

# A Systematic Review of Nonpharmacological and Nonsurgical Therapies for Gastroesophageal Reflux in Infants

Aaron E. Carroll, MD; Michelle M. Garrison, MPH; Dimitri A. Christakis, MD, MPH

**Background:** Nonpharmacological and nonsurgical measures are often recommended for gastroesophageal reflux disease (GERD) in infants, despite ambiguous supporting evidence.

**Objective:** To conduct a systematic review of rigorously evaluated nonpharmacological and nonsurgical therapies for GERD in infants.

**Design/Methods:** We searched online bibliographic databases, including MEDLINE, EMBASE, the Cochrane Collaboration and Clinical Trials Database, and alternative medicine databases for the terms *gastroesophageal reflux* and *infants*. We selected randomized controlled trials of nonpharmacological and nonsurgical GERD therapies in otherwise healthy infants. Data were extracted from the selected articles regarding reflux, emetic episodes and intraesophageal pH.

**Results:** We identified 43 relevant studies, of which 10 met the selection criteria. These studies examined positioning, pacifier use, and feeding changes. Positioning at a 60° elevation in an infant seat was found to increase

reflux compared with the prone position. No significant difference was shown between the flat and head-elevated prone positions. The impact of pacifier use on reflux frequency was equivocal and dependent on infant position. The protein content of formula was not found to affect reflux. Although no study demonstrated a significant reflux-reducing benefit of thickened infant foods compared with placebo, 1 study detected a significant benefit of formula thickened with carob bean gum compared with rice flour (pH < 4 for 5% vs 8% of time). Another study showed that if supplementing with dextrose 5% water or dextrose 10% water, the lower-osmolality fluid was associated with less reflux.

**Conclusions:** Many conservative measures commonly used to treat GERD in infants have no proven efficacy. Although thickened formulas do not appear to reduce measurable reflux, they may reduce vomiting. Further studies with clinical outcomes are needed to answer questions about efficacy definitively.

*Arch Pediatr Adolesc Med.* 2002;156:109-113

**G**ASTROESOPHAGEAL reflux disease (GERD) is a common disease of infancy, with a prevalence of as high as 18% in healthy children, and a frequent reason for visits to primary health care providers.<sup>1</sup> Approximately 50% of all healthy infants will vomit more than twice per day.<sup>2</sup>

A variety of approaches have been used in the treatment of GERD, including pharmacological and nonpharmacological therapies. As many of the pharmacological therapies for reflux, eg, metoclopramide hydrochloride (Reglan) and cisapride (Propulsid), are falling into disfavor or are withdrawn from use, practitioners may rely more on conservative measures as first-line therapy for GERD. These nonpharmacological and nonsurgical

therapies include positioning changes, formula changes, and thickening of infant food.

Although these interventions are commonly recommended,<sup>3</sup> evidence in support of them is sparse. We therefore undertook a systematic review to summarize the current state of the evidence. To maximize clarity and clinical usefulness, we present the results of that review as distinct evidence summaries detailing the potential benefits and harms of each intervention.

## RESULTS

### LITERATURE SEARCH

The systematic literature search identified more than 2500 articles. After excluding articles that did not describe clinical

From the Robert Wood Johnson Clinical Scholars Program (Dr Carroll), the Department of Pediatrics (Drs Carroll and Christakis), and the Child Health Institute (Ms Garrison and Dr Christakis), University of Washington, Seattle.

## METHODS

We searched several bibliographic databases, including MEDLINE (January 1, 1966, through November 30, 2000), the Cochrane Collaboration and Clinical Trials Database (as of November 2000), EMBASE (as of November 2000), and multiple alternative medicine databases. We used the search terms *gastroesophageal reflux disease* and *infants* as medical subject headings and keywords. We restricted the results to studies that were conducted in human infants and published in the English language. We reviewed the titles of all returned articles and the bibliographies of all relevant review articles and selected articles to determine whether the studies examined nonpharmacological and nonsurgical therapies for infants with GERD. Articles were immediately excluded if they included drug or surgical therapies or were obviously not clinical trials.

