



*House of Representatives Study Committee on Pediatric
Acute-Onset Neuropsychiatric Syndrome ("PANS") and
Pediatric Autoimmune Neuropsychiatric Disorder
Associated with Streptococcal Infection ("PANDAS")*

Final Report

**The Honorable Sharon Cooper, Chair
Representative, 43rd District**

The Honorable Karen Bennett
Representative, 94th District

The Honorable David Dreyer
Representative, 59th District

The Honorable Lee Hawkins
Representative, 27th District

The Honorable Richard Smith
Representative, 134th District

Citizen Members

Dr. Suvrat J. Bhargave, Psychiatrist

Dr. Jill Dickerson, Pediatrician

Dr. Silke Von Esenwein, Public Health Practitioner

December 1, 2019

Prepared by the House Budget and Research Office

Introduction

The Georgia House of Representatives created the House Study Committee on Pediatric Acute-Onset Neuropsychiatric Syndrome ("PANS") and Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection ("PANDAS") during the 2019 Legislative Session through the passage of House Resolution 590. PANS and PANDAS create the sudden onset of obsessive-compulsive disorder in children, causing previously healthy and emotionally-adjusted children to experience severe anxiety and emotional disturbances. The committee was formed to identify the barriers to PANS and PANDAS by evaluating awareness, testing, diagnosis, and early linkage to medication and care, and to publish its findings with recommendations.

Representative Sharon Cooper (43rd) chaired the committee, which included four additional House members and three citizen members: Representative Karen Bennett (94th); Representative David Dreyer (59th); Representative Lee Hawkins (27th); Representative Richard Smith (134th); Suvrat J. Bhargava, M.D. (Center for Family Psychiatry); Jill Dickerson, M.D. (Vibrant Kids Pediatrics); and Silke Von Esenwein, M.D. (Emory University). The House Budget and Research Office assigned Mr. Leonel Chancey to assist the committee, while the Office of Legislative Counsel assigned Mr. Vincent Wiegand, Esq.

The committee held three public meetings at the Capitol complex in Atlanta to hear from the National Institute of Mental Health, American Academy of Pediatrics, Intown Pediatric and Adolescent Medicine, Children's Healthcare of Atlanta, Southeastern PANS/PANDAS Association, Therapy Works ATL, and parents regarding their experiences searching for solutions to provide relief for their children with PANS/PANDAS.

During the meetings, committee members heard the various definitions, types of symptoms, historical links, evidence, and treatment recommendations for the intricate issues regarding the PANS/PANDAS auto-immune disorders. The committee also focused on the cost of treatment and medical insurance coverage concerning Georgia's children with PANS/PANDAS. The following speakers testified before the committee:

September 17, 2019 — Susan Swedo, M.D. (National Institute of Mental Health); Deneta Sells, M.D. (FAAP, Intown Pediatrics); and Gabriel Guyana, (Southeastern PANS/PANDAS Association).

October 2, 2019 — Satya Gedela, M.D. (Chief of Neurology, Children's Healthcare of Atlanta); Jill Dickerson, M.D. (Committee Member, Vibrant Kids Pediatrics); Carrie Smith; Jeannie Garvey, Esq; and Katherine Butler.

October 16, 2019 — Kelley Utterback (PACE Foundation); Eric Fier, M.D. (Psychiatrist, Therapy Works ATL); and Jessica Gowen (President, Southeastern PANS/PANDAS Association).

Background

Pediatric Acute-Onset Neuropsychiatric Syndrome (“PANS”) and Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection (“PANDAS”) are distorted autoimmune responses that inflame the brain, resulting in an abrupt onset of neuropsychiatric symptoms. The obsessive-compulsive symptoms include developmental regression, limited eating habits, convulsions, anxiety, depression, hyperactivity, sleep disturbance, urinary problems, irritability, aggression, and sensory sensitivity. Families describe the inception and the symptoms of this disorder as instantaneous, usually appearing within 24–48 hours. This exacerbation is caused by antibodies attacking nerve cells in the brain, triggering interference with neuronal cell signaling.

