

Gastroesophageal Reflux Disease (GERD) in Children: From Infancy to Adolescence

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Abstract

The increased recognition of the difference between the adult and the pediatric populations in terms of the manifestation and the management of gastroesophageal reflux disease (GERD), owes much to the number and nature of high quality clinical research and drug trials conducted in the past decade. The plethora of choices available to treat GERD is unprecedented. A primary care physician clearly understands the investigative and therapeutic options available, and some of the risks associated with them. What makes the physician wary is the absence of a) a clear objective definition of gastroesophageal reflux disease (GERD) in a pediatric population and b) sufficient data to support the use of the armamentarium available. The variety of definitions and terms used in the literature to define GERD adds to the confusion and results in a variety of approaches to manage it.

In light of the new developments, the objective of the review is threefold, 1) to simplify as much as possible the current evidence based pediatric literature in defining

GERD and its common presentations in the three distinct sub-populations of children as newborns and infants (0-12 months), toddlers and children (1-10 years), and adolescents (11-18 years). These cut-off periods are arbitrary and some overlap is inevitable, 2) to review the diagnostic and therapeutic tools available today, and 3) to effectively apply these tools and formulate pathways in some case scenarios, for the esophageal and extra esophageal GERD manifestation in the three distinct age groups specified above.

Keywords: Gastroesophageal, reflux, esophagitis, guidelines.

Introduction

The clear gold-standard definition of the Gastro Esophageal Reflux (GER) and Gastro Esophageal Reflux Disease (GERD) in specific age groups in children has remained elusive. A global, evidence-based consensus on the definition and classification of gastroesophageal reflux disease in the pediatric population, was reached last year by eminent experts from around the world.¹ Specific challenges in infants and young children were also highlighted. The group derived perspectives from an adult consensus already available in the literature.² For all practical purposes, GERD in a pediatric patient is defined as the reflux of gastric contents causing troublesome symptoms and/or complications. Since this is a patient-centered and symptom reporting based definition, it should be reserved for children above the age of 8. For younger children surrogate reporting by parents or caregivers is still necessary since the patient outcome reporting is less reliable at this stage as we can imagine. It is recommended that age specific symptom based questionnaire should be supplemented to increase the

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reliability of reporting. These questionnaires currently are undergoing extensive evaluative validation.

It is important for readers to understand that troublesome symptoms are those that have an adverse effect on a child's well-being and do not represent the parents' agonizing moments.

GER is a physiologic process due to transient relaxation of lower esophageal sphincter (TRLES) and defined as reflux of gastric contents into the esophagus with or without regurgitation and vomiting.

Regurgitation is the passage of gastric contents into the pharynx and/or mouth or expelled out of the mouth. It is a non-specific symptom that in infants, besides GER and GERD, can occur in cow's milk protein allergy as well. Physiologic regurgitation is generally effortless and painless although it could be forceful at times and can occur in up to 70% of completely healthy newborns and infants. It resolves without intervention in 95% of the infants by 12-14 months of age.³⁻⁵ Regurgitation is different from vomiting, which is another non-specific symptom with numerous causes, and defined as forceful expulsion of mostly gastric contents from the mouth with the retrograde intestinal peristalsis, emetic reflex from the CNS and often accompanied by nausea.

Rumination Syndrome

It is a distinct condition and not related to GER or GERD. It is described as the regurgitation of recently swallowed food into the mouth with subsequent mastication and reswallows. Commonly seen in children with neurologic impairment, in adolescent females with eating disorders⁶ and rarely, in young children in cases of self-stimulation,⁷ or deprivation.

Reflux Esophagitis (RE) or Reflux Related Erosive Esophagitis (ERD)

RE is defined endoscopically by visible breaks of the mucosa in the distal esophagus. When reflux-related erosions are present during endoscopy, they should be graded using classifications of erosive esophagitis.⁸⁻¹¹ Findings in the

tissue biopsy or histology from the esophagus that are commonly attributed to RE are non-specific, and therefore, not diagnostic. The role of histology is to diagnose other esophageal disorders with symptoms mimicking GERD but having distinct and specific features, like Eosinophilic Esophagitis, Crohn's disease, infectious esophagitis and Barrett's changes in chronic GERD. In otherwise healthy children reflux esophagitis does not usually recur once treated.

Non-Erosive Reflux Esophagitis (NERD)

NERD is defined as the presence of 'troublesome symptoms' caused by the reflux of gastric contents and by the absence of mucosal breaks during endoscopy as opposed to Erosive Reflux Esophagitis (ERD) described in the preceding paragraph, where there is a visible break in the distal esophageal mucosa. NERD as a diagnosis is reserved for neurologically intact children older than 8 years since it is a clinical diagnosis and dependent on the cognitive ability of a child to report troublesome symptoms reliably and accurately. It is seen predominantly in female population with functional GI disorders and unlike GERD, the troublesome symptoms do not occur during sleep or while lying supine.^{12, 13}

Heartburn

Heartburn is defined as a burning sensation behind the sternum that may take the quality of pain. Also referred to as retrosternal or substernal burning pain, it is a symptom of GERD with or without esophagitis.¹⁴ The symptom is applied in older children (>8y/o) and adolescents who have the cognitive ability to reliably and accurately report it. It can be a part of 'Typical Reflux Syndrome' as mentioned next.

