

بنام خداوند جان و

Disorders of Brain-Gut Interaction (Functional gastrointestinal Disorders)




Laya Amini, MD, Gastroenterohepatologist

Isfahan university of Medical Sciences

May 2026

Definition

- ❓ Disorders of brain-gut interaction (**DBGI**), formerly classified as functional gastrointestinal disorders (**FGIDs**), comprise a group of conditions that relate to the gastrointestinal (GI) tract and can not be completely explained by other underlying etiologies such as GI, anatomic, physiologic, or biochemical abnormalities.
- ❓ Conversely, DBGI are defined as a group of disorders classified by GI symptoms related to any combination of motility disturbances, visceral hypersensitivity, altered mucosal and immune function, gut microbiota, and/or central nervous system processing.



Rome IV criteria, May 2016:

FGID



DBGI

FGID:

- ❓ non specific and potential for stigma

DBGI:

- ❓ not entirely based on diagnoses of exclusion
- ❓ based on objective, unambiguous, and accurate criteria derived from a medical history and clinical examination



❓ DBGI may coexist or interact with other organic GI disorders, such as:

inflammatory bowel disease

celiac disease

chronic pancreatitis

❓ DBGI themselves exist as related entities on a spectrum with considerable overlap.

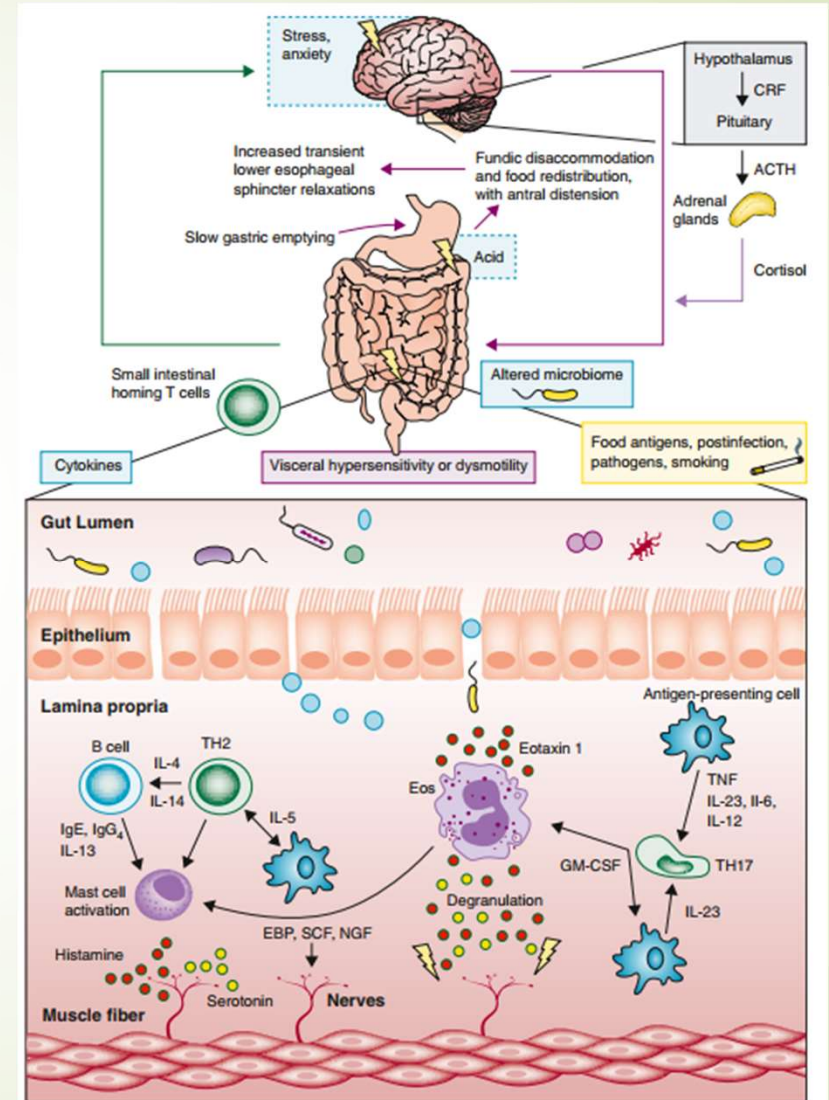
❓ DBGI in children encompass two age-groups: infants/toddlers and children/adolescents.

