
Posttussive emesis as a symptom of asthma in children

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Background: Emesis can be triggered by cough in children, and cough is a common symptom of asthma.

Objective: To explore the association between posttussive emesis and asthma in the pediatric population.

Methods: A questionnaire was distributed to parents of children between the ages of 2 and 17 years in the pediatric and allergy-immunology clinics at our institution from August 16 through November 3, 2008. Prevalence of posttussive emesis was determined and compared among children with physician-diagnosed asthma, children with no evidence of asthma, and those not formally diagnosed as having asthma but with surrogate markers suggestive of asthma. The predictive value of posttussive emesis was compared with those of known markers of asthma. The prevalence of gastroesophageal reflux and pertussis was evaluated because these conditions might also cause posttussive emesis.

Results: The prevalence of posttussive emesis was 33% in our study population of 500 children. Among those with physician-diagnosed asthma ($n = 122$), 56% reported a history of posttussive emesis. For patients not formally diagnosed as having asthma but with surrogate markers suggestive of asthma ($n = 62$), 71% had a history of posttussive emesis. Both of these were significantly higher than in those with no evidence of asthma ($n = 316$), in whom 16% reported a history of posttussive emesis ($P < .0005$). Children with posttussive emesis were significantly more likely to have asthma than those without posttussive emesis (odds ratio, 7.9; 95% confidence interval, 5.2–12). Neither pertussis nor gastroesophageal reflux accounted for the degree of posttussive emesis reported.

Conclusions: Posttussive emesis is more common among children with asthma than among nonasthmatic children. In children with cough and a history of posttussive emesis, asthma should be strongly considered in the differential diagnosis.

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INTRODUCTION

Cough is one of the most common presenting symptoms for children in the outpatient setting and is a frequent cause of consultation with a pediatric subspecialist.^{1,2} Determining the cause of the cough is often a challenge for physicians but is essential for guiding the management of these patients.

The diagnosis of asthma can be elusive, particularly in young children who may have suggestive symptoms but in whom objective data collection can be technically difficult.³ Even in older children, although pulmonary function testing can provide objective evidence of asthma, results may be normal in an asymptomatic child with mild asthma.⁴ Biomarkers, such as exhaled nitric oxide, might be helpful in quantifying inflammation, but its role in routine practice is still being defined.^{5,6} Ultimately the evidence to support a diagnosis of asthma relies on obtaining a thorough history, and

any historical clues that can help distinguish the asthmatic child from the nonasthmatic child will likely improve the management of these children.

Posttussive emesis has historically been associated with *Bordetella pertussis* infections, in which violent coughing paroxysms are often followed by emesis.⁷ Most of the medical literature on posttussive emesis refers to this association with pertussis. An exception is a case series reported by Schreier et al^{8,9} in 1987, in which patients had vomiting as the primary presenting symptom of asthma. These cases are presented as rare exceptions, with the intent of encouraging physicians to broaden the differential diagnosis of the vomiting patient. We hypothesized that posttussive emesis is actually common in children and is more common among those with asthma, thus making it a useful historical clue to help differentiate the origin of a child's cough.

METHODS

A questionnaire was distributed to the parents of patients between the ages of 2 and 17 years in the pediatric and allergy-immunology clinics at the Walter Reed Army Medical Center in Washington, DC, from August 16 through November 3, 2008. The front of the questionnaire contained demographic information and questions regarding whether the child had ever been diagnosed by a physician as having asthma, gastroesophageal reflux (GER), or pertussis. The back of the questionnaire contained asthma surrogate marker

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Has your child:	Never	Rarely	Occasionally	Frequently
Used a short acting inhaler for cough? (i.e. Albuterol, Proventil)				
Used a long acting inhaler for cough? (i.e. Flovent, Pulmicort, Advair)				
Had cough to the point that it caused him/her to throw up?				
Had cough at night when he/she was not otherwise ill?				
Had wheezing noted by a healthcare provider?				
Had shortness of breath more frequent or severe than other children of the same age?				
Been to the emergency room because of breathing problems?				
Been hospitalized overnight due to breathing problems?				

Has your child:	No	Yes
Been diagnosed with allergic rhinitis (hay fever) or eczema?		
Had a first degree relative (parent or sibling) diagnosed with allergies, asthma, or eczema?		