Typical Reflux Syndrome

The term again is reserved for older children and adolescents who have heartburn with or without regurgitation. It is a clinical diagnosis and if no warning signals are present, then a 2-4 week trial of proton pump inhibitor (PPI) could be initiated without additional testing.¹⁵⁻¹⁸

Sandifer Syndrome

This is a dystonic head posturing, torticollis and opisthotonic back movement that has been shown to be an uncommon, but specific manifestation of GERD. It resolves with anti-reflux treatment.

Predisposing Conditions/High Risk Groups

Certain conditions in children put them at a risk for higher incidence, relapse and chronicity of GERD symptoms. These include children with chronic neurologic impairment, repaired esophageal atresia, hiatal hernia, chronic respiratory diseases like cystic fibrosis (CF) and genetic conditions like Down syndrome and Cornelia de Lange syndrome (Fig. 1). Children with family history of Barrett's esophagus, strictures and adenocarcinoma with GERD are also at a higher risk of GERD and its associated complications.¹⁹⁻²¹ Likewise, the complications of severe GERD occur with greatest frequency in children with underlying GERD-provoking conditions.^{19,22}

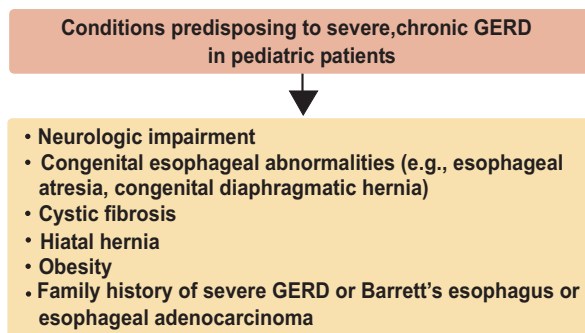


Fig. (1). Conditions predisposing to chronic, severe gastro esophageal reflux disease.

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Role of Genetics

No review remains complete without a statement or two about the role of genetics in any condition under its scrutiny. Although GERD tends to cluster in families, and monozygotic

twins have a higher concordance rate than the dizygotic twins, the search for responsible genes is far from over. It seems worthwhile mentioning a gastro-oesophageal reflux disease susceptibility gene in pediatric and adult GERD patients known as Collagen type III alpha I (COL3A1). COL3A1 has been shown to be genetically associated with Hiatus Hernia (HH) in adult males. The GERD and the HH associated alleles are different, indicating two separate mechanisms leading to disease.²³ More recently, the proteinase-activated receptor-2 (PAR-2) expression was shown to be 7- to 10-fold upregulated ($P < 0.0001$) in the esophageal mucosa of patients with GERD in contrast to the mucosa of patients with NERD. Moreover, the PAR-2 upregulated expression correlated positively with Interleukin-8 (IL-8) expression and with histomorphological alterations in GERD.²⁴

Extra-esophageal Manifestations of GERD

Sandifer syndrome, dental erosions, respiratory (broncho-pulmonary, otological, rhinological, laryngo-tracheal and pharyngeal) manifestations and pathological apnea can all be associated with GERD. Some are definite associations and some remain in the 'possible association' category (Fig. 2). These can occur without the symptoms of esophageal involvement and even in the absence of esophagitis per endoscopic assessment. Combined Multiple Intra-luminal Impedance (MII) and pH Monitoring (MII/pH) may be of value in some of these conditions to prove or disprove their association with GERD.

Diagnosis of GERD

Since the word complication along with 'troublesome' is in the definition of GERD it is essential to clarify that the complications of GERD include strictures, Barrett's Esophagus (BE) and adenocarcinoma of esophagus. The latter two are rare in children but seen in high risk patients like neurologically impaired children, children with repaired esophageal atresia and/or chronic relapsing GERD. Particular attention should be paid to the family history of the child. History and Physical Examination

