Diagnosis and Treatment of PANS/PANDAS

Current Resources for General Pediatricians

ASPIRE
Alliance to Solve PANS & Immune-Related Encephalopathies

Diagnostic Criteria for PANS

Pediatric Acute-onset Neuropsychiatric Syndrome

1. Abrupt, acute onset of
   - Obsessive-compulsive disorder or severe restricted food intake
2. Concurrent presence of additional behavioral or neurological symptoms with similarly acute onset and severity from at least two of the seven following categories:
   - Anxiety, separation anxiety
   - Emotional lability or depression
   - Irritability, aggression, and/or oppositional behaviors
   - Behavioral or developmental regression
   - Deterioration in school performance (loss of math skills, handwriting changes, ADHD-like behaviors)
   - Sensory or motor abnormalities, tics
   - Somatic signs: sleep disturbances, enuresis, or urinary frequency
3. Symptoms are not better explained by a known neurologic or medical disorder
4. Age requirement – None

WHAT ARE **PANS & PANDAS**

PANS Pediatric Acute-onset Neuropsychiatric Syndrome

PANS is a clinical diagnosis based on history and physical examination. PANS diagnostic criteria require an acute onset of OCD and/or eating restrictions, with concurrent symptoms in at least two of seven neuropsychiatric and somatic categories. Infections, metabolic disturbances, other inflammatory reactions and stress can trigger PANS. Infectious triggers include upper respiratory infections, influenza, strep, mycoplasma pneumoniae, and lyme borreliosis, among others. The average age of onset is between 3 and 13, but post-pubertal cases do occur. There is no requisite age of symptom onset for a PANS diagnosis.

PANS
is caused by an infectious trigger or other non-infectious agents such as environmental triggers.

PANDAS Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections

PANDAS, a subset of PANS, is associated with group A Streptococcus (GAS) infections. Not all patients have a positive strep throat culture, and examination must be followed by ASO and ADB immune responses. Onset of symptoms can occur within days of contracting strep, or within several months of the inciting infection.

PANDAS
is associated with group A Streptococcus (GAS) infections.

PANS/PANDAS are misdirected immune responses, often with an encephalitic onset, that result in acute onset of OCD, tics and/or restricted food intake, along with other neuropsychiatric and somatic symptoms. After the initial onset, PANS/PANDAS symptoms follow a relapsing/remitting course. Initial triggers may differ from secondary triggers. During each recurrence, symptoms can worsen, and new symptoms may manifest.

Symptoms can range from mild to severe. In mild cases, children might function well enough to continue to attend school. In severe cases, symptoms can become life-threatening due to extreme food restriction and/or suicidality. Many children with PANS/PANDAS are diagnosed with a psychiatric illness and prescribed psychotropic medications rather than being evaluated and treated for an underlying infection. According to a consortium of experts convened by the National Institute of Mental Health, appropriate treatment for these disorders is a triad that incorporates psychological support (CBT, ERP and/or psychotropic medication), antimicrobial treatment, and immunomodulation.

10 Things You Should Know About PANS/PANDAS

1. Strep throat is NOT the only infectious trigger. Although group A streptococcal (GAS) infections are associated with PANDAS, PANS is a broad-spectrum syndrome that can result from a variety of disease mechanisms and multiple etiologies.

2. Acute onset can be preceded by milder episodes. Mild cases have been documented, and symptoms might look like behavioral problems, isolated tics, and sensory issues, among other issues that require awareness on the part of the parent and provider. These children should be clinically evaluated for PANS/PANDAS.

3. Tics are not always present. While tics were part of the original PANDAS diagnostic criteria,they are not required for a PANS diagnosis.

4. OCD symptoms vary. While the mean age of OCD in children is between the ages of 9 and 10, in children with PANS/PANDAS it can start much earlier. OCD presentation is acute and disruptive to child's normal functioning.

5. Restrictive eating can be a primary symptom. Some children with PANS/PANDAS present with Avoidant Restrictive Food Intake Disorder without OCD or tics. A child with severe food restriction resulting in dramatic weight loss or who refuses fluid intake should be examined for PANS/PANDAS.

6. Children with PANS/PANDAS may experience recurrence of episodes. Some children experience remission of symptoms after treatment with no recurrence, while a portion experience subsequent exacerbation (relapse) incited by a variety of triggers.

7. Prevalence is unknown, due to poor diagnosis. PANS/PANDAS affects as many as 1 in 200 children each year according to the PANS/PANDAS consortium.

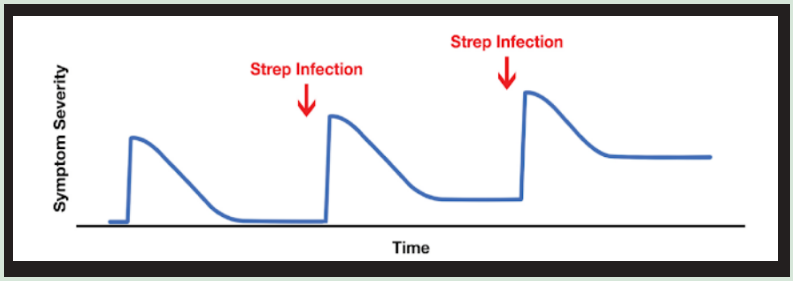
8. Scientific studies strongly support PANS/PANDAS diagnosis. Diagnostic guidelines published by the Journal of Child and Adolescent Psychopharmacology (July 2017) and a recent nationwide study in the Netherlands designed to test PANDAS hypothesis demonstrated that individuals with a positive streptococcal test have an increased risk of neuropsychiatric disorders. The study also demonstrated an increased risk with non-streptococcal throat infections.

