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Differentiating Celiac Disease, Lactose Intolerance, and Irritable Bowel Syndrome in the Primary Care Setting

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ABSTRACT

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The purpose of this paper is to assist nurse practitioners (NPs) and other primary care providers in differentiating between celiac disease (CD), lactose intolerance (LI), and irritable bowel syndrome (IBS) in adults. The Health Source: Nursing/Academic Edition, CINAHL, MEDLINE (EBSCO) search engines were utilized to access systematic reviews and primary research articles published between 2009–2016. Current literature supports that a thorough history and physical must be conducted and alarming symptoms must be investigated to rule out worrisome diagnoses. Based on subtle characteristics gathered from the history and physical, the NP's examination and testing will help distinguish CD, LI, and IBS. Nurse practitioners should use a sequential process of examination and testing (see Figure-1) to distinguish gastrointestinal disorders that share common symptoms.

Keywords: celiac disease, lactose intolerance, irritable bowel syndrome, diarrhea

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and Irritable Bowel Syndrome in the Primary Care Setting

Gastrointestinal (GI) disorders are frequently seen in primary care settings and commonly include celiac disease (CD), lactose intolerance (LI), and irritable bowel syndrome (IBS). However, these disorders are often difficult to differentiate because each condition share common symptoms such as abdominal pain, bloating, gas, and diarrhea. These often vague and commonplace symptoms make the diagnosis difficult and contribute to delay in diagnosis. Patients who develop CD as adults gradually experience abnormal symptoms of diarrhea and steatorrhea, and as a result these patients may perceive their symptoms as being normal (Brody & Murray, 2014). For example, it takes approximately one year (and sometimes even as long as 10 years) for patients with CD to be diagnosed after GI symptoms appear (Ford et al., 2009; Fuchs et al., 2014). Likewise, 10–15% of the population in the United States is affected by IBS, but only 5–7% are actually diagnosed (National Digestive Diseases Information Clearinghouse, 2013), and usually only after their primary care provider (PCP) has referred them to a gastroenterologist (El-Salhy, Lomholt-Beck, & Gundersen, 2011).

Abdominal complaints comprise 30–50% of reported cases in the primary care setting; therefore, nurse practitioners (NPs) must be well versed in GI-related disorders. Although CD, LI, and IBS present with similar symptoms, the pathology differs, and, if misdiagnosed, irreversible GI damage and nutritional deficiencies might result. According to Pironti et al. (2010), patients complaining of chronic diarrhea and/or abdominal pain suffer from microscopic damage due to an underlying pathological process 81% of the time. Therefore, it is imperative that NPs make accurate and timely diagnoses not only to prevent

pathological disease processes from ensuing, but to improve their patient's quality of life (Schuppan & Zimmer, 2013; Strauch & Cotter, 2011; Thom, Longo, Running, & Ashley2009). Accordingly, the purpose of this paper is to introduce NPs to a systematic approach for successfully differentiating CD, LI, and IBS in adults.

Methods

Collectively, there are few systematic reviews and meta-analyses published on distinguishing CD, IBS, and LI; there are, however, a variety of research studies available on these topics individually. Data were accessed through several search engines. First, the Cochrane Database was accessed to identify any meta-analyses studying these disorders conjointly. Next, the Health Source: Nursing/Academic Edition, CINAHL, MEDLINE (EBSCO) search engines were used to access articles published in English between 2009–2015. Search terms included "celiac," "CD," "lactose intolerance," "LI," "irritable bowel," "IBS," and "diagnose."

