

Review

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## What every psychiatrist should know about PANDAS: a review

Germana Moretti\*, Massimo Pasquini, Gabriele Mandarelli,  
Lorenzo Tarsitani and Massimo Biondi

Address: Department of Psychiatric Sciences and Psychological Medicine, "Sapienza" University of Rome, Viale dell'Univeristà 30, 00185, Rome, Italy

Email: Germana Moretti\* - [moretti.ge@tiscali.it](mailto:moretti.ge@tiscali.it); Massimo Pasquini - [massimo.pasquini@uniroma1.it](mailto:massimo.pasquini@uniroma1.it);  
Gabriele Mandarelli - [gabriele.mandarelli@uniroma1.it](mailto:gabriele.mandarelli@uniroma1.it); Lorenzo Tarsitani - [lorenzo.tarsitani@uniroma1.it](mailto:lorenzo.tarsitani@uniroma1.it);  
Massimo Biondi - [massimo.biondi@uniroma1.it](mailto:massimo.biondi@uniroma1.it)

\* Corresponding author

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### Abstract

The term Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus infections (PANDAS) was coined by Swedo et al. in 1998 to describe a subset of childhood obsessive-compulsive disorders (OCD) and tic disorders triggered by group-A beta-hemolytic *Streptococcus pyogenes* infection. Like adult OCD, PANDAS is associated with basal ganglia dysfunction. Other putative pathogenetic mechanisms of PANDAS include molecular mimicry and autoimmune-mediated altered neuronal signaling, involving calcium-calmodulin dependent protein (CaM) kinase II activity. Nonetheless the contrasting results from numerous studies provide no consensus on whether PANDAS should be considered as a specific nosological entity or simply a useful research framework. Herein we discuss available data that could provide insight into pathophysiology of adult OCD, or might explain cases of treatment-resistance. We also review the latest research findings on diagnostic and treatment.

### Introduction

Several studies provide compelling evidence of cortico-subcortical involvement in the pathogenesis of obsessive-compulsive disorder (OCD) [1]. Data emerging from morphological and functional neuroimaging studies suggest specific alterations at the level of orbitofrontal-caudate-thalamic circuits [2,3]. Patients with adult-onset OCD often have a history of ischemic stroke or traumatic brain injury involving the basal ganglia [4-6]. Moreover, indirect evidence of basal ganglia involvement in OCD comes from observations that the symptoms of OCD regress after surgery for cingulotomy and capsulotomy, interventions that disconnect the frontal cortex from basal ganglia [7,8].

Despite advances in the knowledge of the pathogenesis of OCD, little is known about the causative mechanisms underlying specific alterations. Observations of patients with rheumatic fever who had Sydenham's chorea manifesting with classic OCD symptoms have suggested a possible etiological link between group A  $\beta$ -hemolytic streptococcus (GABHS) infection in a subset of OCD patients [9-11]. GABHS has also been implicated in the development of Tourette syndrome [12-14] and autism in children [15].

These clinical reports engendered considerable interest in a possible streptococcal-triggered etiology for OCD. In 1998 the National Institute of Mental Health instituted a

research group that sought to characterize a subgroup of children with OCD and tic disorders (TD), namely "pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections" (PANDAS) [16]. These investigators outlined diagnostic criteria, studied several candidate PANDAS patients and proposed a possible pathophysiologic mechanism according to which a susceptible host might produce antibodies against GABHS that cross-react with neuronal tissue [16]. This mechanism resembles what happens in GABHS post-infection sequelae glomerulonephritis and rheumatic fever. Evidence suggesting a possible association between OCD and GABHS infection also in adults, comes from three case reports describing the abrupt onset of OCD due to GABHS infection [17-19]. In all cases the infection and obsessive-compulsive symptoms both promptly responded to antibiotics.

Recent evidence suggests that specific antibodies targeted to the dominant epitope of GABHS (N-acetyl-beta-D-Glucosamine) might influence neuronal signal transduction thus causing alterations in behavior and movement control. Accordingly, sera from some patients with Sydenham's chorea [20] or PANDAS [21] contain antibodies that induce calcium-calmodulin dependent protein (CaM) kinase II activity.

Despite growing support for an association between GABHS and OCD, the causal relationship between GABHS infection and OCD, its pathophysiology, and its possible clinical implication remain highly controversial. In this paper we will review human studies aimed at verifying the PANDAS construct. Our review focuses primarily on the pathogenetic mechanisms underlying the development of PANDAS. An important unanswered question is whether some patients currently treated for OCD are actually undiagnosed PANDAS in childhood. Knowing more about the pathogenesis of PANDAS might improve our insight into pathogenetic mechanisms of treatment-resistant OCD.

#### **PANDAS: historical perspective**

In 1994 Susan E. Swedo reported the case of a 9-year-old girl with rheumatic chorea and OCD whose neuropsychiatric symptoms responded to plasma exchange [9]. In the ensuing years a growing interest focused on the neuropsychiatric features of rheumatic fever and reports described patients with Sydenham's chorea who in up to 70% of cases manifested obsessive-compulsive symptoms, apparently indistinguishable from those of classic OCD [9,10]. The relationship between GABHS and Sydenham's chorea has long been documented in the medical literature [22]: streptococcal peptides stimulate specific lymphocyte immune responses producing antibodies that might in turn cross-react with various host epitopes, through the

mechanism known as molecular mimicry [23,24]. In analogy to Sydenham's chorea, infections with GABHS may trigger autoimmune responses that cause or exacerbate some cases of child-onset OCD, TD or Tourette syndrome [25].

The first systematic attempt to identify and define a nosological entity characterized by pediatric OCD or TD, triggered by an infection and with a supposed autoimmune pathogenesis, dates back to 1995. In this year Allen and co-workers described 4 patients in whom OCD or Tourette syndrome manifested or worsened after GABHS infection (two cases) and viral infection (two cases), and responded to treatment with plasmapheresis, intravenous immunoglobulin (IVIG) or immunosuppressive doses of prednisone [25]. To summarize the essential features of this subgroup of patients with OCD or TD, Allen et al. coined the acronym PITANDs (pediatric infection-triggered, autoimmune, neuropsychiatric disorders). As possible triggers of the neuropsychiatric manifestations they originally included along with GABHS infection, viral or other bacterial infections [25].

In a later study in 1998, Swedo et al. reappraised and extended the diagnostic criteria for PITANDs, no longer mentioned viral or other bacterial infections and hypothesized the existence of PANDAS [16]. They proposed five diagnostic criteria 1) the presence of OCD or a tic disorder or both, 2) pediatric onset, 3) episodic course of symptom severity with abrupt onset or dramatic symptom exacerbations, 4) temporal association with GABHS infection 5) and association with neurological abnormalities during symptom exacerbations [16]. Whereas the PITANDs hypothesis focused generally on a possible association between "an antecedent or concomitant infection" and neuropsychiatric manifestations, the diagnostic criteria for PANDAS were restricted to GABHS infection.

In a systematic clinical evaluation of 50 children who met the diagnostic criteria for PANDAS, Swedo and colleagues found that these patients typically had a young age at illness onset, an abrupt onset of neuropsychiatric symptoms and frequently manifested neuropsychiatric comorbidities (attention deficit hyperactivity disorder 40%, major depressive disorder 36%, overanxious disorder 28%, separation anxiety disorder 20%, enuresis 12% [16]. GABHS infection preceded 45 (31%) of 144 exacerbations of TD or OCD. Moreover, the onset of behavioral symptoms (irritability, emotional lability, tactile/sensory defensiveness, motor hyperactivity, deterioration in handwriting) was typically associated with exacerbation of OCD or tics, triggered by GABHS infections [16], also in patients who had Sydenham's chorea [9].

Subsequent studies investigating the PANDAS hypothesis yielded controversial results. Some seemed to confirm the association between GABHS infection and OCD or TD exacerbations [26,27], whereas others failed [28,29]. Circumstantial evidence indicating PANDAS as an autoimmune disorder came also from the presence of anti-neuronal (anti-brain, anti-basal ganglia) antibodies in children with PANDAS [30-32] or children with Tourette syndrome [33-35]. Again other studies failed to identify significant differences into auto-antibody levels between patients with PANDAS and controls [36-38]. The discrepancies among the various researches presumably arise partly from methodological problems: for example, the use of rabbit neural antigens having low homology with the human isoforms instead of human antigens [38]. Strong support for PANDAS as an immune-mediated disorder comes from the excellent response of children with PANDAS to immunotherapies (plasma exchange and IVIG) [39].

Prompted by a report that antibiotic prophylaxis diminished recurrences of rheumatic fever, some investigated a possible analogous outcome in patients with PANDAS. The first trial with oral penicillin was unsuccessful [40]. Another prospective longitudinal trial of azithromycin or oral penicillin in 23 children with PANDAS showed that antibiotic prophylaxis, with both molecules, effectively decreased streptococcal infections and neuropsychiatric symptoms exacerbations among children with PANDAS [41].

#### **Diagnostic issues**

As well as stimulating considerable attention the PANDAS hypothesis has generated controversy and skepticism. A major criticism is although the currently proposed diagnostic criteria focus on the occurrence, onset, severity and course of tic or obsessive compulsive symptoms they may fail to distinguish PANDAS from other phenotypes of OCD or tics, and to some degree even from Sydenham's chorea [42,43]. A childhood onset of symptoms (second criterion) may lack the specificity needed to distinguish PANDAS from Tourette syndrome, because in up to 75% of TD cases the manifestations begin during the prepubertal period [44]. Moreover, in a series of 80 patients with TD, 53% of the sample reported a sudden onset of illness [45]. Furthermore, the specificity of a sudden and dramatic onset (third criterion) for the PANDAS subgroup of OCD or TD or both has been questioned because some reports describe cases of sudden-onset of adult OCD or TD after GABHS [17,19,46,47]. Most children enrolled in PANDAS studies manifested several neuropsychiatric comorbidities especially attention deficit hyperactivity disorder, anorexia nervosa, dystonia, trichotillomania, major depressive disorder, or separation anxiety disorder [16,30,31,41]. Whether these manifestations are inde-

pendent, secondary to the development of PANDAS or, at least in some cases, could share a common pathogenetic pathway is unclear. Obviously, the presence of neuropsychiatric comorbidities limits the discriminating specificity of the diagnostic criteria, but in childhood neuropsychiatric disorders this is the rule rather than the exception. The presence of neurological abnormalities (fourth criterion) has been often referred to as the presence of choreiform movements (reported in up to 95% of patients with PANDAS in the acute phase), hence becoming a specific criterion [16]. Those supporting the PANDAS hypothesis have been excluding choreic movements as possible neurological manifestation to avoid possible diagnostic overlap between PANDAS and Sydenham's chorea, who often present OCD or TD comorbidities [10,48]. Some authors suggested that the PANDAS subgroup could represent an attenuated form of Sydenham's chorea and that a dysfunction in the basal ganglia could be a common pathogenetic pathway between choreiform movements and overt chorea [42,49]. Subsequent studies nevertheless showed that choreiform movements (elicited exclusively by a clinician on a neurological examination disclosing stressed posture) could be reliably distinguished from choreatic movements (rapid, involuntary, continuously increasing arrhythmic movements that are present continuously and increase during unrelated voluntary movements) [49,50]. Finally the temporal association (fifth criterion) between GABHS infection, whose incidence in school-age children is high, and the onset or the exacerbation of neuropsychiatric symptoms does not necessarily mean causality, the question awaits an answer from further controlled prospective studies. Streptococci were initially associated with Kawasaki disease and Henoch-Schönlein purpura, but controlled studies eliminated bacteria as a causal factor [42]. Streptococci are not the only infectious agents implicated in Tourette syndrome, other pathogens putatively involved include *Borrelia burgdorferi* and *Mycoplasma pneumoniae* [51].