Figure 1. Asthma surrogate marker questionnaire. Responses were assigned points according to the following: 0, never; 1, rarely; 2, occasionally; and 3, frequently. Respondents who did not report asthma previously diagnosed by a physician and had a total score of 5 or greater were categorized in the probable asthma group.

questions to assess for the presence of symptoms typically correlated with asthma, such as use of inhalers, cough at night, cough with exercise, wheezing, or acute care visits for breathing problems (Fig 1). These questions were scored on a 4-point Likert scale: 0, never; 1, rarely; 2, occasionally; and 3, frequently. Questions relating to family history or personal history of allergic disease were scored as 0 or 1, resulting in a maximum asthma surrogate marker score of 23. History of posttussive emesis was queried within the asthma surrogate marker questions but was not counted toward the asthma surrogate marker score. Questionnaires were returned anonymously at the same clinic visit and incomplete questionnaires were discarded.

Patients were classified into 1 of 3 groups based on their responses: (1) asthma that was previously diagnosed by a physician; (2) no evidence of asthma; or (3) possible asthma. For this study, “possible asthma” was defined as a score greater than or equal to 5 on the questionnaire. This cutoff value was determined by calculating the sensitivity and specificity for each possible score for those with physician-diagnosed asthma. The prevalence of posttussive emesis and other asthma surrogate markers were determined for each group. Odds ratios (ORs) and positive and negative predictive values were calculated for posttussive emesis and for the 10 known asthma surrogate markers.

All patients between the ages of 2 and 17 years with completed questionnaires were included in the study. Patients younger than 2 years were excluded because of the high incidence of physiologic reflux during infancy and the fact that the high number of well-child visits during the first 2 years of life might have skewed the study population toward younger children. It was estimated that a study population of 408 patients would be required to detect a significant difference between groups, assuming a 10% prevalence of asthma in the population and 30% prevalence of posttussive emesis

among asthmatic patients vs 10% prevalence of posttussive emesis in the nonasthmatic population. The posttussive emesis prevalence estimates were based on the clinical experience of the authors.

All analyses were performed with SPSS statistical software, version 12 (SPSS Inc, Chicago, Illinois). Means were compared using a 2-sample *t* test, and proportions were analyzed between groups using the Fisher exact test. The ORs are presented with 95% confidence intervals (CIs). All *P* values are 2-tailed. All responses were anonymous, and the study was conducted under an approved institutional review board human use exempt protocol through the Walter Reed Army Medical Center Department of Clinical Investigation.

RESULTS

The questionnaire was distributed to 660 parents and the estimated compliance with completion of the questionnaire was 76%. The final study population consisted of 500 children with a mean age of 9.15 years and a male:female ratio of 45:55. More than 95% of the questionnaires were completed in the pediatric clinic, where an estimated 40% of patients during the study period were attending a well-child or routine follow-up visit.

Twenty-four percent of the patients had physician-diagnosed asthma, and these patients had a mean age of 9.6 years. Sixty-three percent were classified as not having asthma, and their mean age was 9.3 years. Twelve percent were classified as having possible asthma based on their asthma surrogate marker score. The mean age in this group was 7.3 years, significantly lower than either patients with physician-diagnosed asthma or those with no asthma ($P < .005$).

The overall prevalence of posttussive emesis reported was 33% (164/500). Among children with physician-diagnosed asthma, 56% reported a history of posttussive emesis. Among those with possible asthma, 71% reported a history of post-

tussive emesis. Prevalence in both of these groups was significantly higher than among children with no evidence of asthma, in whom only 16% reported a history of posttussive emesis ($P < .0005$). Figure 2 displays the frequency of reported posttussive emesis for each group. Of note, 58 patients (12%) reported posttussive emesis occurring occasionally or frequently.

Scores on the asthma surrogate marker questionnaire were compared between those with physician-diagnosed asthma and those without the diagnosis. The sensitivity and specificity were calculated for each score, and based on receiver operating characteristic curve analysis, a score of 5 was verified as the best predictive value for physician-diagnosed asthma (87% sensitivity and 89% specificity). Patients with a score of 5 or above and not formally diagnosed as having asthma were considered to have possible asthma. These patients were shown to be statistically similar to patients with diagnosed asthma in the frequency of reported posttussive emesis and in 6 of 10 other asthma surrogate markers (Table 1).

Posttussive emesis was reported nearly 8 times more frequently in patients with physician-diagnosed or possible asthma compared with those with no evidence of asthma (OR, 7.9; 95% CI, 5.2–12). Table 2 describes how posttussive emesis compared with the other asthma predictors queried in terms of ORs and positive and negative predictive values.

