PANDAS:

Fact Sheet about Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections

National Institute of Mental Health

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Overview

What is PANDAS?

PANDAS is short for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections. A child may be diagnosed with PANDAS when:

- Obsessive compulsive disorder (OCD) and/or tic disorders suddenly appear following a strep infection (such as strep throat or scarlet fever); or
- The symptoms of OCD or tic symptoms suddenly become worse following a strep infection.

The symptoms are usually dramatic, happen "overnight and out of the blue," and can include motor and/or vocal tics, obsessions, and/or compulsions. In addition to these symptoms, children may also become moody, irritable, experience anxiety attacks, or show concerns about separating from parents or loved ones.

What causes PANDAS?

The strep bacteria is a very ancient organism which survives in its human host by hiding from the immune system as long as possible. It does this by putting molecules on its cell wall that look nearly identical to molecules found on the child's heart, joints, skin, and brain tissues. This is called "molecular mimicry" and allows the strep bacteria to evade detection for a time.

However, the molecules on the strep bacteria are eventually recognized as

foreign to the body and the child's immune system reacts to them by producing antibodies. Because of the molecular mimicry, the antibodies react not only with the strep molecules, but also with the human host molecules that were mimicked.

The cross-reactive antibodies then trigger an immune reaction that "attacks" the mimicked molecules in the child's own tissues. Studies at the NIMH and elsewhere showed that some cross-reactive "anti-brain" antibodies target the brain, causing OCD, tics, and the other neuropsychiatric symptoms of PANDAS.

Could an adult develop PANDAS?

PANDAS is considered a pediatric disorder and typically first appears in childhood from age 3 to puberty. Reactions to strep infections are rare after age 12, but the investigators recognize that PANDAS could occur (rarely) among adolescents. It is unlikely that someone would experience these post-strep neuropsychiatric symptoms for the first time as an adult, but it has not been fully studied.

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.

Symptoms

How is PANDAS diagnosed?

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.

The 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 (see information below)
- Association with group A Beta-hemolytic streptococcal infection (a positive throat culture for strep or history of scarlet fever)

- Association with neurological abnormalities (physical hyperactivity, or unusual, jerky movements that are not in the child's control)
- Very abrupt onset or worsening of symptoms

If the symptoms have been present for more than a week, blood tests (antistreptococcal titers) may be done to document a preceding streptococcal infection (See Q: What is an anti-streptococcal antibody titer?)

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:

- ADHD symptoms (hyperactivity, inattention, fidgety)
- 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)
- Mood changes (irritability, sadness, emotional lability)
- Sleep disturbance
- Night-time bed wetting and/or day-time urinary frequency
- Fine/gross motor changes (e.g., changes in handwriting)
- Joint pains.

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 may return just as suddenly and dramatically as they did previously.

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 fact, the average grade-school student will have 2 – 3 strep throat infections each year.

PANDAS is considered as a diagnosis when there is a very close relationship between the abrupt onset or worsening or 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.

What is an anti-streptococcal antibody titer?

The anti-streptococcal antibody titer determines whether the child has had a previous strep infection. Two different strep tests are commercially available:

- Antistrepolysin O (ASO) titer,* which rises 3-6 weeks after a strep infection, and
- Antistreptococcal DNAase B (AntiDNAse-B) titer, which rises 6-8 weeks after a strep infection.

**Titer refers to the amount of something, in this case biological molecules in blood that indicate a previous 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 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. See Q: When is a strep titer considered to be abnormal, or "elevated"?

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.)

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

- ADHD symptoms (hyperactivity, inattention, fidgety)
- 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)
- Mood changes (irritability, sadness, emotional lability)
- Sleep disturbance
- Night-time bed wetting and/or day- time urinary frequency
- Changes in muscle movements ranging from small muscles (for example handwriting) to large (walking and running)
- Joint pains.

What if my child's doctor does not understand or does not want to consider PANDAS?

Contact the International OCD Foundation or the PANDAS Network to find a doctor who may be knowledgeable about PANDAS. **Please note:** NIMH does not evaluate the professional qualifications and competence of individual physicians listed on these websites. The resources are provided for general informational purposes only. NIMH does not intend to provide specific medical advice on our Web sites, but rather to help visitors better understand mental health and disorders. NIMH will not provide specific medical advice and urges you to consult with a qualified mental health or health care provider for diagnosis and for answers to your personal questions.

