Gas and Bloating—Controlling Emissions: A Case-Based Review for the Primary Care Provider

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Abstract

The evaluation of the patient with gas and bloating can be complex and the treatment extremely challenging. In this article, a simplified approach to the history and relevant physical examination is presented and applied in a case-oriented manner, suitable for application in the primary care setting.

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Gas-related symptoms (GRSs) such as bloating, belching, and flatulence are common and are a consequence of an incompletely understood interaction between gastrointestinal (GI) motility and gas production.[1] *Bloating* can be defined as a sense of gassiness or a sense of being distended, whereas *belching* (also referred to as *eructation*) reflects the expulsion of excess gas from the esophagus or stomach and may or may not occur in association with bloating. Bloating should be distinguished from abdominal distention, the latter being an objective increase in abdominal girth. Abdominal distension occurs in only 50% of patients who experience bloating.[2] Although occasional flatulence[3] and belching after meals is not considered abnormal, these symptoms can be bothersome, particularly when they occur in excess.[4] An important consideration is that the threshold for a patient to seek medical evaluation is affected by their perception of what is "normal."[5] Although this

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is a useful factor to be aware of, a careful evaluation is required to ensure an organic disorder is not the underlying etiology.

These symptoms occur in both functional GI disorders, such as irritable bowel syndrome (IBS),[1] and in the general population.[6] In a study[7] of a random selection of the general US population, almost 1 in 3 respondents met Rome I criteria for functional bloating. Gas-related symptoms can markedly impair the health-related quality of life of affected patients.[4,6] Despite the increasing number of promising pharmacotherapies and dietary interventions that may help alleviate these symptoms,[8,9] an effective management strategy can be hard to elucidate, frustrating both patients and clinicians. In this review, we will present some key aspects of the history and physical examination that guide the further assessment and management of GRSs. We will then apply these concepts in 4 case scenarios describing commonly encountered clinical phenotypes.

A SIMPLIFIED 5-STEP APPROACH TO THE CLINICAL HISTORY

The initial approach to the patient with GRSs is to obtain a detailed history and perform a physical examination. We propose a simple 5-step approach to the clinical history, supplemented by key physical examination findings, which can facilitate the work-up.

Clarify the Predominant Symptom, as Well as Its Timing of Onset

The predominant symptom, be it belching or bloating, should be ascertained initially to help direct questioning. Next, the timing of the onset of symptoms relative to food ingestion should also be clarified. The onset of symptoms soon after eating suggests a gastric etiology, whereas delayed symptoms may suggest a small bowel origin. A simplified approach to the evaluation of the patient with GRSs is outlined in Figure 1.

Perform a Thorough Dietary Evaluation

Primary care physicians should explore the patient's eating pattern and relationship of symptoms. The patient should be asked to describe how much and how frequently they eat. Eating large meals less frequently may contribute to postprandial discomfort. Eating meals quickly, without thorough chewing, and gulping food may contribute to GRSs.

Some patients may associate their symptoms with ingestion of foods associated with increased intestinal gas production, such as onions, beans, and legumes. Intolerance of food types containing lactose,[10] gluten,[11] and fructose[12] may also be related to gas. The patient may have experienced GRSs improvement with prior dietary modification, and this should be pursued in the history.

The patient should be asked about consumption of large quantities of caffeine or carbonated drinks, as these can contribute to GRSs. Belching, in particular, can be associated with caffeine ingestion because of transient lower esophageal sphincter relaxation (TLESR).[13]

Artificial sweeteners, specifically sugar alcohols such as sorbitol, mannitol, and glycerol, promote gas production, and frequent use of such products should be sought in the clinical history. These are often contained in chewing gum, even if "sugar-free."

Ask About Associated GI Symptoms, Specifically Abdominal Pain, Diarrhea, Constipation, and Weight Loss

The coexistence of abdominal pain, alteration in bowel habit, and abdominal bloating suggests a potential diagnosis of IBS. However, many other conditions leading to GRSs may also cause abdominal pain.

The patient should be questioned with respect to the form and frequency of stool, as well as the ease of stool passage, as constipation can induce GRSs. The presence of incomplete evacuation of stool, straining with defecation, or manual removal of stool suggests a diagnosis of pelvic floor dysfunction. The presence of diarrhea should prompt consideration of small intestine bacterial overgrowth (SIBO) and celiac disease.

Weight loss history should always be sought in patients presenting with GI symptoms. Substantial weight loss raises concern for an underlying neoplasm or malabsorptive conditions, such as celiac disease. Patients with severely restricted caloric intake, sometimes due to dietary intolerance or even functional dyspepsia, may also report marked weight loss.