A recent study has shown that antibody test reactions for *Mycoplasma pneumoniae* differ significantly in patients with Tourette syndrome and healthy controls (59% vs. 3%) [51]. Even though most reports involve GABHS, these data suggest that the autoimmune process underlying post-infective autoimmune neuropsychiatric symptoms may be triggered not only by streptococci but also by other infectious agents.

#### **Physiopathology of GABHS infections**

GABHS is a Gram-positive, extracellular bacterium of spherical to ovoid shape, and is one of the most frequent human pathogens. Several clinical manifestations have been associated with acute GABHS infections, including pharyngitis (strep throat), scarlet fever, impetigo and cellulitis [24]. GABHS produces several extracellular viru-

lence factors including streptolysin S and O, hyaluronidase, opacity factor, NADase and M-like proteins. M protein is the major surface protein and occurs in more than 100 antigenically distinct types, being the basis for the serotyping of strains with specific antisera [24]. Bacterial cell wall M proteins have been found to mimic several cardiac proteins and the group-specific carbohydrate of GABHS resembles the glycoprotein of heart valves. Indirect evidence suggests that M6 and M19 proteins may share common epitopes with brain structures [52]. Group A streptococci also elaborate, to varying degrees, a polysaccharide capsule composed of hyaluronic acid. The description of new virulence factors, not present in the earlier strains, together with a significant increase in the incidence and severity of infections, has suggested that GABHS genome has re-arranged over time. Evidence in recent years suggests that new phage-encoded virulence factors will be identified by sequencing the genomes of additional GABHS strains [53].

An individual's vulnerability to infection-triggered autoimmune disorders depends crucially on genetics. Family-based studies support a genetic predisposition to rheumatic fever [54]. Rheumatic fever is an inflammatory disease that can involve heart, joints, skin and brain. Sydenham's chorea is the most frequent neurological manifestation of rheumatic fever and is characterized by rapid, uncoordinated jerking movements affecting primarily face, feet and hands. Rheumatic fever is believed to be caused by antibody cross-reactivity. This cross-reactivity is a Type II hypersensitivity reaction often referred to as molecular mimicry [54]. Substantial evidence argues for molecular mimicry also in Sydenham's chorea, and anti-GABHS antibodies could cross-react with neuronal tissue [54].

A pioneering study on children with Sydenham's chorea found that 46.6% of sera from 30 patients reacted with neuronal cytoplasm of human caudate and subthalamic nuclei and the presence of anti-neuronal antibody was associated with the severity and duration of clinical attacks [55]. Several subsequent studies investigated the presence of anti-neuronal or anti-brain antibodies in movement disorders. Antineuronal antibodies directed against caudate nuclei were found in 10 of 11 patients with Sydenham's chorea [56]. In a later study, Church and colleagues found higher titers of anti-basal ganglia antibodies in patients with acute Sydenham's chorea than in convalescent patients [57].

#### **Antineuronal autoantibodies**

The presence of systemic anti-basal ganglia autoantibodies has been proposed as possible evidence for an immunological pathogenesis of a subset of OCD. The modulation of intracellular signalling pathways by

autoantibodies has been described in myasthenia gravis [58] (autoantibodies to the acetylcholine receptor blocking neuromuscular transmission) and Graves disease [59] (autoantibodies against thyroid-stimulating hormone). Nonetheless basal ganglia, like most CNS structures, are relatively inaccessible to circulating antibodies owing to the presence of the blood-brain barrier (BBB). Although the mechanism by which circulating antibodies or cytokines might gain access to the CNS is unknown, with the exception of the circumventricular/lamina terminalis region, where the BBB is absent [60], a variety of hypothetical mechanisms exist. For example, circulating antibodies could reach the CNS if an inflammation of the meninges causes a local BBB breakdown. Cytokines, probably crossing the BBB at circumventricular organs, can trigger an immune activation on the CNS side of the BBB. Moreover, peripheral B cells that are cross-reactive to a CNS epitope may cause intrathecal production of antibodies [61].

To test the specificity of the association between anti-brain antibodies and the neuropsychiatric symptoms in PANDAS, Pavone and colleagues compared a group of PANDAS children with patients with uncomplicated (without neuropsychiatric manifestations) GABHS active infection [30]. They found a far higher incidence of anti-brain antibodies in serum from children with PANDAS than in those with active GABHS infection (64% vs. 9%) suggesting that the presence of anti-brain antibodies could not be accounted for by GABHS infection alone [30]. Further support for an immune-mediated pathogenesis of OCD in a subset of patients came from a study by Dale et al. that compared anti-basal ganglia antibody (ABGA) titers among patients with OCD and three control groups (neurological patients, uncomplicated GABHS infection, autoimmune disorders) and found significantly higher antibody expression in the OCD group (42% vs. 4%, 2%, and 10% in the three control groups) [31]. In the same study the authors found that the mean CY-BOCS score in the antibody-negative patients was higher than in the antibody-positive patients, and the latter had lower obsessions of hoarding/saving [31]. Others nevertheless also found anti-brain antibodies in healthy controls [14,33]. Two successive studies found no significant differences for ABGA immunoreactivity between patients with PANDAS vs. controls [36] and between children who met PANDAS criteria and two control groups (healthy controls and patients with TD) [37]. These discrepancies in autoantibody findings could reflect the methods used for antibody detection: enzyme-linked immunosorbent assay (ELISA) and western blotting which can alter the conformation of the antigens and could therefore affect antibody-antigen interactions [31].

Despite existing evidence of brain-specific antibody reactivity, and the isolation of antibodies against basal ganglia evoked by streptococcal cell wall, the mechanism by which molecular mimicry results in a behavioral or movement alteration is still unclear. Recent work by Kirvan and colleagues suggests that the pathogenesis of PANDAS and Sydenham's chorea might involve immune-mediated altered neuronal signaling [20,21]. These investigators first demonstrated that monoclonal antibodies derived from patients with acute Sydenham's chorea and targeted to N-acetyl-beta-D-glucosamine (GlcNAc), the dominant epitope of GABHS, reacted with human lysoganglioside GM1. This lysoganglioside influences neuronal signal transduction [62]. Moreover the autoantibody 24.3.1, from sera of patients with acute Sydenham's chorea induced CaM kinase II activity, whereas serum obtained from convalescent patients did not [20]. A recent work from the same group reported that antibodies which react with lysoganglioside GM1 and induce CaM kinase II activation in neuronal cells are present in PANDAS [21]. Using competitive-inhibition ELISA Kirvan et al. found that soluble lysoganglioside GM1 inhibited 73% of sera from patients with PANDAS binding to GlcNAc (conjugated to bovine serum albumin) but only 23% of sera from controls (OCD, tic disorders, attention deficit hyperactivity disorder, patients not meeting PANDAS criteria) [21]. Moreover, using human neuroblastoma cell cultures, they showed that PANDAS sera specifically induced antibody-mediated activation of CaM kinase II (75% percent of acute PANDAS sera), the degree of activation being superior to non-PANDAS sera and inferior to chorea sera. PANDAS sera depleted of IgG did not activate CaM kinase II. Notably the degree of activation of CaM kinase II was highest in PANDAS patients with isolated tics.

Current data emerging for patients with chorea, PANDAS and OCD seem to suggest that CaM kinase II could be an intracellular mediator of behavioral and motor manifestations in some neuropsychiatric disorders. Along a continuum of activation from low levels (e.g. non-PANDAS OCD) to extremely high levels (rheumatic chorea), CaM kinase II activity seems to be associated in non-PANDAS OCD with simple neuropsychiatric manifestations and in rheumatic chorea with frank motor alterations. No studies have yet shown whether the physiological systems activating this signal cascade interact with possible disease-related (autoimmune ?) triggers. If they do, these interactions could be a new target for possible pharmacological approaches in disorders such as OCD and choreiform disorders.

#### **Peripheral markers**

The research for a possible susceptibility marker for PANDAS mostly focused on identifying peripheral markers. Among proposed peripheral markers of PANDAS suscep-

tibility is monoclonal antibody directed against a non-HLA B-cell marker known as D8/17. This antibody is an IgM first isolated from fusions of spleen cells from mice that had been repeatedly immunized with human B-cells from patients with confirmed rheumatic fever [63,64].

In a study investigating D8/17 in PANDAS, Swedo and colleagues compared 27 children who met the diagnostic criteria with 9 patients with Sydenham's chorea and 24 healthy controls, and found a significantly higher percentage of B cells that bind D8/17 monoclonal antibody in children with both diseases than in controls (89% in Sydenham's chorea, 85% in PANDAS, 17% in controls) [65]. Another study of patients with child-onset OCD or Tourette disorder found 100% positive reactions for D8/17 in patients compared with 5% in the control group [13]. Subsequent studies investigated D8/17 positive B-cells in obsessive-compulsive spectrum disorders, as well as in other neuropsychiatric disorders. High percentages of B-cells expressing D8/17 were found in patients with autism (78%) [15], anorexia nervosa (100%–81%) [66,67], adult OCD (59%–92%) [68,69], tics (61%) [70] and trichotillomania (59%) [68]. Recent studies that used more accurate methods (flow cytometry) nevertheless failed to replicate these results [71,72]. This discrepancy may be due, at least in part, to the difference in the methods used in these studies, but also to the molecular characteristics of the antibody. The antibody that binds to D8/17 is an IgM, known to be relatively unstable and difficult to purify.

Preliminary evidence suggests that D8/17 antigen immunoreactivity may reflect different psychopathological characteristics among patients with obsessive-compulsive spectrum. In a study on repetitive behaviors in autism Hollander and colleagues investigated the presence of D8/17 antigen in a sample of 18 children with autism. They found that the D8/17-positive patients had significantly higher mean children Yale-Brown obsessive compulsive scale (CY-BOCS) compulsion scores than the D8/17-negative patients [15]. These results suggest that psychopathological characteristics could differ in the various clinical subgroups of patients with OCD according to the underlying pathogenetic mechanisms.

#### **Neuroimaging**

In recent years, evidence arising from morphological and functional neuroimaging studies have linked OCD with dysfunction in frontal-subcortical circuits. Strong evidence exists of orbitofrontal cortex involvement but other areas implicated in the pathogenesis of OCD include the anterior cingulate gyrus, amygdala, insula, thalamus, striatum, lateral frontal and temporal cortices [1-3]. Several studies with positron emission tomography (PET) reported increased glucose metabolism in the orbitofron-

tal cortex, caudate, thalamus, prefrontal cortex and anterior cingulate among patients with OCD [73-75]. Current knowledge on the pathophysiology of OCD, despite suggesting an involvement of discrete brain regions, is far from concluding that these abnormalities are the cause of OCD or just an epiphenomenon [2].

