Diagnosis and Treatment of PANS/PANDAS

▶ *Resources for Pediatric Healthcare Providers*

THE UNIVERSITY OF ARIZONA

Distinguishing PANS/PANDAS from Other Disorders

The National Institutes of Health first distinguished the phenomenon of strep-related PANDAS in the late 1990s, and subsequently defined PANS in 2012 to address the wider group of children who may have underlying etiologies separate from documented streptococcal infection. Research is ongoing to clarify the link between inflammation and psychiatric disorders, enhancing the ability to better diagnose and treat youth with a variety of neuropsychiatric disorders.

PANS/PANDAS, while based on a strong biological model supported by active research, does not include currently agreed upon biomarkers. As a result, it relies on a "diagnosis of exclusion" made through comprehensive clinical examination confirming that there are no other known neurological and medical disorders that better explain the symptoms and clinical history of the patient. The clinical symptoms overlap with a variety of psychiatric disorders; however, it is the atypically rapid, severe onset of various problems that distinguishes PANS from psychiatric disorders.

At first glance, a child with PANS and a child with OCD may appear similar. They both have obsessions, compulsions, and anxiety; these symptoms cause significant distress, interfere with daily functioning in school, social activities, family relationships, and normal routines. On closer examination, there are clear differences between these two conditions.

	Pediatric OCD	PANDAS/PANS
Age	First onset typically between 8–12 years old	Typically affects children 4–14 years old
Timeline	Gradual, increasing over time	Acute, dramatic onset of symptoms
Symptoms	A wide range of symptoms, cycling between obsessions that cause anxiety and compulsions to reduce it. ▪ Obsessions may include fears of contamination, pathological doubt, unwanted thoughts and/or images, or the need for symmetry. ▪ Compulsions may involve excessive checking, washing and/or cleaning, reassurance seeking, or counting, ordering, or arranging things.	Sudden, abrupt onset of obsessive-compulsive behavior and/or eating disorder **plus** at least two of the following: ▪ Anxiety, separation anxiety ▪ Emotional lability or depression ▪ Irritability, aggression, and/or oppositional behaviors ▪ Behavioral or developmental regression ▪ Deteriorated school performance (loss of math skills, handwriting changes, ADHD-like behaviors) ▪ Sensory or motor abnormalities, tics ▪ Sleep disturbances, enuresis, or urinary frequency
Cause	Probable familial/genetic link and possible involvement of the cortico-striato-pallidothalamic (CSPT) pathway	Hypothesized to be the result of autoimmune antibodies mistakenly attacking the basal ganglia in the brain following an infection

PANS/PANDAS Diagnosis

Identification and intervention early in the disease cycle is critical for returning affected children to baseline functioning. General pediatricians, as the ones most likely to see these children first, play a key role in initial case-finding and early treatment.

Medical Work Up

- Comprehensive history, including family history. Clarify timing of onset of the condition. Identify OCD and/or ARFID history

- Physical examination for occult infections (adenoids, tonsils, sinuses, urethra, and anus). Look for choreiform movements and dilated pupils
- Rule-out Sydenham chorea and other specific illnesses
- MRI with findings of asymmetry or other abnormalities on examination
- LP if there are concerns for encephalitis
- Swallowing study if obsessional symptoms like vomiting, choking or food restrictions
- EEG to determine types of encephalopathy (regional slowing or epileptiform activity)
- Polysomnography for sleep disturbances Assessment of anti-neuronal antibodies

Supporting Lab Tests

- Strep - throat culture or perianal culture
- Anti streptococcal titers (Supportive but not diagnostic)
  - ASO (anti-streptolysin O)
  - Anti-DNAse B (Anti-deoxyribonuclease B)
- Appropriate testing for infectious triggers
- Thyroid studies including anti-thyroglobulin
- Antinuclear antibody titers
- Quantitative immune globulins
- CBC
- Ferritin
- Vitamin D
- Others indicated by symptoms

Treatment

A three-pronged approach is recommended for treating PANS/PANDAS:

- **Remove the infectious source** with antimicrobial treatments
- **Treat the disrupted immune system** with anti-inflammatory and/or immune modulating interventions
- **Alleviate symptoms** with psychotherapeutic treatments

When there is a high index of suspicion of PANS or PANDAS based on the clinical findings, a trial antibiotic and NSAID course of treatment has the value of potentially being both diagnostic and therapeutic. Follow-up examination will reveal the efficacy of the intervention.

