monograph, 2015; HUMIRA® (adalimumab) product monograph, 2015.

# Pharmacotherapy

## Biologics: therapeutic drug monitoring

- Due to the complex nature of all biologics and the varied outcomes among patients, therapeutic drug monitoring (TDM) offers a way to identify the unique therapeutic window of each patient relative to his/her medication regimen
- TDM allows for personalized assessment, which increases the likelihood of positive treatment outcomes
  - TDM is the measurement of a patient's serum for drug and antibody levels; the blood draw may be done at trough, the lowest drug serum level, just before a scheduled infusion
  - TDM is intended to assist with dosing decisions in individual patients
  - Drug trough levels and drug antibody levels need to be taken into account before considering dose adjustment in CD patients
- TDM is only commercially available for infliximab (Remicade®) and adalimumab (Humira®) AND may not be easily available to all health care providers to use as part of clinical practice

GI Society-Therapeutic drug monitoring, 2015; REMICADE® (infliximab) product monograph, 2015.

# Pharmacotherapy

## Biologics: patient support programs

- Patient support programs are an important resource for patients taking biologics
- These programs have coordinators/nurses that may assist patients in many ways such as coverage issues, clinic appointments, offering information and tools to help guide them through the treatment process

| Biologic(s) | Patient support program |
|---|---|
| • Adalimumab (Humira®) | • Abbvie Care™<br>http://www.abbviecare.ca/humira/ |
| • Infliximab (Remicade®)<br>• Golimumab (Simponi®) | • BIOADVANCE®<br>https://bioadvancemember.ca/ |

AbbVie-Abbvie Care. 2015; Janssen-BIOVANCE, 2015.

# Pharmacotherapy

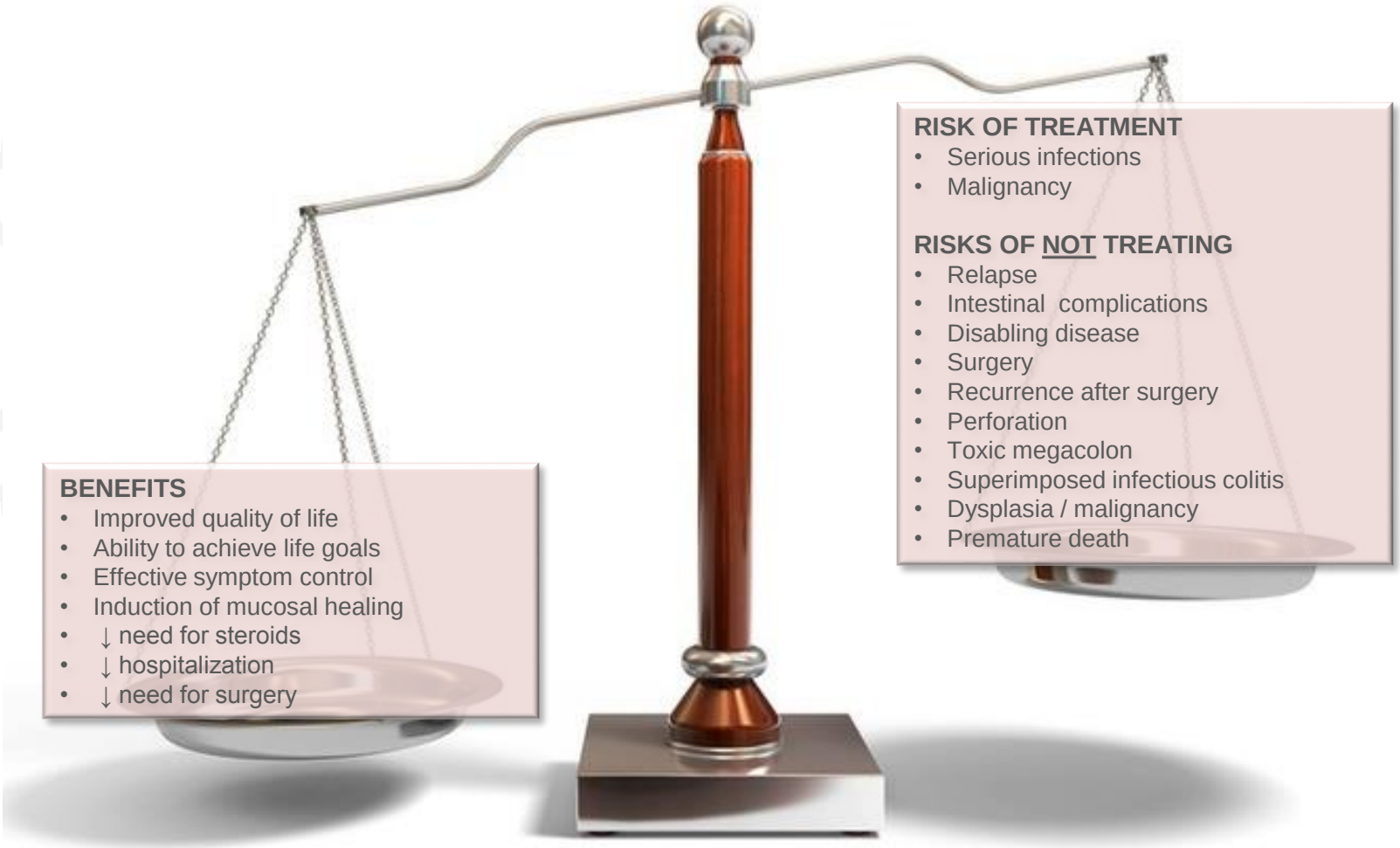
## Biologics: subsequent entry biologics