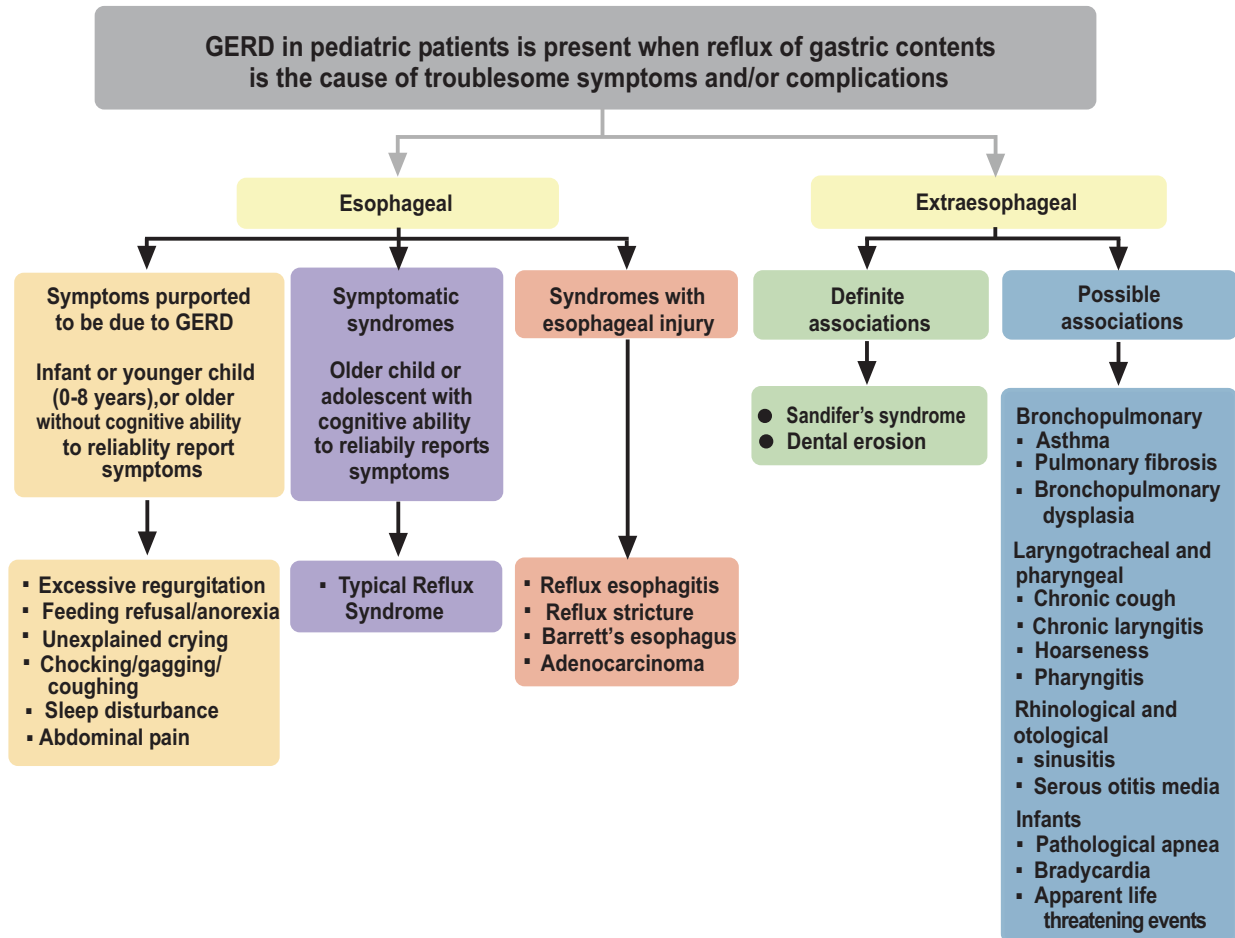


Fig. (2). Esophageal and Extra esophageal GERD.

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may be sufficient to diagnose GERD if the symptoms are typical in older children and adolescent patients.

In infants and toddlers, however there is no specific symptom or symptom complex that is diagnostic for GERD or predictive of response to therapy. Most of the symptoms like regurgitation, excessive crying, irritability, fussiness and arching are non-specific and besides GERD, occur occasionally in otherwise completely healthy babies with physiologic GER and in other conditions like cow's milk protein or soy allergy. In fact GERD and milk protein allergy can co-exist and a two to four week trial of extensively hydrolyzed cow's milk protein formula or an amino acid based formula may

resolve the symptoms initially suggestive of GERD.²⁵⁻²⁷

Besides, regurgitation is neither necessary nor sufficient to diagnose GERD. Quantifying regurgitation and clustering of regurgitation with other symptoms like excessive crying has been shown to improve diagnostic sensitivity and specificity, as evident in the I-GERQ (Infant Gastroesophageal Reflux Questionnaire) scores in one study.²⁸ In infants, normal regurgitation and normal crying, or abnormal crying due to a cause other than GERD, may be mistaken for GERD.^{29,30} Irritability again can be due to multiple reasons like constipation, cow's milk protein allergy, and infections especially urinary tract infections (UTI) and

neurologic impairment. A primary care physician must be familiar with these challenges and use better judgment when facing such a patient.

