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PANDAS: Frequently Asked Questions about Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections

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PANDAS, is an abbreviation for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections. The term is used to describe a subset of children who have Obsessive Compulsive Disorder (OCD) and/or tic disorders such as Tourette Syndrome, and in whom symptoms worsen following strep infections such as "Strep throat" and Scarlet Fever.

The children usually have dramatic, "overnight" onset of symptoms, including motor or vocal tics, obsessions, and/or compulsions. In addition to these symptoms, children may also become moody, irritable or show concerns about separating from parents or loved ones. This abrupt onset is generally preceded by a Strep throat infection.

What is the mechanism behind this phenomenon? At present, it is unknown but researchers at the NIMH are pursuing a theory that the mechanism is similar to that of Rheumatic Fever, an autoimmune disorder triggered by strep throat infections. In every bacterial infection, the body produces antibodies against the invading bacteria, and the antibodies help eliminate the bacteria from the body. However in Rheumatic Fever, the antibodies mistakenly recognize and "attack" the heart valves, joints, and/or certain parts of the brain. This phenomenon is called "molecular mimicry", which means that proteins on the cell wall of the strep bacteria are similar in some way to the proteins of the heart valve, joints, or brain. Because the antibodies set off an immune reaction which damages those tissues, the child with Rheumatic Fever can get heart disease (especially mitral valve regurgitation), arthritis, and/or abnormal movements known as Sydenham's Chorea or St. Vitus Dance.

In PANDAS, it is believed that something very similar to Sydenham's Chorea occurs. One part of the brain that is affected in PANDAS is the Basal Ganglia, which is believed to be responsible for movement and behavior. Thus, the antibodies interact with the brain to cause tics and/or OCD, instead of Sydenham Chorea.

Frequently Asked Questions

Is there a test for PANDAS?

No. The diagnosis of PANDAS is a clinical diagnosis, which means that there are no lab tests that can diagnose PANDAS. Instead clinicians use 5 diagnostic criteria for the diagnosis of PANDAS (see below). At the present time the clinical features of the illness are the only means of determining whether or not a child might have PANDAS.

What are the diagnostic criteria for PANDAS?

Diagnostic criteria are:

- Presence of obsessive-compulsive disorder and/or a tic disorder
- Pediatric onset of symptoms (age 3 years to puberty)
- Episodic course of symptom severity
- Association with group A Beta-hemolytic streptococcal infection (a positive throat culture for strep or history of Scarlet Fever)
- Association with neurological abnormalities (motoric hyperactivity, or adventitious movements, such as choreiform movements).

What is an episodic course of symptoms?

Children with PANDAS seem to have dramatic ups and downs in their OCD and/or tic severity. Tics or OCD which are almost always present at a relatively consistent level do not represent an episodic course. Many kids with OCD or tics have good days and bad days, or even good weeks and bad weeks. However, patients with PANDAS have a very sudden onset or worsening of their symptoms, followed by a slow, gradual improvement. If they get another strep infection, their symptoms suddenly worsen again. The increased symptom severity usually persists for at least several weeks, but may last for several months or longer. The tics or OCD then seem to gradually fade away, and the children often enjoy a few weeks or several months without problems. When they have another strep throat infection the tics or OCD return just as suddenly and dramatically as they did previously.

Are there any other symptoms associated with PANDAS episodes?

Yes. Children with PANDAS often experience one or more of the following symptoms in conjunction with their OCD and/or tics:

1. ADHD symptoms (hyperactivity, inattention, fidgety)
2. Separation anxiety (child is "clingy" and has difficulty separating from his/her caregivers; for example, the child may not want to be in a different room in the house from his/her parents)
3. Mood changes (irritability, sadness, emotional lability)
4. Sleep disturbance
5. Night- time bed wetting and/or day- time urinary frequency
6. Fine/gross motor changes (e.g. changes in handwriting)
7. Joint pains.

My child has had strep throat before, and he has tics and/or OCD. Does that mean he has PANDAS?

No. Many children have OCD and/or tics, and almost all school aged children get strep throat at some point in their lives. In fact, the average grade-school student will have 2 – 3 strep throat infections each year. PANDAS is considered when there is a very close relationship between the abrupt onset or worsening of OCD and/or tics, and a preceding strep infection. If strep is found in conjunction with two or three episodes of OCD/tics, then it may be that the child has PANDAS.

Could an adult have PANDAS?

No. By definition, PANDAS is a pediatric disorder. It is possible that adolescents and adults may have immune mediated OCD, but this is not known. The research studies at the NIMH are restricted to children.

My child has PANDAS. Should he have his tonsils removed?

The NIH does not recommend tonsillectomies for children with PANDAS, as there is no evidence that they are helpful. If a tonsillectomy is recommended because of frequent episodes

of tonsillitis, it would be useful to discuss the pros and cons of the procedure with your child's doctor, because of the role that the tonsils play in fighting strep infections.

What exactly is an anti-streptococcal antibody titer?