Background Information on CD, LI, and IBS

Celiac Disease

Affecting 0.5–1% of people worldwide, CD is a genetically or autoimmune based chronic enteropathy of the small intestine that is caused by an intolerance to gluten (Mehdi, Sakineh, Mohammad, Mansour, & Alireza, 2012; Schuppan & Zimmer, 2013). Gluten is a complex of water-soluble protein that is a component in wheat, barley, bulgur, durum, rye, and spelt. Other foods containing gluten that patients might be unfamiliar with, include beer, candy, gravies, imitation meats or seafood, processed luncheon meats, salad dressings, soy sauce, self-basting poultry, and some soups (The Mayo Foundation, 2013). People who have the genetic predisposition for CD typically carry the HLA-DQ2 or HLA-

DQ8 genes (90% and 10%, respectively) (Schuppan & Zimmer, 2013; Strauch & Cotter, 2011). Patients with genetic-based and autoimmune diseases (especially Turner syndrome, Down syndrome, type I diabetes mellitus [DM 1], and thyroid disease), as well as first-degree relatives of patients with CD, are considered to be high risk for developing CD. This genetic link causes class II human leukocyte antigens to produce autoantibodies against the enzyme tissue transglutaminase (tTG), which becomes activated in the presence of gluten (Schuppan & Zimmer, 2013; Strauch & Cotter, 2011). As this autoimmune process proceeds, it damages the villi lining the mucosa of the small intestine and alters the environment where nutrients are absorbed (Leffler & Schuppan, 2010). Once diagnosed, this inflammation can be managed simply by excluding gluten from the diet (El-Salhy et al., 2011; Ford et al., 2009).

Celiac disease involves a variety of symptoms with both gastrointestinal and systemic manifestations, usually lasting longer than 3 months. A patient typically presents with diarrhea, unexplained weight loss, abdominal distention, bloating, dyspepsia, and flatulence (Schuppan & Zimmer, 2013). It is not uncommon for pain to be specifically located in the right lower abdomen, and even accompanied by a palpable mass, raising suspicions of appendicitis or Crohn's disease (Gikas & Triantafillidis, 2014). Systemic manifestations of CD include migraines, chronic fatigue, depression, irritability, Duhring's dermatitis herpetiformis, oral aphthous ulcers, loss of dental enamel, iron-deficiency anemia, anorexia, osteoporosis, joint pain, growth failure, short stature, delayed puberty, amenorrhea, early menopause, reduced fertility, and epilepsy (Boettcher & Crowe, 2013; Kurppa et al., 2009; Rubio-Tapia, Hill, Ciarán, Calderwood, & Murray, 2013; Strauch & Cotter, 2011). Patients who presented with coexisting musculoskeletal or neurological

disorders, diarrhea, abdominal pain, iron-deficiency anemia, or female, were found to have experience a diagnostic delay before being diagnosed with CD (Fuchs et al., 2014). It is important for NPs to recognize these systemic manifestations to distinguish CD from other bowel disorders.

Lactose Intolerance

Lactose intolerance is the most common metabolic food sensitivity, affecting 60–70% of people worldwide. Approximately 20% of those affected are Europeans and Americans (Carter & Attel, 2013; Perets et al., 2014). Primary lactose deficiency is the most common cause of LI and is found most frequently in South America, Africa, Asia, and descendants from those areas. Secondary lactose deficiency results from injury and inflammation of the brush border of the small intestine, and can also be caused by bacterial overgrowth, gastroenteritis, CD, and disorders that cause rapid gastrointestinal motility (Carter & Attel, 2013; Yang et al., 2013). Lactose intolerance usually begins in childhood, but it is most prevalent in adulthood, because the lactase enzyme progressively decreases over the lifespan (Boettcher & Crowe, 2013; Furnari et al., 2013; Perets et al., 2014). Lactase persistence is a term used to describe the capability of being able to digest lactose as an adult. About two thirds of people in the world do not carry the genetic makeup that allows for lactase production, and are therefore lactase non-persistent. Genetic testing is available to identify people who are lactase non-persistent, and can be screened for the C/C (-13910) genotype (sensitivity 93% and specificity 100%). Additional testing is available for the T/C (-13910) gene, but these patients can either be lactase persistent or non-persistent (Baffour-Awuah et al., 2015).

