

This primary care pathway was co-developed by primary and specialty care and includes input from multidisciplinary teams. It is intended to be used in conjunction with specialty advice services, when required, to support care within the medical home. Wide adoption of primary care pathways can facilitate timely, evidence-based support to physicians and their teams who care for patients with common low-risk gastrointestinal (GI) conditions and improve appropriate access to specialty care, when needed. To learn more about primary care pathways, check out this short video or click here to visit the Primary Care Supports webpage

Celiac Disease (CD) PATHWAY PRIMER

Celiac disease (CD) is a genetic disease which can manifest at any age. It is an immune-mediated disorder wherein the consumption of gluten-containing foods (wheat, barley, rye, contaminated oats, triticale, and may be in foods due to cross contact) causes inflammation of the small bowel. This inflammation leads to small bowel villous atrophy, a histologic hallmark of CD which impacts nutrient absorption. Over time, depending on the severity of the damage, this can lead to nutritional deficiencies, weight loss, diarrhea, osteoporosis, infertility, and rarely GI cancers such as small bowel lymphoma.

Approximately 1 in 100-200 people living in Alberta have CD; roughly 40% of these individuals have not been diagnosed, and likely do not know they have the disease.^{1,2}

CD can present with a myriad of symptoms including both GI and non-GI complaints.

- GI symptoms include irritable bowel syndrome (IBS) like features, characterized by varying bowel habits. Often the stool is looser and more frequent than normal, but some patients have constipation instead.
- In children, diarrhea is more common, but this still only accounts for less than 10% of pediatric presentations.
- Many patients with CD have mild GI symptoms that they do not recognize as problematic. For example, they may consider excessive gassiness as normal; only until they have been on a gluten free diet do patients realize what a truly "normal" bowel habit means.
- In the past, many CD patients also presented with weight loss; however, nowadays a CD diagnosis in
 obese or overweight patients is not uncommon.
- Presenting symptoms or features of CD are listed below.

In the past, many patients with CD also presented with weight loss; however, nowadays a CD diagnosis in obese or overweight patients is common.

Checklist to guide in - clinic review of your patient with suspected CD		
Confirm absence of alarm features (see algorithm box 2). If any alarm features are identified, order necessary workup AND immediately refer for specialist consultation.		
Complete Tissue Transglutaminase (TTG IGA) blood test ONLY if patient is eating sufficient gluten, or willing to do the gluten challenge (see algorithm box 3b)		
Order hemoglobin and ferritin as they often are abnormal (prevalence of iron deficiency anemia (IDA) is 5.5% in patients with biopsy-confirmed CD) ³ * If testing reveals unexplained IDA (alarm feature), refer immediately for consultation		
Depending on the clinical situation (e.g., in a patient with diarrhea), consider ordering a fecal calprotectin (FCP); or, for other undifferentiated GI symptoms, one may also consider ordering a serum C-reactive protein (CRP) (see algorithm box 3a)		



EXPANDED DETAILS

1. Suspected Celiac Disease (CD)^{4,5}

The most prominent features that warrant testing for CD include:

- Chronic diarrhea
- IBS-like bowel habit. Typically, this means diarrhea as a predominant symptom, but can also mean predominant constipation, or alternating bowel habit.
- Recurrent abdominal discomfort/pain, bloating, gas, flatulence
- Iron deficiency anemia. This is also an alarm feature which warrants immediate referral for consultation/endoscopy, in addition to TTG IGA testing.
- First degree relative (parent, sibling, or child) with CD. Having a first-degree relative with CD increases one's lifetime risk of CD up to ten-fold over the general population.
 - All first-degree relatives of a person with CD should be checked for the disease at least once, irrespective of having symptoms.
 - For children with a first degree relative with CD, pediatric guidelines recommend testing from age 2 onwards and every 1-2 years during childhood and adolescence.
 - There are no clear guidelines regarding repeated screening for adults; however, if patients with a first-degree family member develop symptoms even after initial negative screening repeat testing is appropriate.