Esophageal pH Monitoring quantifies esophageal acid exposure with several parameters like the total number of reflux episodes in 24 hours and in which position, for example lying supine or standing. It records the number of reflux episodes that last >5 minutes, the duration of the longest reflux episode, and the percentage of the entire record that esophageal pH is <4.0 which is called reflux index (RI). The test has been validated and has established normative values for children. Clinical value: a) evaluates the efficacy of antisecretory therapy, b) correlates symptoms like chest pain and cough with acid reflux episodes, and c) identifies the children with asthma in whom GERD may be an aggravating factor. The sensitivity, specificity, and clinical utility of pH monitoring for diagnosis and management of possible extra-esophageal complications of GER are not well established (32).³¹ However, many pediatric gastroenterologists find this test clinically useful and often use it.

Combined Multiple Intra-luminal Impedance (MII) and pH Monitoring (MII/pH) has an added advantage in that it detects, in addition to acidic reflux episodes, non-acidic and weakly acidic reflux episodes as well. It is sensitive to the movement of solid, liquid or gas bolus in the esophagus and measures resistance or impedance between the electrodes placed across the length of the esophagus. Clinical Value: a) better than pH monitoring alone in the evaluation of the temporal relation between symptoms, especially respiratory symptoms and GER, b) when combined with video-polysomnography to monitor symptoms it can be a useful tool in correlating reflux episodes with apnea, cough, other respiratory symptoms, and behavioral symptoms³²⁻³⁶ and c) It complements pH probe monitoring by detecting reflux events during post-prandial period when the gastric contents are not so acidic. Normative values for

children have not been established but MII/pH shows promise and once validated, would likely replace pH monitoring alone as the 'gold standard'.

Motility Studies like Esophageal manometry is not sensitive or specific enough to diagnose GERD. Clinical Value: a) identify a motility disorder like achalasia or other motor disorders especially in patients who have failed acid suppression and who have a normal endoscopy.

Endoscopy and Biopsy are clinically valuable in diagnosing reflux esophagitis when there are visible mucosal breaks in distal esophagus. Histology or biopsy findings identify or rule out non-reflux causes of esophagitis and diagnose and monitor Barrett esophagus (BE) and its complications. Histology and biopsy findings are not sensitive or specific enough to diagnose reflux esophagitis. GERD could still be present in the absence of these non-specific reactive changes in histology, which, in the past were presumed to be diagnostic of GERD.

Barium Contrast Radiography should not be used to diagnose GERD as it has poor sensitivity and specificity. Clinical value: a) confirms or rules out anatomic abnormalities of the upper gastrointestinal (GI) tract that may cause symptoms similar to those of GERD for example malrotation and gastric outlet obstruction.

Nuclear Scintigraphy tests are less irradiating and often used. These tests have contributed to improvements in the management of asthmatic children and in anti-reflux intervention success-rate increase. It can also promptly detect alterations in lung perfusion and prevent stable tissue damage.³⁷ However; the standards for interpretation of these tests for the diagnosis of GERD in children are not well established. These may help diagnose pulmonary aspiration in patients with chronic and refractory respiratory symptoms but a negative test does not rule out possible pulmonary aspiration of gastric contents. Gastric emptying studies are recommended only in cases of

symptoms of gastric retention. As of now, the experts do not recommend using Nuclear Scintigraphy to routinely evaluate children with suspected GERD.³¹

Esophageal and Gastric Ultrasonography are not recommended for the routine evaluation of GERD in children although in one recent study, Esophageal Ultrasound (EUS) was able to identify children with Eosino-philic Esophagitis (EE) by measuring the thick-ness of the mucosa in both the proximal and the distal part of the esophagus. The findings were statistically significant when the measurements were compared to the ones in children with GERD.³⁸

Middle ear fluid, pulmonary aspirate for lactose, pepsin or lipid laden macrophages and Esophageal Fluids for bilirubin are tests that are not specific for GER as the cause of rhinological, otological and bronchopulmonary diseases. The role of bile reflux in causing refractory GERD is not quite established. Therefore it is safe to conclude that these tests have limited utility in clinical practice.

Empiric Trial of Acid Suppression as a Diagnostic Test can be beneficial in adolescents with classic GERD symptoms, and a 2-4 week trial of PPI is justified for example in managing 'heartburn' in adolescents (Fig. 3). However, the resolution of symptoms does not always mean that the PPI worked, since placebo effect and natural course could play a role as well. An empiric trial of PPI as a diagnostic test is not advisable since there is no evidence to support it in the literature. The GERD symptoms in infants are less specific and exposing them to the potential adverse events of PPI is not the best practice. It is essential to rule out causes other than GERD before making such a move.

Treatment Modalities Currently Available

Lifestyle Changes in Infants with GERD

Reassurance

For otherwise healthy, thriving infants with symptoms likely due to physiologic GER, parental education, guidance, and support are usually sufficient.

