Post-streptococcal autoimmune disorders of the central nervous system
Lisa A. Snider and Susan E. Swedo

Purpose of review
Autoimmune disease has long been intertwined with investigations of infectious causes. Antibodies that are formed against an infectious agent can, through the process of molecular mimicry, also recognize healthy cells. When this occurs, the immune system erroneously destroys the healthy cells causing autoimmune disease in addition to appropriately destroying the offending infectious agent and attenuating the infectious process. The first infectious agent shown to cause a post-infectious autoimmune disorder in the central nervous system was Streptococcus pyogenes in Sydenham’s chorea. The present review summarizes the most recent published findings of central nervous system diseases that have evidence of a post-streptococcal autoimmune etiology.

Recent findings
Sydenham’s chorea and other central nervous system illnesses that are hypothesized to have a post-streptococcal autoimmune etiology appear to arise from targeted dysfunction of the basal ganglia. PANDAS (pediatric autoimmune disorders associated with streptococcal infections) is the acronym applied to a subgroup of children with obsessive-compulsive disorder or tic disorders occurring in association with streptococcal infections. In addition, there are recent reports of dystonia, chorea encephalopathy, and dystonic choreoathetosis occurring as sequelae of streptococcal infection. Investigators have begun to isolate and describe antistreptococcal–antineuronal antibodies as well as possible genetic markers in patients who are susceptible to these illnesses.

Summary
Clinical and research findings in both immunology and neuropsychiatry have established the existence of post-streptococcal neuropsychiatric disorders and are beginning to shed light on possible pathobiologic processes.

Keywords
Group-A β-hemolytic streptococcal infections, autoimmune disease, post-infectious, central nervous system illness

Introduction
One of the primary roles of the immune response is to provide defense against infection. The immune system must be able to recognize a pathologic agent and target it for destruction (immune response) while ignoring healthy tissue (self-tolerance). Autoimmunity is a dysfunction of the immune system where self-tolerance to healthy tissues has been suppressed or lost. The loss of self-tolerance allows the immune system to produce autoantibodies that erroneously target healthy tissue for destruction. Although our knowledge of the pathobiology of autoimmune disease in the central nervous system (CNS) has expanded greatly, the initial events that lead to the loss of self-tolerance are still unknown. It has been hypothesized that self-tolerance to CNS antigens is broken by several linked events that result in the initiation or induction of anti-CNS immune responses, which produce the inflammation and demyelination seen in these disorders [1].

The concept of molecular mimicry has been hypothesized as a possible mechanism for the induction of autoantibodies [2]. In this model, autoantibodies are produced against healthy tissue because the antigen on a pathologic organism closely resembles the structure of an antigen on healthy tissue. When the immune system induces an antibody to target the pathologic organism for destruction, there is enough overlap that the antigen on the healthy tissue is also recognized. This mistaken recognition results in a functional loss of self-tolerance and the destruction of healthy tissue by the host’s own immune system. Molecular mimicry is just one possible mechanism by which post-infectious autoimmune disorders can occur. A wide variety of inciting organisms and affected tissues have been reported. This review will concentrate on evidence for autoimmune disease in the CNS caused by Streptococcus pyogenes or Group A β-
hemolytic streptococcus (GABHS), the infecting organism in ‘strep throat’ and scarlet fever.

**Pathogenesis of post-streptococcal illness**

GABHS colonize the throat or skin and are responsible for a number of suppurative infections and nonsuppurative sequelae. As pathogens they have developed complex virulence mechanisms to avoid host defenses. GABHS has been investigated for its significant role in the development of post-streptococcal infection sequelae. The basic pathogenesis begins with an infection with GABHS. There are multiple serotypes of GABHS and there is evidence that only specific serotypes will cause rheumatic fever. There is not evidence for this selectivity in any of the other post-streptococcal CNS disorders at this point. Although there is a high prevalence of GABHS throat infections among pediatric populations, only a small percentage of individuals develop post-streptococcal autoimmune illnesses. Studies of families suggest that rheumatic fever is an autosomal recessive illness with limited penetrance [3]. This implies that these illnesses will only develop in a susceptible host that has been infected by a specific GABHS serotype. It is this infection with GABHS that primes the host’s immune system and causes an abnormal response. The healthy tissues of the CNS can become the targets of this abnormal immune response causing neuropsychiatric sequelae through an inflammatory process [3] (Fig. 1).