9. Early diagnosis and treatment lead to improved outcomes. According to NIMH, "preliminary data suggest that with appropriate treatment early in the course of illness, and effective use of antibiotic prophylaxis, we may be able to prevent up to 25%-30% of childhood mental illnesses".

10. Pediatricians CAN diagnose and treat PANS/PANDAS. The 2017 JCAP Treatment Guidelines issued by the PANS Physician Consortium are designed to provide practical clinical guidelines for the management and treatment of children diagnosed with PANS/PANDAS.

UNDERSTANDING **SYMPTOM PATTERNS**

Repeated Flares & Symptom Baseline



Source: NIMH Information About PANS/PANDAS
https://www.nimh.nih.gov/research/research-conducted-at-nimh/research-areas/clinics-and-abs/sbp/information-about-pans-pandas.shtml

Do symptoms return to baseline between flares/exacerbations? Not always. Some symptoms can remit fully while others are reduced but not back to baseline. PANS symptoms can relapse and remit. In between flares, symptoms do not always go back to baseline. Unfortunately, in some cases, subsequent flares can be more severe with a longer duration; symptoms move further away from baseline and can become chronically debilitating. PANS symptoms can remit completely especially if treated quickly and thoroughly. Treatment plans should not only include treatments to clear the current flare but also address symptoms that have not returned to baseline. Ultimately the goal is to relieve symptoms and prevent symptoms from becoming chronically debilitating.

PANS Symptom Severity

The severity of PANS symptoms varies from patient to patient and can vary from flare to flare. Treatment plans reflect the severity of the current PANS flare and case history. Not all patients return to baseline between flares which can affect treatment plans. PANS is a clinical condition identified by an abrupt onset of a specific cluster of symptoms as a result of a variety of etiologies and disease mechanisms. Therefore, tracking symptoms and their onset, severity, and duration is critical to making a clinical diagnosis. Both clinicians and parents can use PANS symptomology rating scale tools to monitor symptom severity.

Mild Symptomology

Mildly severe PANS symptoms interfere with daily life but are manageable and do not completely debilitate the patient. Mild symptoms may present in some situations but not in all. For example, a patient may be able to attend school with some reservations but once back home is definitely anxious about being separated from a parent, needing significantly more attention than when at baseline. Obsessive-compulsive symptoms occupy 1 to 2 hours of the patient's day without escalating to obsessional fears.

- Symptoms interfere with daily life but not in all settings
- Able to attend school but with separation anxiety
- OCD occupies 1-2 hours a day without escalating to obsessional fears
- Other symptoms vary from patient to patient and from flare to flare but are not incapacitating
- Symptoms require some school accommodations

Moderate Symptomology

Moderately severe PANS symptoms interfere with daily life; some symptoms are less manageable, significantly negatively hindering the majority of activities. Obsessive-compulsive symptoms are present 50% to 70% of a patient's waking hours but do not interfere with all activities. For example, a patient may not be able to attend school but may be able to go to a friend's house if a parent is with them. Other symptoms are also moderately severe; they impact the patient most of the day but are not completely incapacitating at all times.

- OCD occupies 50%-70% of the waking day. Impacts daily activities severely but not fully disabling
- Other symptoms are also moderate; impact daily life but not incapacitating
- School attendance may be affected, but the patient may be able to engage in other activities
- Symptoms require increased school accommodations and supports

Severe Symptomology

Severe PANS symptoms can be life-threatening. Serious weight loss can result from obsessional eating restrictions. Severe impulsivity can manifest in life-threatening ways (jumping from heights or moving cars or threatening harm to self or others). Aggressive treatment is necessary. Obsessive-compulsive thoughts occupy 80%-100% of waking hours, obstructing daily functioning (attending school, showering, doing simple tasks). Separation anxiety is extreme; patients will barely leave the house, will not separate from parents, and sleep in their bed. All symptoms, including increased aggression, emotional lability, and irritability, may be equally impacted.

