Relationship of Movements and Behaviors to Group A Streptococcus Infections in Elementary School Children

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Background: *Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus (PANDAS) research is based on the hypothesis that infections trigger changes in behavior and movement in children.*

Methods: *We enrolled 693 children (ages 3 to 12 years) into a systematic, longitudinal study. Data were collected monthly for 8 months (October–May) to determine point prevalence of Group A Streptococcal (GAS) infections, tics, behavior, and choreiform movements. Simultaneous throat cultures were obtained, and relational analyses were made between GAS and movement/observation ratings.*

Results: *Combined behavior/GAS associations (concurrent with or 3 subsequent months to GAS) revealed a strong relationship, relative risk (RR) of 1.71 ($p < .0001$). Detailed analysis revealed that balance/swaying and non-tic grimacing were responsible for a significant proportion of this association ($RR = 2.92$, $p < .0001$). A strong seasonal pattern was found, with fall being more significant for GAS infections and observation ratings ($p < .0001$) compared with winter/spring. Children with repeated streptococcus ($n = 64$) showed higher rates of behavior and distal choreiform observations ($p = .005$).*

Conclusions: *Motor/behavior changes were noted to occur in relationship to positive GAS culture with support that repeated GAS increases risk.*

Key Words: ADHD, behavior, choreiform, group A streptococcus, PANDAS, tics

Investigation into a streptococcal-triggered etiology for obsessive compulsive disorder (OCD) has stimulated renewed interest in the relationship of behavior, tics, and choreiform movements to infection. Neurological symptoms, such as choreiform movements and tics, have been listed as criteria to support a diagnosis of Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcus (PANDAS) (Swedo et al 1998). Subsequently, debate has arisen on the definition of choreiform versus chorea. The word "chorea" derives from the *Greek* choreia, meaning "dance". The modern definition of chorea is an arrhythmic, rapid, often jerky movement that might be simple or complex. Chorea might be the only presenting feature of a disease, as it is in thyrotoxicosis (Pozzan et al 1992), or might be present as part of a spectrum of disease, as in Sydenham's chorea (SC). Chorea might be subtle, limited to a particular body region, and difficult to diagnose. For the purposes of this paper, the term "chorea" will be used to describe unsolicited spontaneous movement (observed in child at rest) and the term "choreiform movement" will be used to describe movement elicited by a clinician exclusively upon neurological examination (stressed posture) and generally manifesting as quick twitches of the fingers or undulating, writhing movements of the fingers, wrists, arms, elbows, or shoulders.

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Sydenham's chorea, a neurological sequelae to Group A streptococcus (GAS) infection, presents as a wide spectrum of symptoms that are both motoric (chorea and dysarthria) and behavioral (emotional lability, fidgetiness, anxiety) (Bronze and Dale 1993; Husby et al 1976; Taranta and Stollerman 1956). In recent outbreaks of rheumatic fever (RF) a large proportion (75% in one study) of individuals had only mild or no history of prior pharyngitis (Congeni 1992). These observations suggest that some strains of GAS associated with RF might not elicit symptoms of pharyngitis and thus escape detection and treatment, so that they are more likely to result in SC/RF. Furthermore, the severity of the adventitious movements range from mild to severe, and only those with impairing symptoms will come to medical attention.

The prevalence of PANDAS among children with OCD and/or tics is not known; one study reported 11% of children with tic disorders experienced abrupt onset or worsening of tics in the 6 weeks after streptococcus infection (Singer et al 2000). Children presenting with PANDAS have a variety of neuropsychiatric symptoms beyond the required sudden onset of OCD or tics, such as separation anxiety, nightmares, personality change, oppositional behavior, and deterioration in math skills and handwriting (Swedo et al 1998). During the acute phase, neurological abnormalities such as hyperactivity, tics, and/or choreiform movements are common but not diagnostic. For example, choreiform movements were noted to be present in over 90% of patients diagnosed with PANDAS (Swedo et al 1998) but are also noted in those without PANDAS course (Murphy et al 2004).

