

## **Sudden and Severe Onset OCD – Practical Advice for Practitioners and Parents**

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“My child was fine last week, last month – and now I have lost her. This is not my child; what has happened??? What do I do??”

For every parent of a child with an illness, especially a mental illness, there is a particular story. But when you meet a parent of a child with PANDAS (typically a child between ages 3-14), you will hear the same panicked story over and over. A child who was happy at home and at school, and was social and athletic, is now walking in circles for hours, washing hands until they bleed, asking the same questions over and over – and over. A child that used to be comforted by a hug is now inconsolable. They may be begging parents for help, begging for a way to end the horror that exists only in their minds. Imagine a child screaming in terror in a corner, and a parent unable to hold them. These parents will tell you in detail about the day or week that their child changed. Here is what life looks like now – children may exhibit some or all of these symptoms:

- Acute sudden onset of OCD
- Challenges with eating, and at the extreme end, anorexia
- Sensory issues such as sensitivity to clothes, sound, and light
- Handwriting noticeably deteriorates
- Urinary frequency or bedwetting
- Small motor skills deteriorate - a craft project from yesterday is now impossible to complete
- Tics
- Inattentive, distractible, unable to focus and has difficulties with memory
- Overnight onset of anxiety or panic attacks over things that were no big deal a few days ago, such as thunderstorms or bugs.
- Suddenly unable to separate from their caregiver, or to sleep alone
- Screaming for hours on end
- Fear of germs and other more traditional-looking OCD symptoms

You will often find these parents on the computer every night, desperate for an explanation that makes sense. They are seeking specialists who can help – and finding

no answers. They are starting to feel crazy themselves, because no one seems to believe what they are going through.

If you are a pediatrician or pediatric therapist faced with this family in your office, this may look daunting. However, let's take a minute to walk through options that *are* available to parents, medical and mental health professionals, and kids suffering from this disorder. These treatment recommendations were developed from interviewing clinicians and researchers around the country, so that you can potentially stop the disease in its tracks while you referring these children for additional help if needed.

### **What is Pediatric Autoimmune Neuropsychiatric Disorder Associated with Strep or PANDAS?**

PANDAS was defined in 1998 by Dr. Sue Swedo. Over the prior decade, Dr. Swedo had been studying Sydenham Chorea where 70% of patients exhibit sudden onset OCD symptoms before or after this classic movement disorder. She and other researchers were finding children who had sudden onset OCD symptoms without the carditis (heart inflammation) or movement disorder normally characteristic of Sydenham Chorea and acute rheumatic fever.

Auto-antibodies have been implicated in the carditis of Acute Rheumatic Fever, and Dr. Swedo theorized that perhaps a related set of antibodies were mistakenly attacking the basal ganglia (part of the brain) rather than the intended streptococcal bacteria triggering the movement disorder/sudden onset of OCD. In July 2010, researchers met at the NIH to discuss the past decade of clinical findings. Of significance, the panel found that while strep throat seems to be a trigger, it may not be the only trigger. Sudden onset OCD could be triggered by other diseases, including Lyme, Mono, Mycoplasma and the flu virus (such as H1N1). Based on this and other clinical reports, the panel modified the research definition of PANDAS.

### **How to Identify a PANDAS Child**

Sudden dramatic onset is the most salient characteristic and differentiates PANDAS from a more frequent pediatric OCD presentation - which involves subclinical symptoms becoming gradually more severe. Incapacitating fears and anxieties seem to come on "overnight" with many parents being able to name the exact day when their child changed. In addition, while the mean age of OCD in children is between 9 and 10 years of age, PANDAS cases can start at a younger age such as 5 or 6, often corresponding with a diagnosis of strep.

***Physicians*** are encouraged to assess for:

- A history of sore throat, fever, exudative pharyngitis, cervical adenopathy (enlarged and tender lymph nodes in the neck), enlarged or damaged tonsils
- Atypical presentations of strep, especially in young children, include abdominal pain and vomiting, vaginal or perianal redness

- In some cases of PANDAS, the strep appeared to be “hiding” in the sinuses or middle ear resulting in a negative throat culture
- It is also possible that non-strep organisms can cause a similar neuropsychiatric illness in vulnerable children. Therefore, it is important to check for mycoplasma, mono, or exposure to Lyme disease.