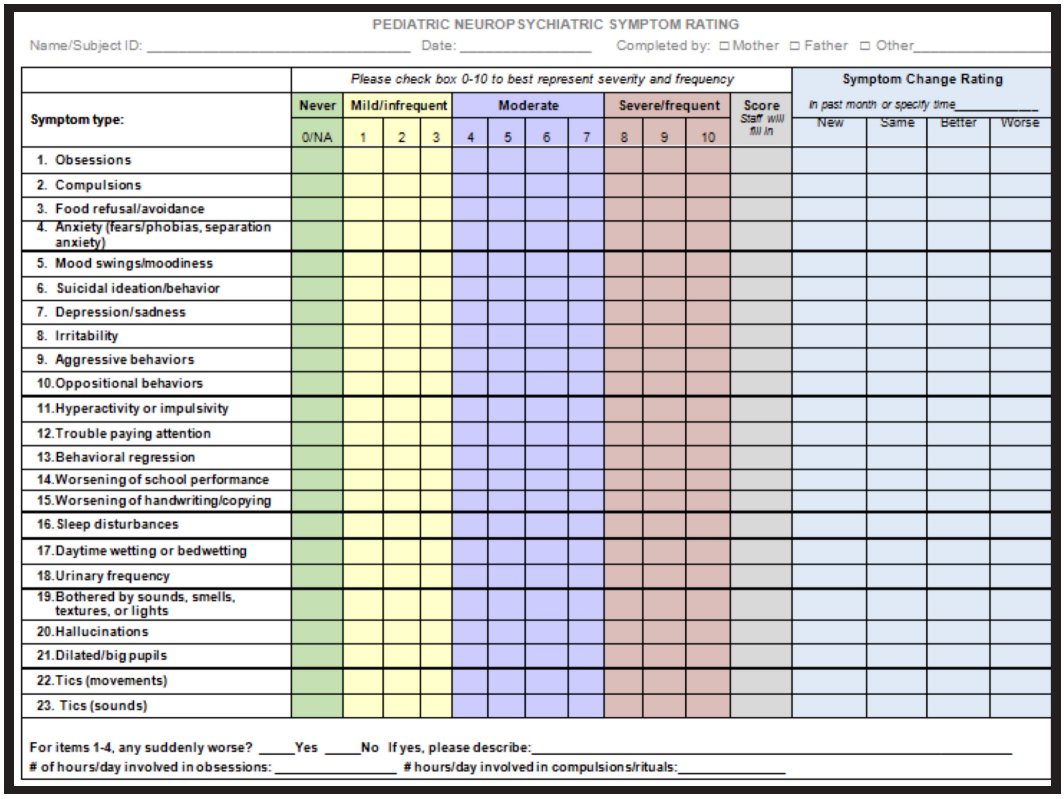
- Neuropsychiatric symptoms can result in life-threatening situations
  - Hazardous impulsivity and/or regression
  - Weight loss (>10%-15% of body mass) due to obsessional food restrictions
- OCD, anxiety, and fears occupy 80%-100% of waking day
- Unable to attend school due to OCD and separation anxiety
- Irritability, depression, aggression, and other symptoms can be equally present

PANS/PANDAS Symptom Rating Scales

There are two useful PANS Symptom Rating Scale tools.

Tracking symptoms, onset, severity, and duration is a critical part of forming a clinical diagnosis and a treatment plan. The **PANS Symptom Scale-Parent Version** includes the core obsessive-compulsive symptoms & associated symptoms and provides an Impairment Rating key to aid in consistency. The **PANS Rating Scale Tracking Chart** is simple to fill out but less detailed in its breakdown of each symptom.

The PANS Symptom Scale-Parent Version was developed by Susan Swedo, MD, Miroslav Kovacevic, MD, Beth Latimer, MD, and James Leckman, MD, along with Diana Pohlman and Keith Moore. The PANS Rating Scale Tracking Chart was developed by Tanya Murphy, MD and Gail Bernstein, MD.



PEDIATRIC NEUROPSYCHIATRIC SYMPTOM RATING

Name/Subject ID: _____ Date: _____ Completed by: ☐ Mother ☐ Father ☐ Other_____

Symptom type:	Please check box 0-10 to best represent severity and frequency											Score Staff will fill in	Symptom Change Rating in past month or specify time_____			
	Never	Mild/infrequent			Moderate				Severe/frequent				New	Same	Better	Worse
	0/NA	1	2	3	4	5	6	7	8	9	10					
1. Obsessions																
2. Compulsions																
3. Food refusal/avoidance																
4. Anxiety (fears/phobias, separation anxiety)																
5. Mood swings/moodiness																
6. Suicidal ideation/behavior																
7. Depression/sadness																
8. Irritability																
9. Aggressive behaviors																
10. Oppositional behaviors																
11. Hyperactivity or impulsivity																
12. Trouble paying attention																
13. Behavioral regression																
14. Worsening of school performance																
15. Worsening of handwriting/copying																
16. Sleep disturbances																
17. Daytime wetting or bedwetting																
18. Urinary frequency																
19. Bothered by sounds, smells, textures, or lights																
20. Hallucinations																
21. Dilated/big pupils																
22. Tics (movements)																
23. Tics (sounds)																

For items 1-4, any suddenly worse? _____Yes _____No If yes, please describe:_____

# of hours/day involved in obsessions: _____ # hours/day involved in compulsions/rituals:_____

Available at: https://aspire.care/symptoms-diagnosis/symptom-tracking-tools

PANS/PANDAS Versus OCD

At first glance, someone with PANS and someone with OCD may appear pretty 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.

