

Prospective Identification and Treatment of Children With Pediatric Autoimmune Neuropsychiatric Disorder Associated With Group A Streptococcal Infection (PANDAS)

Marie Lynd Murphy, MD; Michael E. Pichichero, MD

Background: The current diagnostic criteria for pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS) are pediatric onset, neuropsychiatric disorder (obsessive-compulsive disorder [OCD]) and/or tic disorder; abrupt onset and/or episodic course of symptoms; association with group A β -hemolytic streptococcal (GABHS) infection; and association with neurological abnormalities (motoric hyperactivity or adventitious movements, including choreiform movements or tics).

Objective: To assess new-onset PANDAS cases in relation to acute GABHS tonsillopharyngitis.

Design: Prospective PANDAS case identification and follow-up.

Results: Over a 3-year period (1998-2000), we identified 12 school-aged children with new-onset PANDAS. Each patient had the abrupt appearance of severe OCD behaviors, accompanied by mild symptoms and signs of acute GABHS tonsillopharyngitis. Throat swabs tested positive for GABHS by rapid antigen detection and/or were culture positive. The GABHS serologic tests, when per-

formed (n=3), showed very high antideoxyribonuclease antibody titers. Mean age at presentation was 7 years (age range, 5-11 years). In children treated with antibiotics effective in eradicating GABHS infection at the sentinel episode, OCD symptoms promptly disappeared. Follow-up throat cultures negative for GABHS were obtained prospectively after the first PANDAS episode. Recurrence of OCD symptoms was seen in 6 patients; each recurrence was associated with evidence of acute GABHS infection and responded to antibiotic therapy, supporting the premise that these patients were not GABHS carriers. The OCD behaviors exhibited included hand washing and preoccupation with germs, but daytime urinary urgency and frequency without dysuria, fever, or incontinence were the most notable symptoms in our series (58% of patients). Symptoms disappeared at night, and urinalysis and urine cultures were negative.

Conclusion: To our knowledge, this is the first prospective study to confirm that PANDAS is associated with acute GABHS tonsillopharyngitis and responds to appropriate antibiotic therapy at the sentinel episode.

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GROUP A β -hemolytic streptococcal (GABHS) tonsillopharyngitis occurs in school-aged children and causes sore throat, fever, headache, and abdominal pain. Peak seasonal occurrence is in the winter and spring months in temperate climates. Diagnosis is confirmed by throat culture, and treatment includes antibiotics. The sore throat illness is self-limited and will usually resolve in about 5 days, even without antibiotic treatment. Infection with GABHS leads to the production of serum antibodies, such as antistreptolysin O (ASO) and antideoxyribonuclease B (anti-DNase B). In certain individuals, infection and antibody production lead to end-organ damage, as antibodies cross-react with tissue of the kidney (post-

GABHS glomerulonephritis), heart (rheumatic fever), and brain (Sydenham chorea). Typically, nephritis occurs about 10 days after GABHS throat infection, and rheumatic fever occurs about 18 days after infection, whereas chorea occurs months later.¹ Because the throat culture may no longer be positive, diagnosis of post-GABHS nonsuppurative sequelae depends on a history of a positive throat culture in the preceding months or the presence of elevated titers of at least 1 of the streptococcal antibodies.²

Obsessive-compulsive disorder (OCD) is characterized by obsessions, the intrusive and unwanted thoughts or images that cause anxiety or distress, and compulsions, the actions performed to soothe the distress caused by the obsessions. The disorder is usually diagnosed

From the Elmwood Pediatric Group, University of Rochester Medical Center, Rochester, NY.