❓ Rumination syndrome, functional constipation, and cyclical vomiting span both age-groups

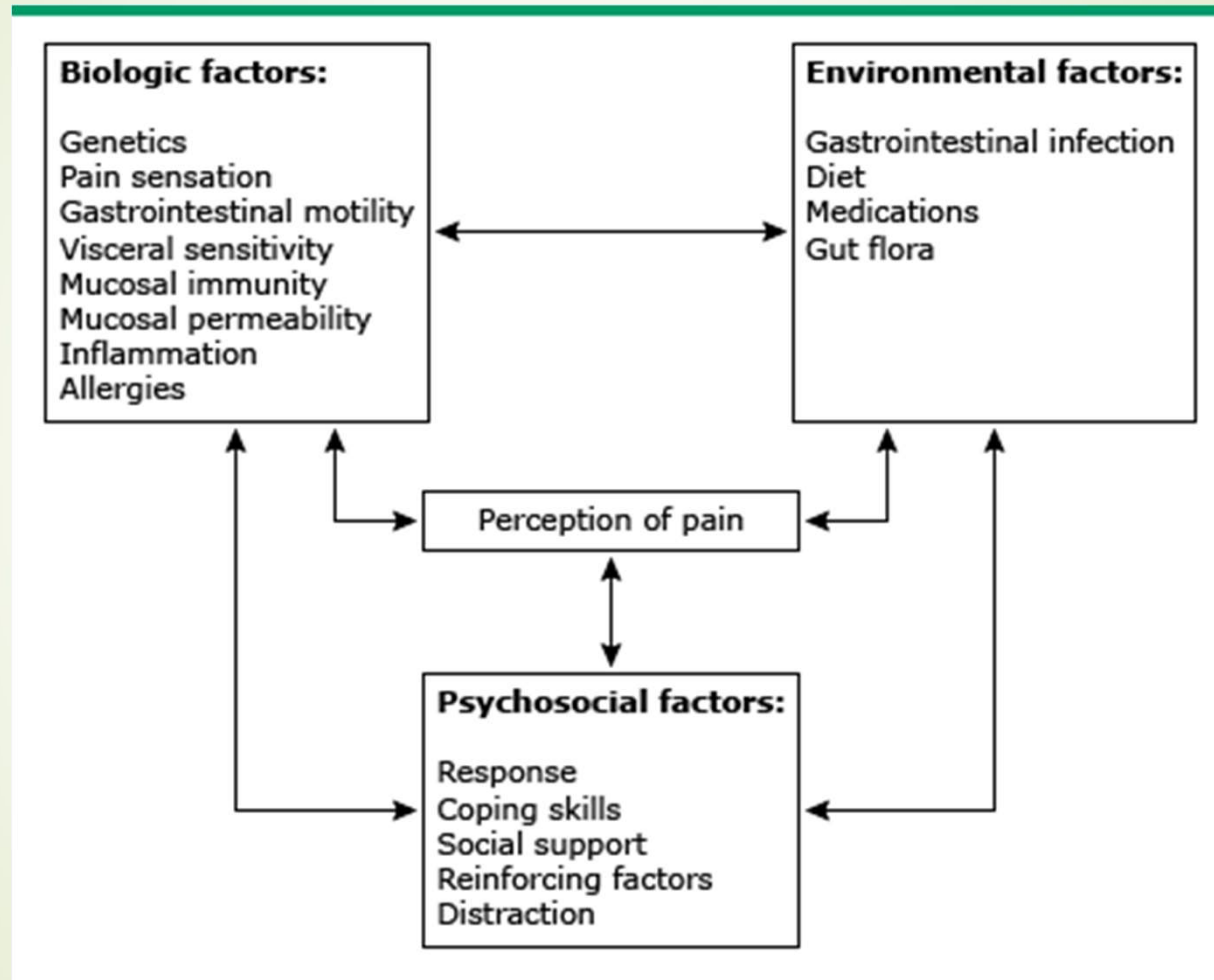
Pathophysiology

a complex interaction between:

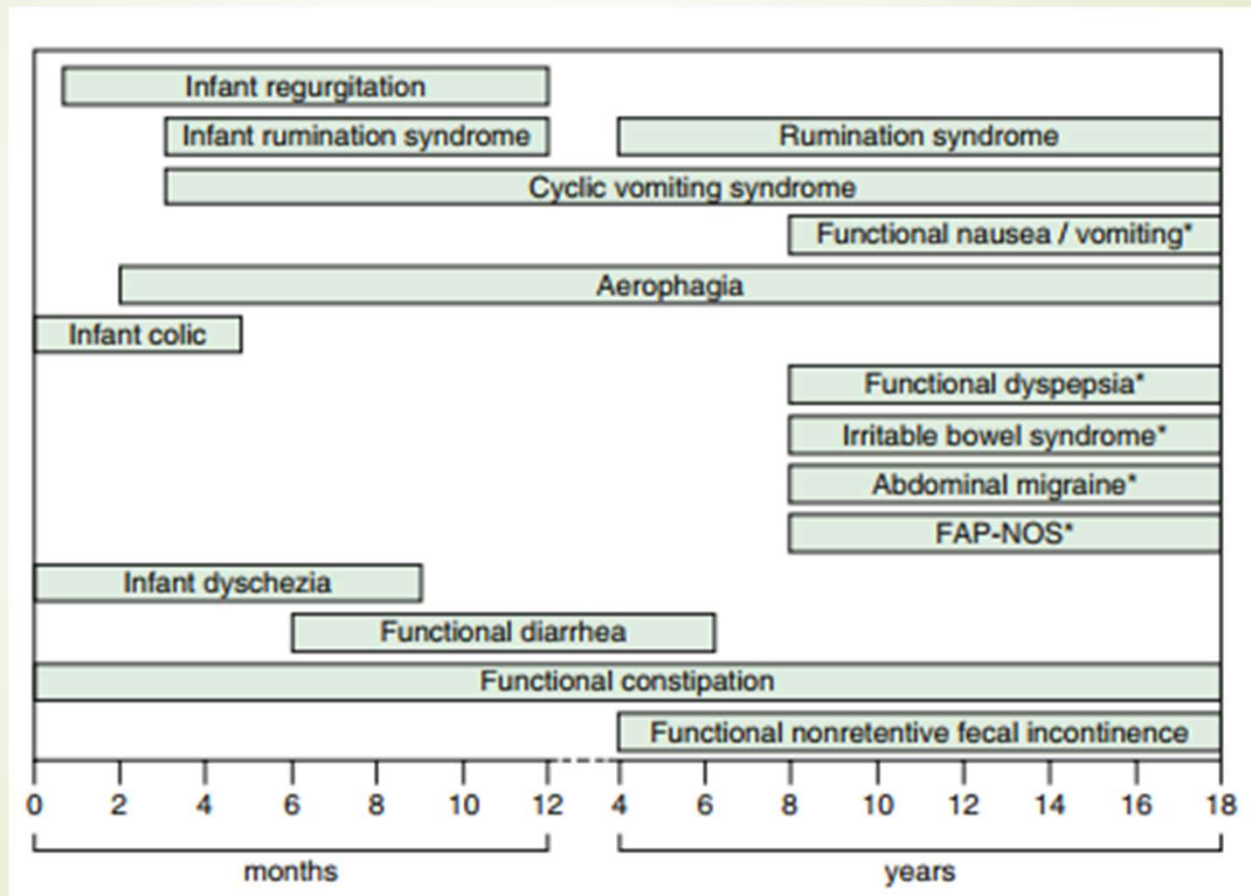
- ❓ gut microbiota
- ❓ host immune responses
- ❓ altered motility
- ❓ visceral hypersensitivity
- ❓ genetic factors
- ❓ the enteric nervous system



Biopsychosocial model of functional gastrointestinal disorders



Age distribution of functional gastrointestinal disorders in infants, toddlers, children, and adolescents





DISORDERS OF BRAIN-GUT INTERACTION IN INFANTS AND TODDLERS



Infant regurgitation

Table 389.1	Diagnostic Criteria for Infant Regurgitation
Must include both of the following in otherwise healthy infants 3wk to 12mo of age:	
<ol style="list-style-type: none">1. Regurgitation 2 or more times per day for 3 or more weeks2. No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing	

Infant Rumination Syndrome

Table 389.2

Diagnostic Criteria for Infant Rumination Syndrome

Must include all of the following for at least 2 mo:

1. Repetitive contractions of the abdominal muscles, diaphragm, and tongue
2. Effortless regurgitation of gastric contents, which are either expelled from the mouth or rechewed and reswallowed
3. Three or more of the following:
 - a. Onset between 3 and 8 mo
 - b. Does not respond to management for gastroesophageal reflux disease and regurgitation
 - c. Unaccompanied by signs of distress
 - d. Does not occur during sleep and when the infant is interacting with individuals in the environment

Table 389.7

Diagnostic Criteria for Cyclic Vomiting Syndrome

Must include all of the following:

1. The occurrence of two or more periods of intense, unremitting nausea and paroxysmal vomiting, lasting hours to days within a 6-mo period
2. Episodes are stereotypical in each patient
3. Episodes are separated by weeks to months with return to baseline health between episodes
4. After appropriate medical evaluation, the symptoms cannot be attributed to another condition

Infant Colic

Table 389.3 Diagnostic Criteria for Infant Colic

For clinical purposes, must include all of the following:

1. An infant who is <5mo of age when the symptoms start and stop
2. Recurrent and prolonged periods of infant crying, fussing, or irritability reported by caregivers that occur without obvious cause and cannot be prevented or resolved by caregivers
3. No evidence of infant failure to thrive, fever, or illness

“Fussing” refers to intermittent distressed vocalization and has been defined as “behavior that is not quite crying but not awake and content either.” Infants often fluctuate between crying and fussing, so that the two symptoms are difficult to distinguish in practice

For clinical research purposes, a diagnosis of infant colic must meet the preceding diagnostic criteria and also include both of the following:

1. Caregiver reports infant has cried or fussed for 3 or more hours per day during 3 or more days in 7 days in a telephone or face-to-face screening interview with a researcher or clinician
2. Total 24-hr crying plus fussing in the selected group of infants is confirmed to be 3 hours or more when measured by at least one prospectively kept, 24-hr behavior diary

Functional Diarrhea(toddler's diarrhea)

Table 389.4 | Diagnostic Criteria for Functional Diarrhea

Must include all of the following:

1. Daily painless, recurrent passage of four or more large, unformed stools
2. Symptoms last more than 4wk
3. Onset between 6 and 60mo of age
4. No failure to thrive if caloric intake is adequate

toddler's diarrhea(Cont.)

- ❑ Nutritional factors such as excessive total calorie intake, excessive dietary intake of the **sugar alcohol sorbitol and the carbohydrate fructose**, coupled with a **low-fat diet**, have been implicated in this osmotic process.
- ❑ Dietary changes such as reducing fruit juice and processed fructose intake are helpful in resolving symptoms.
- ❑ Fiber supplementation may be of some benefit, but evidence is lacking.

Infant Dyschezia

- ❑ apparent discomfort before defecation in an infant less than 9 months of age.
- ❑ strain before defecation for 10-20 minutes with associated screaming, crying, and possible red/purple facial discoloration
- ❑ the result of discoordinated abdominal and pelvic floor musculature contraction, raising the intraabdominal pressure
- ❑ Typically, stools are passed several times daily and are not associated with other health problems or anatomic abnormalities.
- ❑ Reassurance provides the basis of management
- ❑ Laxative, suppository, or digital manipulation is not required and may be counterproductive.
- ❑ Infant dyschezia typically resolves after 3-4 weeks of symptoms.

Functional Constipation

Table 389.5 Diagnostic Criteria for Functional Constipation

Must include 1 mo of at least two of the following in infants up to 4yr of age:

1. Two or fewer defecations per week
2. History of excessive stool retention
3. History of painful or hard bowel movements
4. History of large-diameter stools
5. Presence of a large fecal mass in the rectum

In toilet-trained children, the following additional criteria may be used:

6. At least one episode per week of incontinence after the acquisition of toileting skills
7. History of large-diameter stools that may obstruct the toilet




Table 389.6 Potential Alarm Features in Constipation

Passage of meconium >48 hours in a term newborn
Constipation starting in the first month of life
Family history of Hirschsprung disease
Ribbon stools
Blood in the stools in the absence of anal fissures
Failure to thrive
Bilious vomiting
Severe abdominal distension
Abnormal thyroid gland or newborn screen
Abnormal position of the anus
Absent anal or cremasteric reflex
Decreased lower extremity strength/tone/reflex
Sacral dimple
Tuft of hair on lower spine
Gluteal cleft deviation
Anal scars