	PANS/PANDAS	OCD
Onset	Acute, sudden onset of concurrent symptoms	Gradual onset with cumulative effect
Course	• Episodic • Relapsing-remitting, chronic, progressive, or chronic-static	Not episodic

Symptoms	• Obsessions/Compulsions or severely restricted food intake
	• 2 of the following concurrent symptoms:
	  • Anxiety, separation anxiety
	  • Emotional lability, depression
	  • Aggression, irritability, oppositional behavior
	  • Behavioral/Developmental regression
	  • Deterioration of learning abilities related to ADHD
	  • Sensory & motor abnormalities, tics
	  • Sleep disturbances, enuresis, urinary frequency
		• Obsessions
		• Compulsions

Motor Signs	• Tics • Choreiform movements	Increased findings of neurological soft signs, including choreiform movements
Neurocognitive Deficits	• Attention • Visual-spatial abilities	• Oculomotor response inhibition • Set shifting and inhibition • Cognitive flexibility and planning
Age of Onset	• Typical onset is between 4-14 years of age • PANDAS requires a prepubertal onset • PANS does not have an age requirement	Typical onset is between 8-12 years of age
Gender Ratio	Nearly 5:1 male to female ratio under age 8	• Age <15 years: males slightly > females • Post-puberty: female/male ratio increases
Incidence	Unknown. Estimate is 10%–20% of pediatric OCD	2% of youths

Cause	• PANS-Multiple etiologies and disease mechanisms:
	  • Underlying neurological, endocrine, metabolic disorders
	  • Postinfectious autoimmune and neuroinflammatory disorders like PANDAS
	• PANDAS-Postinfectious autoimmune and neuroinflammatory disorder
		• Probable genetic link
		• Possible involvement of the cortico-striato-pallido-thalamic (CSPT) pathway
		• Chronic avoidance of anxiety-producing stimuli is a contributing factor

Infectious Trigger	• PANS-Association with infection but not required • PANDAS-Required association with strep	Unknown
Involvement of Basal Ganglia	Strong Support	Good Support

SUPPORTING **TESTING, WORKUP & MANAGEMENT**

PANS/PANDAS Supporting Lab Tests

- Strep - 48 hour culture or perianal culture
- Anti streptococcal titers - (Supportive but not diagnostic)
  - ASO *(anti-streptolysin O)*
  - Anti-DNAse B *(Anti-deoxyribonuclease B)*
  - ACHO *(anti-group A carbohydrate antibodies)*
- Positive EBV IgM *(VCA) (EBNA)*
- Lyme Disease and co-infections
- Mycoplasma Pneumonaie IgA & IgM
- Pneumococcal Antibody
- Epstein Barr Virus Panel
- Coxsackie A & B Titers
- Other positive specific autoimmune encephalopathic antibodies: HSV, VZV, EV, HHV-6, Anti-NMDAR, ALE, GAD-65 *(blood & LP)*
- Antinuclear antibody titers
- IgE Level
- IgA, IgM
- IgG *(subclass 1, 2, 3, 4)*
- CBC
- Leukopenia
- Ferritin
- Serum Copper
- B-12
- Vitamin D
- Plasma Amino Acids
- Organic Acids
- Others indicated by symptom
- Increased Circulating Immune Complexes *(c1q, c3d, Raji cells)*

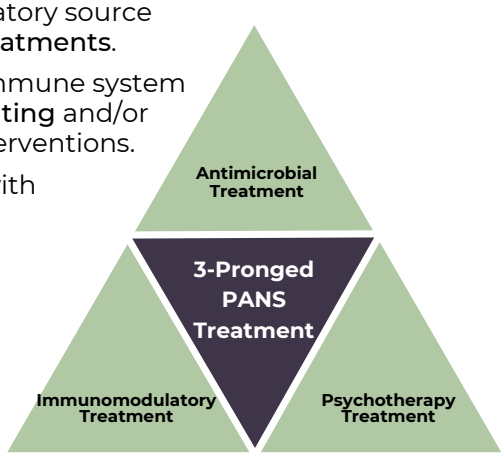
> "The best test is still taking a thorough history and listening to the parents."
>
> *– Dr.Sue Swedo*

Medical Work Up

- Comprehensive history, including family history
- Look for choreiform movements and dilated pupils
- Rule-out Sydenham chorea and other specific illnesses
- Physical examination for occult infections (adenoids, tonsils, sinuses, urethra, and anus)
- 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

Three-Pronged Treatment

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



Overview of Treatment of PANS-JCAP Vol27, 2017 Swedo, MD, Frankovich, MD, MS, Murphy, MD, MS

Making the Strep Connection

While strep is ubiquitous among children, it is not a simple bacteria to test for, nor to eradicate.

- A negative strep test (rapid, culture, or blood work) DOES NOT rule out PANDAS or PANS.
- PANDAS symptoms can start even after a strep infection has been treated.
- Strep does not only affect the throat.
- GAS infection can occur in the throat, sinuses, ears, vagina, anus, and on the skin. If you suspect strep but the throat is clear, consider swabbing elsewhere.
- Streptococcal bacteria can invade host cells and persist in an intracellular environment, effectively allowing them to "hide" from some antibiotics.*
- Rapid strep tests do produce false negatives. If you suspect strep but have a negative rapid swab, consider sending a swab out for culture.
- Some children do not produce ASO or Anti-DNase B titers. These children will not show current or past strep infection on blood work, but they can still have PANDAS.

