

# Gastroesophageal reflux in infants and children

## *When to reassure and when to go further*

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### ABSTRACT

**OBJECTIVE** To review current understanding and approach to diseases resulting from gastroesophageal reflux (GER) in infants and children.

**QUALITY OF EVIDENCE** Very few randomized or blinded controlled trials have been reported in this area. MEDLINE searches for gastroesophageal reflux, gastroesophageal reflux disease, esophagitis, and pulmonary aspiration, using age-limited (all childhood) data, find most articles. Very thorough reviews undertaken by both European and North American societies for pediatric gastroenterology provide up-to-date consensus statements.

**MAIN MESSAGE** Gastroesophageal reflux is a normal phenomenon recognized in infants as “spitting up.” Understanding the mechanism of transient lower esophageal relaxation episodes allows physicians to counsel concerned parents that reflux and spitting up occur universally, but are less visible in children older than 6 to 12 months. In infants and children, GER can result in a variety of diseases and can cause esophageal and tracheopulmonary damage. Investigation of these diseases can be specific and accurate. Therapy is available, but no drug will stop reflux. Some children suffer intractable GER with secondary complications (GERD) despite medical treatment. Failure of therapy could mean patients require surgical intervention.

**CONCLUSION** Visible GER is very common in infants and children and can usually be managed with explanation, reassurance, and simple measures. Diseases caused by GER can be investigated specifically and managed with accurately defined therapy.

### RÉSUMÉ

**OBJECTIF** Passer en revue le savoir et l'approche entourant les maladies résultant du reflux gastro-œsophagien (RGO) chez les nourrissons et les enfants.

**QUALITÉ DES DONNÉES** Il existe très peu d'études contrôlées à double insu rapportées dans ce domaine. La majorité des articles ont été tirés de recensions dans MEDLINE à l'aide des termes « reflux gastro-œsophagien, maladie du reflux gastro-œsophagien, œsophagite et aspiration pulmonaire » et ce, en fonction de limites d'âge (toute l'enfance). Des déclarations consensuelles à jour sont fondées sur des études très rigoureuses entreprises par des sociétés européennes et nord-américaines de gastro-entérologie pédiatrique.

**PRINCIPAL MESSAGE** Le reflux gastro-œsophagien est un phénomène normal reconnu chez les nourrissons comme étant « la régurgitation ». La compréhension du mécanisme des épisodes de relaxation transitoire de l'œsophage inférieur permet aux médecins d'informer les parents que le reflux et la régurgitation se produisent universellement, mais qu'ils sont moins visibles chez les enfants de plus de 6 à 12 mois. Chez les nourrissons et les enfants, le RGO peut causer diverses maladies et des dommages œsophagiens et trachéopulmonaires. L'investigation de telles maladies peut être spécifique et exacte. La thérapie est disponible mais aucun médicament n'arrête le reflux. Certains enfants souffrent de RGO réfractaire avec des complications secondaires en dépit des traitements médicaux. L'échec thérapeutique pourrait signifier la nécessité d'une intervention chirurgicale chez le patient.

**CONCLUSION** Le RGO visible est très courant chez les nourrissons et les enfants et peut habituellement être pris en charge en donnant des explications, en rassurant et par de simples mesures. Les maladies causées par le RGO peuvent faire l'objet d'une investigation spécifique et être traitées grâce à une thérapie définie avec précision.

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*Cet article a fait l'objet d'une évaluation externe.*

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**F**amily physicians and pediatricians commonly see infants and toddlers who “bring up” gastric material. The bringing up might be forceful (projectile) or simply a bubbling out. It is often perceived by caregivers as distasteful and a signal that infants or toddlers are unwell.

Previous explanations and management have not survived the test of time or controlled trials. This paper is written to help physicians be aware of current theory about GER, recognize the difference between simple reflux and reflux disease, and identify suitable investigations where warranted. It also provides an algorithm for managing GER and its associated complications (GERD). In some publications, the term GER is used to denote abnormal reflux. In this paper, abnormal reflux is denoted as GERD or GER with identified complications.