Review the Patient's Medications, and Enquire About Supplements

Medication review is necessary in all patients with chronic unexplained GI symptoms.

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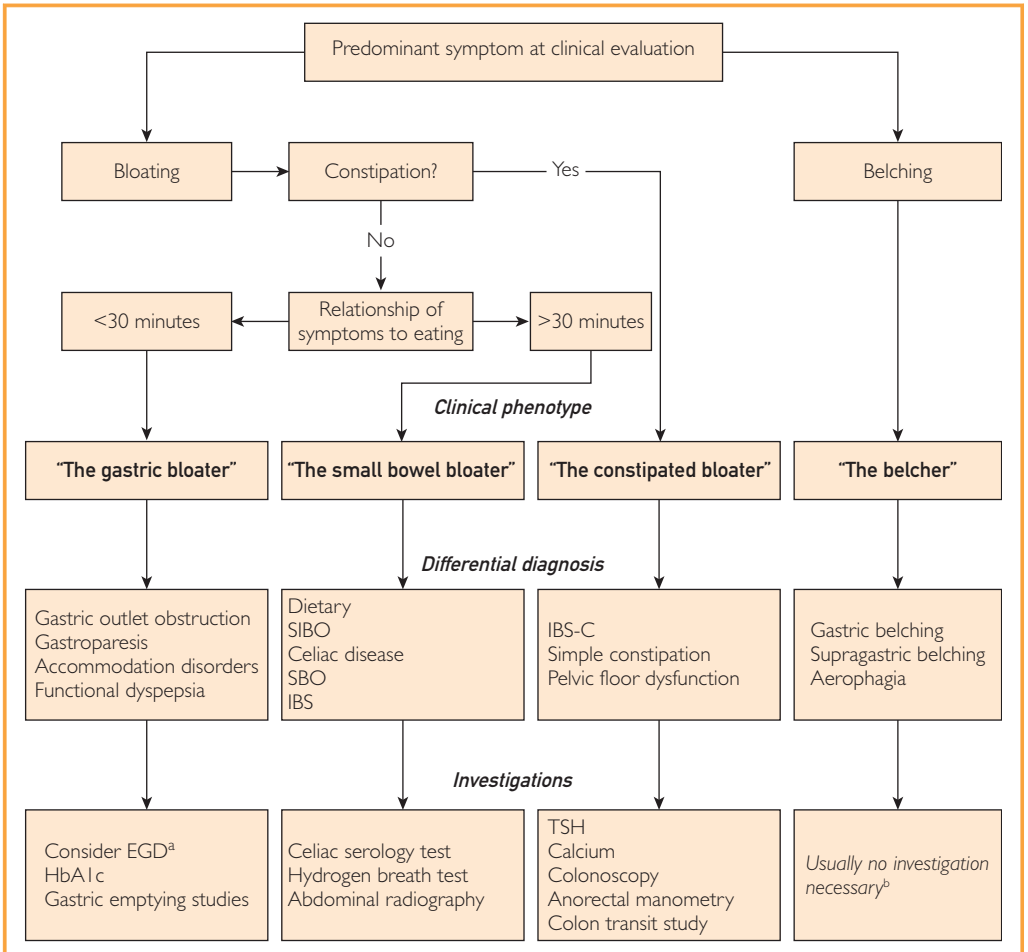

FIGURE 1. A simplified approach to the evaluation of the patient with gas-related symptoms. [a]Indicated in the presence of alarm features: Age > 50 years, upper GI malignancy in a first-degree relative, weight loss, GI bleeding, or iron deficiency anemia, dysphagia, odynophagia, persistent vomiting, abnormal imaging suggesting organic disease (American Society for Gastrointestinal Endoscopy). [b]Consider EGD (+/− gastric biopsies) and/or gastric emptying test to rule-out an organic etiology, in certain patients. EGD = esophagogastroduodenoscopy; HbA1c = glycosylated hemoglobin; IBS = irritable bowel syndrome; IBS-C = irritable bowel syndrome—constipation; SBO = small bowel obstruction; SIBO = small intestine bacterial overgrowth; TSH = thyroid-stimulating hormone.