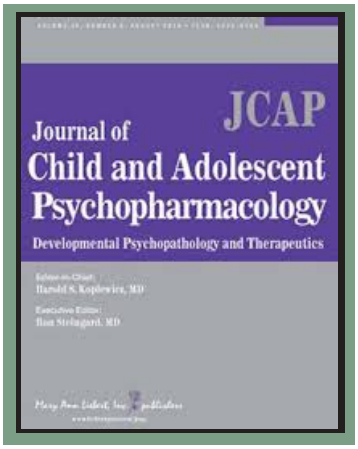
Due to these issues with effectively testing for strep, the consensus treatment guidelines support one trial of antibiotics for children in whom a clinician suspects a strep infection, even if strep testing is negative.

**https://mbio.asm.org/content/7/3/e00661-16.*

RESOURCES FOR **DIAGNOSIS & TREATMENT**

Journal of Child and Adolescent Psychopharmacology

Two recent issues of JCAP have established guidelines for clinical diagnosis and treatment of PANS/PANDAS.



The PANS/PANDAS Research Consortium (PRC) convened by Dr. Swedo, formerly Chief of the Section on Behavioral Pediatrics at the National Institute of Mental Health (NIMH), published two special issues of the Journal of Child and Adolescent Psychopharmacology. The February 2015 issue focuses on clinical evaluation. The July 2017 issue provides detailed guidelines on a combination of psychotherapeutic, antimicrobial, and Immunomodulatory treatments. The PRC consists of a diverse group of clinicians and researchers from complementary fields of pediatrics: general and developmental pediatrics, infectious diseases, immunology, rheumatology, neurology, and child psychiatry.

Diagnostic Evaluation and Treatment Guidelines are Open Access
https://aspire.care/resources/clinicians

Diagnostic Evaluation

Special Issue: Pediatric Acute-Onset Neuropsychiatric Syndrome
Journal of Child and Adolescent Psychopharmacology
February, 2015

Clinical Evaluation of Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS): Recommendations from the 2013 PANS Consensus Conference
Kiki Chang, Jennifer Frankovich, Michael Cooperstock, Madeleine W. Cunningham, M. Elizabeth Latimer, Tanya K. Murphy, Mark Pasternack, Margo Thienemann, Kyle Williams, Jolan Walter, Susan E. Swedo

"The goals were to clarify the diagnostic boundaries of PANS, to develop systematic strategies for evaluation of suspected PANS cases, and to set forth the most urgently needed studies in this field.

Presented here is a consensus statement proposing recommendations for the diagnostic evaluation of youth presenting with PANS".

Treatment Guidelines

Special Issue: PANS-PANDAS Treatment Guidelines
Journal of Child and Adolescent Psychopharmacology
September, 2017

Overview of Treatment of Pediatric Acute-Onset Neuropsychiatric Syndrome
Susan E. Swedo, Jennifer Frankovich, and Tanya K. Murphy

Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part I—Psychiatric and Behavioral Interventions
Margo Thienemann, Tanya Murphy, James Leckman, et al.

Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part II—Use of Immunomodulatory Therapies
Jennifer Frankovich, Susan Swedo, Tanya Murphy, et al.

Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part III—Treatment and Prevention of Infections
Michael S. Cooperstock, Susan E. Swedo, Mark S. Pasternack, et al.

ICD-11

ICD-11 Includes PANDAS Code

In May 2019, the World Health Organization (WHO) adopted the 11th edition of the International Classification of Diseases (ICD-11). This updated version will go into effect on January 1, 2022 in member countries. WHO has already released a preview that will allow countries to plan how to use the new version, prepare translations, and train health professionals. The ICD-11 includes PANDAS for the first time in coding related to post-infectious tics and autoimmune disorders related to the central nervous system.

Access to the new ICD-11 is available online at https://icd.who.int/en/

Disease Mechanisms & Treatment

Supported by novel animal disease models and clinical research, key advances in our understanding of post-infectious basal ganglia encephalitis (BGE) and immune-related encephalopathies have emerged over recent years. Large epidemiological studies continue to support the relationship between infectious triggers and neuropsychiatric disorders, while advances in our understanding of the role of neuroimmune dysregulation are shaping future findings in diagnostic and treatment outcomes. Highlighted are a few recent peered-review research studies and reviews of thereof that are furthering our understanding of post-infectious BGE that will aid future diagnostic and treatment modalities.



Preclinical Animal Models are Advancing Our Knowledge of Post-Infectious BGE

Various pre-clinical animal models are reviewed utilizing group A streptococcus (GAS) exposure to study the mechanisms of immune activation and how these induce long-term neurobehavioral effects associated with neuropsychiatric disorders such as those observed in PANS. These models will help decipher not only novel treatments, but also more specific diagnostic tools.

