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Rome V Pediatric Upper Gastrointestinal Disorders of Gut–Brain Interaction

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Upper gastrointestinal disorders of gut–brain interaction (DGBI) present from infancy through adolescence. The Rome V Criteria have expanded to include DGBI of the esophagus, disorders of air-transit, and feeding disorders, as well as rumination syndrome, cyclic vomiting, chronic nausea syndrome, and functional dyspepsia. This expansion provides a diagnostic framework for patients presenting with chest and throat pain, feeding difficulties, belching, pain with eating, nausea, and vomiting. Given the advances in impedance technology and high-resolution manometry, testing plays a greater role in many of these diagnostic criteria than they have in past Rome iterations. This harmony between symptoms and testing results in more precision in therapeutic approaches that are critically multidisciplinary. The ability to assign new, positive diagnoses across the upper gastrointestinal tract offers new opportunities for pediatric-focused therapeutic trials.

Keywords: Pediatrics; Feeding Disorders; Gastroesophageal Reflux; Neuromodulators.

The Rome V pediatric upper gastrointestinal (GI) disorders mirror some adult diagnoses, while developing several new pediatric diagnoses, particularly within the realm of esophageal and functional feeding disorders, where more specific subtypes are added to provide more diagnostic clarity and targeted management.

G1. Esophageal Disorders

The use of pH-impedance technology has increased the awareness of esophageal DGBI. In the past, nonerosive reflux disease was the all-encompassing diagnosis for children without pathologic amounts of gastroesophageal reflux. The use of pH-impedance testing has allowed for additional phenotyping of patients with significant symptoms that are typically associated with gastroesophageal reflux disease (GERD) (Figure 1).

G1a. Reflux Hypersensitivity

Definitions. Rome V defines reflux hypersensitivity (RH) similarly to adult RH except the description of pain may include not only heartburn and chest pain, but other types of pain or discomfort. The definition in younger children (ie, <8 years) is more complicated due to their inability to describe the pain.[1,2] Therefore, the symptoms must be consistent with pain and more severe than expected based on the developmental stage of the child.

Epidemiology. There are scarce data on the epidemiology of RH in children due to the new pediatric classification.[3,4] In 2 studies of children aged ≥5 years undergoing both endoscopy and pH-impedance testing, 20%–29% of children met the adult Rome IV Criteria for RH.[3,4]

Abbreviations used in this paper: **ANS, autonomic nervous system; ARF, anticipatory restrictive feeding; ARFID, avoidant/restrictive food intake disorder; CBT, cognitive behavioral therapy; CHS, cannabinoid hyperemesis syndrome; CNS, chronic nausea syndrome; CVS, cyclic vomiting syndrome; DGBI, disorders of gut–brain interaction; EoE, eosinophilic esophagitis; FD, functional dyspepsia; FH, functional heartburn; FPFD, functional pediatric feeding disorder; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HD, hypersensitive dysphagia; HRIM, high-resolution esophageal impedance manometry; IPBI, intrapyloric botulinum toxin injection; PDS, postprandial distress syndrome; POTS, postural orthostatic tachycardia syndrome; PPI, proton pump inhibitor; RH, reflux hypersensitivity; RNEPD, reflux-negative esophageal pain disorder; RS, rumination syndrome; SGB, supragastric belching; TCA, tricyclic antidepressant; THC, Δ-9-tetrahydrocannabinol.**

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G1a. Diagnostic Criteria[a] for Reflux Hypersensitivity

Patients <8 years old	Patients >8 years old
Must include *all* of the following: 1. Intermittent symptoms that a. Are thought to be gastroesophageal reflux–related b. Are suggestive of pain c. Are more severe than could be expected based on normal developmental age d. Impact on age-expected daily activities and/or quality of life e. Occur at least 3 days per week 2. Normal macroscopic esophageal findings on endoscopy and absence of histologic evidence of eosinophilic esophagitis. 3. Evidence of triggering of symptoms by acid and/or nonacid reflux events on pH- or pH-impedance monitoring despite normal acid exposure. 4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out.	Must include *all* of the following: 1. Intermittent retrosternal pain, heartburn, throat pain, or burning sensation in the throat that a. Impact on age-expected daily activities and/or quality of life b. Occur at least 3 days per week 2. Normal macroscopic esophageal findings on endoscopy and absence of histologic evidence for eosinophilic esophagitis 3. Evidence of triggering of symptoms by acid and/or nonacid reflux events on pH- or pH-impedance monitoring despite normal acid exposure. 4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out.

[a]Criteria fulfilled for at least 2 months before diagnosis.

Pathophysiology. The mechanisms underlying RH are multifactorial and include reflux episode type (ie, pH, height, and composition), impaired mucosal integrity, central and peripheral sensitization, neuronal positioning in the mucosa, and genetic and psychological factors.[5–14] Patient factors may also impact symptoms, including anxiety, hypervigilance, and sleep disturbances.[15–18]

Clinical evaluation. Both endoscopy and catheter or wireless reflux monitoring are needed to accurately diagnose RH. Diagnosis requires a grossly normal endoscopy without eosinophilic esophagitis (EoE) microscopically and pH-impedance testing (or pH-metry or wireless pH testing) with normal acid exposure (ie, pH <4 for <12% of the time for infants aged <1 year and <6% of the time for children aged >1 year) along with positive symptom association to acid or nonacid reflux (Figure 1).[3,4,19] A positive symptom association includes either a symptom index (ie, the number of symptoms associated with reflux within a 2-minute time window divided by the total number of symptoms) ≥50% or a symptom associated probability (ie, a Fisher exact test to determine the probability that symptom–reflux relationship does not occur by chance) of >95%.

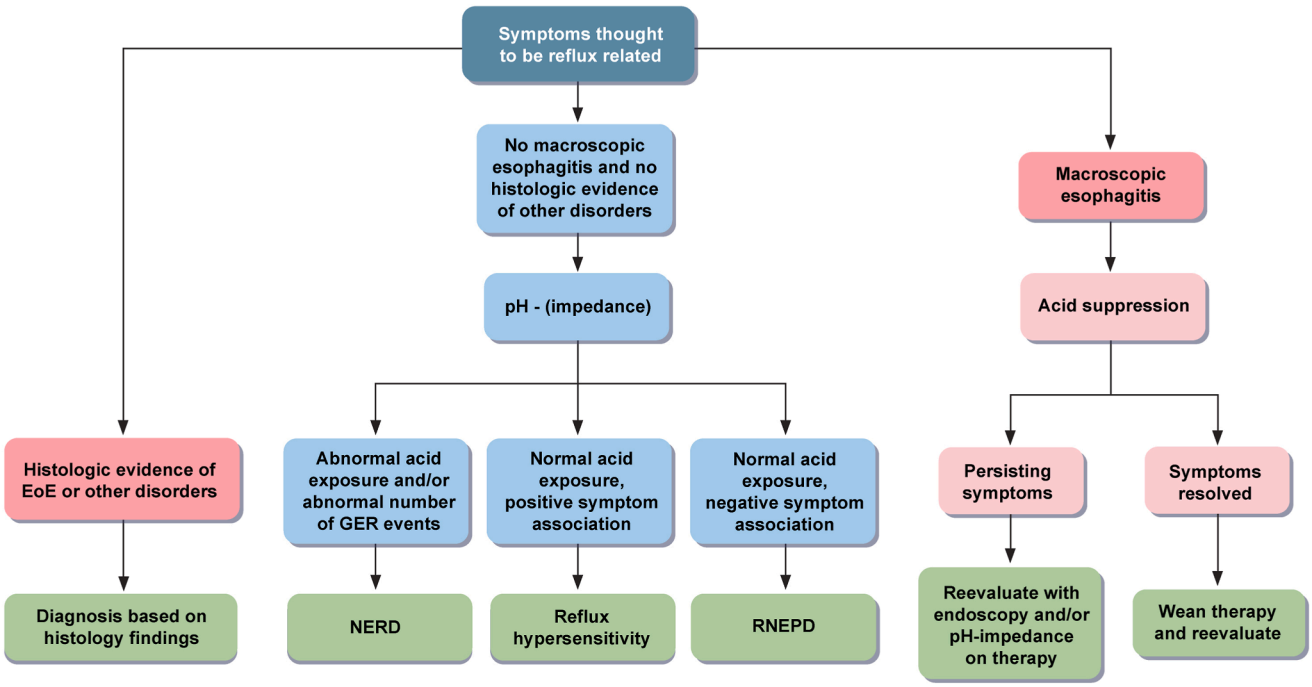

Figure 1. Algorithm for esophageal pain disorders. GER, gastroesophageal reflux.

