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Review Article

Brain-Gut Interaction Disorders in Infants and Preschoolers: How are we Finalizing the Practice of the Rome IV Criteria, and what are the Expectations for the Next Step?

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Abstract

Background: This commentary will delve into our well-lived real-world experience with the seven disorders of brain-gut interaction in infants and preschoolers, and prepare for the transition to the Rome V Criteria. Brain-gut interaction disorders in children is a disease that has been focused on by both General Paediatricians as well as Pediatric Gastroenterologists.

Objective of the Study: The objective of this commentary is to present the Rome IV Criteria and share valuable experiences gathered over the past ten years. Additionally, it offers insights into what the forthcoming Rome V criteria will enhance our understanding of brain-gut interaction disorders. The Rome IV criteria, a set of chronic or recurrent disorders characterized by gastrointestinal symptoms resulting from a combination of altered motility, visceral hyperalgesia, altered mucosal immune function, altered gut microbiota, and altered central nervous system processing. The current Pediatric Criteria Rome IV criteria used are divided into two age groups: newborns and children (0 to 3 years of age), and children and adolescents (4 to 18 years of age). In this text, we explore the experience of approaching infants and Preschoolers.

Conclusion: The Rome IV criteria for infants and preschoolers have enabled us to understand brain-gut interaction disorders better, thereby enriching our diagnostic capacity and treatment options for these children.

Keywords: *Rome IV Criteria; Brain-Gut Interaction Disorders; Infant; Preschoolers*

At sunset, at the end of a good time, marked by a pleasant period of experiences or work, this is how we feel about the end of the application of the Rome IV Criteria to children and adolescents. As we conclude the application of the Rome IV Criteria to children and adolescents, we are just ready, filled with confidence and reassurance for the next step: implementing the Rome V Criteria. This transition represents a significant change in our understanding and management of brain-gut interaction disorders. This Commentary will delve into our well-lived real-world experience with the seven Disorders of Brain-Gut Interaction in Infants and Preschoolers, and prepare for the transition to the Rome V Criteria. Brain-gut interaction disorders in children is a disease that has been focused on by both General Paediatricians as well as Pediatric Gastroenterologists.

The objective of this commentary is to share valuable experiences gathered over the past ten years, accumulated through rigorous clinical practice and research with the Rome IV criteria. These experiences have significantly contributed to our understanding and management of brain-gut interaction disorders. Additionally, it offers insights into what the forthcoming Rome V criteria will enhance our understanding of these disorders.

How to diagnose disorders of brain-gut interaction

The Rome IV criteria, a set of chronic or recurrent symptom-based diagnostic criteria, have significantly reshaped our understanding of brain-gut interaction disorders. These disorders result from a combination of altered motility, visceral hyperalgesia, altered mucosal immune function, changes in gut microbiota, and central nervous system processing. The current Pediatric Criteria Rome IV criteria used are divided into two age groups: newborns and children (0 to 3 years of age), and children and adolescents (4 to 18 years of age). In this text, we explore the experience of approaching infants and Preschoolers [1].

Approaching parents/caregivers and patients with disorders of brain-gut interaction: The vital role of effective communication is a skill that is often underestimated in the management of these conditions. Effective communication is the cornerstone of patient-centered care. Following the guidelines outlined by Drossman [2] and acquiring time-saving skills, you can establish a positive relationship with patients by using clear and concise language, providing written materials for further reference, and being mindful of time constraints. The ultimate goal is to empower patients and parents to alleviate or mitigate the severity of symptoms, enhance their ability to cope with symptoms, reduce the utilization of healthcare resources, prevent harm, improve the cost-effectiveness of medical care, and improve health-related quality of life (Box 1).

1. The acquisition of clinical data is a dynamic process that hinges on active listening and keen observation, making you an integral part of the patient's care.
2. Accept the reality of the disorder, considering that there is no specific biomarker or diagnostic test.
3. Pay attention to the nonverbal messages from parents/caregivers or the patients themselves.
4. It is important to identify how the patient understands the disease from their personal and sociocultural perspective.
5. Work to improve patient satisfaction. This satisfaction is related to the patient's perception of the physician's humanistic approach, technical competence, interest in psychosocial factors, and provision of relevant medical information.
6. Offer empathy, a powerful tool that allows you to truly understand and connect with the patient's pain and distress, fostering a sense of compassion and understanding.
7. Value the patient's feelings.
8. Set realistic goals, taking into account the patient's expectations and the nature of the condition, to foster a sense of responsibility and proactivity in your approach.
9. Patient education is necessary at every visit.
10. Reassure. Patients often experience serious consequences from their illness and may feel helpless, vulnerable, and that their condition is out of their control.
11. The foundation of patient-centered Care is that the patient and physician must agree on the diagnosis and treatment options. This approach, which emphasizes the patient's active involvement in their own Care, is crucial for effective communication and treatment planning in brain-gut disorders.
12. Help the patient take responsibility. Patients with chronic illnesses fare better when they take responsibility for their Care.
13. Set limits. For some patients, it is essential to establish and maintain clear limits regarding frequent phone calls, unexpected visits, lengthy appointments, or unrealistic expectations of Care.