- Subsequent entry biologics (SEBs) are drugs that are similar to the innovator biologic drug
- Currently in Canada, there are no SEBs approved for the treatment of IBD
- SEBs are not considered ‘generic biologics’
  - They are considered similar, but not identical, to the innovator biologic drugs
- Like innovator biologics, SEBs are generated from living cells
- Because their molecular structures are large and manufacturing processes complex, it is challenging to produce exact replica of innovator drugs
  - Health Canada does not support automatic substitution of a SEB for its reference biologic drug
- Differences between a SEB and an innovator drug may result in differences in clinical effects
- Individuals on a biologic innovator drug should be aware of the risks and benefits of switching to an SEB
  - In some cases, substitution of an innovator product with a SEB may lead to the endogenous formation of antibodies that prevent the SEB from having a maximal effect
  - This may occur even if the patient did not demonstrate clinically significant immunogenicity with the original innovator product

Health Canada-SEBs (2010).

# Pharmacotherapy

## Biologics: putting benefits and risks into perspective



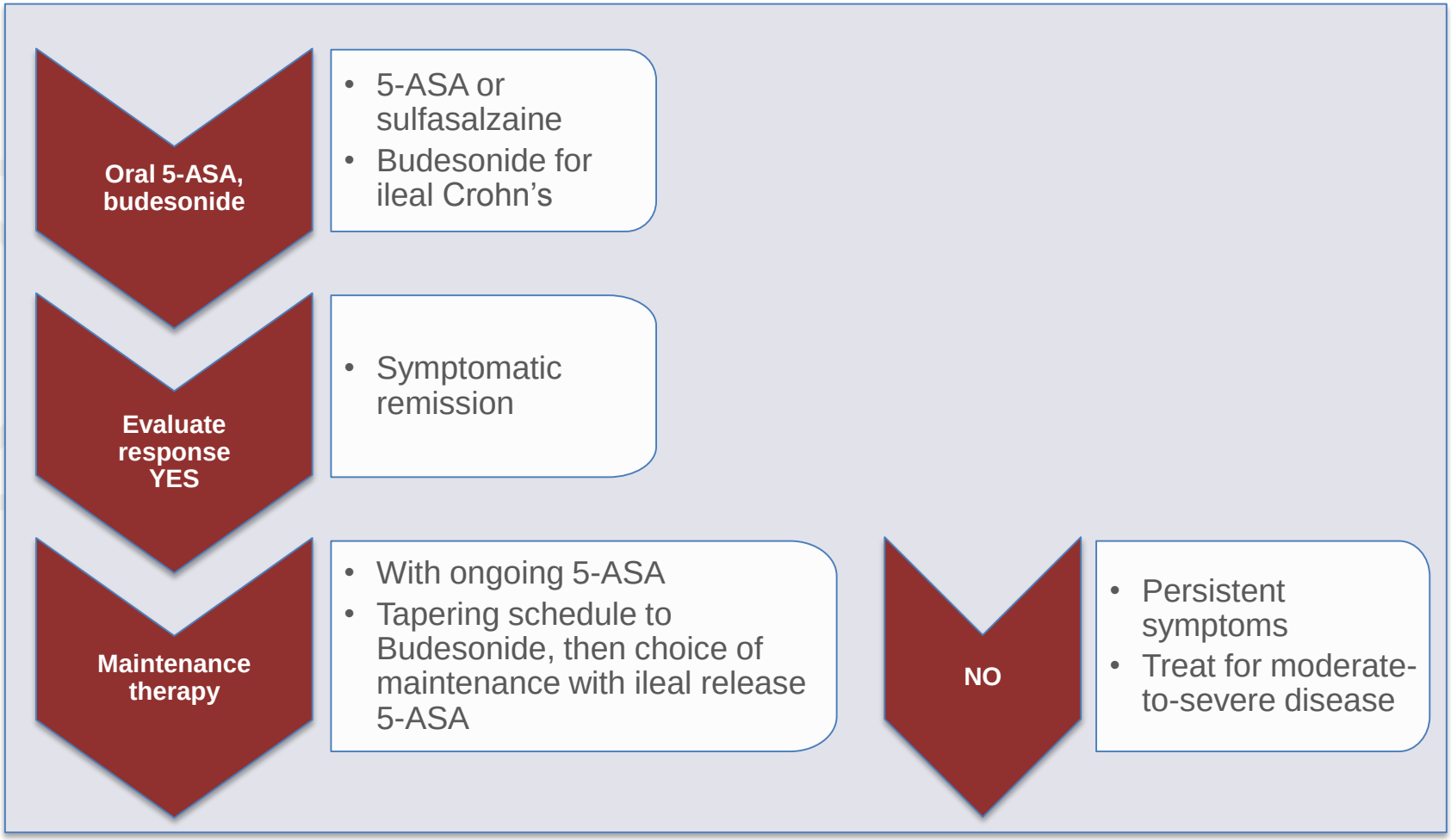

Van Assche *et al*., 2010; Hoentjen, 2009.