In 1996 Giedd et al. first described an association between abrupt exacerbation of OCD symptoms after GABHS infection and an enlargement of basal ganglia [76]. Relatively few imaging studies have investigated CNS alterations in SC, most studies found no pathological changes on MRI. An MRI study of 24 children with SC, however, found volumetric abnormalities in caudate, putamen and globus pallidus [77]. Another study in a patient with Sydenham's chorea detected striatal abnormalities (increased signal intensity on T2-weighted images involving the putamen, globus pallidus, and the head of the caudate nucleus bilaterally) that reversed after recovery [78]. A subsequent longitudinal study with MRI compared 34 patients who met PANDAS criteria with 82 healthy controls and found a significant enlargement of caudate, putamen and globus pallidus in the patients [79]. Interestingly, immunomodulatory treatment (plasma exchange and IVIG) normalized this difference, suggesting that basal ganglia abnormalities are reversible. The same study found no correlation between symptom severity and basal ganglia volume [79].

Further longitudinal studies monitoring the CNS changes such as autoimmune vasculitis and edema and OCD symptoms that are supposed to follow GABHS infection are needed to assess a possible causal role and the involvement of specific CNS regions [80].

#### **Therapeutic strategies**

The neurobiological mechanisms underlying the pathophysiology of OCD remain an intense area of research. One of the most accepted theories supports an alteration of serotonergic brain pathways, mainly because serotonin reuptake inhibitors achieve better clinical efficacy than other pharmacotherapeutic agents [81]. Double-blind, placebo-controlled trials have shown the efficacy of clomipramine and selective serotonin reuptake inhibitors (SSRI) in the treatment of adult OCD [81]. Although fewer, but consistent observations, suggest that clomipramine and SSRI may be equally effective in the treatment of childhood OCD, only clomipramine, fluvoxamine and sertraline have been approved by the FDA for child and adolescent OCD.

Several lines of evidence indicate that an optimal treatment for OCD is combined pharmacotherapy and cognitive behavioral therapy (CBT) [82]. Despite the advances in pharmacological and psychotherapeutic approaches,

up to 40-60% of treated patients are still non-responders or their response is unsatisfactory [83].

Some reports suggest that OCD or tics manifesting in patients with PANDAS respond to serotonergic drugs and combined therapy [84]. CBT and serotonergic drugs have proven efficacy, whether or not the symptomatology is triggered by a GABHS infection. Even in the PANDAS subgroup many patients have an unsatisfactory response. The true percentage of non-responders remains difficult to define but probably approaches that in the non-PANDAS subgroup.

When standard treatments fail and symptoms are severe and disabling, Swedo and colleagues proposed immunomodulatory interventions, tailored to the presumed pathophysiology [84]. In a longitudinal double-blind placebo-controlled trial of 29 children with PANDAS, plasma exchange, IVIG or sham IVIG proved better than placebo in reducing OCD symptoms at 1-month follow-up (58% improvement with plasma exchange, 45% with IVIG) and tics (49% improvement with plasma exchange, 19% with IVIG) as measured by CY-BOCS and Tourette syndrome unified rating scale [39]. The improvements remained stable at 1 year follow-up, and were all statistically significant ( $p < 0.05$ ) with the exception of tics in the group treated with IVIG. Whereas standard therapies (SSRI, cognitive behavioral therapy) have proved efficacious in the PANDAS subset of OCD and TD, immunotherapies were ineffective in children with resistant OCD without a history of GABHS infection [85], suggesting that immunotherapy is specific for PANDAS thus supporting the presumed pathophysiology.

In a prospective longitudinal study 12 children who met the diagnostic criteria for PANDAS, were treated with penicillin or amoxicillin (5 patients), amoxicillin and clavulanate (1 patient), or cephalosporin (6 patients) during acute exacerbation of neuropsychiatric symptoms. In all patients antibiotic therapy effectively resolved OCD, the anxiety symptoms and tics within on average 14 days [26]. Penicillin prophylaxis has proven effective in preventing recurrences of rheumatic fever, and the American Heart Association recommend the use of oral penicillin 250 mg twice a day for prevention [86]. Because of the hypothesized pathophysiologic similarities between Sydenham's chorea and PANDAS some have argued that penicillin prophylaxis would also reduce neuropsychiatric exacerbations in children with PANDAS. In the first controlled trial on antibiotic prophylaxis for PANDAS, 37 children who had been previously diagnosed as PANDAS, were randomized to 4 months of penicillin V (twice daily oral 250 mg) followed by 4 months of placebo, or placebo followed by penicillin. In this study oral penicillin failed to provide adequate prophylaxis for GABHS and subse-

quently for neuropsychiatric symptoms exacerbations [40]. In a subsequent randomized trial Snider and colleagues tried to determine whether the negative results from Garvey were due to inefficacious prophylaxis against GABHS infection, and not to a lack of association between GABHS infection and neuropsychiatric symptoms. The study compared penicillin, considered as an "active placebo", with azithromycin, a drug that had proved efficacious against GABHS infections. In contrast to previous studies, penicillin and azithromycin both effectively decreased GABHS infections and neuropsychiatric exacerbations. The authors therefore concluded that antibiotic prophylaxis may be useful in the management of children with PANDAS [41].

Others later pointed out that the study had several limitations: the small sample size, the use of an "active placebo" and the retrospective methodology used to collect clinical data (symptoms severity, previous GABHS infections) regarding the year before patients were included in the study [87,88]. More important, many patients had neuropsychiatric comorbidities (as in all PANDAS studies) and the study design failed to consider concomitant pharmacological treatments as possible sources of confounding. Current knowledge therefore seems insufficient to support routine antibiotic prophylaxis for the symptoms of PANDAS.

### Conclusion

Despite the encouraging results from recent studies that tested a possible autoimmune pathogenesis of PANDAS also at an intracellular level, and found in CaM kinase II a possible mediator of neuropsychiatric symptoms in this subset of OCD or TD patients, the validity of this nosologic entity is still questioned. The presence of anti-brain antibodies in a subset of patients with OCD, the promising results from immunomodulatory treatment in PANDAS and the possible association between some upper respiratory infections and the sudden onset of OCD, suggest a supportive role for immune triggers in some OCD subtypes. A research area that deserves further investigation regards the possible differences in the psychopathological characteristics of autoimmune-induced and non-autoimmune-induced OCD. Our findings in this review apart from confirming PANDAS as a distinct clinical entity, suggest that PANDAS is a useful research field that could open new insights into the pathogenesis of OCD, even in adults.

### Abbreviations

BBB: blood-brain barrier BBB; CaM kinase II: calcium-calmodulin dependent protein kinase II; CY-BOCS: children Yale-Brown obsessive compulsive scale; GABHS: group A  $\beta$ -hemolytic streptococcus; IVIG: intravenous immunoglobulin; OCD: obsessive-compulsive disorder; PAN-

DAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections; TD: tic disorder

### Competing interests

The authors declare that they have no competing interests.

### Authors' contributions

GM, MP, GM, LT and MB conceived the manuscript and drafted it. All authors read and approved the final manuscript.

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From: "P.A.N.D.A.S. Resource Network" <heidicake1@yahoo.com>  
Subject: Contact Form: P.A.N.D.A.S. Resource Network  
Date: February 22, 2012 2:57:14 PM EST  
To: support@pandasresourcenetwork.org

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Name: heidi oneill  
Email: heidicake1@yahoo.com  
Address: 42 Whitewood Drive  
City: Rocky Point  
State: NY  
Zip: 11778  
Phone: 516.356.9957  
ACN Member?: No  
Forum name:

Options: I need help finding a physician

Reason: Other ideas.

How did you hear about us?: friend

Comments: My son just turned 6 yrs old in January. He had a severe stomach bug of some sort and recently after he came to me out of the blue and stated he is thinking bad words. He has had several nightmares and this calm sweet boy can't sit still anymore. He is extra sensitive and I now noticed a tic. The Pediatrician order blood work on my request and has no markers for strep but his creatine level is high. My son is not the same child within one WEEK. I am beside myself. I did reach out to Dr. Robert Melillo and he stated he has seen cases like this and it could be PANDAS. My son comes to me now on a daily basis and tells me "He licked the wall and scratched the couch" and he didn't do any of those things. I need help and I need it fast. If he is exposed to another strain of something what kind of child could he turn into. I am sure it was from something he had in January. A coworker of mine in which our children are in the same school system had the same symptoms of my son and again the peds said it was a virus well that virus ruptured his appendix and he spent almost 2 wks in the hospital. I can not take this lightly because my carefree son is now worrying and obsessing all the time. PLEASE HELP ME  
Share address with PANDAS researchers?: Please share my information with PANDAS researchers

From: Heidi <heidecake1@yahoo.com>  
Subject: Fw: Tanner O'Neill  
Date: February 24, 2012 4:19:37 PM EST  
To: Lynn Johnson <lynnj0750@msn.com>  
Reply-To: Heidi <heidecake1@yahoo.com>

----- Forwarded Message -----

From: Heidi <heidecake1@yahoo.com>  
To: "JoNel.Aleccia@msnbc.com" <JoNel.Aleccia@msnbc.com>  
Sent: Friday, February 24, 2012 2:29 PM  
Subject: Tanner O'Neill

Hey Jonel,

As I begin to write this I try not to cry. Tears of sadness than joy. Lynn told me to be strong but I am obviously having a hard time. My son's name is Tanner. He was born on January 12th, 2006. He was a large baby, weighing over 10lbs at birth. He met all his milestones as predicted by his pediatrician. When he was 14 months he started to string his sentences. He rarely would get any illnesses. We would just take him for his routine visits. When he was about 3 1/2 he started to get the typical ear infections or viruses as any normal kid. At that time we noticed he started to stammer on his first word of a sentence. Everyone told me it was a phase that children do this. He then would be at his peak of health and the stammering was mysteriously non-existent. I never associated the two until you read further in our story. Everyone has told me how sweet my son is and what a great kid. He listens, excellent focus and just a joy to be around. He entered preschool at the age of 4 and he had illness after illness, ear infections, viruses, everything that you would expect in when all children are together.

The preschool teacher told me he is in the top of his class and the only thing that ever concerned her is that he seems to worry. My husband and I were perplexed at the idea that our 4 yr old worries and we never saw it. We dismissed it and said it was a phase. December of 2010 my father broke his jaw and this immediately followed an illness that Tanner was just getting over and my son's stammering came back with a vengeance. As parents we felt he was affected by the idea and appearance of his grandfather. The stammering subsided after a couple of weeks and we were on the road again to a fluent intellectual child that excelled in preschool. Summer of 2011 was uneventful except for mom changing jobs. I began my career at Brain Balance Achievement Centers. This new career focuses on children of Neurological Disorders.

Now it came to Kindergarten and just like any kid my son was so excited. He started off his year fabulous! He sicknesses started again and he started to perform rituals. Again, you think it is a phase. The rituals subsided and as usual the stammering got better. Now winter of 2011/2012. January of 2012 there was a vicious unknown virus going around his school. My son caught this virus and again complained of a severe stomach ache for two weeks. I brought him to the pediatrician and they said it was just a virus but now had another ear infection. At the same time my friend, who's son went to the Middle School, caught the virus and wound up in the hospital after two weeks with a ruptured appendix. At the end of January my son would come to me and say, "two feathers are coming out of my stuffed puppy" and I would respond there are no feathers and don't worry about it. This would go on every night. Okay, another phase?