Treatment. *Empiric acid suppression trial.* An empiric proton pump inhibitor (PPI) trial is often an initial step for typical symptoms such as heartburn or chest pain, particularly when testing is unavailable. However, although PPI response is often used diagnostically for GERD, PPI response does not reliably predict reflux phenotype[3,4]; 0%–67% of pediatric patients with acid RH had at least some symptomatic improvement with PPI use.[3,4] Empiric acid suppression trials should be time-limited up to 8 weeks and further diagnostic testing (ie, endoscopy, pH-impedance, and CYP2C19 gene testing if possible) should be pursued if there is no symptom improvement.[20] Histamine-2 receptor antagonists can also treat esophageal hypersensitivity and are a first-line therapy for patients awaiting endoscopy.

Prokinetics. Two pediatric studies found that 43%–66% of patients with RH improved when starting PPI and/or prokinetics, but neither study addressed which patients improved with the use of prokinetics alone.[21,22]

Neuromodulators. Selective serotonin reuptake inhibitors have been studied in adults with RH; 62% of adults receiving 20 mg of citalopram had complete symptom resolution compared with 33% of patients receiving placebo.[23] Similarly, tricyclic antidepressants (TCAs, eg, imipramine and nortriptyline) have been used successfully to treat typical symptoms in adults.[24,25] There are no equivalent pediatric studies of selective serotonin reuptake inhibitors or TCAs.

Cognitive behavioral therapy and other psychological interventions. Although there are no pediatric studies, a randomized trial of adults with nonerosive reflux disease and mood disorders found cognitive behavioral therapy (CBT) (alone or in combination with medications) superior to medications (eg, omeprazole and domperidone) alone.[26] Esophageal-directed hypnotherapy, acupuncture, deep breathing, and biofeedback may also be helpful.[27–30]

G1b. Reflux-Negative Esophageal Pain Disorder

Epidemiology. Patients with reflux-negative esophageal pain disorder (RNEPD) have a visually normal upper endoscopy and no evidence of pathologic acid reflux with negative reflux-symptom correlation by pH-impedance (or pH-metry or wireless testing). This is equivalent to functional heartburn (FH) in adults. However, unlike adult FH, symptoms of RNEPD may include intermittent retrosternal pain, heartburn, throat pain, or burning sensation in the throat, at least 3 times per week for 2 months.[31] Younger children may present with crying or repeatedly pointing to areas of discomfort. Two studies found that 38%–44% of pediatric patients with normal endoscopy undergoing pH-impedance testing met criteria for FH per the adult Rome IV definition.[3,4]

Pathophysiology. Visceral hypersensitivity likely plays a main pathogenetic role, as these patients have intact mucosal integrity, normal mucosal nerve location, and normal esophageal refluxate clearance. The presence of microscopic esophagitis does not preclude a diagnosis of RNEPD, as 20%–23% of children with RNEPD had microscopic esophagitis, which did not correlate with symptom severity.[3,4]

There is also a role for gut–brain interplay in symptom perception. In adults, patients with FH often report other DGBI, have increased symptom hypervigilance, and exhibit more psychological comorbidities compared with healthy volunteers.[15,32–37] Stress also increases pain perception to esophageal stimuli.[38–40]

Clinical evaluation. Symptoms are nonspecific in children, complicating a symptom-based RNEPD diagnosis.

G1b. Diagnostic Criteria[a] for Reflux-Negative Esophageal Pain Disorder

Patients <8 years old	Patients >8 years old
Must include *all* of the following: 1. Intermittent symptoms that a. Are thought to be gastroesophageal reflux–related b. Are suggestive of pain c. Are more severe than could be expected based on normal developmental physiology for age d. Impact on age-expected daily activities and/or quality of life e. Occur at least 3 days per week f. Cannot be fully explained by another medical condition after appropriate evaluation 2. Normal macroscopic esophageal findings on endoscopy and absence of histologic evidence of eosinophilic esophagitis 3. Normal esophageal acid exposure on pH- or pH-impedance monitoring 4. No temporal correlation between symptoms and acid or nonacid reflux events on pH- or pH-impedance monitoring	Must include *all* of the following: 1. Intermittent symptoms of retrosternal pain, heartburn, or throat pain or burning sensation in the throat that a. Occur at least 3 days per week b. Impacts on age-expected daily activities and/or quality of life c. Cannot be fully explained by another medical condition after appropriate evaluation 2. Normal macroscopic esophageal findings on endoscopy and absence of histologic evidence of eosinophilic esophagitis 3. Normal esophageal acid exposure on pH- or pH-impedance monitoring 4. No temporal correlation between symptoms and acid or nonacid reflux events on pH- or pH-impedance monitoring

[a]Criteria fulfilled for at least 2 months before diagnosis.

To separate it from GERD, nonerosive reflux disease, or RH, diagnostic testing (ie, endoscopy and pH-impedance testing) is required for children with persistent symptoms that could be interpreted as GERD (Figure 1).

Treatment. The treatment of patients with RNEPD is multimodal, involving medication and CBT. An empiric trial of acid suppression is often attempted before testing. In 1 pediatric study, 25%–75% of patients showed partial or complete symptom resolution.[3,4] However, response to acid suppression may be a placebo response because RNEPD is not caused by acid reflux. For treatment-refractory patients, it is critical to do further testing, as antireflux surgery is not indicated.[41,42]

Because RNEPD falls on the spectrum of visceral hypersensitivity, neuromodulators should be the mainstay of therapy. Although there are no pediatric trials, in an adult trial of PPI-refractory heartburn, fluoxetine led to more heartburn-free days than omeprazole or placebo.[43] In addition, there are some limited adult data suggesting that melatonin may be helpful in reducing symptoms in patients with FH compared with nortriptyline or placebo.[44]

G1c. Diagnostic Criteria[a] for Disorders of Esophageal Air-Transit

Symptoms that:
1. Are related to the passage of esophageal air
2. Impact on age-expected daily activities and/or quality of life
3. Occur at least 3 days per week
4. After appropriate evaluation, the symptoms cannot be fully explained by other medical condition

Subgroups include:
G1c.i. Aerophagia syndrome
G1c.ii. Supragastric belching syndrome

[a]Criteria fulfilled for at least 2 months before diagnosis.