**Quality of evidence**

MEDLINE was searched for primary references for GER (childhood) back to January 1980 using MeSH/meta derived terms to ensure that complications, drug therapy, dietary therapy, and pulmonary aspiration were reviewed. Secondary references back to 1958 were reviewed where relevant. In literature and in practice, GER in infants and children has been subject to few controlled trials and has lacked standardized nomenclature. Understanding of the basic physiology of the lower esophageal sphincter (LES) has only gradually improved.

Randomized controlled trials are referenced; they deal exclusively with drug therapy. This article provides up-to-date guidance based on current knowledge and investigations (using randomized controlled trials where available) and best evidence from consensus statements of both the North American Society of Pediatric Gastroenterology and Nutrition (NASPGN)<sup>1</sup> and the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN),<sup>2</sup> along with 30 years of subspecialty clinical experience in pediatric gastroenterology.

**Definition**

Gastroesophageal reflux is the *effortless* passage of gastric contents into the esophagus. It can consist of gas (eructation, or burp) or fluid (positing, wet burp, “spitting up” in infants, or, incorrectly, vomiting). In normal children and adults, this occurs several to many times a day, but fluid rarely reaches the mouth.

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**Table 1. Manifestations of gastroesophageal reflux disease (GERD)**

| AREA                  | DISEASE                                 | RESULT  |
|-----------------------|---|---|
| Normal growth         | Excessive GER                           | Failure to thrive                                     |
| Esophagus             | Inflammation or ulcer                   | Pain, spasm, dysphagia, odynophagia, bleeding, anemia |
| Esophagus             | Scarring to stricture                   | Dysphagia, food impaction, food regurgitation         |
| Esophagus             | Chronic inflammation                    | Barrett esophagus, carcinoma                          |
| Esophagus             | Inflammation and distention             | Esophagobronchial reflex, wheezing                    |
| Larynx                | Inflammation                            | Hoarseness, obstructive apnea                         |
| Tracheobronchial tree | Acid damage or inflammation, aspiration | Cough, wheezing, “bronchitis,” pneumonia              |
| Teeth                 | Acid damage                             | Dentine damage by acid                                |
| Pharynx               | Pharyngitis                             | Referred pain to external ear canal, otalgia          |

It relieves gastric fundic distension and, in infants, is actively promoted by caregivers during and after feeding. Refluxed liquid material might be visible in the mouth or invisible and heard as bubbling or churning in the chest (like a coffee percolator). Children might be seen to swallow.

Vomiting is the *active* expulsion of gastric contents from the stomach. It requires use of voluntary muscles, including the diaphragm and abdominal wall muscles, and a stimulus that can be central or peripheral. It generally includes recognition by one of the body senses of a potentially noxious situation. Vomiting includes reverse peristalsis that might empty the proximal duodenum and is frequently associated with autonomic activity resulting in sweating, pallor, and a general feeling of illness.

In the history, the essential elements for diagnosing GER are that no retching is involved initially and that children neither appear nor act nauseated. The distance the material is propelled is *not* diagnostic. Some infants and children learn to actively expel distasteful refluxed material and thus appear to vomit.

**Table 2. Investigation of gastroesophageal reflux disease (GERD)**

| SYMPTOM  | INVESTIGATION                            | REASON FOR INVESTIGATION  |
|--|--|---|
| Simple GER   | History and physical examination         | Reassurance and explanation   |
| Severe GER   | Barium upper GI series                   | Upper gut partial obstruction or anomaly?   |
| Severe GER   | Trial of whey-based or monomeric formula | Allergic enteropathy? Any improvement?  |
| Severe GER   | Nuclear medicine gastric emptying scan   | Delayed emptying? Pulmonary aspiration?   |
| Esophagitis  | Trial of PPI (1-2 mg/kg/d for 4-6 weeks) | Major improvement or not?   |
| Esophagitis  | Upper endoscopy                          | Presence of esophagitis? Upper gut partial obstruction or anomaly? H-type TE fistula? |
| Recurrent cough, choking, episodic chest pain, apneic spells | pH probe                                 | Correlation of acid reflux with <i>documented</i> symptoms?                           |
| Recurrent cough, choking, wheezing                           | pH probe, double probe technique*        | Correlation of acid reflux into hypopharynx with <i>documented</i> symptoms?          |
| Cough, wheezing, bronchitis, pneumonia                       | Bronchoscopy                             | Edema of laryngeal folds? Lipid-laden macrophages? H-type TE fistula?                 |
| Choking, coughing with feeding                               | Video fluoroscopic swallowing study      | Primary disorder of mouth or pharynx coordination? H-type TE fistula?                 |

