

One-Year Follow-up of Symptoms of Gastroesophageal Reflux During Infancy

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ABSTRACT. *Objectives.* 1) Determine what percentage of infants outgrow regurgitation over 1 year. 2) Determine whether they develop feeding or mealtime problems. 3) Determine whether they develop frequent respiratory illnesses, including ear, sinus, and upper respiratory infections, or wheezing episodes.

Design. One-year follow-up survey of parents of children identified at 6 to 12 months of age as those who regurgitate (case subjects) and matched control subjects.

Participants. Sixty-three case subjects and 92 control subjects attending 12 different (urban, suburban, and rural) practices in the Pediatric Practice Research Group in the Chicago area.

Primary Outcome Measures. The Infant Gastroesophageal Reflux Questionnaire–Shortened and Revised Form and the Children’s Eating Behavior Inventory (CEBI).

Results. At 1-year follow-up, no parents of case or control subject described spitting up as currently a problem. The parent of only one control subject (and no case subject) reported spitting up one or more times a day. Parents of subjects were more likely than those of control subjects to report frequent feeding refusal: odds ratio = 4.2, adjusted by age (95% confidence interval: 1.4–12.0). Case and control subjects had comparable average total CEBI scores (case subjects, $\bar{x} = 83 \pm 10$ vs control subjects, $\bar{x} = 82 \pm 11$) and comparable average proportion of items identified as a problem ($8\% \pm 11\%$ case subjects vs $6\% \pm 9\%$ control subjects). Case subjects were more likely to respond positively to two CEBI questions indicating specific feeding problems: 1) “my child takes more than an hour to eat his/her meals” (8% case subjects vs 0% control subjects) and 2) “I get upset when I think about our meals” (14% case subjects vs 4% control subjects). The frequencies of ear, sinus, and upper respiratory infections and of episodes of wheezing were comparable in both groups.

Conclusions. 1) Infants with daily or problematic regurgitation at 6 to 12 months of age outgrew this within the following year. 2) Infants with daily or problematic regurgitation were more likely to develop feeding problems. 3) There was no increase in respiratory illnesses in infants with a history of regurgitation. *Pediatrics* 1998; 102(6). URL: <http://www.pediatrics.org/cgi/content/full/102/6/e67>

102/6/e67; gastroesophageal reflux, infants, practice-based research, epidemiology, feeding problems, natural history.

ABBREVIATIONS. GER, gastroesophageal reflux; IGER–SF, Infant Gastroesophageal Reflux Questionnaire–Shortened and Revised Form; CEBI, Children’s Eating Behavior Inventory.

Information on the natural history of regurgitation is important so that practicing physicians can give valid anticipatory guidance to parents regarding this common symptom and monitor infants appropriately with this problem for later difficulties. Although many complications of gastroesophageal reflux (GER) have been described,^{1–4} the likelihood of these is unknown because longitudinal data regarding the natural history of GER are lacking. Carre,⁵ based on retrospective analysis, reported that GER resolved without treatment by 2 years of age in 60% to 65% of patients who also had associated hiatal hernias. Because these patients reflect a subset of patients requiring subspecialty care, the data cannot be generalized to children seen in a primary care setting.

Available clinical information suggests that feeding and mealtime problems can be a part of the natural history of some infants with GER. Refusal to eat has been described as a manifestation of GER.³ In a retrospective chart review of 600 children younger than 2 years of age with GER, Dellert and colleagues found 25 (4%) with resistance to oral feedings severe enough to result in tube feedings for nutritional support.² No published prospective study has examined the prevalence of feeding problems in infants with GER. Recent studies suggest that GER is sometime associated with respiratory illness, but the prevalence of the association is also unclear.⁶

To determine the prevalence of symptoms associated with overt GER during the first year of life, we have reported on the findings of a cross-sectional survey.⁷ We now report on the 1-year follow-up of this cohort of children with symptoms consistent with GER and of matched control subjects.

The data address the following questions: 1) What percentage of children outgrow their regurgitation? 2) How often do feeding or mealtime problems in general and food aversion specific to milk follow regurgitation during infancy? 3) Are infants who regurgitate at increased risk for respiratory illnesses,

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including ear, sinus, and upper respiratory infections or wheezing episodes?

