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Practical algorithms for managing common gastrointestinal symptoms in infants

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ABSTRACT

Objective: In early infancy, various gastrointestinal symptoms (e.g., constipation, regurgitation, crying/fussiness, infantile colic, and excessive gas) are common problems and may result in numerous visits to pediatricians. Worldwide, this often results in switching infant formulas because parents (and sometimes doctors) believe these symptoms reflect a formula intolerance. However, in many cases, these infants are growing and developing normally. This study was performed to offer family pediatricians consensus-based algorithms on the management of the most common gastrointestinal symptoms in infants.
Methods: A group of pediatric gastroenterologists and pediatric allergists from Europe, USA, Latin America, and Asia developed guidelines and practical algorithms to assist general pediatricians in addressing this challenge.
Results: Five such practice recommendations were developed after a thorough literature review. These algorithms should not be considered as an "evidence-based guideline"; on the contrary, the authors are convinced that challenging these proposals will result in updated and improved versions.
Conclusion: To date, these algorithms, based on the published literature, are the result of a broad consensus of pediatric gastroenterologists from different continents.

Introduction

Functional gastrointestinal (GI) symptoms are very frequent in infants [1]. In formula-fed infants, general practitioners and family pediatrics very often change the formula. The authors developed practical algorithms on the management of these functional GI symptoms. Because double-blinded, placebo-controlled, prospective intervention trials are very limited in this field, these algorithms are based on a consensus among opinion leaders from different parts of the world. Evidence is used wherever it was available. The authors met twice face to face and then by e-mail and teleconferencing. The concept was started by one of the authors (P. A.); however, there was no financial contribution or help from this author's company (Abbott Nutrition) in any aspect.

Regurgitation

Daily regurgitation has a prevalence ranging from 86.9% at 2 mo of age to 7.6% at 1 y [2]. The presence of regurgitation is related to the volume of food ingested: the larger the volume ingested, the longer the gastric emptying time, the higher the intragastric pressure, and the more frequent the transient

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spontaneous relaxations of the lower esophageal sphincter, which predispose an infant to gastroesophageal reflux (GER) [3].

Diagnosis

Regurgitation is defined as the passage of refluxed contents into the pharynx or mouth or from the mouth [4]. Vomiting is defined as a central nervous system reflex involving autonomic and skeletal muscles. GER refers to the movement of gastric content retrograde and out of the stomach. GER is a physiologic process occurring several times per day in all healthy individuals. According to pH-metric criteria, most GER episodes are shorter than 3 min, occur in the postprandial period, and cause few or no symptoms [5]. According to the Rome III criteria, the diagnosis of regurgitation in a healthy infant 3 wk to 12 mo of age should include regurgitation at least two times per day for at least 3 wk and the absence of nausea, hematemesis, aspiration, apnea, failure to thrive, difficulty in feeding or swallowing, and an abnormal posture [1]. More than 50% of all infants meet these criteria (Fig. 1).

Management

The great majority of infants with regurgitation are normal. However, in the infant with recurrent regurgitation, a good medical history and a complete physical examination are mandatory to rule out red flags that can suggest a pathologic condition. One important parameter is the child's anthropometric percentiles to know whether the child is growing properly. Physiologic regurgitation should not be diagnosed in an infant with vomiting and poor weight gain [6]. The management of physiologic regurgitation includes parental education; for example, parents need to know that overfeeding exacerbates regurgitation. In infantile regurgitation, thickened anti-regurgitation (AR) formula decreases the frequency and volume of regurgitation. A prone (anti-Trendelenburg) position is not recommended because of the risk of sudden infant death syndrome [7]. In addition, studies have not shown that anti-secretory drugs or prokinetic agents are of benefit in infants with physiologic regurgitation [8]. A subset of infants with an allergy to cow's milk protein (CMP) may exhibit regurgitation and vomiting indistinguishable from that associated with physiologic GER [5]. In these infants, vomiting frequency decreases significantly (usually within 2 wk) after the elimination of CMP from the diet, and re-introduction causes the recurrence of symptoms. Studies support the use of extensively hydrolyzed or amino acid formulas (aaFs) in formula-fed infants with bothersome regurgitation and vomiting lasting up to 4 wk [5].

Most episodes of regurgitation in healthy individuals are shorter than 3 min, occur in the postprandial period, and cause few or no symptoms [9]. In contrast, GER disease (GERD) is present when the reflux of gastric contents causes troublesome symptoms and/or complications [10]. In this case, the cause of GERD should be identified. The management of GERD includes lifestyle changes, pharmacologic therapy, and, seldom, surgery. Nutritional management of GER includes thickened AR formula, which, by improving the viscosity of what is ingested, relieves regurgitation symptoms, decreases crying, improves sleep, decreases the frequency and total volume of vomiting, and improves weight gain [11]. AR formulas containing processed rice, corn, or potato starch, guar gum, or locust bean gum are available in Europe, Latin America, Asia, and the USA [5]. The effect of the thickener on the absorption of vitamins and minerals has been investigated [12] but has not been demonstrated in vivo. If a commercial AR formula is not available, thickening may be done at home with locust bean gum or rice, corn, or wheat cereal. However, if cereals are used, the caloric intake is increased (possibly causing excessive weight gain). Locust bean gum does not increase the caloric density. Also, "home thickening" of a regular formula increases the osmolarity, which in turn increases the number of lower esophageal sphincter relaxations, which may cause more reflux and regurgitation. Patients with regurgitation/vomiting and persistent failure to thrive should be referred to a pediatric specialist [8].