DISORDERS OF BRAIN-GUT INTERACTION IN OLDER CHILDREN AND ADOLESCENTS



Nausea and Vomiting Disorders

- 1)Cyclic Vomiting Syndrome
- 2)Functional Nausea and Vomiting
- 3)Rumination Syndrome
- 4)Aerophagia

Functional Nausea and Vomiting

Table 389.8 Diagnostic Criteria* for Functional Nausea and Functional Vomiting

FUNCTIONAL NAUSEA

Must include all of the following fulfilled for the last 2 mo:


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

FUNCTIONAL VOMITING

Must include all of the following:

1. On average, one or more episodes of vomiting per week
2. Absence of self-induced vomiting or criteria for an eating disorder or rumination
3. After appropriate evaluation, the vomiting cannot be fully explained by another medical condition

*Criteria fulfilled for at least 2mo before diagnosis.

- 
- ❑ Importantly, these conditions occur **without** coincident abdominal pain.
 - ❑ The presentation may be accompanied by **autonomic symptoms** such as diaphoresis, pallor, tachycardia, and dizziness.
 - ❑ The differential diagnosis includes anatomic, inflammatory, infectious, and motility etiologies.
 - ❑ Anxiety and other behavioral conditions can be present with these DBGI and should be evaluated for and managed accordingly.
 - ❑ children with functional nausea or functional vomiting should undergo **psychologic evaluation**.
 - ❑ In children with psychologic comorbidities, cognitive-behavioral therapy or other psychologic interventions are appropriate.
 - ❑ Cyproheptadine and transcutaneous gastric stimulation may be effective in the management of nausea.

Rumination Syndrome in Children

Table 389.9

Diagnostic Criteria* for Rumination Syndrome in Children

Must include all of the following:

1. Repeated regurgitation and rechewing or expulsion of food that:
 - a. Begins soon after ingestion of a meal
 - b. Does not occur during sleep
2. Not preceded by retching
3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out

*Criteria fulfilled for at least 2 mo before diagnosis.



Rumination Syndrome in Children(treatment)

- ❑ Because rumination syndrome is essentially a learned habit, therapy focusing on **managing the habit** has proven effective.
- ❑ **Deep breathing exercises** to counteract the noxious stimulus are often employed to change the pressure differential and prevent regurgitation of gastric contents.

Aerophagia

- ❑ often seen in **neurocognitively impaired** patients
- ❑ involves excessive air swallowing occurring throughout the day with progressive abdominal distention and with repetitive passage of gas via belching and/or flatus.
- ❑ Symptoms cannot be attributed to any other causes.
- ❑ In children with age-appropriate cognition and neurologic status, chewing gum and gulping down liquids may be risk factors for aerophagia.
- ❑ Abdominal pain, nausea, and early satiety are possible associated GI symptoms; sleeping difficulty, headaches, and dizziness are also reported.
- ❑ **Anxiety** is a frequent comorbidity.
- ❑ Treatment is multidisciplinary and may include behavioral therapy, deep breathing, and potentially medications to relieve anxiety.



Abdominal Pain Disorders

- 1) Functional Dyspepsia (FD)
- 2) Irritable Bowel Syndrome (IBS)
- 3) Abdominal Migraine
- 4) Functional Abdominal Pain Not Otherwise Specified (FAP-NOS)

Functional Dyspepsia

Table 389.10 Diagnostic Criteria* for Functional Dyspepsia

Must include one or more of the following bothersome symptoms at least 4 days/mo:

1. Postprandial fullness.
2. Early satiation.
3. Epigastric pain or burning not associated with defecation.
4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Within functional dyspepsia, the following subtypes are now adopted:

1. Postprandial distress syndrome includes bothersome postprandial fullness or early satiation that prevents finishing a regular meal. Supportive features include upper abdominal bloating, postprandial nausea, or excessive belching.
2. Epigastric pain syndrome, which includes all of the following: bothersome (severe enough to interfere with normal activities) pain or burning localized to the epigastrium. The pain is not generalized or localized to other abdominal or chest regions and is not relieved by defecation or passage of flatus. Supportive criteria can include (1) burning quality of the pain but without a retrosternal component and (2) the pain is commonly induced or relieved by ingestion of a meal but may occur while fasting.

*Criteria fulfilled for at least 2 mo before diagnosis.

Functional Dyspepsia(Cont.)