Figure 3 illustrates the number of patients in the study group by age and the prevalence of reported posttussive emesis by age group. Although it appears to be more common among younger children, posttussive emesis was reported

Table 1. Parental Responses by Asthma Category

	Asthma, No. (%) (n = 122)	Possible asthma, No. (%) (n = 62)	No asthma, No. (%) (n = 316)
Admissions for breathing problems	37 (30) ^a	13 (21) ^a	4 (1)
Controller use	78 (64) ^{a,b}	13 (21) ^a	2 (1)
Emergency department visits for breathing problems	83 (68) ^{a,b}	28 (45) ^a	12 (4)
Exercise cough	80 (66) ^a	40 (65) ^a	30 (9)
Family history of atopy	91 (75) ^a	48 (77) ^a	137 (43)
Night cough	93 (76) ^a	51 (82) ^a	62 (20)
Personal history of atopy	66 (54) ^a	27 (44) ^a	70 (22)
Posttussive emesis	68 (56) ^a	44 (71) ^a	52 (16)
Reliever use	108 (89) ^{a,b}	40 (65) ^a	25 (8)
Shortness of breath	92 (75) ^{a,b}	23 (37) ^a	16 (5)
Wheeze	95 (78) ^a	40 (65) ^a	14 (4)

^a $P < .005$ for asthma and possible asthma vs no asthma.

^b $P < .005$ for asthma vs possible asthma (remainder $P \geq .05$).

among all ages in the study group. The proportion of study participants who reported ever having posttussive emesis was 42% among children aged 2 to 6 years, 36% among children aged 7 to 11 years, and 18% among children aged 12 to 17 years. For patients younger than 6 years, the predictive value of posttussive emesis for asthma was higher than for the group as a whole (OR, 9.1; 95% CI, 4.6–18).

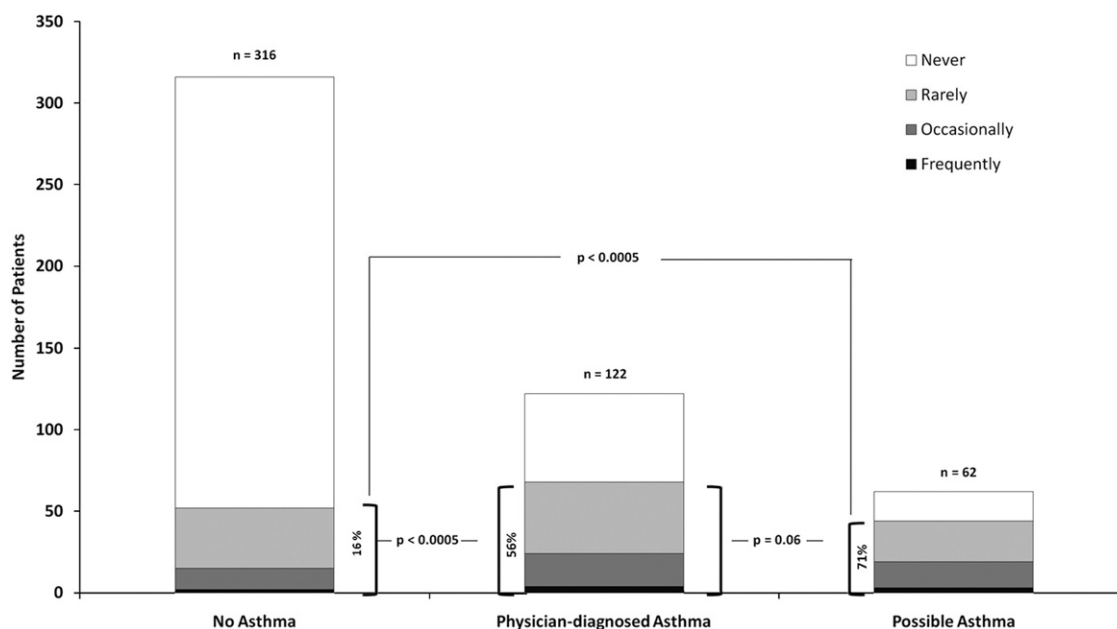


Figure 2. Frequency of reported posttussive emesis by asthma diagnosis group. Responses to the posttussive emesis question from patients without asthma, possible asthma, and reported physician-diagnosed asthma were compared. A statistical comparison of the proportions of each group reporting posttussive emesis of any frequency (rarely, occasionally, and frequently) was conducted using the Fisher exact test, with the lowest proportion in the no asthma group and highest in the possible asthma group.