Specific to GRSs, the patient should be questioned with respect to psyllium-containing products, which may contribute to excess gas production. Metformin and opiates are also associated with GRSs.[14,15]

Explore the Patient's Comorbidities, and Ask About Risk Factors for SIBO

The use of continuous positive airway pressure for obstructive sleep apnea is associated with GRSs, typically with morning symptoms following overnight use.[16] New users may require alteration in continuous positive airway pressure settings to minimize these effects. Patients receiving home oxygen therapy can also experience gaseous symptoms. Approximately 25% of patients experience gas-bloat syndrome after Nissen fundoplication surgery, and a history of the same should be sought.[17]

Small intestine bacterial overgrowth can manifest as GRSs.[18] Risk factors for SIBO should be sought in the history[18] and include the following:

1. *Structural:* small bowel diverticula, and strictures due to Crohn disease, radiation, or nonsteroidal anti-inflammatory drugs

2. *Surgical:* Roux-en-Y surgery (blind and afferent loops) and ileocecal valve resection
3. *Dysmotility:* scleroderma, narcotics, diabetes mellitus, and amyloidosis
4. *Reduced acid (achlorhydria):* acid suppressive therapy, gastric resection, atrophic gastritis, and advancing age
5. *Miscellaneous:* celiac disease, cirrhosis, immunodeficiency, and pancreatic insufficiency

PHYSICAL EXAMINATION: KEY FINDINGS

Clues to the etiology of gaseous symptoms may be encountered by patient observation during the history-taking process. Occasionally, a patient presenting for evaluation of belching will be observed to belch excessively when attention is focused on this symptom. The patient may even volunteer a demonstration of "belching" during the interview process. Improvement in belching may also be observed as the patient is distracted. These observations suggest a diagnosis of supragastric belching, a learned behavior that is often associated with anxiety disorders.

Examination of the abdomen may reveal distention related to small bowel ileus or mechanical obstruction or less likely gastric outlet obstruction (GOO), whereby patients may also manifest a succussion splash. Nongaseous etiologies for abdominal distension should also be considered, including ascites, organomegaly, and increased adiposity. Bowel sounds should be carefully auscultated, with the presence of high-pitched bowel sounds suggesting mechanical obstruction whereas reduced or absent bowel sounds could suggest GI ileus or dysmotility.

A detailed digital rectal examination should also be performed looking for evidence of fecal impaction or signs of pelvic floor dysfunction. Signs of pelvic floor dysfunction include increased perineal descent (ie, descending perineum syndrome), decreased perineal descent, or abnormal sphincter tone and failed relaxation of the puborectalis muscle with simulated defecation.

CASE EXAMPLES

Case 1: "The Gastric Bloater"

A 28-year-old woman presents for evaluation of a 2-week history of postprandial epigastric discomfort and bloating. She recently experienced a self-limited episode of viral gastroenteritis. Her symptoms occur within 15 minutes of eating. She does not take nonsteroidal anti-inflammatory drugs. An 8-week trial of proton pump inhibitor therapy was not helpful. Laboratory testing included a glycosylated hemoglobin level of 5.2%. Esophagogastroduodenoscopy (EGD) revealed solid food retained within the stomach, but the endoscope was advanced to the duodenum without difficulty. A gastric emptying scintigraphy study found delayed gastric emptying.

The presence of symptoms such as epigastric discomfort and upper abdominal bloating occurring soon after eating suggests the symptoms are likely gastric in origin. Potential explanations for such symptoms would include GOO, gastroparesis, abnormalities of gastric accommodation, and functional (nonulcer) dyspepsia. Gastric outlet obstruction may be caused by neoplasm, chronic peptic ulcer disease, or complications of pancreatitis and is often associated with vomiting of undigested or partially digested food. If suspected, EGD is the appropriate investigation, with a normal study effectively excluding GOO. *Gastroparesis* is a disorder defined by delayed gastric emptying in the absence of mechanical GOO and is most frequently associated with diabetes.[19] With her recent gastroenteritis, this patient has a frequently overlooked risk factor for gastroparesis.[20] The clinical history of gastroenteritis combined with the evidence of delayed gastric emptying on her scintigraphy study, in the setting of a normal glycosylated hemoglobin test, suggests a diagnosis of postinfectious gastroparesis.

Our patient's abnormal gastric emptying study was not consistent with an abnormality of gastric accommodation. Gastric accommodation involves relaxation of the gastric fundus within minutes of eating food, and the resultant reduction in accommodation may lead to early postprandial GRSs. This condition may be diagnosed by scintigraphic measurement of accommodation. Lastly, a diagnosis of functional dyspepsia is suggested by the presence of chronic upper abdominal pain, bloating, or discomfort, usually present for 6 months or more, in the absence of alternative explanation or organic disease (including normal EGD).[21] Our patient had an alternative explanation for her symptoms.

