Iron Deficiency Anemia (IDA) Pathway for Colorectal Cancer Diagnosis

Quick Links: Primer & Expanded details | Provider resources | Patient resources | Provide feedback

1. Signs of IDA

(**Both** must be present to meet criteria for high risk iron deficiency anemia)

- Anemia:
  Hb <130 g/L in men,
  Hb <120 g/L in women

AND

- Iron Deficiency:
  Serum ferritin below lower limit of normal

2a. Rule out celiac disease

(Click on arrow for more detailed guidance)

- TTG blood test (anti-transglutaminase antibody): negative (past 5 years or current) **AND/OR**
- Prior normal duodenal endoscopic biopsy (taken during gastroscopy)

b. Address Gynecology causes

- Heavy menstruation

3. Is there high risk rectal bleeding?

(**ALL** must be present to meet criteria for high risk rectal bleeding):

- Blood visibly present in/on stool **OR** in the toilet **AND** not just on the tissue paper
- New onset or worsening **AND** persistent rectal bleeding (not just a single episode; present most days of the week for more than 2 weeks)
- Bleeding is unexplained (i.e., **absence of complete colonoscopy within last 2 years**)

No / Yes

Follow high risk rectal bleeding pathway

Investigation that should be carried out:

4. Medication review

Especially anti-platelet agents and/or anti-coagulants

5. Baseline investigations (within 8 weeks of referral)

CBC (Required), Serum Ferritin (Required), TTG (Required),
Serum Iron, TIBC, Transferrin saturation, Creatinine, Alkaline Phosphatase, Bilirubin, ALT , CRP (if indicated)

Note: For patients with signs of IDA, FIT should not be done

6. Physical exam

Consider rectal exam, especially if there is also a change in bowel habit or lower abdominal pain

7. Consider alarm symptoms concerning for colorectal or other GI cancer

- Significant diarrhea, as can occur in IBD
- Unintentional weight loss (≥ 5-10% of body weight over 6 months)
- Significant and progressive change in bowel habit
- Significant abdominal pain

Alarm feature should be unexplained (i.e., not investigated by lower endoscopy within the last 2 years)

Yes / No

8. Urgent criteria for IDA pathway for colorectal cancer diagnosis

- IDA with Hb <110 g/L (Men) / <100 g/L (Women)

OR

- IDA with alarm symptom concerning for colorectal or other GI cancer

8. Refer for urgent endoscopy (gastroscopy and/or colonoscopy); should be evaluated in < 2 weeks

For referral: See Alberta Referral Directory (www.albertareferraldirectory.ca) and fax to:
Edmonton (SHARP-GI) Fax: 780-670-3607
Calgary (GI-CAT) Fax: 403-944-6540

9. Semi-urgent criteria for IDA pathway for colorectal cancer diagnosis

- IDA with:
  Hb between 110 - 130 g/L (Men)
  Hb between 100 - 120 g/L (Women)

9. Refer for semi-urgent endoscopy (gastroscopy and/or colonoscopy); should be evaluated in < 8 weeks

For referral: See Alberta Referral Directory (www.albertareferraldirectory.ca) and fax to:
Edmonton (SHARP-GI) Fax: 780-670-3607
Calgary (GI-CAT) Fax: 403-944-6540

EXPANDED DETAILS

Pathway Primer

- This pathway has been developed in part to ensure **early diagnosis of patients presenting with iron deficiency anemia (not previously investigated) at high risk of colon cancer or other GI cancers**, such as gastric and esophageal cancer.
- It is recognized there are several **other causes of iron deficiency anemia**.
- It is important that iron deficiency anemia is appropriately investigated and in a timely manner.

- **GI Causes of Iron Deficiency Anemia**
    - Iron Deficiency Anemia (IDA) has many causes but this pathway focuses on *GI causes of IDA*
    - Common causes of IDA without obvious evidence of GI tract bleeding (blood in stool, melena) include:
        - heavy menstruation in women
            - *It is important to know in women whether they are still menstruating or whether they have had a hysterectomy*
        - colon cancer
        - other GI tract cancers, including esophageal and gastric cancer
        - peptic ulcer disease
        - celiac disease
        - inflammatory bowel disease (IBD)
        - chronic GI blood loss from small vascular or mucosal lesions, often associated with use of anti-platelet agents, NSAIDS and anti-coagulants
        - chronic GI blood loss due to other causes
        - poor iron intake
            - *Poor iron intake is a rare cause of significant iron deficiency. It is generally advisable that patients are investigated for other cause of iron deficiency.*

- Celiac disease causes IDA because of impaired absorption of iron, not because of excess GI tract blood loss. Testing for celiac disease, by the TTG blood test (anti-transglutaminase anti body), is important in the work-up of IDA. It is no longer required to also order an IgA level when ordering TTG.