February of 2012 my son recovered and seemed to be back to normal but February 11th we were out with friends and my husband and I noticed his stammering was out of control. It took him 14 repetitions of the first word to get his sentence out. It was so noticeable that his little friend said, "Tanner why do you keep saying the word she?" My husband I figured now it is time to really push the school for speech since they discounted it earlier. The week of Valentines Day the rituals started again, rubbing walls, the floor, etc... He came to me and started saying "Mommy, I licked the wall and touched the door, and my hand scratched the TV". None of this was true and I said why are you saying that and he responded, "I don't know mommy". Now I started to take note of his changes. My gut told me something is wrong. Immediately after that the nightmares started. It was a recurrent dream about a creature. Friday the 17th I was taking my little daughter to preschool and after I dropped her off he told me he was thinking bad words. I asked him what bad words and he proceeded to curse. I told him it was okay and I got upset knowing something wasn't right. He then told me several things about what he licked, touched, scratched and he didn't do any of those things. He stated he worries all the time now and SOMETHING WAS WRONG WITH HIS BRAIN.

That Friday night he came off the school bus came in the house and unloaded about everything he touched, licked. He always started it by "I think I licked the \_\_\_\_\_". It was almost some kind of release. I was beside myself.

We came home and put the kids to bed and I told my husband something is wrong and it is not a phase. Saturday, 2/18/2012, came and I took the kids out to the park to get some fresh air. My son looked off but he began to play. I noticed he was rubbing his chin on his jacket and he kept doing it. As he was running to another play ground a little girl ran into he fell and he cried uncontrollably and we left. He then had the strangest outburst in the car screaming at the top of his lungs! This was not my son. I immediately called my husband at work and told him everything. My husband was speechless. Sunday I began to vacuum to clean my house and he covered his ears and said it was too loud. I grabbed my husband and said this is not right. We decided that it was going to be a daddy and son day. They went bowling and my husband said he had a disconnected daze in the car and he was rubbing his chin with jacket again. The day was long trying to keep everyone busy. That night he said he was thinking bad words again and I told him it was okay. Monday morning he woke up and said his ear hurt so we went to our local pediatrician. I asked the pediatrician privately that I wanted him to be tested and this was not normal. He gave me a script for a blood test but discounted what I said and said it was a phase. Monday was Presidents day and we had a playdate, his friend Tyler. I started to notice my son was scrunching his mouth as a tic! Panic set in!! He kept running up to me and my husband telling us what he licked, touched and scratched, and again he never did anything of the sort. The tics were always with his mouth pushing his lips up. He played with his friend all day as I watched his new behaviors. I sat in my room that night and my gut just told me something was not right. Tuesday, February 21st, I had a business meeting with the founder of the Brain Balance Program Dr. Robert Melillo. We discussed our program and procedures and then I just said Rob I have to talk to you. I told him what my son was doing and the odd sudden onset of behaviors. He proceeded to tell me it is PANDAS. He explained the reasoning behind why my son is acting so odd. We also discussed his speech issue and he told me it has all to do with the Basal Ganglia of the brain and how the antibodies he is producing is attacking this region. He also told me it is an Auto Immune Disorder. I knew I was correct and I didn't care if the pediatrician did not believe me. That afternoon I received word that my son's blood test CBC and Metabolic panel were normal but the others were still not in. Well the next day they came in and they were normal (for what they tested) so am I just going crazy as I watch my son change! I then went on the website and placed an email for some help with PANDAS. Twenty minutes later Lynn Johnson called me and I exploded with tears. She told me to breathe and I am not crazy! I started to tell her my story and she said honey it's PANDAS and it was going to be okay! She made some calls and now I was going to be in Connecticut the next day to have him evaluated at the Brain Balance in Norwalk Conn by Dr. Mark Goldenberg. She called me back and the next thing I knew this angel from heaven got me an appointment with Dr. Bouboulis. Thursday we went over by the Ferry to Conn and had our evaluation with Dr. Goldenberg and he had seen PANDAS children before and it is an autoimmune disorder. I had my visit with Dr. Bouboulis and his wonderful PA Jennifer and told me it was going to be okay. I started my son on the treatment of medication and within one day I am already seeing improvement!!!! He isn't rubbing the walls, he isn't thinking bad thoughts... GOD BLESS the amazing people in my life Dr. Robert Melillo and this angel LYNN and DR. BOUBOULIS. Please feel free to contact me (516) 356-9957  
My fear is of another mother going through this and not being so fortunate. This message has to get out!!

**From:** "P.A.N.D.A.S. Resource Network" <Info@PANDASResourceNetwork.org, tkletecka@yahoo.com>  
**Subject:** Contact Form: P.A.N.D.A.S. Resource Network  
**Date:** February 26, 2012 2:05:13 PM EST  
**To:** info@pandasresourcenetwork.org

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Thank you for submitting your information to the PANDAS Resource Network. Although we try to respond to everyone individually, the sheer volume of requests occasionally makes that impossible. In the mean time, please take advantage of the information on PANDASResourceNetwork.org.

Here is the information we've received from you:

Name: Tammy Kletecka

Email: tkletecka@yahoo.com

Address: 2524 19th Ave

City: Rockford

State: Illinois

Zip: 61108

Phone: 815-980-9272

ACN Member?: No

Forum Name: Tammy Kletecka

How did you hear about us?: search

Reason: I am interested in starting a local support group

Skill Details:

Options: Other

Comments: My eight year old daughter recently lost her mind for no apparent reason, was diagnosed with OCD in the emergency room, where they wanted to ship her off to a hospital. I did an internet search- found you, and pleaded the idea with her Pediatrician. He agreed to do a 48 hour strep as she recently had an ear infection weeks prior. Today is Sunday so we don't have the results. However, they went ahead and ordered her antibiotics and 48 hours later (BINGO) she's substantially better. We have been able to touch her, and there are less contaminated areas. Today we even persuaded her to leave the house for breakfast, where she only washed her hands four times. She has stopped sweating at us, and seems to be looking more like her old self. Thank you! I can't wait to share this info with her pediatrician on Monday, for now I am just going to cross my fingers for a full recovery. I am also concerned about the anti-depressants they gave her three days ago. I don't feel that they were really helping anyway.

Share address with PANDAS researchers?: Please share my information with PANDAS researchers

**Subject:** PANDAS story from Allen, TX

**From:** Jeff & Kirsten Fair (faircasa@yahoo.com)

**To:** mediastories@yahoo.com;

**Date:** Sunday, March 27, 2011 11:51 AM

Hello,  
I received this email address from the PANDAS Resource Network with a request for anyone willing to share their story.

Our 7-yr old daughter was diagnosed with PANDAS in February 2011. The diagnosis was at once a relief and a terrifying reality. Since then we have found new doctors, started aggressive antibiotic treatment, cognitive behavior therapy, and even joined a local support group. We have witnessed a miracle in our daughter's condition. She is by no means "cured" and we understand from speaking with other families that we'll have years of treatment ahead. But we were so deeply in despair before getting a diagnosis and information before. From Nov 2010 to Mar 2011, we went from true darkness to optimism, hope, and excitement about the future. The only way we figured out this medical mystery was by talking to others and relentlessly searching for information. I personally spent over 300 hours researching on the Internet and on the phone with physicians in that several month period. With a busy family of 3 children, this disorder definitely turned our lives upside down. We are a family of strong Christian faith, and I know that doesn't get mentioned on TV much, but I cannot tell our story without saying that is ultimately what we believe pulled us through, kept us together, and led us to the right people who could help. Our pediatrician essentially said he didn't even know for sure if he believed PANDAS was a real disorder, so we thankfully found another local doctor who did. There is so little awareness of this illness, even among physicians and therapists, it's extremely difficult for parents who are in crisis mode to get help. Because the symptoms present as "mental," you get sent to psychiatrists and therapists who ultimately cannot help a PANDAS child on their own. It is a medical condition which requires medical treatment, and not just psychiatric drugs (in most cases, psychiatric drugs like SSRIs actually are more harmful than helpful for PANDAS patients). This disorder turns lives upside down. Marriages are strained. Siblings are devastated. Parents grieve the loss of their child even while he or she is still alive and needing major help. Going on with your usual activities is no longer possible; we stopped soccer, ballet, church, playdates, going to restaurants, going shopping, having friends over for dinner, and vacations. Our daughter could not go to school, sleep in her own bed, eat a normal variety of food, do any normal activities. It was a huge ordeal with screaming to get her in the car to go to a doctor's appointment. All of this happened in a span of about a week. She had previously been the most outgoing, well-adjusted, bright and happy child you could imagine. She had always loved school and all her activities, was a wonderful student in gifted and talented classes, and had lots of friends. Thankfully after starting strong antibiotics she has almost completely recovered. We still have moments of difficulty, but we know this takes some time. She is still going to therapy also to help with some coping mechanisms when she feels symptoms returning. This is the strangest disorder, and it's scary that scientists and doctors still don't understand it completely. But we are committed to helping in every way we can...not just for our daughter but for the overall research and awareness effort. Even locally, I'm so happy if I can help another parent find resources and hope. Thank you for listening to our stories and doing what you can do increase awareness of this mysterious illness. Far too many children and families have suffered already.

Full of hope in Texas,

Kirsten Fair

214-929-6772 (please call/email if you have any questions or would like more information)

faircasa@yahoo.com

**Subject:** PANDAS/PITANDS Story  
**From:** Shari Hanneman (Hanneman@wi.rr.com)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 10:17 AM

We understand you are interested in participants for a story on PANDAS/PITANDS. Our family would be interested in participating. Particularly, our 11 year old daughter has PANDAS and she is very willing to help raise awareness and help other children who are suffering from the debilitating disease.

Our daughter was diagnosed with PANDAS in December, 2010 and was treated with high dose Intravenous Immunoglobulin in early February, 2011. She is at 6 weeks post IVIg and has made significant improvements. She has gone from a completely non-functioning child in November 2010 to competing and winning a dance competition last weekend.

The PANDAS Resource Network has been instrumental in helping us to navigate through the diagnosis, treatment, and recovery process of PANDAS.

Please let us know how we can help!

Shari Hanneman

Franklin, WI

414-761-0663 (h)

414-510-6522 (c)

**Subject:** Our PANDAS Story  
**From:** Deborah Conner (deborah\_conner@yahoo.com)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 10:18 AM

I am writing today to bring a fairly unknown and misdiagnosed illness to your attention. Many doctors are unaware that it exists. This illness is called PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections). Our daughter, now age 10, came down with a strep infection on 1/19/2009. She went to bed on 1/21/2009 with strep but on an antibiotic and with no other symptoms. She woke on 1/22/2009 with OCD thoughts and behaviors. It took a week for me to realize that something was dreadfully wrong. I contacted our pediatrician thinking that it was an allergic reaction to an antibiotic. Luckily, he knew of PANDAS and made the diagnosis. For the next few days, we battled to get our daughter in to see specialists and finally saw a psychiatrist, neurologist, and psychologist who agreed that it was PANDAS and have helped us manage this condition. It took approximately 10 weeks for the symptoms to lessen considerably and at this point, our daughter is nearly symptom free. This condition can recur with future strep infections and can worsen with each consecutive infection. We do see flares in behavior when she is exposed to strep or mycoplasma pneumonia.