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The management approach for patients with early postprandial bloating is tailored to the underlying etiology. This patient should receive formal instruction from an experienced GI dietician with respect to a gastroparesis diet (eating small meals frequently or reducing dietary fat intake). She can be reassured that postinfectious gastroparesis is usually self-limiting and should improve with time.[20] Those patients whose gastroparesis is related to a systemic condition such as diabetes mellitus or connective tissue disease (eg, scleroderma) should have targeted treatment of their underlying condition. A prokinetic, such as metoclopramide, may be considered in cases refractory to dietary modification.[22] If metoclopramide is prescribed, the use of the liquid formulation at a dose of 5 to 10 mL, 30 minutes before meals and at bedtime, may optimize the clinical response.[23]

Patients with confirmed abnormal gastric accommodation may also benefit from the principles of a "gastroparesis diet." Buspirone at a dose of 5 to 10 mg, 30 minutes before meals, has been reported to be beneficial in some of these patients.[24] If GOO is found, this will usually require surgical intervention.

Finally, many patients will be diagnosed with functional dyspepsia, a diagnosis of exclusion. Similar dietary instruction should occur, as well as avoidance of other precipitants, identified by a diet and symptom diary.[21] If symptoms persist, and local prevalence of *Helicobacter pylori* is more than 10%, this diagnosis should be sought (*H pylori* breath test, stool antigen, or biopsy at EGD) and treated if present.[21] A trial of acid suppressive therapy may be of benefit, especially if the primary symptom is epigastric pain.[21] Amitriptyline has also been shown to be beneficial,[25] and if prescribed for this indication, a starting dose of 25 mg at nighttime, increasing in 25-mg increments every 2 weeks, may be considered. For those patients with predominant postprandial fullness and bloating, a trial of either metoclopramide or buspirone may also be beneficial.

Case 2: "The Small Bowel Bloater"

A 45-year-old woman presents with a long-standing history of substantial abdominal bloating with pain, occurring 1 to 2 hours after eating, with pain relieved by defecation. She also describes episodic loose stool lasting on average for 7 days each month. She denies weight loss. She does not ingest excess caffeine, carbonated drinks, chewing gum, or artificial sweeteners. She has not had abdominal surgery. Prior testing has included normal celiac serology, a normal hydrogen breath test, and an unremarkable plain film of the abdomen.

Upper abdominal bloating that occurs over an hour after eating suggests a small bowel origin. The differential diagnosis includes dietary-related ingestion (foods, lactose, gluten, and FODMAPs [fermentable oligo-, di-, monosaccharides, and polyols]), celiac disease, SIBO, small bowel obstruction (SBO), or IBS. A focused history has helped to rule out many of the usual diet-related causes of abdominal bloating. Our patient had normal celiac serology, and normal abdominal radiography, making SBO less likely. Previous abdominal surgery predisposes to SBO due to adhesions and should always be sought in the history of patients presenting with GRSs. This risk increases in those with multiple abdominal operations and those with a history of SBO secondary to adhesions.

Patients with SIBO will often have concomitant diarrhea. Although no perfect test exists for diagnosing SIBO, the normal hydrogen breath test combined with the absence of risk factors outlined earlier in the review makes this diagnosis unlikely. The diagnosis of SIBO can be made by EGD, with small bowel aspirate and culture revealing more than 100,000 organisms/mL. A noninvasive alternative test is the hydrogen breath test, which involves ingestion of substrate with monitoring of hydrogen in exhaled breath every 15 to 30 minutes. In nondiabetic patients, glucose is the substrate used, and a positive test involves an increase in hydrogen by 12 ppm. In diabetic patients, lactulose is the substrate used, with an increase by 20 ppm indicative of a positive test. Management of SIBO includes treatment of identifiable risk factors, replacement of nutritional deficiencies (eg, vitamin B_{12}), and antibiotics, such as ciprofloxacin 250 mg twice a day for 7 to 10 days. A cyclic antibiotic for the first 7 to 10 days each month can also be used for some cases with high risk of persistent or recurrent SIBO (eg, patients with scleroderma).

Our patient has had a thorough evaluation with no etiology apparent. Her presentation of bloating and diarrhea, coexisting with abdominal pain relieved by defecation, is most