METHODS

Sample

Parents of healthy infants 6 to 12 months old were identified in 1995 as case subjects (with regurgitation) or control subjects (no regurgitation) from a survey of 948 parents of 0- to 12-month-olds⁷ (355 were 6 months or older) attending 12 different practices in the Pediatric Practice Research Group (affiliated with Children's Memorial Hospital).^{8,9} Children 6 months of age and older were chosen to be followed because based on a previous study,⁷ they were likely to have "outgrown" their regurgitation at follow-up. No children had any known medical or behavioral problems that would predispose them to GER disease or feeding problems. Case subjects were identified by parents who described that spitting up was a problem for their child (28%) or reported that their child spit up one or more times a day (10%). Although the previous study suggests that these symptoms can commonly occur at this age, we hypothesized that these factors might have an impact on subsequent feeding behavior. Control subjects were matched to case subjects by age and practice strata.

Follow-up Procedure

This report is based on data obtained when the parents completed mailed follow-up surveys 1 year later. From June to September 1996, follow-up surveys (described below) were mailed to 192 parents. Surveys were not mailed to 163 eligible parents because they did not consent to follow-up. When parents did not respond, up to three additional surveys were mailed. Eighty-one percent of eligible participants (63 case and 92 control subjects) completed the follow-up questionnaires.

Tools

Parents were asked to complete two surveys concerning their child: The Infant Gastroesophageal Reflux Questionnaire–Shortened and Revised Form (IGER–SF) and the Children's Eating Behavior Inventory (CEBI). They also were asked several additional questions regarding the child's health history and milk consumption. The IGER–SF is based on The Infant Gastroesophageal Reflux Questionnaire, an instrument developed by Orenstein and colleagues to improve history-taking of infants with suspected GER.¹⁰ The IGER–SF had been completed by the parents in the initial study.⁷ Studies using the IGER have found this tool to be reliable and valid,^{10–12} and the IGER–SF also has been found to be reliable.⁷

The CEBI is a valid and reliable instrument that assesses eating and mealtime problems in children.¹³ It consists of 40 items: 28 pertain to the child's food preferences, motor skills, and behavioral compliance; and 12 assess parent–child behavior interaction, parents' feelings about feeding the child, and interactions between family members. For each item, the respondent indicates on a 5-point Likert response scale how often the behavior occurs and whether it is perceived as a problem (yes/no). The scale generates two scores: the total eating problem score is based on the Likert scale responses and indicates the frequency of the problem listed; a second score indicates how many of the 40 items are perceived to be a problem (range, 0% to 100%).

Six additional questions were asked at follow-up that had not been asked at baseline: four on the frequency of ear, sinus, and upper respiratory infections and of wheezing episodes; and two on the frequency and enjoyment of milk consumption.

The reliability of the CEBI was assessed using test–retest consistency. Case subjects and control subjects were compared on the various measures. Mean, median, and standard deviation were calculated for numerical variables, and percentage was calculated for categorical variables. Mean values were compared using the two-sample *t* test and analysis of variance with age as the covariate. Proportions were compared using the χ^2 or Fisher's exact test. Multiple logistic regression analysis was used to calculate odds ratios for discrete outcomes.

This study was approved by the Institutional Review Board at Children's Memorial Hospital.

RESULTS

Reliability of the Survey Instruments

To assess CEBI reliability, 27 parents were called within 2 weeks after they returned the follow-up surveys, and the CEBI questionnaire was repeated over the telephone. The median proportion of agreement for each question on the survey for the 5-point Likert response scale was 0.82, with a range of 0.23 to 1.00. The median proportion of agreement for each item indicating whether it was perceived as a problem was 0.94, with a range of 0.66 to 1.00.

Description of Study Respondents

Table 1 presents the characteristics of the study subjects and responding parents. Surveys were completed from 155 parents attending 12 pediatric offices (range, 2 to 52 surveys/office). The only characteristic that was statistically different between case and control groups was initial age; the mean difference between the case subjects (range, 7.2 months) and control subjects (range, 8.2 months) was not clinically significant. Most of the parent respondents were mothers who were white and college graduates.

IGER–SF and Respiratory Symptoms

Tables 2 and 3 show the symptoms of GER initially and at 1-year follow-up. Initially, by definition, case subjects but not control subjects reported that spitting up was a problem for their child or reported that their child spit up one or more times a day. At 1-year follow-up, no parents of case or control subjects described spitting up as currently a problem. Only one control subject and no case subject was reported to spit up one or more times a day (Table 1). At baseline, both case and control subjects rarely reported feeding refusal. At 1-year follow-up, case subjects were more likely than were control subjects to report frequent feeding refusal (Table 2) (odds ratio = 4.2 adjusted by age; 95% CI: 1.4–12.0).