During her illness, our daughter experienced separation anxiety, mood changes, obsessive/compulsive behavior, and sleep disturbances.

We have researched this illness and spoken with Dr. Madeline Cunningham (<http://www.ouhsc.edu/mi/faculty/cunningham.html>) who is currently doing a research study on it at the University of Oklahoma.

An intriguing study was done at the University of Florida which states: "In an eight-month study of 693 children in a Florida public school system, University of Florida researchers found that shortly after the number of strep infections in the group increased, there was a corresponding rise in involuntary movements and disruptive behaviors — symptoms that could indicate a neurological cause." Here is a link to the rest of the article: <http://news.ufl.edu/2007/02/06/strep-tic/> .

It is my goal that more people be made aware of this illness so correct diagnosis can be made for all children experiencing this result of strep. Strep is such a common illness that I feel educating the public is of extreme importance. Had we not had a pediatrician who was aware of this illness, we would still be out there searching and wondering why our daughter suddenly changed.

I currently lead the Dallas area PANDAS support group. Another PANDAS mom who originally co-led this group with me now leads the Grapevine/Fort Worth group. During this time of year, I am contacted on a

regular basis by newly diagnosed families desperate to find answers and doctors that can help. I have been amazed by the strength of the families in our support group.

Please contact me with any questions that you may have. Thanks!

Deborah Conner

I can do all things through Him who strengthens me. Philippians 4:13

**Subject:** PANDAS  
**From:** Amy & Paul Sevigny (pakasevigny@comcast.net)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 10:40 AM

Here is our story of how a PANDAS diagnosis has affected our family!

1 year ago, almost to the day, we got a phone call from our oldest daughters school nurse, stating she was crying uncontrollably in her office, complaining of an upset stomach. I went to pick her up and my normal acting, healthy, happy child looked like she had been ran over by a truck: pale, wide eyed, panic stricken and hysterical- her specific complaints were of a stomach ache. Because, her sister had been diagnosed with strep a few days earlier, I called the doctor to have her seen- she said no need to be seen and treated her with an antibiotic for 10 days. Our once very happy child spiraled down hill from there, she was now leaving class daily and crying in the nurses office and eventually refusing to go to school- she did go but was completely unfunctioning for the last several months of her 4th grade. She also had many physical symptoms: constant complaints of a stomach ache, inability to eat (losing about 10 pounds in a month), sleeping problems, paleness etc... Her emotions/anxiety, panic attacks got so bad we quickly became in contact with a therapist (thinking something major must have happened to her, that she is not able to tell us)- on email contact her history with a strep infection was mentioned to the therapist- thank god she counseled us to ask for a blood strep test from the doctors, low and behold our daughters levels were very high- she was put on another course of antibiotics- this time until school was out for the year- we slowly saw progress and our healthy happy child began to return. She has had a few reoccurrences and is now quickly put on antibiotics for a strep infection or exposure.

We are happy to have our little girl back now, but live in a constant state of panic that we could lose her again at any moment, as her change was over night last year!

The thing that we would like to get out and that we find so frustrating is that the medically community would have been very happy to discount her strep infection and her bodies immune response, and label her as new onset anxiety, ocd etc... and would have been happy to treat her for that, but with the proper treatment (antibiotics) she has recovered, but the reality is could relapse at any moment.

There is so much more to our story: struggle to find a doctor to treat her properly, insurance denials for the specialist etc....

With all this said, we loved to share our story, but would never do anything to negatively affect my child and make her situation worse. Please use our information, **contact us for details and permission** etc..to help with your story and please get the word out!!!! These kids need help and these families need help (this whole disorder has changed all of us!)

Thank you for your time- Amy and Paul Sevigny (pakasevigny@comcast.net)

**Subject:** PANDAS in Charlotte  
**From:** Dillon and Claire Bowles (dillonandclaire@carolina.rr.com)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 2:00 PM

I am a physician and my child was diagnosed with PANDAS in January of 2009. We went to 14 doctors over 2 years before the diagnosis was made. Twice we were given the diagnosis of ADHD in the process. This was a disease that I had never heard of even though I went to medical school. My son's case was fairly severe by the time we were diagnosed (severe anxiety, OCD, rages, sleep issues, tics, chorea to the extent he was unable to walk at times). We have undergone treatment( plasmaphoresis) at Georgetown Hospital in DC and now are treated locally by several physicians who were willing to help. My second son was diagnosed last year and because he was caught early he has been much easier to treat. He is almost 6 months out from his last IVIG treatment and completely symptom free. I continually try to spread the word not only with parents, but amongst the medical community. I am always willing to share our story and help other families.

Claire S Bowles, MD

Charlotte, NC

**Subject:** PANDAS story---Lexington, KY  
**From:** Sarah Alleman (salleman920@gmail.com)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 2:15 PM

Dear Producers,

Thank you very much for shining more light on PANDAS. This condition has wreaked havoc with our family and countless others. The short story is that it makes you question everything you've ever done as a parent in regards to your child's health, discipline, and overall well-being. And you also review your entire health history and question it as well. It means that you often can't enjoy minor things like a picnic at the park or little league or school programs. It means that you are constantly on guard and vigilant about any atypical behavior you see...any snuffle or cough you hear...and you see the danger of germs everywhere. You don't have time to clean your house, balance the checkbook, or take a shower. When you do get out of the house and are at the grocery store, you don't have a list, so you spend a lot more money than you need to spend. It's hard to consider even leaving your child with someone else, so you don't get a break from it. BUT nobody knows all of this stuff because if you ask us how we are, we'll probably say fine or give a vague answer about difficulties that belie what is really going on in the four walls of our home. And this is happening with so many families who are undiagnosed (but wondering what is happening to their child), misdiagnosed with an alphabet soup of mental illnesses, and those of us "lucky" enough to have the PANDAS label and know what we are dealing with for our kids. It may start with strep, but so many other infections and viruses trigger symptoms that fear is everywhere. Web sites like Pandas Resource Network, forums, and social networking are literally a lifeline to drowning parents who have children suffering from PANDAS. They let us know that we are not alone in this struggle. Many doctors don't want to diagnose or treat this condition due to the so-called "controversy." For those of us who see the effects of this condition on a daily basis, there is no controversy. We need help. We need more people to know about PANDAS. We need more research. We need a cure and/or effective treatment that are easy for everyone to obtain. We appreciate the work of the PANDAS experts so very much, but every pediatrician should be able to recognize the signs. At a minimum, checking for infection before medicating a child for a mental illness should be standard operating procedure. And the effects this condition likely has on the juvenile justice system and other aspects of society (such as education) are unknown. These seemingly innocuous childhood illnesses can have MAJOR effects. Parents need to know this and be forewarned since early treatment is so important for recovery. And as you'll see in our case, we did seek help and couldn't find it locally.

Here is our family's story. There are no short PANDAS stories. And this is the abbreviated version...there is more, but this is a start.

Our 7 year old son Jesse suffers from PANDAS. We suspect early onset due to some strange behaviors when he was a toddler, but it was a diagnosed bout of strep throat at the end of December 2009 that brought HUGE behavior changes. He got sick with what looked like a virus while out of town visiting relatives. (He had received his 2nd H1N1 shot 2 weeks before which may be related to a weakened immune system and the subsequent strep.) By the time I had him to the doctor, his fever was gone and he seemed a bit better. The strep swab was positive to the doctor's surprise. That's when I realized that my son was likely asymptomatic to strep and wondered if I had missed any other infections. He's also asymptomatic to ear infections and had only two diagnosed/treated bouts with that. He did suffer

from many sinus infections as a child. We removed his adenoids for snoring just before he was 3, and his tonsils were removed just before he turned 4.5 due to chronic tonsillitis.

After that strep throat, Jesse's behavior changed at the end of January 2010, and he began getting in a lot of trouble in kindergarten despite having hardly any issues the first part of the year. We had numerous meetings with the school trying to figure out what was happening there.

We took Jesse to the pediatrician to rule out diabetes, anemia, UTI, strep, ear infections and other physical causes (none). I actually visited our pediatrician EIGHT times between February and May to check for illnesses or to discuss behavior changes. We went to the ophthalmologist to check his vision (fine). (Jesse's gifted, which probably helps him compensate a lot with the PANDAS issues.) We had an occupational therapy evaluation. We had evaluations done by a psychologist we had used for previous IQ testing and ended up with an anxiety diagnosis. We also saw another psychologist. Jesse was exhibiting behaviors at school and at home. We'd see rages, obsessions, fears, age regression, tantrums, inability to reason with him, ADHD symptoms, perfectionism, sensory seeking, insomnia/sleep issues, and more.

I found PANDAS in May 2010 and called my pediatrician thinking I had found the answer. I was told that it couldn't be PANDAS because he'd had subsequent negative strep tests...not a possibility. My goal at that point became to get Jesse out of school without him being suspended since he was always in so much trouble. He had outdoor recess taken away in early May. Let me say that again...MY KINDERGARTEN SON WAS NOT ALLOWED TO GO OUTDOORS FOR RECESS. He would have issues where he wouldn't want to come back inside, and the school couldn't/wouldn't deal with it. I was called numerous times to come to the school. In some cases when I got to the school, it was clear Jesse was having a panic attack or rage of some sort. We ended the year with notes from our doctor allowing us to send Jesse only half days. I could hardly look at or talk to the teacher or principal, and I had been Room Mom! In addition to all this, my husband was diagnosed with some health issues in April, so we were also dealing with that.

The summer showed improvement, and we had him in occupational therapy. We assumed that school had been a big part of the issue (and still do believe there was MUCH stress in that environment). We had applied to a Montessori school and decided to homeschool if we did not get into the private school. (We were waitlisted at Montessori.) I still have trouble driving by our neighborhood school due to the issues we experienced, and I often go the back roads to avoid exposure to the building.

At the end of August, Jesse caught what looked like a cold. In the next weeks (just as I was starting to homeschool), he started a vocal tic. Then a breathing tic. Then developed a strange fear of his hands after watching a cartoon. Then a rage happened. I took him to the doctor with some PANDAS info in hand and asked for a strep test. She did the swab, and it was negative. The doctor told me I needed to get him to the psychiatrist and put him on SSRIs to help his anxiety. There were PANDAS patients at their practice, and they didn't act like Jesse was acting. I asked her to run the strep titers, and I was able to get him some antibiotics. She did not feel it was PANDAS and noted in the chart that he "seemed fine." Two days later on Saturday, I get an early call from the nurse saying his culture showed positive for strep, and she complimented the doctor on making that call. I corrected her and said that it wasn't the doctor, it was me. And I asked if the titers were back...they weren't. I called the office on Monday and expected the doctor to consider PANDAS again due to the strange presentation of strep throat. NOPE. Not PANDAS because the strep titers weren't high enough according to the doctor. (Wrong. I now know that some kids don't have a rise in titers, but the positive culture showed strep involvement.) She also told me that if it was PANDAS that the antibiotics would have cleared the symptoms within 24-hours. (Wrong. There's no research that says that. And those particular symptoms did clear within about 6 days.) She gave me the name of a neurologist I could call on my own if I wanted to pursue PANDAS, and she told me to get him on SSRIs. I sought a second opinion with a doctor who after reviewing our entire medical file and spreadsheets I had prepared showing illnesses and resulting treatments/behaviors said my son likely had PDD-NOS citing info from some

evaluations done when he was a toddler due to a speech delay. His speech delay was resolved, and other QUALIFIED doctors had screened him for autism and did not give that diagnosis. (Those behaviors from toddlerhood began after an illness, and that is why we suspect early onset. My son is not autistic. It's that screening that I believe clouded the entire PANDAS diagnosis locally because they kept going back to that for an answer even tho' it was not there.) And as for SSRIs, they are contra-indicated for PANDAS patients. We also had proven mental changes with infections and still couldn't get a local doctor to help. After we were diagnosed, we were able to find a local doctor willing to take us on as patients after a referral from friends and several calls to other specialists. He does not have any other PANDAS patients, but he has been open to reading the materials I've given him and is interested in our case.