# Section 4

## Treatment algorithms

# Treatment algorithm

## Mild-to-moderate

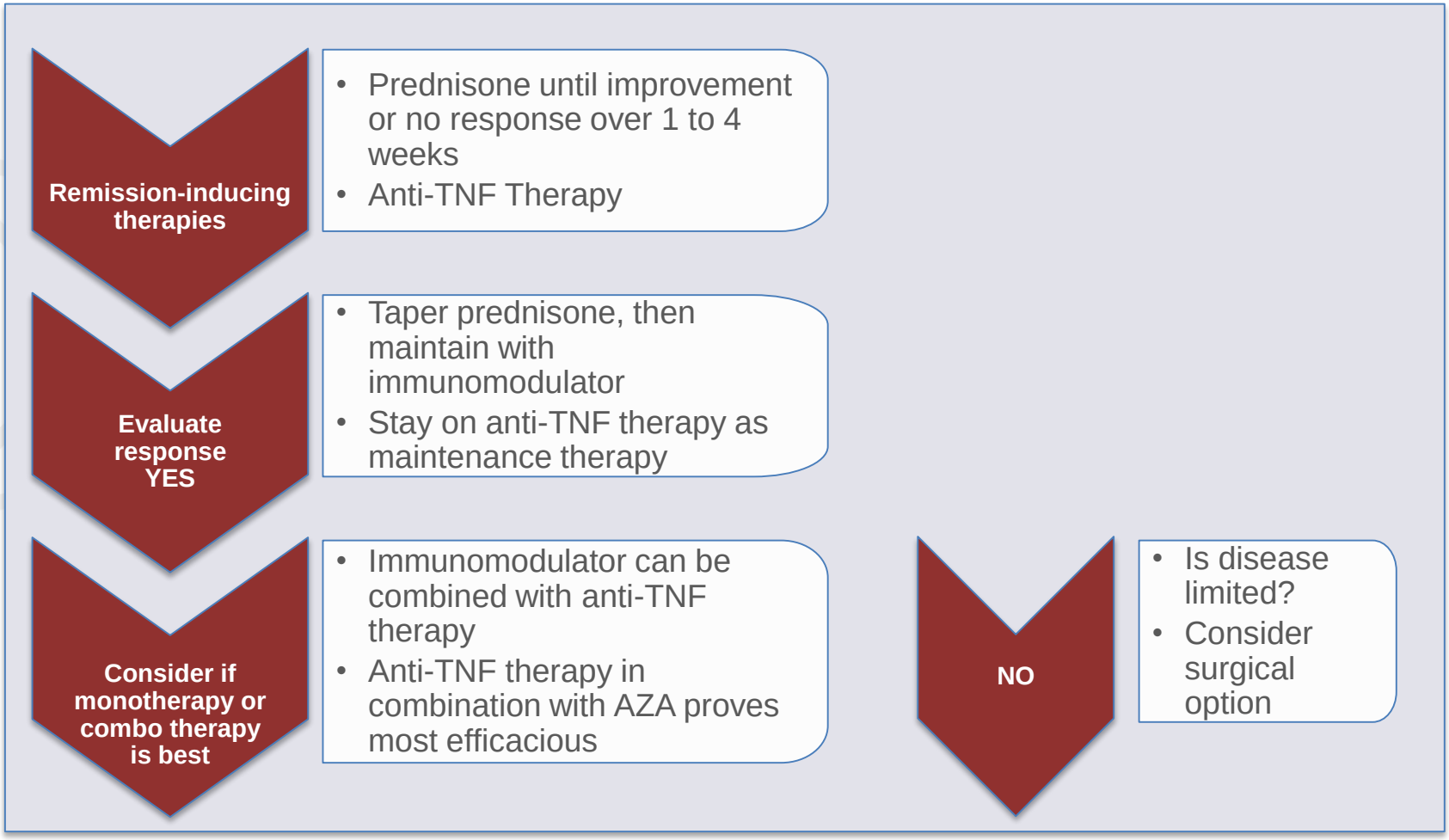



5-ASA, 5-aminosalicylic acid.

American College of Gastroenterology,1997 Annual Meeting. Hanauer, 1997.