When red flags are present, there are a few conditions that are often found. CMP allergy (CMPA) should be suspected in an infant with recurrent regurgitation and/or vomiting associated with eczema and/or wheezing. In this case, elimination of CMP should start with an extensive hydrolysate. The guidelines define a therapeutic hypoallergenic formula as one that is tolerated by at least 90% (with 95% confidence) of infants with CMPA [13]. These criteria are met by extensively hydrolyzed formulas based on whey, casein, or another protein source and by amino acid–based formulas. They will probably also be met by (extensive) rice hydrolysates. It is best that all supplementary food is stopped during the diagnostic elimination diet. Also, a trial of a milk-free diet for the breast-feeding mother is appropriate for infants not responding to management [1]. GER and/or regurgitation are almost never an indication to stop breast-feeding.

Infantile colic

Infantile colic was first described by Wessel et al. in 1954 [14] as "crying lasting three or more hours a day, at least three days a week for at least three weeks." In 2006, the Rome III criteria defined it as "episodes of irritability, fussing, or crying that begin and end for no apparent reason and last at least three hours a day, at least three days a week, for at least one week" [1]. The incidence varies from 5% to 20% [15]. Colic occurs equally in breast- and bottle-fed infants and in both sexes [15]. The etiology is unknown and multiple hypotheses have been proposed, including altered GI function; variable food intolerance, sometimes related transient low lactase activity; CMPA; GER; intestinal microflora imbalance; etc. [16].

Diagnosis

The cardinal symptom is excessive and persistent loud crying, which mostly tends to occur late in the afternoon. During each episode, the child appears distressed, irritable, and fussy and contracts the legs, becomes red-faced, and frequently has episodes of borborygmi. In any patient with suspected infantile colic, it is necessary to consider CMPA, GER, and transient low lactase activity by searching for the patient's clinical symptoms (Fig. 2) [17].

Management

There are no uniform criteria for a specific therapeutic regimen. The first recommended step is to look for potential "red flags" (Fig. 2); if not present, evaluate the feeding technique; then, reassure the caregivers and offer general advice, emphasizing the self-limiting nature of the condition. For breast-fed infants, clinicians should advise mothers to continue breast-feeding but can sometimes recommend that the mothers avoid cow's milk from their own diet. The elimination diet should be continued for a minimum of 2 wk and should

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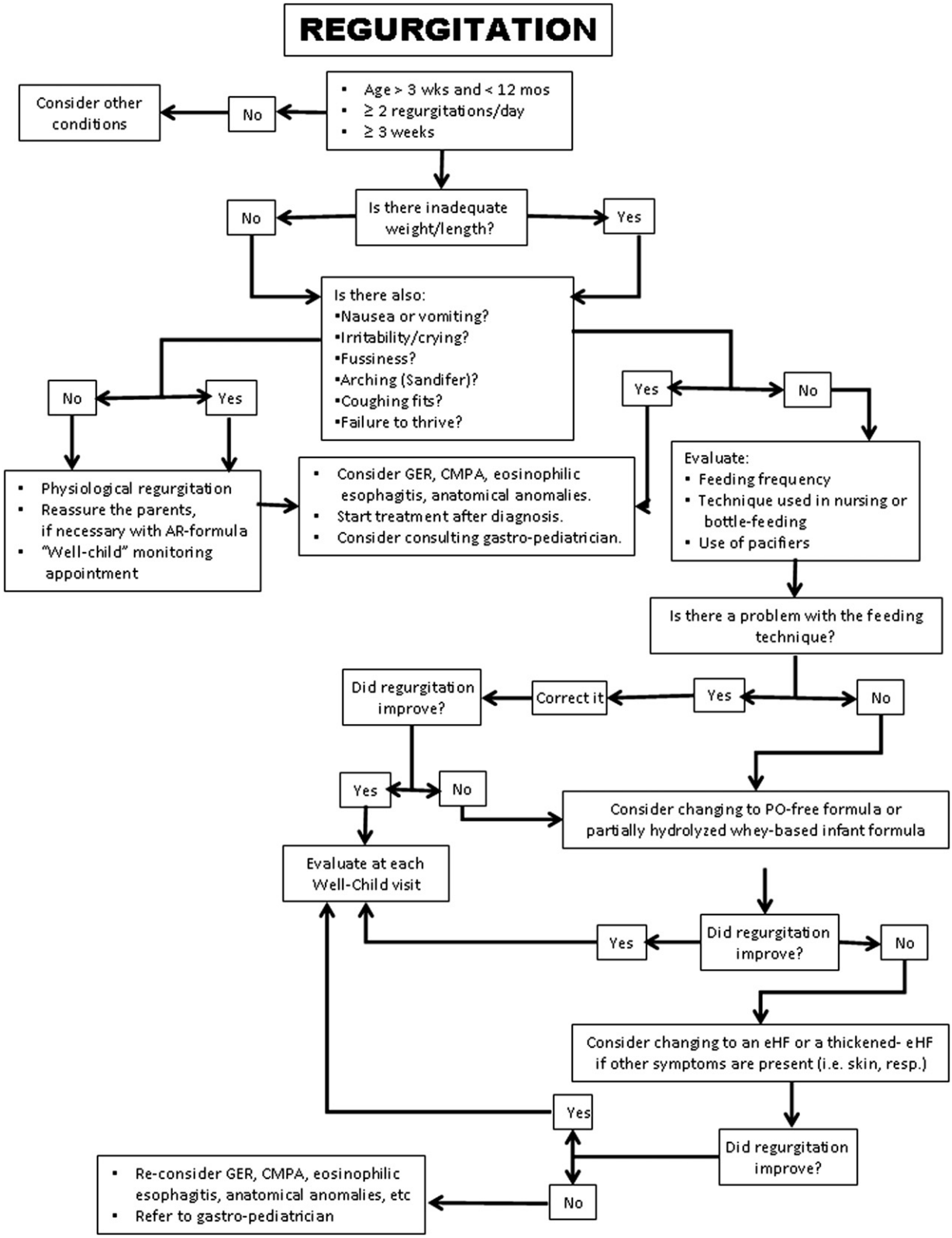