Neuropsychiatric consequences of childhood group A streptococcal infection: A systematic review of preclinical models

Mora S, Martín-González E, Flores P, Moreno. M. Brain Behav Immun. 2019 Feb 25. pii: S0889-1591(19)30214-4. doi: 10.1016/j.bbi.2019.02.027. PMID: 30818033

PANS/PANDAS Characterized as Pediatric Acquired Encephalopathies Responsiveness

This review summarizes autoimmune encephalitis in children. PANS/PANDAS is included as a subgroup of acquired encephalopathy with focal neurological deficits of infectious and/or immune origin.

Autoimmune encephalitis in children: clinical phenomenology, therapeutics, and emerging challenges

Dale RC, Gorman MP, Lim M. Curr Opin Neurol. 2017 Jun;30:334-344. doi:10.1097/WCO.0000000000000443. PubMed PMID: 28234797

Role of Autoimmunity in the Breakdown of the Blood-Brain Barrier

This review summarizes available rodent models for elucidating the mechanisms for both humoral (antibody) and cell mediated (T cell) autoimmune responses. Understanding the potential routes for antibody entry into the central nervous system (CNS) is crucial to elucidating how autoantibodies generated in response to Group A Streptococcus or other pathogens mediate disease pathogenesis in PANS/PANDAS.

Hello from the Other Side: How Autoantibodies Circumvent the Blood-Brain Barrier in Autoimmune Encephalitis

JPlatt MP, Agalliu D, Cutforth T. Front Immunol. 2017 Apr 21;8:442. doi: 10.3389/ mmu.2017.00442. PMID: 28484451

Large Prospective Studies Support Post-Infectious Mediated Development of Neuropsychiatric Symptoms

A population-based cohort study based on the Danish nationwide registry of a total of 1,098,930 individuals identified an 84% increased risk of developing any mental disorder as a result of infections requiring hospitalizations (HRR of 1.84, 95% CI, 1.69-1.99). These findings provide evidence for the involvement of infections and an immune-mediated etiology with a wide range of mental disorders in children and adolescents.

A Nationwide Study in Denmark of the Association Between Treated Infections and the Subsequent Risk of Treated Mental Disorders in Children and Adolescents

Köhler-Forsberg, Petersen L, Gasse, Mortensen, Dalsgaard, Yolken, Mors, Benros. JAMA Psychiatry. 2018 Dec 5. doi:10.1001/jamapsychiatry.2018.3428. PMID: 30516814

New Studies Reveal the Role of Autoimmunity in the Susceptibility and Development of Pediatric Neuropsychiatric Disorders

Case studies identify the role of maternal autoimmunity as a risk factor for neuropsychiatric disorders in children by mechanisms involving maternal immune activation in utero. As reviewed by Pape et. al., it is now well accepted that immune dysregulation plays a key role not only in classical autoimmune brain diseases, but also in neuropsychiatric disorders such as PANS.

Maternal thyroid autoimmunity associated with acute-onset neuropsychiatric disorders and global regression in offspring

Jones HF, Ho ACC, Sharma S, Mohammad SS, Kothur K, Patel S, Brilot F, Guastella AJ, Dale RC. Immune-Neurodevelopment Study Group. Dev Med Child Neurol. 2019 Aug;6. doi.org/10.1111/dmcn.14167 PMID: 30720202

Immunoneuropsychiatry - novel perspectives on brain disorders

Pape K, Tamouza R, Leboyer M, Zipp F. Nat Rev Neurol. 2019 Jun;15(6):317-328. doi:10.1038/s41582-019-0174-4. PMID: 30988501

Correlation between Streptococcus Infections and PANDAS

The findings reported represent one of the **largest retrospective studies conducted on the association between streptococcal infections and PANDAS.** Children with a previously positive streptococcus test had an 18% higher risk of any mental disorder, 51% higher risk of OCD, and 35% higher risk of tic disorders, which are diagnostic criteria for PANDAS. Study findings support the association of streptococcal and non-streptococcal infections in the diagnosis of PANS.

Association of Streptococcal Throat Infection With Mental Disorders: Testing Key Aspects of the PANDAS Hypothesis in a Nationwide Study

Köhler-Forsberg, Petersen L, Gasse, Mortensen, Dalsgaard, Yolken, Mors, Benros. JAMA Psychiatry. 2018 Dec 5. doi:10.1001/jamapsychiatry.2018.3428. PMID: 30516814

Connecting the Immune System to the Brain

The research findings challenge the dogmas regarding the immune privilege status of the central nervous system (CNS) and its isolation from the immune system by the blood-brain barrier. Functional meningeal lymphatic vessels capable of carrying immune cells and interstitial fluids from the CNS are identified and characterized. Findings provide novel understanding on how autoimmune encephalopathies, like PANS/PANDAS, can develop when these unique lymphatic vessels malfunction.

Structural and functional features of central nervous system lymphatic vessels

Louveau A, Smirnov I, Keyes TJ, Eccles JD, Rouhani SJ, Peske JD, Derecki NC,Castle D, Mandell JW, Lee KS, Harris TH, Kipnis J. Nature. 2015 Jul 16;523(7560):337-41. doi: 10.1038/nature14432. PMID: 26030524.