consistent with IBS—diarrhea (IBS-D) as per the Rome criteria.[26] Again, initial management should focus on dietary interventions, which are often overlooked.[27] Up to 60% of patients with IBS associate symptoms with eating a meal. Possible explanations include food intolerances, gastrocolic response, microbiome/fermentation, gas handling, or psychological factors.[28] The basic principles of IBS management are outlined in Figure 2. Reassurance and education are critical initial steps. The traditional IBS diet emphasizes a greater focus on how and when to eat rather than on what foods to ingest—3 meals and 3 snacks a day; reduced intake of fatty foods, spicy foods, coffee, and alcohol; and avoidance of carbonated drinks, gums, and sweeteners.[29] Other recommended diets include the low FODMAP diet, which has been shown to reduce GRSs in patients with IBS as compared with the standard diet.[8,30] Interestingly, in a recent randomized trial,[31] both these diets were equally efficacious. The third diet to consider is a gluten-free diet, irrespective of the presence of celiac disease. Gluten has been shown to alter bowel function in patients with IBS-D[32] and is associated with more frequent stool and increased small bowel permeability, especially when HLA-DQ2 or -DQ8 positive.[11] A recent study[33] found that patients with IBS-D had a sustained symptom improvement upon a gluten-free diet. For patients with episodic pain, a trial of hyoscyamine or dicyclomine should be considered.[34,35] For patients with continuous pain, neuromodulation with amitriptyline may be more beneficial.[36] Cognitive behavioral therapy has also been shown to be helpful in certain patients.[37] The complementary medicine, STW 5, has also been shown to have some benefit.[38] In patients with IBS-D, 25% may have bile acid malabsorption, and thus a trial of a bile acid sequestrant may be worthwhile.[39]

Moreover, the Food and Drug Administration recently approved rifaximin, a gut-selective antibiotic that is not systemically absorbed,[40] and eluxadoline, a new oral agent with mixed opioid effects, for the treatment of IBS-D.[41] Of note, there is limited evidence that probiotics may be beneficial in reducing GRSs in patients with IBS.[9]

Case 3: "The Constipated Bloater"

A 51-year-old woman presents for evaluation of chronic bloating. She has also had constipation for many years, with recent worsening. She has used methylcellulose without benefit, while polyethylene glycol caused increased bloating and abdominal discomfort, without

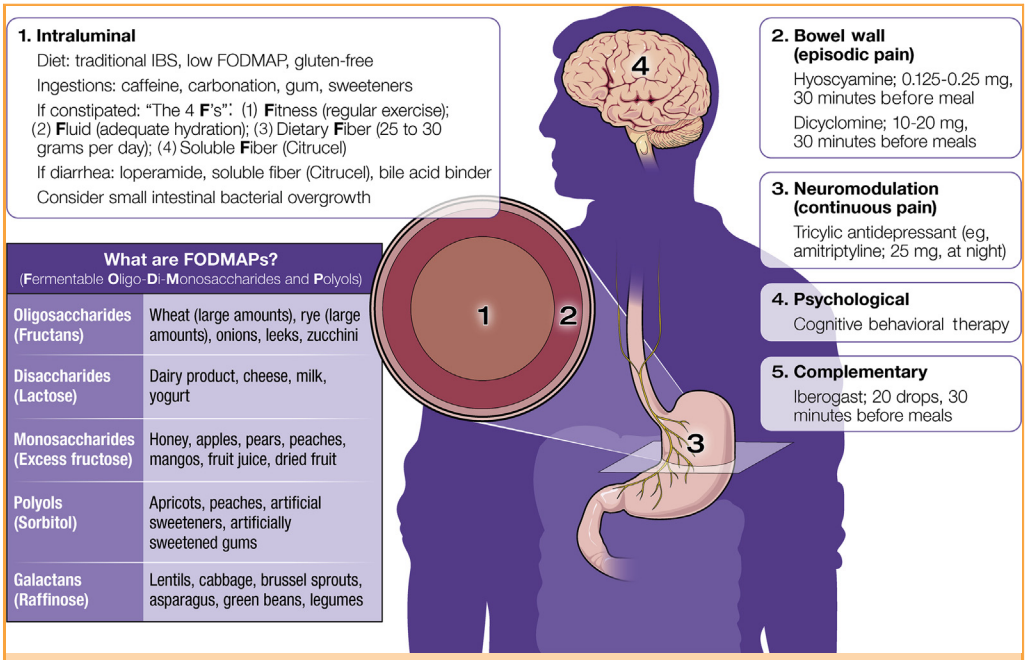

FIGURE 2. Basic principles of irritable bowel syndrome management. IBS = irritable bowel syndrome.

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improving the constipation. The patient spends lengthy periods in the restroom, straining to have a bowel movement. On digital rectal examination, decreased movement of the perineum and failed relaxation of the puborectalis muscle with simulated defecation are noted.

Constipation is a common cause of GRSs. The most common etiologies include IBS-constipation, simple constipation, or constipation associated with pelvic floor dysfunction. Although constipation is often due to inadequate dietary fiber or fluid intake or lack of physical activity, consideration also needs to be given to the possibility of motility disorders or colonic pathology. Systemic conditions such as hypothyroidism or hypercalcemia and medication use (eg, narcotics and calcium channel blockers) may also be contributing factors. Although most patients with uncomplicated constipation do not require investigation, the clinical presentation can identify a subset of patients in whom investigations are indicated. Colonoscopy should be pursued when marked alteration in bowel habit is associated with unexplained concerning symptoms such as hematochezia or weight loss. Anorectal manometry is indicated for patients with symptoms or signs suggestive of pelvic floor dysfunction, as in this case, and is the diagnostic test of choice.