Meanwhile, our son was slipping into more symptoms. OCD. Vocal tics. Insomnia. Age regression. ADHD. Fears. Sensory seeking. Rages. Tantrums. Perfectionism. And more. We couldn't take him out of the house, and he showed no signs of wanting to leave. He wanted to watch TV and would rage when we turned off the set. He stayed up all night and slept all day. Homeschool was impossible. We also found an ear infection at an urgent treatment center that the second doctor had missed. We treated it with antibiotics and saw a huge difference, but the symptoms came back. We got another course of antibiotics, but the symptoms didn't go away that time. I believe if our first doctor had helped us instead of hindering, we may not have lost Jesse like we did in Oct and Nov.

In mid-Oct, I contacted a PANDAS expert in Chicago and sent my son's records. We had a call, and he said he was 95-100% sure it was PANDAS. We scheduled IVIg because we had seen antibiotics fail. We had IVIg in mid-Nov 2010. (We were lucky that insurance did pay...for many families it is not approved.) It took about two weeks to see results, but Jesse responded very well. We had about a month of really good behavior, which meant we were able to put up a Christmas tree and celebrate (something we thought we were going to skip). In early Jan, Jesse did show several days of PANDAS behavior and improved. Recently, we have seen symptoms return, and we're in consultation with our PANDAS expert to see what some recent test results (including mycoplasma pneumonia) will mean for us.

Overall, our son is a funny, wickedly smart, spirited 7-year-old. PANDAS is robbing him of many aspects of his childhood...and us of many aspects of parenthood. I should be researching the best popsicle stick structures to build or summer camps. Instead, I'm Googling mycoplasma effects and immune system functions and checking the forum and Facebook all day. Even when you have a "good" day you can't fully enjoy it due to the knowledge that tomorrow might be bad. We will help Jesse, but there's been a cost...and not just a financial one. Our story is to be continued...we hope for a happy ending.

Thank you again for your interest in PANDAS and your continuing coverage. This research and advances will likely help so many other children and shed light on other conditions. I strive to help my own child, but I'm glad to have the opportunity to help other kids too.

All the Best!

Sarah Jane Alleman

Lexington, KY

**Subject:** PANDAS Letter Our story  
**From:** Shirley Tapia (tapiash1@yahoo.com)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 2:35 PM

My name is Shirley Tapia and I have an 8 yr. Ethan Tapia who has been affected by PANDAS. My son was a very funny little guy, very mild tempered and a lot of fun to be around. He has always been a very healthy child. Ethan lost most of his expressive language. He was evaluated by a speech therapist and his score resembled a score of an 18 month to 2 yr old. He was having sensory issues. We could not get him to wear his clothes. We had to buy him rayon shorts, pants and shirts. We took Ethan to his Pediatrician and she strongly believed he had Autism. I had a hard time believing that. A child cannot get Autism over night.

On the morning of October he woke up with a strange blink. We took him to the eye doctor and they said he was fine. A few days later he started jerking his shoulders. It looked like he was having seizures. We saw 3 different neurologists and they all confirmed he was not having seizures. They recommend we see a neuro psychologist. We took him to a neuro and they diagnosed him with tourettes, ocd and Add. They put him on meds and ethan had a horrible reaction. I took him off the meds and began researching. During the time that we were visiting all the doctors Ethan developed a fear of germs. He would shower 6 to 7 times a day. He would constantly do his laundry. He would include everything in his room. Shortly after the OCD started he started with melt downs. He couldn't communicate his feelings so he became violent. He would bust and throw objects. Blood would gush out of his nose when he was really upset. I was exhausted. I stayed up all night researching and researching. One night I came across an article on PANDAS. I contacted a specialist and we started drawing blood. All of his titers were normal and nothing showed strep. I continued to research and that's when I came across on Cam Kinase. It stated a child may have normal titers if the infection had been sometime time ago. Well the last time Ethan was sick it was a throat infection and it was a year prior to testing. There were probably symptoms before but it didn't appear drastically until he was given the Flu mist and it aggravated his symptoms.

I decide to contact Dr. Cunningham and have his blood drawn. The results were very high. Regardless of research I new he had PANDAS.

I live in NM and no one was convinced or wanted to treat him. After researching I found a doctor in A California who would treat him. My husband and I drove to California to see a doctor who specialized in PANDAS. Since the start of treatment last May he has been on antibiotics, steroids and has had 3 IVIG. He ha made a lot of progress. He is communicating and all symptoms are pretty much gone. He has flair ups but it is nothing compared to what we went through last year.

PLEASE, PLEASE help us get the word out. Not as many parents have the money or as proactive as many of us have been. If I was not so stubborn my son would probably be on meds and be severly mentally ill. This is a condensed story but I would to tell you more. PANDAS shook my families' world and now it's time we shake the World. PANDAS RESOURCE NETWORK has been our life saver!

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**Subject:** PANDAS nightmare  
**From:** Gliebe Diane (dgliebe@fuse.net)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 3:11 PM

Please allow me to share the story of my daughter McKenna.

My happy, healthy, sweet and funny 10 year old daughter ceased to exist this past summer. We lost her completely to debilitating OCD a symptom of this disease. She stopped talking, walking, and eating. She lived in a catatonic state for months. Pointing at things she wanted, screaming and sobbing uncontrollably for hours a day. (I have documented on video.) We saw several doctors who tried hard to make her well with medicine and cognitive behavior therapy. None of it worked.

We participated in a research study through Dr. Madeleine Cunningham at the University of Oklahoma. By their research parameters, she tested positive for PANDAS. That confirmed to us what we believed to be true all along, McKenna had the autoimmune disease PANDAS.

Unable to get treatment in Cincinnati, we traveled to New Jersey to see Dr. Catherine Nicolaiades. I knew from my research she had helped other PANDAS patients get well, and I believed she was our hope. She was. Dr. Nicolaiades started McKenna on antibiotic treatment 1 month ago. Four days into treatment, we could see it was working. Everyday we are seeing her brain heal. What a beautiful thing. Everyday we experience victories; eating dinner with us, walking outside, answering a telephone. All of which were impossible a month ago.

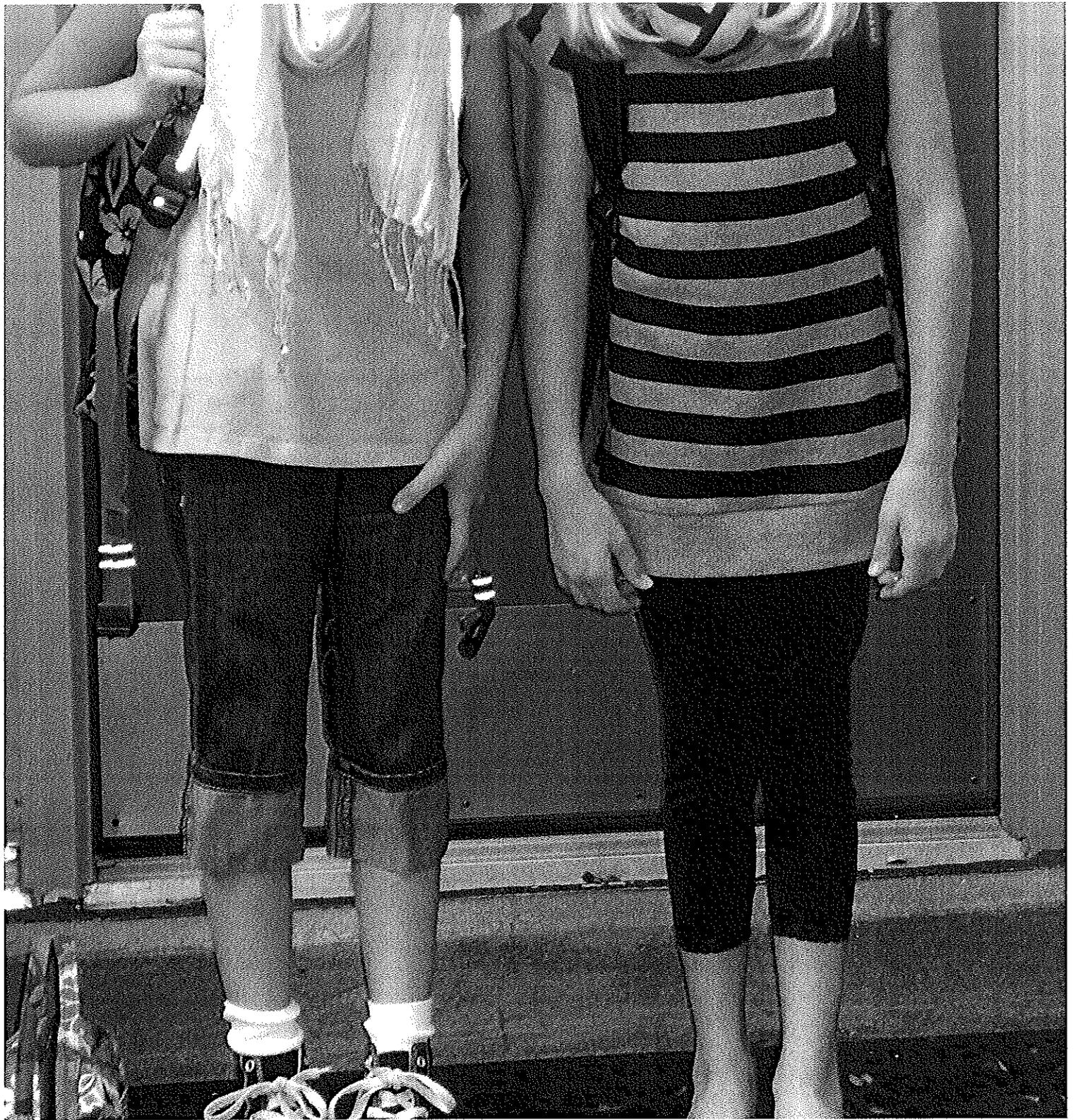
It is incredibly scary to deal with a disease that so few doctors know how to treat. It completely stopped our lives. I lost their Dad to heart disease three and a half years ago, and I was not about to lose my daughter too. I promised McKenna I would not stop searching for the answers until she was well. I know now, that day is coming.

Sincerely,  
Diane Gliebe-Meyer

513-474-9218

picture McKenna (on left) her twin Bryn (on right)





**Subject:** Pandas  
**From:** Laurie Owens (minnesotaowens@comcast.net)  
**To:** mediastories@yahoo.com;  
**Cc:** minnesotaowens@comcast.net;  
**Date:** Tuesday, March 22, 2011 4:17 PM

Dear Producers,

Thank you for doing a story about Pandas!!!