During the meeting at NIH last year, researchers and clinicians across the country began to revise the criteria defining this illness in children. Based on that conference, because there are non-strep causes of sudden onset illness, researchers changed the name of the disease to PANS: Pediatric Acute-Onset Neuropsychiatric Syndrome.

***Mental and medical professionals*** should look for:

- Abrupt, dramatic onset of OCD is the first diagnostic criterion for PANS. For those familiar with the CYBOCS (Childhood Yale Brown Obsessive Compulsive Scale) scores, some clinicians look for an increase in total score of more than 16 in the course of a few days. Children may have mild “quirks” or even some signs of OCD prior to this abrupt dramatic onset. In retrospect some clinicians suggest that mild micro-episodes may even have occurred in the past. However, in the space of a few days, they “fall off a cliff”, dramatically causing a significant decrease in the child’s ability to function. Impairment is significant. Parents can usually name the day that the crisis occurred and have vivid memories of the first obsessions or compulsions because of their extreme nature. As an example, a normally joyful, balanced emotionally, independent, social child may turn into a child that has extreme temper tantrums that are out of character, and can no longer leave a parent’s side without accommodation. Panic attacks and unusual anxieties are not uncommon. In addition to the typical obsessional fears and compulsive behaviors, this criterion also may be satisfied by the sudden severe onset of food avoidance, anorexia and eating restrictions. Clinically, these occur as solitary symptoms among PANS patients, as well as from complications resulting from obsessional fears of choking, vomiting or of contaminated foods.
- Although there appears to be uniformity in the acuity and severity of onset of the co-occurring symptoms, there is great variability in the nature of the symptoms accompanying the OCD. As a result, the second major criterion for PANS is the concurrent acute onset of additional symptoms from at least two of the following seven categories:
  1. anxiety (particularly acute separation anxiety and irrational fears)
  2. emotional lability and/or depression
  3. irritability, aggression and/or oppositional behaviors
  4. behavioral (developmental) regression
  5. sudden deterioration in school performance
  6. sensory or motor abnormalities (particularly dysgraphia/ trouble with handwriting)
  7. somatic/physical signs and symptoms

As in most of psychiatry, PANS is a clinical diagnosis, meaning that there are currently no laboratory or genetic tests that can confirm the diagnosis. As such, a second opinion to find consensus on the diagnosis of PANS between two experienced physicians may be useful.

### **Additional Medical Testing to Consider Prior to Onset of Treatment**

Many physicians report that a throat culture appears to be key (even if there are no signs or symptoms of pharyngitis). Due to the difficulty in properly sampling these children, a two-swab sample should be taken to check for bacterial colonization. The first swab should be a rapid strep test. It is very important that the culture is obtained properly by vigorously swabbing across the entire pharynx, behind both tonsils and the uvula. If the child doesn't gag and protest, the swab is probably inadequate. If negative, use the second swab for a 4-hour agar plate culture. If these are both negative, consider testing for Lyme disease, Mycoplasma, vitamin D, Ferritin and thyroid. Many children with recurrent upper respiratory infections have immune deficiencies and would benefit from an immune function assessment such as blood counts measuring quantitative immunoglobulins and a referral to a pediatric immunologist.

Finally, many physicians rely on antibodies to the exotoxins of streptococcus to confirm a prior infection measuring ASO and AntiDNaseB. These tests have fixed windows where the measurement may begin to be positive 1-8 weeks after initial infection. Typically two measurements are required. The first should be obtained as soon as possible after the suspected infection and the second at least six weeks later. It is currently unknown whether carrying the bacteria without an active infection alone is sufficient to cause symptoms in PANS children.

If test results are all normal, it does not rule out a diagnosis of PANS, and exposure to infections from close contacts should be considered.