Most patients with constipation will benefit from ensuring dietary fiber intake of approximately 20 g/d, maintaining excellent hydration, increasing physical activity (if this is feasible), and in some cases initiation of supplementary fiber (eg, methylcellulose, 2 heaped tablespoons per day). Patients with constipation associated with excess gas or bloating may have worsening of their symptoms with psyllium products. Therefore, if fiber supplementation is being pursued, this group of patients may see more benefit from a non—psyllium-containing product such as methycellulose. For those patients not responding to these measures, an osmotic laxative such as polyethylene glycol should be pursued. Worsening of GRSs after fiber supplementation or osmotic laxatives may be a clue to the underlying pelvic floor dysfunction. The most effective intervention for dysynergic defecation is pelvic floor retraining using biofeedback therapy, with studies showing up to an 80% improvement at 6 months after a 2-week program.[42] Stimulant laxatives are usually reserved for patients with dysmotility disorders, those on narcotic pain medications, and those unresponsive to other interventions for constipation. For those patients with GRSs due to narcotic-induced constipation, measures should be taken to reduce or discontinue narcotic dose, if appropriate. Two novel agents—lubiprostone and linaclotide—have been approved for the treatment of chronic idiopathic constipation and IBS-constipation.[43] However, relatively small response rates and higher costs will likely make these medications second-line therapy, for now.[43]

Case 4: "The Belcher"

A 35-year-old man presents for evaluation of belching that has been present for 1 year. The patient states that at times he will belch up to 50 times/min. During the consultation, he has an episode of frequent belching, lasting for 15 seconds. His wife states that he often belches when anxious and never belches while asleep.

Belching may reflect normal physiology or may be pathological, a manifestation of conditions such as aerophagia or supragastric belching. In the process of eating, ingestion of small quantities of air is normal. Gas is also produced within the GI tract. These sources can contribute to intestinal gas and may ultimately be passed as flatus or may rise into the fundus of the stomach, leading to TLESR. These TLESRs occur approximately 25 to 30 times/d in normal individuals and represent the mechanism for "physiologic" belching. Supragastric belching usually occurs as a result of diaphragmatic contraction, decreased intrathoracic pressure, or air entering the esophagus and then being expelled as the diaphragm relaxes. This is an abnormal learned behavior that may lead to multiple "belches" per minute, especially when attention is focused on the symptom or when the patient is anxious. Our patient's presentation is most consistent with supragastric belching. *Aerophagia* (*air swallowing*) refers to the process of swallowing excessive amounts of air and may be seen in patients who eat in a hurried manner, do not chew their food thoroughly, and gulp during eating. Although there is also an association with anxiety disorders, the symptom is generally not reproduced

during the history-taking process and does not become more prominent with focused attention.

The approach to managing patients whose primary symptom of belching depends on the diagnosis, which is generally apparent after clinical assessment. Many patients with excess belching will benefit from dietary reduction of high gas forming foods such as onions, beans, and legumes. Eating small meals, chewing food thoroughly, and minimizing ingestion of carbonated drinks may also be helpful. Occasionally, with more difficult to control physiologic belching, baclofen can be prescribed as a short-term therapeutic trial (reduces TLESRs).[44] Patients with suspected aerophagia should also be advised to eat slowly, deliberately chewing their food and not gulping. However, this group of patients and those with supragastric belching will usually benefit most from behavioral therapy consultation and specifically instruction with respect to the potential benefits of diaphragmatic breathing as a means to decreasing aerophagia and supragastric belching.[45]

CONCLUSION

Evaluation of the patient with GRSs can often be complex and time-consuming. To this end, a methodical approach can facilitate diagnosis and management. One such simplified approach to the relevant history and physical examination is presented and applied to the clinical cases described in this review. This approach should help with limiting the differential diagnosis and directing testing and should help primary care physicians evaluate and treat a large percentage of patients with GRSs. Referral to a gastroenterologist should be considered in more complex or refractory cases.