Box 1: *Approaching parents/caregivers and patients with disorders of brain-gut interaction.*

Practice with disorders of brain-gut interaction in infants and preschoolers

As healthcare professionals, the implementation of the Rome IV Criteria in diagnosing brain-gut interaction disorders is a crucial responsibility that we hold. A clear and concise clinical history and physical examination are the foundation of these diagnoses, designed to be easy to use and facilitate accurate assessment and diagnosis, minimizing the need for extensive laboratory testing. Providing precise, predefined diagnoses is integral to helping patients and caregivers better understand and accept the diagnosis, despite the absence of demonstrable underlying organic disease.

Infant colic

Rome IV Criteria

Child under 5 months of age when symptoms begin or end

• Crying, fussing, or irritability in recurrent and prolonged periods reported by parents/caregivers that occur without an apparent cause and cannot be prevented or resolved by the parents/caregivers

• No evidence of failure to thrive, fever, or a defined illness.

For research purposes, the diagnosis requires two additional criteria

• Occurs from birth to 5 months of age

• Episodes lasting three or more hours daily, three or more days per week for one or more weeks, when recorded prospectively in a 24-hour behavior diary.

"Fussing" refers to intermittent, distressed vocalization and is a unique behavior that falls between crying and being awake and content. Understanding this distinction is key to the diagnostic process. [1]

Figure A

Infant colic is a syndrome characterized by prolonged periods of crying and difficult-to-soothe behavior. The crying is categorized into physiological (physical and emotional needs), pathological (organic factors), and nonspecific crying (with no apparent reason) [3]. Certainly, crying is a powerful form of communication for newborns, as it helps them connect with their parents, who are their primary source of protection. Crying during the first months of life reflects physiological maturational changes in neurobehavioral development. There is no difference between sexes, type of feeding (breastfeeding or formula), gestational age (term or preterm), time of year, or socioeconomic status. However, it is more common in firstborns. A reduction in crying accompanies the child's development. It is not associated with warning signs or "red flags" that might suggest organic disease. The main characteristics of infant colic are shown in box 2.

Colic is a functional gastrointestinal disorder, a benign and self-limiting process. It is characterized by a variable combination of age-dependent, chronic, or recurrent symptoms not explained by structural factors or biochemical abnormalities.
The condition usually presents in the second or third week of life, typically peaks at 6 weeks of age, and generally resolves spontaneously by 3 to 4 months of age.
These episodes of fussiness exhibit a diurnal pattern, with a higher concentration of crying in the late afternoon and early evening, as well as a slight increase in the early morning. It does not appear to be related to environmental events.
It is characterized by paroxysms of excessive, inconsolable crying, agitation, and irritability with no apparent cause in an otherwise healthy infant. It is unpredictable and spontaneous.
It typically presents with high-pitched crying, unsoothable crying, facial expressions appearing to show pain, abdominal distension, increased gas, flushing, curling of the legs over the abdomen, and arching of the back. The child appears to have difficulty passing gas and having bowel movements. prolonged crying.

Box 2: *Characteristics of infant colic.*

Diagnosis

Questions should be asked about the child's behavior, the time of day, and the duration of crying episodes. History of apnea, cyanosis, or difficulty breathing, vomiting, and regurgitation. Assess prenatal and perinatal problems, sleep history, nutrition, bowel movements, urination, and history of psychosocial problems. Clothing should be removed to facilitate a thorough examination. Wessel., *et al*.'s 'rule of threes' criteria, which involves the infant crying for more than three hours a day, for more than three days a week, for at least three weeks, is challenging to apply in clinical practice due to its subjective nature and the potential for parental misinterpretation.

Treatment

Infant colic can be managed through dietary, pharmacological, and behavioral strategies. The pediatrician's role as a counselor and educator is crucial, as they guide parents and play an integral part in the process, making families feel supported and reassured, knowing they have a knowledgeable and caring professional on their side. The pediatrician will provide a diagnosis, educate parents about the nature of infant colic, and guide them in implementing the strategies for managing it. After diagnosis, parents should be educated about the benign and self-limiting nature of infant colic. It is crucial to emphasize the parents' role in the treatment, as they are the ones who will implement the strategies. Therefore, the basis of treatment lies with the parents, empowering them to take an active and responsible role in their child's well-being.