G1c.i. Diagnostic Criteria for Aerophagia Syndrome

Must include both of the following:
1. Excessive air swallowing that results in bothersome signs or symptoms
2. Abdominal distention due to intraluminal air that increases during the day

Supportive criteria:
1. Increased flatus
2. Increased belching and/or gastric venting when a feeding tube is present
3. Intraluminal impedance measurement supporting the diagnosis; note that absence of aerophagia during the measurement does not exclude the diagnosis
4. Abdominal x-ray showing that intraluminal air is the cause of the distention

G1c.ii. Diagnostic Criteria for Supragastric Belching Syndrome

Must include *all* of the following:
1. Bursts of repetitive belching originating from the esophagus
2. Does not fulfill criteria for functional dyspepsia, physiological reflux–related esophageal pain disorder, and reflux-negative esophageal pain disorder

Supportive criteria:
1. Does not occur during sleep
2. No air expulsion during distraction or speech
3. Impedance and/or impedance-manometry measurement can support the diagnosis but absence of supragastric belching during the measurement does not exclude the diagnosis

G1c. Disorders of Esophageal Air-Transit

Understanding disorders of air-transit has become clearer using pH-impedance testing and high-resolution impedance manometry (HRIM). With the ability to detect directionality of air movement, clinicians can differentiate subtypes of belching as related to supragastric belching, aerophagia, or GERD.

G1c.i. Aerophagia Syndrome

Definition. Normally, most liquid and solid boluses that children swallow are preceded by small amounts of air.[45,46] However, aerophagia syndrome is defined as a pattern of excessive air swallowing leading to a typical symptom pattern, with abdominal distention that increases over the day and/or excessive belching and flatulence.

Epidemiology. Prevalence in healthy children ranges from 0.5% to 6.3% and varies in different regions of the world.[47–49] Prevalence is higher (7%) in children visiting a pediatric gastroenterology clinic.[50] There is substantial overlap between aerophagia and other DGBI.[51–53]

Rationale for change in criteria. Aerophagia, a normal physiologic phenomenon, should only be considered a syndrome if it impacts quality of life and causes symptoms. Previously, increased flatus was considered a major criterion but because flatus may go unnoticed, it is no longer a major criterion. Since the recognition of supragastric belching (SGB), excessive belching as a clinical symptom is a supportive criterion. Patients with abdominal bloating without evidence of intra-abdominal air do not fall into this category.

Pathophysiology. When air swallowing is excessive, gas can result in luminal distention throughout the GI tract. In the stomach, vagal tension receptors are activated, resulting in increases in transient lower esophageal sphincter relaxations and gastric belching. In the large intestine, luminal distention causes bloating, pain, and flatulence.

Clinical evaluation. Clinical history will typically include a pattern of gradually worsening abdominal distention associated with belching and flatulence during the day. Early satiety, abdominal pain, nausea, and loss of

appetite may occur and can worsen over the day. In addition, a more acute presentation can be seen in patients who have episodes of intense air swallowing, which can lead to gastric or intestinal volvulus and/or respiratory distress due to the increased abdominal pressure.[54] Repetitive behaviors that may increase air swallowing, like chewing gum or drinking carbonated beverages, should be assessed.

If the clinical picture lacks alarm symptoms (eg, weight loss and anemia), testing is not needed. If there is diagnostic uncertainty, pH-impedance testing or HRIM may be indicated.

An abdominal x-ray may show large volumes of intestinal air without air-fluid levels and can help to differentiate between intestinal air and other causes of distention (eg, constipation, abdominophrenic dyssynergia, and ileus).

Treatment. No therapeutic trials exist. However, in patients with severe distention, a nasogastric tube or an existing gastrostomy tube can be used to vent air from the stomach.[55] If colonic distention is present, rectal decompression may be appropriate. In patients with chronic stable symptoms, a conservative approach is sufficient. Speech therapy or CBT aimed at reducing the air swallowing may be tried. Benzodiazepines can be considered in severe cases. Circumstantial evidence suggests that infants swallow less air using different bottle or nipple systems.[56]

G1c.ii. Supragastric Belching Syndrome

Definition. SGB is defined as esophageal air ingestion immediately followed by active expulsion from the esophagus back into the pharynx.[57] It can occur in healthy children, but is considered a disorder when it is excessive and impacts daily activities.

Epidemiology. In children with symptoms suggestive of GERD, SGB was found during pH-impedance testing in 7 of 287 (2.4%) and, of these, 3 had more than 13 episodes per 24 hours, which is considered the abnormal cutoff in adults.[46,58] In patients with symptoms suggestive of rumination—the effortless regurgitation of gastric contents—3 of 16 (18.7%) showed a pattern of predominantly SGB on HRIM rather than rumination.

Pathophysiology. SGB is a voluntary yet subconscious behavior. Two mechanisms are described in adults.[59] First, patients create negative thoracic pressures, leading to the suction of air into the esophagus when the upper esophageal sphincter opens. Immediately after the air has entered the esophagus, it is expelled. Second, patients may push air into the esophagus by tongue retraction and then expel the air.[59] SGB can be an unintentional reaction to an unpleasant feeling such as pressure retrosternally or in the abdomen.[60]

Clinical evaluation. Most patients present with excessive belching as the primary symptom. However, the symptoms may sound like hiccups to patients or parents. Often no tests are needed, as the story of multiple repeated belches is nearly pathognomonic for SGB. SGB typically occurs outside of meal periods and does not occur during sleep. pH-impedance or HRIM can be performed to confirm the diagnosis. However, absence of belching during testing does not exclude the diagnosis, as events can be sporadic.

Treatment. In a single randomized trial of behavioral interventions in adults, which included education about the disorder, warning signs for oncoming events, and breathing exercises, patients who received the behavioral interventions had higher rates of symptom improvement lasting up to 6 months.[61] Specific speech therapy interventions have been described and were successful in an open trial.[62]

G2. Functional Pediatric Feeding Disorders

The prevalence of pediatric feeding disorders have been increasing. Currently, the 2 terms to describe these disorders—avoidant/restrictive food intake disorder (ARFID) and pediatric feeding disorders—have been used to describe a range of different signs and symptoms in children, making it challenging to determine the most appropriate therapies for each patient. The goal of defining functional pediatric feeding disorders (FPFDs) is to provide more clarity about which therapies are most appropriate for patients without a structural cause for symptoms.

G2. Diagnostic Criteria[a] for Functional Feeding Disorders

Altered feeding patterns that (a) interfere with functioning; (b) occur for at least 3 times per week; and (c) cannot be attributed to an underlying medical or skill-based diagnosis that has been effectively evaluated and managed.

The diagnosis should have at least 1 of the following components:

1. Evidence of nutritional compromise (micronutrient deficiency, macronutrient deficiency)
2. Use of supplemental enteral or parenteral nutrition
3. Active or passive avoidance behaviors
4. Use of a restricted/selective diet or a diet that is not developmentally appropriate to treat symptoms
5. Lack of developmentally expected self-feeding
6. Excessive use of routine feeding strategies (eg, chewing, liquid wash down, pacing) to complete a meal

[a]Criteria fulfilled for at least 1 month before diagnosis.

G2a. Diagnostic Criteria for Hypersensitive Dysphagia

A feeding disorder characterized by perception of liquids and/or solid foods passing abnormally through the oropharynx or esophagus that is associated with *all* of the following characteristics:

1. No evidence of pharyngeal or esophageal mucosal or structural abnormalities
2. Absence of major esophageal motor disorders
3. No evidence of bolus transit abnormalities

G2b. Diagnostic Criteria for Anticipatory Restrictive Feeding

A functional feeding disorder driven by the anticipation of aversive experiences while eating and is associated with 1 or more of the following:

1. Significant weight loss (or failure to achieve expected weight gain or faltering growth in children)
2. Significant nutritional deficiency
3. Dependence on enteral feeding or oral nutritional supplements
4. Marked interference with other psychosocial functioning

G2c. Diagnostic Criteria for Hunger Dysregulation Disorders

A feeding disorder that is characterized by either:

1. **G2c.i.** Reduced hunger drive: The patient will not voluntarily eat or drink calorically appropriate foods after periods of age-appropriate fasting AND the patient requires prompting and/or scheduling of meals in order to insure adequate intake.
2. **G2c.ii.** Excessive hunger drive: The patient has excessive hunger manifested by inability to stop eating even after finishing a meal and excessive eating between meals even after completing a full meal.