? Pathophysiologic mechanisms:

- impaired gastric accommodation
- visceral hypersensitivity
- food allergy
- delayed gastric emptying
- post-viral gastroparesis

? Differential diagnosis:

- GI etiologies of epigastric pain, including gastritis, esophagitis, and pancreatitis, among others.

Functional Dyspepsia(Cont.)

? Treatment:

- ? a trial of **dietary and lifestyle changes** including avoiding spicy foods, caffeine, fatty foods, and nonsteroidal anti inflammatory drugs (NSAIDs).
- ? **Gastric acid reduction** therapy
- ? Assessment by a pediatric gastroenterologist and upper endoscopy
- ? **cyproheptadine** (to improve gastric accommodation in patients with early satiety)
- ? attempts to treat visceral hypersensitivity
- ? Low-dose tricyclic antidepressant therapy with **amitriptyline** may have efficacy in refractory cases.
- ? **prokinetic medications** such as erythromycin or metoclopramide(for early satiety)
- ? **Percutaneous electrical stimulation of the stomach** is a potential option for patients with FD refractory to standard therapy.

Table 389.11

Alarm Symptoms Usually Needing Further Investigations in Children with Chronic Abdominal Pain

- Pain that wakes up the child from sleep
- Persistent right upper or right lower quadrant pain
- Significant vomiting (bilious vomiting, protracted vomiting, cyclical vomiting, or worrisome pattern to the physician)
- Unexplained fever
- Genitourinary tract symptoms
- Dysphagia
- Odynophagia
- Chronic severe diarrhea or nocturnal diarrhea
- Gastrointestinal blood loss
- Involuntary weight loss
- Deceleration of linear growth
- Delayed puberty
- Family history of inflammatory bowel disease, celiac disease, and peptic ulcer disease

Table 389.12

Alarm Signs Usually Needing Further Investigations in Children with Chronic Abdominal Pain

- Localized tenderness in the right *upper* quadrant
- Localized tenderness in the right *lower* quadrant
- Localized fullness or mass
- Hepatomegaly
- Splenomegaly
- Jaundice
- Costovertebral angle tenderness
- Arthritis
- Spinal tenderness
- Perianal disease
- Abnormal or unexplained physical findings
- Hematochezia
- Anemia

Irritable Bowel Syndrome (IBS)

Table 389.13

Diagnostic Criteria* for Irritable Bowel Syndrome

Must include all of the following:

1. Abdominal pain at least 4 days/mo associated with one or more of the following:
 - a. Related to defecation
 - b. A change in frequency of stool
 - c. A change in form (appearance) of stool
2. In children with constipation, the pain does not resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not irritable bowel syndrome)
3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

*Criteria fulfilled for at least 2 mo before diagnosis.




Table 389.14	Recommendations for Treatment of Irritable Bowel Syndrome
---------------------	--

RECOMMENDATIONS FOR TREATMENT OF IRRITABLE BOWEL SYNDROME (IBS)

- Mild symptoms often respond to dietary changes.
- Antispasmodics can be used as needed for abdominal pain or postprandial symptoms.
- Antidepressants can improve abdominal pain and global symptoms. They may be considered for patients with moderate to severe symptoms.

IBS WITH CONSTIPATION (IBS-C)

- Fiber may relieve constipation in patients with mild symptoms.
- Polyethylene glycol can increase the frequency of bowel movements but may not improve overall symptoms or abdominal pain.
- Lubiprostone or linaclotide can be tried in patients whose symptoms have not responded to polyethylene glycol.

IBS WITH DIARRHEA (IBS-D)

- Taken as needed, loperamide can reduce postprandial urgency and stool frequency, but it does not improve global symptoms.
- Rifaximin and eluxadoline have been modestly more effective than placebo in relieving symptoms.

IBS (Cont.)