- **Definition of Iron Deficiency Anemia**
    - For diagnosis of IDA, *both* the Hemoglobin (Hb) and iron stores *must be low.*
    - ***Anemia* is present when Hb is <130 g/L in men and <120 g/L in women.**
    - ***The following criteria have been set***
        - **<u>URGENT</u>**
            - IDA with Hb <110 g/L (Men) / <100 g/L (Women), **OR**
            - IDA with alarm symptom concerning for colorectal or other GI cancer:
                - Significant diarrhea, as can occur in IBD
                - Unintentional weight loss (≥ 5-10% of body weight over 6 months)
                - Significant and progressive change in bowel habit
                - Significant abdominal pain
        - **<u>SEMI-URGENT</u>**
            - IDA with:
                - Hb between 110 - 130 g/L (Men)
                - Hb between 100 - 120 g/L (Women)
    - **Serum ferritin is the best test for diagnosis of iron deficiency.**
        - *Iron deficiency* is defined as serum ferritin below the lower limit of normal. In Alberta, lab guidelines state that the lower limit of normal is 30 ug/L for men and 20 ug/L for women.
        - Ferritin is more accurate than serum iron or TIBC (total iron binding capacity) and transferrin saturation.
        - A transferrin saturation <16% supports the diagnosis of IDA.
        - The caveat of a serum ferritin is that it is an acute phase reactant, meaning that it is elevated when active inflammation, such as can be seen in IBD, is present.
        - In individuals with active inflammation (ongoing infection or active IBD) a ferritin <100 ug/mL supports the diagnosis of iron deficiency.

The Iron Primer listed below further explains the diagnosis of iron deficiency.

Iron Primer

Evaluation of measures of iron storage can be challenging. Gastrointestinal (occult) blood loss is a common cause of iron deficiency and should be considered as a cause when iron deficiency anemia is present.

- Two main serological tests best evaluate iron stores (ferritin, transferrin saturation) – neither of which are perfect.
- The first step is to evaluate a **serum ferritin**:
  - If the serum ferritin is low, it is diagnostic of iron deficiency, with high specificity (98% specificity).
  - Ferritin is an acute phase reactant, which may be elevated in the context of acute inflammation and infection. If you suspect this to be the case, order a transferrin saturation (see below).
    - However, if the ferritin is above 100 ug/L and there is no concurrent significant chronic renal insufficiency, iron deficiency is very unlikely – even in the context of acute inflammation/infection.
- The second step is to evaluate **transferrin saturation**:
  - The transferrin saturation is a calculated ratio using serum iron and total iron binding capacity. Serum iron alone does **not** reflect iron stores.
  - Low values (less than 10%) demonstrate low iron stores in conjunction with a ferritin <100 ug/L.
- In the absence of abnormal iron indices, anemia may be from other causes other than (occult) blood loss (e.g., bone marrow sources, menstruation).

EXPANDED DETAILS

This pathway focuses on IDA as the main presentation.

1. Signs of IDA

- For diagnosis of IDA, *both* the Hemoglobin (Hb) and iron stores *must be low.*
- ***Anemia* is present when Hb is <130 g/L in men and <120 g/L in women.**
- **Serum ferritin is the best test for diagnosis iron deficiency.**
  - Iron deficiency is defined as serum ferritin below the lower limit of normal. In Alberta, lab guidelines state that the lower limit of normal is 30 ug/L for men and 20 ug/L for women (as of Nov 2021)
  - Ferritin is more accurate than serum iron or TIBC (total iron binding capacity) and transferrin saturation.
  - A transferrin saturation <16% supports the diagnosis IDA.
  - The *caveat* of a serum ferritin is that it is an acute phase reactant, meaning that it is elevated when active inflammation, such as can be seen in IBD, is present.
  - In individuals with active inflammation (ongoing infection or active IBD) a ferritin <100 ug/mL supports diagnosis of iron deficiency.