# Treatment algorithm

## Moderate-to-severe

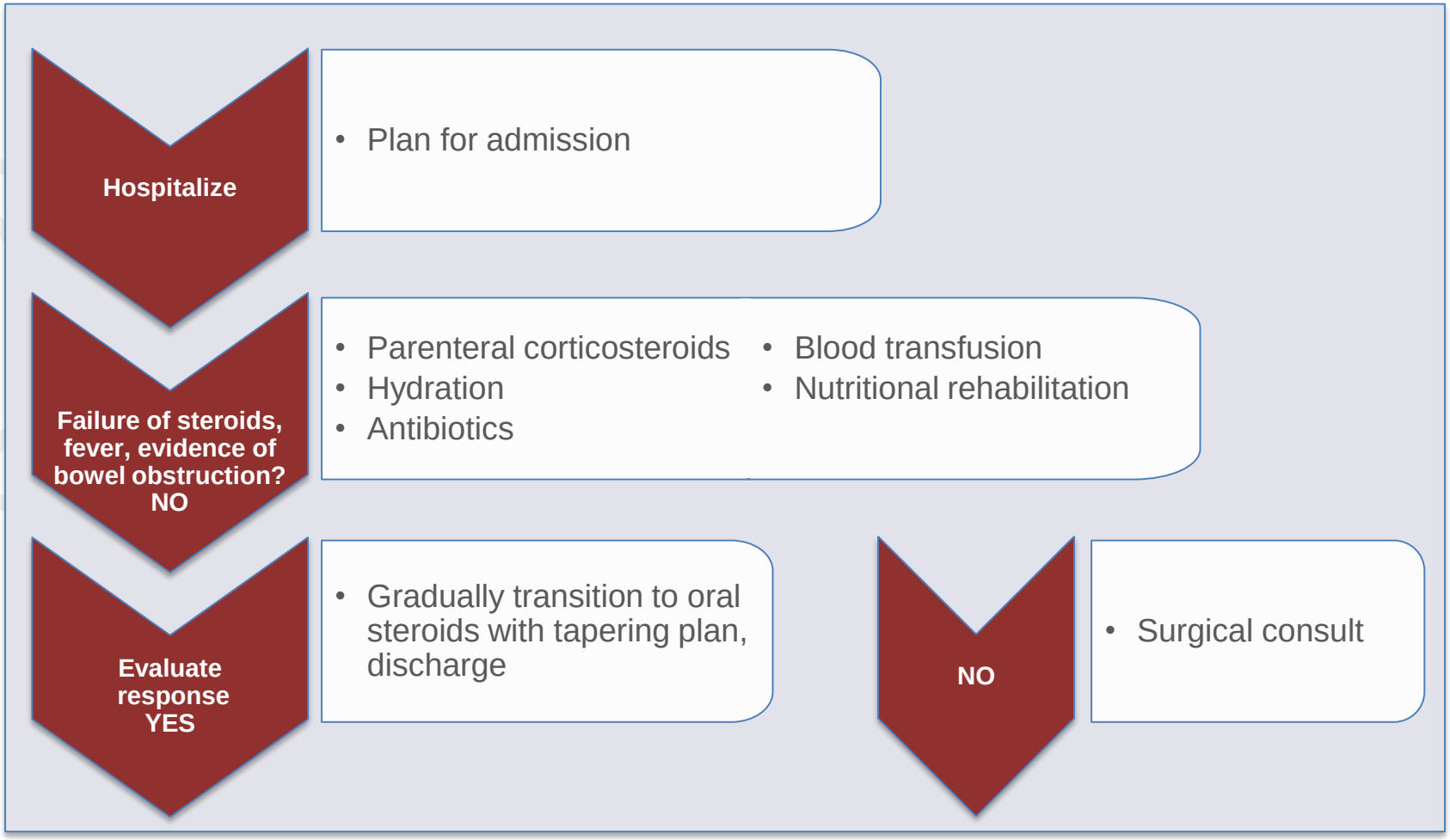



AZA, azathioprine; TNF, tumour necrosis factor.

American College of Gastroenterology,1997 Annual Meeting. Hanauer, 1997.

# Treatment algorithm

## Severe-to-fulminant




American College of Gastroenterology,1997 Annual Meeting. Hanauer, 1997.

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# Section 5

## Self-assessment quiz

# Self-assessment quiz

- Now that you have reviewed the module content, you have the opportunity to test your knowledge and understanding of the material by completing a self-assessment
- The assessment consists of 5 multiple choice questions
- Please attempt each question before looking at the answer key, which is located on page 40
- The answer key provides the rationale for each answer and indicates where the correct answer can be found in the module

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# Question 1

Which of the following is characteristic of a patient with mild-to-moderate Crohn's disease?

a) Absence of toxicity

b) Cachexia

c) Persistent vomiting

d) Significant anemia

# Question 2

Which of the following is characteristic of Crohn's disease in remission?

a) Failure to respond to medical intervention

b) Increased dependency on corticosteroids

c) No inflammatory sequalae with improving inflammatory markers

d) Surgical intervention completion with gross residual disease

# Question 3

Which of the following is a class of medication used to control inflammation for patients with Crohn's disease?

a) Angiotensin receptor blockers (ARBs)

b) Immunomodulators

c) Incretin mimetics

d) Statins

# Question 4

Which of the following medications is an example of a glucocorticoid (steroid)?

a) Amoxicillin

b) Prednisone

c) Methotrexate

d) Infliximab

# Question 5

Which of the following statements is true?

