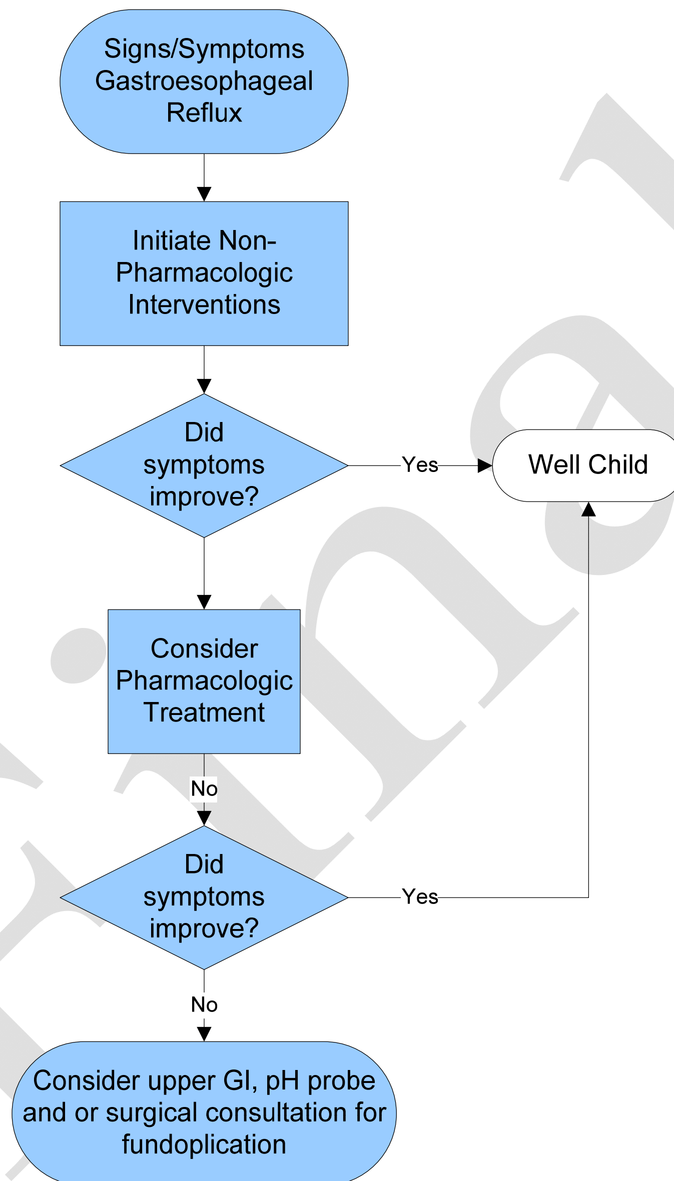
Children's Mercy Hospitals and Clinics
Evidence Based Practice Clinical Practice Guide

Gastroesophageal Reflux in the ICN



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<u>Definition/ Epidemiology</u>: Premature infants and chronically ill infants appear prone to GE reflux and the complications that can arise due to GE reflux.

- Gastroesophageal reflux in the neonate occurs in 22-85% of preterm infants (Tipnis & Tipnis, 2008).
- Twenty five percent of very low birthweight infants are treated with acid suppression therapy at discharge (Tipnis & Tipnis, 2008).

- In term infants, vomiting is a common symptom of gastroesophageal reflux and recurrent vomiting occurs in 50% of infants from 0-3 months, 67% in four month old infants and 5% in 10-12 month old infants (Bhatia & Parish, 2009).

Objective of Guideline: To standardize the care of infants in the ICN with gastroesophageal reflux (GE Reflux).

Target Users: Neonatologists, Neonatal & Perinatal Fellows, Hospitalists, Neonatal Nurse Practitioners, ICN Nurses, Medical Residents.

Guideline Inclusion Criteria: Infants on the Neonatal Service with signs and symptoms of GE Reflux.

Guideline Exclusion Criteria: Infants and children not on the Neonatal Service.