Lactose is a disaccharide sugar found in dairy products such as milk, yogurt, and cheese that requires the lactase enzyme to break it down into glucose and galactose. Inadequate levels of the lactase enzyme result in abdominal discomfort, bloating, gas, and diarrhea, because undigested lactose in the colon is fermented by bacteria (Boettcher & Crowe, 2013; Campbell et al., 2010; Carter & Attel, 2013). People with LI can generally tolerate 12 grams of lactose (1 cup of milk) with symptoms typically beginning when 40 grams of lactose are ingested. However, if minute amounts of lactose cause distressing symptoms, a rare disorder called congenital lactase deficiency should be considered (Bolin 2009; Campbell et al., 2010; Yang et al., 2013). Studies have shown that diarrhea pre-dominant IBS (IBS-D) patients release greater amounts of inflammatory cells after lactose ingestion compared to the average person, and find symptom relief with a lactose-free diet (Yang et al., 2014). Although lactose intolerance is quite common, it can be difficult to differentiate when it coexists with other disorders, such as IBS and CD.

Irritable Bowel Syndrome

Irritable bowel syndrome affects 10–15% of the world's population (but most cases are concentrated in North America), is a set of GI symptoms resulting from irregular relaxation and contraction of the bowel (National Digestive Diseases Information Clearinghouse, 2013). These symptoms are thought to originate from an alteration in the neuromuscular function of the smooth muscle lining of the large bowel, which normally relaxes and contracts in a coordinated rhythm (Bolin, 2009; Ford et al., 2009; Mayo Foundation for Medical Education and Research, 2011). Evidence has supported the idea that there may be a connection between excessive microflora in the gut, as well as excessive inflammation and cytokine activity (Simsek, 2011; Yang et al., 2014). Risk factors for IBS include female

gender, being between the ages of 20–40, and having psychosocial issues such as anxiety, depression, personality disorders, and abuse (Chapman, Chen, & Leaver, 2015; Simsek, 2011). The four subtypes of IBS are IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), mixed IBS (IBS-M), and unsubtyped IBS (IBS-U). It is notable that IBS-D is the subtype most frequently confused with other bowel disorders. These patients typically experience diarrhea and abdominal cramping that mainly occurs in the mornings and after meals. Other complaints include mucus in the stool, fecal incontinence, feelings of incomplete evacuation, and pain relieved by defecation (Yang et al., 2013; Yang et al., 2014). Anorexia, steatorrhea, nocturnal pain or diarrhea, progressive pain, and bloody stools are abnormal and considered inconsistent with the diagnosis of IBS-D, thus requiring further testing (Chapman et al., 2015). Irritable bowel syndrome does not cause permanent damage to the colon or increase the risk for colorectal cancer, although it does severely impact patients' quality of life. There is a possibility that CD and IBS-D can coexist simultaneously, but there are conflicting results supporting routine screening of these concurrently (Bakhshipour et al., 2012; Cash, 2011; El-Salhy et al., 2011; Shahbazkhani et al., 2003).

Current Recommendations for Diagnosing CD

Serological Testing

Diagnosis of CD first begins with serological screening for antibodies (Kurppa et al., 2009; Tortora et al., 2014). The first-line serological test is the tissue transglutaminase antibody (IgA a-tTG), which has high sensitivity (90–98%) and specificity (95–97%), is inexpensive, reliable, and easy to interpret. A "Total IgA" level should be tested simultaneously because 2% of people with CD have an IgA deficiency and, therefore, might falsely test negative for IgA a-tTG. Patients who have an IgA deficiency with the initial