There are also many non-specific symptoms and signs that can constitute the first presentation of CD, the most frequent of which are listed below. **Practitioners should have a low threshold for testing for CD with the following:**

Other GI symptoms and signs

- Weight Loss
- Diarrhea
- Recurrent oral ulcers
- Mildly abnormal liver enzymes (often less than or equal to five times upper limit of normal). CD is present in 3-4% of patients with chronic unexplained mildly elevated transaminases; 27% of newly diagnosed patients with CD may have abnormal serum transaminases.⁶
- Lactose intolerance, which may present with gassiness, bloating, loose stool, mild abdominal discomfort, and rarely severe abdominal pain. Small bowel villous atrophy in untreated CD can lead to lactase deficiency and subsequent lactose intolerance. This abnormality will normalize with a gluten-free diet.

Non-GI Symptoms

- Short stature
- Fatigue/malaise
- Recurrent non-specific headaches
- Difficulty concentrating ("foggy brain")
- Anxiety or mood disturbances
- Recurrent joint aches and pains
- (Early-onset adult) osteoporosis; CD can also present initially as osteopenia.
- Amenorrhea, infertility, recurrent miscarriages
- Peripheral neuropathy presenting as numbness or tingling in the hands/feet.
- Skin rash (dermatitis herpetiformis)⁷

Rare Symptoms/Signs

- Epilepsy with occipital calcifications
- Dental hypoplasia
- Unexplained ataxia
- Anemia secondary to folate or Vitamin B12 deficiency

Patients with these medical conditions have a higher risk of developing CD:

- Personal history of autoimmune conditions, e.g., thyroid disease, diabetes mellitus type 1
- Personal history of certain genetic conditions e.g., Down syndrome (Trisomy 21) or Turner syndrome



2. Alarm Features

Adults

- Onset of symptoms after age 50
- Diarrhea that awakens the patient from sleep
- Visible blood in stool
- Unintended weight loss (more than 5% of original body weight over a 6–12-month period)
- Unexplained iron deficiency anemia (see Iron Deficiency Anemia Pathway)
- Family History (first-degree relative) of colorectal cancer ^{8,9} (See Alberta Colorectal Cancer Screening Guideline)

Pediatrics

• Visible blood in stool

NOTE: if patient has any alarm features, do the following:

- Start workup as described below (see 3a and 3b)
- Refer patient for GI consultation *Do not wait for lab results before referring

3. Celiac Disease Workup and Requirements for Testing and Diagnosis

3a. Investigations/Workup

Initial investigations and workup to be completed:

- A detailed medical history and physical examination should be performed to assess for:
- Other conditions that mimic CD such as inflammatory bowel disease or irritable bowel syndrome (see IBS Pathway).
- Drugs which can cause GI side effects especially diarrhea or constipation. Common culprit drugs are proton pump inhibitors, non-steroidal anti-inflammatories, laxatives, antacids, iron/calcium/magnesium supplements, antidepressants, opioids, metformin, cannabis (which can cause nausea, vomiting, disturbed bowel habit), and some herbal products.
- Laboratory investigations:
 - TTG IGA blood test is the ONLY laboratory test required to screen for CD in Alberta. A patient **must** be eating adequate gluten at the time of the test for accurate results (see 3b below).
 - Do not order other blood tests for CD such as anti-tissue transglutaminase immunoglobulin G antibody (TTG IGG), Anti-Endomysial Antibody (Anti-EMA) or gliadin deamidated antibody IgG and Immunoglobulin A.
 - The standard TTG IGA test performed by laboratories in Alberta automatically detects if the patient
 has sufficient IgA to run the TTG IGA. If there is insufficient IgA, the laboratory will automatically
 reflexively pivot to tests that use an IgG antibody. The subsequent testing is slightly different (TTG
 IGG or Anti-EMA) in in Calgary and Edmonton but will be done automatically in place of the TTG IGA.
- For patients that are eating gluten, the TTG IGA is highly accurate (greater than 95% positive predictive value). A positive test is excellent in being able to detect patients who truly have CD and distinguish them from patients who do not have CD (true positives and true negatives).
- Although a positive TTG IGA result has a greater than 95% accuracy in diagnosing CD, a referral for GI specialist consultation/endoscopic biopsy is still recommended to confirm the diagnosis before committing the patient to a life changing lifelong gluten free diet.
- As iron deficiency is common in CD, consider ordering hemoglobin and ferritin if not performed within the last 6 months.³
- Consider other differentials (e.g., IBS, IBD):
- Consider ordering fecal calprotectin and/or serum CRP to rule out IBD, especially if significant diarrhea.