a) It is important to weigh the risks and benefits of biologic therapy

b) People who take biologics are likely to suffer a lower quality of life

c) The potential benefits of therapy with biologics have not been established

d) The risks of biologic therapy generally outweigh the benefits

# Answer key

1. **The correct answer is a.** Absence of toxicity is characteristic of a patient with mild-to-moderate Crohn's disease. See page 10 for more information on this topic.

2. **The correct answer is c.** No inflammatory sequalae, with improving inflammatory markers, is characteristic of remission. See page 13 for more information on this topic.

3. **The correct answer is b.** Immunomodulators, such as methotrexate and azathioprine, are a class of medications used to control inflammation for patients with Crohn's disease. See page 18 for more information on this topic.

4. **The correct answer is b.** Prednisone is an example of a glucocorticoid (steroid). See page 20 for more information on this topic.

5. **The correct answer is a.** It is important to weigh the risks and benefits of biologic therapy. See page 28 for more information on this topic.

# Congratulations!

You have completed the 5th module of the program.

Based on what you learned in Module 5, you should be able to:

- Summarize the treatment goals of Crohn's disease
- Assess disease activity and diagnose and grade disease severity using the Symptomatic Assessment Questionnaire
- Describe the current pharmacotherapy options for Crohn's disease
- Advise on treatment strategies based on disease severity using the treatment algorithms for Crohn's disease

If you have answered the quiz questions correctly and achieved the learning objectives, you are ready to move on to Module 6, which will focus on intestinal bowel disease and surgery.

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