testing for the "IgA a-tTG" and "Total IgA levels" should instead be tested for the IgG anti-DGP serum antibody (Brody & Murray, 2014; Ford et al., 2009; Leffler & Schuppan, 2010; Schuppan & Zimmer, 2013; Thom et al., 2009). It is imperative that patients are not on a gluten-free diet at the time of lab work because the absence of gluten in the diet gives falsely normal test results. Patients who have negative serology as a result of being on a gluten-free diet can be screened via the IgA a-tTG and IgG anti-DGP, and, if either serology is positive, can proceed to upper endoscopy with small bowel biopsy. If these patients were on a gluten-free diet and their serology tests are negative, they can be screened for HLA-DQ2/DQ8 genes. If these genetic markers are negative, it can be assumed that they do not have CD. On the other hand, if they are positive, these patients should participate in a gluten challenge diet. Gluten should be present in the diet for at least 2 weeks (optimally 8 weeks), after which serological testing can be performed. If serology is negative, then the patient should continue a gluten diet for 6 more weeks and be retested for the IgA a-tTG, Total IgA, and IgG anti-DGP serum antibodies (Brookes & Murray, 2014; Schuppan & Zimmer, 2013).

Endoscopy

If serology is positive, or if there is a high probability of CD, patients should be referred to a gastroenterologist for an upper endoscopy and small bowel biopsy (Kurppa et al., 2009; Rubio-Tapia et al., 2013). As mentioned earlier, CD risk factors include having a first-degree relative with CD; an autoimmune predisposition, especially type 1 diabetes mellitus and thyroid disease; or Down syndrome. A person with severe diarrhea, weight loss, and anemia is at moderate to high risk for having CD (Leffler & Schuppan, 2010). During endoscopy, at least four biopsies from the duodenum, and at least two biopsies from the

duodenal bulb must be obtained for accurate results. These samples are graded according to the MARSH III criteria, which categorizes the severity of the patchy, inflamed lesions of the small bowel. Debate exists regarding other non-invasive approaches to confirm CD, but endoscopy with duodenal biopsy is considered the "gold standard" for diagnosis (Kurppa et al., 2009; Schuppan & Zimmer, 2013; Strauch & Cotter, 2011).

Alternative Testing for CD

Current trends include the use of alternative, less-invasive methods to rule out CD, especially for the elderly and high-risk populations who might not tolerate endoscopy. Capsule endoscopy, where an encapsulated camera is ingested and passed through the GI tract, may be performed if the patient refuses endoscopy and no alarm symptoms are present. Another option, although not the preferred method, is to use a combination of antibody titers to predict the amount of damage caused to the small intestine. Tortora and his team (2014) found that the presence of a-tTG levels (> 62.4) accompanied by elevated EMA levels (> 45 U/mL) were diagnostic for small bowel damage. Rapid CD tests are available over-the-counter, but there is little evidence that they are diagnostic for CD. Korkut et al. (2010) reported that the rapid BioCard Celiac Test was accurate in identifying all patients who had biopsy-proven CD. However, more research must be conducted to determine if these rapid tests will be feasible for use in primary care clinics. Ultimately, endoscopy is the most effective way to diagnose CD, but capsule endoscopy, antibody titers, and rapid CD tests are alternative options in a non-compliant patient (Bolin, 2009; Schuppan & Zimmer, 2013; Strauch & Cotter, 2011).

Current Recommendations for Diagnosing LI

The diagnosis of LI typically involves eliminating dietary lactose for 2 weeks to determine if symptoms improve. It is sufficient to diagnose a patient with LI if GI complaints resolve with a lactose free-diet. However, patients who refuse to adhere to a trial of lactose elimination should proceed with the Lactose Hydrogen Breath Test (HBT) (sensitivity [69–100%] and specificity [89–100%]), which is non-invasive and cost-effective. During the HBT, individuals are given 2g/kg of lactose and are tested for hydrogen detected in their breath at baseline (fasting for at least 12 hours) and in 30-minute intervals for 3 hours. Participants who have a persistent rise in their hydrogen breath level by 20 ppm are considered HBT positive (Ghoshal, Kumar, Chourasia, & Misra, 2009; Perets et al., 2014; Yang et al., 2013). Efficacy of testing for LI using the HBT was found to be dependent on whether there was adequate preparation. False positive results are seen with inadequate pretest fasting or recent smoking (within 6 hours of testing), and false negative results occur with antibiotic use, diabetes, bacterial overgrowth of the small intestine, gastric emptying issues, or underlying pulmonary disorders because these factors can affect the amount of hydrogen levels detected in the breath of patients (Carter & Attel, 2013). An alternative option to the HBT is the Lactose Tolerance Test (LTT), but the LTT has a lower sensitivity (77–96%) and specificity (76–94%). The HBT is also more convenient because it monitors the presence of hydrogen, which is a byproduct of undigested lactose, whereas the LTT requires consecutive blood samples to monitor for glucose absorption in the blood to indicate whether or not lactose is being broken down in the small bowel (Furnari et al., 2013).

