Summary of the 2018 NASPGHAN-ESPGHAN Pediatric Gastroesophageal Reflux Clinical Practice Guideline[1]

Focus on Infants

BACKGROUND

In 2018, an updated guideline was published on gastroesophageal reflux (GER*) and GER disease (GERD*) in infants and children, which included additional new data on the benefits and harms of interventions, and the need to provide guidance for both primary care physicians, dietitians, and pediatric gastroenterologists.[1]

The summation of the guideline's approach to infants with frequent regurgitation or vomiting suspected of GERD is shown in the algorithm (Figure 1).

OVERVIEW OF RECOMMENDATIONS

The summation of the guideline's approach to infants with frequent regurgitation or vomiting suspected of GERD is presented in the following algorithm. The key algorithm decision points are expanded further below.

INFANT WITH SUSPICION OF GERD

There are a number of challenges to defining GER and GERD in the pediatric population. Reported symptoms of infant GERD vary widely and may include excessive crying, back arching, regurgitation and irritability, yet many of these symptoms occur in all babies even those without GERD. To date, there is no gold standard diagnostic tool for GERD; it is a symptom based diagnosis. The definitions are shown below.

***DEFINITIONS:**

GER: *the passage of gastric contents into the esophagus with or without regurgitation and vomiting.*
GERD: *when GER leads to troublesome symptoms and/or complications.*
Refractory GERD: *GERD not responding to optimal treatment after 8 weeks.*

HISTORY AND PHYSICAL EXAM

In the infant with recurrent regurgitation or 'spitting', a thorough history and physical examination as outlined in Tables 1-2 is essential.

PRESENCE OF ALARM SIGNS

Referral of infants with GERD to the pediatric gastroenterologist is recommended if there are alarm features (Table 3), or symptoms suggesting an alternative underlying gastrointestinal disease (Table 4).

Diagnostic tests are not recommended in the investigation of GERD in infants with the exception of the specific instances detailed in the full guidelines report.[1] Barium contrast studies or ultrasonography can be performed to exclude anatomical abnormalities. Referral to a pediatric gastroenterologist is recommended for consideration of GI studies such as endoscopy, manometry, pH-metry or pH-impedance.

FIGURE 1: *Management of the symptomatic infant.*

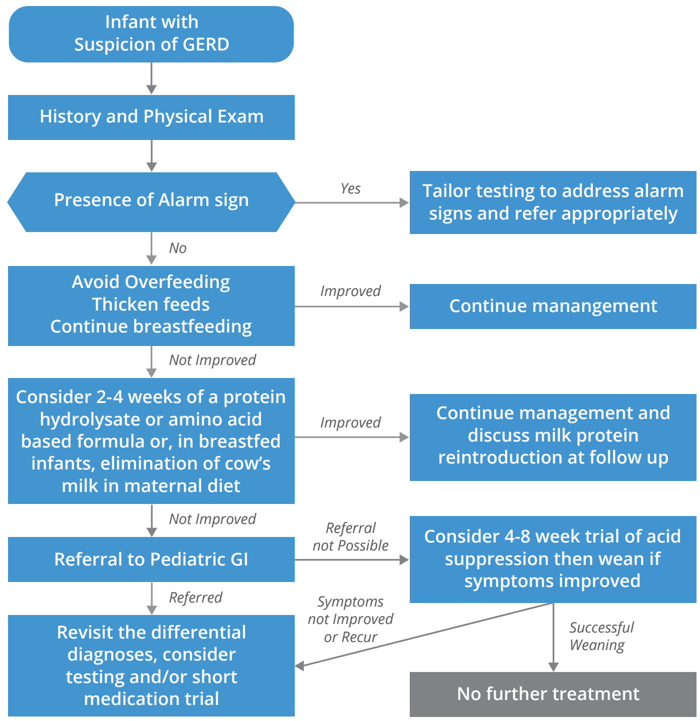

TABLE 1: *Clinical History of Disease Assessment.*

Age of onset
Feeding and dietary history
Length of feeding period
Volume of each feed
Type of formula
Method of mixing formula
Quality of milk supply (breastfeeding)
Volume of feeds
Additives to the feed
Restriction of allergens
Time interval between feeds
Growth trajectory
Family medical history
Pattern of regurgitation/spitting/vomiting
Nocturnal
Immediately post prandial
Long after meals
Digested vs. undigested
Possible environmental triggers
Family psychosocial history
Second-hand tobacco smoke exposure
Prior pharmacological and dietary interventions
Presence of warning signs

TABLE 2: *Common symptoms and signs to identify GERD in infants.*

SYMPTOMS	SIGNS
General Discomfort/irritability* Failure to thrive Feeding refusal Dystonic neck posturing (Sandifer syndrome)	General Dental erosion Anemia
Gastrointestinal Recurrent regurgitation Hematemesis Dysphagia/odynophagia	Gastrointestinal Esophagitis Esophageal stricture Barrett's esophagus
Airway Wheezing Stridor Cough Hoarseness	Airway Apnea spells Asthma Recurrent otitis media Recurrent pneumonia associated with aspiration

**If excessive irritability and pain is the single manifestation it is unlikely to be related to GERD*

THERAPY

FIRST-LINE APPROACH

While evidence is lacking for improvement in GER, the following modifications are without risk or cost and so should be considered before more costly or risky interventions.