At 1-year follow-up, there were no significant differences between case subjects and control subjects in refusal of feeding when hungry, irritability, irritability with feeding, back-arching, choking or gagging with feeding, or abdominal pain. The mean frequencies in the past 6 months of ear infections (1.8 for case subjects vs 1.7 for control subject), sinus infections (1.3 for case subjects vs 1.2 for control subjects), and wheezing (1.2 for case subjects vs 1.2 for control subjects) were comparable in both groups ($P > .05$). The proportion of parents reporting frequent upper

TABLE 1. Characteristic of Infants and Their Parents Enrolled in the Study

Characteristic	Case (<i>n</i> = 63)	Control (<i>n</i> = 92)	<i>P</i>
\bar{x} Initial age in months (range)	7.2 (6–12)	8.2 (6–12)	< .001
\bar{x} Birth weight (kg) (range)	3.5 (2.1–4.4)	3.6 (2.3–4.9)	NS
Gender (% male)	57	49	NS
Race (% white)	97	92	NS
Maternal education (% college graduate)	60	63	NS

TABLE 2. Symptoms of GER: Initial and at 1-Year Follow-up

	% Positive	
	Case	Control
Spitting up a problem		
Initial	38	0
1-year follow-up	0	0
Spitting up ≥ 1 time/day		
Initial	94	0
1-year follow-up	0	0

TABLE 3. Feeding Refusal: Initial and 1-Year Follow-up

	% Positive	
	Case	Control
Feeding refusal		
Initial	0	3
1-year follow-up	19	9

respiratory infections in the past year also was comparable (16% for case subjects vs 9% for control subjects; $P > .05$).

CEBI and Milk Consumption

Case and control subjects were similar in the average total CEBI scores (case subjects, $\bar{x} = 83 \pm 10$ vs control subjects, $\bar{x} = 82 \pm 11$; $P = .5$), and the proportion of items identified as problems ($8\% \pm 11\%$ case subjects vs $6\% \pm 9\%$ control subjects; $P = .2$). Parents of case subjects were more likely to report two feeding issues as problems: 1) "my child takes more than an hour to eat his/her meals" (8% case subjects vs 0% control subjects; $P = .01$), and 2) "I get upset when I think about our meals" (14% case subjects vs 4% control subjects; $P = .05$). On two other questions, parents of case subjects tended to report more problems than did parents of control subjects, but the difference did not reach statistical significance. These include 1) "my child takes food between meals without asking" (10% case subjects vs 2% control subjects; $P = .07$), and 2) "I let my child have snacks between meals if he/she doesn't eat meals" (16% case subjects vs 6% control subjects; $P = .06$).

Reports of daily consumption of milk and whether the child likes milk were similar between groups.

DISCUSSION

These data provide the first prospective longitudinal information regarding the natural history of GER during infancy and the subsequent development of feeding problems.

Natural History

The children followed in this study were normal infants and not known to have GER disease. Consistent with clinical experience, the data show that infants who regurgitated at 6 to 12 months of age were no longer doing so 1 year later. The natural history of regurgitation is important for anticipatory guidance because regurgitation is a common symptom during infancy. Based on these data, physicians can predict that when regurgitation lasts past 6 months of age it usually resolves over the following year. Toddlers

who continue to regurgitate regularly after that merit additional evaluation.

Feeding Problems

Reflux is well known to cause the unpleasant sensation of "heartburn" in older children and adults, and recent evidence by Feranchak on a small sample of infants ($N = 8$) suggests that it also is perceived as an unpleasant experience in infants.¹⁴ In that prospective study using split-screen video and pH probe monitoring, behaviors suggestive of discomfort (crying or frowning) were associated temporally with the onset of reflux in 17% of episodes.

It is widely known that food aversion may be seen when someone develops gastroenteritis and then subsequently avoids a particular food temporally associated with the illness, even though that food may not have been responsible for the malaise. Food aversions also are seen after chemotherapy or radiation therapy in cancer patients, with avoidance of foods consumed around the time of their noxious treatments.^{15,16} Classical conditioning would suggest that infants with uncomfortable reflux would learn to associate eating with discomfort and thus subsequently tend to avoid eating.