2. a. Rule out celiac disease

- It is important that a *TTG blood test to rule out celiac disease* is ordered.
- This is not required if it was done in the past (<5 years) or the patient previously had a normal duodenal endoscopic biopsy (taken during gastroscopy).
- It is no longer required to also order an IgA level when ordering TTG
- Although celiac disease is often associated with other GI symptoms, iron deficiency anemia can be its only manifestation.
- If celiac disease longstanding (>6 months) and patient compliant with gluten free diet AND/OR anemia out of keeping with degree/duration of heavy menstruation, **proceed** with referral.

2. b. Address gynecology causes

- It is important to know in women whether they are still menstruating or whether they have had a hysterectomy.

3. Is there high risk rectal bleeding?

- Rectal bleeding (blood visibly present in/on stool OR in the toilet AND not just on the tissue paper) is defined as high risk if it is new onset or worsening AND persistent (not just a single episode, present most days of the week for more than 2 weeks).
    - The incidence of colorectal cancer has been rising among patients less than age 50, but the absolute risk remains low. Adult patients of all ages can have high risk rectal bleeding, but the bleeding must be accompanied by the presence of other alarm features to be suitable for this pathway.
- Follow the High Risk Rectal Bleeding Pathway for Colorectal Cancer Diagnosis if high risk rectal bleeding is present.

4. Medication review

- New medications may be implicated, especially anti-platelet agents and/or anti-coagulants.
- Use of anti-coagulation or anti-platelet agents increases the risk of bleeding, but, if present, it still means the patient needs to be investigated for the cause.

5. Baseline investigations

- Baseline investigations to identify concerning features or clear etiologies **MUST** include:
    - CBC, Serum Ferritin, TTG

  Additional recommended blood tests:
    - Serum Iron, TIBC, Transferrin saturation, Creatinine, Alkaline Phosphatase, Bilirubin, ALT
    - CRP (if indicated, especially if there is possibility of inflammatory cause, such as ulcerative colitis or Crohns disease)

6. Physical exam

- Consider rectal exam, especially if there is also a change in bowel habit or lower abdominal pain.

7. Consider alarm symptoms concerning for colorectal or other GI cancer

- *Alarm symptoms*, when present, are important to consider and will determine urgency of referral for endoscopic evaluation. (Features should be unexplained, i.e. not investigated by lower endoscopy in the last 2 years):
    - Significant diarrhea, as can occur in IBD
    - Unintentional weight loss (≥5-10% of body weight over 6 months)
    - Significant and progressive change in bowel habit
    - Significant abdominal pain

- *Other features*, when present, are important to consider and may influence triage of the referral for endoscopic evaluations:
    - IDA onset age >40
    - Family history of inflammatory bowel disease (IBD) or colorectal cancer (first-degree relative)
    - Evidence of GI bleeding
    - Nocturnal symptoms

8. Urgent criteria for IDA pathway for colorectal cancer diagnosis

- If there is IDA with:
    - **Hb which has dropped to <110 g/L (Men) / <100 g/L (Women),** OR
    - **At least one of the following alarm symptom concerning for colorectal or other GI cancer:**
        - Significant diarrhea, as can occur in inflammatory bowel disease (IBD)
        - Unintentional weight loss (≥ 5-10% of body weight over 6 months)
        - Significant and progressive change in bowel habit
        - Significant abdominal pain

The referral is urgent meaning the patient should be evaluated (gastroscopy and colonoscopy) in **<2 weeks**.