GI—gastrointestinal, PPI—proton pump inhibitor, TE—transesophageal.  
\*Double probe technique is performed with one probe in the hypopharynx and a second probe in the esophagus at the standard position.<sup>9</sup>

The apparent vomiting occurs after reflux is seen to be happening, however, and children return to normal activities immediately after.

### Why reflux?

Gastroesophageal reflux occurs as a result of transient LES relaxation to a zero gradient between gastric and esophageal lumens or of an “LES pressure drift” during which the pressure differential between the LES and the lower esophagus gradually

decreases to zero and can remain atonic for minutes to an hour or more.<sup>3</sup>

Transient LES relaxations are not associated with swallowing and are likely modulated by the filling volume of the fundus or body of the stomach, and by the central nervous system.<sup>4</sup> The concept of a weak esophageal sphincter is no longer tenable.

Why do infants appear to have excessive GER while older children and adults appear not to have it? Three reasons are evident: the volume of ingested food per kilogram of body weight is five to eight times greater in infants than adults<sup>5</sup> (greater gastric filling), an infant’s esophageal capacity is 5 to 10 mL while an adult’s is about 180 mL (less reservoir), and an infant’s intra-abdominal esophagus is extremely short while an adult’s is about 3 cm<sup>2,6,7</sup> (less flap valve action in the abdomen).

Before 6 months of age, GER occurs much more frequently while infants are sitting or propped up. Neurologically handicapped children are at great risk of GERD and primary swallowing disorders.<sup>8</sup> Investigation of potential GERD in such infants and children should, therefore, be early and aggressive.

### Gastroesophageal reflux with complications

Damage to tissues (at microscopic or macroscopic levels) resulting from GER indicates disease (GERD) (Table 1). In clinical practice, both esophageal discomfort and pulmonary symptoms are common reasons for concern and consultation. Table 2 summarizes pertinent investigations.

Esophagitis can be silent or symptomatic. Incidence of mild peptic esophagitis is unknown because it is frequently silent until a piece of food (usually meat) sticks in the lower esophagus or until more serious signs or symptoms present, sometimes years later.

In infants, visible or occult gastrointestinal bleeding or anemia might be the presenting sign of erosive esophagitis with no other history or signs. Failure to thrive associated with pain or fussiness during feeding or refusal to feed, usually after a short interval of sucking, can also indicate GERD with esophagitis. In older children, food sticking in the esophagus or chest or high epigastric pain could signal esophagitis.

Recurrent respiratory symptoms that might include cough, choking, wheezing, bronchitis, or pneumonia (although most frequently associated with infection or allergy) are now also well recognized as complications of GER. In infants with persistent or recurrent pulmonary symptoms not otherwise explained, GER should be considered as the cause. Wheezing via the esophagobronchial reflex or by direct contact with

laryngotracheobronchial mucosa through aspiration can result from GER. Direct aspiration can result in recurrent bronchitis or pneumonia. Respiratory symptoms are relatively much more frequent in children with a primary swallowing disorder. Infants and children who cough, choke, or become apneic while swallowing (either food or refluxate) can usually be shown to have primary hypopharyngeal dysfunction with penetration of the vallecula-laryngeal area by pharyngeal contents.<sup>9,11</sup>

In addition to the major complications of GER noted above, dental damage (recognized by dentists as erosion of dentine usually in the posterior teeth) and otalgia<sup>12</sup> in the absence of visible ear disease could both be the result of acid reflux into the pharynx or mouth.

### When to investigate GER

Most simply, physicians should investigate GER when parents mention it in the office. The best and simplest investigation is a careful history. This is normally the only investigation required.