Tourette syndrome (TS) is more prevalent in the community than previously thought. Approximately 1% of school-age children are reported to have TS (Baron-Cohen et al 1999; Kadesjo and Gillberg 2000). In a study that investigated the prevalence and characterization of tics and problem behaviors in 553 elementary-school-age children, the monthly prevalence of motor tics ranged from 3.2% to 9.6% and problem behaviors ranged from 2.6% to 11% (Snider et al 2002). A seasonal correlation of tics and behaviors has been previously reported to occur with winter months (Kovalenko et al 2000; Murphy et al 2004; Snider et al 2002). Other researchers have investigated the possible

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association of a documented illness such as upper respiratory infection (URI) (Giulino et al 2002; Perrin et al 2004) at or near the time of OCD/tic onset. One found a relationship between URI and sudden/dramatic symptom onset ($p = .02$) along with a trend for the infection/sudden onset group to have higher scores on instruments measuring symptoms of attention-deficit/hyperactivity disorder (ADHD) (Giulino et al 2002). Associations were found between GAS and parent report of a recent change in certain behaviors, such as harder time paying attention, increased fidgetiness/restlessness, unusual clinginess/harder time with separation, unusual noises, repetitive behaviors, unusual urinary problems, and seeming more negative than usual (7 of 30 variables examined). This correlation was significant when comparing ill children with well children; there was no difference in GAS-infected children and those presumed to have viral infection (Perrin et al 2004). Perhaps one of the strongest studies to support the GAS association was a recent case-control study that used population-based data from a large health maintenance organization and assessed whether GAS infection was associated with increased risk for OCD or TS (Mell et al 2005). Patients with OCD or TS were more likely than control subjects to have had prior streptococcal infection in the 3 months before onset date and that having multiple GAS infections within a 12-month period was associated with a markedly increased risk for TS (odds ratio = 13.6) (Mell et al 2005).

The extent of GAS's contribution in the expression or manifestation of choreiform movements is not delineated. Group A streptococcus has already proven to be etiologically related to the onset of SC and RF and is postulated to serve as a trigger for some cases of childhood OCD. In a study that compared neuropsychiatric course and GAS titer fluctuations, streptococcal titers positively correlated with obsessive compulsive severity rating changes (Murphy et al 2004). The subject group that exhibited a PANDAS course showed a positive relationship between increase in tic severity and choreiform assessment 12 weeks later, suggesting a longer latency in choreiform movement presentation after tic exacerbation (Murphy et al 2004).

Finding a relationship between an infectious agent and a clinical disorder does not prove causality but is often the first step in documenting an etiologic relationship (Falkow 2004; Fredericks and Relman 1996). Because GAS infection is common, an association with tics and/or choreiform movements occurring by chance is possible. Recently, Luo et al (2004) reported no clear relationship between new GAS infections and symptom exacerbations in unselected pediatric patients with OCD and/or TS. However, 5 subjects demonstrated acute exacerbations of symptoms that were linked to GAS by serologic assay and 3 of these had previously been identified as "probable PANDAS" by diagnostic interview (Luo et al 2004), suggesting that a subgroup of patients might be at risk for GAS-induced neuropsychiatric fluctuations.

To date, choreiform movements have not been assessed in a large population prospectively and concurrently with streptococcal cultures. The purpose of this study was to determine whether an association exists between choreiform movements, tics, and behavior with GAS infection by systematic, longitudinal observation of a population of pre-kindergarten–6th-grade students.

Methods and Materials

Community-Based, Longitudinal Study Design

A community-based design offers the benefits of being less likely to be plagued by sample selection bias, variability in case identification, and problems with syndrome definition (Fallon and Schwab-Stone 1992). For purposes of convenience sampling, we used a school-based design as an approximation for community-based design. Although not equivalent to random sampling, this design enables access to diverse populations of school-age children, thus increasing the heterogeneity of the sample and minimizing possible selection bias. This design might miss severely affected individuals who are unable to attend school owing to illness or home-schooling, but these individuals represent a very small proportion of the population (Jankovic 1992; Owens and Murphy 2004). A longitudinal study design was chosen to study time lag effects of GAS on behavior and motor symptoms.

Subjects

This study was reviewed and approved by the University of Florida Institutional Review Board–01. The subject population was recruited from 3 schools in the Putnam County, Florida school system (total school enrollment = 3000). At school open houses, the investigators described the nature of this study and answered associated questions. Written consent from the parent/guardian and written assent from the student was obtained for all participants. If either the parent or student declined consent/assent, then the child was not included in the study. Educational materials about the signs and symptoms of streptococcal illnesses and the importance of seeking appropriate medical attention were given to all parents regardless of participation. Participating parents completed a brief questionnaire regarding their child's general health. On the questionnaire, parents were asked (but not required) to indicate child's ethnicity and whether child was in exceptional student education (ESE) classes for learning or behavior problems. In Florida, by law the ESE classification includes those students placed in mentally handicapped and learning disabled as well as gifted classes; however, in this study, students in gifted classes were not included in our ESE categorical assignment.