Clinical Questions Answered by Guideline:

1. Does breast milk decrease the incidence or severity of GE reflux in infants?
2. In infants in the ICN does changing position decrease GE reflux?
3. Are thickened feedings by mouth effective, safe and helpful in the treatment of GE reflux in healthy infants?
4. For infants in the ICN with suspected GE reflux does treatment with erythromycin, H2 Blockers or proton pump inhibitors improve symptoms?
5. In infants in the ICN with suspected GE reflux does treatment with erythromycin, sucralfate, bethanecol or metoclopramide improve symptoms?
6. For infants in the ICN, does a pH study assist in diagnosing GE reflux?

Differential Diagnosis:

Gastrointestinal Obstruction Pyloric stenosis Malrotation with intermittent volvulus Intestinal duplication Hirschsprung disease Antral/duodenal web Foreign body Incarcerated hernia Appendicitis **Other gastrointestinal disorders** Achalasia Gastroparesis Gastroenteritis Peptic ulcer Eosinophilic esophagitis/gastroen-teritis	Food allergy Inflammatory bowel disease Pancreatitis **Neurologic** Hydrocephalus Subdural hematoma Intracranial hemorrhage Intracranial mass Infant migraine Chiari malformation **Infectious** Sepsis Meningitis Urinary tract infection Pneumonia Otitis media Hepatitis	**Metabolic/endocrine** Galactosemia Hereditary fructose intolerance Urea cycle defects Amino and organic acidemias Congenital adrenal hyperplasia **Renal** Obstructive uropathy Renal insufficiency **Toxic** Lead Iron Vitamins A and D Medications—ipecac, digoxin, theophylline, etc	**Cardiac** Congestive heart failure Vascular ring **Others** Pediatric falsification disorder (Munchausen syndrome by proxy) Child neglect or abuse Self-induced vomiting Cyclic vomiting syndrome Autonomic dysfunction

(Vandenplas, et al., 2009.)

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Practice Recommendations:

Signs and symptoms of Gastroesophageal (GE) Reflux in neonates:

Signs and Symptoms of GE reflux

- Gagging
- Choking with frequent swallowing
- Vomiting
- Irritability during and after feedings
- Dysphagia
- Self limiting the volume of oral feeding
- Turning away from a feeding
- Nasal congestion
- Chronic cough
- Reactive airway disease
- Retching
- Rumination
- Grimacing upon swallowing
- Refusal to feed
- Oral aversion
- Arching
- Apnea, with or without bradycardia
- Hoarseness of cry
- Stridor
- Recurrent pneumonia

(Pediatric Care On-Line, 2009)

Treatment:

Treatment options can be classified into non-pharmacologic and pharmacologic treatments.

Non-Pharmacologic Treatment:

There are four non-pharmacologic interventions found in the literature:

- Promoting the use of breast milk.
- Changing from a cow milk protein based formula to an amino acid based formula.
- Altering the position of the infant during and after feedings.
- Thickening oral feedings.

Promoting the use of breast milk.

Feedings of breast milk may decrease the frequency and duration of reflux episodes indirectly, as it promotes more rapid gastric emptying time. (Heacock, Jeffery, Baker, & Page, 1992; Ewer, Drubin, Morgan, & Booth, 1994; Van Den Driessche et al., 1999).

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Changing from a cow milk protein based formula to an amino acid based formula.
Vomiting in infants can be a sign of cow milk protein allergy. Decreased vomiting has occurred within 24 hours after changing to a hypoallergenic formula. A 1-2 week trial of a hypoallergenic formula, Neocate® or EleCare®, may be beneficial to rule out protein allergy (Ravelli, Tabanelli, Volpi, & Ugazio, 2001).