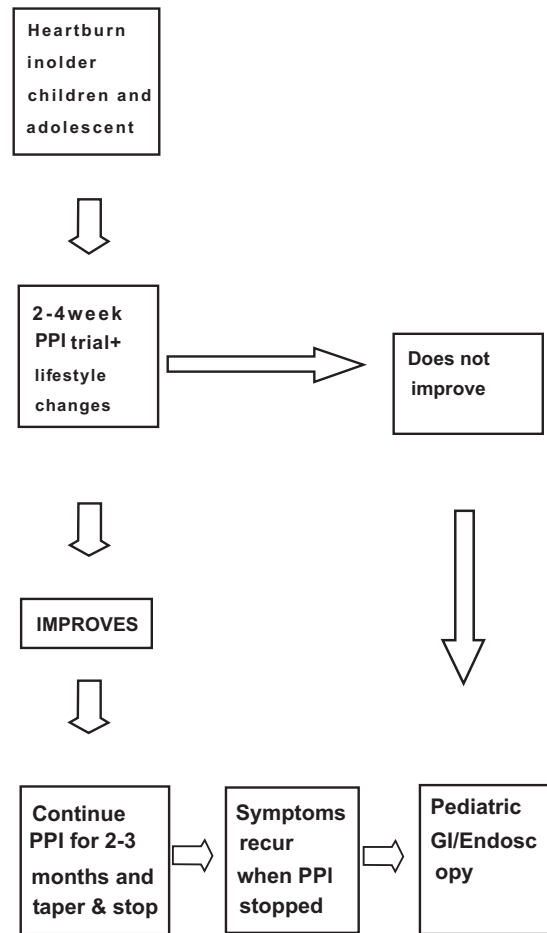


Fig. (3). Clinical pathway to manage 'heartburn' in older children and adolescents in clinical practice.

(Inspired from NASPGHAN-ESPGHAN guidelines 2009).

Diet

Milk protein allergy sometimes can present with symptoms indistinguishable from GERD.^{27,39,40} Therefore, formula-fed infants with recurrent vomiting may benefit from a 2- to 4-week trial of an extensively hydrolyzed protein formula that has been evaluated in controlled trials.^{27,41} Similarly breast-fed infants with regurgitation and vomiting may benefit from a trial of avoidance of cow's milk and eggs by their mothers.^{42,43} Use of commercially thickened antiregurgitant (AR) formulae containing processed rice, corn or potato starch, guar gum, or locust bean gum, may decrease visible regurgitation but does not reduce the frequency of esophageal reflux episodes. AR formulae decrease overt regurgitation and vomiting frequency and volume compared with unthickened formulae⁴⁴⁻⁴⁶ or formulae thickened with rice cereal.⁴⁷⁻⁵² The latter also

has a disadvantage of inadvertently increasing calories per feed and the need for making a large bore nipple hole for the bottle feeding infant.

Position During Sleep

It has been shown by pH monitoring that the prone positioning decreases the amount of acid esophageal exposure when compared with that measured in the supine position.⁵³⁻⁵⁷ However, prone and lateral positions are associated with an increased incidence of sudden infant death syndrome (SIDS).⁵⁸⁻⁶⁰ The risk of SIDS outweighs the benefit of prone or lateral sleep position in GER; therefore, in most infants from birth to 12 months of age, supine positioning during sleep is recommended unless the risks of dying from GERD outweighs the risk of that from SIDS.

Lifestyle Changes in Children and Adolescents with GERD

Diet

There is no sufficient evidence to recommend a routine elimination of any specific food for the management of GERD in older children and adolescents. Expert opinion suggests that children and adolescents with GERD should avoid caffeine, chocolate, alcohol, and spicy foods if they provoke symptoms.⁶¹⁻⁷² We can extrapolate from adult studies where obesity, large meal volume, and late night eating⁷³ are associated with symptoms of GERD.

Position During Sleep

Adults who sleep with the head of the bed elevated have been shown to have fewer and shorter episodes of reflux and fewer reflux symptoms.⁷⁴⁻⁷⁶ Other studies in adults have shown that reflux increases in the right lateral decubitus position.^{77,78} Therefore prone or left-side sleeping position and/or elevation of the head of the bed for adolescents with GERD may be of benefit in select cases.

Pharmacologic Therapies

Histamine-2 Receptor Antagonists (H2RAs) are anti-secretory agents that are superior to placebos, have a rapid onset of action, and, like buffering agents, may be used on-

demand for symptoms of GERD. Unfortunately, their long term use is limited due to the tachyphylaxis or tolerance.