We analyzed studies for adequate inclusion criteria, randomization, and allocation concealment. Although considerable disagreement exists regarding how pathologic GERD should be defined, we accepted any study that defined GERD as reflux into the esophagus with a pH of less than 4.0 for at least 5% of the time, as diagnosed by means of pH probe study findings. Although this cutoff is frequently used as a diagnostic criterion in research and clinical practice, it may or may not adequately correlate with symptomatic reflux in infants.

To meet selection criteria, a study had to randomize otherwise healthy, full-term infants with GERD to treatment and control groups. Crossover trials were accepted if infants were exposed in random order to both treatment and control protocols. Allocation concealment was only considered a requirement for inclusion when all reviewers agreed that it would be feasible to blind such a study, and that the absence of effective blinding could bias the outcome. For example, although blinding may not be feasible in a study of infant positioning, the results of a pH probe are unlikely to be affected by parent or provider knowledge of allocation. All disagreements were resolved via consensus.

Unless otherwise indicated, data are given as mean  $\pm$  SEM.

trials or that examined drug or surgical therapy, 35 articles remained and were assessed by all 3 reviewers (A.E.C., M.M.G., and D.A.C.). Articles were most commonly excluded at this stage because they did not describe trials,<sup>4-9</sup> or the trials did not specifically study therapies for GERD,<sup>10-13</sup> infants with compound medical problems<sup>14-17</sup> or premature infants were included,<sup>18-21</sup> and a control group or proper randomization was missing.<sup>1,22-25</sup> Other studies were eliminated because they included therapies judged to be pharmacological in nature.<sup>26,27</sup> Ten randomized controlled trials (RCTs) met selection criteria. Of these, 2 RCTs studied positioning<sup>28,29</sup>; 3 studied thickened infant food<sup>30-32</sup>; 4 studied formula changes<sup>33-36</sup>; and 1 studied nonnutritive sucking.<sup>37</sup> Characteristics of these studies are summarized in the **Table**.

Two of the trials investigated the effect of positioning. One studied the placement of the infant upright in a seat vs lying prone; the other examined the effect of elevation of the head of the bed.

*Does placement upright in an infant seat reduce the amount of reflux?*

**There is no evidence to support this intervention.** One RCT<sup>29</sup> found that placement in an infant seat (inclined at 60°) was detrimental with respect to GERD. Infants were randomized and studied in paired 2-hour trials using the pH probe to measure reflux. Infants in the seat spent a greater proportion of time in a state of reflux (28.2%  $\pm$  6.4%) than did those in the prone position (12.8%  $\pm$  3.7%) and had significantly more episodes of reflux (16.0  $\pm$  2.4 vs 10.1  $\pm$  2.3). Although the infant seat has been considered a treatment for GERD, evidence suggests that it actually exacerbates reflux.

*Does elevating the head of the bed reduce the amount of reflux?*

**There is no evidence to support this intervention.** One RCT<sup>28</sup> found no difference in any measure of reflux between infants in the prone position and those in the prone position with the head of the bed inclined at 30°. Infants were randomized and underwent pH probe studies for 3-hour sessions in a crossover trial that measured the amount of reflux, number of episodes, average length of episodes, number of long episodes, and length of the longest episode. Among the 90 infants with GERD, no difference was seen between the positions for any of these measures.

## NONNUTRITIVE SUCKING

*Does pacifier use reduce reflux?*

**There is no evidence to support this intervention.** Orenstein<sup>37</sup> studied 48 infants randomized to a prone or seated position. In each position, infants underwent pH probe examination with and without pacifiers in random order for 3 hours. In the prone position, pacifier use increased the number of episodes of reflux in 2 hours (7.2  $\pm$  1.1 to 12.8  $\pm$  2.3 [ $P$  = .04]). In the seated position, pacifier use decreased the number of reflux episodes in 2 hours (21.1  $\pm$  3.1 to 14.8  $\pm$  2.6 [ $P$  = .03]), but not enough to compensate for the negative effects of the seated position. Total reflux time and reflux clearance were not significantly affected by pacifier use in either position.