Avoid Overfeeding

Modifying feeding volumes and frequency according to age and weight to avoid overfeeding in infants with GERD is suggested.

Thicken Feeds

Use of thickened feedings for treating visible regurgitation/vomiting in infants with GERD is suggested. Whenever thickening formula, using rice cereal with low or no arsenic is recommended, for its ability to thoroughly dissolve, affordability and long track record of use in infants.

Continue Breastfeeding

While breastfeeding is always encouraged, some infants with significant reflux need thickened feeds. Pumped breast milk can be thickened with commercial thickeners such as carob bean-based thickeners. Each commercial thickener has varying age restrictions and recommendations may vary based on the brand and regarding the institutional policies. Breastmilk cannot be thickened with cereal as the cereal is digested by the amylases in breast milk.

The following modifications are not recommended because of lack of data:

- positional therapy
- massage therapy
- prebiotics
- probiotics
- herbal medications

SECOND-LINE APPROACH

After optimal non-pharmacological treatment has failed, a 2 to 4-week trial of extensively hydrolyzed protein-based or amino acid-based formula is suggested in infants suspected of having GERD, given that symptoms of GERD and cow's milk protein allergy are identical.

TABLE 3: *'Red flags' suggesting more worrisome disorders requiring further investigation and management.*

SIGNS AND SYMPTOMS	REMARKS
General	
Weight loss	Suggests a variety of conditions, including systemic infections
Lethargy	
Fever	
Excessive irritability/pain	
Dysuria	May suggest urinary tract infection, especially in infants
Onset of regurgitation/vomiting >6 months increasing/persisting >12-18 months of age	Late onset as well as symptoms increasing or persistings after infancy, based on natural course of the disease, may indicate a diagnosis other than GERD.
Neurological	
Bulging fontanel/rapidly increasing head circumference	May suggest raised intracranial pressure for example due to meningitis, brain tumor or hydrocephalus
Seizures	
Macro/microcephaly	
Gastrointestinal	
Persistent forceful vomiting	Indicative of hypertrophic pyloric stenosis (infants up to 2 months old)
Nocturnal vomiting	May suggest increased intracranial pressure
Bilious vomiting	Regarded as symptom of intestinal obstruction. Possible causes include Hirschsprung disease, intestinal atresia or mid-gut volvulus or intussusception
Hematemeisis	Suggests a potentially serious bleed from the esophagus, stomach or upper gut, possibly GERD-associated, occurring from acid-peptic disease.* Mallory-Weiss tear† or reflux-esophagitis.
Chronic diarrhea	May suggest food protein-induced gastroenteropathy‡
Rectal bleeding	Indicative of multiple conditions, including bacterial gastroenteritis, inflammatory bowel disease, as well as acute surgical conditions and food protein-induced gastroenteraphty rectal bleeding‡ (bleeding caused by proctocolitis)
Abdominal distension	Indicative of obstruction, dysmotility, or anatomic abnormalities

GERD = gastroesophageal reflux disease
*Especially with non-steroidal anti-inflammatory drugs
†Associated with vomiting.
‡More likely in infants with eczema and/or a strong family history of atopic disease.

TABLE 4: *Alternative underlying diseases with GERD-like symptoms.*

Gastrointestinal obstruction Pyloric stenosis Malrotation with volvulus Intussusception Hirschsprung disease Antral/duodenal web Foreign body Incarcerated hernia Superior mesenteric artery (SMA) syndrome	Other gastrointestinal disorders Achalasia Gastroparesis Gastroenteritis Peptic ulcer Eosinophilic esophagitis Food allergy/intolerance Inflammatory bowel disease Pancreatitis Appendicitis
Neurologic Hydrocephalus Subdural hematoma Intracranial hemorrhage Intracranial mass	Infectious Sepsis/meningitis Urinary tract infection Upper/lower airway infection Otitis media Hepatitis
Metabolic/endocrine Congenital adrenal gland hyperplasia/adrenal crisis Galactosemia Hereditary fructose intolerance Urea cycle defects Amino and organic acidemias Fatty acid oxidation disorders Metabolic acidosis	Others Pediatric condition falsification (PCF)/factitious disorder by proxy (FDP) Child neglect or abuse Self-induced vomiting Cyclic vomiting syndrome Rumination syndrome
Toxic Lead poisoning Other toxins	Renal Obstructive uropathy Renal insufficiency
Cardiac Heart failure Vascular ring Autoimmune dysfunction	