PARTICIPANTS AND METHODS

This prospective study was conducted at the Elmwood Pediatric Group, a primary care, pediatric office practice in suburban Rochester, NY. Patients were identified and followed during a 3-year time period, from 1998 to 2000. Children presenting with the abrupt, explosive onset of a significant new behavioral problem, such as OCD, tic disorder, age-inappropriate separation anxiety, or late age-onset attention-deficit/hyperactivity disorder (ADHD) were considered for admission to the study group. Children with long-standing behavioral symptoms presenting for initial care were not included. Once the explosive onset of behavior was identified, the presence of GABHS infection was investigated. If GABHS infection was present (positive throat culture at presentation or recorded in the medical record in recent prior weeks) or had occurred recently (as documented by an elevated ASO or anti-DNase B titer) a diagnosis of PANDAS was made, antibiotic treatment was rendered, and the patient was observed prospectively. Behavioral symptoms were reported by parents and/or observed in the office. Severity was estimated by the inability to attend school normally or the degree to which symptoms interfered with family routines.

No patient had been previously diagnosed with acute rheumatic fever, Sydenham chorea, Tourette syndrome, or ADHD. One child had transient Bell palsy after varicella. Another child had acute onset of OCD behavior in 1997, but she entered our study group during a recurrence of OCD symptoms when it was first recognized that she had PANDAS. Subsequent medical record review was used to determine the GABHS history in prior years. As with patients presenting with rheumatic fever, the presence of GABHS infection was determined by throat swabs tested by rapid antigen-detection assay (Acceava; Thermo BioStar, Inc, Boulder, Colo) or throat culture on sheep blood agar plates in the Elmwood Pediatric Group office laboratory (Clinical Laboratory Improvement Act level 3 certified). The GABHS antibody titers (ASO and anti-DNase B) were quantitated at commercial laboratories. Analyses of anti-neuronal antibodies were performed as previously described¹⁵ (courtesy of John Zabriskie, PhD).

Once identified, patients with PANDAS were followed prospectively to document improvement of the OCD behavior by parent report and, in some cases, independent psychiatric evaluation. Improvement in tic behavior was documented by a physician. Serial titers or follow-up throat cultures documented resolution of the initial acute GABHS infection. Patients were instructed to return for evaluation if fever, sore throat, or recurrence of behavioral symptoms occurred. The time course of onset was again documented, patients were examined, and rapid antigen-detection assay or throat culture for GABHS was performed. If there was no evidence of GABHS on initial throat culture, patients were instructed to return in 3 days for another culture.

in adolescence in men and early adulthood in women, and it has a lifetime prevalence of 2% to 3%. Comorbid conditions include depression, tics, and anxiety disorders. Typically, there is a slow, insidious onset over months to years before diagnosis.³ Children with Sydenham chorea also exhibit OCD.⁴ In one series, 70% of those with Sydenham chorea had sudden-onset OCD.⁵

Pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS) is a recently described entity that may be similar in mechanism to other nonsuppurative post-GABHS disorders. Unlike typical patients with OCD, children with PANDAS develop sudden-onset OCD or tic behavior shortly after GABHS infection. The working criteria for a diagnosis of PANDAS are (1) presence of OCD and/or tic disorder; (2) pediatric onset; (3) abrupt onset and episodic course; (4) association with GABHS infections; and (5) association with neurological abnormalities, such as motoric hyperactivity, choreiform movements, or tics.^{6,7}

To date, most knowledge about PANDAS has been obtained by studying patients with a known tic disorder or long-standing OCD in research facilities and referral centers.^{6,8-12} The authenticity of PANDAS has been questioned.^{13,14} We describe 12 patients in a primary care practice identified at the onset of a first episode of PANDAS and followed prospectively to address questions about age of onset, sex predominance, seasonal occurrence, relationship to GABHS infection, and response to antibiotic treatment. We conclude that there is an association between sudden onset of neuropsychiatric symptoms, especially OCD, and GABHS tonsillopharyngitis in some previously healthy children.

RESULTS

CASE REPORT

A 5-year-old boy suddenly developed frequent daytime urination (**Table**; patient No. 7). The onset was pinpointed to one evening. He voided, then immediately felt the urge to void again, producing only drops of urine. This behavior peaked in the morning when he was trying to catch the school bus. There was no fever, dysuria, or incontinence. The symptoms did not occur through the night.