A patient who has a negative HBT or LTT but continues to display abnormal GI symptoms after consuming lactose may receive genetic testing or undergo a biopsy-based Lactose Intolerance Quick Test (LIQT), which has a sensitivity, specificity, and positive predictive value nearing 100%. A biopsy sample, taken during endoscopy, from the duodenum is incubated with lactose for 20 minutes and observed for a reaction. However, because of its high cost and invasiveness, the PCP should order LIQT testing very conservatively. Genetic testing of the C/C (-13910) and T/C (-13910) genes is an alternative option, but is also costly (Carter & Attel, 2013; Furnari et al., 2013; Perets et al., 2013).

Current Recommendations for Diagnosing IBS-D

Unfortunately, there are no specific tests that directly detect IBS-D; the diagnosis is made only after ruling out other diseases that have similar GI symptoms (El-Salhy et al., 2011). Alarm symptoms such as rectal bleeding, anemia, and weight loss are consistent with a pathological illness, and should be investigated aggressively. This investigation should include invasive testing such as endoscopy and colonoscopy and a consultation with gastroenterology. For cases of chronic diarrhea (lasting longer than 2 to 4 weeks) the most basic serological tests should include a complete blood count, C-reactive protein, and CD serology (Chapman et al., 2015). Additional tests include stool studies, especially if the patient has recently traveled abroad or been hospitalized. Essentially, the patient's specific clinical history and background should dictate the provider's choice of testing (Bolin, 2009; Ford, 2009; National Digestive Diseases Information Clearinghouse, 2013).

If there are no alarm symptoms that need to be investigated, the ROME III criteria questionnaires provide a positive approach to diagnose IBS. After the exclusion of other

diagnoses, the ROME III criteria can be used to substantiate a diagnosis of IBS. Examples of the ROME III criteria include the presence of recurrent abdominal pain or discomfort for at least 3 days/month in the last 3 months that is associated with *two or more* of the following: Improvement with defecation, onset associated with a change in frequency of stool, or a change in form or appearance of stool (Chapman et al., 2015; Gikas & Triantafillidis, 2014; Rome Foundation, 2006). A positive Rome III screening correlates with a three-fold greater likelihood of having IBS (Ford et al., 2013).

On the other hand, there is controversy regarding the use of subjective questionnaires to substantiate a final diagnosis of IBS-D. Research has shown that questionnaires, including the ROME III criteria, have a sensitivity and specificity of approximately 70%. This is attributed to the fact that such questionnaires are solely based on patient-reported symptoms (Bolin, 2009; Chapman et al., 2015). In fact, 20–50% of patients with confirmed CD meet the ROME criteria for IBS, highlighting the potential inaccuracy of questionnaires (Korkut et al., 2010; Rubio-Tapia et al., 2013). In order to address gaps in the ROME III criteria, Pimentel et al. (2010) developed a questionnaire that focuses on irregular bowel patterns, such as monitoring intensity of symptoms and their changes over time. It includes questions regarding unpredictable bowel habits that occurred on a daily basis, and were correlated most specifically with three or more weekly variable stool forms (Pimentel et al., 2010). Because IBS-D is technically a diagnosis of exclusion, the key factor is first to exclude life-threatening illnesses and to keep CD and LI in the differential when assessing a patient for IBS-D.