Guide parents to carry the child as much as possible (at least three hours a day), and respond to crying quickly (within ninety seconds), reducing failures in both the short and long term. The child learns that you are ready, willing, and able to meet their needs. Encourage parents to seek help from supportive family or friends, as their support can make a significant difference. Learn and practice stress reduction techniques. A pamphlet on colic, which includes information on the causes of colic, tips for soothing a colicky baby, and when to seek medical help, should be provided to parents/caregivers. This pamphlet is a comprehensive guide that can help parents understand and manage infant colic effectively.

Practices with infantile colic

The finding that prolonged crying in children with infantile colic is more likely to occur in the afternoon or evening and often worsens at night, when parents are returning home, trying to prepare dinner, and relaxing from the day's activities, provides a good bond with parents and reinforces later behaviors. Infants with Colic are healthy, eat well, gain weight adequately, and have no other symptoms. In fact, Colic is not a sign of serious illness, bad temperament, bad behavior, or inadequate parenting. At the appointment, parents may be tired and worried that their child may have a severe disorder. Colic is a source of great suffering for children, parents, family members, and caregivers. However, understanding that infant colic is a regular part of development can help alleviate some of the anxiety and stress parents may feel. So, Pediatricians should be confident when guiding families with a colicky child, reassuring them that this is a regular part of their child's development.

Future directions: In the short term, it is necessary to resolve the controversies regarding the use of probiotics in infantile colic.

Functional constipation

Functional constipation (FC) can begin at any time in children under 4 years of age, but the highest incidence appears during the period of anal toilet training. Boys have a higher incidence of faecal incontinence. The developmental process of FC Retention behaviour plays a crucial role in the pathophysiology of children under the age of 4. Unpleasant experiences, such as painful bowel movements, cause the child to retain their stool voluntarily, leading to a vicious cycle, resulting in harder and more difficult-to-pass stools.

Rome IV Criteria

The Pediatric Rome IV criteria, a comprehensive set of guidelines, diagnose Functional Constipation (FC) in children up to 4 years of age. The diagnosis requires at least one of the following findings: two or fewer bowel movements per week, excessive fecal retention, painful or hard bowel movements, or a history of large-diameter stools. Also, the presence of a large fecal mass in the rectum.

The Pediatric Rome IV criteria for diagnosing Functional Constipation (FC) in children up to 4 years of age have been further refined. The novelty was to incorporate the use of children with anal toilet training to differentiate toilet-trained and non-toilet-trained children. The following additional criteria may be used to enhance the diagnosis: At least one episode of fecal incontinence per week after toilet training has been achieved. A precise publication evaluated the impact of incorporating toilet-training status in the Pediatric Rome IV criteria for FC in infants and toddlers [1].

Figure B

Recently, in two well-presented reviews, the authors provided a comprehensive explanation of FC. One in a well-crafted arrangement illustrates the manuscript [4]. The second one presents the ten "hard" questions in FC for pediatric ages. The issues are listed and commented on, just as they afflict us in our daily lives, in the Management [5]. The most important recommendation is the last one: "A strict follow-up is highly recommended to avoid persistence of FC symptoms." Additionally, in 2024, an extraordinary book with a special chapter on Constipation and soiling, offering insightful observations on the mental health approach [6].

Clinical history and physical examination

The clinical approach should consider: At what age did Constipation begin? This is crucial, especially in the first year of life, as a differential diagnosis with Food Allergy is sometimes necessary. A guideline helps us with this issue [7]. What is the shape, size, and frequency of bowel movements? The Bristol Score can be easily applied after the age of two [8] or a Stool Form Scale for children [9]. The Retention posture, characterized by standing rigidly with the buttocks contracted, walking on tiptoe, legs crossed, leaning against furniture, or sitting with legs stretched out, is frequently observed in clinical practice. These details from the clinical history and physical examination are vital in understanding and managing FC.

Investigation

Constipation can be a manifestation of a severe organic disorder, with low incidence/prevalence compared to FC (Celiac disease, hypothyroidism, cystic fibrosis, hypercalcemia, hyperkalemia, opiates, phenobarbital, anticholinergics, Hirschsprung's disease, spinal cord abnormalities, imperforate anus, and anteriorly displaced anus). However, constipation alone did not increase the likelihood above the population prevalence. An excellent text addresses the yield and cost of performing screening tests for FC in children [10].

Tests, if necessary, such as in refractory constipation, may include immunoglobulin A, tissue transglutaminase IgA, thyroid function, and calcium levels. Celiac disease may be considered if Constipation develops early with the introduction of gluten and is associated with iron deficiency anemia and poor growth. Allergy testing is not recommended for diagnosing cow's milk protein allergy in children with constipation, as these are usually non-IgE-mediated forms. A trial of cow's milk and soy protein withdrawal for four weeks may be indicated in children with intractable constipation.