## THICKENED INFANT FOOD

Four RCTs studied the effect of thickened food on GERD. Two studies compared formula thickened with rice flour with placebo, 1 studied carob bean gum–thickened formula vs placebo, and 1 compared the 2 thickening agents.

*Does thickening food with rice flour reduce the amount of reflux?*

**There is no evidence to support this intervention.** Bailey et al<sup>31</sup> randomized infants to receive plain apple juice or apple juice thickened with rice flour. Infants received

## Characteristics of Included Studies

Study	No. of Study Subjects		Age Range	Intervention	Outcomes Measured
	Treated Group	Control Group			
Orenstein <sup>28</sup>	100	100*	4-26 wk	Positioning	Reflux duration and frequency
Orenstein et al <sup>29</sup>	9	9*	0.5-4.2 mo	Infant seat	Reflux duration and frequency
Borrelli et al <sup>30</sup>	12	12	5-11 mo	Thickened formulas (Nutrilon AR)†	Reflux duration and frequency, clinical score, emesis
Bailey et al <sup>31</sup>	52	52*	4 d-14 mo	Thickened juice	Reflux duration and frequency
Orenstein et al <sup>32</sup>	20	20*	4-34 wk	Thickened formula	Clinical score, emesis
Khoshoo et al <sup>33</sup>	3	3*	3-12 mo	Whey- or casein-based formula	Reflux duration and frequency, emesis
Vandenplas et al <sup>34</sup>	10	10	1 wk-4 mo	Carob bean gum–thickened formula	Reflux duration and frequency, clinical score
Tolia et al <sup>35</sup>	28	28*	1-11 mo	Casein-predominant, soy-based, or whey-predominant formula	Reflux duration
Sutphen and Dillard <sup>36</sup>	19	19*	0.7-13.2 mo	D5W, D10W or Polycose solution‡	Reflux duration
Orenstein <sup>37</sup>	48	48*	1.5-28 mo	Pacifier	Reflux duration and frequency

\*Indicates cross-over trials, in which each patient serves as his or her own control.

†Nutrilon AR is manufactured by Nutricia, Boca Raton, Fla.

‡D5W indicates dextrose 5% water; D10W, dextrose 10% water; and Polycose, glucose polymer solution (Ross Laboratories, Columbus, Ohio).

at least 3 feedings of both juice types during 20 to 24 hours in the following 4 positions: prone, prone and elevated 30°, supine, or unrestricted. Reflux was measured by means of a pH probe for 2 hours postprandially. There was no difference between the 2 types of juice in any position, except in the 30° elevated prone position, in which reflux time was increased with thickened juice. Orenstein et al<sup>32</sup> assessed reflux by means of technetium Tc 99m sulfur colloid 500- $\mu$ Ci scintigraphy in 20 infants undergoing paired feeding consisting of infant formula alone or formula thickened with rice cereal. The feedings were given 48 to 72 hours apart, and the infants underwent 90-minute postprandial studies. The type of formula had no statistically significant impact on the amount of reflux. However, a significant decrease was found in the number of episodes of frank emesis (1.2  $\pm$  0.7 vs 3.9  $\pm$  0.9 per 90 postprandial minutes).

*Does thickening food with carob bean gum preparation reduce the amount of reflux?*

**There is no evidence to support this intervention.** In one RCT,<sup>34</sup> 20 infants were randomized to receive the control formula (80% casein and 20% whey) or the thickened formula. Both groups also received positional treatment and parental reassurance. Parents kept a regurgitation diary for 1 week, and a 24-hour pH study was performed before and after treatment. Both groups noted improvements compared with baseline, but no significant difference was found in pH monitoring results between the control and treatment groups. There were some intra-group improvements, which led the authors to conclude that thickened formulas reduced the reflux index. However, no significant differences were found between the groups before and after the trial. Parental diaries recorded improvement in the number of regurgitations in both groups, with no significant difference between them.