Subject Demographics

We enrolled 703 pre-kindergarten–6th-grade children (23.4% of total school population). Ten children were only seen once during the October–May observation period and are not included in this analysis. Of the 693 subjects who were seen between 2 and 8 times, 365 (53%) were boys and 328 (47%) were girls. The mean number of visits/child was 7.2 (± 1.1). The ethnic distribution of participants was as follows: 60% white, 13% African American, 16% Hispanic, 3% American Indian/Asian/Polynesian, and 8% declined to answer. The average age of the subjects was 8.04 (± 2.06). There were 32 subjects (4.6%) in the 3–4 year age range, 228 subjects (32.9%) in the 5–6 year range, 185 subjects (26.7%) in the 7–8 year age range, and 248 subjects (35.8%) in the 9–12 year age range.

Throat Cultures

Children who were participating in the study came to a specifically designated room in their school (one classroom at a time). Each child received a numerical ID and then proceeded to the throat culture station where a licensed laboratory technician conducted the procedure. The child's assigned number was written on the culture dish. Any observations regarding the child's health or appearance of oral structures, was noted on an observation sheet. The school nurse was called the following day with the names of the students with positive throat cultures. The school nurse notified the parent that their child had tested positive for GAS and stated that the child could be treated at no

charge with either penicillin or erythromycin provided via the study or the family could choose to seek private treatment. The laboratory technician was blinded to behavior and neurological assessment collection and data.

Direct Observation

The study employed direct observation for the assessment of neurological symptoms. Observation ratings were performed by a doctoral-level professional experienced in child assessment; the rater was blinded to the throat culture collection and results. After having had a throat culture, the child then proceeded to the direct observation station where the choreiform screening took place. The rater saw the children in groups of approximately 5, marking their numbers on an observation sheet. While the children were waiting in line for their turn at the choreiform screening they were observed at rest for 3 min with tics and behaviors noted. Tics were classified into 6 categories: facial, shoulder, arms/hands/fingers, legs, vocal, and other. Behaviors were classified into 9 categories: fidgets in line, twirls hair, excessive touching/tapping, picking skin/nose, cracking joints, hitting/shoving/pulling hair, balance/swaying, grimacing (non-tic facial movements), and other.

The rater instructed the children to hold their arms extended straight in front of them with their palms downward and fingers separated for approximately 20 sec and then instructed them to stand with their arms extended and their palms upward (fingers separated) for 20 sec. The children were to keep their eyes closed until they were instructed to open them. The rater observed the children for the 40-sec period, recording any choreiform movements that occurred. Choreiform movements were classified as "distal" (fingers, hands, wrists) or "proximal" (arms, elbows, shoulders). In addition, "pronator drift" (wrist turned inward toward body when in arms-outstretched, palms-down position) was noted when present. Choreiform movements were scored as 0 = none, 1 = 2–5 isolated twitches, 2 = 6–10 twitches in bursts, or 3 = continuous (Touwen 1979). Only choreiform scores of 2 or 3 were used in the data analysis to best decrease the potential for false positives. Disruptive behaviors, tics, and choreiform movements were additionally classified as "isolated" (observed only on one visit) or "persistent" (observed on 2–8 visits). If symptoms were deemed significantly severe by the rater to possibly warrant treatment, the child's guardian was contacted by one of the investigators and treatment options discussed.

Data Analysis

For each child, behavior, neuropsychiatric symptoms, and GAS infections were recorded at each visit. In analysis, the GAS records were matched by their longitudinal relationship with the current symptom. For example, the influence of a visit-1 infection on a visit-3 symptom was considered the same as a visit-3 infection on a visit-5 symptom, because both indicated a 2-visit latent period. The first task was to determine how many previous infections (measured by time lags) should be included in the prediction model. Two × two contingency tables were used to test the relation between each previous GAS infection, ordered by visit lags, and every behavior and neuropsychiatric symptom. After determination of influential time lags, relative risk (RR), defined as the probability ratio of having the symptom or behavior with a previous GAS infection versus with that of not having a previous GAS infection was calculated. The estimation was adjusted for issues in the clustering of data, (i.e., RR was estimated for each school and then combined with the best linear combinator by the inverse variance weight method—the minimum variance unbiased linear estimator for the overall RR). The variance of the RR was computed from the logarithmic transformation of the RR (Agresti 2002). The RR analysis considered each subject as the sampling unit. This analysis dichotomized the children by presence of GAS infection (+GAS) or not (−GAS).