This obsession with urine and the compulsive need to repeatedly urinate increased over 7 days, along with the acute onset of an age-inappropriate separation anxiety. He cried for hours when his mother left for work and he was left in the care of his father.

On examination, marked tonsillopharyngeal erythema, an impetiginous lesion at the corner of the lip, and moderate cervical adenopathy were present without fever or tonsillar enlargement. A throat culture was positive for GABHS. A cephalosporin was prescribed, and within 6 days, his compulsive need to urinate ended, his separation anxiety improved, and he was attending school normally.

A month later, the patient returned with another abrupt onset of compulsive urination, separation anxiety before school, and a mild sore throat. On examination, the posterior pharynx was intensely red, without enlargement of the tonsils, fever, or adenopathy. Throat culture and rapid antigen-detection assay were both nega-

Demographic and Disease Characteristics of 12 Patients With PANDAS*

Patient No./Sex/Age, y	Month of OCD Onset	Sudden Onset	OCD Behaviors†	Tics/ADD	No. of Recurrences
1/M/10	April	Y	1, Confessions, household items	N	0
2/M/5	October	Y	1	Tics	0
3/F/10	September	Y	2	N	0
4/M/5	October	Y	2	N	0
5/F/6	October	Y	2, 3	N	1
6/F/7	December	Y	1, 4	N	0
7/M/5	February	Y	1, 2	N	1
8/M/9	March	Y	Fear of failure	ADD	0
9/F/6	April	Y	2, Symmetry	N	2
10/M/5	April	Y	2	Blinking tic	2
11/M/5	November	Y	Negativity	Blinking tic	4
12‡/F/6	March	Y	1, 2, 3, 5, Colors	N	6

*PANDAS indicates pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection; OCD, obsessive-compulsive disorder; ADD, attention-deficit disorder; M, male; and F, female.

†For OCD behaviors: 1 indicates fear of harm to self or others/avoids separation; 2, urinary frequency/toilet hygiene; 3, germ related; 4, hoarding germs; and 5, hand washing.

‡Patient joined the study when OCD recurred and PANDAS was first diagnosed.

tive for GABHS. The patient was instructed to have another throat swab in 72 hours, which was positive for GABHS. He was treated with a cephalosporin, and, in 5 days, his OCD behaviors and anxiety had normalized. The findings from the follow-up examination were normal, the throat culture was negative for GABHS, and symptoms did not recur during 12 months of follow-up.

AGE, SEX, AND SEASONAL PATTERN

Data summarizing age, sex, month of OCD onset, neuropsychiatric symptoms, and recurrences for the 12 cases of PANDAS in our series are shown in the Table. Mean age was 7 years (age range, 5 years 4 months, to 10 years 11 months). The sex ratio showed a predominance of boys (1.4:1), and the months of initial OCD episode were September through April.

NEUROPSYCHIATRIC SYMPTOMS

All patients had abrupt onset of neuropsychiatric symptoms, and 7 (62%) of 12 patients could pinpoint the day symptoms started. All patients had obsessive thought patterns, 75% of which were germ- or illness-related, causing compulsive hand washing or excessive toilet hygiene rituals. One child compulsively hoarded items her germs had touched. Seven children (58%; including 4 [80%] of the 5 girls) exhibited a pattern of compulsive daytime urinary urgency, frequency, and wiping without fever, dysuria, or nighttime symptoms and without evidence of urinary tract infection by urinalysis or urine culture. Forty-two percent of patients experienced a new onset of extreme and age-inappropriate separation anxiety when leaving their mothers. This symptom was manifest especially in the morning before the school bus arrived, with children physically clinging to their parents' legs and refusing to part. The oldest child in the series was able to verbalize his obsessive, irrational fear of dying or being sent to prison, but the younger children with this compulsive need to be with their mothers could not verbalize the thoughts leading to this behav-