Fig. 1. Algorithm. AR, anti-regurgitation; GER, gastroesophageal reflux; CMPA, cow's milk protein allergy; PO, palm oil; eHF, extensively hydrolyzed cow's milk formula.

continue if the infant responds well. For formula-fed infants, the elimination of CMP and the use of an extensively hydrolyzed protein formula are an effective treatment of infantile colic [15]. Experience has shown that partially hydrolyzed formulas can be a useful option when CMPA is a not a potential cause of the colic or when the extensive hydrolysate would be

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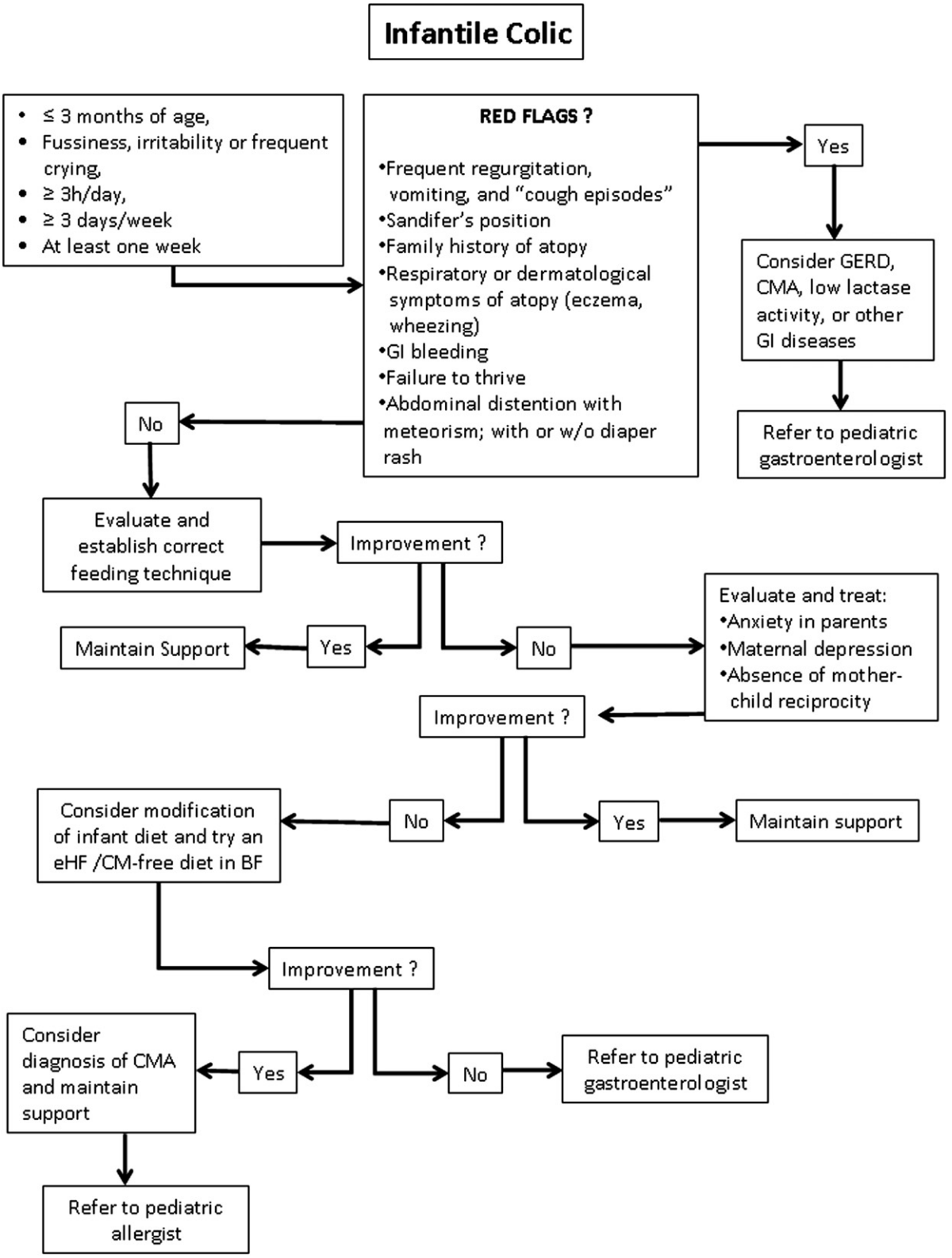

Fig. 2. Algorithm. GI, gastrointestinal; GERD, gastroesophageal reflux disease; CMA, cyclic motor activity; eHF, extensively hydrolyzed cow's milk formula; CM, cow's milk; BF, breast feeding.

too expensive [15]. In fact, various randomized controlled trials have reported the efficacy of whey-based partially hydrolyzed formulas. In some cases, these formulas are lactose reduced or lactose free and have added prebiotics, showing, with varying levels of evidence, a decrease in the number of crying episodes per week and total crying time [9]. However, the role of lactose

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can be questioned, because soy formula was not associated with a benefit [18].

The efficacy of dicyclomine, dicycloverine, or cimetropium has been evaluated. The latter has shown a high rate of lethargy, motion sickness, and/or somnolence [19]. Simethicone has shown no difference from placebo [20]. Other randomized controlled trials have studied glucose or saccharose solutions, with varying effects on crying time [21]. Clinical trials have studied the efficacy and safety of probiotics in infantile colic; and although the results are promising, the magnitude of the effect and the quality of the evidence are not yet sufficient for a solid recommendation [22]. Several studies have been performed with proton pump inhibitors in distressed infants and all failed to show any benefit [23–26].

