



Complete Summary

GUIDELINE TITLE

Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children.

BIBLIOGRAPHIC SOURCE(S)

Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, Gerson WT, Werlin SL. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr 2001;32(Suppl 2):S1-31. [336 references] [PubMed](#)

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SCOPE

DISEASE/CONDITION(S)

- Gastroesophageal reflux (GER)
- Gastroesophageal reflux disease (GERD)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assist the primary and specialist medical provider in the evaluation and management of gastroesophageal reflux in infants and children

TARGET POPULATION

Infants and children with suspected or confirmed:

- Gastroesophageal reflux (GER)
- Gastroesophageal reflux disease (GERD)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnostic Approaches

1. History and physical examination
2. Barium contrast radiography
3. Esophageal pH monitoring
4. Endoscopy and biopsy
5. Scintigraphy
6. Empiric therapy

Treatment Options

1. Lifestyle changes
 - Feeding changes in infants
 - Positioning therapy for infants
 - Lifestyle changes in children and adolescents
2. Pharmacological therapies
 - Acid suppressants
 - Histamine-₂ receptor antagonists (e.g., cimetidine, nizatidine, ranitidine, famotidine)
 - Proton pump inhibitors (e.g., omeprazole, lansoprazole, rabeprazole)
 - Antacids (e.g., aluminum or magnesium hydroxide)
 - Prokinetic therapy (e.g., cisapride, metoclopramide, bethanechol)
 - Surface agents (e.g., sucralfate, sodium alginate)
3. Surgical treatment for gastroesophageal reflux disease (GERD), such as Nissen fundoplication

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic tests
- Rate of symptomatic relief
- Rate of weight gain and growth
- Esophagitis healing
- Prevention and control of respiratory and other symptoms
- Medication and treatment side effects

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Articles on diagnosis, treatment, and complications were searched separately. Articles published in English between January 1966 and March 1999 on gastroesophageal reflux (GER) in children were searched using Ovid and PubMed. Letters, abstracts, editorials, case reports, reviews, and articles related to premature infants and children with neurological impairments were excluded.

The search strategies for diagnosis yielded 169 articles, 129 articles after exclusion criteria were applied, while the search strategy for treatment yielded 770 articles. After exclusion criteria were applied, there were 23 articles related to non-pharmacological treatment (positioning and dietary changes), 42 to pharmacological treatment (prokinetics and acid-suppressants) and 70 to surgical treatment (fundoplication). Searches on specific complications of GER yielded the following: 140 before and 20 after application of exclusion criteria for apnea and apparent life-threatening events; 91 before and 27 after exclusion criteria for asthma; 18 before and 9 after exclusion criteria for eosinophilic esophagitis; and 83 before and 34 after exclusion criteria for pulmonary disease. Subsequently, additional articles were identified and reviewed. When the pediatric literature was insufficient, the adult literature was also considered.

NUMBER OF SOURCE DOCUMENTS

354+

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Categories of the Quality of Evidence

I Evidence obtained from at least one properly designed randomized controlled study.

II-1 Evidence obtained from well-designed cohort or case-controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-controlled analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Articles were evaluated using published criteria. To evaluate inter-rater reliability, both clinical epidemiologists independently reviewed twenty-nine of the therapy articles on respiratory complications. Concordance using the criteria was 48% with all differences attributable to case series (Level IIa) and descriptive studies (Level III) evidence. If case series and large case reports were considered equivalent, the concordance was 100%.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Nominal Group Technique)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Committee based its recommendations on integration of the literature review with expert opinion. Consensus was achieved through Nominal Group Technique, a structured, quantitative method. Using the methods of the Canadian Preventive Services Task Force, the quality of evidence of each of the recommendations made by the GER Guideline Committee was determined and is summarized in the Appendix.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

All comments submitted by peer review were considered and where appropriate, modifications were made.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full text for additional information, including detailed information on dosing, possible side effects, and other interventions.

Each recommendation is identified as falling into one of five categories of evidence, indicated by a bracketed Roman numeral. The five categories represent varying levels of clinical confidence regarding the recommendation.

Definitions for the categories of evidence (I, II-1, II-2, II-3, III) are provided at the end of the Major Recommendations field.