A repeated (longitudinal) categorical response regression model was used to find the relation between each symptom and the influence of the GAS infection and other covariates, such as race, gender, ESE, and age. The presence or absence of a symptom or behavior formed the dichotomous response for the longitudinal model. The logarithmic link is used in the SAS (Cary, North Carolina) program to produce RR for all the covariates. The within subject covariance structure was assumed to be autoregressive, but the results from SAS GENMOD procedure are not sensitive to this assumption. In other words, the generalized estimating equation (GEE) output from SAS will give consistent estimates even if the covariance is mis-specified. A mis-specified covariance will make the conclusion less precise, but the p value is on the conservative side (Agresti 2002). Bonferroni adjustments for multiple comparisons were not presented in the table but are mentioned in the results.

Results

Of the 693 children observed, tics were noted at least once (isolated) in 14.1% and disruptive behaviors were noted in 30.2%. Persistent (noted 2–8 times) tics occurred in 1.6% of children and persistent disruptive behaviors occurred in 17.2%. Table 1 illustrates the observations made by the categories of isolated and persistent. Both (persistent) tics and problem behaviors were observed more often in boys than girls (3:1). The majority of the children (85.4%) were not placed in ESE classes; however, consistent with the literature (Packer 2005), we did find a significant relationship ($p = .01$) between tics and ESE, with

Table 1. Prevalence of Symptoms Overall and with Multiple GAS Infections

	ISOLATED (Observed One Time)				PERSISTENT (Observed 2–8 Times)			
Observation	Overall Group %	Repeated GAS Group %	95% CI If $p < .05$	p	Overall Group %	Repeated GAS Group %	95% CI If $p < .05$	p
Tics	14.1	12.5		.40	1.6	.0		TFD
Behavior	30.2	35.9		.14	17.2	26.5	(1.06, 2.94)	.02
Distal Choreiform	15.2	23.4	(1.28, 3.67)	.002	3.2	15.6	(3.41, 9.50)	.0001
Proximal Choreiform	22.4	32.8	(1.05, 2.77)	.015	9.1	1.6		TFD
Pronator Drift	17.5	23.4		.08	4.3	4.7		TFD

P value on the association on whether the Repeated Group A streptococcus (GAS) caused more of the observation to occur. CI, confidence interval; TFD = Too few data to make statistical inference.

Table 2. Associations of Subject Characteristics with Observed Symptoms

Symptom	Tics	Choreiform Movements		Pronator Drift	Behavior
		Proximal	Distal		
Gender[a]	(1.84, 11.9)	(1.10, 1.69)	(1.08, 2.08)	ns ($p = .67$)	(1.07, 2.27)
Age[b]	ns ($p = .82$)	(1.03, 1.13)	ns ($p = .43$)	ns ($p = .11$)	ns ($p = .06$)
ESE[c]	(1.15, 6.55)	ns ($p = .46$)	ns ($p = .61$)	ns ($p = .95$)	ns ($p = .53$)
Race (AfAm)[d]	ns ($p = .79$)	ns ($p = .13$)	(.32, .84)	ns ($p = .35$)	(1.01, 2.51)
Race (Hisp)[d]	ns ($p = .42$)	ns ($p = .72$)	(.35, .92)	ns ($p = .78$)	(1.03, 2.97)

All intervals in this table are 95% relative risk (RR) confidence intervals when the effect is statistically significant at .05 level.
[a]The gender row is the RR of boys versus girls. The boys have higher risks in all categories except Pronator Drift.
[b]The 95% RR confidence intervals when age is increased by 1 year (i.e., risk increases with age).
[c]RR of being in exceptional student education (ESE) versus not in ESE.
[d]RR of being African-American or Hispanic versus White.

ESE students having a higher rate of tic findings (Table 2). Only 5 children (.7%) developed persistent (2 or more consecutive months) choreiform symptoms after a GAS infection. Of the 693 children cultured monthly, 195 students (28%) tested positive for GAS during the 8-month observation period. Of that group, 64 repeatedly (2–6 times; mean = 2.6) tested positive for GAS (M/F = 1.7:1), with 45 subjects having at least 2 consecutively positive cultures. During the observation period, 4.6% had 4 or more positive throat cultures suggesting likely carrier state. Table 1 also shows the observations made in this smaller cohort ($n = 64$) by the categories of isolated and persistent. Those with repeated GAS infections showed higher rates of behavior ($p = .05$) and distal choreiform ($p = .001$) observations.