Other studies have evaluated the role of additional familial caregivers' support; counseling therapies; car rides during colic episodes; a decrease of stimulating actions (such as changing diapers); chiropractic, spinal massages; or even the use of herbal options. Unfortunately, none of these trials was of sufficient methodologic quality to allow a recommendation [27,28].

Infantile colic is a condition that has many different causal and contributing factors. This multifactorial aspect makes it unlikely that a single intervention will be found that is associated with significant improvement in an unselected patient population. Thus far, there is only some evidence for a beneficial effect of extensive and, to a lesser extent, partial hydrolysates.

Fussiness, gassiness accompanied by crying

Although many infants are distressed because of fussiness and gassiness, almost all these infants also cry a lot, and therefore caregivers are more focused on the crying than the other signs and symptoms. Therefore, in these cases, a good medical history is critical. Infants usually communicate and express themselves by crying. This may be due to a variety of reasons, ranging from hunger or a desire for attention to a severe life-threatening illness. Healthy children starting at a very early age cry 20 min to 3.5 h/d [29]. By the time parents present to the emergency room with their crying child, caregivers are often anxious, frustrated, and sleep deprived. These emotions contribute to the difficulty of making an evaluation of the non-verbal crying infant and lead to most emergency room visits occurring in cases of "non-serious" diseases, aggravated by insufficient caretaker knowledge and information [30]. The best available evidence strongly indicates, but does not yet confirm, that unsoothable crying bouts and fussiness are common and specific to early infancy, not affected by parenting, and probably due to neurodevelopmental changes that are a normal part of development. In contrast, overall 24-h bouts of crying are substantially decreased when parents adopt methods of care that involve more physical contact and greater responsiveness [31]. Prolonged crying and fussiness in the first 3 mo may be due to food intolerance and other organic disturbances in a very small number of cases [31]. This section refers to infants with fussiness and/or gassiness accompanied by crying (the "colicky baby"). This kind of crying is different from the crying related to "infantile colic" that has been defined previously. Therefore, the algorithms for "colic" and "fussiness, gassiness accompanied by crying" are slightly different.

Diagnosis

Symptoms such as fussiness or excessive gas in the great majority of cases are not associated with any medical condition. A fussy infant is one who is easily upset and given to bouts of ill temper. The presence of a certain amount of air in the digestive tract is normal; however, when there is an excess, symptoms/signs such as abdominal distention and even pain can be present. Improper feeding techniques are an important cause of aerophagia. Some red flags may alert doctors to the potential presence of an organic condition (in decreasing order of evidence): 1) positive physical examination; 2) frequent regurgitation, vomiting, diarrhea, blood in stools, or weight loss/failure to thrive; 3) lack of a diurnal rhythm; 4) positive family history of migraine, asthma, atopy, or eczema; and 5) maternal drug ingestion. Low lactase activity or secondary lactose malabsorption in fussy babies can be associated with excessive gas and soft stools with or without the presence of diaper rash [32]. The clinical history and physical examination are the cornerstones for evaluating young infants whose chief complaints include crying, irritability, screaming, or fussiness. In fact, it has been found that the clinical history and physical examination can help pediatricians in identifying the etiology in 66.3% of cases [33]. Additional testing should be performed based on the clinical findings (Fig. 3).

Management

Fussiness, crying, and excessive gas production may be normal at a young age. There is strong evidence that the introduction of structured parenting based on behavioral principles from about 6 wk of age is likely to help prevent night waking and signaling after 12 wk [30]. A noteworthy finding is that no benefits from this approach were apparent before 6 wk of age. Where no organic disturbances are found, the available evidence provides no basis for advising parents in general that changes in their care are likely to resolve crying problems in 1- to 3-mo-old infants. This is particularly true of the prolonged, unsoothable crying bouts that seem to be central to parents' concerns in early infancy. Instead, once an organic disturbance is considered and the infant's healthy growth and development are confirmed, the focus of intervention should be on containing the crying and providing parents with information and support. Important elements advocated by an expert group [34] are 1) examining the notion that crying means there is something "wrong" with a baby at this age and introducing alternatives (e.g., that it signals a reactive or vigorous baby); 2) viewing the first 3 mo of infancy as a developmental transition that all babies go through more or less smoothly; 3) reassuring parents that it is normal to find crying aversive and discussing the dangers of "shaken baby syndrome"; 4) discussing ways of containing/minimizing the crying and highlighting the positive features of the baby; 5) considering the availability of support and the development of coping strategies that allow individual parents to take time out and "recharge their batteries"; 6) empowering parents and reframing the first 3 mo as a challenge they can overcome, with positive consequences for themselves and their relationships with their babies; and 7) continuing to monitor the infant and the parents. In formula-fed infants, when low lactase activity is suspected and the child has gassiness, diarrhea, and in some cases diaper rash and the parents really focus on this, lactose may be withdrawn from the diet temporarily. In some cases, GERD may cause crying and fussiness. However, all placebo-controlled studies evaluating the efficacy of proton pump inhibitors in these infants failed to show benefits.