ior. Four (33%) of 12 children had clear-cut neurologic abnormalities. Two boys had recurrent tics, including head tilting, nodding, and eye blinking. One of these patients showed negative and aggressive behaviors. One boy had transient ADHD-like symptoms, including fidgeting, memory impairment, and deterioration of handwriting. No patients had classic chorea, but the 1 patient most severely affected exhibited choreiform finger movements. All patients were emotionally labile and exhibited motoric hyperactivity during these episodes.

The first 4 patients were referred for psychiatric evaluation because the severity of their symptoms interfered with daily activities. Three were incapacitated and unable to leave the home. In each patient, OCD with or without anxiety was confirmed by history, but the patients had already improved following antibiotic treatment by the time of psychiatric evaluation several weeks later. Subsequent patients with similar symptoms and severity were followed through the pediatric office without referral to psychiatric care. The severity of the illness was determined by parental report. All patients met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*¹⁶ criteria for severe OCD because they were unable to attend or function at school or child care. The Children's Yale-Brown Obsessive-Compulsive Scale¹⁷ criteria of time spent, interference, distress, resistance, and control over obsessions would place these children in the category of severe to extreme severity.

ASSOCIATION BETWEEN OCD SYMPTOMS AND GABHS INFECTIONS

Evidence of a clear-cut, temporal relationship between the abrupt onset and/or exacerbation of OCD symptoms and acute GABHS tonsillopharyngitis infection was established by prospective throat swab testing in most patients. Antistreptococcal antibody titers were obtained in a subset for whom the throat cultures were not concurrently positive with behavior changes. A notable feature of the tonsillopharyngitis episodes was the lack of sever-

ity. Few children had fevers, and their sore throats were mild. The tonsillopharynx was moderately to intensely red, but exudate was scant or absent and cervical adenopathy was minimal. None of these children displayed the typical features of classical severe GABHS tonsillopharyngitis, although 1 patient had scarlet fever rash.

There was a latent period between GABHS infection at a remote time and GABHS infection triggering PANDAS. The Elmwood Pediatric Group practice had cared for most patients since birth and all for at least a year before the onset of PANDAS. Eleven (92%) of 12 patients had a documented GABHS illness (range, 1-7 illnesses) prior to the GABHS illness that triggered OCD; 1 had no documented prior GABHS illness but had febrile lobar pneumonia associated with a sore throat. Eight (67%) of 12 patients had 4 or fewer episodes of GABHS infection before they developed PANDAS; the 4 patients who had no recurrences of OCD were all in this group. Four (33%) of 12 patients had 5 or more episodes of GABHS infection; the patients with the most OCD recurrences, and the most severe OCD, were in this group.

SENTINEL EPISODE OF OCD

When new-onset OCD symptoms occurred, evidence of GABHS infection in recent weeks was sought to establish the diagnosis of PANDAS. Ten (83%) of 12 patients had a throat culture or rapid antigen-detection assay negative for GABHS within 3 months before the new GABHS infection associated with OCD, which suggests that they were not carriers; 7 of these patients had a negative rapid antigen-detection assay or throat culture within 1 month before the new infection. Documented GABHS infection from throat swabs during a clinical episode of pharyngitis (in 1 case, scarlet fever) occurred at presentation in 6 of 12 patients or within 1 month in 4 of 12 patients prior to the initial episode of OCD, for a total of 10 (83%) of 12 patients. Of the remaining 2 patients, 1 had clinical pharyngitis with a negative rapid antigen-detection assay 11 days before the new GABHS infection but a documented elevated anti-DNase B titer (>1360) at onset of OCD. One patient (with 7 previous episodes of GABHS) had documented GABHS 3 months before and underwent a tonsillectomy without antibiotic treatment 1 month prior to the onset of OCD. She was included in the study when we first recognized PANDAS at a recurrence of the GABHS infection. Nine (75%) of 12 patients had a documented follow-up throat culture negative for GABHS within 1 month of treatment. Of the remaining 3, 1 had a decrease in anti-DNase B titer over 6 months (>1360 to 960). The remaining 2 had clinical improvement but no throat culture obtained at the end of treatment.