The small number of repeated GAS infections prevented us from doing a combined analysis of repeated GAS infection and other covariates. The primary analysis dealt with all the GAS infections, single or multiple. A comprehensive search by 2×2 contingency tables showed that the GAS influence on behavior did not last more than 3 visits (e.g., p values were high after more than 3 time lags). Thus, only GAS infection data for the current and previous 3 visits were used to assess RR. The risks were computed for each school, then combined with the best linear combination as described in the data analysis section. The results are shown in Table 3. This table shows that the association of GAS with the individual neuropsychiatric symptoms was weak, although all the GAS+ results demonstrated higher risk (RR > 1). When all neurological symptoms were combined (i.e., Distal Choreiform, Proximal Choreiform, Pronator Drift), the statistical significance reached .03. However, the association between GAS+/GAS− and behavior was strong ($p < .0001$). Even with the Bonferroni adjustment for multiple testing, this result remained significant, suggesting that GAS infection increased abnormal behaviors in this sample.

Subsequently, a repeated categorical response model was used for the GAS/symptom-behavior relationship with the effect of covariates race, gender, age, and ESE. The results are given in Table 2.

A very strong seasonal effect was found. In the association of GAS and all recorded observations, the fall had a much higher incident rate (all with $p < .0001$) compared with winter or spring (Table 4). In looking at the infection pattern, the peak incidence of GAS positive cultures was in October, with 9.43%. Antibiotic therapy provided to the schools might have contributed to a decreasing GAS rate, with a peak again in February, after the holiday break (Figure 1).

Table 3. Relationship Between Symptom Groups and GAS (Concurrent to Previous 3 Visits)

Symptom/Behavior	GAS+[a]	GAS−[b]	RR[c]	95% CI[d]	p[e]
Tics	14/195	29/498	1.29	(.28, 25.6)	.20
Distal Choreiform	48/195	119/498	1.09	(.81, 1.46)	.29
Proximal Choreiform	84/195	203/498	1.06	(.88, 1.29)	.26
Pronator Drift	24/195	41/498	1.57	(.98, 2.54)	.031
Combined Neurological Symptoms	122/195	272/498	1.14	(1.00, 1.32)	.028
Behavior (all)	68/195	91/498	1.71	(1.31, 2.24)	.00006
Balance/Swaying and Non-Tic Grimacing	37/195	28/498	2.92	(1.83, 4.66)	.00004

[a]Group A streptococcus (GAS)+ column shows the number of symptoms with GAS+ / total number of GAS+ subjects.
[b]GAS− column shows the number of symptoms without GAS/total number of GAS-free subjects.
[c]RR is the relative risk estimated from the combined schools.
[d]95% CI is the 95% confidence interval for the RR.
[e]The p value for GAS+/symptom association.

Discussion

Several studies have attempted to find associations between GAS and OCD and/or tics with mixed results. In this study, tics did not show an association with prior GAS infections. The low number of subjects displaying persistent tics and the brief assessment of each subject restricted the likelihood of finding an association between tics and GAS during the observation period. Group A streptococcus seemed to significantly increase the risk of finding behavior symptoms consistent with ADHD. Those with repeated GAS infections seemed to also have an increased risk of having behavior symptoms observed on more than one assessment. In a result similar to other reports, ADHD-like behavioral changes were found to be strongly associated with concurrent (Perrin et al 2004) or prior streptococcus infection (Peterson et al 2000). For example, Perrin et al (2004) reported that ADHD

Table 4. Seasonality of GAS+ Cultures and Observations

Variable	Fall[a]	Winter[b]	Spring[c]	p
Positive GAS	8.9%	5.8%	3.7%	.0001
Behaviors	23.2%	7.6%	3.5%	.0001
Tics	6.3%	1.9%	.5%	.0001
Distal Choreiform	5.1%	1.8%	2.4%	.0001
Proximal Choreiform	7.1%	2.9%	7.2%	.0001
Pronator Drift	5.9%	2.6%	.1%	.0001

[a]Fall is defined as October and November.
[b]Winter is defined as January and February.
[c]Spring is defined as March and April.