Constipation

In infants younger than 4 mo, the feeding pattern has a key role in the stool pattern. Healthy breast-fed babies may defecate

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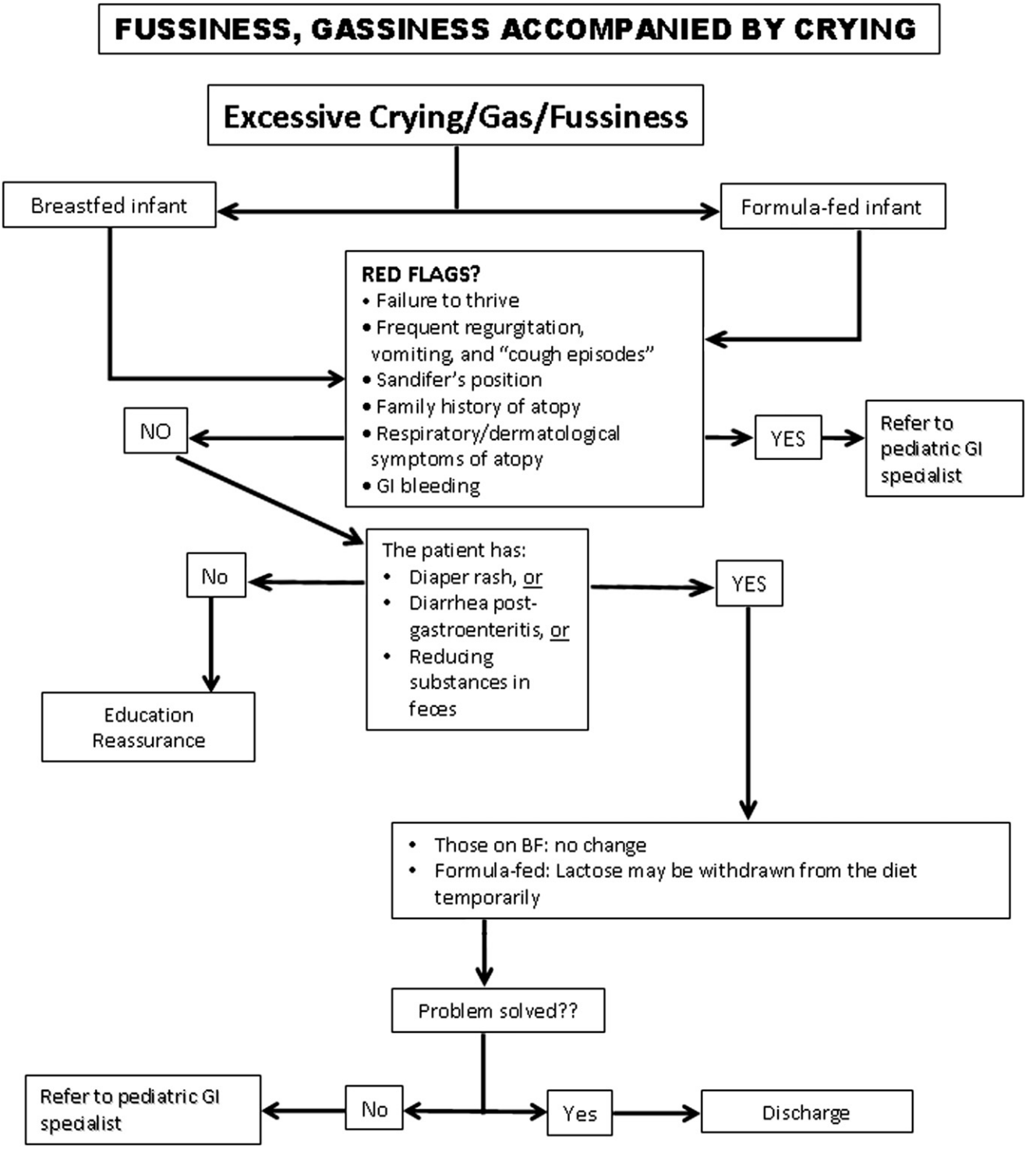

Fig. 3. Algorithm. GI, gastrointestinal; BF, breast feeding.

as frequently as 12 times per day or as infrequently as once in 3 or 4 wk [1]. In this age group, hard stools are found only in 1.1% of exclusively breast-fed versus 9.2% of formula-fed infants (0.001) [35]. Unpublished data have confirmed that 10% of formula-fed infants continue to have hard stools, despite the use of probiotic- or prebiotic-enriched formula. Firm or hard stools are often seen with the change from breast milk to infant formula or after the introduction of solids. Harder stools are frequent in infants fed with formulas containing palm olein oil or palm oil as the main source of fat [36].

Diagnosis

A thorough medical history and physical examination are the cornerstones for establishing the etiology of infant constipation. Failure to pass meconium within 24 to 48 h after birth should