RESPONSE TO ANTIBIOTIC TREATMENT AT THE SENTINEL PANDAS EPISODE

All patients were treated with 10 days of an antibiotic effective for eradication of GABHS infection. It is the practice of the Elmwood Pediatric Group to prescribe penicillins or cephalosporins when GABHS infection occurs. Five of our patients received penicillin (or amoxicillin because of taste preference); 1 patient received amoxicillin/

clavulanate potassium, and 6 received a cephalosporin. In each sentinel episode in our series, initiation of antibiotic therapy appeared to lead to prompt improvement in OCD symptoms. In the 4 patients with no subsequent recurrences, behavior was normal in 5 to 21 days. The mean time to resolution of symptoms was similar in patients treated with penicillin or amoxicillin (14 days) compared with those treated with a cephalosporin; however, 2 patients treated with a cephalosporin showed the fastest symptom resolution (5 and 6 days).

RECURRENCE OF PANDAS

Six (50%) of 12 patients had at least 1 distinct recurrence of OCD. Two patients had 1 recurrence, 2 had 2, 1 had 4, and 1 had 6, for a total of 16 recurrent episodes in these 6 patients. The 2 patients with the most recurrences both experienced more than 6 episodes of GABHS prior to the GABHS infection that triggered PANDAS. Both patients developed a waxing and waning course. In every instance, the recurrence of PANDAS behavior was associated with a GABHS infection. Fourteen (87%) of the 16 recurrent OCD episodes were preceded by a documented throat culture negative for GABHS 1 to 3 months prior to illness, suggesting that the patients were not chronic GABHS carriers. All recurrent cases had a documented throat culture or rapid antigen-detection assay positive for GABHS. All patients were treated with antibiotics (usually a cephalosporin), all had prompt improvement of their OCD symptoms, and all had a documented throat culture negative for GABHS after treatment. In no instance did a new recurrence of OCD occur in the absence of a new GABHS infection, nor did a GABHS infection occur without OCD symptoms recurring. In the patients with 1 or 2 recurrences, they occurred 1 to 6 months later. In each patient with multiple recurrences, the recurrences spanned the entire 3-year study period. Some parents identified a recurrence of behavioral symptoms even before the culture was positive for GABHS. They were instructed to return in 72 hours, and throat cultures were then positive. The OCD symptoms were similar to prior symptoms at recurrence.

SEROLOGIC TESTING

Serologic tests for acute GABHS were conducted on 3 children. Titers for anti-DNase B were elevated above the laboratory reporting range (>1360) for 2 patients at the onset of the neuropsychiatric episodes. Two patients also had elevated ASO titers (2- to 3-times the normal level) at the time of the PANDAS diagnosis. One patient was tested for antineuronal antibodies⁹ and they were detected.

COMMENT

The identification and prospective observation of 12 children with PANDAS provided an opportunity to address several important questions about the disorder.

AGE, SEX, AND SEASONAL OCCURRENCE

The children with PANDAS had an age of onset (5-12 years old) and seasonal occurrence (September-April)

similar to the peak age and seasonal occurrence of GABHS tonsillopharyngitis,¹ which is not surprising because PANDAS is associated with GABHS infection. In our practice, the peak of GABHS infection occurs between September and April.¹⁸ Boys were more commonly identified with PANDAS. Tics, GABHS, and OCD are more common in men.¹ The age of onset of classic OCD is much different than in our patient group; OCD usually has its onset in late adolescence or early adulthood.³ Previous studies of PANDAS have defined the disorder as prepubertal, with a predominance of boys affected.⁷

NATURE OF OCD SYMPTOMS

The nature of the OCD symptoms in our series is similar to other reports of OCD. Germ-related behaviors included repeated hand washing, hoarding of items germs had touched, and excessive toilet hygiene rituals. In most studies, women show more washing behaviors, and men show more checking behaviors, aggressive behaviors, and comorbid tics.³ The specific complaint of compulsive urinary frequency was more common in this series than in general reports of obsessive-compulsive behavior.