3b. Requirements for Celiac Disease Testing and Diagnosis

- For patients consuming a gluten-containing diet: order TTG IGA
- For patients consuming a gluten-free diet: complete the Gluten Challenge (see below) before ordering TTG IGA

NOTE: It is impossible to diagnose a patient with celiac disease if they are on a gluten free diet.



- Patients with an elevated TTG IGA should <u>not</u> commence a gluten-free diet while awaiting referral for gastroscopy with small bowel biopsy.
 - It can be difficult for patients to continue/resume eating gluten. For information on the disadvantages to a GFD when it is not medically necessary, see #4 (below).
 - If you strongly feel the patient cannot continue eating gluten, consider an advice service to help you decide on next steps before starting your patient on the GFD
 - If the patient chooses to eliminate gluten after a confirmed-positive TTG IGA, they will need to **restart and complete** a Gluten Challenge before gastroscopy can be done to confirm CD.

Gluten Challenge¹⁰

- At minimum 2 servings of gluten containing food per day x 1-2 months
 - Examples: 2 slices of bread, 1 bagel/pita/wheat tortilla, 1 cup pasta, or 1.5 cups cereal.
 - To assess adequacy, a repeat TTG IGA can be ordered 4 weeks after starting the gluten challenge.
 - If positive, the patient is consuming enough gluten to proceed for the gastroscopy/small bowel biopsy.
 - If negative, a longer duration or higher intake of gluten is recommended prior to the gastroscopy/small bowel biopsy.
- A gluten challenge in children is discouraged if they are malnourished or during certain times of development:
 - Before 5 years of age
 - Prior to the formation of permanent dentition
 - During the pubertal growth spurt
 - Consider consulting a pediatrician before starting a gluten challenge

4. Unable to Diagnose CD

If patient is unwilling or unable to complete the gluten challenge prior to the TTG IGA test, it may not be possible to definitely diagnose CD.

Counsel the patient that:

- It is important to make a definitive diagnosis of CD, as this diagnosis has lifelong dietary implications and requires lifelong monitoring.
- CD is associated with risk of developing other diseases (e.g., type I diabetes/other autoimmune diseases, osteoporosis, heart disease, rarely intestinal cancer, etc.) and possibly having untreated CD may increase the risk of developing them.
- Having a formal diagnosis can improve dietary adherence, which has more dietary restrictions for patients with CD compared to patients with gluten intolerance or gluten sensitivity.
- Eating gluten free is burdensome and more expensive.¹¹ Being formally diagnosed can help with resource access, including for tax credits.
 - A tax deduction may be available to offset some of the extra food costs for patients with CD.
- A gluten-free diet is not necessarily a healthier diet. In fact, gluten-free processed foods can be high in sugar and fat and low in specific micronutrients if not well-managed with dietitian support.
- Making a definitive CD diagnosis via direct testing is preferred. However, for patients that are unwilling to eat gluten, a <u>negative</u> Human Leukocyte Antigen (HLA-DQ2 and HLA-DQ8) genetic test may help to rule out CD.
 - Virtually all patients (99%) who have CD carry the HLA-DQ2, HLA-DQ8 or both genes. If the genetic test is negative, one can say with 99% certainty that the patient does not have nor will develop CD.
 - However, if the genetic test is positive, we still do not know if the patient has CD.
 - 30-40% of the general population have at least one of these genes but only 4% of these will develop CD over their lifetime.¹²
 - Patients who have both genes have a 30% chance of developing CD over their lifetime.