Treatment

Initial treatment of FC typically involves pharmacological approaches, which consist of fecal disimpaction, maintenance therapy, and a gradual weaning process. One of the most significant therapeutic failures is failing to achieve adequate disimpaction and introduce

maintenance pharmacological treatment. Diet therapy as an initial strategy has also been challenging, considering the time it takes for children to adapt their usual diet to one with an adequate/higher concentration of dietary fiber. Rectal therapies, such as enemas and suppositories, are rarely necessary and do not speed recovery.

The primary treatment for FC is the use of oral laxatives, which should be initiated early to achieve a faster therapeutic effect. Laxatives such as Polyethylene Glycol 3350, lactulose, or Magnesium hydroxide are the preferred initial treatment for this age group. The reasons for treatment failure include an insufficient dose, duration, adherence, recurrence of triggering factors, or an incorrect diagnosis. Adherence can be affected by the taste and amount of laxative the child receives. Early initiation of oral laxatives is crucial, making us proactive and responsible in our approach to FC.

Practices with functional constipation

Diagnostic information depends on parents/caregivers. In infants referred for FC, associated symptoms may include irritability, decreased appetite, and early satiety, which typically resolve after a bowel movement. Specifically, in cases of first-year onset at the first visit to a specialized clinic, there is a delay in referrals, the worst symptoms, and excessive use of rectal laxatives [11]. Regarding Food Allergy, the document from the European Academy of Allergy and Clinical Immunology recognizes the common cold as a possible allergic condition not mediated by immunoglobulin E [6].

Toilet training should be implemented once constipation is under control. FC should not be confused with infantile dyschezia, which represents poor coordination between increased intra-abdominal pressure and pelvic floor muscle relaxation during bowel movements, but passes stools of normal consistency. Routine abdominal radiography is not recommended for diagnosing FC. However, it may be helpful in a child in whom fecal impaction is suspected, but physical examination is unreliable or not possible. Abdominal radiography can be used to confirm the result of fecal disimpaction.

Future directions: New medications are on the way to join the FC therapeutic arsenal. Serotonergic agents (Prucalopride), Prosecretory (Lubiprostone, linaclotide, and plecanatide) are on their way, some encountering obstacles and others at a fast pace [12]. These developments hold promise for future improvements in treatment options. However, we constantly encounter difficulties when applying the Recommendations for pharmacological clinical trials in children with FC [13].

Functional diarrhea

Rome IV Criteria

The Rome IV criteria, a stable and reliable set of guidelines, have remained unchanged since their introduction. The cardinal features of FD include daily, painless, chronic loose stools, which are mushy or watery, foul-smelling, light in color, with no blood, and containing undigested food particles. Several times a day (usually more than four times a day). Bowel movements begin upon waking and become softer and more frequent throughout the day, but do not occur at night in an otherwise healthy and growing child if caloric intake is adequate.

It is important to note that the symptoms of functional diarrhea occur between 6 and 60 months of age and persist for more than 4 weeks [1, 14].

Figure C

Functional diarrhea is a clinical diagnosis using the current Rome criteria. There are no symptoms/signs of maldigestion or macronutrient malabsorption. The child does not appear sickly based on their appearance and the frequency of their bowel movements.

Episodes of diarrhea are usually triggered by an intercurrent infection, especially after viral gastroenteritis, respiratory tract infection, tooth eruption, and biopsychosocial stress. Factors involved in FD: the diet is often characterized by an increased intake of fluids and fruit juices, which contain excess fructose and sorbitol (such as apples and pears), as well as those with high osmolarity (such as soft drinks). The relationship between diet and possible etiopathogenesis remains unchanged. Therefore, the dietary approach, which is the cornerstone of treatment, provides a reliable and effective method for managing FD, offering reassurance to both healthcare professionals and patients.

Investigation

Laboratory investigation: Complete blood count shows no anemia or eosinophilia. Routine urine and culture, faecal parasitology, leukocyte, carbohydrate, and fat tests in the stool, and stool culture (all negative). Food allergy screening is negative.

Treatment

Functional diarrhea is often treated as carbohydrate intolerance or food protein allergy. The '4 Fs' treatment approach, which includes fluid, fiber, fructose, and fat, is readily incorporated into the treatment. Improvement typically occurs within a few days to a few weeks after starting therapy. However, there is no evidence to support the use of pharmacotherapy [15]. In more severe cases or when there is a delay in the clinical response to dietary measures, offering a morning dose of Loperamide can be considered. It can be used for short periods and discontinued once the diet returns to normal.