G2d. Diagnostic Criteria for Medically Triggered Functional Feeding Disorder

A feeding disorder that:

1. Developed in the context of a medical condition but the feeding dysfunction persisted after the medical disorder has resolved or is adequately treated and cannot be attributed to the underlying medical condition
2. Manifests as a regression or lack of progression of feeding patterns or skills that previously achieved and cannot be attributed to the medical condition

Definitions. Pediatric feeding disorders affect 5%–20% of children and are associated with significant morbidity, decreased quality of life, and increased resource utilization.[63,64] Until now, functional feeding disorders have only been addressed in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition[65] and the definitions lacked the specificity needed to guide diagnostic testing and therapies. The Rome V Committee felt their inclusion was critical because: (1) many patients present to gastroenterologists for evaluation, the placement of feeding tubes, and/or parenteral nutrition; and (2) many of the patients presenting with DGBI also have concurrent functional feeding disorders that need to be addressed.

The definition of ARFID in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition[65] created confusion in the realm of pediatric feeding disorders, stating: ARFID is "an eating or feeding disturbance (eg, apparent lack of interest in eating or food; avoidance based on the sensory characteristics of food; concern about aversive consequences of eating) as manifested by persistent failure to meet appropriate nutritional and/or energy needs."[65]

By merging examples of different feeding disorders under a single term, ARFID, the definition lacks needed granularity to refer patients for appropriate therapies. Therefore, we propose that the term ARFID should be eliminated and replaced by more precise terms (Figure 2).

In the case of FPFD, impairments may include the inability to efficiently take adequate diverse nutrition, eating difficulties outside of preferred settings, and challenging mealtime behaviors. Symptoms should be present for at least 4 weeks to allow for symptom resolution if triggered by acute events (eg, infection) and for appropriate targeted testing to exclude other diagnoses (eg, EoE, which is present in up to 15% of patients).[66] As these are new diagnoses, the relative proportions of subgroups are not known. In 1 study of children with ARFID, 43%–82% had a lack of interest in eating (the new "hunger dysregulation" diagnosis), 21%–68% had sensory-driven food refusal, and 11%–21% had swallowing difficulties (the new "hypersensitive dysphagia" [HD] diagnosis).[67]

G2a. Hypersensitive Dysphagia

Children with HD present with sensations of food feeling stuck despite normal esophageal anatomy, motor function, and bolus clearance. This diagnosis is equivalent to the "functional dysphagia" diagnosis in adults, with some key differences. First, HD includes both oropharyngeal and esophageal sensations because children cannot often differentiate locations or they will not put food in the mouth or will chew and spit food or drinks. Second, normal bolus transit (as measured by HRIM or esophagram if the former is not available) was added to the definition.

G2b. Anticipatory Restrictive Feeding

Anticipatory restrictive feeding (ARF) is characterized by the fear of an aversive experience with eating (eg, nausea, pain, bloating, gagging, choking, or vomiting). Clinically, these patients may present with significant diet restrictions resulting in elimination of entire food groups, specific food textures, or food temperatures. Children may express experiences of anxiety, disgust, or fear when consuming new, symptom-triggering, or nonpreferred foods. ARF differs from a medically triggered functional feeding disorder in that the latter is associated with the loss or halting of feeding milestones or skills with the development of a medical illness. ARF does not have a loss of skills or milestones but is associated with fear of eating. ARF is common in children with concurrent DGBI and the majority (>80%) of these patients have underlying GI symptoms.[68,69]

G2c. Hunger Dysregulation Feeding Disorder

There are 2 subtypes: (1) reduced hunger drive and (2) excessive hunger drive. With reduced hunger drive, patients are rarely if ever hungry or thirsty. In contrast, the

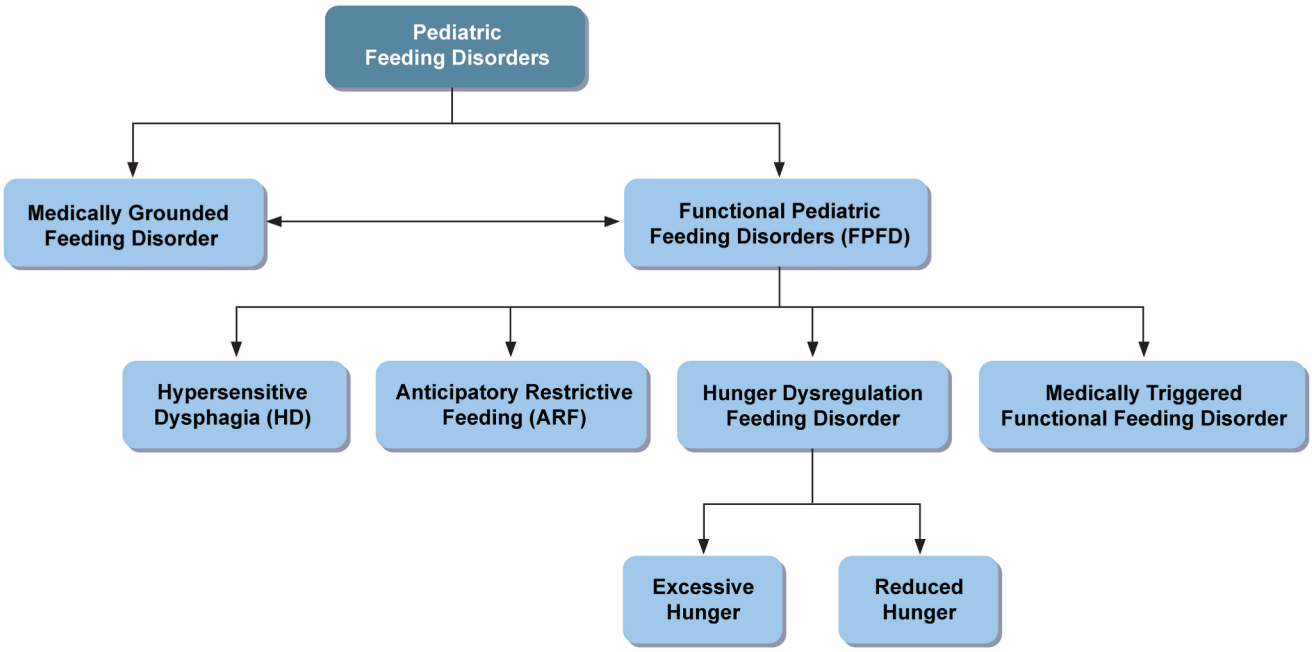

Figure 2. Algorithm for pediatric feeding disorders. Patients may have a medically grounded feeding disorder that develops into a functional feeding disorder or visa versa.

excessive hunger drive patients manifest with excessive drive to eat. These feeding disorders typically manifest early in childhood, including during toddlerhood and even infancy.

