



**ASPIRE Professional
Advisory Board**

February 18, 2024

Susan Swedo, MD
Scientist Emerita
National Institute of
Mental Health

Dritan Agalliu, PhD
Assistant Professor
Departments of
Neurology and Pathology
& Cell Biology Columbia
University

Margo Thienemann, MD
Co-Director PANS Clinic
and Director Psychiatric
Services, Stanford
University

Mark Pasternack, MD
Unit Chief, Pediatric
Infectious Disease, Mass
General for Children

**Fern Aaron Zagor, LCSW,
ACSW**
Principal Consultant,
Fern Zagor

**Nancy H. O'Hara, MD,
MPH, FAAP**
Integrative Pediatrics,
New England Center of
Health

Sydney Rice, MD, Msc
Developmental
Pediatrics, Co-Director
Childhood Autoimmune
Encephalopathy Clinic,
University of Arizona

**Anu French, MD, FAAP,
ABoIM**
Integrative Pediatrician
SSM Health Cardinal
Glennon Pediatrics

Shannon L. Delaney, MD
Psychiatry, Child &
Adolescent Psychiatry
Private Practice

Christina Hift, MD, FAAP
Infectious Disease &
Pediatric Rheumatology,
Private Practice

Dear Chairlady Esther Helton and the House Insurance
Subcommittee,

On behalf of the Alliance to Solve PANS and Immune Related Encephalopathies (ASPIRE), we the members of the ASPIRE Professional Advisory Board, write to express our strong support for **HB 2463** AN ACT to amend Tennessee Code Annotated, Title 8; Title 56 and Title 71, relative to pediatric medical disorders and **HB2484** AN ACT to amend Tennessee Code Annotated, Title 8; Title 56 and Title 71, relative to pediatric medical disorders. These bills will significantly improve the health and well-being of patients with PANS and ease the financial and emotional burdens of their families.

Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) is characterized by the abrupt and dramatic onset of obsessive-compulsive symptoms, restricted intake of food or fluids (sometimes to the point of starvation or dehydration), anxiety, depression and suicidality, emotional lability, personality changes, sensory hypersensitivity, cognitive deficits and physical symptoms, such as arthralgias, urinary dysfunction, and severe insomnia. As its name implies, PANS affects children, primarily those aged 4 - 9 years. A viral or bacterial infection triggers most cases; when Group A streptococcal infections (such as strep throat or impetigo) triggers symptoms, the disorder is known as Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS). In recent months, a number of studies have proven that PANS/PANDAS is a form of autoimmune encephalopathy—or inflammation of the brain. Treatment of PANS/PANDAS involves a three-pronged approach that utilizes psychiatric medications to provide symptomatic relief, antibiotics to eliminate the source of neuroinflammation and immune-modulating therapies to treat disturbances of the immune system. When these therapies are instituted promptly, many children recover completely and return to full functioning.

Delays in obtaining treatment not only prolong the child's suffering needlessly but also increase the risk that the PANS/PANDAS symptoms will become entrenched, leading to long-term psychiatric, neurologic, and cognitive dysfunction.



Unfortunately, there are currently several barriers that delay or prevent treatment of PANS/PANDAS. At the outset, families are confronted with a paucity of physicians available to treat PANS/PANDAS. Insurance coverage for PANS/PANDAS would address this concern through efforts to educate providers and raise awareness about PANS/PANDAS. Without such measures, many families must travel long distances to access treatment at great emotional and monetary expense. For others, the inability to travel due to financial circumstances or the severity of a child's illness postpones or precludes therapeutic interventions entirely.

Lack of insurance coverage for PANS/PANDAS further delays or, in some cases, completely prevents access to treatment. Particular difficulties are experienced with obtaining reimbursement for intravenous immunoglobulin (IVIG) and other immunotherapies. Insurers routinely deny insurance coverage, and a lengthy cycle of repeated denials and appeals frustrates both healthcare providers and families. More importantly, the denials/appeals process prolongs the patients' suffering and family trauma and increases the risk of serious neurological and psychological harm, long-term disability or even loss of life. Faced with continual denial of care, many families attempt to self-pay for the treatments, forcing them to take on heavy credit card debt, deplete retirement/college funds or sell their homes to raise funds to pay for a treatment that should be covered by insurance.

While we acknowledge that the cost of immunotherapies (particularly IVIG) is substantial, it is small in comparison with the cost of emergency interventions, inpatient psychiatric treatment, and/or pediatric hospitalizations for the complications of severe PANS/PANDAS, such as starvation/dehydration, aggressive behaviors, and self-injury or suicidality. Delayed or denied care also carries a risk of long-term care for serious neurological, emotional, and behavioral disabilities. In addition to the increased expenditures for medical care, untreated PANS/PANDAS also increases education-related costs, as children often require specialized, individualized instruction and significant accommodations for cognitive, neuropsychological, and psychological dysfunction.