- *Certain group of patients such as those with chronic advanced kidney disease or elderly individuals with anemia of chronic disease may have baseline Hb levels below the normal range (i.e., Hb is <130 g/L in men and <120 g/L in women).*
- *A significant unexplained drop in Hb from their baseline is a reason for referral for endoscopy.*

- Investigations that will assist with triage:
    - Information over period in which Hb drop occurred:
        - CBC (Required)
        - Serum Ferritin (Required)
        - TTG (Required)
        - Serum Iron, TIBC and Transferrin saturation
        - Creatinine
        - ALT, Alkaline Phosphatase, Bilirubin
        - CRP (if there is possibility of inflammatory cause)
    - Medications: especially anti-platelet agents and/or anti-coagulants
    - Physical exam: describe findings of rectal exam if completed, especially if there is also a change in bowel habit or lower abdominal pain

9. Semi-urgent criteria for IDA pathway for colorectal cancer diagnosis

- If there is IDA with:
    - **Hb between 110 - 130 g/L (Men) / 100 - 120 g/L (Women)**

The referral is semi-urgent meaning the patient should be evaluated (gastroscopy and colonoscopy) in **<8 weeks**.

- Investigation that will assist with triage:
    - Information over period in which Hb drop occurred:
        - CBC (Required)
        - Serum Ferritin (Required)
        - TTG (Required)
        - Serum Iron,TIBC and Transferrin saturation
        - Creatinine
        - ALT, Alkaline Phosphatase, Bilirubin
        - CRP (if there is possibility of inflammatory cause)
    - Medications: especially anti-platelet agents and/or anti-coagulants
    - Physical exam: describe findings of rectal exam if completed, especially if there is also a change in bowel habit or lower abdominal pain

Back to algorithm

BACKGROUND

About this Pathway

- The creation of the Colorectal Cancer Diagnosis Pathway builds on the success of previous pathways including lung, breast and prostate cancer. Building out multiple cancer diagnosis pathways has begun to create end-to-end pathways for cancer patients in Alberta on a provincial scale with the goals of expedited cancer diagnosis and providing better support to patients through that process.
- Initial work on this pathway was started in May 2019 and is being implemented over two years. Patients, providers and administrators from relevant areas were brought together to gather information on current experiences with colorectal diagnosis, collect data on how the system is performing and review best practice evidence. Provincial principles of care, strategic areas for improvement in Alberta and a provincial measurement and reporting framework were defined.
- Primary Care providers were engaged to co-design pathways with patients, gastroenterologists, colorectal surgeons, and GI intake programs.
- Local implementation teams will be engaged in work around planning and pathway roll-out, determination of barriers and facilitators, and shared learnings with other sites. Performance dashboard reports will be developed and disseminated to provide feedback to clinical teams on pathway performance and outcomes. Sustainability planning will be initiated early with implementation teams to ensure successful transition of pathways to operations at the end of the initiative.

Authors & Conflict of Interest Declaration

This pathway was reviewed and revised under the auspices of the Cancer Strategic Clinical Network (CSCN) in 2020 by a multi-disciplinary team led by family physicians, gastroenterologists and colorectal surgeons.

Pathway Review Process

Specialty access pathways undergo scheduled review every three years, or earlier, if there is a clinically significant change in knowledge or practice. The next scheduled review is June 2028. However, we welcome feedback at any time. Please email comments to albertapathways@primarycarealberta.ca.

Disclaimer

This pathway represents evidence-based best practice, but does not override the individual responsibility of healthcare professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified healthcare professional. It is expected that all users will seek advice of other appropriately qualified and regulated healthcare providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

PROVIDER RESOURCES

Advice Options

Non-urgent gastroenterology advice is available to support family physicians, nurse practitioners, and specialists.

- Electronic advice is available across the province via Alberta Netcare eReferral (responses are received within five calendar days). Visit www.albertanetcare.ca/learningcentre/eReferral.htm for more information.
- Non-urgent telephone advice connects to specialists in real time via a tele-advice line.
    - In the Calgary Zone at specialistlink.ca or by calling 403-910-2551.
    - In the Edmonton and North Zones by calling 1-844-633-2263 or visiting www.pcnconnectmd.com.

PATIENT RESOURCES

Description	Website
Iron Deficiency Anemia Care Instructions	myhealth.alberta.ca/Health/aftercareinformation/pages/conditions.aspx?hwid=uf8380
Anemia Care Instructions	myhealth.alberta.ca/Health/aftercareinformation/pages/conditions.aspx?hwid=uf8147
Iron Test	myhealth.alberta.ca/Health/pages/conditions.aspx?hwid=hw41550&
Celiac Disease Care Instructions	myhealth.alberta.ca/Health/aftercareinformation/pages/conditions.aspx?hwid=abp7938