Proton Pump Inhibitors (PPI) are superior to H-2RAs and placebos in healing of erosive esophagitis and relief of GERD symptoms⁷⁹⁻⁸¹ by their potent anti-secretory action and they do not exhibit tolerance with long term use. They could be of benefit in older children and adolescents with GERD. At this point, no placebo-controlled PPI treatment trial for the typical GERD symptoms has shown significant symptom improvement in infants and none of the PPIs has been approved for use in infants below 12 months of age. When initiating treatment it is prudent to start with the smallest effective dose and stick with once a day dosing about 30 minutes before the meals. The not so common but serious adverse effects of acid suppression include increased risk of community-acquired pneumonias and GI infections besides candidemia and necrotizing enterocolitis (NEC) in preterm infants.⁸²⁻⁸⁶

Prokinetic agents include metoclopramide, erythromycin, bethanechol, cisapride, domperidone or baclofen, and they work by reducing the frequency of transient relaxations of the lower esophageal sphincter (TLESR). The risk versus benefit ratio of all of them is high and there is insufficient evidence of their clinical efficacy. Therefore, their routine use in pediatric GERD cases is not justified. They are good candidates to be studied in well designed control trials in children with GERD.

Gastric acid-buffering agents like alginate, and sucralfate are useful on demand for occasional heartburn or reflux symptoms. They should not be used on a long term basis for GERD as they have certain absorbable components that may be harmful if used for a length of time. They are not recommended for chronic GERD in children.

Anti-reflux surgery in the form of open or laparoscopic fundoplication as well as endoluminal approaches have been shown to benefit a select group of children with chronic-relapsing GERD. Patients who have failed

medical therapy, those who are dependent on long-term medical therapy, the ones who have been non-adherent to the medical therapy and children with GERD-related respiratory complications like asthma or recurrent aspiration are generally considered for these surgeries. Ironically, children who most need the surgery i.e. those with underlying disorders predisposing them to the most severe GERD like neurologic impairment are at the highest risk for operative morbidity and postoperative failure. It is essential therefore to rule out all non-GERD causes of the child's symptoms, confirm the diagnosis of chronic relapsing GERD, discuss with the parents the pros and cons of surgery and to assure that the caregivers understand the potential complications, symptom recurrence and sometimes the need to be back on medical therapy. Since the vomiting and regurgitation in children with neurologic impairment could be centrally mediated, fundoplication in the effort to control vomiting, can backfire, and leave these children with troublesome retching.

Common Clinical Scenarios in Infants, Children and Adolescents with Suspected GERD: Evaluation and Management

The most recent pediatric gastroesophageal reflux clinical practice guidelines from the joint recommendations of North American Society for Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) is a very thorough, well researched and comprehensive document for further review for the readers who are interested. Some scenarios of GERD that a primary care physician often encounters in his/her clinic are addressed in this section. The NASPGHAN-ESPGHAN guidelines³¹ have been a major source of reference for the following scenarios.

Infants

Recurrent Regurgitation and Vomiting

Since there are numerous causes of vomiting, a detailed history, a thorough physical exam and supporting investigations are absolutely indispensable.

Neurologically Intact Infant with Uncomplicated Recurrent Regurgitation

Normal, uneventful history, normal growth parameters, unremarkable physical exam and absence of warning signs should generally be sufficient to establish the diagnosis of uncomplicated GER and parental education, reassurance, and anticipatory guidance should suffice. In formula-fed infants, thickening the formula with a tablespoonful of cereal per ounce of formula with a larger bore nipple hole or using the commercially available anti-regurgitation (AR) formula should reduce the frequency of overt regurgitation and vomiting. Pharmacologic therapies are not recommended and often not needed.

Neurologically Intact Infant with Recurrent Vomiting and Poor Weight Gain

Failure to Thrive (FTT) cases should not be labeled physiologic GER. A detailed history including diet history and preparation of formula feeds if not breastfeeding, physical exam, observation of the parent/caregiver-child interaction including the child's feeding and swallowing can guide a physician toward further management. Minimal laboratory investigations to extract maximum information would be urinalysis (screen for urinary tract infection (UTI) and renal tubular acidosis (RTA)), complete blood count (CBC) for anemia, infections, malignancy etc., serum electrolytes, blood urea nitrogen, and serum creatinine for acid-base imbalance, metabolic acidosis or alkalosis and renal impairment. Additional testing should be held pending the results of these screening tests. Depending on the index of suspicion of the physician, some choices are: a) 2-week trial of extensively hydrolyzed formula or amino acid-based formula to exclude cow's milk allergy, b) increase caloric density of formula by thickening feeds if need be, and c) educate the parents regarding the daily nutrition and formula volume needs for normal infant growth. Frequent and close monitoring of caloric intake and weight changes can be accomplished by arranging follow ups in the outpatient setting, failing which, the patient should be admitted for in-

patient monitoring, further evaluation, possible naso-gastric tube feedings and pediatric gastroenterology consultation.