5. If the TTG IGA result is positive, patient likely has CD

- Refer patient for biopsy to confirm CD diagnosis.
- Patient MUST consume sufficient gluten prior to biopsy (see Gluten Challenge, above)

For pediatric patients:

• A pediatric gastroenterologist can make a diagnosis without biopsy according to current pediatric guidelines; however pediatric patients should still be referred to GI consultation while consuming a gluten containing diet.

6. Celiac Disease NOT suspected

6a. If the TTG IGA result is negative OR the biopsy does not confirm celiac disease, it is very unlikely that patient has CD

- Based on the predominant GI symptoms, consider referring to other pathways such as IBS, chronic diarrhea, chronic constipation, or chronic abdominal pain for recommendations on further assessment and management.
- The patient may instead have gluten intolerance or non-celiac gluten sensitivity.

6b. Gluten Sensitivity/Intolerance is NOT Celiac Disease

- Gluten ingestion may cause symptoms in the absence of true celiac disease this is referred to as gluten intolerance or non-celiac disease gluten sensitivity. Such patients may have GI symptoms and non-GI symptoms, such as chronic fatigue, concentration difficulties ("foggy brain") and joint pains that are perceived to be or are truly related to gluten intake. However, if their TTG IGA is normal (while eating gluten) and duodenal biopsies are negative, the patient does not have CD.
- Patients with gluten sensitivity should **never** have an elevated TTG IGA at any time. If they do, they likely have CD and should be referred accordingly.
- Most individuals who believe they are gluten sensitive and have fewer symptoms on a low-gluten diet are not actually following a 100% gluten-free diet. TTG IGA tests and small bowel biopsies are usually normal in these patients; however, the TTG IGA and histology will not be reliable if they are truly eating gluten-free.

7. General principles of management, possibly in conjunction with a GI specialist

- Continuous long-term follow up by health professionals (GI specialist, family physician and/or dietitian) is important.
- The lifelong cornerstone of treatment of CD is being 100% gluten-free (avoiding wheat, rye, barley, contaminated oats, triticale and associated cross-contamination). This is very difficult, expensive, and requires a major change in eating habits.
- Gluten free products can be high in fat, sugar, and salt, and often low in fiber, iron, and B vitamins. This may put the patient at risk of cardiometabolic and other disorders¹³ if the diet is not optimized.
- Women of child-bearing age may warrant folate monitoring or supplementation.

We strongly recommend early referral to a dietitian in long term follow up. Registered Dietitians complete nutritional assessments, address nutrient deficiencies, provide education and support on food labelling, nutrient content of gluten-free foods, food preparation, cross-contamination, dining out, etc. See Referral to a Registered Dietitian (below).