Our first knowledge of Pandas came one year ago on St. Patrick's Day. Our "healthy" son headed to school just like he ordinarily did. The morning was uneventful. At 9:30 am I received a call from school that our son was moving very strangely and that I needed to get to school as soon as possible. When I arrived at school, our son was having trouble controlling his arms, shoulders, and facial expressions. His shoulders were shrugging up and down very quickly. I helped him get in to the car. I drove to a hospital where a doctor who knows our son is affiliated. While I drove him to the hospital his arms flailed about, hitting the car seats and window. His face made frequent uncontrolled "grimaces." His speech was very labored.

I brought him to the emergency department. His regular doctor examined him and ordered blood work. My son was discharged several hours later. Doctors weren't sure why he was experiencing the movements, but thought it may have been due to a dosage reduction of a medication from a couple of weeks earlier. My husband and I brought our son home and kept him home for a couple of days to "watch him."

Over the next few days the movements became fewer. Our doctor phoned us a week later to report that our son's strep antibody titers were elevated. Our doctor believed our son's movements were due to a reaction to a recent strep infection. The doctor said our son had Pandas. We had no idea what that was. However, our son had stayed home from school with a sore throat exactly 21 days earlier before the onset of movements.

The day after the diagnosis my husband and I met with our son's teachers for his regularly scheduled conferences. It was very strange because our son had a different teacher for every class, and all of them remarked about his new "concerns" with eraser particles, sharpie smells, germs, going blind. Our son had never been overly concerned with germs. I also began to notice that my 13 yo son who used to love sitting in the front seat of the car had started sitting in the back seat with a baseball hat and/or sunglasses to shield his eyes. He had been asking me about his concerns with going blind from looking at the sun recently. I thought it was strange, but I did not think much about it at first.

Spring break came and went. Our son's fears were increasing exponentially. He was no longer sleeping alone. He insisted on sleeping on our floor every single night. He struggled at school because his OCD became so debilitating. He was experiencing huge panic attacks. He could not be left alone. He was afraid of everything. He became homebound by the middle of April. His fears increased and he seemed to add things to his list of worries each day. He began hallucinating.

As you may imagine, this took quite a toll on our family. We have 2 younger children who witnessed this tragedy right before their eyes. Our son's panic attacks frequently turned to rage. It all made no sense to our younger kids. Since our son was unable to attend school, I stayed home from part time work to be with him. This created a financial strain.

To make matters worse, none of the doctors or institutions we first contacted in our area had a whole lot of knowledge about PANDAS. Few were interested in learning about the latest studies and research. Several doctors seemed downright skeptical of our story. The MAJOR medical institutions located near us had no interest in helping our son. "We don't treat PANDAS," said the very famous clinic. Our neurologist said "PANDAS is controversial. I fall on the side of non-believers. What can I do for you?"

Since we exhausted every avenue we could think of locally, we decided to seek treatment from people outside our local area. Fortunately we became connected with the PANDAS Resource Network. It was through the network that we were able to connect with doctors and the latest research from experts in the PANDAS community. We also realized what we were experiencing was happening to others.

We have found treatment from doctors hundreds of miles away who are knowledgeable about PANDAS. They are motivated to help our son. Our son has had IVIG and plasmapheresis. We have spent countless hours learning about this devastating illness. We have spent thousands of dollars to seek treatment for our son. The treatments have benefitted our son tremendously, although this is a chronic illness and he continues to experience exacerbations. Today our biggest hurdle is local knowledge, ongoing care, and coverage for treatment from our insurance. Insurance providers rarely pay for IVIG or plasmapheresis for PANDAS. The really scary thing.....siblings are thought to have a 40 to 50% chance of becoming PANDAS kids as well. Very, very scary.

Thank you for listening to the many stories. Out of respect for our kids we ask that you keep the identities and details of our story private.

Sincerely, Laurie Owens

**Subject:** A tale of two stories of PANDAS/PITANDS

**From:** wpackfans@aol.com (wpackfans@aol.com)

**To:** mediastories@yahoo.com;

**Date:** Tuesday, March 22, 2011 5:30 PM

My name is Jessica Barton and I have two children: Noah, 11, and Jessalyn, 7.

One year ago this month, Jessalyn was diagnosed with strep and was put on an antibiotic. Almost overnight, she turned into a different child....one I did not recognize. My social butterfly could not sleep, cried constantly, could not be separated from me and began to fear leaving the house. After three rounds of antibiotics (and continued neuropsychiatric symptoms), the pediatrician asked me if I had ever heard of PANDAS. I went home and stayed up all night researching it.

After compiling my research, it dawned on me that my son, Noah, also had many of the symptoms of PANDAS--symptoms that had shown up overnight over 2 1/2 years prior. He had been diagnosed with a tic disorder, ADD and depression. He had been on medication for over 2 years to help with the symptoms of his diagnoses.

I decided to have him checked for strep. It was negative. The doctor then said PANDAS was a closed door. I had been so sure that Noah also had PANDAS that I ignored the doctor and began to dig deeper. After weeks of frantic online searching, I found Dr. Trifiletti in New Jersey who told me that there were other bacterial triggers for this disease--triggers that change the acronym for the disease from PANDAS to PITANDS. He did bloodwork on Noah and discovered that Noah was indeed positive--not for strep, but for mycoplasma pneumoniae. His antibodies were over 8 times the normal upper limit.

Dr. T took on both of my children as patients last June. Fortunately, Jessalyn's case was easy to treat. In some children, if the first exacerbation is caught and treated aggressively and early, resolution of that exacerbation can be relatively quick. Jessalyn is back to being my social butterfly. I have to watch that she does not get strep, but other than that, she is fine.

Noah's case is a bit different. He had been misdiagnosed and mistreated with psychotropic drugs for over 2 years.....all the while the real culprit was blooming in his body, attacking his brain, causing tics, obsessions, frustration, sadness, anger, confusion and ultimately, rejection by his peers. This delay in receiving the correct diagnosis was caused by the complete ignorance of the local medical community, and I am sad to say, by my own ignorance and complete reliance on that community. This delay has also made Noah's case so much more difficult to treat. He is slowly getting better, but it has been and continues to be an agonizing process. Noah loses a bit of ground with his peers, with his life, each day he has PITANDS that is not under control. Let me repeat--it has now been over 3 1/2 years since his tic first manifested. If only a doctor, friend, teacher, principal, or fellow parent had said to me at the onset of that first exacerbation, "I saw this segment on a disease called PANDAS/PITANDS on TV and some kids start ticing overnight, just like Noah has. Maybe you should look into that." Instead there was no awareness of this horrible disease out there, and as a result I put psychotropic drugs into my child that his body and embattled brain did not need, possibly damaging something in the process. I cannot unring that bell, and will always have to live with myself for that choice.

I beg for you to do all you can to make PANDAS/PITANDS more recognizable, more mainstream. Do all you can so that other children will have experiences like Jessalyn's.....not Noah's. Do all you can so other mothers don't have to live with the guilt I carry for mistreating my son.

**Subject:** PANDAS Story

**From:** thmhenry@aol.com (thmhenry@aol.com)

**To:** mediastories@yahoo.com;

**Date:** Tuesday, March 22, 2011 6:29 PM

My daughter Margaret was six years old when she experienced overnight symptoms of severe OCD after witnessing our dog throw up. She would check everyone in the house about every few

minutes sometimes for hours a day. She went from being a bright, happy, fearless six year old to a child who suddenly had severe separation anxiety, severe anxiety and obsessions around

throw up, and a snorting tic that was so bad we ended up changing schools because her classmates constantly made fun of her tic, calling her a pig. We immediately knew that something

was terribly wrong and got her right into her physician who suspected OCD. One thing we clearly knew was that our daughter was not the same child we knew a few weeks before, and that she

drastically changed overnight. At the time, we didn't really even know what OCD was so I got on the internet to research it and heard about PANDAS. We clearly remembered that she was

very sick right before her symptoms began and so we went back to the doctor and asked him about PANDAS. He insisted that Margaret did not have symptoms of PANDAS and did not test

her for strep. As our physician for many years, we believed he must be right. A year later I convinced another doctor to test her for strep but by that time her levels were in the normal

range. So, we found a therapist who worked with Margaret intensively with exposure therapy and her symptoms gradually improved. We worked with doctors from one of the best Children's

Hospitals in the country, so felt like she was in the best care. We also thought the therapy she received was the reason for her symptoms improving. Two years later, her symptoms markedly

improved. Then at age nine, she left for overnight camp about a month after a bout of mycoplasma pneumonia. When she returned from camp, she completely stopped eating, refused to leave

the house, her severe OCD returned, she had several panic attacks a day, was suicidal, suffered light/noise sensitivity, had severe impulse control problems, frequently jumping out the

window and running into the street, tantrums, aggression. She was so sick she needed to be watched at all times 24/7. School became almost impossible for her and her grades dropped

two grade levels that year, and was eventually diagnosed with dysgraphia (caused by PANDAS) All of this in a NINE year old !!! My husband and I tried hospitalizing her, but we were uninsured

so were denied. We contemplated intensive therapy for her in Florida, across the country for us, but we couldn't even get her out of the house, let alone an airplane. And then, once again, she

gradually began improving. We also continued to suspect PANDAS and frequently insisted she get tested when she got sick, but without those strep titers, it was virtually impossible to prove

PANDAS, particularly given the fact that most doctors are nbelievers. Three years later, she continued to have symptoms, but not to the same extreme. Then I happened to find on Pandas

Resource Network that Mycoplasma Pneumonia can be involved in episodes following the initial Strep trigger. That was

what I needed ! I was now 99% convinced that Margaret indeed had

PANDAS. Through PRN I was able to find doctors who could treat and diagnose her. She tested positive for Mycoplasma pneumoniae three years after exposure to it. It had

crossed the Blood brain barrier triggering her symptoms. She also participated in the study with Madeline Cunningham and her bloodwork tested in the high PANDAS range. She was put on

full time antibiotics and within two weeks she was completely back to the child I knew before her first episode at age six. After two months she was taken off the antibiotic and her symptoms

returned so she has now been taking it for six months and is doing great ! Obviously we are both happy and sad at the same time knowing full well that If it were not for PRN

and all the parents and Dr's involved in the Network that there was a great likelihood Margaret would have suffered a lifetime of mental illness. My sadness comes from the fact that so many

doctors failed to recognize and treat her, and there is no doubt there are many children misdiagnosed with OCD and tourettes. I am happy because there are dedicated mothers and a few

doctors who know the unimaginable suffering that occurs with PANDAS. And thanks to them, Margaret is thriving and loves life once again !! PANDAS Resource Network gave Margaret

back her childhood ! Both Margaret and I are more than happy to be reached for further questions or information. Our phone number in Seattle is 206-322-7642. Thanks.

Brett Henry (Margarets mother)

**Subject:** PANDAS Survivor  
**From:** Phil and Gwen (pgmolfino@comcast.net)  
**To:** mediastories@yahoo.com;  
**Date:** Tuesday, March 22, 2011 7:55 PM

Not sure who this email is destined for, but we have a very important story to tell. A story about suffering, the failure of mainstream medicine, and the second chance that we were given through the Pandas Resource Network. They connected us with a doctor who treated our OCD/PANDAS son and reversed most of his symptoms within three days.