Infant with Apnea

Current data strongly suggest that GER is not the cause of apnea in most infants.⁸⁷ Although reflux causes physiologic apnea, it causes pathologic apneic episodes in a small number of newborn and young infants and in exceptional cases like neurodevelopment disorders. There is no data to confirm GERD as a cause of apnea in premature babies either. In cases where GERD causes pathological apnea, the infant is more likely to be awake and the apnea is more likely to be obstructive.

Infant with Acute Life Threatening Event (ALTE)

ALTE is described as episodes of combinations of apnea, color change, change in muscle tone, choking, and gagging and GERD has frequently been suspected to be the cause. However, reflux of gastric acid seems to be related to ALTE in <5% of infants with ALTE.⁸⁸ For a clinician, a clear temporal relation based on history, observation or testing in an individual infant is more important in making a connection. Impedance/pH recording in combination with polysomnographic recording could be used to document a relationship between pathologic apnea and GERD. Therefore it is essential to consider causes other than GERD in making a diagnosis of ALTE although the yield may not be high for the tests looking for other causes as well especially if the physical exam is normal.⁸⁹

Infants with Unexplained Crying and Irritability

As discussed earlier, these symptoms are non-specific and may be present in many conditions in infancy like UTI, constipation, neurologic disorder and milk protein allergy. If there are no significant findings on history and physical exam, the parents should be reassured, their anxieties should be allayed, their questions answered and the anticipatory guidance should remain the mainstay of management. If symptoms persist, a trial of extensively hydrolyzed milk protein formula or an amino acid based formula may prove beneficial. Monitor-

ing of pH with or without impedance measurement may show a correlation of GERD with the troublesome symptoms. Caution is advised before initiating a time-limited empiric trial of acid suppression therapy due to the adverse effects of the medicines and the self limiting course of the illness in most cases.

Infant with Bronchopulmonary Dysplasia (BPD)

There is an association between GERD and bronchopulmonary dysplasia in neonates and infants, but the cause-and-effect relationship is uncertain.

Toddlers and Young Children

A Young Child with Vomiting and Abdominal Pain

After 18 months of age it is rare for GERD to start causing these symptoms. A search to confirm GERD by pH/MII or endoscopy and ruling out mechanical obstruction like malrotation etc. by barium contrast radiography is important. Based on the history, physical exam and focused laboratory assessments, alternative diagnosis could be arrived at. Endoscopy and biopsy may be helpful in detecting *H pylori* gastritis with or without ulcer or eosinophilic esophagitis.

A Young Child with Sinusitis and Otitis Media

One retrospective case control study showed that neurologically intact children with GERD have two-fold increased risk of sinusitis, laryngitis, pneumonia and bronchiectasis, and less otitis media.⁹⁰ However, selection bias and variable definition of GERD cases may have affected the outcomes. Some other studies in children report an association between acid reflux and serous otitis media.^{91,92} Controlled treatment trials in pediatric patients with GERD to show the causal relationship between GERD and these conditions have not been done to make any substantial recommendations at this point.

A Child with Difficult to Control Asthma

Many studies have demonstrated an association between asthma and measurements of reflux by pH probe or pH/MII. These studies have shown that 60% to 80% of children with

asthma have abnormal pH or pH/MII recordings.⁹³ A study of 77 children 3 to 14 years old with difficult-to-control asthma found that 66% had abnormal Reflux Index (RI) on pH testing.⁹⁴

It is not known if the pH or pH/MII recordings can identify children who would potentially benefit from anti reflux medical or surgical therapy. Some uncontrolled case series using nonobjective parameters have shown a dramatic improvement in asthma symptoms in children after anti-reflux surgery.⁹⁵ In the absence of heartburn or regurgitation, unexplained asthma is less likely to be related to GERD. In a select group of patients, like patients with heartburn, nocturnal asthma, or steroid-dependent, difficult to control asthma, if there is a positive finding on a pH probe or Impedance study, then a PPI trial could be initiated that might prove beneficial. Long-term PPI treatment is often needed to control symptoms.

A Young Child with Recurrent Pneumonia

Reflux causing recurrent pneumonia has been reported in otherwise healthy infants and children.⁹⁶⁻⁹⁸ Recurrent pneumonia and interstitial lung disease may be the complications of GER due to aspiration of gastric contents. Currently there is no test that can determine whether GER is causing recurrent pneumonia. An abnormal esophageal pH test may increase the probability that GER is a cause of recurrent pneumonia but is not a proof thereof. Nuclear scintigraphy can detect aspirated gastric contents when images are obtained for 24 hours after enteral administration of a labeled meal, but more often than not, the aspiration occurs during swallowing rather than the aspiration of refluxed material. Some experts have advocated a trial of naso-gastric tube feeding to exclude aspiration during swallowing as a potential cause of recurrent disease. Similarly, the question as to whether the anti-reflux surgery would be beneficial in a certain case of GERD, could be answered indirectly by feeding via naso-jejunal tube and observing for symptom resolution. Often a physician, running out of options feels compelled to give anti reflux surgery a chance to save a patient's severely impaired lungs from further

deterioration. This may turn out to be in the best interest of the patient, despite the lack of solid proof to establish GER as the cause.