Altering the position of the infant during and after feedings.
The following positions have been shown to be beneficial in decreasing episodes of reflux:

- Prone. Caution needs to be exhibited using the prone position close to discharge with the association to SIDS.
- Left (side down) lateral.
- Right (side down) lateral for 1 hour after feeding, then turning to left (side down) lateral until the next feeding.
- Elevating the head of the bed has not been shown to decrease GER in healthy, term infants. Consider head of the bed elevation for infants with respiratory issues or other specific clinical reasons. (Bhat, Rafferty, Hannam, & Greenough, 2007; Corvaglia, et al., 2007; Craig, Hanlon-Dearman, Sinclair, Taback, & Moffatt ,2004; Omari, et al, 2004: vanWick, et al., 2007.)

Thickened feedings
Thickening feeds has been shown to have moderate effect on regurgitation scores and reflux index. However, the addition of thickener changes the calorie concentration of the feeding. Consider the use of thickened feedings only in specific clinical situations, such as potential airway compromise or recurrent emesis. (Craig, Hanlon-Dearman, Sinclair, Taback, & Moffatt, 2004; Horvath, Dziechciarz, & Szajewska, 2008).

Pharmacologic Treatment: (see Medication Table)
Medications should be reserved for infants who fail non-pharmacologic measures. The research evaluating the use of prokinetic agents and acid suppression agents is low quality. Further research (if performed) is likely to have an important influence on our confidence of the study results.

Prokinetic agents
There is weak evidence that supports the use of prokinetic agents (specifically erythromycin) in treatment for feeding intolerance that may indirectly decrease GE reflux by increasing gastric emptying. (Ng, Gomez, Rajadurai, Saw, & Qauk, 2003; Arguelles-Martin, Gonzalez-Fernandez, &Gentles, 1989)

Acid suppression agents
Acid suppression agents (H2 blockers and Proton Pump Inhibitors) increase gastric pH, but have not been shown to reduce the symptoms of GE reflux. Potential adverse effects from medications causing gastric acid suppression include: necrotizing enterocolitis, altered gastric colonization, and increased pneumonia rate (Omari, Haslam, Lundborg, & Davidson, 2007; Salvatore, Hauser, Salvatoni, & Vandenplas, 2006; Vandenplas, Salvatore, & Hauser, 2005; Barron, Tan, Spalding, Bakst & Singer, 2007; Fontana et al, 1993.).

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Medication	Trade name	Category	Dose	Max dose	Formulations	Pt. charge	Contraindications	Adverse Effects
Erythromycin	EES, EryPed	Antibiotic/prokinetic	Oral 10mg/kg/dose	Oral: 250mg/dose	200mg/5mL suspension,	$14	Hepatic impairment	Liver toxicity
					400mg tab	$14		
Ranitidine	Zantac	H2 antagonist	Oral: 2-4mg/kg/day	Oral: 150mg/dose	15mg/mL solution	$38		Thrombocytopenia
			IV: 2mg/kg/day	IV: 50mg/dose	2.5mg/mL injection	$32		
Lansoprazole	Prevacid	Proton Pump Inhibitor	Oral: 1mg/kg/dose	Oral: 30mg	3mg/mL suspension	$27		
					15mg tablets	$28		
					30mg capsules	$32		
Omeprazole	Prilosec	Proton Pump Inhibitor	Oral: 1mg/kg/dose	Oral: 40mg	2mg/mL suspension	$34		
					10mg capsules	$25		
					20mg capsules	$27		
Sucralfate	Carafate	GI miscellaneous	Oral: 0.5-1 gram/dose	Oral: 1 gram	100mg/mL suspension	$18		
Bethanecol	Urecholine	Cholinergic agent	Oral: 0.6mg/kg/day	Oral: 50mg	1mg/mL suspension	$18	GI obstruction, hyperthyroidism,PUD, cardiac dx	Hypotension, salivation
					10mg tablet	$17		
Metoclopramide	Reglan	Prokinetic	Oral: 0.2mg/kg/dose	Oral: 10mg	1mg/mL solution	$13	GI obstruction, history of EPS, siezure disorder	EPS, sedation, anxiety, NMS, methemoglobinemia
					10mg tablet	$14		
			IV: 0.2mg/kg/dose	IV: 10mg	2.5mg/mL injection	$23		

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Use of pH probe testing

A pH probe with impedance measurement, which detects both acid and non-acid reflux, is preferred over conventional pH probe testing. At CMH&C, both pH and impedance are measured. Even with the impedance measurement, diagnosis of GE reflux is problematic (Condino, et al., 2006; Tolia, Wuerth, & Thomas, 2005).