*Is thickening food with carob bean gum more successful than rice flour in reducing reflux?*

**Yes.** In 1 crossover RCT,<sup>30</sup> 24 infants received a traditional formula thickened with rice flour or a formula thickened with carob bean gum, and formulas were alter-

nated in a nonrandom alteration study. All infants underwent 24-hour pH probe studies. The infants were then randomized to receive 1 of the 2 formulas for the next 2 weeks, with parents scoring their reflux symptoms on diary cards. Parental diaries showed reduction over time in the symptomatic scores for both formulas. The mean ( $\pm$  SD) reductions were significantly greater, however, with the carob bean gum–thickened formula (symptomatic score reduction, 70.4%  $\pm$  6.0% vs 48.7%  $\pm$  6.2% [ $P < .01$ ]; reduction in episodes of emesis, 58.1%  $\pm$  5.6% vs 34.1%  $\pm$  8.8% [ $P < .05$ ]).

## FORMULA CHANGES

Two RCTs investigated the effect of formula composition on GERD, with equivocal results.

*Does the composition of formula have any effect on reflux?*

**There is no evidence to support this intervention.** Tolia et al<sup>35</sup> randomized 28 infants to receive casein-predominant, soy-based, and whey-predominant formulas in random order. The infants were given 1 serving of each formula on 3 consecutive days and then underwent measuring for gastric emptying time and reflux by means of scintigraphy. No difference was seen in spitting and vomiting between the formulas. The differences in volume of reflux for each formula were not statistically significant. Another small study<sup>33</sup> monitored reflux in 3 infants with GERD by means of a 24-hour pH probe for casein- and whey-based formulas. All 3 infants showed improvement in emesis while receiving the whey-based formulas (1.3  $\pm$  0.6 vs 4.3  $\pm$  0.6 [ $P < .01$ ]), although the difference between the formulas, based on the results of the pH probe testing, was not statistically significant.

## CALORIC DENSITY AND OSMOLALITY

*Does the caloric density or osmolality of feedings affect reflux?*

**Possibly.** Sutphen and Dillard<sup>36</sup> studied the effect of dextrose 5% water (D5W), dextrose 10% water (D10W), and a glucose polymer solution (Polycose; Ross Laboratories, Columbus, Ohio) when rehydrating chil-

### What This Study Adds

Nonpharmacological and nonsurgical measures are often recommended for infant gastroesophageal reflux disease, although the evidence in support of them is ambiguous. This review systematically evaluated rigorous studies of these therapies to document their efficacy. Through this review, we hope to make it clear to practitioners that many of these therapies have no proven efficacy. More studies of nonpharmacological and nonsurgical measures are necessary in the future.

dren with carbohydrate solutions. Nineteen infants underwent pH probe monitoring as they received each solution 1 time in a random order while undergoing the pH probe study. The total minutes of esophageal reflux were significantly lower while receiving the D5W and glucose polymer solutions than while receiving the D10W solution (mean  $\pm$  1 SD, 12.0  $\pm$  11.3 and 12.6  $\pm$  8.0, respectively, vs 28.6  $\pm$  28.4 [ $P < .05$ ]). No significant difference was found in the results in the first postprandial hour, but results became significant when observed for 2 hours postprandially.