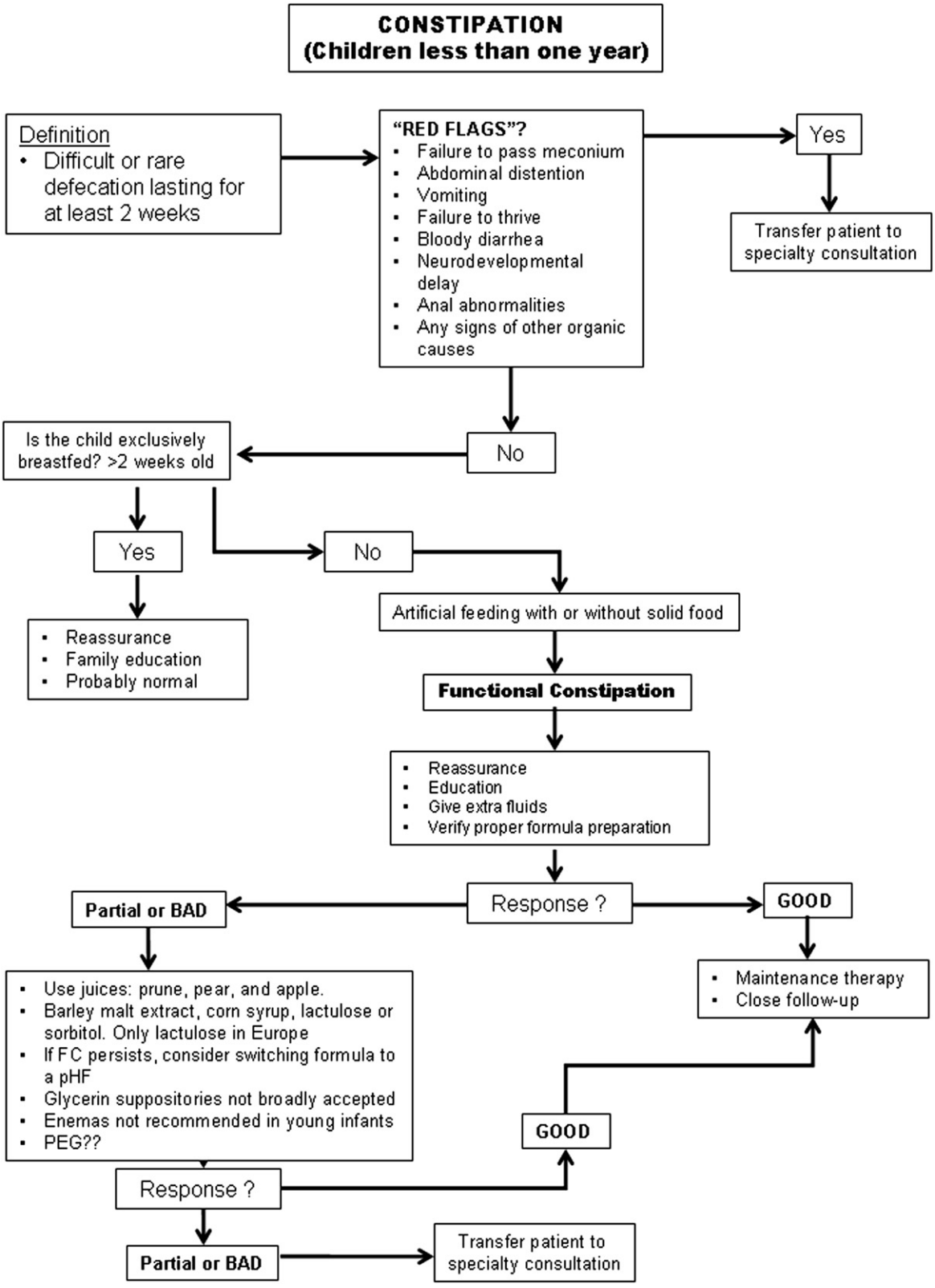

Fig. 4. Algorithm. FC, functional constipation; pHF, partially hydrolyzed cow's milk formula; PEG, polyethylene glycol.

raise a suspicion of Hirschsprung's disease [37]. The normal defecation pattern of infants must be known by the health care professional to differentiate abnormal from normal to properly educate and advise parents and to avoid unneeded treatments. It is crucial to establish what the parents mean when using the term *constipation*: the length of time the condition has been

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Table 1
Classification of gastrointestinal food allergy syndromes*

IgE-mediated	Mixed non-IgE/IgE-mediated	Non-IgE–mediated
Immediate gastrointestinal hypersensitivity	allergic eosinophilic esophagitis	food protein-induced enterocolitis syndrome
Oral allergy syndrome	allergic eosinophilic gastritis	allergic enteropathy
	allergic eosinophilic gastroenterocolitis	allergic proctocolitis

IgE, immunoglobulin E
* Adapted from the Singapore Ministry of Health Food Allergy Clinical Practice Guidelines [44].

present, the frequency of bowel movements, the consistency and size of the stools, whether defecation is painful, whether blood has been present in the stool, and whether the child seems to experience abdominal pain. For infants, many experts recommend using the definition proposed by Biggs and Dery [37]: "difficult or rare defecation lasting for at least two weeks." The diagnosis of functional constipation (FC) is made by the medical history and physical examination. No testing is necessary if there are no arguments for an organic cause. The younger the infant, the higher the risk of an anatomic or organic cause, although FC remains the most frequent condition at any age. Anorectal examination should evaluate the perianal sensations, anal position and tone, the size of the rectum, the presence of an anal wink, the amount and consistency of stool, and its location within the rectum. Specific tests must be performed if other clinical data are present (i.e., pain, failure to thrive, intermittent diarrhea, abdominal distention) [1,37]. Although CMPA has been shown to be a cause of constipation in a subset of children, the exact proportion is unclear and the pathophysiologic mechanisms have remained elusive (Fig. 4) [38].

Management

The first step in treatment is parental education. Doctors should address the myths and fears about FC and point out that FC is one of the most common, non-dangerous problems in pediatrics and that it usually disappears. Dietary recommendations may help. If the probability of any organic condition is low, reassurance and close follow-up should be enough. If the infant is receiving a standard infant formula, it is recommended that the infant should continue with the same formula. In some regions, it is popular to use magnesium-rich mineral water to prepare the infant formula. However, there is no evidence to support this practice, and mineral intake in these circumstances is above the recommendations. Juices that contain sorbitol, such as prune, pear, and apple juices, can decrease constipation. Glycerin suppositories—not well accepted by all experts—could be helpful in acute constipation, when rectal emptying is needed. Evidence does not support the use of mineral oil (risk of lipoid pneumonia due to aspiration) or enemas (e.g., phosphate). Infant formulas containing partially or extensively hydrolyzed proteins, fortified with prebiotics and/or probiotics, and without palm oil as the main source of fat in the oil blend offer a good alternative for managing FC [39,40]. There are some formulas commercialized as "anti-constipation formulas." However, there is only limited evidence of their efficacy [41].