If giardia intestinalis is positive, two possibilities should be analysed:

1. The diagnosis of functional diarrhea occurs concomitantly with Giardiasis (the age group with the highest prevalence, and the clinical presentation of the two entities can be very similar. In this situation, when treating Giardiasis alone, there is no clinical improvement. Then, initiate treatment for functional diarrhea.
2. The clinical is due solely to Giardiasis (observe the clinical response after appropriate treatment).

Practices with functional diarrhea

Bowel movements typically begin upon waking and become softer and more frequent throughout the day, but do not occur at night. However, 25% of mothers reported that their child passed stools in their sleep during periods of significant clinical exacerbation. So, these criteria have been abandoned [16].

Related to parasitic diseases, Giardiasis is a common problem in some geographical areas. So, chronic diarrhea due to Giardiasis may occur in the same age group as FD and presents with very similar clinical features (watery, foul-smelling stools). Stool for ova and parasites Investigation is mandatory in these children.

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Future directions: Although the Rome IV criteria define FD as a disorder exclusive to children younger than 5 years old, it is essential to consider the potential for extending the age range. The diagnosis of FD should be considered for inclusion in children aged 8–18 years, reflecting the evolving understanding of this condition. This also underscores the need for further research in this area, inviting healthcare professionals to contribute to the advancement of medical knowledge [17].

Infant dyschezia

Roma IV Criteria

Infant Dyschezia is a condition defined as straining and crying for at least 10 minutes before the successful passage of soft stools in an infant <9 months old without any other health problems [1].

The most widely accepted proposed explanation for Infant Dyschezia is a disturbance in the defecation process. This is characterized by a specific issue with the pelvic floor muscles, where there is incoordination leading to contraction of the abdominal muscles and the relaxation of the anal sphincter.

Figure D

In most infants, infant dyschezia symptoms begin in the first months of life and resolve spontaneously after 3-4 weeks. This transient nature of the condition should provide reassurance to parents. The child responds to the urge to defecate with a Valsalva maneuver, but does not synergistically relax the pelvic floor. During defecation, it represents poor coordination between increased intra-abdominal pressure and relaxation of the pelvic floor muscles. Infants strain for 10 to 20 minutes, scream, cry, and have a plethoric or purple face while attempting to defecate. These symptoms/signs can be very distressing for parents [18].

One study evaluated risk factors such as the infant's age, sex, onset of first meconium, current diet, history of hospitalization, socio-emotional status, and the parents' number of children, age, education levels, occupations, and income. However, only the number of children in the family (being an only child), a complementary diet, and social-emotional disturbance were significant factors. The highest prevalence is in infants aged 7-9 months [19]. Also, another study, being a systematic review and meta-analysis, concludes that there were no associations between infant dyschezia and sex, birth weight, prematurity, newborn hospital stay (>4 days), neonatal antibiotic use, time of commencing breastfeeding, type of feeding, bottle/pacifier usage, or type of first consumed food. Concerning maternal factors, no associations were found between Infant Dyschezia and number of miscarriages, parity, education level, or family type, symptoms of postpartum depression, or psychiatric symptoms. This should help parents feel less guilty or responsible for their child's condition [20].

Investigation

A detailed clinical history and physical examination are essential. However, despite straining before defecation, stools are always normal. The physical examination is regular. A wrong diagnosis occurred in 28.5% of cases, confusing them with FC, abdominal Colic, cow's milk allergy, and Hirschsprung's disease [19]. Laboratory tests are not indicated.

Treatment

There is no specific treatment for dyschezia, except reassurance from parents/caregivers. Educate by guiding the patient toward a transient functional process, without the need for investigation, ensuring access is available. It is important to emphasize that manipulating the anal area or prescribing laxatives is an unnecessary intervention. This should give healthcare providers confidence in their approach to management [18].

Practices with infant dyschezia

As assessed in the literature, risk factors for developing infant dyschezia are rare and will not contribute much to the diagnosis. However, if an incomplete clinical history, infantile dyschezia can be confused with infantile colic or FC. In addition, two studies reported that infant dyschezia was not associated with the subsequent development of FC [21,22].

Future directions: Infant dyschezia is related to the kind of complementary feeding.

Rumination in infants and preschoolers

Rome IV Criteria

The Rome IV Criteria define the symptoms of rumination syndrome as those persisting for at least 2 months. These symptoms are characterized by repeated contractions of the abdominal muscles, diaphragm, and tongue; regurgitation of gastric contents into the mouth, which are then either voided or rechewed and re-swallowed. It is essential to note that the onset of these symptoms typically occurs between 3 and 8 months of age, which is a crucial factor in identifying rumination syndrome in pediatric patients. The syndrome does not respond to treatment for gastroesophageal reflux disease or regurgitation; does not occur during sleep or when the child is interacting with people in the environment; and is not accompanied by signs of distress [1].