One of the first case studies occurred in 1995 with four boys aged 10 to 14 years old.¹ Their symptoms ranged from moderate to severe, with two boys showing evidence of recent strep infections, while the other two showed histories of past viral illnesses. Two were treated by plasma exchange, and two with intravenous immunoglobulin (IVIG) or prednisone. All four boys had significant responses immediately after receiving treatment. These autoimmune diseases are often mistaken with pediatric Obsessive-Compulsive Disorder (OCD).

Pediatric OCD is typically found around eight years old, where children experience repeating obsessions such as fear of contamination, pathological doubt, counting, or arranging items in a specific order.² OCD results from a probable genetic link that is gradually more severe over time. The mysterious difference with PANS/PANDAS is that PANS typically results in autoimmune antibodies mistakenly inflaming the brain following infection of mycoplasma, mononucleosis, Lyme, and H1N1. PANDAS emerges following a strep infection, which can affect children as early as the age of four years old. Unfortunately, a reliable laboratory or imaging test for PANDAS is yet to be available. Diagnosis relies on continuous observation of clinical courses, including laboratory tests documenting the streptococcal infection.

Testimony presented to the committee illustrates the historical links between OCD and Sydenham chorea during the discovery of PANS/PANDAS. In 1922, Dr. E.M. Hammes claimed that “Mental symptoms may occur at any stage in the course of Sydenham’s Chorea.”³ With Sydenham chorea, there is a neurological appearance of acute rheumatic fever that causes brain inflammation produced by cross-reactive antibodies. Dr. Hammes describes patients to have periods of depression and suicidal thoughts. In one observation, he witnessed a woman who became hallucinogenic and was tube-fed because of the fear that her food was poisonous.

The lack of understanding of PANS/PANDAS has devastated families with relapsing episodes that are life-threatening if a child does not receive prompt medication. Interventions can take weeks to begin showing signs of progress and may need adjustments when symptoms often fluctuate. Without appropriate medical care, out-of-pocket medical expenses are disastrous when not covered by insurers. Until further conclusive studies are released, families are still waiting for consensus treatment guidelines. Following testimony from multiple medical experts, the committee presents the following findings and recommendations to the Georgia House of Representatives.

¹ A.J. Allen, M.D., H.L. Leonard, M.D., and Susan Swedo, M.D., “Case Study: A new infection-triggered, autoimmune subtype of pediatric OCD and Tourette’s syndrome,” *Journal of the American Academy of Child and Adolescent Psychiatry*, 34(3):307-11, March 1995.

² International OCD Foundation, “Is it OCD, or is it PANDAS/PANS?” July 8, 2015.

³ E.M. Hammes, M.D., “Psychosis Associated with Sydenham Chorea,” *Journal of the American Medical Association*, September 2, 1922

Committee Findings

The conventional treatment for PANS/PANDAS is a combination of antibiotic medications to treat the triggering infection and immune deficiency. Therapy can show positive results as soon as four weeks when doctors catch the illness early. For patients not diagnosed or treated in a timely matter, some intense approaches are needed, such as steroids and psychiatric medications. In severe cases, Intravenous immunoglobulin (IVIG) therapy helps strengthen a child's immune system to fight infections as well as prevents white blood cells from harming brain cells with the supplement of new precise antibodies.

Families located within the southeastern United States have very little success in finding a significant clinic or children's hospital that will provide care for this illness. Other families have no other choice but to try the expensive IVIG treatment, which costs around \$200 per kilogram of body weight per round (approximately \$10,000 per pound for a 100-pound child).⁴ Some insurance providers will cover immunoglobulin therapy only if it is determined medically necessary. Testimony revealed that few families have the disposable income to seek care and treatment that can cost hundreds of thousands of dollars.⁵ However, it is rare to find support due to medical criteria and guidelines for PANS/PANDAS lacking uniformity among medical experts.