The anti-streptococcal antibody titer determines whether there is immunologic evidence of a previous strep infection. Two different strep tests are commercially available: the antistreptolysin O (ASO) titer, which rises 3-6 weeks after a strep infection, and the antistreptococcal DNAase B (AntiDNAse-B) titer, which rises 6-8 weeks after a strep infection.

What does an elevated anti-streptococcal antibody titer mean? Is this bad for my child?

An elevated anti-strep titer (such as ASO or AntiDNAse-B) means the child has had a strep infection sometime within the past few months, and his body created antibodies to fight the strep bacteria. Some children create lots of antibodies and have very high titers (up to 2,000), while others have more modest elevations. The height of the titer elevation doesn't matter. Further, elevated titers are not a bad thing. They are measuring a normal, healthy response – the production of antibodies to fight off an infection. The antibodies stay in the body for some time after the infection is gone, but the amount of time that the antibodies persist varies greatly between different individuals. Some children have "positive" antibody titers for many months after a single infection.

When is a strep titer considered to be abnormal, or "elevated"?

The lab at NIH considers strep titers between 0-400 to be normal. Other labs set the upper limit at 150 or 200. Since each lab measures titers in different ways, it is important to know the range used by the laboratory where the test was done – just ask where they draw the line between negative or positive titers.

It is important to note that some grade-school aged children have chronically "elevated" titers. These may actually be in the normal range for that child, as there is a lot of individual variability in titer values. Because of this variability, doctors will often draw a titer when the child is sick, or shortly thereafter, and then draw another titer several weeks later to see if the titer is "rising" – if so, this is strong evidence that the illness was due to strep. (Of course, a less expensive way to make this determination is to take a throat culture at the time that the child is ill.)

Should an elevated strep titer be treated with antibiotics?

No. Elevated titers indicate that a patient has had a past strep exposure but the titers can not tell you precisely when the strep infection occurred. Children may have "positive" titers for many months after one infection. Since these elevated titers are merely a marker of a prior infection and not proof of an ongoing infection it is not appropriate to give antibiotics for elevated titers. Antibiotics are recommended only when a child has a positive rapid strep test or positive strep throat culture.

What are the treatment options for children with PANDAS?

The treatments for children with PANDAS are the same as if they had other types of OCD or tic disorders. Children with OCD, regardless of whether or not their illness is strep triggered, benefit from cognitive behavioral therapy and/or anti-obsessional medications. A recent study showed that the combination of an SSRI medication (such as fluoxetine) and cognitive behavioral therapy was the best treatment for OCD, and that medication alone or cognitive behavioral therapy alone were better than no treatment, or use of a placebo (sugar pill). It often takes time for these treatments to work, so the sooner therapy is started, the better it is for the child.

Children with strep triggered tics should be helped by the same tic medications that doctors use to treat other tic disorders. Your child's primary physician can help you decide which type of specialist your child may need to see to receive these treatments.

Can penicillin be used to treat PANDAS or prevent future PANDAS symptom exacerbations?

Penicillin and other antibiotics kill streptococcus and other types of bacteria. The antibiotics treat the sore throat or pharyngitis caused by the strep by getting rid of the bacteria. However, in PANDAS, it appears that antibodies produced by the body in response to the strep infection are the cause of the problem, not the bacteria themselves. Therefore one could not expect antibiotics such as penicillin to treat the symptoms of PANDAS. Researchers at the NIMH have been investigating the use of antibiotics as a form of prophylaxis or prevention of future problems. At this time, however, there isn't enough evidence to recommend the long-term use of antibiotics.

What about treating PANDAS with plasma exchange or immunoglobulin (IVIG)?

The results of a controlled trial of plasma exchange (also known as plasmapheresis) and immunoglobulin (IVIG) for the treatment of children in the PANDAS subgroup was published in "The Lancet", Vol. 354, October 2, 1999. All of the children participating in the study had clear evidence of a strep infection as the trigger of their OCD and tics, and all were severely ill at the time of treatment. The study showed that plasma exchange and IVIG were both effective for the treatment of severe, strep triggered OCD and tics, and that there were persistent benefits of the interventions. However, there were a number of side-effects associated with the treatments, including nausea, vomiting, headaches and dizziness. In addition, there is a risk of infection with any invasive procedure, such as these. Thus, the treatments should be reserved for severely ill patients, and administered by a qualified team of health care professionals.

The NIMH is currently enrolling participants in an IVIG clinical trial for PANDAS. More information can be found at: <http://intramural.nimh.nih.gov/pdn/>.

Of note, a separate study was conducted to evaluate the effectiveness of plasma exchange in the treatment of chronic OCD (Nicolson et al: An Open Trial of Plasma Exchange in Childhood Onset Obsessive-compulsive Disorder Without Poststreptococcal Exacerbations. "J Am Acad Child Adolesc Psychiatry 2000," 39[10]: 1313-1315. None of those children benefited,

suggesting that plasma exchange or IVIG is not helpful for children who do not have strep triggered OCD or tics.

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