Abbreviations and Acronyms: **EGD** = esophagogastroduodenoscopy; **GI** = gastrointestinal; **GOO** = gastric outlet obstruction; **GRSs** = gas-related symptoms; **IBS** = irritable bowel syndrome; **IBS-D** = irritable bowel syndrome—diarrhea; **SBO** = small bowel obstruction; **SIBO** = small intestine bacterial overgrowth; **TLESR** = transient lower esophageal sphincter relaxation

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REFERENCES

1. Ringel Y, Williams RE, Kalilani L, Cook SF. Prevalence, characteristics, and impact of bloating symptoms in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2009; 7(1):68-72:quiz 3.
2. Houghton LA, Lea R, Agrawal A, Reilly B, Whorwell PJ. Relationship of abdominal bloating to distention in irritable bowel syndrome and effect of bowel habit [published correction appears in *Gastroenterology*. 2006;131(6):2029. Agrawal, Anvrag [corrected to Agrawal, Anurag].]. *Gastroenterology*. 2006; 131(4):1003-1010.
3. Levitt MD, Furne J, Olsson S. The relation of passage of gas an abdominal bloating to colonic gas production. *Ann Intern Med*. 1996;124(4):422-424.
4. Halder SL, Locke GR III, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ III. Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. *Aliment Pharmacol Ther*. 2004;19(2):233-242.
5. Talley NJ, Boyce P, Jones M. Identification of distinct upper and lower gastrointestinal symptom groupings in an urban population. *Gut*. 1998;42(5):690-695.
6. Tielemans MM, Jaspers Focks J, van Rossum LG, et al. Gastrointestinal symptoms are still prevalent and negatively impact health-related quality of life: a large cross-sectional population based study in the Netherlands. *PLoS One*. 2013; 8(7):e69876.
7. Drossman DA, Li Z, Andruzzi E, et al. U.S. householder survey of functional gastrointestinal disorders: prevalence, sociodemography, and health impact. *Dig Dis Sci*. 1993;38(9): 1569-1580.
8. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*. 2014;146(1):67-75.e5.
9. Hungin AP, Mulligan C, Pot B, et al; European Society for Primary Care Gastroenterology. Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice—an evidence-based international guide. *Aliment Pharmacol Ther*. 2013;38(8):864-886.
10. Deng Y, Misselwitz B, Dai N, Fox M. Lactose intolerance in adults: biological mechanism and dietary management. *Nutrients*. 2015;7(9):8020-8035.
11. Vazquez-Roque MI, Camilleri M, Smyrk T, et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. *Gastroenterology*. 2013;144(5):903-911.e3.
12. Choi YK, Kraft N, Zimmerman B, Jackson M, Rao SS. Fructose intolerance in IBS and utility of fructose-restricted diet. *J Clin Gastroenterol*. 2008;42(3):233-238.
13. Lohsiriwat S, Puengna N, Leelakusolvong S. Effect of caffeine on lower esophageal sphincter pressure in Thai healthy volunteers. *Dis Esophagus*. 2006;19(3):183-188.
14. Dujic T, Zhou K, Donnelly LA, Tavendale R, Palmer CN, Pearson ER. Association of Organic Cation Transporter 1 With Intolerance to Metformin in Type 2 Diabetes: A GoDARTS Study. *Diabetes*. 2015;64(5):1786-1793.
15. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. *Ther Adv Chronic Dis*. 2016; 7(2):121-134.
16. Engleman HM, Asgari-Jirhandeh N, McLeod AL, Ramsay CF, Deary IJ, Douglas NJ. Self-reported use of CPAP and benefits of CPAP therapy: a patient survey. *Chest*. 1996;109(6): 1470-1476.
17. Tian ZC, Wang B, Shan CX, Zhang W, Jiang DZ, Qiu M. A meta-analysis of randomized controlled trials to compare long-term outcomes of Nissen and Toupet fundoplication for gastroesophageal reflux disease. *PLoS One*. 2015;10(6): e0127627.
18. Grace E, Shaw C, Whelan K, Andreyev HJ. Review article: small intestinal bacterial overgrowth—prevalence, clinical features,