The American Medical Association has not published policies or guidelines for the treatment of PANS/PANDAS. The clinical characteristics of the illness are the most common way of verifying if a child will have an irregular course of symptoms. With some parents, educators, and medical providers unaware of the disease, children are more likely to be diagnosed improperly with learning disabilities or behavioral issues. The World Health Organization's system of medical coding, known as the International Classification of Disease for documenting diagnoses, diseases, and symptoms, released a new code for PANDAS, but it will not become effective until 2022.⁶

A few clinics have opened nationally since 2012, beginning with the Stanford PANS clinic, which is the first multi-disciplinary PANS clinic in the world.⁷ Dr. Jennifer Frankovich and her clinical team were the first to create a clinical database of patients and controlled biospecimens. In addition to creating clinical data, Dr. Frankovich is working alongside ten different science labs to reveal the details of the illness. In 2017, the Arizona Children's Postinfectious Autoimmune Encephalopathy (CPAE) clinic was established. CPAE studies conditions where infections activate an autoimmune reaction in the brain that changes neurologic functions. They are the first clinic in the U.S. to apply a diverse model for PANS/PANDAS, including the management of immune deficiency, preventative use of antibiotics, immune-suppressive drugs, immunomodulatory IVIG, and stem cell transplants.⁸ Their advanced delivery of care continues to investigate new treatments to improve outcomes.

⁴U.S. Department of Health and Human Services, "Analysis of Supply, Distribution, Demand, and Access Issues Associated with Immune Globulin Intravenous (IGIV)," February 1, 2007.

⁵Jeannie Garvey, Esq., PANS/PANDAS House Study Committee meeting, public comment, October 2, 2019.

⁶World Health Organization, "WHO releases new International Classification of Diseases (ICD 11)," June 18, 2018.

⁷Stanford Medicine, Stanford Children's Health PANS Clinic, November 13, 2019. <https://med.stanford.edu/pans/about.html>

⁸University of Arizona Health Sciences, Children's Post Infectious Autoimmune Encephalopathy Center (CPAE), "Clinical Research," August 28, 2019. <https://peds.arizona.edu/cpae>

The Controversy with PANS/PANDAS

Doctors still find PANS/PANDAS to be contentious despite the growing awareness. The most common approach to challenging the existence of PANDAS is the strength of association with strep infections to the recurrence of behavioral tics. Some earlier studies have failed to confirm the link between prior streptococcal infections and PANDAS diagnosis.⁹ However, the children in the studies may not have been identified cases of acute rheumatic fever. Furthermore, unsuccessful attempts to associate the severity of PANDAS to strep infections does not cancel the existence of the disease.

The second criticism argues the lack of evidence showing symptoms as an autoimmune development. Research has proposed the basis for PANDAS as a molecular malfunction in which antibodies produced against streptococcal proteins also target the brain. The challenge remains as studies have inconsistently demonstrated changes in the levels of antibodies in the bloodstream as a PANDAS patient recuperates or declines.¹⁰ Inconsistent antibody levels could be due to controlled sera, the bright yellow fluid obtained when separating whole blood into its solid and liquid elements, used in medical studies instead of children with the illness. For example, animal tests have shown a strong correlation when rodents are slowly injected with Group A streptococcus.¹¹

Infected rodents show similar behavior and motor problems consistent with PANDAS. Further studies have found that human antibodies will attach to brain cells in mice, but will become nonbinding after a patient receives IVIG treatment.¹² However, skepticism remains on PANDAS's legitimacy. As Dr. Wendy Edwards explains, "I would say the majority of people still do not accept that this is a real thing. It is not in the textbooks yet. Medicine is very slow about getting stuff into textbooks. There are a lot of great websites for physicians, and there are wonderful research articles out there, it has been published in legitimate medical journals, and yet, physicians are very slow to change their minds about things."¹³

For decades, Dr. Susan Swedo has worked unremittingly to solve the mysteries surrounding this autoimmune disorder, including a 1998 publication specifically linking abrupt neurological changes and strep infections in children.¹⁴ Her research found that children who tested positive for streptococcal infection were more likely to have both OCD and tics as opposed to those who tested negative. When tics or OCD are measured separately, there is no significant association relative to streptococcal infection. Dr. Swedo's evidence shows the possibility that children who present both OCD and tics are more likely to have had streptococcal infections.