Rumination syndrome, a unique disorder of gut–brain interaction, is characterized by the regurgitation of food or fluid shortly after eating. This regurgitation, which does not involve retching, is often effortless. Individuals affected by this syndrome either spit out or re-swallow the regurgitated material, which is a key aspect that sets it apart from other gastrointestinal disorders.

Figure E

Rumination syndrome, a functional disorder, often brings about distressing medical and psychosocial consequences. These include weight loss, malnutrition, dehydration, anxiety, fear of eating, social isolation and withdrawal, missing school or moving to online school, and an overall impaired quality of life. The condition itself is deeply distressing to patients and families, regardless. Risk factors for infant rumination include: Sensory and/or emotional deprivation; institutionalized infants in orphanages; emotionally distant infants, and abandoned infants [23-25].

Diagnosis

The diagnosis of rumination syndrome is clinical and requires a comprehensive medical history to avoid misdiagnosis. Patients/parents often report frequent vomiting, leading to an erroneous diagnosis of gastro-oesophageal reflux disease in the majority of cases. Many patients with rumination have been misdiagnosed as PPI-refractory GERD, highlighting the need for a thorough anamnesis.

Rumination may start during food intake or 10-15 minutes after having finished eating, and the events may persist for up to two hours. Rumination may present with fluids alone or with solid foods. Fluid intake characteristically facilitates the rumination of solid foods.

Investigation

However, due to a general lack of awareness of the disease, patients are often subjected to seeing several physicians and undergo a series of upper gastrointestinal tract endoscopy and radiological studies. They are administered ineffective treatments, entailing a significant increase in expenses, a decrease in quality of life, and adverse psychological effects, before reaching the ultimate diagnosis. This emphasizes the urgent need for early diagnosis to prevent diagnostic delay or underdiagnosis [26,27].

The Rome criteria state that diagnostic tests to rule out an organic disorder are not essential when the clinical diagnostic criteria are met. In clinical practice, observing a patient's behavior, especially when they are exposed to foods that cause symptoms, can be a useful diagnostic tool. This consideration, however, is not currently included in the diagnostic algorithms.

Practices with rumination

- It is often associated with long periods of social deprivation.
- There is inadequate interaction between the child and the mother/caregiver.
- The child exhibits "self-stimulation" behavior caused by poor mother-child interaction.
- The child's needs are not met due to insufficient interaction during feeding and poor reciprocal interaction.
- The infant learns to stimulate and "self-feed" by ruminating.
- Nonpharmacological treatment is the choice [28].

Infant regurgitation

Rome IV Criteria

Include the following in healthy infants 3 weeks to 12 months of age:

1. Regurgitation ≥2 times per day for ≥ weeks.

2. Crucially, the absence of aspiration, apnea, abnormal posturing, failure to thrive, feeding difficulties, hematemesis, retching, or swallowing difficulties is a key component of the Rome IV Criteria [1]

Two years after the Rome IV Criteria, a Joint Committee of NASPGHAN and the ESPGHAN published guidelines on gastro-esophageal reflux (GER) and GER disease (GERD) in 2018, a testament to the credibility of the information [29].

Figure F

Infant regurgitation, also known as gastroesophageal reflux (GER), is a physiological process that occurs after feeding newborns/infants. Episodes are short, asymptomatic, limited to the distal esophagus, and have no complications. This self-limiting nature of GER should provide reassurance to caregivers and healthcare providers. The peak incidence in infants occurs between 3 and 4 months of age, decreases after six months of age, and resolves in 95% by 1 year of age. The incidence of GER in premature infants born less than 34 weeks of gestation is approximately 22% [30]. GER becomes Gastroesophageal Reflux Disease (GERD) when reflux causes troublesome symptoms and/or complications, such as poor weight gain, feeding difficulties, or respiratory symptoms. In infants, it is challenging to distinguish between pathologic and physiologic conditions [31-33].

History and physical examination

Generally, regurgitation does not occur before the age of 1 week or after the age of 6 months. Effortless vomiting or regurgitation is characteristic of GER. GER is a functional, self-limiting condition that occurs several times a day in healthy infants, lasting less than 3 minutes, and with few symptoms. However, in patients with recurrent respiratory symptoms, difficulty with weight gain, and children with medically complex conditions, suspected of GERD should be considered. The history should include: the age of onset of symptoms, as well as feeding details (time interval between feedings, length of feeding period, volume of each Feeding, type of formula, methods of formula preparation, foods added to the formula, and any allergen restrictions). Additionally, the pattern of regurgitation (nocturnal,

immediately after meals, long after meals, digested versus undigested), as well as previous pharmacologic and dietary interventions, should be considered.