current and developing diagnostic tests, and treatment. *Aliment Pharmacol Ther*. 2013;38(7):674-688.
19. Camilleri M. Novel diet, drugs, and gastric interventions for gastroparesis. *Clin Gastroenterol Hepatol*. (2016 Jan 4) http://dx.doi.org/10.1016/j.cgh.2015.12.033. [Epub ahead of print].
20. Naftali T, Yishai R, Zangen T, Levine A. Post-infectious gastroparesis: clinical and electerogastrographic aspects. *J Gastroenterol Hepatol*. 2007;22(9):1423-1428.
21. Talley NJ, Ford AC. Functional dyspepsia. *N Engl J Med*. 2015; 373(19):1853-1863.
22. Parkman HP, Hasler WL, Fisher RS; American Gastroenterological Association. American Gastroenterological Association medical position statement: diagnosis and treatment of gastroparesis. *Gastroenterology*. 2004;127(5):1589-1591.
23. Camilleri M, Parkman HP, Shafi MA, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-37: quiz 38.
24. Tack J, Janssen P, Masaoka T, Farré R, Van Oudenhove L. Efficacy of buspirone, a fundus-relaxing drug, in patients with functional dyspepsia. *Clin Gastroenterol Hepatol*. 2012;10(11): 1239-1245.
25. Talley NJ, Locke GR, Saito YA, et al. Effect of amitriptyline and escitalopram on functional dyspepsia: a multicenter, randomized controlled study. *Gastroenterology*. 2015;149(2):340-349. e2.
26. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders [published correction appears in *Gastroenterology*. 2006;131(2):688]. *Gastroenterology*. 2006;130(5):1480-1491.
27. Mayer EA. Clinical practice: irritable bowel syndrome. *N Engl J Med*. 2008;358(16):1692-1699.
28. Camilleri M. Peripheral mechanisms in irritable bowel syndrome. *N Engl J Med*. 2012;367(17):1626-1635.
29. McKenzie YA, Alder A, Anderson W, et al; Gastroenterology Specialist Group of the British Dietetic Association. British Dietetic Association evidence-based guidelines for the dietary management of irritable bowel syndrome in adults. *J Hum Nutr Diet*. 2012;25(3):260-274.
30. Staudacher HM, Lomer MC, Anderson JL, et al. Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. *J Nutr*. 2012;142(8):1510-1518.
31. Böhn L, Störsrud S, Liljebo T, et al. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology*. 2015;149(6):1399-1407.e2.
32. Biesiekierski JR, Newnham ED, Irving PM, et al. Gluten causes gastrointestinal symptoms in subjects without celiac disease: a double-blind randomized placebo-controlled trial. *Am J Gastroenterol*. 2011;106(3):508-514:quiz 515.
33. Aziz I, Trott N, Briggs R, North JR, Hadjivassiliou M, Sanders DS. Efficacy of a gluten-free diet in subjects with irritable bowel syndrome-diarrhea unaware of their HLA-DQ2/8 genotype. *Clin Gastroenterol Hepatol*. 2016;14(5):696-703.e1.
34. Poynard T, Regimbeau C, Benhamou Y. Meta-analysis of smooth muscle relaxants in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2001;15(3):355-361.
35. Ruepert L, Quartero AO, de Wit NJ, van der Heijden GJ, Rubin G, Muris JW. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. *Cochrane Database Syst Rev*. 2011;(8):CD003460.
36. Chao GQ, Zhang S. A meta-analysis of the therapeutic effects of amitriptyline for treating irritable bowel syndrome. *Intern Med*. 2013;52(4):419-424.
37. Altayar O, Sharma V, Prokop LJ, Sood A, Murad MH. Psychological therapies in patients with irritable bowel syndrome: a systematic review and meta-analysis of randomized controlled trials. *Gastroenterol Res Pract*. 2015;2015:549308.
38. Ottillinger B, Storr M, Malfertheiner P, Allescher HD. STW 5 (Iberogast®)—a safe and effective standard in the treatment of functional gastrointestinal disorders. *Wien Med Wochenschr*. 2013;163(3-4):65-72.
39. Slattery SA, Niaz O, Aziz Q, Ford AC, Farmer AD. Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea. *Aliment Pharmacol Ther*. 2015;42(1):3-11.
40. Pimentel M, Park S, Mirocha J, Kane SV, Kong Y. The effect of a nonabsorbed oral antibiotic (rifaximin) on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med*. 2006;145(8):557-563.
41. Lembo AJ, Lacy BE, Zuckerman MJ, et al. Eluxadoline for irritable bowel syndrome with diarrhea. *N Engl J Med*. 2016;374(3): 242-253.
42. Chiarioni G, Salandini L, Whitehead WE. Biofeedback benefits only patients with outlet dysfunction, not patients with isolated slow transit constipation. *Gastroenterology*. 2005;129(1):86-97.
43. Thomas RH, Luthin DR. Current and emerging treatments for irritable bowel syndrome with constipation and chronic idiopathic constipation: focus on prosecretory agents. *Pharmacotherapy*. 2015;35(6):613-630.
44. Blondeau K, Boecxstaens V, Rommel N, et al. Baclofen improves symptoms and reduces postprandial flow events in patients with rumination and supragastric belching. *Clin Gastroenterol Hepatol*. 2012;10(4):379-384.
45. Chitkara DK, Van Tilburg M, Whitehead WE, Talley NJ. Teaching diaphragmatic breathing for rumination syndrome. *Am J Gastroenterol*. 2006;101(11):2449-2452.