Diagnostic Approaches

History and Physical Examination

In most infants with vomiting, and in most older children with regurgitation and heartburn, a history and physical examination are sufficient to reliably diagnose gastroesophageal reflux (GER), recognize complications, and initiate management. [III]

Upper Gastrointestinal (GI) Series

The upper gastrointestinal (GI) series is neither sensitive nor specific for the diagnosis of GER, but is useful for the evaluation of the presence of anatomic abnormalities, such as pyloric stenosis, malrotation and annular pancreas in the vomiting infant, as well as hiatal hernia and esophageal stricture in the older child. [III]

Esophageal pH Monitoring

Esophageal pH monitoring is a valid and reliable measure of acid reflux. Esophageal pH monitoring is useful to establish the presence of abnormal acid reflux, to determine if there is a temporal association between acid reflux and frequently occurring symptoms, and to assess the adequacy of therapy in patients who do not respond to treatment with acid suppression. Esophageal pH

monitoring may be normal in some patients with gastroesophageal reflux disease (GERD), particularly those with respiratory complications. [II-2]

Endoscopy and Biopsy

Endoscopy with biopsy can assess the presence and severity of esophagitis, strictures and Barrett's esophagus, as well as exclude other disorders, such as Crohn's disease and eosinophilic or infectious esophagitis. A normal appearance of the esophagus during endoscopy does not exclude histopathological esophagitis; subtle mucosal changes such as erythema and pallor may be observed in the absence of esophagitis. Esophageal biopsy is recommended when endoscopy is performed to detect microscopic esophagitis and to exclude causes of esophagitis other than GER. [II-2]

Nuclear Scintigraphy

The role of nuclear scintigraphy (milk scan) in the diagnosis and management of GERD in infants and children is unclear. [III]

Empiric Medical Therapy

A trial of time-limited medical therapy for GER is useful for determining if GER is causing a specific symptom. [III]

Treatment Options

Diet Changes in the Infant

There is evidence to support a one- to two-week trial of a hypoallergenic formula in formula fed infants with vomiting. Milk-thickening agents do not improve reflux index scores but do decrease the number of episodes of vomiting. [I]

Positioning of the Infant

Esophageal pH monitoring has demonstrated that infants have significantly less GER when placed in the prone position than in the supine position. However, prone positioning is associated with a higher rate of the sudden infant death syndrome (SIDS). In infants from birth to 12 months of age with GERD, the risk of SIDS generally outweighs the potential benefits of prone sleeping. Therefore, non-prone positioning during sleep is generally recommended. Supine positioning confers the lowest risk for SIDS and is preferred. Prone positioning during sleep is only considered in unusual cases where the risk of death from complications of GER outweighs the potential increased risk of SIDS. When prone positioning is necessary, it is particularly important that parents be advised not to use soft bedding, which increases the risk of SIDS in infants placed prone. [I]

Positioning of the Child and Adolescent

In children older than one year it is likely that there is a benefit to left side positioning during sleep and elevation of the head of the bed. [I]

Lifestyle Changes in the Child and Adolescent

It is recommended that children and adolescents with GERD avoid caffeine, chocolate and spicy foods that provoke symptoms. Obesity, exposure to tobacco smoke and alcohol are also associated with GER. It is not known whether lifestyle changes have an additive benefit in patients receiving pharmacological therapy. [III]

Acid-suppressant Therapy

Histamine-₂ receptor antagonists (H₂RAs) produce relief of symptoms and mucosal healing. Proton pump inhibitors (PPIs), the most effective acid suppressant medications, are superior to H₂RAs in relieving symptoms and healing esophagitis. Chronic antacid therapy is generally not recommended since more convenient and safe alternatives (H₂RAs and PPIs) are available. [I]

Prokinetic Therapy

Cisapride is available in the USA only through a limited-access program. Cisapride reduces the frequency of symptoms, including regurgitation and vomiting. However, because of concerns about the potential for serious cardiac arrhythmias in patients receiving cisapride, appropriate patient selection and monitoring as well as proper use, including correct dosage (0.2 mg/kg/dose QID [four times per day]) and avoidance of co-administration of contraindicated medications, are important. Other prokinetic agents have not been shown to be effective in the treatment of GERD in children. [I]

Surgical Therapy

Case series indicate that surgical therapy generally results in favorable outcomes. The potential risks, benefits and costs of successful prolonged medical therapy versus fundoplication have not been well studied in infants or children in various symptom presentations. [II-3; III]

Evaluation and Management of Infants and Children with Suspected GERD

The approach to the evaluation and management of infants and children with GERD depends upon the presenting symptoms or signs. Below is a summary of conclusions and recommendations derived from an integration of the research evidence with clinical experience for various clinical presentations. Where there are no randomized studies, the recommendations are based on the consensus opinion of the GER Guideline Committee.