We hypothesized that the association of GER with eating would result in food aversion and mealtime problems. The data are consistent with this hypothesis. Feeding problems—including feeding refusal, meal times >1 hour, and parent reports that they feel "upset" during mealtime—were much more frequent after 1 year in patients with reflux than in control subjects. However, behavioral feeding problems are common even in control toddlers (for example, 9% of parents of control subjects reported feeding refusal), indicating that the etiology of feeding problems at this age is multifactorial.

We also hypothesized that infants who regurgitate would selectively avoid milk, because milk products (including formula) are consumed commonly during the months of regurgitating. Our data did not support this hypothesis. We presume that this is because the infants consumed a sufficient variety of foods while regurgitating to make their food aversion non-specific.

The data that feeding problems are more frequent after reflux suggest that it may be useful to screen infants with significant regurgitation for the development of subsequent feeding and mealtime problems. Additional research is needed to explore this possibility.

Additional studies also are needed to clarify the cause and nature of the feeding refusal and mealtime problems described. Although it seems likely that their etiology is usually behavioral, there are other possibilities. It is possible that the development of an undiagnosed esophagitis might explain these feeding problems. Alternately, Hyman suggests that the developing nervous system of infants exposed to acid in their esophagus may be vulnerable to develop an increased sensitivity to pain from GER, even in the absence of tissue damage.³

Respiratory Problems

The relationship between GER and various respiratory disorders is controversial.⁶ This study did not find that infants who regurgitated were more likely to experience an increased frequency of ear, sinus, or upper respiratory infections or wheezing episodes. It would be useful to confirm this negative finding with medical documentation regarding infections. Even if confirmed by such data, the negative findings on a cohort of basically healthy children may not be generalizable to ill patients with GER who present for specialty care.

Methodologic Considerations

Although regurgitation is a more frequent symptom of GER in infants than in older children,¹ it represents only a small percentage of actual reflux episodes. Yet most children who regurgitate do not receive radiologic or pH studies, and clinical decision-making usually is based solely on history such as the information obtained by the IGER-SF. It would be of interest to repeat the analysis we have performed in a representative cohort of pH-proven GER, but this may not be feasible.

Some Remaining Unanswered Questions

Additional studies are needed to determine whether an actual change in feeding behavior or a difference in parental perception explains the feeding problems described in this study. The data reported do not address whether physicians should be treating uncomplicated regurgitation in infants or what sort of treatments are most effective to reduce GER and the development of later symptoms. Future research should include randomized placebo-controlled trials of treatments for GER during infancy, with outcome measures that include not only reductions in regurgitation but also a reduction in later development of feeding and mealtime problems.

APPENDIX

The following pediatricians and nurse practitioners participated in the initial data collection for this study: Ilham Algayed, MD; Peter Baker, MD; Michael Bauer, MD; Barbara Bayldon, MD; Eileen Beaty, MD; Irwin Benuck, MD; Susan Bishop, MD; Constance Blade, MD; Pamela Boyd, MD; Kathleen Brady, MD; David Brotzman, MD; Richard Burnstine, MD; Karen Burton, MD; Walter Campbell, MD; Sheila Citron, MD; David Claus, MD; Joe Cooler, MD; Bob Cullen, MD; Michael Danzer, MD; Brenda Darrach, MD; Arthur Dechovitz, MD; Virginia DePaul, MD; David Dobkin, MD; Ann Doege, MD; James Downey, MD; Michael Eisenfeld, MD; David Farnsworth, MD; Diane Fondriest, MD; Irene Freeman, MD; Susan Fullerton, MD; H. Garry Gardner, MD; Timothy Gelleski, MD; Melanie Goodell, MD; Patrick Gries, MD; Christienne Grunenwald, MD; Deborah Gulson, MD; Sumner Hagler, MD; Linda Hamilton, MD; Alice Harrington, MD; Barbara Hartz, MSN; Liz Hawkes, MD; Mary Higgins, MD; Laurie Hochberg, MD; Julie Holland, MD; Pamela Huang, MD; Leela Jain, MD; Jerome Kaltman, MD; Regina Kammel, MD; Alex Kaminsky, MD; Kay Kelly, MD; Marta Killner, MD; T. Randall Kinsella, MD; Theresa Kracic,

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