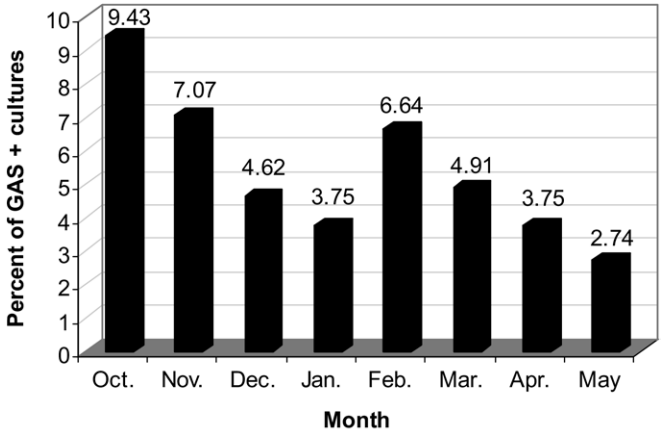

Figure 1. Monthly distribution of Group A streptococcus positive (GAS+) cultures.

symptoms were more commonly reported in children ill with a viral infection or with GAS than in well children. In a study examining streptococcal titers and basal ganglia volumes in children with OCD, tics, and/or ADHD, the most striking finding was that those children with ADHD had elevated titers, but there was no relationship with OCD or tic disorder (Peterson et al 2000). Interestingly, ADHD might be a risk factor for developing SC in children with RF (Mercadante et al 2000). For behaviors (balance/swaying and grimacing) more consistent with those seen in SC, we found a very significant association between GAS infection and symptom manifestation.

The role of GAS subclinical infections and carrier states for increasing neuropsychiatric risk is unknown. A school study examining the characteristics of GAS carrier state found that the majority of the children with GAS positive cultures were carriers (Martin et al 2004); however, others argue that GAS carriage rates are low (Ginsburg et al 1985; Hoffmann 1985; Pichichero et al 1999). Although 28% of children in this study attended school with pharyngeal GAS present at some point during the 8 months of observation, two-thirds of the children with a positive culture were positive only once. Furthermore, only 4.6% had persistently positive cultures. However, those subjects with 2 or more cultures positive for GAS were even more likely to have increased choreiform and behavior ratings and were more likely to be boys (63%). Mell et al (2005) found that multiple streptococcus infections increased the odds ratio for TS from 2 to 13. Given the male preponderance of ADHD and PANDAS, we found the idea that the male gender might be a risk factor for repeated GAS infections to be intriguing. These findings present several possibilities: 1) common childhood behavioral symptoms are most susceptible to change during and after common childhood illnesses; 2) pre-existing ADHD predisposes increased risk for developing infections; 3) pre-existing ADHD predisposes an association with other more dramatic neuropsychiatric manifestations, such as tics and OCD. The specificity of the infection along with CNS and immune vulnerability due to environmental or genetic risk likely interact to produce increased behaviors during and after infections.

A seasonal increase of observed behaviors was found in this study similar to earlier reports of neuropsychiatric symptom increases (Kovalenko et al 2000; Murphy et al 2004; Snider et al 2002). Seasonal variations are observed in many chronic illnesses, such as bipolar disorder (Shin et al 2005), multiple sclerosis (Goodkin and Hertsgaard 1989), and lupus (Hasan et al 2004). The seasonality relationship to the incidence of many autoimmune diseases is hypothesized to be due to immune changes in human susceptibility to a particular pathogen (Dowell 2001). Rheumatic fever has seasonal peaks (late spring) that correlate with preceding GAS peaks (late winter) (Tolaymat et al 1984). This study showed a seasonal peak corresponding to the fall season, which was likely influenced by the detection and treatment of many asymptomatic children.

The strengths of this prospective, systematic investigation were the large number of students cultured and observed, the ethnic diversity of the study population, and the fact that repeated cultures and observations were completed in tandem. The results are limited, however, by features of the study design. Although there was only one rater for the behavior, tic, and choreiform assessment, multiple checks were incorporated into the study design. The observations were also carried out in a structured rating setting rather than a naturalistic setting (classroom), which could have changed the subject's behavior (i.e., suppressed tics, increased fidgeting). Higher rates than expected were found on some of the observed behaviors and fewer than expected were found on others (tics), but assessment was brief and not definitive enough to indicate a disorder. Monthly assessments for GAS present an underestimate of the true GAS prevalence. To best determine carrier state versus subclinical infection, serial titers would have been useful as well as more frequent cultures and better assessment of treatment compliance.

Conclusions

The purpose of this study was to determine whether an association exists between choreiform movements, tics, and behavior with GAS infection by systematic, longitudinal observation of a population of pre-kindergarten–sixth-grade students. Group A streptococcus does seem to increase risk for behaviors and movements. However, more research is needed to explore the role of GAS in childhood neuropsychiatric symptoms, particularly for those with a history of repeatedly positive throat cultures.

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