**Sydenham’s chorea**

Sydenham’s chorea, the neuropsychiatric manifestation of rheumatic fever, has been proposed as a possible medical model for post-streptococcal autoimmune neuropsychiatric disorders [4]. Molecular mimicry is implicated in this illness through the demonstration of antineuronal antibodies in serum samples from patients with Sydenham’s chorea [5]. These antineuronal antibodies are postulated to arise in response to an infection with GABHS and then to cross-react with antigens from neurons in the basal ganglia. The first antineuronal antibodies isolated from patients with Sydenham’s chorea were found to react with cytoplasm from the caudate and subthalamic nucleus. In these 30 Sydenham’s chorea patients, the presence of antineuronal antibodies correlated with the severity and duration of the chorea [5]. These results were replicated in 11 children diagnosed with Sydenham’s chorea at the National Institute of Mental Health (NIMH). Antineuronal antibodies directed against human caudate tissue were demonstrated in 10 of the 11 patients [6].

Post-mortem studies as well as functional and structural brain imaging support the involvement of the basal ganglia in Sydenham’s chorea. In a study conducted at the NIMH, 24 patients with Sydenham’s chorea were compared with 48 matched controls using cerebral magnetic resonance imaging. The Sydenham’s chorea group showed increased volumes of the caudate, putamen, and globus pallidus when compared with the controls [7]. The current evidence for Sydenham’s chorea being a post-streptococcal autoimmune disorder is growing stronger. Once preliminary work on the bioactivity of these antineuronal antibodies has been established, the pathobiology of this illness will be confirmed.

**PANDAS**

Swedo and colleagues [8] published the first description of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) in 1998. This cohort of children had the abrupt onset of obsessive-compulsive disorder (OCD) or tic disorder following an infection with GABHS. Five criteria were established for inclusion in the PANDAS subgroup: presence of OCD and/or a tic disorder, prepubertal onset, acute onset and episodic course of symptom severity, association with GABHS infection, and association with neurologic abnormalities. The children had a very young age of illness onset, 6.3 (± 2.7 SD) years for tics and 7.4 (± 2.7 SD) years for OCD. Children in the PANDAS subgroup were also found to have larger volumes of the caudate, putamen, and globus pallidus than healthy children by cerebral magnetic resonance imaging [9] (Table 1).

In children with severe symptoms who met criteria for the PANDAS subgroup, immunomodulatory treatment with plasma exchange (PEX) and intravenous immunoglobulin (IVIG) was found to be effective in lessening the neuropsychiatric symptom severity [10]. A double-blind randomized study compared PEX with IVIG and sham IVIG (placebo) for the treatment of tics and obses-
GABHS at presentation, but elevated antistreptococcal antibody titers. The remaining child had a tonsillectomy performed 1 month prior to onset because of a history of recurrent GABHS infections during the previous year. In the children who did not experience a recurrence of neuropsychiatric symptoms, a complete resolution of OCD symptoms occurred in 5–21 days [11**].

In order to determine if a parent-reported upper respiratory infection might be a valid screening tool for children found to be in the PANDAS subgroup, 83 consecutive children and adolescents referred to an academic child psychiatry clinic with the primary diagnosis of OCD were evaluated for symptoms of an upper respiratory infection at the onset of their neuropsychiatric symptoms. The children with a history of an upper respiratory infection were more likely to experience a sudden rather than insidious onset of OCD symptoms and also to have a comorbid tic disorder. To determine that a child meets criteria for membership in the PANDAS subgroup, however, a prospectively determined association between neuropsychiatric symptoms and GABHS infection must be established. Validated biomarkers will be necessary to confirm a retrospective diagnosis. Until they are available, a history that abrupt onset OCD began around the time of an upper respiratory infection should alert a clinician to look prospectively for a GABHS association [12*].