Discussion

Numerous gastrointestinal issues exist, and even as signs and symptoms manifest themselves, identifying the specific issue can be complicated. Complaints of abdominal pain, bloating, gas, and diarrhea are often present in CD, LI, and IBS and contribute to a delay in diagnosis. For example, ordering a series of stool studies is appropriate if the patient has recently traveled internationally or has been hospitalized. Likewise, when CD is the top differential, it is crucial that the NP screens for a family history of CD and other autoimmune diseases. The NP must also thoroughly evaluate the patient for systemic manifestations of CD such as anemia, dermatitis herpetiformis, dental enamel defects, aphthous ulcers, infertility, and osteoporosis. When IBS-D is highly suspected, at the very least a CBC, CRP, and CD serology should be analyzed. On the other hand, it is possible for different combinations of CD, LI, and IBS to coexist.

Limitations

There are several limitations of this literature review, many of which are attributable to the fact that some information was gathered from studies performed worldwide. Celiac disease, LI, and IBS each have an effect on specific international populations, and synthesizing data into one composition of evidence could influence the results that were obtained. Many of the studies that were pertinent to LI involved persons of Asian descent. The majority of these studies were performed on adults ages 18–75, and results might not be as valuable in assisting NPs in addressing GI issues in the pediatric population. There was no personal benefit, bias, or monetary gain in the process of collecting published literature.

Conclusion

Celiac disease, LI, and IBS present with similar common symptoms, which can be misleading and contribute to a delay in diagnosis. The NP must be exceptionally thorough in obtaining the patient's history and performing the physical examination in order to identify subtle clues that would direct him or her toward the correct diagnosis. A patient's age, ethnicity, gender, family history, psychosocial history, recent travel and hospitalization, diet, and timing of symptoms should be addressed. It is critical that patients with alarm symptoms (fatigue, weight loss, nocturnal diarrhea, and blood in the stool) are referred to gastroenterology for more aggressive testing, which would likely involve endoscopy. The NP can use the algorithm (Figure-1) and table (Table-1) provided when he or she encounters patients presenting with symptoms such as abdominal pain, bloating, gas, and diarrhea. These should be referenced and utilized in accordance with the patient's clinical history and physical examination. However, the NP should also consider other differentials and order additional testing that would be appropriate for the individual's presentation. The purpose of this paper is to prepare NPs to identify patients who are affected by CD, LI, or IBS in order to quickly and efficiently provide treatment options and improve their patients' quality of life. Therefore, it is critical for NPs to be prepared with a process to distinguish bowel disorders, prioritize differential diagnosis, and order appropriate tests that would guide them in their diagnosis of CD, LI, and IBS, and furthermore prepare them with tests that consulting specialists might anticipate.