Cow's milk protein allergy

Although systematic prevalence studies are lacking, cow's milk is one of the most common causes of food allergy in infants and young children globally [42]. CMPA often presents with GI disturbances such as vomiting and diarrhea. Making the diagnosis is critical in its management, because avoidance of CMP results in the resolution of symptoms, whereas unnecessary dietary restrictions and elimination diets may result in impaired growth or malnutrition [43].

Classification and clinical features

According to the definition proposed by the World Allergy Organization, CMA is a hypersensitivity reaction brought on by specific immunologic mechanisms to cow's milk [44]. CMPA is not a single entity but a heterogeneous group of disorders that can be classified in different categories: 1) immunoglobulin E (IgE)-mediated, 2) mixed IgE/non-IgE–mediated, and 3) non-IgE–mediated allergies.

The IgE-mediated CMPA is caused by an immediate hypersensitivity to CMP, which is often associated with atopic conditions: atopic eczema, asthma, and/or allergic rhinitis. GI symptoms such as vomiting, abdominal colic, and occasionally diarrhea accompany systemic manifestations of the skin (urticaria, angioedema) and respiratory tract (rhinitis, wheezing, stridor), and pallor or flaccidity (hypotension), which occur soon after allergen exposure (usually within 1 h). Anaphylaxis is the most serious manifestation of IgE-mediated CMPA [44]. In som infants, it may be very difficult to separate "reflux" from "CMPA" symptoms.

Mixed IgE/non-IgE- and non-IgE–mediated allergies constitute a mixed group of disorders that have been well defined clinically, although their immunologic mechanisms may not be well understood [44].

Table 2
Clinical features helpful in distinguishing among GI food allergy syndromes*

	Vomiting	Diarrhea	Growth	Common food allergens	Other	Onset
Food protein-induced enterocolitis syndrome	prominent	prominent	normal	milk/soy/others	re-exposure: severe, subacute symptoms	days to 1 y
Allergic eosinophilic esophagitis	common	minimal	may be affected	milk/soy/egg/wheat/peanut	reflux-type symptoms, obstruction/ dysphagia, abdominal pain	any age
Allergic eosinophilic gastroenterocolitis	prominent	prominent	poor	milk/soy/egg/wheat/fish	strictures, dysmotility, ascites, anemia, GI bleeding	any age
Allergic enteropathy	variable	moderate	poor	milk/soy	hypoalbuminemia, edema	2–24 mo
Allergic proctocolitis	absent	minimal, bloody	normal	breast milk/soy		days to 6 mo

GI, gastrointestinal
* Adapted from the Singapore Ministry of Health Food Allergy Clinical Practice Guidelines [44] and Sicherer SH: Enterocolitis, proctocolitis, and enteropathy. In: Paediatric allergy. 510–7.

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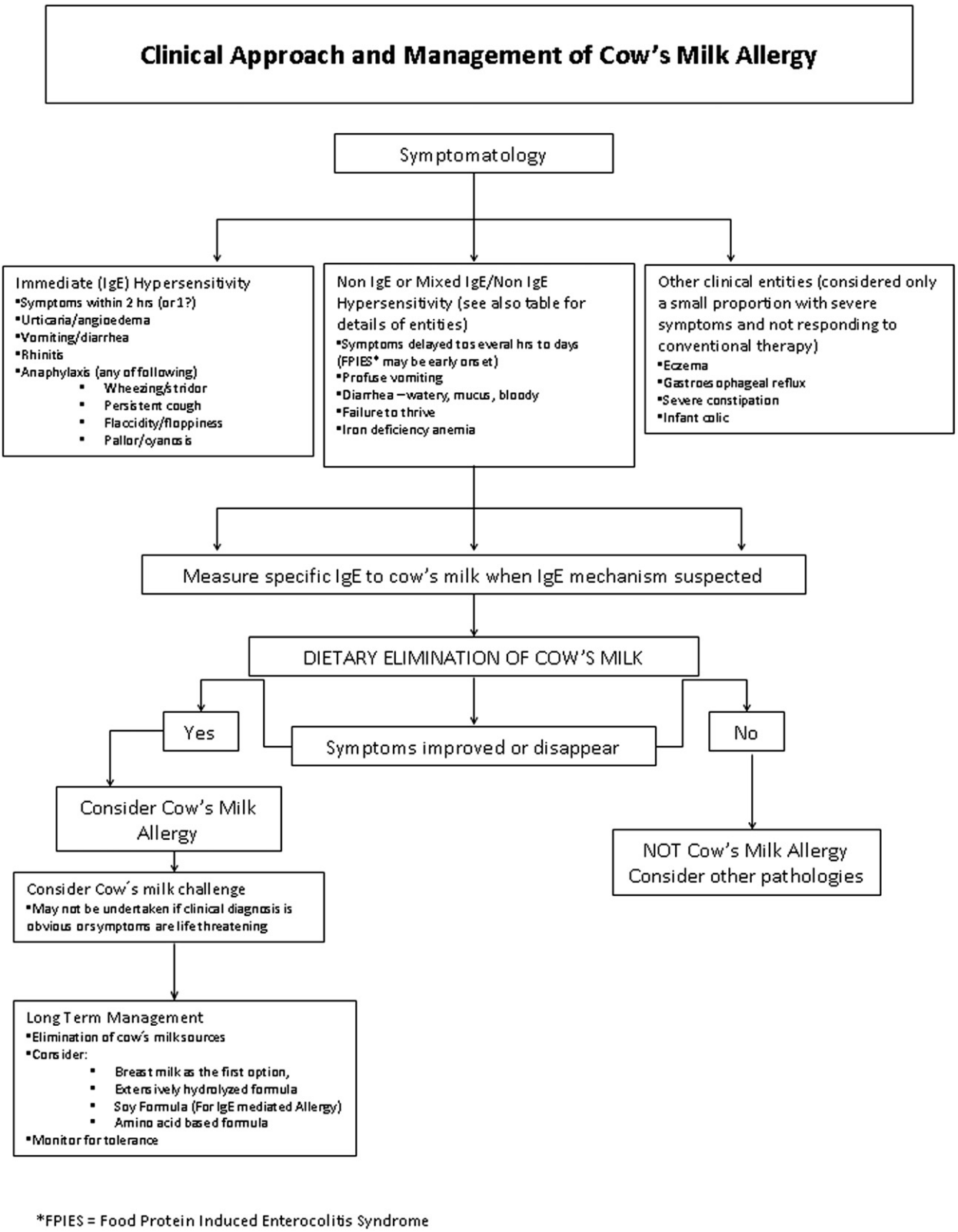