Since the AAP Redbook publication in 2018, written in 2017, there have been several critical advances in research. In 2017, the PANS Research Consortium (PRC) published treatment guidelines in the *Journal of Child and Adolescent Psychopharmacology*. (7, 8, 9, 10) These guidelines are divided into four sections and represent best practice recommendations: Overview (1), Part I-psychiatric and behavioral interventions (2), Part II-use of immunomodulatory therapies (3), and Part III-treatment and prevention of infections (4). In 2017 and 2020, two papers from Columbia University explain the mechanism of PANDAS by elucidating how the autoantibodies enter the CNS due to persistent microglial activation as a result of



multiple Group A Streptococcus infections (5,6). In 2020, a double-blind study out of Yale demonstrated that antibodies from children with PANDAS bind specifically to striatal cholinergic interneurons and alter their activity. “These findings provide strong evidence for striatal CINs as a critical cellular target that may contribute to pathophysiology in children with rapid-onset OCD symptoms, and perhaps in other conditions.” (7). A 2020 study on IVIG for PANS provides further support of IVIG use for a small but significant subset of children who meet the criteria. (8) These studies are only a small sample of the scientific advancements being made in PANS PANDAS.

In closing, we ask that you alleviate the burdens placed on families, physicians, and other community members who strive to serve the critical needs of children with PANS/PANDAS. Please enable their doctors to make appropriate medical decisions free from administrative and time constraints posed by insurance coverage denials. We urge you to join your fellow legislators in Arkansas, Delaware, Indiana, Illinois, Kansas, Minnesota, Massachusetts, Maryland, New Hampshire, Oregon, and Rhode Island require insurance coverage for PANS/PANDAS treatment. Your leadership on this important issue will help ensure children with PANS/PANDAS receive appropriate treatment, enabling them to experience all the joys of childhood and reach their full potential.

Thank you for your time and consideration. Please don't hesitate to contact us if we can provide additional information and answer any questions that may arise.

ASPIRE Professional Advisory Board

Susan Swedo, MD
Scientist Emerita
National Institute of Mental Health

Contact Information:

Gabriella True, PAB Secretary and Board President

Email: gabriella@aspire.care Mobile: 562-480-7560

Sources:

- 1 - Swedo SE, Frankovich J, Murphy TK. Overview of treatment of pediatric acute-onset neuropsychiatric syndrome. *J Child Adolesc Psychopharmacol.* 2017;27:562-5. <https://doi.org/10.1089/cap.2017.0042>
- 2 - Thienemann M, Murphy T, Leckman J, et al. Clinical management of pediatric acute-onset neuropsychiatric syndrome: Part I- psychiatric and behavioral interventions. *J Child Adolesc Psychopharmacol.* 2017;27:566-73. <https://doi.org/10.1089/cap.2016.0145>
- 3 - Frankovich J, Swedo S, Murphy T, et al., 2017. Clinical management of pediatric acute-onset neuropsychiatric syndrome: Part II— use of immunomodulatory therapies. *J. Child. Adolesc. Psychopharmacol.* 2017;27:574-93. <http://doi.org/10.1089/cap.2016.0148>
- 4 - Cooperstock MS, Swedo SE, Pasternack MS, Murphy TK. for the PPC. Clinical Management of pediatric acute-onset neuropsychiatric syndrome: Part III—treatment and prevention of infections. *J Child Adolesc Psychopharmacol.* 2017;27:594- 606. <http://dx.doi.org/10.1089/cap.2016.0151>.
- 5 - Maryann P. Platt, Kevin A. Bolding, Charlotte R. Wayne, Sarah Chaudhry, Tyler Cutforth, Kevin M. Franks, Dritan Agalliu. Th17 lymphocytes drive vascular and neuronal deficits in a mouse model of postinfectious autoimmune encephalitis. *Proceedings of the National Academy of Sciences Mar 2020, 117 (12) 6708-6716; DOI: 10.1073/pnas.1911097117*
- 6 - Cutforth, Tyler & Platt, Maryann & Agalliu, Dritan. Hello from the Other Side: How Autoantibodies Circumvent the Blood-Brain Barrier in Autoimmune Encephalitis. (2017). *Frontiers in Immunology.* 8. 10.3389/fimmu.2017.00442.
- 7 - Antibodies Bind to Striatal Cholinergic Interneurons and Alter Their Activity
Jian Xu, Rong-Jian Liu, Shaylyn Fahey, Luciana Frick, James Leckman, Flora Vaccarino, Ronald S. Duman, Kyle Williams, Susan Swedo, and Christopher Pittenger. *Am J Psychiatry* 16 Jun 2020 DOI: 10.1176/appi.ajp.2020.19070698
- 8 - Isaac Melamed, Roger Kobayashi, Maeve O'Connor, Ai Lan Kobayashi, Andrew Schechterman, Melinda Heffron, Sharon Canterberry, Holly Miranda, Nazia Rashid. Benefits of IVIG in Pediatric Acute-Onset Neuropsychiatric Syndrome. *Neurology Apr 2020, 94 (15 Supplement) 2411*