If there is no evidence of pulmonary disease, anemia, difficulty or pain during feeding, or failure to thrive, no further investigation is required. Parents should be assured that GER is normal and that it becomes less evident as infants mature. Most toddlers have "outgrown" it by 1 year old.

The advent of proton pump inhibitor (PPI) acid suppression has made management of GERD with esophagitis and GERD with mild laryngeal symptoms much more effective. A clinical diagnosis and trial of treatment, along with explanation and reassurance, will manage most cases. Investigation is required if there is doubt as to whether GER is causing observed signs or symptoms; to evaluate the extent of disease to be treated or the results of treatment; or if there are complicating factors, either anatomic or physiologic, that might affect management.

Patterns of practice of individual physicians and the investigative and specialty resources available will help decide when referral is required. Referral is likely if interventional investigation, such as endoscopy or pH probe, is required. Referral is also required for complex developmentally delayed children with recurrent chest problems who sometimes require tube feeding or surgery.

### What investigations are available?

Invasive investigation is *not* warranted if the diagnosis is already apparent. For example, it is not useful to perform a pH probe simply to "prove reflux" in a baby with visible reflux.

### History, physical examination, and observation.

History, physical examination, and observation of a child feeding are the most useful investigations under every circumstance. Is there dysphagia or odynophagia, coughing, or choking during feeding? Does an infant express pain when swallowing or when refluxing? Does an infant waken at night crying in pain, and is there refluxed material on the bedding? Has blood ever been seen in refluxed material? Does an infant have persistent wheezing or productive cough, worse after feeding or refluxing? Is there unexplained anemia?

Beyond that, investigation is guided by the disease to be confirmed. Since GER is universal, no test can confirm it; GER alone is not a disease!

**pH probe.** A pH probe is most useful for correlating suspect symptoms (eg, chest pain, respiratory changes) that might suggest GERD. pH changes seen on the record might lead physicians to draw inferences from that correlation. The study must be interpreted with specific reference to patients' signs and symptoms and not simply by reference to a computer-derived "reflux index" or score.<sup>13,14</sup> Nonspecific irritability, failure to thrive, and colic are unlikely to be clarified by pH probe because it proves neither esophagitis nor esophageal pain in infants. To prove them requires esophageal biopsy or a Bernstein test (infusion of normal saline vs one-tenth normal hydrochloric acid into the esophagus in a random, blinded fashion to simulate acid reflux).

**Double probe.** A double probe pH study (upper probe in the hypopharynx) is ideal for demonstrating penetration of the hypopharynx by refluxate and for correlating with respiratory symptoms.<sup>9</sup> Currently, this study is rarely available.

### Barium meal or upper gastrointestinal series.

These tests are useful *only* to identify anatomic abnormalities of the upper gastrointestinal tract. They are *not* of any use in diagnosing GER<sup>10</sup> (because GER is universal, and the mechanisms used in radiology are nonphysiologic) or mild esophagitis. In addition, the swallowing mechanism is not routinely or effectively assessed during a routine upper gastrointestinal barium series.

### Video fluoroscopic swallowing study (VFSS).

A VFSS, or modified barium swallow, is most useful for assessing mastication and swallowing mechanisms. It is usually performed with both a feeding expert, such as a speech pathologist, and a radiologist

present. This study identifies disorders of pharyngeal-hypopharyngeal coordination, including penetration of the nasal cavity, vallecula, and larynx, and full tracheal aspiration.

**Esophageal motility studies.** These studies identify abnormal peristalsis in the esophagus. Extended upward, motility studies can help assess hypopharyngeal-cricopharyngeal peristalsis-relaxation relationships. The resting pressure of the LES is, in general, no longer considered a risk factor for GER because any pressure at all will prevent reflux at rest.

**Gastric emptying scan.** This scan assesses gastric half-emptying time, which is a reflection of gastric peristalsis and pyloric function. Slow gastric emptying could predispose patients to increased-volume GER. Also, episodes of GER can be seen on the scan, and occasionally, so can episodes of pulmonary penetration.