Table 2. Predictive Values of Asthma Surrogate Markers

Predictor	OR (95% CI)	PPV, %	NPV, %
Admissions	29 (11–79)	93	70
Controller use	154 (41–576)	98	77
Emergency department visits	39 (20–73)	90	81
Exercise cough	18 (11–29)	80	82
Family history of allergic disease	4.1 (2.7–6.0)	50	80
Night cough	15 (9.4–23)	70	86
Posttussive emesis	7.9 (5.2–12)	68	79
Reliever use	48 (28–82)	86	89
Shortness of breath	31 (18–56)	88	81
Wheeze	59 (32–111)	91	86

Abbreviations: CI, confidence interval; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value.

Histories of pertussis and GER were evaluated as potential confounders that might lead to posttussive emesis. Twelve patients reported having been diagnosed as having pertussis (2.4%), and 10 of these 12 reported a history of posttussive emesis. Seven of these patients also had physician-diagnosed asthma.

Nearly 10% of our study population reported having been diagnosed as having GER (48/500). Twenty-seven of these patients (56%) had either physician-diagnosed or possible asthma (17 diagnosed, 10 possible), and 21 patients did not have evidence of asthma. Among those with no evidence of asthma, GER was associated with posttussive emesis (OR, 3.0; 95% CI, 1.2–7.7). Among those with either physician-diagnosed or possible asthma, there was no significant asso-

ciation between GER and posttussive emesis (OR, 1.3; 95% CI, 0.6–3.1).

DISCUSSION

In this survey of children attending the outpatient clinic of a large academic medical center, posttussive emesis was significantly associated with both physician-diagnosed asthma and possible asthma. Posttussive emesis had a predictive value similar to well-established markers of asthma.¹⁰ These results suggest that asking about posttussive emesis during evaluations of children with cough may improve our ability to recognize and treat patients with asthma.

In addition to being more common among asthmatic children, posttussive emesis was also more common among those with GER who did not also have asthma. There was not a significant association among asthmatic patients with GER primarily because there were many patients with asthma but no GER who reported having posttussive emesis. It is possible that the underlying mechanism for posttussive emesis in GER and in asthma is the same and that many asthmatic patients simply have undiagnosed GER.

Posttussive emesis was also more common among the few patients who reported being diagnosed as having pertussis. Although the incidence of pertussis has increased in recent years, this has been noted primarily with waning immunity in the adolescent and adult population.^{11,12} It is possible that pertussis was underdiagnosed, but pertussis could not account for the 33% of patients who reported posttussive emesis in this highly immunized study population or for the frequency of reported posttussive emesis. Because the diag-

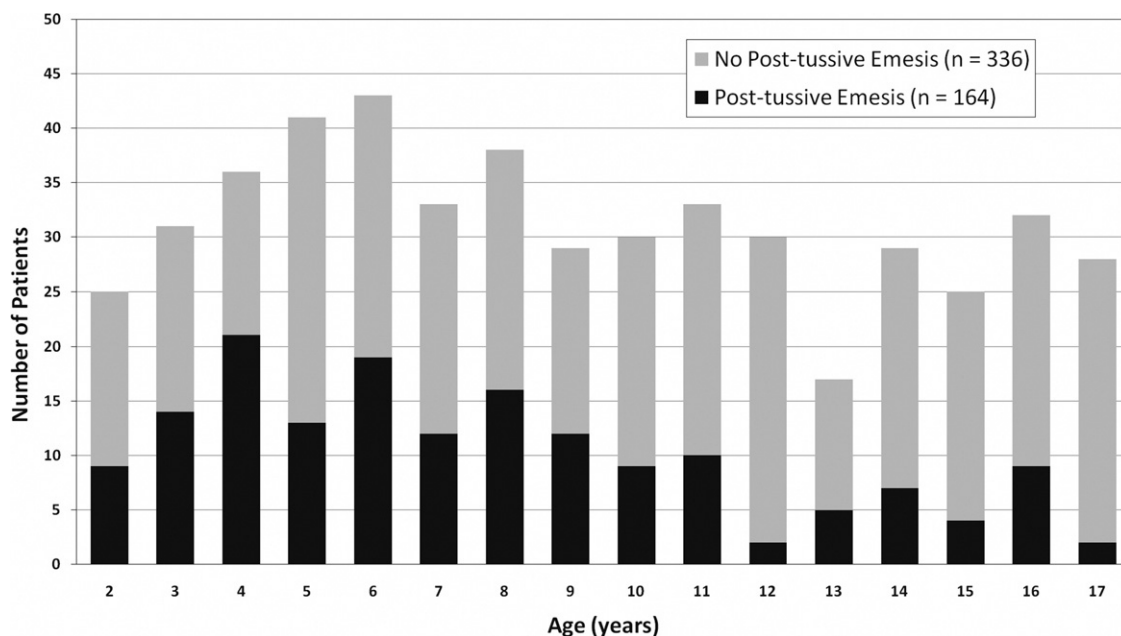


Figure 3. Age distribution of responses to the posttussive emesis question. The black portion of each stacked bar represents the number of patients responding yes to any frequency of posttussive emesis, and the shaded portion represents those responding never. The total number of responses was 500.

nosis of pertussis can be difficult to confirm, it is also possible that some of the patients diagnosed as having pertussis were simply asthmatic. Posttussive emesis should certainly be a red flag for pertussis, but it should not be considered pathognomonic.