Our lives were utterly destroyed overnight. For four months we mourned the "loss" of our son, got educated, regularly disappointed, and finally saved. If you'd like to hear about our story, we'd be happy to share it.

Phil and Gwen Molfino

**Subject:** PANDAS child

**From:** Rashida Qureshi-Keys (rqureshikeys@hotmail.com)

**To:** mediastories@yahoo.com; corselius@verizon.net; ckeys@ciena.com; nurses@advanced-allergy.com;

**Date:** Wednesday, March 23, 2011 9:46 AM

My son's story is a little different. Blake is 13 now, and honestly, he was an odd bird from infancy. He clung to me, was fearful of everything, and spoke very little, even though he was capable. He struggled in school, made no friends, chewed his fingernails obsessively. At age 7 he started being treated for ADHD and anxiety and depression. I feared for my child everyday what the future would hold. Meanwhile, his brother and sister, one older and one younger, had tonsils out, had typical childhood infections, etc. I had no idea that ALL my kids had strep, not just the ones with sore throats. Fastforward 5 years, Blake's condition got even worse. He developed a self mutilation behavior, pulling the skin around his neck so tightly, the skin on the front has stretch marks. He eventually lost expressive speech, able only to answer yes /no questions, and unable to initiate verbal communication. He lost the ability to write and do math. He could no longer sit in a classroom at all. He was removed from school at the beginning of seventh grade. He received a diagnosis of high functioning autism. We were devastated and furious. What did not make sense though, was that his condition continued to decline. I knew that was not consistent with any form of autism. I prayed and prayed and googled! Lo' and behold, PANDAS. By the grace of God, Blake's tests were all positive. As you may know, thirty percent of kids with PANDAS may not test positive for strep antibodies. But Blake's tests were all positive, which was terrific because none of the specialists we had seen to that point had ever heard of PANDAS. He went on to have the Cunningham test, which further supported the diagnosis. After 8 months of antibiotics, my son can speak to us again, and I know that he is not autistic in any sense. He has motivation, which he did not have at all prior. He can bathe, brush his teeth, take his medication, even cook for himself! He jokes with us, understands sarcasm, and is super bright. PANDAS had literally suppressed his "SELF" all his life. I am thoroughly enjoying getting to know my son. Blake is now under the care of Dr. B, receiving regular IVIG, and I don't fear for his future anymore, I am looking forward to it.

Rashida A. Qureshi-Keys  
3018290622

**Subject:** Re: Read this one  
**From:** Mediastories (mediastories@yahoo.com)  
**To:** mediastories@yahoo.com;  
**Cc:** lynnj0750@msn.com;  
**Date:** Thursday, March 24, 2011 4:24 AM

Sent from my iPhone

On Mar 23, 2011, at 12:35 PM, "Owens, Chris J." <Chris.J.Owens@supervalu.com> wrote:

My wife sent in details about my son which would make a great contribution to the story (a copy is below). We want to protect him because he is embarrassed by his illness so his anonymity is important. Also, we are fearful of reprisals from the insurance industry do to their sinister behavior in the area of treatment. If you want to really hit on a timely and interesting back story associated with PANDAS, it would be how it exposes immoral practices in the health insurance industry related to this childhood illness. Their lack of understanding of the ailment seems to lead them into a default "rejection" of the best treatment regime, something called IVIG.

Insurance companies use the typical fallback position of "investigational" even though most the clinical studies call for IVIG as a recommend treatment. (Most other countries that practice western medicine use IVIG to treat it). They force families and physicians into the difficult position of arguing the obvious to someone who has no vested interest in proper care. In fact, one could argue they have the opposite motivation of the parents, doctors and patient. The epidemiology is clear that PANDSAS is a fairly common autoimmune issue. If they cover the treatment and diagnosis increases, then the # of IVIG treatments go up and their costs go up. So, rather than support using a relatively inexpensive, commonly used treatment option, they deny coverage. Many families choose financial ruin to pay for the treatment out of pocket because the Insurance industry does not support any reasonable treatments.

If you want to draw some viewers, run a story on a debilitating illness that attacks kids. If you want to draw a lot of viewers, run a story about an illness where the insurance industry is fighting against a common, relatively inexpensive treatment that could cure most of these kids...

*cjo*

<image001.png>**Chris Owens** ~ O:952-294-6934 ~ m:952-913-5008 ~  
chris.j.owens@supervalu.com

**From:** Laurie Owens <minnesotaowens@comcast.net>

**Date:** March 22, 2011 3:17:58 PM CDT

**To:** mediastories@yahoo.com

**Cc:** Me Owens <minnesotaowens@comcast.net>

**Subject:** Pandas

Dear Producers,

Thank you for doing a story about Pandas!!!

Our first knowledge of Pandas came one year ago on St. Patrick's Day. Our "healthy" son headed to school just like he ordinarily did. The morning was uneventful. At 9:30 am I received a call from school that our son was moving very strangely and that I needed to get to school as soon as possible. When I arrived at school, our son was having trouble controlling his arms, shoulders, and facial expressions. His shoulders were shrugging up and down very quickly. I helped him get in to the car. I drove to a hospital where a doctor who knows our son is affiliated. While I drove him to the hospital his arms flailed about, hitting the car seats and window. His face made frequent uncontrolled "grimaces." His speech was very labored.

I brought him to the emergency department. His regular doctor examined him and ordered blood work. My son was discharged several hours later. Doctors weren't sure why he was experiencing the movements, but thought it may had been due to a dosage reduction of a medication from a couple of weeks earlier. My husband and I brought our son home and kept him home for a couple of days to "watch him."

Over the next few days the movements became fewer. Our doctor phoned us a week later to report that our son's strep antibody titers were elevated. Our doctor believed our son's movements were due to a reaction to a recent strep infection. The doctor said our son had Pandas. We had no idea what that was. However, our son had stayed home from school with a sore throat exactly 21 days earlier before the onset of movements.

The day after the diagnosis my husband and I met with our son's teachers for his regularly scheduled conferences. It was very strange because our son had a different teacher for every class, and all of them remarked about his new "concerns" with eraser particles, sharpie smells, germs, going blind. Our son had never been overly concerned with germs. I also began to notice that my 13 yo son who used to love sitting in the front seat of the car had started sitting in the back seat with a baseball hat and/or sunglasses to shield his eyes. He had been asking me about his concerns with going blind from looking at the sun recently. I thought it was strange, but I did not think much about it at first.

Spring break came and went. Our son's fears were increasing exponentially. He was no longer sleeping alone. He insisted on sleeping on our floor every single night. He struggled at school because his OCD became so debilitating. He was experiencing huge panic attacks. He could not be left alone. He was afraid of everything. He became homebound by the middle of April. His fears increased and he seemed to add things to his list of worries each day. He began hallucinating.

As you may imagine, this took quite a toll on our family. We have 2 younger children who witnessed this tragedy right before their eyes. Our son's panic attacks frequently turned to rage. It all made no sense to our younger kids. Since our son was unable to attend school, I stayed home from part time work to be with him. This created a financial strain.

To make matters worse, none of the doctors or institutions we first contacted in our area had a whole lot of knowledge about PANDAS. Few were interested in learning about the latest studies and research. Several doctors seemed downright skeptical of our story. The MAJOR medical institutions located near us had no interest in helping our son. "We don't treat PANDAS," said the very famous clinic. Our neurologist said "PANDAS is controversial. I fall on the side of non-believers. What can I do for you?"

Since we exhausted every avenue we could think of locally, we decided to seek treatment from people outside our local area. Fortunately we became connected with the PANDAS Resource Network. It was through the network that we were able to connect with doctors and the latest research from experts in the PANDAS community. We also realized what we were experiencing was happening to others.

We have found treatment from doctors hundreds of miles away who are knowledgeable about PANDAS. They are motivated to help our son. Our son has had IVIG and plasmapheresis. We have spent countless hours learning about this devastating illness. We have spent thousands of dollars to seek treatment for our son. The treatments have benefitted our son tremendously, although this is a chronic illness and he continues to experience exacerbations. Today our biggest hurdle is local knowledge, ongoing care, and coverage for treatment from our insurance. Insurance providers rarely pay for IVIG or plasmapheresis for PANDAS. The really scary thing.....siblings are thought to have a 40 to 50% chance of becoming PANDAS kids as well. Very, very scary.

Thank you for listening to the many stories. Out of respect for our kids we ask that you keep the identities and details of our story private.

Sincerely, Laurie Owens

**Subject:** [No Subject]

**From:** Kerry Ebersole (kerry.ebersole@yahoo.com)

**To:** mediastories@yahoo.com;

**Date:** Tuesday, March 22, 2011 9:38 PM

PANDAS and PITANS needs more media attention and more research so that families do not have to suffer like our family suffered and like many other families have suffered. My nine year old daughter went from being sweet, smart and outgoing to angry, challenged, and anti-social essentially overnight. She was terrified as was I. I will never forget the fear in her eyes because she did not know what was happening to her. Can you imagine your nine year old child telling you that she thought she wanted to kill you? That she would rather kill herself than have to suffer like she was? To not have any idea what had happened?

When we first went to a psychiatrist she did tell us about PANDAS. Unfortunately, the lab messed up my daughter's test results and it had been a three hour process to get her blood drawn due to her OCD and anxiety. The psychiatrist told us it didn't matter what the results were as the treatment for OCD and PANDAS was the same. We also went to 4 therapists. None of them mentioned PANDAS, the symptoms of PANDAS, or the treatment for it. It wasn't until I went to the OCD conference that I met a woman who told me that my daughter seemed just like her daughter who had been diagnosed with PANDAS and that I should look into it. Easier said than done. It was hard to find a doctor near our home who believed in it or treated for it. This is unforgivable when a national renowned children's hospital is in our backyard. The one doctor I found and called never called back despite numerous messages.

One year after her sudden onset, we found a doctor in the next state who sent us for bloodwork and upon receipt of the results and his evaluation of her, diagnosed her with PANDAS. A normal school age child's strep titers are around 170. The test only measured up to 1,380 and my daughter's results were greater than the test could measure. Since the time of her diagnosis, we have been to two other PANDAS doctors, (none of which are in our home state) to continue with her treatment. We have been to other doctors nearby who not only don't believe in it but some are even disdainful. I am sure that if it happens to someone they love, they will become a believer on the spot.

It is now two years post our onset and we are back to 90-95%. We got back to this level after the treatment for PANDAS began. I do wonder if we would be back to 100% if we did not have to suffer for one year without the proper treatment. I also think of all of the things we went through in that year and that my daughter suffered needlessly all because of lack of the information.

And yet, we are one of the lucky ones. There are still so many families out there that are still fighting, still have no idea what is going on or how to get help.

I fully support Dr. Bouboulis and P.A.N.D.A.S. Resource Network for spreading the word about PANDAS/PITANS. We could not have made it this far without Dr. B and I am thankful everyday for what he has done for us. He has given me back the sweetest sounds- my daughter's laughter and singing which one year ago, I never thought I would hear again.

Doing a story on PANDAS/PITANS can save lives!

Kerry