### **Treatment Options and Strategies to Consider for PANS**

While acknowledging the need for additional research, we also cannot sit idly by while children scream in terror. We have to help children suffering today. Clinicians around the country have started treating our kids. Best practices suggest that one develop a treatment plan based on interventions with the minimum effective dose, an intervention with the best cost/benefit ratio (less intrusive, minimal short term and long term side effects, good at preventing relapse, easy to administer, tolerated well) and treatments that have the most research behind them. Research can include controlled studies (better) and case reports (good but less informative). We will rate each of the following treatments currently being used as a guide for professionals and parents to consider when trying to determine the best course of action. This is said with the caveat that at this point in time PANDAS and PANS treatments are drastically under researched. Please see the end of this article for more about how to help on this front.

**IVIG:** The original research studies investigating possible treatment options were done by giving children IVIG (intravenous immunoglobulin). Essentially, this treatment gives a

child antibodies from a myriad of donors. We don't know exactly how IVIG works, but it appears to help in a number of autoimmune illnesses.

In PANDAS, IVIG reduced the OCD symptom severity for 82% of children suspected of having PANDAS in a small study

(<http://intramural.nimh.nih.gov/pdn/pubs/pub-5.pdf>) that is now being repeated at the NIH ([http://clinicalstudies.info.nih.gov/cgi/detail.cgi?A\\_2011-M-0058.html](http://clinicalstudies.info.nih.gov/cgi/detail.cgi?A_2011-M-0058.html)). IVIG is offered to children in a clinical environment – but is often not covered by insurance and is expensive. While IVIG is usually considered quite safe for treating auto-immune disorders, there are several risks. Nausea, vomiting, and headache are not uncommon and in rare instances, aseptic meningitis or allergic reactions may occur. Although most side effects are not harmful in the long term, they are unpleasant and therefore IVIG therapy is generally recommended only for severe or persistent cases or as indicated for immune deficiency disorders.

**Antibiotics:** Dr. Swedo also did research showing that using antibiotics as a prophylaxis to prevent strep successfully reduces neuropsychiatric exacerbations (<http://www.ncbi.nlm.nih.gov/pubmed/15820236>). Another study will start soon as a collaboration between Harvard and the University of South Florida. They will be examining a common treatment course successfully used by clinicians: using antibiotics in children with PANDAS. Early in the disease if strep is present, this is an obvious course. But no research has yet been done on why many clinicians find that a longer term course of antibiotics often seems to offer great hope to families suffering from this disease –even after the actual triggering illness is over.

As such, some physicians have found the following particularly helpful for new, sudden onset cases:

- Use antibiotics for 3-6 weeks initially. Use of augmentin has anecdotally been found to be more effective at a relatively high dose as well as the cephalosporins (cephalexin, cefdinir) and azithromycin. Consider using probiotics but not at same time of the day; allow 2-3 hour window between. If no improvement is seen after 3-4 weeks, a physician may consider an alternate class of antibiotic treatment. If symptoms completely remit, a trial off the antibiotic may be attempted. If symptoms return, additional treatment may be warranted.

However, in many cases, a physician will see a child a several weeks after the initial onset, or in a second exacerbation. In that case, some clinicians have recommended the following:

- A throat culture can still be very informative at this point as well as antibody levels. Then treat with antibiotics as above while waiting for the results. If there is a marked reduction in symptoms, gradually wean. With a recurrence, antibiotics are reintroduced and continued as needed. Try to gather retrospective information, ask for detailed pediatrician records to be forwarded and nail down the exact timing of testing and labs. Since prior testing may have been limited, a trial of antibiotics appears to be low risk.

**Exposure and Response Prevention (an intervention under the broader umbrella “Cognitive Behavior Therapy or CBT):** Unlike traditional onset OCD, where research clearly guides a mental health and medical professional’s decision making about how to proceed with treatment, PANS onset OCD is still under researched. As we wait for studies to be completed we still need to develop treatment strategies that can address the pain and suffering of children and families now. For many PANS children, the suddenness of onset and the migratory nature of the obsessions/compulsions can make Exposure and Response Prevention therapy or ERP challenging; however, a combination of a medical intervention and traditional ERP might be the best course of action at this point in time. For some children an initial treatment with antibiotics or IVIG results in significant relief of symptoms. For those with slow or partial remission of symptoms, ensuring that ERP is included seems to be critical. Children develop habits and fears quickly and they may use ERP treatment to teach their brain to ignore the irrational fear signals they have been receiving. ERP teaches a child concrete tools to overcome OCD thoughts on a daily basis. Many clinicians find that learning ERP allows the entire family to function more calmly during future exacerbations, while seeking medical help. Some recent but preliminary work by a group at University of South Florida found strong effects for this approach in children with PANDAS (Drs. Storch & Murphy).