Corticosteroids May Shorten Duration of Flares in PANS/PANDAS Patients

Corticosteroids may be a helpful intervention in new-onset and relapsing/remitting PANS/PANDAS cases. Clinical remission may occur sooner. Longer courses may lead to more durable remissions.

Pediatric Acute-Onset Neuropsychiatric Syndrome Response to Oral Corticosteroid Bursts: An Observational Study of Patients in an Academic Community-Based PANS Clinic

Kayla Brown, Cristan Farmer, Bahare Farhadian, Joseph Hernandez, Margo Thienemann, and Jennifer Frankovich. 2017 Sep;27(7):629-639. doi: 10.1089/cap.2016.0139. PMID: 28714753

NSAIDs May Shorten Duration of Flares in PANS/PANDAS Patients

NSAIDs given within 30 days of flare onset or prophylactically may shorten neuropsychiatric symptom duration in new-onset and relapsing/remitting PANS/PANDAS patients.

Effect of Early and Prophylactic Nonsteroidal Anti-Inflammatory Drugs on Flare Duration in Pediatric Acute-Onset Neuropsychiatric Syndrome: An Observational Study of Patients Followed by an Academic Community-Based PANS Clinic

Kayla D. Brown, Cristan Farmer, G. Mark FreemanJr., Ellen J. Spartz, Bahare Farhadian, Margo Thienemann, and Jennifer Frankovich. JCAP.2017 Sep;27(7):619-628. doi: 10.1089/cap.2016.0193 PMID: 28696786

Majority of Newly-Acquired Streptococcus Infections are Asymptomatic

The prospective study examining the immunological response to infection by group A streptococcus (GAS) was performed in serum samples obtained from pediatric subjects. Study examined the immune response to 13 shared GAS antigens and 18 type-specific M peptides, but found no novel pattern of immune responses. Importantly, the study found that **65% of new streptococcus infections did not result in symptoms despite a detectable immunological response.** This finding is supported by previous research and suggests **the majority of GAS infections remain undetected and contribute to the burden of the disease when left untreated.**

Prospective Longitudinal Analysis of Immune Responses in Pediatric Subjects After Pharyngeal Acquisition of Group A Streptococci Autoimmune encephalitis in children: clinical phenomenology, therapeutics, and emerging challenges

Hysmith ND, Kaplan EL, Cleary PP, Johnson DR, Penfound TA, Dale JB. J. Pediatric Infect Dis Soc. 2017 Jun 1;6(2):187-196. doi: 10.1093/jpids/piw070. PMID: 28204534

A Double-Blind Randomized Placebo-Controlled Pilot Study Points to Efficacy Azithromycin in PANS Patients

This double blind pilot study suggests azithromycin may be helpful in treating PANS diagnosis patients, especially those with elevated levels of both OCD and tic symptoms.

A Double-Blind Randomized Placebo-Controlled Pilot Study of Azithromycin in Youth with Acute-Onset Obsessive–Compulsive Disorder

Tanya K. Murphy, Erin M. Brennan, Carly Johnco, Ellisa Carla Parker-Athill, Branko Miladinovic, Eric A. Storch, and Adam B. Lewin. JCAP.S2017 Sep;27(7):6 40-651. doi: 10.1089/cap.2016.0190. PMID: 28358599

Therapeutic Plasma Apheresis as a Treatment for Severely Ill Patients with PANS Associated with Streptococcal Infections

Therapeutic plasma apheresis should be reserved for treatment of severely affected PANDAS patients. It appears to be a safe, well-tolerated, and beneficial treatment option.

Therapeutic Plasma Apheresis as a Treatment for 35 Severely Ill Children and Adolescents with PANS Associated with Streptococcal Infections

M. Elizabeth Latimer, Nathan L'Etoile, Jakob Seidlitz, and Susan E. Swedo. JCAP 2015 Feb;25(1):70-5. doi: 10.1089/cap.2014.0080. PMID: 25658452

Clinical Studies Identify Autoantibodies as Predictive Markers for IVIG Treatment Responsiveness

In an open-labeled IVIG study in children with comorbid ASD and PANS/PANDAS, anti-tubulin and anti-D2R (as measured by the Cunningham panel) were associated with responsiveness to IVIG treatment, suggesting these autoantibodies could be biomarkers to select for positive IVIG treatment outcomes. Research continues to explore serum biomarkers and genetic risk factors that can provide a diagnostic tool and/or complement diagnosis of PANS/PANDAS.