One criterion for inclusion in the PANDAS subgroup is a prepubertal age of onset. A recent case report described a 28-year-old male who had the onset of debilitating OCD at 25 years of age following a sore throat. His pharyngitis went untreated for 3 weeks before he was brought to medical attention and treated with antibiotics. As his pharyngitis resolved, he developed acute OCD symptoms that severely interfered with his life. Since this patient had a post-pubertal onset of symptoms he cannot be included in the PANDAS subgroup. The report suggests that the subgroup may be larger than originally described, but inclusion of adult cases must await the development of more specific diagnostic tests [13*]. Children undergoing tonsillectomy for recurrent streptococcal pharyngitis who also have OCD and tic disorders have had reported improvements in their neuropsychiatric symptoms following surgery [14]. Since otolaryngologists evaluate a large proportion of pediatric patients with recurrent GABHS infections it is important that these subspecialists are aware of the association of GABHS infection and the onset of neuropsychiatric symptoms (Table 2).

### Obsessive–compulsive disorder

OCD is generally conceptualized as a neurobiologic disorder with a multifactorial etiology. There is increasing evidence that a post-streptococcal autoimmune-

---

**Table 1. The five clinical criteria of the PANDAS subgroup**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Presence of obsessive–compulsive disorder and/or tic disorder</td>
<td>A 28-year-old male who had the onset of debilitating OCD at 25 years of age following a sore throat.</td>
</tr>
<tr>
<td>(meeting DSM-IV criteria),</td>
<td>As his pharyngitis resolved, he developed acute OCD symptoms that severely interfered with his life.</td>
</tr>
<tr>
<td>(2) Prepubertal symptom onset,</td>
<td>Since this patient had a post-pubertal onset of symptoms he cannot be included in the PANDAS subgroup.</td>
</tr>
<tr>
<td>(3) Episodic course characterized by acute, severe onset and dramatic</td>
<td>The report suggests that the subgroup may be larger than originally described, but inclusion of adult cases must await the development of more specific diagnostic tests.</td>
</tr>
<tr>
<td>symptom exacerbations.</td>
<td>Children undergoing tonsillectomy for recurrent streptococcal pharyngitis who also have OCD and tic disorders have had reported improvements in their neuropsychiatric symptoms following surgery.</td>
</tr>
<tr>
<td>(4) Neurological abnormalities (e.g. choreiform movements) present</td>
<td>Since otolaryngologists evaluate a large proportion of pediatric patients with recurrent GABHS infections it is important that these subspecialists are aware of the association of GABHS infection and the onset of neuropsychiatric symptoms (Table 2).</td>
</tr>
<tr>
<td>during symptom exacerbations.</td>
<td></td>
</tr>
<tr>
<td>(5) Temporal relationship between GABHS infections and symptom</td>
<td></td>
</tr>
<tr>
<td>exacerbations.</td>
<td></td>
</tr>
</tbody>
</table>

PANDAS, pediatric autoimmune disorders associated with streptococcal infections; GABHS, Group A β-hemolytic streptococcus.
mediated process is occurring in the PANDAS subtype of OCD. Both radiologic and immunologic evidence supports this postulated etiology. Radiologic evidence from imaging studies of children in the PANDAS subgroup implicates the basal ganglia as the primary site of dysfunction [15*]. Magnetic resonance imaging studies on these children have revealed reduced caudate nucleus volumes in children with longstanding OCD but acutely increased volumes after the onset of neuropsychiatric symptoms [15*]. This acute increase in volume could be secondary to a post-infectious inflammation, while the reduced volumes found in chronic OCD could be secondary to another process or repeated bouts of inflammation. The serologic evidence documenting that Sydenham’s chorea is a post-streptococcal autoimmune disease is now being acquired from children in the PANDAS subgroup. Both antineuronal antibodies against the basal ganglia and cytokine profiles similar to those found in Sydenham’s chorea have been reported in the PANDAS subgroup [15*].

There is a growing body of evidence that post-streptococcal autoimmunity plays a role in pediatric OCD. To explore the possible association between compromised immune function and OCD, adult OCD patients were compared with patients with other psychiatric disorders to determine if there was a higher incidence of recurrent infections or other evidence of compromised immune function among the patients with OCD. A chart review from an anxiety disorders clinic revealed an increased rate of immune related syndromes among OCD patients in comparison to other anxiety and mood disorder groups. One implication of this finding is that prolonged immunologic stress may be a risk factor for OCD. It is possible that immunologic stress may compromise the blood brain barrier and permit the influx of antineuronal antibodies into the central nervous system [16**].