### COMMENT

Although often used, these nonpharmacological, nonsurgical approaches to the management of infant GERD lack a sound evidence base. None of the interventions discussed in this review significantly improved reflux. Thickening infant formulas, however, reduced the frequency of frank emesis. Medical textbooks are often used as a proxy for the prevailing opinions of experts.<sup>38</sup> In the case of GERD, many textbooks continue to recommend the use of conservative measures, including thickening of juice and formula and upright positioning, despite their lack of proven efficacy.<sup>39-45</sup>

Many pediatricians and pediatric gastroenterologists prescribe these therapies despite their lack of evidence, often as a means of including parents in the treatment plan when reassurance seems insufficient. Although no evidence suggests that these nonpharmacological therapies are unsafe, they often carry hidden burdens. Wedges (devices that keep infants sleeping at an incline) can be expensive and cumbersome to use, and reliance on them may lead to undue anxiety on occasions when parents fail to use them. Thickening infant foods necessitates bottle feeding, thereby requiring that breastfeeding mothers express breast milk rather than nurse directly. This may be inconvenient and may have an impact on mother-child bonding.

The limitations of this study are that we included only articles and textbooks written in the English language. The number of well-designed clinical trials of nonpharmacological and nonsurgical therapies for reflux is small. Therefore, a potential effect of some of these therapies may have been missed because of the small sample size. This review does not prove that these therapies do not work; it illustrates that no conclusive evidence exists to prove that they do work. Certainly, more studies are needed to answer questions about efficacy definitively.

This systematic review, like others before,<sup>46</sup> identified significant gaps in what we know about treating GERD in infants. No quality RCTs have examined changes in feeding volume or frequency. Another area for potential improvement in future research is in the outcome measures used. Thus far, most of the studies have used pH probes to diagnose and monitor GERD. Although pH probes are an objective measure, and thus not subject to bias, they may not reflect clinical symptoms, which constitute the outcome of greatest interest to parents. One potential scoring system might be the 25-point Infant Gastroesophageal Reflux Questionnaire GERD score based on 11 items, including frequency and amount of vomiting, feeding, weight gain, comfort, crying, hiccups, arching, and apnea.<sup>47</sup> This test was shown to have a 100% positive predictive value and 94% to 98% negative predictive value in a clinical study of its validity.<sup>47</sup> Despite potential problems with bias and comparability between studies, clinical scores may be a more clinically relevant outcome measure in the study of infant GERD.

Accepted for publication September 28, 2001.

Corresponding author: Aaron E. Carroll, MD, Robert Wood Johnson Clinical Scholars Program, H-220 Health Sciences Center, Box 357183, Seattle, WA 98195-7183 (e-mail: acarro@u.washington.edu).

### REFERENCES

1. Bagucka B, De Schepper J, Peelman M, Van de Maele K, Vandenplas Y. Acid gastroesophageal reflux in the 10 degrees-reversed-Trendelenburg-position in supine sleeping infants. *Acta Paediatr Taiwan*. 1999;40:298-301.
2. Orenstein SR, Izadnia F, Khan S. Gastroesophageal reflux disease in children. *Gastroenterol Clin North Am*. 1999;28:947-969.
3. Tsou VM, Bishop PR. Gastroesophageal reflux in children. *Otolaryngol Clin North Am*. 1998;31:419-434.
4. Lynn MR. Use of infant seats for gastroesophageal reflux. *J Pediatr Nurs*. 1986; 1:127-129.
5. Blecker U, Van Hauthem H, Lanciers S, Peeters S, Vandenplas Y. The effect of different feeds on the incidence of postcibal gastro-oesophageal reflux in infants as measured by oesophageal pH monitoring. *Eur J Gastroenterol Hepatol*. 1992;5:47-50.
6. Cucchiara S, De Vizia B, Minella R, et al. Intra-gastric volume and osmolality affect mechanisms of gastroesophageal reflux (GOR) in children with GOR disease [abstract]. *J Pediatr Gastroenterol Nutr*. 1995;20:468.
7. Sajwaj T, Libet J, Agras S. Lemon-juice therapy: the control of life-threatening rumination in a six-month-old infant. *J Appl Behav Anal*. 1974;7:557-563.
8. Heacock HJ, Jeffery HE, Baker JL, Page M. Influence of breast versus formula milk on physiological gastroesophageal reflux in healthy, newborn infants. *J Pediatr Gastroenterol Nutr*. 1992;14:41-46.
9. Kravitz H. Comparison of newborn infants in raised and horizontal cribs. *IMJ III Med J*. 1975;147:389-390.
10. Tolia V, Kauffman RE. Comparison of evaluation of gastroesophageal reflux in infants using different feedings during intraesophageal pH monitoring. *J Pediatr Gastroenterol Nutr*. 1990;10:426-429.
11. Orenstein SR. Effects on behavior state of prone versus seated positioning for infants with gastroesophageal reflux. *Pediatrics*. 1990;85:765-767.
12. Billeaud C, Guillet J, Sandler B. Gastric emptying in infants with or without gastro-oesophageal reflux according to the type of milk. *Eur J Clin Nutr*. 1990;44: 577-583.
13. Fabiani E, Bolli V, Pieroni G, et al. Effect of a water-soluble fiber (galactomannans)-enriched formula on gastric emptying time of regurgitating infants evaluated using an ultrasound technique. *J Pediatr Gastroenterol Nutr*. 2000;31:248-250.
14. Meyers WF, Herbst JJ. Effectiveness of positioning therapy for gastroesophageal reflux. *Pediatrics*. 1982;69:768-772.
15. Carre I. Postural treatment of children with a partial thoracic stomach ("hiatus hernia"). *Arch Dis Child*. 1960;35:569-580.
16. Khoshoo V, Zembo M, King A, Dhar M, Reifen R, Pencharz P. Incidence of gas-