The Infant with Recurrent Vomiting

In the infant with recurrent vomiting, a thorough history and physical examination, with attention to warning signals, is generally sufficient to allow the clinician to establish a diagnosis of uncomplicated GER (the "happy spitter"). An upper GI series is not required unless there are signs of gastrointestinal obstruction. Other diagnostic tests may be indicated if there are symptoms of poor weight gain, excessive crying, irritability, disturbed sleep, feeding or

respiratory problems. In the infant who has uncomplicated GER, parental education, reassurance and anticipatory guidance are recommended. Generally no other intervention is necessary. Thickening of formula and a brief trial of a hypoallergenic formula are other treatment options. If symptoms worsen or do not improve by 18 to 24 months of age, re-evaluation for complications of GER is recommended. Generally this includes an upper GI series and consultation with a pediatric gastroenterologist. [III]

The Infant with Recurrent Vomiting and Poor Weight Gain

In the infant with vomiting and poor weight gain it is recommended that the adequacy of calories and the effectiveness of swallowing be assessed. If there is poor weight gain despite adequate caloric intake, a diagnostic evaluation to uncover other causes of vomiting or weight loss is generally indicated. Tests may include a complete blood count, electrolytes, bicarbonate, urea nitrogen, creatinine, alanine aminotransferase, ammonia, glucose, urinalysis, urine ketones and reducing substances, and a review of newborn screening tests. An upper GI series to evaluate anatomy is also recommended. Treatment options include thickening of formula, a trial of a hypoallergenic formula, increasing the caloric density of the formula, acid suppression therapy, prokinetic therapy and, in selected cases, prone positioning. Further management options include endoscopy with biopsy, hospitalization, tube feedings and rarely surgical therapy. Careful follow-up is necessary to assure adequate weight gain. [III]

The Infant with Recurrent Vomiting and Irritability

Normal infants typically fuss or cry intermittently for an average of two hours daily, which may be perceived as excessive by some parents. A symptom diary may be useful to determine the extent to which the infant is irritable and has disturbed sleep. As in all infants with vomiting, other causes of vomiting need to be excluded. Expert opinion suggests two diagnostic and treatment strategies. Empiric treatment with either a sequential or simultaneous two-week trial of a hypoallergenic formula and acid suppression may be initiated. If there is no improvement, either esophageal pH monitoring to determine the adequacy of therapy or upper endoscopy with biopsy to diagnose esophagitis may be performed. If there is no response to therapy and these studies are normal, it is unlikely that GER is contributing to symptoms. Alternatively, evaluation could begin with esophageal pH monitoring to determine if episodes of irritability and sleep disturbance are temporally associated with acid reflux. [III]

The Child or Adolescent with Recurrent Vomiting or Regurgitation

In otherwise normal children who have recurrent vomiting or regurgitation after the age of 2 years, management options include an upper gastrointestinal (GI) series, upper endoscopy with biopsy, and prokinetic therapy. [II-2; III]

Heartburn in the Child or Adolescent

For the treatment of heartburn in children or adolescents, lifestyle changes accompanied by a two- to four-week therapeutic trial of an H₂RA or PPI are recommended. If symptoms persist or recur, the child can be referred to a

pediatric gastroenterologist for upper endoscopy with biopsy and in some cases long-term therapy. [III]

Esophagitis

In the infant or child with esophagitis, initial treatment consists of lifestyle changes and H₂RA or PPI therapy. In patients with only histopathological esophagitis, the efficacy of therapy can be monitored by the degree of symptom relief. In patients with erosive esophagitis, repeat endoscopy is recommended to assure healing. [I]

Dysphagia or Odynophagia

In the child with dysphagia (difficulty swallowing) or odynophagia (painful swallowing), a barium esophagram is recommended. If the initial history is suggestive of esophagitis, upper endoscopy may be performed as the initial diagnostic test. Treatment without prior diagnostic evaluation is not recommended. In the infant with feeding refusal, because a large variety of disorders may contribute to infant feeding difficulties, empiric therapy for GER is generally not recommended. However, if there are other signs or symptoms suggestive of GERD then a time-limited course of medical therapy can be considered. [III]

Apnea or Apparent Life-threatening Events (ALTE)

In patients with ALTEs recurrent regurgitation or emesis is common. However, investigations in unselected patients with ALTE have not demonstrated a convincing temporal relationship between esophageal acidification and apnea or bradycardia. There are no randomized studies to evaluate the usefulness of esophageal pH monitoring in infants with ALTE. In patients with frequent ALTE in which the role of GER is uncertain, esophageal pH monitoring may be useful to determine if there is a temporal association of acid reflux with ALTE. The evidence suggests that infants with ALTE and GER may be more likely to respond to anti-reflux therapy when there is gross emesis or oral regurgitation at the time of the ALTE, when episodes occur in the awake infant, and when the ALTE is characterized by obstructive apnea. Therapeutic options include thickened feedings and prokinetic and acid suppressant therapy. Since most infants improve with medical management, surgery is considered only in severe cases. [II-2; III]