Reports of post-streptococcal autoimmunity in PANDAS have spurred interest in studying immune parameters in non-PANDAS OCD. Studies that have assessed immunologic measures in patients with OCD have not found consistent evidence of this connection in non-PANDAS OCD [17**]. Although OCD is felt to have a genetic basis, no specific genetic factors have been conclusively identified to date. This has led researchers to look for possible environmental risk factors that may be interacting with underlying genetic susceptibility in individuals with OCD. The similarities between Sydenham’s chorea, PANDAS and OCD with respect to genetic susceptibility have encouraged researchers to look for a post-streptococcal association for non-PANDAS OCD. To date, however, there is no evidence for this among nonselected patients with OCD [18*].

### Movement disorders

In the past decade there has been increasing evidence that movement disorders can develop in the context of streptococcal infections. Reports to date suggest that post-streptococcal neurologic sequelae include extrapyramidal movement disorders such as chorea, tics, and dystonia [19*]. The relationship between tic disorders and GABHS infection has been reported in the literature frequently, yet very few studies have looked systematically for evidence of GABHS infection in children with tic disorders. A well designed case-control study of the relationship between childhood tic disorders and GABHS infections in Italian school-aged children was conducted using mean antistreptolysin O (ASO) titer. (ASO titers become elevated 4–6 weeks after a preceding GABHS infection.) In the children with a tic disorder, mean ASO titer was significantly higher compared with that of controls [20**].

A variety of movement disorders have been proposed to have an immune-mediated or post-streptococcal etiology. In the recent literature there are three clinical reports of particular interest. Two children with serologic evidence of a recent GABHS infection presented with infantile bilateral striatal necrosis, a dystonic movement disorder with basal ganglia imaging abnormalities. Both

### Table 2. Current treatment guidelines for children in the PANDAS subgroup

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Assessment for GABHS infection by 48 h culture in a young child with abrupt onset OCD and/or tic disorder. A positive culture should be treated promptly with a standard 10-day course of antibiotics.</td>
</tr>
<tr>
<td>(2)</td>
<td>If the abrupt onset of the OCD and/or tic symptoms occurred at least 4–6 weeks prior to the visit, then a blood test for antistreptococcal antibody titers (ASO and anti-Dnase B) should be done (along with a 48 h throat culture) to attempt to document a preceding GABHS infection. Antibiotic treatment of elevated titers is inappropriate in the absence of a positive GABHS culture.</td>
</tr>
<tr>
<td>(3)</td>
<td>Prospective assessment for GABHS infections in a child with an episodic course of symptoms should be done. Throat cultures for GABHS should be obtained at the time of relapse of OCD and/or tic symptoms or antistreptococcal titers should be drawn 4–6 weeks later.</td>
</tr>
<tr>
<td>(4)</td>
<td>The decision to begin antibiotic prophylaxis should be based on clinical indications in each individual child after obtaining evidence that they are in the PANDAS subgroup. The prompt diagnosis and adequate treatment of GABHS infections in this subgroup of patients is clearly indicated.</td>
</tr>
<tr>
<td>(5)</td>
<td>Treatment with immunomodulatory therapies (like plasma exchange and intravenous immunoglobulin) should be reserved for children with acute, severe symptoms who fit the PANDAS designation. These treatments carry significant risks and should be used only for the most severely affected patients.</td>
</tr>
</tbody>
</table>
of these children had antineuronal antibodies reactive against the basal ganglia [21]. Paroxysmal dystonic chorea was an episodic, nonkinesiogenic (not induced by movement), extrapyramidal movement disorder. A sporadic case of this disorder was described in an 8-year-old boy who was found to have serum antibasal ganglia antibodies and a history of a preceding GABHS infection [22]. A childhood syndrome of immune-mediated choreatic encephalopathy was reported in four previously healthy girls aged 3–8 years. These girls presented with encephalopathy and an extrapyramidal movement disorder without evidence of a preceding streptococcal infection but with cerebral spinal fluid specific oligoclonal bands [23*].

An 8-month longitudinal observational study of school-aged children was conducted to determine the monthly point prevalence of motor tics. The investigators found that the incidence of motor tics was significantly higher during the winter months of November through February when compared with the spring months of March through June. Although no direct streptococcal infection rates were determined, this time period overlaps with the high seasonal prevalence of streptococcal infections seen in this age group. This study provides indirect evidence of a temporal correlation between GABHS infections and tic disorders [24].