G2d. Medically Triggered Functional Feeding Disorder

The key feature to this diagnosis is that (1) the underlying medical disorder needs to have been successfully treated and (2) there is a halting of oral progression or a regression of oral skills (ie, skills needed for children to eat and drink safely and efficiently such as chewing, bolus propulsion, and sensory processing of oral contents) coinciding with a clear medical event. Often, these patients present during late infancy or toddlerhood in the context of severe GERD or EoE when these patients continue to only consume a liquid diet despite complete mucosal healing and no evidence of bolus retention. In contrast, if a patient has EoE and develops a food impaction, is successfully treated for EoE, but then does not want to eat any solid food for fear that it will get stuck, that patient would have ARF because the fear of eating is at the root of the feeding disorder. Finally, if the patient has active EoE and does not eat solid food, this is a medically triggered pediatric feeding disorder (because there is persistent inflammation and potentially esophageal dysmotility) but not a medically triggered functional feeding disorder. The term "functional" is added when there is no structural reason to explain the inability to take solid or liquid food.

Epidemiology. Feeding problems are estimated to occur in from 25% to 45% of children in the general population, in 33% of children with developmental disabilities, and in up to 80% of children with severe cognitive disabilities.[70–72] Medical and oral problems occurred more often in patients aged <2 years, and behavioral or functional feeding problems occurred more often in children aged >2 years.[73] In a large cohort of young children with feeding disorders, 86% of the patients had a medical disorder; 61% had an oropharyngeal dysfunction, and 18% had a behavioral problem.[73]

Pathophysiology. There are no studies for these new diagnoses. Ghrelin, oxytocin, cholecystokinin, and peptide YY have all been studied in adults and/or children with ARFID, with no clear signal emerging as a causative factor for symptoms.[69,74–76] One common cause for feeding-related anxiety is the initial restriction of food in an effort to improve GI symptoms. This could be driven by well-intentioned self or family observation, medical recommendations, or online social media.[77,78]

Clinical evaluation. All structural and skill-based etiologies should be assessed or managed before starting any behavioral treatments. If diagnostic testing is not available, behavioral interventions can be trialed but, if these interventions are ineffective, then reassessment of the medical condition and feeding skills is necessary.

Key questions providers should ask patients and families are shown in Table 1. History should be multimodal and is accomplished via clinical histories, school reports, video recordings of mealtimes, and neuropsychological testing. Cultural meal practices need to be considered. Because feeding disorders increase caregiver stress, diminish parental confidence, and result in negative parent–child interactions, assessment of whole family wellbeing is important.[79,80]

History, signs, and symptoms that may suggest a diagnosis other than an FPFD are shown in Supplementary Table 1 and Supplementary Figure 1. Mealtime or feeding assessment is critical to assess for feeding skills and to

Table 1. Suggested Questions to Consider for Functional Feeding Diagnoses

Disorder	Key questions
General	How long does a meal take to complete?
	Do you need your food cut up in small pieces?
	Do you chew your food more than others?
	How much liquid do you drink with each meal?
	Does feeding happen overnight?
	What happens if meals are off schedule?
	What are preferred foods?
	What are avoided foods?
	Has there been weight loss? Gain?
	Are meals stressful for you? For your family?
	Are there any allergies?
	Are there any cultural requirements for meals?
	How do you eat at home compared to school?
	Can you go out to eat as a family?
	Do you need to bring food with you when you leave the house and if so, why?
	Do you have issues wearing clothes with tags or walking on sand or grass barefoot?
	Are you bothered by loud noises?
HD	Do you feel that liquids, solids or both get stuck?
	Are there particular foods that get stuck?
	What makes the stuck feeling go away?
	How much liquid do you need to drink at a meal?
	How much chewing is required during a meal?
ARF	Do you experience worry about eating?
	What symptoms have been associated with a meal? After a meal?
	Are there foods that you typically worry about eating and what happens if you try to eat them?
	Are you able to go out to eat with friends?
Hunger dysregulation disorder	How long can you go without eating?
	What happens if you cannot eat due to a change in schedule, fasting for medical procedures?
	Do you need to lock up food between meals?
	Do you graze on food throughout the day?
Medically triggered functional feeding disorder	Can you pinpoint when the feeding trouble started?
	Are you able to eat age-appropriate food consistencies (liquids, semisolids, solids) before the medical condition started?
	Have you had any infections?
	Do you take any medications?
	Have you received any new medical diagnoses?
	When was the last assessment of medical conditions?
	What testing have you recently had done?

watch for avoidance behaviors, tantrums, or oral pocketing of food.[81]

Unlike many other DGBI, significant testing may be required before an FPFD diagnosis can be made because of the medical masqueraders (Figure 2) that may mimic an FPFD.[73] Testing by feeding diagnosis is shown in Supplementary Table 2. Upper GI endoscopy is almost always recommended for pediatric feeding disorders because EoE can present with symptoms mimicking an FPFD; 25%–50% of patients with EoE have dysphagia and feeding issues and 15% of children with feeding issues have EoE.[82–84] Laboratory testing for celiac disease, thyroid disease, a complete blood count, and electrolytes are indicated and, potentially expanded laboratory testing for iron, vitamin A, C, D, B12, carnitine, folate, liver function tests, thiamin, and zinc, depending on the history.[83,85]

Treatment. For the majority of patients, outpatient nutritional management is feasible and preferred. Nutritional management may include the addition of vitamins, addition of nutritionally complete formula or calorically dense additives, or strategic rotation of preferred foods. If there is significant weight loss, barium imaging for evaluation of superior mesenteric artery syndrome may be needed. Changes in vital signs (eg, low heart rates and hypotension) may merit urgent inpatient nutritional rehabilitation. In addition, restrictive diets such as the low fermentable oligo-saccharides, di-saccharides, monosaccharides, and polyols diet, gluten-free diets, and dairy-free diets are not usually recommended for symptom control as they may increase meal-related anxiety, thus worsening or triggering an FPFD.[86]

Although enteral tubes may play an important role in urgent nutritional rehabilitation, the majority of patients do not need enteral tube support. In the ARFID literature, 20%–46% of patients were reliant on some form of enteral support, although the approach to ARFID has recently moved away from enteral tube use toward multidisciplinary behavioral therapies.[67] Intravenous parenteral nutrition is not recommended for FPFD.

Medications are often trialed for FPFD subtypes. For patients lacking a hunger drive, cyproheptadine has been found to increase appetite and improve gastric accommodation.[87,88] A retrospective review of intrapyloric botulinum toxin injections (IPBIs) in 85 young children with feeding disorders found some improvement with IPBIs.[89] Although the mechanism is not known, improvements in gastric accommodation or sensory perception have been suggested. In small case series, neuromodulators such as TCAs, gabapentin, and mirtazapine may be beneficial.[90–92] In addition to the medications above, it is important to treat any underlying mental health issues either through psychological interventions or, when needed, medications (eg, fluoxetine, escitalopram, sertraline, olanzapine, and mirtazapine).[93,94] Finally, for patients with GI symptoms triggering ARF, it is important to maximize symptom control to improve behavioral outcomes.

Behavior management techniques are designed to strengthen adaptive behaviors and reduce challenging behaviors. The goal in HD is to help the child overcome fears through a combination of exposure therapy, including discrimination training, along with cognitive restructuring methods.[95,96] Children with ARF benefit from environmental control methods including repeated exposures to new and nonpreferred foods, and interventions that focus on the schedule to promote appetite.[97,98] Teenagers with ARF may benefit from CBT.[99] Patients with ARF are also encouraged to develop fear/avoidance hierarchies paired with graded exposure to the feared foods, allowing for nontraumatic experiences. Behavioral management of dysregulated hunger typically involves a combination of medical management of hunger cues along with strict behavioral environmental controls. Patients with medically triggered functional feeding disorder often require interdisciplinary care with gastroenterologists, deglutologists, psychologists, and other members of the care team.[100]

G3. Gastroduodenal Disorders

Highlights of this Rome V iteration include updates in the prevalence literature for these disorders and increased expansion of therapeutic options.