"C-E-L-I-A-C" – principles of CD management

- **C**onsultation with a Registered Dietitian for nutrition education and for recommended vitamin and mineral supplementation
 - See Alberta Referral Directory (search: nutrition counselling)
 - Visit Alberta Health Services Nutrition Services for programs and services offered by Zone
 - Patients can access workshops and classes facilitated by dietitians at ahs.ca/NutritionWorkshops (search "celiac")
 - If a patient has a nutrition question, they can call 811 and ask to talk to a dietitian or visit ahs.ca/811 to complete a self-referral form
- Education about the disease through Celiac Canada and the importance of testing first degree family members
- Lifelong adherence to a strict gluten-free diet and of evaluation of compliance. See compliance scoring tool at Celiac Canada: Gluten Free Diet Compliance Score
- dentification and treatment of nutritional deficiencies
 - Screen and treat for iron deficiency at presentation (CBC, ferritin)
 - For patients with malabsorption or malnutrition, consider additional tests (e.g., 250H vitamin D, folate, vitamin B12)
 - Consider an age-appropriate and gluten-free multivitamin and mineral supplement.
 - Consider other initial testing to identify complications and coexisting conditions at presentation:
 - Hemoglobin A1c, thyroid stimulating hormone
 - Alanine transaminase (ALT), aspartate transferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), and bilirubin
- Access to an advocacy group such as the local chapters of Celiac Canada
- **C**ontinuous long-term follow up
 - If patient has seen a GI, establish who will do the follow up testing.
 - In general, a repeat TTG IGA should be done in 6 months after starting a gluten-free diet. In most patients the TTG IGA should improve by 6 months, but it may take up to 2 years to fully normalize. (Frequency of testing depends in part on how much the TTG IGA is improving)
 - Once the TTG IGA is normal:
 - Do a lifelong annual TTG IGA, hemoglobin, and possibly ferritin. Follow up any abnormal baseline testing (HbA1C, liver chemistry, thyroid tests, etc.)
 - Iron and other nutrient deficiencies (specifically ferritin, folate, vitamins D and B12) should improve.
 - o Symptoms such as bloating, diarrhea should also improve.
 - In a small proportion of patients, the TTG IGA will decrease but not fully normalize within two years. In this case:
 - o consider re-referral to a GI, especially if TTG IGA remains markedly abnormal.
 - consider re-referral to a Dietitian to explore patient's diet. Poor compliance to a GFD is a common (90%) reason why TTG IGA does not normalize. This could be due to a knowledge gap, food insecurity, or more.
 - Vaccinations
 - Patients with CD are at increased risk for pneumococcal infections; pneumonia vaccination is recommended in all people more than 65 years.
 - Encourage annual influenza vaccination.
 - If CD is diagnosed in an adult, consider doing a bone density as there is an increased risk of osteopenia and osteoporosis at a younger age.
 - One-time DEXA scan (considered after one year on GFD in individuals at risk for developing osteopenia or osteoporosis)¹⁴
 - Follow up biopsies can be considered at one year after diagnosis. This helps to prove that the GFD is working and may also be a motivator for patients to stick to a GFD. This is more often done in adults than children. The decision to re-biopsy is often made by the GI specialist. Repeat biopsy should be considered if TTG IGA is not improving despite adherence to a GFD.



• If patient has an unsatisfactory response to management

- In a small percentage of patients with CD the TTG IGA does not fully normalize by 1-2 years. These patients and those with persistent or new-onset symptoms (even well after their diagnosis) may need to be reassessed by a GI specialist.
- Consider using an advice service before re-referring for GI specialist consultation.

• Refer patient for Consultation/Endoscopy if:

- Suggested by advice service.
- Patient has any alarm features (see # 2, above)

Still concerned about your patient?

The primary care physician is typically the provider who is most familiar with their patient's overall health and knows how they tend to present. Changes in normal patterns, or onset of new or worrisome symptoms, may raise suspicion for a potentially serious diagnosis, even when investigations are normal and typical alarm features are not present. There is evidence to support the importance of the family physician's intuition or "gut feeling" about patient symptoms, especially when the family physician is worried about a sinister cause such as cancer. A meta-analysis examining the predictive value of gut feelings showed that the odds of a patient being diagnosed with cancer, if a GP recorded a gut feeling, were 4.24 times higher than when no gut feeling was recorded ¹⁵

When a "gut feeling" persists in spite of normal investigations, and you decide to refer your patient for specialist consultation, document your concerns on the referral with as much detail as possible. Another option is to seek specialist advice to convey your concerns.



BACKGROUND

About this Pathway

- Digestive health primary care pathways were originally developed in 2015 as part of the Calgary Zone's Specialist LINK initiative. They were co-developed by the Department of Gastroenterology and the Calgary Zone's specialty integration group, which includes medical leadership and staff from Calgary and area Primary Care Networks, the Department of Family Medicine, and Alberta Health Services.
- The pathways were intended to provide evidence-based guidance to support primary care providers in caring for patients with common digestive health conditions within the patient medical home.
- Based on the successful adoption of the primary care pathways within the Calgary Zone, and their impact on timely access to quality care, in 2017 the Digestive Health Strategic Clinical Network (DHSCN) led an initiative to validate the applicability of the pathways for Alberta and to spread availability and foster adoption of the pathways across the province.