- troesophageal reflux with whey- and casein-based formulas in infants and in children with severe neurological impairment. *J Pediatr Gastroenterol Nutr.* 1996;22:48-55.
17. Kelly KJ, Lazenby AJ, Rowe PC, Yardley JH, Perman JA, Sampson HA. Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula. *Gastroenterology.* 1995;109:1503-1512.
  18. Vandenas Y, Sacre L, Loeb H. Effects of formula feeding on gastric acidity time and oesophageal pH monitoring data. *Eur J Pediatr.* 1988;148:152-154.
  19. Sutphen JL, Dillard VL. Medium chain triglyceride in the therapy of gastroesophageal reflux. *J Pediatr Gastroenterol Nutr.* 1992;14:38-40.
  20. Sutphen JL, Dillard VL. Effect of feeding volume on early postcibal gastroesophageal reflux in infants. *J Pediatr Gastroenterol Nutr.* 1988;7:185-188.
  21. Blumenthal I, Lealman GT. Effect of posture on gastro-oesophageal reflux in the newborn. *Arch Dis Child.* 1982;57:555-556.
  22. Vandenas Y, Sacre-Smits L. Gastro-oesophageal reflux in infants: evaluation of treatment by pH monitoring. *Eur J Pediatr.* 1987;146:504-507.
  23. Vandenas Y, Sacre L. Milk-thickening agents as a treatment for gastroesophageal reflux. *Clin Pediatr (Phila).* 1987;26:66-68.
  24. Tobin JM, McCloud P, Cameron DJ. Posture and gastro-oesophageal reflux: a case for left lateral positioning. *Arch Dis Child.* 1997;76:254-258.
  25. Orenstein SR, Whittington PF. Positioning for prevention of infant gastroesophageal reflux. *J Pediatr.* 1983;103:534-537.
  26. Sutphen JL, Dillard VL, Pipan ME. Antacid and formula effects on gastric acidity in infants with gastroesophageal reflux. *Pediatrics.* 1986;78:55-57.
  27. Gouyon JB, Boggio V, Fantino M, Gillot I, Schatz B, Vallin A. Smectite reduces gastroesophageal reflux in newborn infants. *Dev Pharmacol Ther.* 1989;13:46-50.
  28. Orenstein SR. Prone positioning in infant gastroesophageal reflux: is elevation of the head worth the trouble? *J Pediatr.* 1990;117(pt 1):184-187.
  29. Orenstein SR, Whittington PF, Orenstein DM. The infant seat as treatment for gastroesophageal reflux. *N Engl J Med.* 1983;309:760-763.
  30. Borrelli O, Salvia G, Campanozzi A, et al. Use of a new thickened formula for treatment of symptomatic gastroesophageal reflux in infants. *Ital J Gastroenterol Hepatol.* 1997;29:237-242.
  31. Bailey DJ, Andres JM, Danek GD, Pineiro-Carrero VM. Lack of efficacy of thickened feeding as treatment for gastroesophageal reflux. *J Pediatr.* 1987;110:187-189.
  32. Orenstein SR, Magill HL, Brooks P. Thickening of infant feedings for therapy of gastroesophageal reflux. *J Pediatr.* 1987;110:181-186.