Older Children and Adolescents

A 13 Year Old Boy with Dental Erosions

A causative association between GERD and dental erosion has been reported⁹⁹ and the severity of dental erosions seems to be correlated with the presence of GERD. Young children and children with Neurologic impairment appear to be at the greatest risk of dental erosions. Data in adolescents however, is equivocal.^{100,101} Drinking excessive juices, bulimia, and racial and genetic factors determining enamel and saliva characteristics can all cause dental erosions. In the absence of an established protocol to manage dental erosions within the context of GERD, the best course of action is to work in consultation with the patient's dentist.

A 15 Year Old Girl with Heartburn

Heartburn is defined as burning sensation behind the sternum that may cross the pain threshold. Also referred to as retrosternal or substernal burning pain it is a symptom of GERD with or without esophagitis.¹⁴ The most common cause of heartburn in older children and adults is GERD and generally acidic reflux, although non acid or weakly acidic reflux and duodeno-gastric reflux can contribute to heartburns.^{102,103} Other causes of heartburn include eosinophilic esophagitis, functional heartburn or NERD, esophageal infections, medications and Crohn's disease.¹⁰⁴⁻¹⁰⁶ Unlike adults, cardiac causes of heartburn are rare in children and adolescents. Recent consensus statements suggest that typical heartburn is a reliable indicator for GERD in neurologically intact older children and adolescents if it is the dominant symptom.^{1,2,31}

A 14 year Old Boy with Difficulty Swallowing

Dysphagia, or difficulty in swallowing is not a common presentation of GERD. It is often an anatomic or a neurologic issue. Strictures following erosive esophagitis and eosinophilic esophagitis can present as dysphagia. Therefore if history and physical exam are non-

revealing, then barium contrast radiography and upper endoscopy with a pediatric gastroenterology consultation should be considered seriously. Therapy with acid suppression without earlier evaluation is not recommended. In young children, feeding refusal can be secondary to dysphagia or odynophagia (painful swallowing), and a thorough physical exam, that includes looking for oro-pharyngeal inflammation and swallowing function, is necessary. In any case of dysphagia, acid suppression without a thorough diagnostic evaluation is not advisable.

An Obese Adolescent with Regurgitation and Epigastric Pain

Pediatric literature is scarce and conflicting when it comes to obesity and its association with GERD.^{107,108} However, adult literature suggests that obesity and incremental weight gain are associated with a significantly higher prevalence and increased severity of GERD, Barrett's esophagus, and esophageal adenocarcinoma.^{109,110}

A 16 Year Old Boy with Hoarseness and Nocturnal Cough

Often an otolaryngologist would come across a finding of posterior laryngeal nodularity and suspect GERD in a patient with chronic or nocturnal cough. Although the physician may very well be on the mark, and granted that chronic laryngitis, chronic cough or hoarseness may be associated with GERD, the fact remains that these conditions are multifactorial and acid reflux could just be an aggravating factor. It is not known how much acid reflux is actually needed to cause pathology of the larynx. MII/pH may show the association between the two but the normative data from specific pediatric age groups are not yet available.¹¹¹ Meticulously controlled studies are needed to compare the superiority or lack there-off of the various diagnostic tools to diagnose extraesophageal GERD.

A High School Student with GERD and H pylori Infection

Paucity of pediatric literature in this area of research precludes a straightforward solution

to this problem. The clinical judgment would be to target the greater evil of the two. Is there a positive or negative association between *H pylori* infection and gastroesophageal reflux disease? Does one depend on the other for sustenance or protection? The answers are controversial and seem to vary with the geography and the ethnicity of the people studied in a given region. One recent study from Asia, screening a large cohort of healthy adult population, found that current infection with *H pylori* had a strong protective effect on reflux esophagitis. The study also found, that after successful eradication of *H pylori* infection, the latter's protective effect on reflux esophagitis was lost and the incidence of reflux esophagitis increased to the level of *H pylori*-negative subjects.¹¹² Since the study was limited to a homogeneous ethnic population in a specific region, it is difficult to extrapolate from it and then apply to general pediatric population. Much work is urgently needed in this area.

Summary

This article provides an overview of the latest developments in the field of gastroesophageal reflux disease (GERD) in children for General Practitioners, Family Physicians and Pediatricians who routinely play a significant primary care physician's role in the care of pediatric patients. Defining GERD in infants, young children and adolescents have been fraught with difficulties but significant inroads have been made upon these challenges. An attempt has been made here to consolidate the information into tools for effectively evaluating and managing these children in clinical practice.

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