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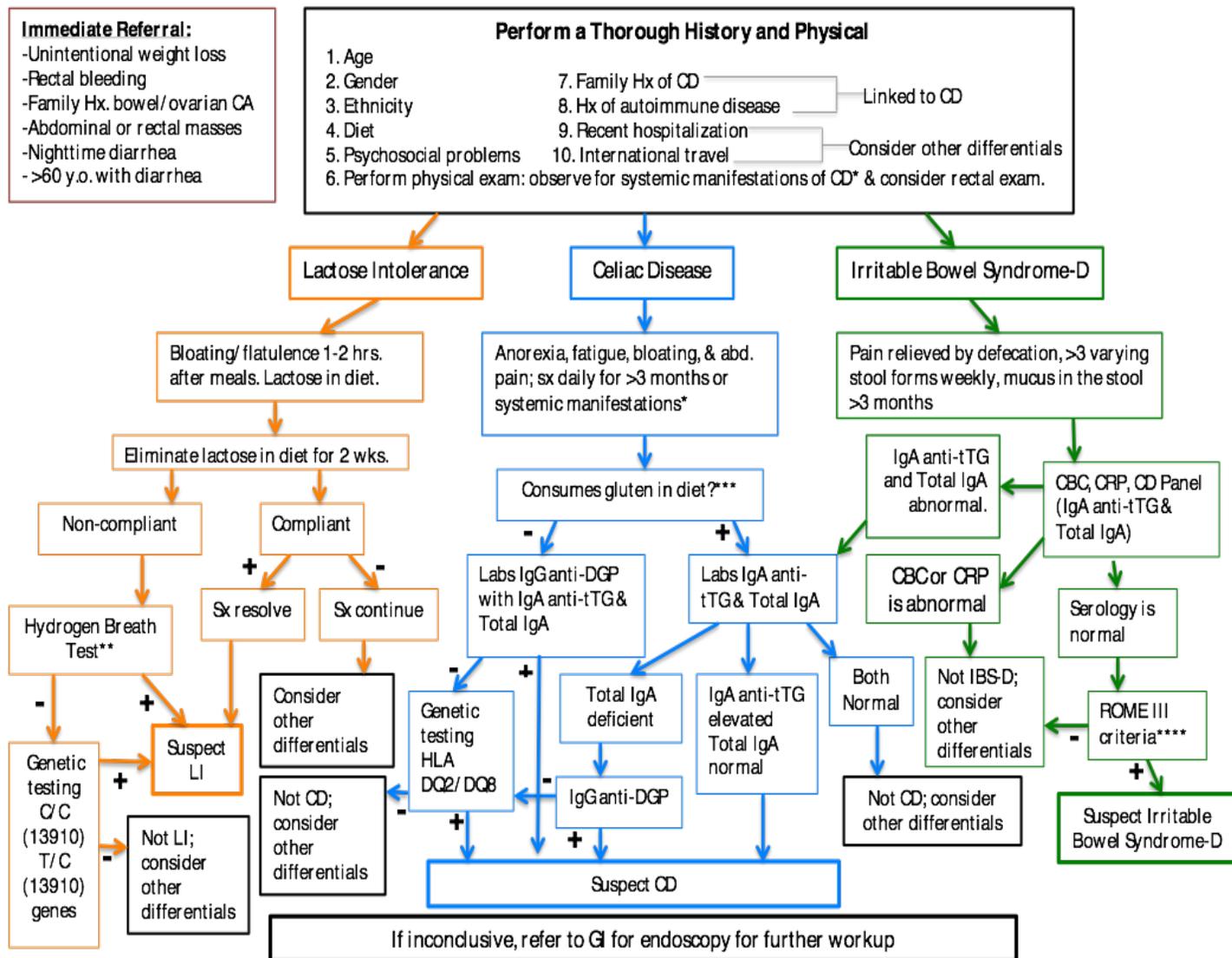Association, 11*(3), 262–268.e261. doi: 10.1016/j.cgh.2012.11.034

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Table-1. Characteristics differentiating CD, LI, and IBS

Disease Type	Population	Risk Factors	Signs & Symptoms	Timing of Symptoms	Tests
Celiac Disease	1% of world Males and females All ages All ethnicities, but most prevalent in Europeans	Genetics: HLA-DQ2 & DQ8 genes 1° or 2° relative with CD Having another autoimmune disease	*Typical symptoms:* Anorexia Diarrhea Bloating Abdominal pain *Systemic symptoms**	Daily Symptoms present gradually Symptoms have been present longer than 3 mos.	IgA-tTG & Total IgA. If Total IgA is deficient, then test the IgG anti-DGP If serology is positive, proceed with endoscopy & duodenal biopsy
Irritable Bowel Syndrome	10–15% worldwide Females Ages 20–40 North America	*Mental health history* (anxiety, depression, personality disorders, history of abuse) *Family history*	Pain relieved by defecation Varying stool forms (>3/wk) Mucus in the stool Bloating Abdominal Pain Cramping Diarrhea	Usually > 3 mos. Waking hours (mornings and after meals)	Process of elimination. CBC, CRP, and (IgA-tTG/ Total IgA) Rome III Criteria
Lactose Intolerance	60–70% worldwide Increases with age All ethnicities, but most common in Asians, African Americans, Indians, Hispanics	*Genetics:* C/C (-13910) & T/C (-13910) *Injury or diseases affecting the small intestine:* (i.e., bacterial overgrowth, CD, post-surgery or chemotherapy etc.)	Diarrhea Nausea Bloating Abdominal Cramping Flatulence Vomiting	Post-lactose ingestion (usually 1–2 h after meals)	Lactose Elimination diet for 2 wks. Hydrogen Breath Test Lactose Intolerance Quick Test *Genetic Testing* C/C (-13910) & T/C (-13910)