It is important to acknowledge that posttussive emesis can be seen in conditions other than asthma, but asthma might be the most common condition resulting in posttussive emesis simply because of the frequency of cough in these patients. A higher negative predictive value than positive predictive value was observed. Taken together, the absence of a history of posttussive emesis may be more helpful in ruling asthma out as a diagnosis than the presence in establishing a diagnosis of asthma.

Posttussive emesis was more prevalent in children younger than 6 years, and the predictive value for asthma was higher among this age group than for older children. In this age group in whom pulmonary function testing can be technically difficult, asking about posttussive emesis might be particularly helpful in screening for asthma. Recall bias from underreporting by older children may partially explain this difference.

In addition to grouping patients as having physician-diagnosed asthma and no asthma, we thought it was important to identify patients with possible asthma. Patients with a diagnosis of asthma who are coughing will be treated for their asthma, but children whose conditions have not been formally diagnosed might escape recognition and proper treatment. Interestingly, the possible asthmatic group had a higher prevalence of posttussive emesis than the physician-diagnosed asthma group. Assuming that appropriate treatment of cough reduces the likelihood of posttussive emesis, this might reflect suboptimal treatment among the possible asthmatic children.

The prevalence of physician-diagnosed asthma in our study population (24%) was higher than in other published reports,^{10,13} which is not surprising considering the patients were selected from a pediatric and allergy-immunology clinic in a busy tertiary care center (as opposed to a mailed questionnaire sampling the general population). It is also possible that selection bias might have occurred, with patients having chronic cough or asthma being more likely to complete the questionnaire. With more asthmatic patients in our study population, the overall prevalence of posttussive emesis is likely an overestimate. We do not believe the higher prevalence of asthma encountered necessarily influenced the discordance of posttussive emesis seen between the asthma vs no asthma groups.

Objective measures, such as pulmonary function testing and bronchoprovocation challenge, can help establish the diagnosis of asthma in children old enough to perform them correctly. We did not use these measures because we included children as young as 2 years. Instead, we chose parental report of having been diagnosed as having asthma and a minimal score on an asthma screening tool to identify those most likely to have asthma. A possible limitation to the

study is the fact that the asthma surrogate marker questionnaire has not yet been validated, although the individual components have been shown to correlate with asthma in other asthma screening tools.^{14–19} To our knowledge, there are no available validated survey instruments that assess for the combined presence of asthma and posttussive emesis. If this screening tool is validated in the future, asking about symptoms within the past year and providing guidance regarding the frequency of symptoms would likely make it a better tool for evaluating current asthma.

The exact mechanism to explain posttussive emesis in asthma is uncertain, but a number of possibilities exist. It could be as simple as cough frequency; with asthmatic children coughing more often and being more likely to eventually cough and vomit. Another possibility is that children with asthma and hyperinflated lungs have flattening of the diaphragm and decreased gastric volume capacity, resulting in a higher likelihood of overfilling the stomach and resultant emesis. A third possibility is that increased negative intrathoracic pressure during inspiration in children with asthma results in a thoracoabdominal pressure gradient that is relatively more positive on the abdominal side of the diaphragm.^{20,21} This pressure gradient might change the anatomical configuration of the antireflux barrier or somehow affect lower esophageal sphincter tone, making reflux and emesis more likely in these children.

Previous literature regarding posttussive emesis focused almost exclusively on pertussis. We provide evidence that it is also a common symptom among children with asthma. Validation of asthma diagnostic and screening tools that incorporate posttussive emesis as a parameter should be considered. Future studies should also evaluate possible pathophysiologic mechanisms and whether these mechanisms also apply to other disease associations such as GER and asthma.

Despite recent technological advances in the field of asthma diagnostics, a thorough history remains the most powerful tool at the disposal of health care professionals. Questions on symptoms such as night cough and cough with exercise when a child is otherwise well have proven helpful in sorting out who might benefit from an inhaled β -agonist and who probably would not. Adding the question, “Does your child cough to the point that he/she throws up?” might also prove helpful in screening for asthma and in managing children with cough.

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