Investigation

For most pediatric patients, a history and physical examination without any warning signs is sufficient to diagnose GER and initiate treatment strategies with confidence. The collection of clinical information through questionnaires can aid in diagnosis, monitoring therapeutic response, and involving parents and caregivers in the diagnostic and treatment process. The most easily applicable questionnaire is the Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R), which is a validated tool that assesses the frequency and severity of regurgitation, feeding difficulties, and other symptoms associated with GERD. Diagnostic tests should be used to document the presence of reflux into the esophagus and establish a causal relationship between reflux and symptoms. Also, evaluate treatment effectiveness. Parental involvement is crucial in this process, as it empowers parents to feel an integral part of their child's Care and well-being.

Treatment

- Medication is not indicated for the management of infant regurgitation, and in most cases, no treatment is necessary.
- However, thickening formula, postural therapy, and lifestyle changes should be considered if regurgitation is frequent and problematic. On the other hand, thickened formulas are associated with increased weight gain. Overfeeding should be avoided, as it can aggravate reflux.
- Because breastfed infants are less likely to regurgitate than formula-fed infants, breastfeeding should be encouraged [35].

Practices with infant regurgitation

Reflux-related symptoms are among the top concerns parents discuss with their pediatricians during routine checkups. The pressure is immense for healthcare professionals to intervene. It is crucial to manage these concerns carefully, making parents feel heard and understood in their worries about their child's health.

Repetitive regurgitation or vomiting present during the first 2-3 weeks of life, or starting after the age of 6 months, other diagnoses should be considered. Warning signs that prompt further investigation include blood in the vomit, significant projectile vomiting, poor weight gain, feeding refusal, or respiratory symptoms. It is crucial to rule out infections, anatomical anomalies, and metabolic disorders. Special attention to the dietary history, since cow's milk protein allergy may mimic GERD.

It is occasionally difficult to differentiate between GERD, with its more intense symptoms, and GERD, with mild symptoms and exclusively gastrointestinal manifestations. This situation can influence decision-making regarding treatment.

GER and GERD constitute disorders that place a significant burden on pediatricians. Therefore, we must consider the possibility of underdiagnosis, overdiagnosis, and unnecessary treatment. Careful differential diagnosis is crucial to prevent over- or under-treatment, thereby ensuring the best Care for our young patients.

Cyclic vomiting syndrome

Early recognition of cyclic vomiting syndrome (CVS) is crucial. It is characterized by recurrent episodes (with predictable periodicity) of sudden onset of nausea and vomiting that can last from hours to days. Attacks are separated by symptom-free intervals of weeks to

Rome IV Criteria

Diagnoses for Cyclic Vomiting Syndrome include all of the following:

1. Periods of unremitting paroxysmal vomiting (two or more) with or without retching, lasting hours to days within 6 months.
2. Episodes are stereotypical, separated by weeks to months in each patient.
3. A return to baseline health between episodes [1].

In 2025, the Practice Guidelines: "North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition 2025 guidelines for management of cyclic vomiting syndrome in children" were introduced. These evidence-based guidelines supersede the former recommendations and provide the best practices for the management of pediatric CVS [36].

Figure G

months. The median age of symptom onset ranges from 3 to 7 years, but it can occur at any age, from childhood to adulthood. A younger age at symptom onset is associated with a longer disease duration. Two-thirds of cases resolve. However, a proportion may develop migraines in late adolescence or adulthood. There is a slight female predominance. It is poorly recognized and likely underdiagnosed, with a delay in diagnosis described as 13 to 40 months. Due to the intensity and severity of the episodes, patients often require hospital care, resulting in missed school days and lost workdays for parents. These crises result in a compromised quality of life.

Clinical history and physical examination

It typically presents in four phases:

1. Prodromal: Sensation that an episode is about to begin. Irritability, nausea, paleness, followed by sweating with or without abdominal pain. This phase lasts from a few minutes to several hours.
2. Vomiting: Vomiting and nausea lasting 20 to 30 minutes at a time. The child remains immobile and unresponsive or writhes and groans with intense abdominal pain. This phase can last from hours to days, being the most extended of the phases. Once vomiting begins, abortion attempts usually fail.
3. Recovery begins with the cessation of nausea and vomiting, an improvement in appetite, and a return to normal health, either immediately or gradually.
4. Asymptomatic (Interepisodic) A phase of well-being between episodes when the child is completely asymptomatic. Extending this phase aims to improve daily activities and quality of life.

Optimal treatment is based on recognizing the phases of CVS.