Outcome Measures:

Percentage of infants discharged on pharmacologic treatment:

- erythromycin
- omeprazole
- lansoprazole
- ranitidine

Percentage of infants < 32 weeks post menstrual age status post pH probe.

Potential Cost Implications:

We propose that total costs will be decreased following implementation of the guidelines due to increased use of non-pharmacologic interventions and the use of lower cost, efficacious medications.

Potential Organizational Barriers:

Largest organization barrier will be old held ideas about "reflux precautions" such as elevation of the head of the bed. There is no supporting evidence that shows benefit from "reflux precautions".

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How guideline was piloted:
1. Steve Olsen, MD presented at Neonatal Noon Conference on January 6, 2010.
2. Nancy Mohr presented at ICN Committee Meeting on February 10, 2010
3. Steve Olsen, MD, presented at ICN Nursing Updates on February 2, 2010, February 8, 2010, and February 18, 2010.
4. Group meetings with Neonatal Nurse Practitioners by Nancy Mohr, OT in June, 2010.

Guideline Preparation: This guideline was prepared by The Office of Evidence Based Practice (EBP) in collaboration with content experts at Children's Mercy Hospitals and Clinics. Development of this guideline supports the Department of Clinical Effectiveness's initiative to promote care standardization that builds a culture of quality and safety that is evidenced by measured outcomes. If a conflict of interest is identified the conflict will be disclosed next to the team members name.

ICN Reflux Clinical Practice Guideline
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No external funding was obtained in the development of this guideline.

Development Process:
The review summary documents the following steps:
1. Review of existing internal and external guidelines and standards
   a. Internal guidelines: Gastroesophageal Reflux Guideline for children external to the ICN
   b. External guidelines: No external guidelines were identified
2. Review preparation
   a. PICOT questions established
   b. Team leaders confirmed search terms used
3. Databases searched
   a. AHRQ National Guideline Clearinghouse
   b. Medline

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   c. Cochrane
   d. CINAHL
4. Critically analyze the evidence
   a. Guidelines
      i. AGREE criteria were used to analyze published clinical guidelines
   b. Literature
      i. CASP tools were used to analyze the literature (e.g. study limitations, consistency of results, directness of evidence, precision and reporting bias)
      ii. GRADE criteria evaluated the literature based on:
         1. The balance between desirable and undesirable effects
         2. Patient values and preferences
         3. Resource utilization

      The table below defines how the quality of the evidence is rated and how the recommendation is established based on the type of evidence:

Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies.
Moderate	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies.
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence.
Very Low	Evidence for at least 1 of the critical outcomes from unsystematic clinical observations or very indirect evidence.
Recommendation	Type of Evidence
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Weak	Desirable effects closely balanced with undesirable effects

5. Recommendations for the guideline were developed by a consensus process incorporating the three principles of EBP (current literature, content experts, and patient and family preference [when possible])

Approval Process: Guidelines are reviewed and approved by the Content Expert Team, the Office of EBP, and other appropriate hospital committees as deemed suitable for the guidelines intended use. Dr. William San Pablo, Gastroenterologist at Children's Mercy Hospitals and Clinics was the external reviewer of this guideline. Guidelines are reviewed and updated as necessary every 3 years within the Office of EBP at CMH&C. Content expert teams will be involved with every review and update.

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Disclaimer:

The content experts and the Office of EBP are aware of the controversies surrounding GE Reflux in the neonate. When evidence is lacking or inconclusive, options in care are provided in the guideline.

These guidelines do not establish a standard of care to be followed in every case. It is recognized that each case is different and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time.

It is impossible to anticipate all possible situations that may exist and to prepare guidelines for each. Accordingly these guidelines should guide care with the understanding that departures from them may be required at times.

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