Fig. 5. Algorithm. IgE, immunoglobulin E.

Table 1 lists the conditions that might be caused by CMPA. These entities are not confined to CMPA and may also be triggered by other food allergens. Table 2 presents the clinical distinction of these disorders, of which food protein-induced enterocolitis is the most serious because a severe reaction may be life-threatening (Fig. 5).

Diagnosis and management

The central principle in managing patients with food allergy is the avoidance of the food known to have caused the reaction. For growing children, elimination diets need to be individually tailored to ensure that the child receives a safe and healthy diet until tolerance to CMP is achieved. In some parts of the world, there is a tendency for medical practitioners to overdiagnose food allergy and prescribe elimination diets that are not adequately supervised. This practice could adversely affect the child's growth [45–50]. In other parts of the world, however, there is a tendency to underdiagnose CMPA. It is therefore essential that an accurate diagnosis of CMPA be made.

In infants with symptoms suggestive of an IgE-mediated reaction, an elimination diet should be advised. Skin prick or specific IgE tests can be performed but are not necessary. Increased IgE is related to the duration of the allergy [44]. A cow's milk challenge is the gold standard for the diagnosis of CMPA but does not provide proof that the immune system is involved. In this regard, it is worth noting that IgE sensitization based on a positive cow's milk IgE test without a positive clinical history is not conclusive of CMPA. These children would require confirmatory challenge testing. Intradermal and atopy patch testing are not recommended standard procedures for the diagnosis of CMPA [51].

Children with CMPA should also be monitored for resolution of the allergy. Most children with IgE-mediated CMPA will ultimately achieve tolerance, with reported rates of resolution of 19% by 4 y of age, 42% by 8 y, and 79% by 16 y [52]. Children who have an IgE-negative allergy become tolerant sooner.

Regarding formula replacement, most guidelines agree that a CMP formula should be replaced by a hypoallergenic formula [53]. According to most guidelines, soy is not recommended as the first line. However, recommendations differ depending on the type of reaction, the age of the patient, availability of the formula, and the costs involved. Rice hydrolysates, which are on the market in a growing number of countries, may soon figure in these recommendations because they are CMP-allergen free, contain extensively hydrolyzed rice protein and thus have low residual allergenicity, and are cheap compared with extensive cow's milk–based hydrolysates. However, clinical experience is too limited to recommend them.

The World Allergy Organization Diagnosis and Rationale for Action against CMPA (WAO-DRACMA) guidelines recommend that, in children with IgE-mediated CMPA at low risk for anaphylactic reactions, an extensively hydrolyzed cow's milk formula (eHF) be used [34,44]. They acknowledge that there is very low-quality evidence for this recommendation but have chosen to favor eHF over aaF because of the high cost of the latter. In children at high risk of anaphylactic reactions, they suggest aaF rather than eHF (conditional recommendation/very low-quality evidence). This recommendation gives priority to avoid anaphylactic reactions over the cost of aaF. The WAO-DRACMA recommends eHF over soy formula in IgE-mediated CMPA but states that "there is very sparse evidence suggesting a possible benefit from using eHF compared to soy formula" and advocates the need for more research. Although soy protein has been used in infant feeding for more than 100 y, the popularity of soy infant formulas varies substantially in different parts of the world. The world is divided into "soy-popular countries" such as the USA and "soy-avoiding countries" such as France [54]. In fact, the Agence Française de Sécurité Sanitaire des Aliments based its position primarily on the limited knowledge and uncertainties regarding the presence of isoflavones in soy formulas [55].

The American Academy of Pediatrics recommends that infants with IgE-mediated CMPA should be given an eHF rather than soy formula. Its article on infant soy formula reported that about 10% to 14% of infants with CMPA are sensitized to soy [56]. However, there is evidence that true rates of soy allergy are much lower. In a prospective cohort study of 13 019 infants performed by Katz et al. [57], the incidence of IgE-mediated CMPA was 0.5% (66 of 13 019 subjects). Interestingly, 64 of these infants could tolerate soy and none of the 66 had a documented allergy to soy. Reported rates of soy allergy in non-IgE–mediated CMPA are much higher (up to 50%), so it is reasonable to avoid recommending soy formula in this group of infants [58]. However, in IgE-mediated CMPA, it is not unreasonable to suggest that soy formula be used as the first choice over eHF or aaF in infants [44].

Conclusion

Healthy infants presenting with common functional GI problems often go through a series of unnecessary changes of formulas. Opinion leaders from different continents have reached a consensus on their diagnosis and management and provided recommendations for their appropriated management.

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