Other Treatments:

- ❑ reduce or restrict foods that may provoke symptoms or cause gas (**FODMAPS**) [fermentable oligo-di-monosaccharides and polyols].
- ❑ **Probiotics** (effective in reducing symptoms in children with IBS, likely through production of short-chain fatty acid)
- ❑ **pepper mint oil** (effective in reducing pain)
- ❑ **Cognitive behavioral therapy** is important to identify possible psychosocial stressors and to help identify coping mechanisms to maximize daily function and quality of life.
- ❑ **transcutaneous neurostimulation** (limited data)

Abdominal migraine

Table 389.15 Diagnostic Criteria* for Abdominal Migraine

Must include all of the following occurring at least twice:

1. Paroxysmal episodes of intense, acute periumbilical, midline, or diffuse abdominal pain lasting 1 hour or more (should be the most severe and distressing symptom)
2. Episodes are separated by weeks to months
3. The pain is incapacitating and interferes with normal activities
4. Stereotypical pattern and symptoms in the individual patient
5. The pain is associated with two or more of the following:
 - a. Anorexia
 - b. Nausea
 - c. Vomiting
 - d. Headache
 - e. Photophobia
 - f. Pallor
6. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

*Criteria fulfilled for at least 6 mo before diagnosis.

Abdominal Migraine(Cont.)

? common triggers:

- * sleep hygiene disruption
- * fatigue
- * travel

? differential diagnosis:

- anatomic obstructions of GI or urologic tract
- infectious or inflammatory conditions
- hepatobiliary and pancreatic disorders
- neurologic and metabolic conditions
- psychiatric disorders

Abdominal Migraine(Cont.)

? Treatment:

- ? Preventing exposure to known triggers
- ? Acute episodes may be treated similarly to migraine headaches with abortive medications such as triptans.
- ? Prophylaxis: cyproheptadine, amitriptyline, and propranolol may be effective

***A large number of children may have their symptom pattern evolve into migraine headaches as they progress toward adulthood

Functional abdominal pain not otherwise specified (FAP-NOS)

- ❑ describes pain that occurs at least 4 times per month with either intermittent or continuous abdominal pain not associated with a particular activity or coincident to another physiologic event such as menses or eating and cannot be explained by any other underlying medical condition. These episodes occur in less than a 2-month span.
- ❑ it is a **DBGI of exclusion**, as it does not meet criteria for either IBS,FD, or abdominal migraine
- ❑ Psychosocial stressors may play a role, and behavioral approaches may be helpful to identify and manage stressors and other exacerbating factors.
- ❑ Pharmacologic data is limited, but small trials have suggested efficacy of **amitriptyline** and **citalopram**, though it should be noted that the latter is associated with suicidal ideation in adolescent patients.



DEFECATION DISORDERS

 **Functional constipation**

 **Nonretentive fecal incontinence (NFI)**


Functional constipation in children and adolescent

Table 389.16 | Diagnostic Criteria for Functional Constipation in Children with Chronic Abdominal Pain

Must include two or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome:

1. Two or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years
2. At least one episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large-diameter stools that can obstruct the toilet

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



Functional constipation in children and adolescent(Cont.)

Management:

- ❑ disimpaction of the rectal stool ball followed by maintenance therapy with osmotic laxatives to soften stools for ease of passage
- ❑ dietary changes to optimize fiber intake (a general rule is that daily fiber intake in grams can be approximated by adding age in years plus 5 to 10)
- ❑ behavioral approaches similar to those employed for younger children

Nonretentive fecal incontinence (NFI)

- ❑ describes the passage of stool in the **absence of fecal retention** that occurs in inappropriate settings for a specific society and culture, and that occurs without evidence of another or underlying medical condition in a child 4 years of age or older over at least a 1-month period.
- ❑ These patients otherwise have **normal defecatory patterns** and function, as well as normal colonic transit time, differentiating and distinguishing them from functional constipation.
- ❑ Another key difference is that children with NFI will have passage of their **entire rectal contents** as opposed to the smears or small amounts of stool in patients with functional constipation and encopresis.
- ❑ **Psychologic comorbidities** are frequent in children with NFI.

NFI(Cont.)

How to diagnose?

- ❑ otherwise normal defecation frequency
- ❑ absence of an abdominal or rectal mass
- ❑ a normal neurologic exam
- ❑ a normal transit marker study

How to manage?

- ❑ involvement of behavioral health professionals
- ❑ proactive regular toilet use

Unfortunately, biofeedback therapy, helpful in other disorders of defecation dynamics, has not proven beneficial in children with NFI.