G3a. Rumination Syndrome

Definition. Rumination syndrome (RS) is an acquired behavioral disorder characterized by repetitive and volitional, although subconscious, episodes of regurgitation of gastric contents.

Epidemiology. The reported prevalence ranges between 0% and 9.7%, with no differences in both gender and age.[48,101,102]

Justification for changes in diagnostic criteria. Pre-Previous pediatric criteria on rumination distinguished

G3a. Diagnostic Criteria[a] for Rumination Syndrome

Must include *all* of the following symptoms for minimum 2 months, starting after 3 months of age:

1. Repeated, seemingly effortless regurgitation of gastric contents that is:
   a. Reswallowed and/or rechewed and/or expelled during or immediately after a meal or ingestion of fluids
   b. Does not occur during sleep
2. Does not respond to standard management for gastroesophageal reflux disease or infant regurgitation.

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out.

Supportive criteria:

1. The repeated regurgitation of gastric contents might occur during or after physical or psychological stress.
2. High-resolution esophageal impedance manometry may help confirm the diagnosis in cases of unusual symptomatology or family skepticism. High-resolution esophageal impedance manometry allows for prompt identification of the rumination episodes, with the sensitivity maximized by an extended recording after a test meal.

[a]Criteria fulfilled for at least 2 months before diagnosis with onset of symptoms after 3 months of age.

among infants, children, and adolescents. Although RS differs by age in pathophysiology, diagnosis, and treatment, shared clinical features support unified criteria. "Seemingly effortless" regurgitation remains appropriate, as abdominal and diaphragmatic contractions often go unnoticed. Regurgitation after fluid intake was added due to its common occurrence. The exclusion of retching was removed, as some children may experience it before episodes. The revised criteria require lack of response to GERD treatment—or, in infants, troubling regurgitation—before diagnosing RS. Descriptions of repetitive muscle contractions in infants were removed, as they reflect pathophysiology rather than clinical criteria.

Pathophysiology. RS involves unconscious contraction of the abdominal wall, increasing intragastric pressure and triggering regurgitation.[103,104] This is facilitated by intercostal muscle contraction and relaxation of the upper esophageal sphincter and esophagogastric junction, leading to retrograde flow. Relaxation of esophagogastric junction includes diaphragmatic relaxation, transient lower esophageal sphincter relaxation, and lower esophageal sphincter displacement.[103] HRIM reveals pressure spikes ("R waves") with retrograde bolus movement.[105]

Triggers may include unpleasant postprandial sensations (eg, nausea, burning, and reflux), which act as premonitory urges and successful treatment often improves these sensations.[106,107] These may result from gastric sensory-motor dysfunction or neuroimmune changes.[108] Delayed gastric emptying is seen in up to 45% of pediatric RS cases.[106] Increased mast cells, eosinophils, and intraepithelial lymphocytes have also been observed.[108]

Learned behaviors, body image concerns, and self-soothing tendencies (especially in infants or neurologically impaired children) may initiate or sustain rumination.[105] RS symptoms may follow physical (eg, viral illness to 43%, nonviral illness 11%) or psychological (eg, anxiety and trauma) triggers in 7%.[109] Impaired caregiver interactions may also contribute.[110]

Clinical evaluation. RS presents as effortless, repetitive regurgitation during or shortly after meals, sometimes triggered by fluids or activity. The regurgitated material reaches the mouth and is either spit out or reswallowed, depending on social circumstances. Episodes do not occur during sleep and may be preceded by nausea or after a burst of coughing or hiccupping. RS can overlap with other DGBI.[105] Up to 40% of affected children experience weight loss but severe malnutrition and disorders like postural orthostatic tachycardia syndrome (POTS) are less common.[103,110] Clinical observation during or after meals is often sufficient for diagnosis.[111] Confirmatory tests, such as HRIM (R-wave), 24-hour pH-impedance monitoring, or upper endoscopy and contrast studies may be needed for atypical presentations or when there is diagnostic uncertainty.[109,112,113]

Younger children with RS are more likely to have developmental delays and less likely to have psychiatric comorbidities.[111] In older children, up to 70% of children have at least 1 psychiatric comorbidity.[109,110] Anxiety, depression, and eating disorders are most common, although attention-deficit hyperactivity disorder, obsessive-compulsive disorder, and adjustment disorder have been reported.[111]

Treatment. The first step is to explain the pathophysiology and offer reassurance to families that no further testing is needed and that effective therapies exist.[114] In fact, 23% of children diagnosed with RS showed self-resolution of symptomatology without treatment after only the initial counseling.[115] In infants and young children, management focuses on supporting the caregiver–infant relationship, providing family support to maximize developmental progress, and addressing potential triggers (eg, neurologic, dietary, positional, or stress-related). The treatment in older children and adolescents focuses on implementing behavioral strategies, modulating food and liquid intake, managing mental health–related issues, and implementing diaphragmatic breathing around mealtimes.[107,116]

Diaphragmatic breathing is the first-line therapy and is effective both in-person and via telemedicine. Modifications using imagery or toys may help younger children.[107,116] CBT complements diaphragmatic breathing, targeting premonitory urges and maladaptive behaviors. Teaching children to reswallow regurgitated material reinforces control and maintains nutrition.[107,116]

Patients with psychological comorbidities should be referred to a mental health care professional, as their presence is associated with both poor treatment outcomes and longer treatment durations.[116–118] In children and adolescents experiencing severe symptoms or medical complications, an intensive inpatient multidisciplinary program may be required.[116–118]

Baclofen may be an adjunctive therapy, although data in children are limited. A recent retrospective study in children found that baclofen is safe and is effective in almost 50% of children.[119] Other drugs and interventions (eg, antireflux surgery and botulinum toxin) are not routinely recommended.

Complete remission rates vary (16%–74%), but most patients show significant improvement, especially younger children.[115,117,118] Long-term outcomes are generally positive, with sustained behavioral strategies, although symptom flares may occur with stress or illness.[117]

G3b. Cyclic Vomiting Syndrome

Definition. Cyclic vomiting syndrome (CVS) is a disorder characterized by stereotypical episodes of repetitive nausea, vomiting, and/or retching dispersed with symptom-free periods.[120]

Rationale for change in diagnostic criteria. The revised criteria provide terminology that would be accepted internationally by both clinicians and researchers. A subcategory on cannabinoid hyperemesis syndrome (CHS) is included based on a rising prevalence and recognition in children.[121]

Epidemiology. CVS is a common condition but often underrecognized. Prevalence rates reach up to 2% in infants, toddlers, and school-aged children.[120] Misdiagnoses, especially as viral gastroenteritis, often delay diagnosis by up to 10 years.[122] CVS leads to significant disability,

G3b. Diagnostic Criteria for Cyclic Vomiting Syndrome

1. Stereotypical episodes of acute onset, repetitive vomiting multiple times per hour
2. ≥4 discrete episodes in the prior 12 months, lasting 2 hours to 7 days
3. Episodes at least 1 week apart
4. Return to baseline health between episodes
5. After appropriate evaluation, the symptoms cannot be fully explained by other medical conditions

Supportive remarks:

1. History or family history of migraine headaches
2. Episodes associated with listlessness, diaphoresis, photophobia, unrelenting nausea, abdominal pain, and/or incessant retching after emptying stomach
3. Less acute or intermittent symptoms such as abdominal pain and nausea can be present between episodes