NEUROPSYCHIATRIC SYMPTOMS ONSET AND GABHS INFECTION

At the sentinel episode of neuropsychiatric symptoms, onset was sudden and dramatic and, in every case, was associated with concurrent GABHS tonsillopharyngitis or a GABHS throat infection in the previous 4 weeks. A positive throat culture or rapid antigen-detection assay demonstrated the association. Streptococcal serologic tests (ASO and/or anti-DNase B) were conducted for 3 children and followed sequentially. However, as Swedo et al⁶ and others^{12,13} have pointed out, positive antistreptococcal titers obtained at the time of neuropsychiatric symptom exacerbation are not sufficient to prove that a child has PANDAS because titers may remain elevated for several months following an acute infection. After entering the study, cultures negative for GABHS were documented before the next positive GABHS culture associated with recurrence of PANDAS behavior changes.

The number of prior episodes of GABHS infection was the only factor that appeared to predict a more severe, relapsing course of PANDAS. The patients who did not have recurrences had fewer episodes of GABHS prior to PANDAS onset, and those with the most severe and relapsing course had the most episodes of GABHS before the onset of PANDAS. Those with the most recurrences developed more significant behavioral symptoms, which then began to wax and wane. Their OCD symptoms became more chronic and persistent. This result is consistent with the increased incidence and severity of OCD seen with recurrences of Sydenham chorea.¹⁹

The association of GABHS infection with symptom exacerbation was determined prospectively for all episodes. Data from rheumatic fever studies demonstrate that a GABHS infection can precede chorea symptoms by several months,² although the lag between subsequent infections and symptom exacerbation is much shorter, often only a few days to a week apart, suggesting an immuno-

logical memory response. Our finding of a new acute GABHS throat infection that triggers PANDAS preceded by a GABHS infection at least 6 months earlier is consistent with the same immune response pattern. Possibly, in the early stage of GABHS infection, an antibody is stimulated that may precipitate behavioral effects even days before the quantity of GABHS is sufficient to be detected by rapid antigen-detection assay or throat culture.

RESPONSE TO ANTIBIOTIC TREATMENT

Surprisingly, with antibiotic treatment appropriate for GABHS infection, our patients exhibited dramatic, rapid resolution of their sentinel OCD, anxiety, and tic symptoms. Resolution of symptoms occurred an average of 14 days after treatment began. This is in marked contrast to typical OCD, which evolves slowly and requires extensive treatment with cognitive behavioral therapy and/or medication to alleviate symptoms over months to years.³ Compulsive wiping and washing rituals disappeared first, and the obsessive thought patterns presumed to lead to the separation anxiety cleared more slowly (usually within several weeks) but completely. The rapid, apparent response to treatment suggests to us the possibility of a GABHS-associated toxin that is a mediator of PANDAS. We speculate about this possibility because such a response would not seem as likely if the process were autoimmune antibody-mediated. These observations did not occur in the context of a double-blind, randomized, controlled trial, so further examination of these potentially important findings is clearly needed.