Authors & Conflict of Interest Declaration

This pathway was reviewed and revised under the auspices of the DHSCN in 2023, by a multi-disciplinary team led by family physicians and gastroenterologists. For more information, contact the DHSCN at Digestivehealth.SCN@ahs.ca.

Pathway Feedback and Review Process

Primary care 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 Spring 2027 however, we welcome feedback at any time. Please email comments to Digestivehealth.SCN@ahs.ca.

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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 health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.



PROVIDER RESOURCES

Advice Options for Adults

Non-urgent advice is available to support family physicians.

- Gastroenterology electronic advice is available through Alberta Netcare eReferral (responses are received within five calendar days). View the eReferral Quick Reference page for more information.
- Non-urgent telephone advice connects family physicians and specialists in real time via a tele-advice line. Family physicians can request non-urgent advice from a gastroenterologist:
 - In the Calgary Zone at specialistlink.ca or by calling 403-910-2551. This service is available from 8:00 a.m. to 5:00 p.m. Monday to Friday (excluding statutory holidays). Calls are returned within one (1) hour.
 - In the Edmonton, Central, and North Zones by calling 1-844-633-2263 or visiting pcnconnectmd.com This service is available from 9:00 a.m. to 6:00 p.m. Monday to Thursday and from 9:00 a.m. to 4:00 p.m. Friday (excluding statutory holidays and Christmas break). Calls are returned within two (2) business days.

Advice Options for Pediatrics

Non-urgent advice is available to support family physicians.

- Non-urgent electronic advice is available through Alberta Netcare eReferral (responses are received within five calendar days). View the eReferral Quick Reference page for more information.
 - Community pediatrics advice is available in the Calgary Zone
 - Pediatric gastroenterology advice is available in the Edmonton Zone
- Non-urgent telephone advice connects family physicians and specialists in real time via a tele-advice line. Family physicians can request non-urgent advice from a pediatrician:
 - In the Edmonton and North Zones by calling 1-844-633-2263 or visiting pcnconnectmd.com .This service is available from 9:00 a.m. to 6:00 p.m. Monday to Thursday and 9:00 a.m. to 4:00 p.m. Friday (excluding statutory holidays and Christmas break). Calls are returned within two (2) business days.
 - In the Calgary Zone at specialistlink.ca or by calling 403-910-2551. This service is available from 8:00 a.m. to 5:00 p.m., Monday to Friday (excluding statutory holidays). Calls are returned within one (1) hour.

Nutrition Services (Adults and Pediatrics)

To refer your patient to a Registered Dietitian:

- Visit Alberta Referral Directory and search for nutrition counselling.
- To learn more about programs and services offered in your zone, visit ahs.ca/Nutrition.
- Health Link has Registered Dietitians available to answer nutrition questions. If a patient has a nutrition question, they can complete a self-referral at ahs.ca/811 or call 811 and ask to talk to a dietitian.

Resources	
Nutrition Guideline for Health Professionals: Gluten-free Diet	Nutrition Guideline: Gluten-free Diet (ahs.ca)
Canadian Celiac Association Resources (celiac.ca)	Resources & Brochures
	Celiac Disease: Oral and Dental Complications
	Celiac Disease for Health Professionals



Patient Resources

Description	Website
General information on celiac disease	MyHealthAlberta - Celiac Disease
Talk to a dietitian	Click <u>Health Link</u> or call 8-1-1 and ask to talk to a Dietitian
Nutrition Education Materials	Alberta Health Services-Nutrition
Going Gluten Free class through Alberta Healthy Living Program	Celiac Disease-Going Gluten Free (search 'Celiac')
Canadian Celiac Association Resources (celiac.ca)	What is Celiac Disease Pamphlet
	Gluten Free Diet Brochure
	Celiac Disease Myths and Facts
	Celiac Disease Blood Testing
	Celiac Disease and Seniors
	Gluten-free Food Guide for Children & Youth

PATIENT PATHWAY

<u>Celiac Disease patient pathway</u>



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