



PANDAS

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Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcal Infections, or PANDAS, is a common autoimmune disorder with far-reaching movement, behavioral, and cognitive consequences. Although we focus on the pediatric population as part of the PANDAS syndrome in this review, immune-mediated OCD/Tics/Neuropsychiatric Disorders can also affect adolescent and adult populations and should always be considered when specific signs and symptoms emerge.

As noted by Dr Sue Swedo at the NIH in the late 1990's, PANDAS involves antibodies from a streptococcal infection reacting with brain tissue (specifically the basal ganglia) and triggers movement and behavioral problems. Rheumatic Fever is an older known disorder that illustrates this same disease process, in which antibodies from a streptococcal infection attack the heart valves, joints, and brain and result in heart disease, arthritis, and Sydenham's Chorea. Although bacteria set the vicious cycle in motion, the real damage in this type of autoimmune disorder stems from the antibodies and the inappropriate immune response.

Although the exact mechanism of the autoimmune process involved with PANDAS is still under investigation, research published in The Journal of Neuroimmunology in 2006 by Kirvan, et al suggests the mechanism involves antibody-mediated cell-signaling post group A streptococcal infections. The antibodies produced in group A streptococcal infections are thought to penetrate the blood brain barrier (BBB) and activate a brain enzyme (CaM kinase II) with multiple functions that are negatively impacted in various neuropsychiatric disorders. The article notes that those with PANDAS have higher CaM kinase II activation than those with non-PANDAS OCD, tic, and ADHD groups not associated with streptococcal infection.

Although PANDAS is a clinical diagnosis, the traditional criteria for PANDAS include:

1. OCD and/or Tic Disorder
2. Pediatric onset of symptoms (age 3 to puberty) – sudden/dramatic onset
3. Episodic course of symptom severity (waxes and wanes)
4. Association with group A beta-hemolytic streptococcal infection (such as through a positive throat culture for strep or history of Scarlet Fever)
5. Association with neurologic abnormalities (such as motoric hyperactivity, choreiform movements, etc)

Clinical experience reveals that traditional criteria for PANDAS do not capture the full scope and complexity of what is involved with the presentation, diagnosis, and treatment



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of this disorder. One must also consider the presence of other signs/ symptoms/ comorbidities, frequent lack of known strep exposure/illness, specific lab abnormalities (or lack thereof), and response to treatment.

Other signs, symptoms, and comorbid diagnoses noted in children with PANDAS include irritability, personality changes, aggression, uncontrolled agitation, fear about bedtime regimen, fidgetiness, emotional lability, anxiety, enuresis, motoric symptoms (tics, handwriting changes, motoric hyperactivity, compulsive rituals), sensory defensiveness, impulsivity, depression, dysthymia, separation anxiety, anorexia, ADD, and ADHD.

Laboratory tools are limited and the traditional abnormalities of increased blood strep titers (ASO and DNaseB antibodies) and a positive throat culture are not always present. Therefore, normal levels of strep antibodies and negative cultures do not exclude the PANDAS diagnosis. Streptococcal bacteria found in gastrointestinal testing may provide a clue given other signs and symptoms consistent with PANDAS, but it is not enough to make a diagnosis. The emerging research noted above involving CaM kinase and anti-neuronal antibodies is promising and has important diagnostic and therapeutic implications. These newer tests are particularly helpful when blood ASO and DNaseB antibodies and other tests are negative in a child in whom PANDAS is suspected, however they are not yet commercially available.

As mentioned earlier, the real problem is thought to be the damage resulting from the inappropriate immune response to the bacterial infection. Damage from the antibodies recurs with each subsequent streptococcal exposure and PANDAS flare. Research studies have shown that antibodies alone are enough to cause the behavioral and movement problems noted in those with PANDAS. This is a crucial point, in that adequate PANDAS treatment requires comprehensive immune therapy, in addition to antibiotics. One is not enough without the other, and immune therapy is likely the more important of the two treatment arms.

Treatments to consider for PANDAS (one should discuss with primary doctor involved, but referral to an Immunologist experienced in PANDAS diagnosis and treatment is also recommended):

1. Antibiotics (used daily for treatment and sometimes less frequently for prophylaxis – zithromax, omnicef, penicillin, IM bicillin, clindamycin, etc)
2. Immune Modulation Therapy
 - a. Corticosteroids (short-term use of tapering dose – positive response often indicates the patient is more likely to respond positively to IVIG, but no response does not mean IVIG will be ineffective)
 - b. Intravenous immunoglobulin (IVIG) -- derived from human blood; pooled from many donors; can provide antibodies in those who are lacking



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- them; can help to inactivate antigens and slow down an overactive immune system that is functioning inappropriately; case reports and studies show effectiveness
- c. Plasmaphoresis – a type of plasma transfusion to remove antibodies; various case reports reveal positive results, but lack of long-term studies
 - d. Other natural anti-inflammatory and immune supporting therapies (curcumin, essential fatty acids, transfer factor/colostrum, probiotics, etc)
3. Natural antimicrobial therapies
 - a. Probiotics, including *Saccharomyces Boulardii*
 - b. Xylitol
 - c. Antimicrobial herbs (Berberine, etc)
 4. Removal of adenoids and tonsils (no good studies on this; may even worsen signs and symptoms in some cases; but can still consider in certain cases where appropriate after referral to ENT Physician familiar with PANDAS).
 5. Medications like SSRI's (Prozac, Zoloft, etc) can often act as a "patch" for OCD or other symptoms, but should only be considered for short-term use in certain cases

PANDAS is a devastating autoimmune disorder in children that highlights another link between chronic and recurrent infection and neuropsychiatric and behavioral problems. Ongoing clinical experience and emerging research reveals the depth and scope of problems stemming from PANDAS is much more far-reaching than previously thought. While OCD and tics are still common, other issues like anxiety, bedtime fears, enuresis, aggression, and deficits in learning, attention, and social interaction are among the many manifestations that result from PANDAS and impair the daily functioning and cognitive progress for many children. Heightened clinical suspicion and more appropriate and comprehensive treatment with antibiotics and immune-modulating therapy will transform PANDAS from a devastating chronic illness with episodic flares into a treatable disorder.