AUTHENTICITY OF GABHS DIAGNOSIS

By definition, because these children displayed symptoms and signs of GABHS tonsillopharyngitis, albeit milder than the classic case, they were not carriers. The negative cultures before and after onset of OCD and before and after recurrences of OCD episodes further argue against the notion that these children were carriers. Third, GABHS carriers do not show antibody increases in response to streptococcal antigens. Although more than 60% of patients with rheumatic fever show significantly elevated ASO titers, those with chorea are less likely to exhibit elevated ASO titers, and multiple antibody tests, including anti-DNase B, may be needed to document bona fide GABHS infection.² When obtained, serologic test results showed the children had very elevated anti-DNase B and/or elevated ASO titers. However, we were struck by the absence of a strong inflammatory response (symptoms and signs) elicited by the GABHS strain infecting our patients. This is similar to the experience documented by Veasy et al²⁰ during recent acute rheumatic fever outbreaks.

Characterization of these strains of GABHS that are prone to the induction of PANDAS in the susceptible host will be of interest. The factors that confer susceptibility to the development of PANDAS, the possible association D8/17 B-lymphocyte antigen as a marker trait,²¹ the immune response associated with the development of the clinical symptoms, and identification of the anatomical structures involved in the expression of the clinical symptoms of PANDAS need to be explored. Might these chil-

What This Study Adds

The possible association between streptococcal infections and the sudden onset of neuropsychiatric disorders such as OCD and tic disorder has been described in the psychiatric literature and in patients with long-standing Tourette syndrome seen in research centers. This is the first prospective study in a primary care setting to confirm an association between sudden onset of a first episode of OCD, anxiety, ADHD, or tic disorder and streptococcal throat infections. It is also the first study to document the disappearance of neuropsychiatric symptoms during antibiotic treatment for streptococcal sore throat, the recurrence of behavioral symptoms with streptococcal sore throat, and the subsequent disappearance of symptoms with appropriate antibiotic treatment.

dren be rendered less susceptible by prevention of GABHS infection through antibiotic prophylaxis? Would immunization against GABHS, when it becomes available, be of benefit, or would it induce autoimmune antibodies?

The possibility that pathogens other than GABHS can induce neuropsychological symptoms⁶ was not confirmed in our study. Our findings do not support the postulate that GABHS needs to be the initial autoimmunity-inciting event, but that subsequent symptom exacerbations can be triggered by viruses, other bacteria, or noninfectious immunological responses.⁶ Previous PANDAS studies included children with long-standing Tourette syndrome.⁶ Our study and application of the PANDAS diagnostic criteria to an unselected private practice population suggest tics are not as common as previously reported, although several boys in our series had tics.

Comorbid symptoms (emotional lability, separation anxiety, and oppositional and age-inappropriate behaviors) were also episodic and temporally related to PANDAS in our patients. Some of these symptoms were present in all our patients, so we consider them manifestations of the PANDAS phenomenon. We concur with Swedo et al⁶ that perhaps the PANDAS syndrome should be expanded to include primary diagnosis of late-onset ADHD and age-inappropriate separation anxiety disorders, as well as OCD and tic disorders. In any case, the abrupt onset of OCD at an early age is quite distinct from the usual pattern of OCD characterized by gradual onset presenting in adolescence or early adulthood.³ The present study also identifies urinary frequency and urgency and associated toilet hygiene rituals as another OCD behavior common in patients with PANDAS.

The design of our study does not allow a determination of the incidence of children with neuropsychiatric disorders who have PANDAS. However, if physicians look for this disorder, the average community-based practitioner may see 1 to 3 new cases per year. This is far more common than rheumatic fever or poststreptococcal glomerulonephritis. Physicians caring for children should be aware of PANDAS because our study strongly suggests that appropriate antibiotic treatment directed at GABHS eradication at the sentinel episode of PANDAS may be of benefit. Fur-

ther studies to examine the best method of eradicating GABHS from the oropharynx and presumed circulating autoantibodies should be undertaken.

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Corresponding author and reprints: Michael E. Pichichero, MD, Elmwood Pediatric Group, University of Rochester Medical Center, 601 Elmwood Ave, Box 672, Rochester, NY 14642 (e-mail: michael_pichichero@urmc.rochester.edu).

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