If the result is unremitting and worsening symptoms, referral is warranted for further investigation and treatment. Recommended treatment for more complex cases calls for a multi-disciplinary approach encompassing psychiatry and behavioral interventions and immunomodulatory therapy.

Clinical consultation is available and ongoing investigational research is being conducted at various sites nationally and internationally, including the University of Arizona's CPAE Center of Excellence.

Further information regarding clinical resources specializing in CPAE, PANS and PANDAS can be found at
https://pacefoundation4kids.org/clinics

Children's Postinfectious Autoimmune Encephalopathy Center

Website *www.peds.arizona.edu/cpae*
Email *cpae@bannerhealth.com*
PO Box 245073
Tucson, Arizona 85724

The Children's Postinfectious Autoimmune Encephalopathy (CPAE) Center of Excellence at the University of Arizona Steele Center, developed in partnership with Banner University Medicine and in cooperation with the NIH/NIMH, is the first in the U.S. to implement an integrated model of basic science, clinical research, clinical care, and teaching to address a spectrum of neuro-psychiatric disorders that are often misdiagnosed, underdiagnosed, and undiagnosed in children.

Guidelines for Accessing PANS/PANDAS Treatment in Arkansas

To make treatment for children with Postinfectious Autoimmune Encephalopathy (PANS/PANDAS) more accessible in Arkansas:

1. The Arkansas Children's Hospital Childhood Post-infectious Autoimmune Encephalopathy (CPAE) Center of Excellence, should provide information on the medical standard-of care guidelines for diagnosing and treating Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) and Pediatric Acute-onset Neuropsychiatric Disorders Associated with Streptococcus (PANDAS).
   A. The information should incorporate the guidance provided by the NIH/NIMH in conjunction with the The PANS/PANDAS Research Consortium https://www.pandasppn.org/guidelines/ along with other medical references such as https://www.pandasppn.org/research-library/
   B. The guidelines should also include summary sheets and flowcharts describing PANS/PANDAS diagnosis and treatment (e.g. https://www.pandasppn.org/pans/)
   C. By way of example, the guidelines might stipulate that:
      - A licensed physician (e.g. Pediatrician, Psychiatrist, Developmental Pediatrician, etc.), after having treated with two or more less-intensive therapies (e.g. limited course of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, selective serotonin reuptake inhibitors (SSRIs), behavioral therapy, short-course antibiotic therapy) have been tried and were not effective, AND
      - A consultation and recommendation is issued by a pediatric sub-specialist (e.g., pediatric neurologist, neurologist, immunologist, rheumatologist, infectious disease) for IVIG treatment, THEN
      - Up to 3 monthly immunomodulatory courses of intravenous immunoglobulin (IVIG) therapy is recommended for treatment of PANDAS and PANS, ADDITIONALLY
      - A reevaluation at 3 months by the pediatric sub-specialist is required for continued therapy of IVIG. This evaluation must

include objective clinical testing, which must be performed pre-treatment and post-treatment to demonstrate significant clinical improvement.

2. The Arkansas Children's Hospital CPAE Center should offer access to live or tele-health CPAE clinical training for the sub-specialists named above, as CPAE clinic time permits.
3. The Arkansas Children's Hospital CPAE Center physicians should conduct medical grand rounds at professional gatherings of Arkansas sub-specialists, ER physicians, etc.
4. The Arkansas Children's Hospital CPAE Center should also assist in the development of PANS/PANDAS webpages on the Arkansas Department of Health website, the UAMS Health website and the Arkansas Children's Hospital website.
5. The Arkansas Children's Hospital CPAE Center physicians should review IVIG prescriptions for PANS/PANDAS patients, at the request of Medicaid, private insurance companies and State Health Department.