Treatment

What are the treatment options for children with PANDAS?

Treatment with Antibiotics

The best treatment for acute episodes of PANDAS is to treat the strep infection causing the symptoms (if it is still present) with antibiotics.

- A throat culture should be done to document the presence of strep bacteria in the throat (oropharynx).
- If the throat culture is positive, a single course of antibiotics will usually get rid of the strep infection and allow the PANDAS symptoms to subside.

If a properly obtained throat culture is negative, the clinician should make sure that the child doesn't have an occult strep infection, such as a sinus infection (often caused by strep bacteria) or strep bacteria infecting the anus, vagina, or urethral opening of the penis. Although the latter infections are rare, they have been reported to trigger PANDAS symptoms in some patients and can be particularly problematic because they will linger for longer periods of time and continue to provoke the production of cross-reactive antibodies.

The strep bacteria can be harder to eradicate in the sinuses and other sites, so the course of antibiotic treatment may need to be longer than that used for strep throat.

Tips for Parents or Caregivers

- Sterilize or replace toothbrushes during/following the antibiotics treatment, to make sure that the child isn't re-infected with strep.
- It might also be helpful to check throat cultures on child's family members to make sure that none are "strep carriers" who could serve as a source of strep bacteria.

Management of Neuropsychiatric Symptoms

Children with PANDAS-related obsessive-compulsive symptoms will benefit from standard medications and/or behavioral therapies, such as cognitive behavioral therapy (CBT). OCD symptoms are treated best with a

combination of CBT and an SSRI medication, and tics respond to a variety of medications.

Children with PANDAS appear to be unusually sensitive to the side-effects of SSRIs and other medications, so it is important to "START LOW AND GO SLOW!!" when using these medications. In other words, clinicians should prescribe a very small starting dose of the medication and increase it slowly enough that the child experiences as few side-effects as possible. If symptoms worsen, the dosage should be decreased promptly. However, SSRIs and other medications should not be stopped abruptly, as that could also cause difficulties.

For the latest research on the treatment of PANDAS, please visit Information on PANDAS.

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

Plasma exchange or immunoglobulin (IVIG) may be a consideration for acutely and severely affected children with PANDAS. Research suggests that both active treatments can improve global functioning, depression, emotional ups and downs, and obsessive-compulsive symptoms. 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**. Clinicians considering such an intervention are invited to contact the PANDAS research group at the NIMH for consultation.

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't 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.

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 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.

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.

Clinical Trials

What are clinical trials?

Clinical trials are part of clinical research and at the heart of all medical advances. Clinical trials look at new ways to prevent, detect, or treat disease. Treatments might be new drugs or new combinations of drugs, new surgical procedures or devices, or new ways to use existing treatments. The goal of clinical trials is to determine if a new test or treatment works and is safe. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, visit NIH's Clinical Trials and You.

How do I find clinical trials for PANDAS?

Around the Nation and Worldwide

NIH conducts clinical research trials for many diseases and conditions, including PANDAS. To search for other diseases and conditions, you can visit www.ClinicalTrials.gov. The ClinicalTrials.gov website has a searchable registry and results database of federally and privately supported clinical trials conducted in the United States and around the world.

ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.

Search NIH Clinical Research Studies

The NIH maintains an online database of clinical research studies taking place at its Clinical Center, which is located on the NIH campus in Bethesda, Maryland. Studies are conducted by most of the institutes and centers across the NIH. The Clinical Center hosts a wide range of studies from rare diseases to chronic health conditions, as well as studies for healthy volunteers. Visitors can search by diagnosis, sign, symptom, or other key words at http://clinicalstudies.info.nih.gov/.

To learn about studies being conducted at NIMH, visit the Pediatrics and Developmental Neuroscience Branch (PDNB) webpage.

Join a National Registry of Research Volunteers

Research Match(https://www.researchmatch.org/)is an NIH-funded initiative to connect 1) people who are trying to find research studies, and 2) researchers seeking people to participate in their studies. It is a free, secure registry to make it easier for the public to volunteer and to become involved in clinical research studies that contribute to improved health in the future.

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