Episodes often start in the morning upon awakening and rarely persist for more than 3 days. The number of attacks varies substantially from child to child. Associated symptoms may include: loss of appetite, abdominal pain, diarrhea, fever, dizziness, headache, and photophobia/phonophobia. Complications such as dehydration and hematemesis (Mallory-Weiss syndrome) may occur in more severe cases.

Warning symptoms/signs: Bilious vomiting, severe abdominal pain or tenderness, attacks precipitated by fasting, intercurrent illness, or a protein-rich meal. On physical examination, severe changes in mental status, abnormal eye movements, papilledema, motor asymmetry, or gait abnormality.

Laboratory evaluation

Basic metabolic panel: Sodium, potassium, chloride, bicarbonate, urea, creatinine, glucose, and subsequent anion gap. Complete metabolic panel: Includes all tests of the basic metabolic panel associated with: bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AP), gamma-glutamyl transferase (GGT), amylase, lipase, total protein, albumin, lactate, ammonia, plasma carnitine, acylcarnitines, and serum amino acids. Urine: urinary amino acids, ketone bodies, D-aminolevulinic acid, and porphobilinogen.

Treatment

The goal of CVS treatment is to control symptoms during an acute episode and prevent future attacks. Provide the patient with a letter explaining the diagnosis and necessary treatment, including instructions for action during acute episodes, guidance on seeking emergency room care, and recommendations for avoiding unnecessary laboratory tests.

The current guidelines [36] provide more comprehensive, evidence-based guidance by employing systematic reviews, assessments of the certainty of evidence, and consideration of additional extensive pediatric migraine research evidence.

The management is based on CVS severity:

1. **Mild:**

- ≤ 4 episodes/year
- < 24 hours duration
- No IV therapy required
- Function not impaired

Abortive: Nonpharmacological, stress reduction.

2. **Moderate:**

- More than four episodes/year, but < 1 episode/month
- Episodes with a 24–48-hour duration
- Occasional ED visits/hospitalizations
- Function moderately impaired

Prophylactic: Pharmacological

β-blockers (propranolol)

5-HT2A antagonists cyproheptadine)

NK-1 antagonist (aprepitant)

TCA (amitriptyline, nortriptyline)

3. Severe/Refractory:

- ≥ 1 episode/month
- ≥ 48 hrs duration
- Repeated ED visits/hospitalizations
- Function severely impaired

Prophylactic: Pharmacological

Consider combination therapy if all agents

Refractory: Anticonvulsants (topiramate, valproate)

Intensive outpatient or inpatient rehabilitation

Suppose the patient does not respond to the initial treatment. It is important to consider re-evaluation for alternative etiologies, ensuring the best possible Care for the patient.

Moderate or severe/refractory:

- Abortive: Pharmacological
- NSAIDs + triptans (migraine features)
- NK-1R-antagonist (aprepitant)
- 5-HT3R-antagonist (ondansetron)
- Sedatives (anti-histamines, melatonin).

Nonresponsive

- Early presentation for IV fluid therapy
- IV 5-HT3R-antagonist ondansetron)
- IV NK-1R antagonist (fosaprepitant)
- IV NSAID if pain/migraine features
- Sedatives (IV anti-histamines or IV benzodiazepines).

Practices with cyclic vomiting syndrome

The diagnosis of cyclic vomiting syndrome (CVS) is a complex process that requires the expertise of healthcare providers. It can be made through careful history taking to rule out warning signs and symptoms that may be related to structural or organic etiologies. Laboratory, radiological, and endoscopic examinations are standard in the vast majority of cases.

Observe the clinical presentation:

1. Is the vomiting truly cyclical (vomiting in bouts, interspersed with symptom-free periods) or simply recurrent?
2. Are there neurological or developmental abnormalities?

3. Is there encephalopathy with seizures?
4. Are the seizures precipitated by illness, fasting, high-fat, or high-protein meals?

Supportive measures

- Patients should receive lifestyle advice and education about the disease.
- This should include managing anxiety and avoiding previously identified triggers: sleep deprivation, exhaustion, stress, anxiety, excitement (start of vacation, holidays).
- Most cases are reversible with risk factor control and appropriate treatment.

Prophylactic medications are recommended in children with frequent (≥ every 4-6 weeks) or severe (exceeding 2 days or requiring hospitalization) episodes. NASPGHAN recommends cyproheptadine for children under 5 years of age and amitriptyline for those 5 years of age and older, with propranolol as a second-line agent. Amitriptyline, a tricyclic antidepressant, is the most effective and widely used agent [37].

Conclusion

The Rome IV Criteria for Infants and Preschoolers have enabled us to gain a clearer understanding of Brain-Gut Interaction Disorders, thereby enriching our diagnostic capacity and treatment of these children.

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