Systemic Symptoms for CD: Iron-deficiency anemia, lactose intolerance, chronic fatigue, joint pain, osteoporosis, migraines, depression, irritability, epilepsy, vitamin deficiencies, protein-calorie malnutrition, short stature, failure to thrive, delayed puberty/early menopause, infertility, dental enamel defects, recurrent aphthous stomatits, dermatitis herpetiformis, and other autoimmune disorders.

Figure-1. Systematic Approach for Differentiating CD, LI and IBS

Immediate Referral:
- Unintentional weight loss
- Rectal bleeding
- Family Hx. bowel/ovarian CA
- Abdominal or rectal masses
- Nighttime diarrhea
- >60 y.o. with diarrhea

Perform a Thorough History and Physical
1. Age
2. Gender
3. Ethnicity
4. Diet
5. Psychosocial problems
6. Perform physical exam: observe for systemic manifestations of CD* & consider rectal exam.
7. Family Hx of CD
8. Hx of autoimmune disease — Linked to CD
9. Recent hospitalization
10. International travel — Consider other differentials

Lactose Intolerance

Bloating/flatulence 1-2 hrs. after meals. Lactose in diet.

Eliminate lactose in diet for 2 wks.

Non-compliant | Compliant

Hydrogen Breath Test** (− / +)

Genetic testing C/C (13910) T/C (13910) genes (+ / −)

Not LI; consider other differentials

Sx resolve (+) | Sx continue (−)

Suspect LI

Celiac Disease

Anorexia, fatigue, bloating, & abd. pain; sx daily for >3 months or systemic manifestations*

Consumes gluten in diet?*** (− / +)

Labs IgG anti-DGP with IgA anti-tTG & Total IgA (− / +)

Genetic testing HLA DQ2/DQ8 (−)

IgG anti-DGP (− / +)

Consider other differentials

Not CD; consider other differentials

Labs IgA anti-tTG & Total IgA

Total IgA deficient | IgA anti-tTG elevated Total IgA normal | Both Normal

Not CD; consider other differentials

Suspect CD

Irritable Bowel Syndrome-D

Pain relieved by defecation, >3 varying stool forms weekly, mucus in the stool >3 months

CBC, CRP, CD Panel (IgA anti-tTG & Total IgA)

IgA anti-tTG and Total IgA abnormal.

CBC or CRP is abnormal

Serology is normal

Not IBS-D; consider other differentials

ROME III criteria**** (− / +)

Suspect Irritable Bowel Syndrome-D

If inconclusive, refer to GI for endoscopy for further workup

* Systemic manifestations: iron deficiency anemia, joint pain, osteoporosis, migraines, depression, irritability, epilepsy, vitamin deficiencies, protein-calorie malnutrition, short stature, failure to thrive, delayed puberty/early menopause, dental enamel defects, recurrent apthous stomatitis, dermatitis herpetiformis.
** False (+) results: inadequate pretest fasting, smoking within 6 hrs. of testing. False (−) results: Bacterial overgrowth of the small intestine, Diabetes Mellitus, antibiotic use, gastric emptying issues, underlying pulmonary disorders.
*** If the patient has been on a gluten free diet, the serology may by falsely negative. Patient should consume gluten for at least 2 weeks, and ideally 8 weeks. Consider testing at 6 weeks, if negative, consider retesting 6 weeks later.
**** ROME III criteria and other questionnaires for IBS have sensitivity and specificity of 60-70%.