**Upper gastrointestinal endoscopy.** Endoscopy can obtain tissue for histologic assessment of esophagitis, Barrett esophagus (metaplastic changes of the esophagus with malignant potential),<sup>15</sup> gastritis or duodenitis, or ulcer, and for identifying anatomic abnormalities. It does not, however, assess function.

**Bronchoscopy.** Bronchoscopy is essential for assessing inflammatory changes in the laryngeal area and in the tracheobronchial tree and for obtaining tissue for examination for lipid-laden macrophages. Endoscopy of the trachea or esophagus is also useful for diagnosing tracheoesophageal fistula.

### Management of simple GER

An explanation of why GER occurs and simple instructions, such as how to position an infant (left side or prone),<sup>16</sup> when to give smaller and more frequent feeds, and how to use formula thickeners (benefit unclear<sup>17,18</sup>), are usually sufficient.<sup>19</sup> Prone positioning has been shown in controlled studies<sup>16,20</sup> to be superior to supine for reducing GER, but statistically it increases risk of sudden infant death syndrome (SIDS). The American Academy of Pediatrics in its position paper on SIDS accepts the prone position only if it is required for infants with GERD.<sup>21</sup>

### Management of GERD with esophageal disease

If the history indicates GER and symptoms fit esophagitis, then a trial of therapy with a PPI is appropriate. A PPI, such as 1 to 2 mg/kg of omeprazole twice daily

## Table 3. Summary of management of gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD)

### 1. Initial investigation by history and physical examination to identify whether patients have simple GER or confirmed evidence of GERD

#### 2. Uncomplicated GER

- Careful history and physical examination
- Reassurance and explanation
- Thickened feeds: 15 mL of rice cereal to 30 mL of formula or commercial thickening agents<sup>17,18</sup>
- Careful feeding and the passage of time

#### 3. Uncomplicated GER not responding to 2 above

- Trial of whey-based formula<sup>26</sup>

#### 4. For GERD with esophagitis

- As in 2 or 3 above, and
- A PPI such as 1-2 mg/kg of omeprazole once or twice daily 15 minutes before meals
- Continue for 1-3 months and reevaluate

#### 5. For GERD with respiratory tract symptoms, stepwise progression

- As in 4 above for 4 weeks, plus video fluoroscopic swallowing study (VFSS)
- If reflux or aspirate continue, try nasogastric or nasojejunal feeding
- If reflux or aspirate continue, do a gastric emptying scan
- If scan results are normal, do fundoplication and gastrostomy
- If results are abnormal, do fundoplication, gastrostomy with pyloroplasty

#### 6. Cough not associated with feeding or history of GER

- Careful history
- Gastric emptying scan for reflux or aspiration
- pH probe for GER *correlated with symptoms*
- If negative, bronchoscopy for lipid-laden macrophages
- If both negative, GER cannot be proven as cause of lower respiratory tract illness

#### 7. Apparent life-threatening event (also termed "missed sudden infant death syndrome" and might be associated with choking spells)

- As in 4 above
- Sleep study with pH probe, if possible
- If 1° swallowing disorder, VFSS
- If *no* choking with feeds, consider laryngotracheobronchoscopy and pH probe for abnormal reflux

**Editor's key points**

- Gastroesophageal reflux (GER) is the common, physiologic, effortless regurgitation of stomach contents; it is different from vomiting caused by active muscle contractions.
- It can result in damage to esophageal, laryngeal, and bronchial tissue and can cause disease and symptoms in the gastrointestinal tract and respiratory system.
- If history and examination indicate no damage or associated disease, explanation and reassurance are sufficient. Further testing is not required.
- Investigation and management should be specifically directed at likely diseases, such as esophagitis, bronchial involvement, or severe choking spells (missed sudden infant death syndrome).