Asthma

In patients where symptoms of asthma and GER co-exist, and in infants and toddlers with chronic vomiting or regurgitation and recurrent episodes of cough and wheezing, a three-month trial of vigorous acid suppressant therapy of GER is recommended. In patients with persistent asthma without symptoms of GER, esophageal pH monitoring is recommended in selected patients who are more likely to benefit from GER therapy. These include patients with radiographic evidence of recurrent pneumonia; patients with nocturnal asthma more than once a week; and patients requiring either continuous oral corticosteroids, high-dose inhaled corticosteroids, more than two bursts per year of oral corticosteroids or those with persistent asthma unable to wean medical management. If esophageal

pH monitoring demonstrates an increased frequency or duration of esophageal acid exposure, a trial of prolonged medical therapy for GER is recommended. [III]

Recurrent Pneumonia

GER can cause recurrent pneumonia in the absence of esophagitis or when esophageal pH monitoring is normal. There is insufficient evidence to provide recommendations for a uniform approach to diagnosis and treatment. Diagnostic evaluation may include flexible bronchoscopy with pulmonary lavage for lipid-laden macrophages, nuclear scintigraphy and assessment of airway protective mechanisms during swallowing.

Upper Airway Symptoms

Hoarseness, chronic cough, stridor and globus sensation can be associated with GER in infants and children. There is insufficient evidence to provide recommendations for diagnosis and treatment.

Definitions:

Categories of the Quality of Evidence

I Evidence obtained from at least one properly designed randomized controlled study.

II-1 Evidence obtained from well-designed cohort or case-controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-controlled analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

CLINICAL ALGORITHM(S)

The original guideline contains algorithms for:

- The management of an infant with uncomplicated gastroesophageal reflux (GER)
- The management of an infant with vomiting and poor weight gain
- The management of a child or adolescent with chronic heartburn
- The continued management of a child or adolescent with esophagitis
- The management of a child or adolescent with persistent asthma and suspected GER

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see Major Recommendations).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis and treatment of gastroesophageal reflux disease
- Effective treatment may relieve the patient's symptoms, promote normal weight gain and growth, heal inflammation caused by refluxed gastric contents (esophagitis), and prevent respiratory and other complications associated with chronic reflux of gastric contents.

POTENTIAL HARMS

Risks associated with treatment of gastroesophageal reflux disease (GERD) in infants and children include complications connected with pharmacological therapies and surgery.

Drug Adverse Effects: see Table 3 in the original guideline for a drug-specific description of adverse effects and precautions. A partial list of adverse effects by drug class is listed below:

- Histamine-₂ receptor antagonists (H₂RAs): rash, headache, dizziness, constipation, diarrhea, and other adverse effects
- Proton pump inhibitors: headache, diarrhea, abdominal pain, nausea, rash, constipation, vitamin B12 deficiency, elevated transaminases, and other adverse effects
- Prokinetics (cisapride): rare cases of serious cardiac arrhythmias, drug interactions

Surgical Complications

Surgical complications include breakdown of the wrap (0.9% to 13%), small bowel obstruction (1.3% to 11%), gas bloat syndrome (1.9% to 8%), infection (1.2% to 9%), atelectasis or pneumonia (4.3% to 13%), perforation (2% to 4.3%), persistent esophageal stricture (1.4% to 9%) and esophageal obstruction (1.4% to 9%). Other complications not reported in enough detail to estimate complication rates include dumping syndrome, incisional hernia and gastroparesis.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The guideline is not intended for the management of neonates less than 72 hours old, premature infants or infants and children with either neurologic impairments or anatomic disorders of the upper gastrointestinal tract.
- The recommendations are a general guideline and are not intended as a substitute for clinical judgment or as a protocol for the management of all patients with this problem.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, Gerson WT, Werlin SL. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 2001; 32(Suppl 2):S1-31. [336 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001

GUIDELINE DEVELOPER(S)

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
- Professional Association

SOURCE(S) OF FUNDING

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

GUIDELINE COMMITTEE

Gastroesophageal Reflux (GER) Guideline Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Colin D. Rudolph, MD, PhD; Lynette J. Mazur, MD; Gregory S. Liptak, MD; Robert D. Baker, MD, PhD; John T. Boyle, MD; Richard B. Colletti, MD; William T. Gerson, MD; Steven L. Werlin, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

American Academy of Pediatrics - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) Web site:

- [HTML Format](#)
- [Portable Document Format \(PDF\)](#)

Print copies: Available from NASPGHAN, PO Box 6, Flourtown, PA 19031; Telephone (215) 233-0808; Fax (215) 233-3939; E-mail naspghan@naspghan.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on June 9, 2003. The information was verified by the guideline developer on June 16, 2003.

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