Intravenous immunoglobulin for the treatment of autoimmune encephalopathy in children with autism

Connery K, Tippett M, Delhey LM, Rose S, Slattery JC, Kahler SG, Hahn J, Kruger U, Cunningham MW, Shimasaki C, Frye RE. Transl Psychiatry. 2018 Aug 10;8(1):148. doi: 10.1038/s41398-018-0214-7. PMID: 30097568

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PANDAS Physicians Network
PPN
A Division of The Foundation for Brain Science and Immunology

PANDAS Physicians Network

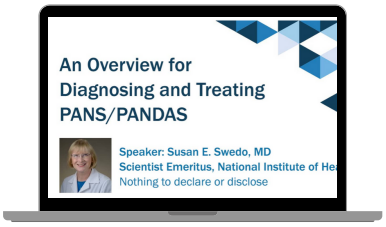
PPN is an organization dedicated to helping medical professionals better understand PANDAS and PANS through real-time information and networking. PPN Guidelines for Diagnostics and Therapeutics are developed by PPN special advisors from Harvard, Yale, Stanford, Columbia, Georgetown, NIH, and NIMH whohave worked with, treated, or studied the patients or aspects of the disorder. Because PANDAS & PANS are interdisciplinary disorders, all the relevant disciplines are represented on the PPN committees and the special advisory council.

It's free to become a member of the PPN.
Benefits include:

- Communicate and ask questions to your peers.
- Receive email alerts on new research, guidelines, and treatment protocols
- Option to be recognized as a practitioner who works with PANS/PANDAS patients
- Receive occasional members only benefits

On Demand CME Activity
An Overview for Diagnosing and Treating PANS/PANDAS - Susan E. Swedo, MD, Scientist Emeritus at the NIH

- Learn the criteria PANS & PANDAS, differences between PANS & PANDAS and OCD, how to determine if symptoms are related to post-streptococcal autoimmunity, and how develop a treatment plan.



www.pandasppn.org

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Objectives:

- Recognize the signs and symptoms of PANS in patients.
- Administer the appropriate first line treatments to PANS patients.
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- Educate and counsel PANS patients and their families on care at home and at school.

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- Michael Wilson, MD, Neurology, UCSF
- Richard Frye, MD, PhD, Neurology, University of Arizona
- Jennifer Frankovich, MD, Rheumatology, Stanford

www.neuroimmune.org

Children's Postinfectious Autoimmune Encephalopathy Center

Children's Postinfectious Autoimmune Encephalopathy Center

Banner - Diamond Children's
Multispecialty Clinic
535 N. Wilmot Rd. Ste 101
Tucson, AZ 85711

www.peds.arizona.edu/cpae

The Children's Postinfectious Autoimmune Encephalopathy (CPAE) Center of Excellence at the UA 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 neuropsychiatric disorders that are often misdiagnosed, underdiagnosed, and undiagnosed in children.

Referral Process:
Fax referral to the CPAE Clinic at 520-694-4486

Questions? Please email our RN patient navigator
Jessica Jones West at CPAE@bannerhealth.com

SUPPORT FOR **Families & Patients**

SEPPA

ASPIRE is incredibly grateful to SEPPA for their selfless assistance in the establishment of our national organization. Their service to the Southeast provides an excellent model for other regions to follow.

SEPPA
Southeastern PANS/PANDAS Association

The Southeastern PANS/PANDAS Association is a group of medical professionals and parents who raise awareness of and expand access to care for Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) and a subset of PANS called Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS). SEPPA support parents, providers, and policy makers in their efforts to heal and take care of children with PANS/PANDAS.

Mission:
SEPPA works for children and families with PANS/PANDAS to expand access to timely, accurate diagnosis and treatment and insurance-based medical care for children, adults, and caregivers affected by PANS, PANDAS, and related neuroimmune disorders in the Southeastern US.

www.sepans.org

ASPIRE

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Alliance to Solve PANS & Immune-Related Encephalopathies
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MENDING MINDS FOUNDATION

Mending Minds Foundation
mminds.org

MIDWEST PANDAS/PANS PARENT ASSOCIATION

MPPA
Midwest PANDAS/PANS Association
midwestpandas.com

PRAI
FINDING ANSWERS FOR CHILDREN WITH NEUROIMMUNE DISORDERS

PRAI
Pediatric Research and Advocacy Initiative
praikids.org

PANDAS Network
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Children's Autoimmune cabda Brain Disorder Association

CABDA
Children's Autoimmune Brain Disorder Association
cabdatexas.org

THE FOUNDATION FOR CHILDREN WITH NEUROIMMUNE DISORDERS

The Foundation for Children with Neuroimmune Disorders
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NEPANS
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Northwest PANDAS/PANS Network
nwppn.org

Our Mission

To improve the lives of children and adults affected by PANS, PANDAS, and immune-related encephalopathies.

Our Vision

We aspire to create a world where children and adults affected by PANS, PANDAS and related encephalopathies obtain a timely diagnosis from informed providers and receive effective, proven and affordable treatments and support in all areas of daily living, without discrimination.

ASPIRE
Alliance to Solve PANS & Immune-Related Encephalopathies

Who We Are

We are experienced leaders in the PANS advocacy community. We are parents, providers and experts in our field who believe collaboration and empowered action are the keys to the world we seek: one where no one suffers through PANS and immune-related encephalopathies without access to a knowledgeable provider, insurance coverage for standard-of-care treatments or the support that comes with public awareness.

We work collaboratively to improve the quality of life for those affected by PANS, PANDAS and immune-related encephalopathies. We focus our efforts on empowering and connecting our community with tools and resources for advocacy, education, support, and awareness.

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