  33. Khoshoo V, Fried M, Pencharz P. Incidence of gastroesophageal reflux with casein and whey-based formulas. *J Pediatr Gastroenterol Nutr.* 1993;17:116-117.
  34. Vandenas Y, Hachimi-Idrissi S, Casteels A, Mahler T, Loeb H. A clinical trial with an "anti-regurgitation" formula. *Eur J Pediatr.* 1994;153:419-423.
  35. Tolia V, Lin CH, Kuhns LR. Gastric emptying using three different formulas in infants with gastroesophageal reflux. *J Pediatr Gastroenterol Nutr.* 1992;15:297-301.
  36. Sutphen JL, Dillard VL. Dietary caloric density and osmolality influence gastroesophageal reflux in infants. *Gastroenterology.* 1989;97:601-604.
  37. Orenstein SR. Effect of nonnutritive sucking on infant gastroesophageal reflux. *Pediatr Res.* 1988;24:38-40.
  38. Antman EM, Lau J, Kupelnick B, Mosteller F, Chalmers TC. A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts: treatments for myocardial infarction. *JAMA.* 1992;268:240-248.
  39. Werlin S. Dysphagia. In: Hoekelman R, ed. *Primary Pediatric Care.* 4th ed. St Louis, Mo: Mosby-Year Book Inc; 2001:1039-1043.
  40. Rudolph C. Gastroenterology and nutrition. In: Rudolph A, ed. *Rudolph's Pediatrics.* 20th ed. East Norwalk, Conn: Appleton & Lange; 1996:993-1122.
  41. Roy CC, Silverman A, Alagille D. Gastroesophageal reflux: sucking and swallowing disorders and diseases of the esophagus. In: Roy CC, Silverman A, Alagille D, eds. *Pediatric Clinical Gastroenterology.* 4th ed. St Louis, Mo: Mosby-Year Book Inc; 1995:163-170.
  42. Shaffer S. Gastroesophageal reflux. In: Liacouras C, ed. *Clinical Pediatric Gastroenterology.* New York, NY: Churchill Livingstone Inc; 1998:181-186.
  43. Gold D, Pettei M. Gastroesophageal reflux. In: Finberg L, ed. *Saunders Manual of Pediatric Practice.* Philadelphia, Pa: WB Saunders Co; 1998:494-496.
  44. Wasserman D. Gastroesophageal reflux. In: Schwartz M, ed. *The 5 Minute Pediatric Consult.* 2nd ed. Philadelphia, Pa: Lippincott William & Wilkins; 2000:378-379.
  45. McEvoy C. Sucking and swallowing disorders and gastroenterology. In: McMillan J, ed. *Oski's Pediatrics: Principles and Practice.* 3rd ed. Philadelphia, Pa: Lippincott William & Wilkins; 1999:319-320.
  46. Berg A. Clinical practice guideline panels: personal experience. *J Am Board Fam Pract.* 1996;9:366-370.
  47. Orenstein SR, Shalaby TM, Cohn JF. Reflux symptoms in 100 normal infants: diagnostic validity of the Infant Gastroesophageal Reflux Questionnaire. *Clin Pediatr (Phila).* 1996;35:607-614.