**SSRIs:** Most clinicians experienced in treating children with PANDAS do not initially recommend SSRIs, especially given the very young age of many of the children. However, as the disease course continues, they may find relief with the use of SSRIs *in much lower doses* than is normally recommended for children with OCD. Close monitoring is strongly recommended, as very young children may have more adverse behavioral or neurological effects. Occasionally, mood stabilizers have been reported as helpful, as the presence of mood volatility in PANS/PANDAS is a major limitation in the use of SSRIs. Please see this link for more information:

**<http://www.primarypsychiatry.com/asp/articleDetail.aspx?articleid=561>**

**Plasmapheresis:** Dr. Swedos’ original study included both IVIG and plasmapheresis. Plasmapheresis was the more immediate and effective option in the original study. However, as the most expensive and invasive treatment option, this is rarely used in a clinical setting, and is beyond the scope of this article. For more information, see the original research study **<http://intramural.nimh.nih.gov/pdn/pubs/pub-5.pdf>**, or read more about plasmapheresis online:.

**Steroids:** As with all autoimmune diseases, doctors have found that anti-inflammatory medications (such as corticosteroids) can be effective in both short and long term use. However, these can be very damaging to children in long-term use and should only be considered in careful consultation. Some parents or clinicians have found that short-term use of steroids can help auto-immune, triggered OCD once the initial infection is cleared. Behavioral side effects are sometimes seen in steroid therapies (especially mood symptoms) and can overlap with PANS symptoms. Should additional research studies come available, IOCDF will publish those findings.

**Ibuprofen and NSAIDs:** Some parents have reported that non-steroid anti-inflammatories (such as Ibuprofen) do seem to help symptoms. This has led some researchers to consider that perhaps it is the anti-inflammatory effects of the antibiotics, IVIG and steroids on the blood-brain barrier that is resulting in improved symptoms. While long-term use of NSAIDs carries its own issues, some pediatricians prescribe a low-dose NSAID during significant episodes. Please consult with your doctor as there are multiple other issues to consider when using this approach.

### **Summary, Conclusions, and Going Forward**

As noted previously, in the absence of research, we cannot recommend doing nothing for these children. Their suffering is intense. And the risk of long-term damage cannot be ignored. We also do not know if some of these children remit spontaneously later in adolescence. We do not know if some of them grow into adults with the most treatment resistant OCD due to permanent basal ganglia damage. While we research those questions, offering treatment options at the local level, especially in the first few months after onset, could be critical to the long term success for these kids. One prospective study conducted in a pediatrician's office suggests that first-onset PANDAS symptoms may remit following successful treatment of the strep infection with antibiotics. Unfortunately, there has not been a follow-up report on these children, so it is unknown if some children experience a second exacerbation following successful treatment of the initial onset of PANDAS symptoms.

Like Sydenham Chorea, PANS provides a window into a whole new way of treating mental illness as a faulty immune response. There are many researchers across the nation who have developed hypotheses about the cause, contributing factors, and treatment. They need funding to move forward with this seed research, before developing larger grant proposals. If you are interested in learning more, or in contributing towards this research, the IOCDF welcomes your call or donation. Dr. Madeleine Cunningham often ends her presentations on PANDAS with this compelling quote: **"If auto-antibodies are proven to play a role in mental disorders, then it will change the way mental illness is diagnosed and treated forever."** Being a part of this change - whether you are a treating physician, a researcher, a parent or a donor - might change your life forever too.

### **Additional reading:**

What every Psychiatrist should know about PANDAS:

**<http://www.cpementalhealth.com/content/4/1/13>**

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