**HB2721: Peer Reviewed Studies**

**Confirming Appropriate Use of Antibiotics and Immunotherapy For Treatment of PANDAS/PANS**

**ABX**
Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS). Orefici G, Cardona F, Cox CJ, Cunningham MW. Ferretti JJ, Stevens DL, Fischetti VA, editors. *Streptococcus pyogenes: Basic Biology to Clinical Manifestations* [Internet]. Oklahoma City (OK): University of Oklahoma Health Sciences Center; 2016 Feb 10. “PANDAS is clearly a subtype of PANS (Murphy, et al., 2015b; Murphy, Parker-Athill, Lewin, Storch, & Mutch, 2015a; Chang, et al., 2015) and not all PANS cases have an underlying streptococcal infection—but all PANDAS cases are associated with streptococcal infections, at least temporally. When these diseases appear, treatment with antibiotics can be successful, and a treatment trial of cefdinir by Murphy and colleagues indicated that therapy with cefdinir, a β-lactam antibiotic, provided notable improvements in tic symptoms rated by the Yale Global Tic Severity Scale (YGTSS) and OCD symptoms rated by the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS). However, the differences within the groups as a whole were not significant. β-lactam antibiotics have been proposed to be neuroprotective above and beyond their antibiotic efficacy (Murphy, Parker-Athill, Lewin, Storch, & Mutch, 2015a).”

**ABX**
http://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2089440
The role of tonsillectomy in the treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Demesh D, Virbalas JM, Bent JP. JAMA Otolaryngol Head Neck Surg. 2015 Mar;141(3):272-5. doi: 10.1001/jamaoto.2014.3407. “Ten patients met strict diagnostic criteria for PANDAS. Comparisons were made between parental reports of symptom severity at diagnosis, after antibiotic treatment (in 10 patients), and after tonsillectomy (in 9). From a baseline severity score of 10, antibiotics alone improved symptoms to a median (interquartile range [IQR]) score of 8 (6.5-10.0) (P = .03). Nine children who subsequently underwent tonsillectomy reported symptom improvement in comparison with treatment with antibiotics alone, including those with no response to antibiotics.”

**ABX**

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3440267/
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. Tan J, Smith CH, Goldman RD. Can Fam Physician. 2012 Sep;58(9):957-9. “Positive results have been found using antibiotic prophylaxis and immunomodulatory therapy in children with PANDAS.”

**ABX**

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**ABX**

**ABX**
Antibiotic prophylaxis with azithromycin or penicillin for childhood-onset neuropsychiatric disorders. Snider LA, Lougee L, Slattery M, Grant P, Swedo SE. Biol Psychiatry. 2005 Apr 1;57(7):788-92. “Penicillin and azithromycin prophylaxis were found to be effective in decreasing streptococcal infections and neuropsychiatric symptom exacerbations among children in the PANDAS subgroup.”

**ABX**

**IVIG and PEX**
Therapeutic Plasma Exchange and Intravenous Immunoglobulin for Obsessive-Compulsive Disorder and Tic Disorders in Childhood, Perlmutter, Susan J et al. The Lancet, 1999, Volume 354, Issue 9185, 1153 – 1158 “Plasma exchange and IVIG were both effective in lessening of symptom severity for children with infection-triggered OCD and tic disorders.”

**IVIG and PEX**
Fernández Ibieta MAn Pediatr (Barc). 2005 May;62(5):475-8. Neuropsychiatric Disorders Associated with Streptococci: A Case Report “Current recommendations include penicillin treatment of each exacerbation with positive throat culture, and more aggressive therapies (intravenous immunoglobulin or plasmapheresis) when symptoms are severe.”

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For optimum symptom relief, it is necessary to utilize a combination of immunomodulatory therapy, antibiotic prophylaxis, and targeted symptom treatments, as described at the PANDAS Physicians Network (PPN) (www.pandasppn.org). The website presents a systematic graduated approach to treatment of PANDAS/PANS based on the best practice standards of expert clinicians from across the United States. In addition to providing suggestions for recognition and diagnosis of PANDAS/PANS, it also offers guidance in the management of patients with varying levels of severity. For reference, the PANDAS Physicians Network website: https://www.pandasppn.org/therapeutic-options-for-pandas-and-pans/
cases, whereas those with long considered early, because NSAIDs or a short course of oral corticosteroids may be sufficient for symptom remission in recent patients given no treatment; (2) Patients given early treatment do better; (3) When patients fail first (especially those presenting with severe symptoms): (1) Patients given immunotherapy do better than patients given no therapy. (2) Patients given treatment early do better than those given treatment late. (3) If a patient does not respond to first line therapy, second line therapy improves outcomes.

**IVIG and PEX**

http://dx.doi.org/10.1089/cap.2016.0148 Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part II—Use of Immunomodulatory Therapies. Frankovich Jennifer, Journal of Child and Adolescent Psychopharmacology. July 2017. “Choosing the optimal immunomodulatory treatment pathway for the patient with PANS/PANDAS requires consideration of the disease severity and trajectory, as well as an understanding of the PANS symptoms in the broader context of infection and inflammatory disease. The general “principles” used to treat other brain inflammatory diseases (AE, NPSLE, etc.) likely apply to PANS (especially those presenting with severe symptoms): (1) Patients given immunotherapy do better and relapse less frequently than patients given no treatment; (2) Patients given early treatment do better; (3) When patients fail first-line therapy, second-line therapy improves outcomes and reduces relapses (Titulaer et al. 2013; Nosadini et al. 2015). Immunomodulatory therapy should be considered early, because NSAIDs or a short course of oral corticosteroids may be sufficient for symptom remission in recent-onset cases, whereas those with long-standing symptoms often require more intensive and prolonged immunotherapeutic interventions.”