**Acute disseminated encephalomyelitis**

Acute disseminated encephalomyelitis (ADEM) is an immune-related inflammatory disease of the CNS, affecting predominantly gray matter. Viruses, bacteria and live vaccines have all been implicated as possible pathogens. In a recent case series, 10 patients with ADEM occurring in association with a preceding GABHS infection had significantly elevated antibasal ganglia antibodies when compared with patients with ADEM without preceding GABHS infection, encephalitis, or a recent streptococcal infection [25**]. A case of ADEM in a 10-year-old boy with concomitant acute glomerulonephritis has also been reported following a GABHS infection [26*]. By evaluating patients with ADEM systematically for evidence of a recent GABHS infection, investigators have been able to define a subgroup characterized by basal ganglia involvement, dystonic movement disorders, behavioral disturbance, and the presence of defining autoreactive antibodies against the basal ganglia [26*].

**Antineuronal antibodies**

Antibodies to nuclear and cytoplasmic antigens are frequently observed in autoimmune disorders. The picture is less clear with regard to antinuclear antibodies in Sydenham’s chorea, tic disorders, and PANDAS. In a cohort of children referred to a neurodevelopmental clinic serum antibodies against human caudate were found to be significantly higher in the children with new onset movement disorders (Tourette’s syndrome, chronic motor or vocal tics, chorea, choreiform movements) than those without movement disorders [27]. The presence of antibodies directed against the caudate and putamen were also found to be significantly higher in a cohort of children presenting with new onset OCD or pervasive obsessive–compulsive symptoms than clinical controls without such symptoms [28].

There have been multiple reports of the isolation of antineuronal antibodies from patients with Tourette’s syndrome. Serum antibodies against human caudate, but not to the putamen or globus pallidus, were found to be significantly higher in patients with Tourette’s syndrome over controls [29]. Antibodies against a neuron-like HTB-10 neuroblastoma cell have been demonstrated in children with Tourette’s syndrome, but were also found in a healthy control group [30]. In a more recent study, Tourette’s syndrome patients were found to have significantly higher levels of total antineural and antinuclear antibodies than healthy controls [31**]. Similar results have also been described in patients with Sydenham’s chorea. Acute Sydenham’s chorea patients had significantly higher titers of anti-basal ganglia antibodies than patients with convalescent Sydenham’s chorea, rheumatic fever without Sydenham’s chorea, or healthy pediatric controls [32*].

There is substantial evidence for elevated antineuronal antibodies in children with Tourette’s syndrome, but further work needs to be done to define the specific antibodies and determine their functional abilities. Recent work has focused on possible animal models of Tourette’s syndrome, which has allowed more specific immunohistochemical studies to be done. Stereotypies and episodic utterances, hypothesized to be analogous to the involuntary movements seen in Tourette’s syndrome, were induced in rats by intrastriatal microinjections of gamma globulins from patients with Tourette’s syndrome. Post infusion immunohistochemical analysis confirmed the presence of gamma globulin selectively bound to striatal neurons [33]. An increased rate of oral stereotypies has also been demonstrated in rats who had bilateral infusions into the ventrolateral striatum with sera from patients with Tourette’s syndrome. The oral stereotypies were significantly increased in the rats infused with the sera from patients with the highest levels of antineuronal antibodies [34].

**D8/17 immunologic marker for central nervous system disorders**

Elevated D8/17 expression on B lymphocytes is a known susceptibility marker of rheumatic fever and has also been reported among patients with OCD [35,36]. An overexpression of D8/17 on B lymphocytes was found in
a group of patients with tic disorders when compared with healthy volunteers [37**]. Although overexpression of D8/17 on B lymphocytes has been reported among several groups of patients with OCD and tic disorders, recent data suggest that the discriminatory ability of D8/17 expression to identify patients with streptococcal related OCD or tic disorders has declined from the initial findings [38]. Methodological limitations of the current D8/17 assay need to be addressed prior to its use as a diagnostic tool in post-streptococcal OCD or tic disorders [39*].

**Conclusion**

The primary evidence for post-streptococcal autoimmune CNS disease is provided by studies of Sydenham's chorea, the neurologic manifestation of rheumatic fever. Reports of OCD, tic disorders and other neuropsychiatric symptoms occurring in association with GABHS infections suggest that a variety of CNS sequelae may be triggered by post-streptococcal autoimmunity; however, many questions remain unanswered. In order for this field to advance, carefully designed clinical trials must be conducted on well defined neuropsychiatric disorders that have a post-streptococcal onset. These trials should continue to refine the phenomenology of these illnesses, determine antineuronal antibodies specific to the disorders, determine the pathobiologic processes and biologic activity of the antineuronal antibodies, and advance our understanding of the risk factors and possible markers for disease state that allow for improved diagnosis and treatment.