THIRD-LINE APPROACH

- Referral to the pediatric gastroenterologist is recommended if infants with GERD are refractory to optimal treatment as described above. Otherwise if referral is not possible:
  - Use of proton pump inhibitors (PPIs) for a maximum of 4 to 8 weeks as first-line treatment of reflux-related erosive esophagitis in infants with GERD is suggested.
  - If PPIs are not available, or contra-indicated, use of histamine-2 receptor antagonists (H_2RAs) for 4 to 8 weeks in the treatment of reflux related erosive esophagitis in infants is suggested.
- Apart from the above medications, pharmacological treatment of infants with GERD is not recommended.
- **The goal for medication therapy is to use the lowest doses of medication for the shortest time possible as these medications do have side effects.**

REFRACTORY GERD

- For infants not responding to 4 to 8 weeks of optimal therapy (PPI or H_2RA) for GERD, evaluation of treatment efficacy and exclusion of alternative causes of symptom is recommended.
- Referral of infants with GERD to the pediatric gastroenterologist is recommended if patients cannot be permanently weaned from pharmacological treatment by 6 to 12 months of age.
- Antireflux surgery should only be considered in infants with GERD under certain circumstances and transpyloric/jejunal feedings in refractory cases of GERD is an alternative approach.[1]

Reference

1. *Rosen R, Vandenplas Y, Singendonk M, Cabana M, DiLorenzo C, Gottrand F, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018 Mar;66(3):516–54.*

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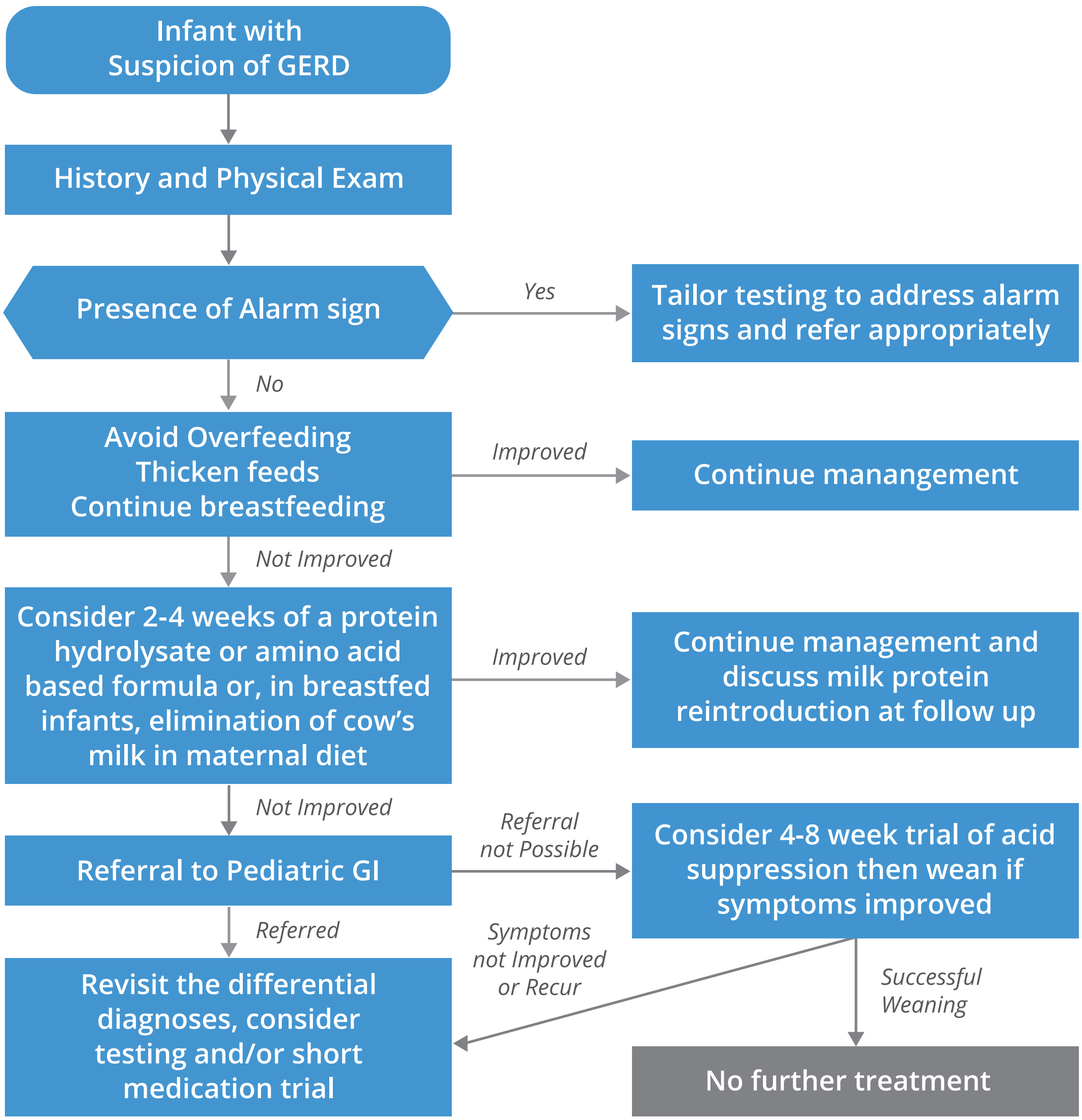
FIGURE 1: *Management of the symptomatic infant.*



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