G3b.i. Diagnostic Criteria for Cannabinoid Hyperemesis Syndrome

1. Stereotypical episodes of vomiting resembling cyclic vomiting syndrome in terms of onset, duration, and frequency
2. Presentation after prolonged (eg, 1–2 years), excessive (eg, near daily) cannabis use
3. Resolution of vomiting episodes by sustained (at least 6 months) cessation of cannabis use

Supportive remarks:

1. May be associated with pathologic bathing behavior (prolonged hot baths or showers)
2. Diagnosis strengthened by positive urine Δ-9-tetrahydrocannabinol test

including an average of 24 missed school days per year and more quality of life impairment than other DGBI.[123]

Pathophysiology. Although the exact mechanisms are unclear, several overlapping pathways have been proposed. CVS is often considered a migraine-equivalent disorder due to similarities in symptoms, triggers, mitochondrial polymorphisms, and treatment response.[124] Mitochondrial dysfunction is supported by maternal inheritance patterns and metabolic abnormalities during attacks. Autonomic nervous system (ANS) imbalance is documented in pediatric CVS.[125] Symptoms like diaphoresis, palpitations, and listlessness are common and patients develop dysautonomia over time.[126] Stress-related activation of the hypothalamic–pituitary–adrenal axis and elevated morning corticotropin-releasing factor levels may delay gastric emptying, which can contribute to episodes.[127–129] Dysfunctional signaling in the brainstem and hypothalamus may trigger emetic responses to stress involving autonomic dysregulation and activation of the vomiting reflex.

Clinical evaluation. CVS is diagnosed based on stereotypical high-intensity vomiting or retching episodes that occur in cycles, often several times per hour, lasting from hours to 1 week, with return to baseline between episodes. Associated symptoms often include pallor, nausea, abdominal pain, diaphoresis, and other signs of sympathetic overactivity. The committee supports the clinical evaluation outlined in the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for children aged 0–18 years, which includes limited diagnostic testing with barium imaging and laboratory tests.[120] Early symptom onset and fasting or high-protein–triggered episodes may indicate an underlying neurometabolic disorder, and metabolic testing should be performed during vomiting episodes—before intravenous fluid administration—for optimal diagnostic yield. In adolescents, consider CHS, characterized by recurrent severe vomiting, nausea, and abdominal pain linked to chronic cannabis use.[120]

Diagnosis is clinical but supported by tests to rule out mimics, especially if red flags (eg, bilious vomiting, neurologic symptoms, and hepatomegaly) are present or if no response to standard treatment occurs within 2 months.

Specific subtypes are important to help target therapy appropriately. These include migraine-associated, menstrual-triggered ("catamenial"), and the more severe Sato-variant CVS. Although migraine-associated CVS often responds to typical abortive and/or prophylactic migraine interventions, calendar-timed and catamenial CVS may benefit from therapies initiated immediately before the anticipated cycle.[120] Comorbid anxiety is very common (occurring in 59% of school-aged children), and a subset of children with a particularly low threshold for stress-triggered episodes may benefit from mindfulness and behavioral interventions.[120,130,131]

Treatment. The committee supports the treatment approach outlined in the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition CVS guidelines.[120] Effective treatment requires a stepwise, individualized approach based on episode severity, disability, and psychosocial impact. Management includes lifestyle changes, behavioral interventions, and alternative therapies for all patients, abortive and/or prophylactic medications, or emergency care based on severity. Lifestyle interventions focus on trigger avoidance and early recognition of prodromal symptoms. Abortive treatments (eg, antimigraine, antiemetic, analgesic, and sedative agents) should be given early, using nonoral routes when possible. Emergency care involves intravenous medications to manage nausea, pain, and induce sleep—often the only effective relief during the emetic phase. Early emergency department treatment reduces hospital admissions. Prophylactic medications are considered for frequent or prolonged episodes that impair functioning. Complementary approaches like mitochondrial supplements, neuromodulation, and mindfulness interventions along with treatment of comorbidities are essential.

G3b.i. Cannabinoid Hyperemesis Subgroup

Epidemiology. CHS, a subtype of CVS, requires cannabis cessation counseling and medical management.[132,133] Although more common in adults, CHS also affects teens, who may underreport cannabis use,

complicating diagnosis. Limited data suggest adolescent CHS may be more common in females and causes symptoms throughout the day, unlike the morning pattern seen in adults.[134]

Pathophysiology. The pathophysiology remains poorly understood but is thought to affect genetically susceptible individuals.[133] Prolonged cannabinoid receptor-1 activation by Δ-9-tetrahydrocannabinol (THC) may disrupt the endocannabinoid system, leading to cannabinoid receptor-1 down-regulation and altered stress and temperature regulation through the transient receptor potential vanilloid system and other neurotransmitters.[132,134]

Clinical evaluation. The clinical evaluation of CHS is identical to that of CVS. CHS typically occurs after years of near-daily cannabis use and should only be diagnosed if symptoms improve with sustained cessation, helping avoid misdiagnosis in patients with CVS with occasional THC use.[120,133] Hot bathing, although common in CHS, also occurs in CVS. A positive urine THC test can support diagnosis, with higher THC-COOH levels indicating chronic use.[120,133] Providers should account for false-positive results and prolonged detection of THC in urine.

Treatment. CHS treatment mirrors CVS and includes abortive and preventive therapies.[120,132,133] Long-term management centers on cannabis cessation and TCAs like amitriptyline. As sudden cessation may cause withdrawal and relapse, gradual reduction and lower-THC products may improve success.

G3c. Chronic Nausea Syndrome

Definition. Nausea, a common symptom, is an unpleasant feeling, usually in the epigastrium or throat, associated with a sense of needing to vomit.[135] Chronic nausea syndrome (CNS) is now recognized as a disabling condition often linked to multiple comorbidities.

Rationale for change in diagnostic criteria. Since its inclusion in Rome IV, studies have confirmed the prevalence of functional nausea and its link to comorbidities like POTS and other autonomic disorders, suggesting it may be part of a broader syndrome. Rome V now uses the term "chronic nausea syndrome" to better reflect this. The diagnostic criteria remain similar to Rome IV. Vomiting is excluded from the definition, as children typically present with nausea alone.

Epidemiology. Chronic or intermittent nausea affects 15%–23% of school-aged children, with higher rates in girls and private school students.[135–137] It often coexists with other DGBI, especially pain-related disorders and functional constipation.[137,138]

Nausea is linked to poor school and social functioning, high somatization, anxiety, depression, and reduced quality of life.[137,138] Children with nausea tend to have more upper GI symptoms and comorbidities like headaches, fatigue, sleep issues, and POTS.[5,138] Using strict Rome IV criteria, functional nausea is rare (0.7%). Nausea is also a fundamental symptom in episodic DGBI, such as abdominal migraines and CVS, and many patients with chronic nausea fulfill criteria for POTS.[138–140]

Pathophysiology. The cause remains unclear but likely involves complex interactions between the brain, gut, ANS, and psychological factors (eg, anxiety and depression).[140–143] Symptoms may result from alterations in gastric electrical rhythm, abnormalities of gastric accommodation, and amplified or attenuated CNS signaling. Other symptoms may be triggered by environmental circumstances or psychiatric comorbidities. Nausea often co-occurs with physiologic changes such as diaphoresis, eye blinking, salivation, palpitations, and pallor.[140–143] Morning nausea may reflect ANS dysfunction or school-related stress.