**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:• of special interest• of outstanding interest


11 Murphy ML, Picchiero ME. Prospective identification and treatment of children with pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS). Arch Pediatr Adolesc Med 2002; 156:356–361. A prospective case study that identified 12 children with new-onset PANDAS from a general pediatric practice over a 3-year period. This group of children in the PANDAS subgroup had decreased in their neuropsychiatric symptoms after appropriate antibiotic therapy for GABHS tonsillitis diagnosed at the onset of the sentinel episode.

12 Giulino L, Gammon P, Sullivan K, et al. The parenteral report of upper respiratory infection at the onset of obsessive-compulsive disorder suggestive of pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection? J Child Adolesc Psychopharmacol 2002; 12:157–164. Children with symptoms of an upper respiratory infection at the time of onset of OCD symptoms were more likely to experience a sudden rather than insidious onset of symptoms and have a comorbid tic disorder.


16 Dinn WM, Harris CL, McGonigal KM, Raymond RC. Obsessive–compulsive disorder and immunocompetence. Int J Psychiatry Med 2001; 31:311–320. This article explores the putative relationship of immunologic stress and OCD by investigating whether adult OCD patients demonstrate a higher incidence of recurrent infections and other conditions suggested of compromised immune function compared with members of other psychiatric groups. A chart review from a private psychiatric clinic specializing in the treatment of anxiety disorders revealed an increased rate of immune related syndromes among OCD patients in comparison to other anxiety and mood disorder groups.

17 Murphy TK, Petitto JM, Voeller KK, Goodman WK. Obsessive compulsive disorder: is there an association with childhood streptococcal infections and altered immune function? Semin Clin Neuro-psychiatry 2001; 6:266–276. This article reviews the neuropsychiatric findings in OCD and Tourette’s syndrome with an emphasis on PANDAS and its association with Sydenham’s chorea. It also reviews the existing studies that have assessed immunologic measures in patients with OCD and Tourette’s syndrome.


20 Cardona F, Orefici G. Group A streptococcal infections and tic disorders in an Italian pediatric population. J Pediatr 2001; 138:71–75. A well designed case-control study of the relationship between childhood tic disorders and GABHS infections in Italian school-aged children. In the children with a tic disorder, mean ASO titer was significantly higher compared with that of controls.


A case series of 10 patients with acute disseminated encephalomyelitis, an immune-related inflammatory disease of the CNS, with a preceding GABHS infection. Enzyme-linked immunosorbent assay results showed significantly elevated antibasal ganglia antibodies in these patients when compared with patients with acute disseminated encephalomyelitis without preceding GABHS infection, encephalitis, or a recent streptococcal infection.


A case of acute disseminated encephalomyelitis, an immune-related inflammatory disease of the CNS, secondary to a GABHS infection in a 10-year-old boy.


Laboratory evidence of a role for antineuronal antibodies in neuropsychiatric disorders using indirect immunofluorescent assays and Western blot techniques. Tourette’s syndrome patients had significantly higher levels of total antineural and antinuclear antibodies than did healthy controls.


Patients with acute Sydenham’s chorea had significantly higher titers of anti-basal ganglia antibodies than patients with convalescent Sydenham’s chorea, rheumatic fever without Sydenham’s chorea, or healthy pediatric controls.


Elevated DB/17 expression on B lymphocytes is a known susceptibility marker of rheumatic fever. An overexpression of DB/17 on B lymphocytes was found in a group of patients with tic disorders when compared with healthy volunteers. Although these patients were unselected with respect to PANDAS criteria, it is possible that a subgroup of the patients with tic disorders may have an overexpression of this marker signifying a potential streptococcus-related association.


A review of the recent studies on DB/17 suggesting that the discriminatory ability of DB/17 expression to identify patients with streptococcal related OCD or tic disorders has declined from the initial findings.


A replication of the overexpression of DB/17 on B lymphocytes in patients with OCD and tic disorders with a discussion of the methodological limitations preventing this marker from being used as a diagnostic test.