⁹ Perrin EM, Murphy ML, Casey JR, et al., "Does group A beta-hemolytic streptococcal infection increase risk for behavioral and neuropsychiatric symptoms in children?" *Arch Pediatr Adolesc Med.* 158:848-856. 2004.

¹⁰ Gilbert DL, Mink JW, Singer HS, "A pediatric neurology perspective on pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection and pediatric acute-onset neuropsychiatric syndrome. *J Pediatr.* 199:243-251, 2018.

¹¹ Lotan D, Benhar I, Alvarez K, et al., "Behavioral and neural effects of intrastriatal infusion of anti-streptococcal antibodies in rats," *Brain Behavior Immun.*, 38:249-262, 2014.

¹² Frick LR, Rapanelli M, Jindachomthong K, et al., "Differential binding of antibodies in PANDAS patients to cholinergic interneurons in the striatum," *Brain Behavior Immun.*, 69:304-311, 2018.

¹³ Jackie Dunham, "Woman shares harrowing experience of son's erratic behaviour after strep," *CTVNews*, October 9, 2018.

¹⁴ Susan E. Swedo, M.D., Henrietta L. Leonard, M.D., et al., "Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections: Clinical Description of the First 50 Cases," *The American Journal of Psychiatry*, February 1, 1998.

Committee Recommendations

The substantial unrest faced by patient families involves different areas. Despite the lack of evidence-based guidelines, randomly controlled trials, or flexible consensus, doctors should still care for PANS/PANDAS patients until quality data is available. Families continue to find that medical care providers are often in conflict or unaccustomed to the diagnoses of PANS/PANDAS. New awareness and education for the evidence-based legitimacy of the diagnosis will help to understand the acute advent of symptoms, which can offer early intervention, laboratory examination, and treatment procedures. Education should extend across specialties, including pediatrics, emergency room care, family medicine, internal medicine, and psychiatry.

Organizations such as the PACE Foundation and the Southeastern PANS/PANDAS Association should continue the campaign to cure pediatric autoimmune neurological diseases. Standardized protocols need to enhance strep screenings, antibiotics coverage, immunotherapy, and other related services. If circumstances do not improve, additional funding will be needed for training providers, including school nurses and specialized education staff, to bring awareness about PANS/PANDAS. Telemedicine training is essential to train providers in rural/underserved areas along with improved data collection and analysis mechanisms to help understand the prevalence and outcomes of the illness. Georgia families have described feeling overwhelmed, frustrated, and exhausted by the process of accessing treatment options.

The unreliable medical coverage by insurers is by far the most significant hindrance for families, and stabilization across different payers would go a long way towards improving their health and stress level. Better access includes uniformity across insurance providers, understanding the stepwise treatment needed to maintain control of the disorder, and the cost related to necessary therapies. Children in Georgia who face delayed diagnosis could soon see relief at Children's Healthcare of Atlanta (CHOA) with the potential pilot clinic to fight PANS/PANDAS. According to Dr. Satya Gedela, Chief of Neurology, the pilot clinic will consist of a specific group of children with clear clinical diagnostic criteria and a prospective study that would help doctors with diagnosis and response to some of the treatments available. A CPAE clinic will enable increased awareness and provide medical care for children with complicated illnesses that need numerous visits to multiple specialists.

In Dr. Gedela's testimony before the committee, he said, "I believe there is a group of patients with this unique clinical condition who would benefit from diagnosis and giving a specific treatment."¹⁶ If a child does not fit the clinical criteria for PANS/PANDAS, the multi-disciplinary team will refer the child and family to the correct specialty within the hospital system. Another medical expert, Dr. Ellen Wald, acknowledges the 100 years that delayed acceptance of strep infections causing acute rheumatic fever and declares, "PANDAS and PANS are real entities. Their prevalence is unknown, and continued study is essential."¹⁷

¹⁶ Satya Gedela, M.D., Children's Healthcare of Atlanta, Georgia House Study Committee on Pediatric Acute-Onset Neuropsychiatric Syndrome ("PANS") and Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection ("PANDAS"), October 2, 2019

¹⁷ Ellen R. Wald, M.D., "A Pediatric Infectious Disease Perspective on Pediatric Autoimmune Neuropsychiatric Disorder Associated With Streptococcal Infection and Pediatric Acute-onset Neuropsychiatric Syndrome," *The Pediatric Infectious Disease Journal*, Volume 38, July 2019.