**Points de repère du rédacteur**

- Le reflux gastro-œsophagien (RGO) est la régurgitation physiologique sans effort du contenu stomacal qui se produit de manière courante; il diffère du vomissement causé par des contractions musculaires actives.
- Il peut se traduire par des dommages au tissu de l'œsophage, du larynx et des bronches, et causer des maladies et des symptômes à l'appareil gastro-intestinal et au système respiratoire.
- Si l'anamnèse et l'examen n'indiquent aucun dommage ou maladie afférente, il suffit de rassurer les parents et de leur donner des explications. Il n'est pas nécessaire de procéder à d'autres épreuves.
- Il faudrait diriger spécifiquement l'investigation et la prise en charge vers d'éventuelles maladies comme l'œsophagite, les troubles bronchiques ou de graves épisodes d'étouffement (syndrome manqué de mort subite infantile).

15 minutes before meals, is reasonable; PPIs reduce both acid load and total volume of gastric secretions. Failure of PPI therapy requires reassessment of compliance and then diagnosis.

Although H<sub>2</sub> blockers might be satisfactory for mild esophagitis, PPIs are more effective and will heal disease not healed by H<sub>2</sub> blockers.<sup>22</sup> If signs and symptoms improve, no further investigation is required, and PPI therapy can be continued for several months if required.<sup>23,24</sup> Withdrawal of cisapride from the market has left a void in management of GER; no other prokinetic drug is as effective, although metaclopramide, domperidone, bethanechol, and erythromycin have all been studied. None produce a consistently positive effect, and their side effects can be clinically severe. The NASPGN continues to support use of cisapride

under suitable conditions.<sup>25</sup> If symptoms do not abate, further investigation is warranted (Table 2).

**Management of GERD with respiratory symptoms or disease**

If hypopharyngeal function is normal (by history or VFSS), a 1-month trial of PPI therapy is reasonable. If PPI therapy clears respiratory symptoms, it can be continued as required. If evidence indicates lack of coordination in primary swallowing, the most effective management is a trial of direct nasogastric or nasojejunal feeding. If this clears symptoms, physicians will need to decide how long to continue it and whether fundoplication and feeding gastrostomy is required. Persistent pulmonary symptoms in the face of reflux that fails to respond to medical treatment usually require fundoplication. Table 3<sup>17,18,26</sup> summarizes management of GER and GERD.

**Prognosis**

Visible GER usually clears gradually during infancy. Most neurologically normal infants seem much improved by 6 months. Statistically, 60% clear by 12 months and > 80% by 18 months.<sup>1,27,28</sup> Many factors are likely involved: decreased volume of intake, larger-capacity esophagus, better trunk muscle tone, more time in an upright position, and a longer intra-abdominal esophageal segment. Gastroesophageal reflux that has advanced to GERD, however, requires active treatment because, even in infancy, complications can ensue.

A practice-based survey of older children in 16 pediatric practices<sup>29</sup> indicated that 2% to 8% of children between 3 and 17 years have symptoms consistent with GER or GERD. Percentages were higher when children were asked than when parents were asked. Developmentally delayed children and adults have a far higher incidence of continuing signs or symptoms of GER and GERD<sup>7,30,31</sup> and are at greater risk of developing Barrett esophagus, esophageal stricture, and carcinoma of the esophagus.

Fundoplication should be reserved for infants or children with GERD *who fail to benefit from aggressive medical management* and continue to have life- or tissue-threatening reflux. Before fundoplication, physicians must decide whether to simultaneously perform feeding gastrostomy.

**Conclusion**

Gastroesophageal reflux occurs in all humans as a result of transient relaxations of the LES. In infants, who have a small esophagus and high-volume intake, the refluxed material frequently overflows

the esophagus and results in visible spitting up or regurgitation. Medical therapy, apart from explanation, reassurance, and simple feeding changes, is neither required nor effective.

Refluxed material might result in tissue damage due to gastric acid or foreign materials (food). Medical management is directed toward identifying the site and extent of damage (disease) and instituting medical or surgical treatment to heal the damage and prevent further effects of reflux. The introduction of PPIs into the therapeutic armamentarium has greatly improved outcomes of treatment. Interventional approaches, using nasointestinal tube feeding, gastrostomy, and fundoplication, are useful. Withdrawal of cisapride from the market has left physicians with no safe and effective prokinetic agent for treating GERD. ❖

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