Clinical evaluation. Before diagnosing CNS, other causes like mucosal disease, obstruction, or motility disorders should be considered. Nausea can be hard to describe, so child-friendly language or pictograms may help.[144] Routine laboratory tests may be done, but extensive testing rarely provides alternative diagnoses.[138] Diagnostic endoscopy is not recommended unless "red flags" are present.[138] Gastric-emptying studies are also not routinely needed unless vomiting is severe, the diagnosis is unclear, or the nausea is intractable. When associated with vomiting, a more detailed central nervous system assessment with imaging or a motility evaluation may be considered. Like in other DGBI, diagnostic tests should only be performed in the presence of other alarm signs or features (eg, weight loss, severe pain, and bilious vomiting).[138]

Treatment. CNS is difficult to treat and lacks standardized therapies.[135,138,140,145] Hypnotherapy may be more effective than standard medical care, especially short term.[146] Medications like ondansetron, domperidone, cyproheptadine, aprepitant, and amitriptyline have shown some benefit, although evidence is mostly anecdotal.[146] Neuromodulators like mirtazapine may help but can cause adverse effects and are best reserved for refractory cases.[147]

Interventions like IPBI and gastric electrical stimulation have shown promise in select patients, although data are limited.[148,149] IPBI may help even without delayed gastric emptying, with effects lasting up to 3 months.[150] Other emerging treatments include percutaneous nerve field stimulation.[151]

Supportive care—including hydration, sleep, exercise, and salt intake—may help, especially in patients with POTS. A multidisciplinary approach involving education,

G3c. Diagnostic Criteria[a] for Chronic Nausea Syndrome

Must include *all* of the following:

1. Bothersome nausea as the predominant symptom, occurring at least twice per week
2. Not associated with vomiting
3. After appropriate evaluation, the nausea cannot be fully explained by another medical condition

[a]Criteria fulfilled for at least 2 months before diagnosis.

reassurance, psychological support, and functional maintenance is key for optimal outcomes.

G3d. Functional Dyspepsia

Definition. Function dyspepsia (FD) describes upper GI discomfort that may include a variable combination of features, including epigastric pain, postprandial upper abdominal fullness, early satiety, bloating, nausea, belching, and vomiting. Two main subtypes have been identified: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS).[152–154]

Justification. The Rome V committee revised the pediatric criteria to align with adult standards; the required symptom frequency for PDS was increased from 1 to 3 times per week, reflecting typical meal patterns and preliminary pediatric data. A postprandial episode is now defined as occurring within 2 hours of a developmentally and culturally appropriate meal.

Epidemiology. In children, a meta-analysis reported a global FD pooled prevalence of 2.1%, although rates vary widely by region—from 2.8% in Japan to nearly 30% in Argentina.[155] In an Italian study of 100 children, 17% had epigastric pain syndrome, 47% had PDS, and 36% had overlapping symptoms. Symptom overlap and transitions between subtypes were common over a 6-month follow-up.[152]

G3d. Diagnostic Criteria[a] for Functional Dyspepsia

Must include 1 or more of the following bothersome symptoms:

1. Postprandial fullness
2. Early satiation
3. Epigastric pain or burning

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Two subtypes:

G3d.i. Postprandial distress syndrome

G3d.ii. Epigastric pain syndrome

[a]Criteria fulfilled for at least 2 months before diagnosis.

G3d.i. Diagnostic Criteria for Postprandial Distress Syndrome

Must include 1 or more of the following bothersome symptoms at least 3 days per week:

1. Bothersome postprandial[a] fullness that occurs with completion of a developmentally and culturally appropriate meal
2. Early satiation that prevents finishing a developmentally and culturally appropriate meal

Supportive features include upper abdominal bloating, postprandial nausea, discomfort, or excessive belching.

[a]Postprandial means that symptoms are triggered within 2 hours after meal intake.

G3d.ii. Diagnostic Criteria for Epigastric Pain Syndrome

Must include 1 or more of the following bothersome symptoms (interferes with function or quality of life) at least 1 day per week:

1. Pain or burning localized to the epigastrium
2. The pain is not present in any other abdominal or chest region
3. Symptoms can be induced or worsened postprandially or can occur independently of meals but postprandial distress syndrome criteria are not fulfilled
4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition, including functional abdominal pain or irritable bowel syndrome

Pathophysiology. FD is a heterogeneous disorder likely associated with different underlying pathophysiologic mechanisms. Common abnormalities include impaired gastric accommodation (40%), hypersensitivity to gastric distention (30%), and abnormal gastric emptying (25%). Other contributors include central sensitization, low-grade inflammation, genetic predisposition, and psychological factors (anxiety).[156,157] Fifty percent of pediatric patients with FD had an abnormal electrogastrography, and 47% showed delayed gastric emptying.[158–160] In a study of 104 children with dyspeptic symptoms, gastric emptying was abnormal in 50% and only nausea correlated with the percentage of food retention at 4 hours.[156] In a study of 16 children with FD undergoing barostat testing, there was a lower gastric accommodation and a lower discomfort threshold compared with non-FD patients and there was no relationship between gastric emptying and barostat findings.[161,162]

Duodenal eosinophilia and mast cell activity, sometimes with food triggers, may also contribute to FD by affecting gut nerve signaling.[163,164] *Helicobacter pylori* infection is not typically associated with pediatric FD and does not require routine testing.[165]

Clinical evaluation. Diagnosis requires clinical judgment, as symptoms overlap with other conditions. Unnecessary testing should be avoided whenever possible. Ultrasound or hepatobiliary iminodiacetic acid scan is reserved for specific cases with right upper quadrant pain. Upper endoscopy (ie, esophagogastroduodenoscopy) is not routinely required in children unless alarm signs are present.[166] Risk factors for abnormal esophagogastroduodenoscopy include male sex, multiple alarm features, and Black race. Expert consensus supports esophagogastroduodenoscopy in selected cases, for example, older children, symptoms lasting longer than 6 months, family history of ulcers, or significant impact on daily life. Gastric emptying may be indicated in intractable patients with PDS.

Treatment. Clinicians should explain the biopsychosocial nature of FD, discuss symptom triggers, and introduce the concept of the gut–brain axis.[167,168] Treatment remains primarily supportive.

Despite many patients reporting food-related symptoms, no specific diet is consistently effective in children.[169] Recommendations, however, may include (1) slow and regular eating, (2) avoidance of high-fat food items, (3) reduction in coffee and alcohol consumption, (4) Mediterranean diet, (5) increase in fresh food intake, and (6) decreased intake of ultraprocessed foods.

A course of acid suppression may be used for epigastric pain syndrome symptoms. In refractory cases, low-dose TCAs and other neuromodulators are often considered, despite limited evidence for benefit.[170–172]

Occasionally, prokinetic agents such as prucalopride or domperidone may be beneficial when available, particularly in those with PDS and abnormal gastric emptying. A review of 57 children treated with mirtazapine for functional nausea or PDS found an 82% response rate and, in the PDS group, 76% improved, with 45% reporting complete relief.[147] Common adverse effects included weight gain (16%) and dysphoria (9%). Cyproheptadine may also be an effective treatment for FD.[171]

In a trial of 100 children with chronic nausea or FD, hypnotherapy showed a trend toward better outcomes at 3 and 6 months and was more effective in functional nausea but not in FD.[173] For treatment-resistant cases, peripheral auricular stimulation may be promising. In a pediatric study of FD, combined intrapyloric botulinum toxin and pyloric dilation improved symptoms in 76% of patients vs 49% in controls, with better outcomes in those with delayed gastric emptying.[174]

Conclusions

Rome V opens the field for new research into the prevalence and natural history of new disorders and the efficacy of psychological and medical interventions for new and old disorders alike.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2026.01.039.

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