Specific education points to emphasize

- ❑ This type of abdominal pain is **common**, occurring in approximately 10 to 20 percent of children.
- ❑ The pain is **not life-threatening** and does not require activity restriction.
- ❑ The pain is **real**; it is thought to be caused by a heightened sensitivity to the normal function of the stomach and bowel.
- ❑ Like other types of pain, this type can be triggered, exacerbated, or maintained by **environmental** (eg, gastrointestinal infection, medications) and **psychosocial** factors, including stress, anxiety, and social reinforcement (eg, attention, staying home from school)
- ❑ Management of pain involves avoiding triggers and improving **copng skills**; the pain may persist, but the child's and family's quality of life can be improved.
- ❑ Chronic pain, regardless of the etiology, can be associated with **depression or anxiety** (both as a cause and an effect).

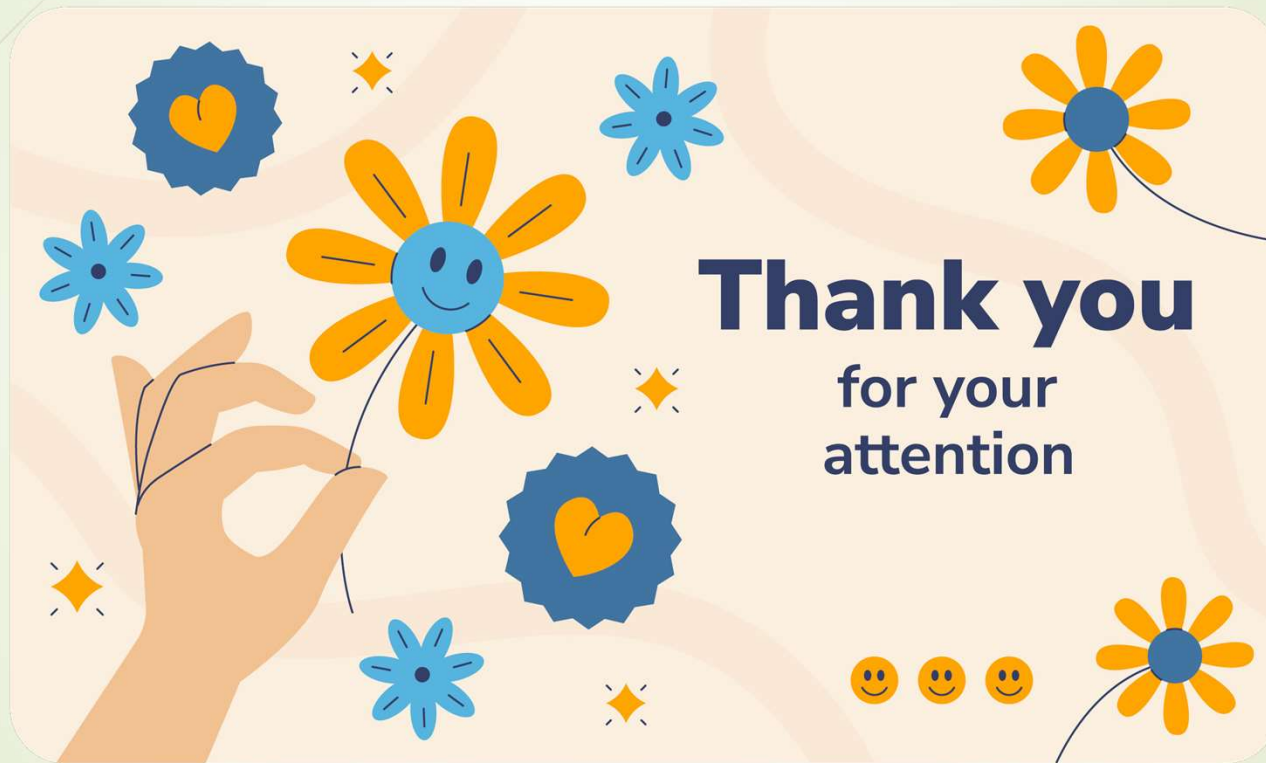
Interventions to improve coping

- ❑ **Relaxation techniques**(Deep breathing, Progressive muscle relaxation,etc.)
- ❑ **Distraction techniques**(conversation, games, television, mental arithmetic, or encouraging the child to use their imagination to think about pleasant things when confronted with pain.)
- ❑ **Guided imagery or hypnotherapy**
- ❑ **CBT**(a psychotherapy approach that helps a patient recognize the links between thoughts, feelings, and behaviors)



Prognosis

- With appropriate support and management, DGBI resolve over several months in the majority of children



Thank you
for your
attention