The following are recommendations by the study committee:

Policy Goals:

- Provide access to insurance-based care for all Georgia children with PANS/PANDAS.
- Provide for improved awareness and early diagnosis of PANS/PANDAS among medical and behavioral health practitioners that enables early detection/diagnosis and treatment to reduce cost, duration, and complexity of treatment and impact of the illness on the child, family unit, and community.
- Provide for training of the medical and behavioral health providers and school personnel who are most likely to interact with children who have PANS/PANDAS in order to rapidly identify possible PANS/PANDAS cases and appropriately evaluate (or refer for evaluation) those children.
- Classification of PANS/PANDAS as an identifiable disease by Georgia’s Department of Public Health (DPH), which will require an opportunity to gain statistics and offer public health information to the public.
- Provide education for the public to provide increased awareness of the illness.
- Provide for diagnosis and treatment coverage of children with PANS/PANDAS by Medicaid, the State Health Benefits Plan, and the University System of Georgia healthcare plan starting in the fiscal year 2020-2021 and beyond.
 - Implement the next steps in 2021-2022 to provide legislation for insurance coverage by private/non-ERISA insurers following evidence obtained through CHOA’s CPAE clinic as well as data gathered once the Georgia Department of Public Health classifies PANS/PANDAS as an ‘identifiable disease.’
 - Language should allow for coverage of treatments *including, but not limited to*, those cited in the July 2017 Journal of Child and Adolescent Psychopharmacology’s treatment guidelines.
 - Consider a provision allowing insurers and Medicaid to seek second opinions on treatment from CHOA’s CPAE clinic as a way to provide evidence of successful practices and reduce insurer’s objections.
- Stipulate that the CPAE clinic be named “Children’s Healthcare of Atlanta CPAE Clinic” as a condition for access to government funding.
- Designate legislative funding of \$125,000 per year for two years to sponsor a medical community CPAE Disorder Awareness Program at CHOA CPAE Clinic.
- Authorize \$250,000 per year for two years to enable the CHOA CPAE clinic to partner with Arizona’s CPAE Center of Excellence to develop a telemedicine service designated to help rural physicians diagnose and treat CPAE disorders.
- Provide for telemedicine services developed and delivered by the new CHOA CPAE clinic, in consultation with the Arizona CPAE clinics, through DPH’s telemedicine/telehealth network.
- Publication of an information page on DPH’s web site for the identification, diagnosis, and treatment of PANS/PANDAS.
- Establish a webpage with CHOA CPAE content.

- Create a Medicaid waiver program modeled after the Katie Beckett Waiver program to allow PANS/PANDAS families to qualify for Medicaid based on a PANS/PANDAS diagnosis for an initial period of two years with renewal available based on the child's medical status and ongoing treatment needs.
- Name the waiver the 'James Mangino' waiver. It is named after a child in Georgia who is affected by the illness and whose mother helped to start the fight for covered services and bring increased awareness in Georgia.
- Provide for CHOA's CPAE clinical team and qualified nonprofit entities to deliver live and web-based training for medical, behavioral health, and school-based providers.
- Publication of an information page on DBHDD's web site on identification, diagnosis, and treatment of PANS/PANDAS.
- Line item funding appropriation for training provided by CHOA's CPAE clinical staff or a qualified nonprofit entity for APEX program providers on recognizing PANS/PANDAS and making referrals for further medical evaluation.
- Line item funding for the Georgia Department of Education's Division for Special Education Services and Supports to provide PANDAS-focused training to inform special education administrators and teachers on how PANS/PANDAS impacts children in the classroom. This training can bring together the Individuals with Disabilities Act (IDEA) conference and the office's regular webinar training programs.