**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

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Intravenous immunoglobulin (IVIG) is widely accepted as a standard treatment for post-infectious autoimmune encephalopathy.[1] Two types of autoimmune encephalopathy are produced by infections with Group A streptococcal bacteria: Sydenham chorea (the neurologic manifestation of acute rheumatic fever) and PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections).[2] In randomized controlled trials, IVIG has been shown to be useful in reducing symptom severity and shortening the course of illness in both disorders.[3-5] IVIG also has been used with benefit in hundreds of cases of immune-related Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). Thus, the PANS/PANDAS Treatment Guidelines recommend consideration of its use for treatment of all moderate-severe cases of PANS/PANDAS (see attachment).[6-7]

Development of the PANS/PANDAS treatment guidelines began in May 2014 at a meeting held at the National Institutes of Health in Bethesda, Maryland. Refinements and modifications were made over the ensuing two years by three workgroups of the PANS/PANDAS Clinical Research Consortium; they separately addressed 1) use of psychiatric medications and behavioral interventions; 2) use of antimicrobials; and 3) use of anti-inflammatory and immunomodulating therapies. The three workgroups followed similar procedures, first reviewing the published literature and drawing upon their combined clinical experience with more than 1,000 children with PANS/PANDAS to formulate an initial set of recommendations, which were then sent to a separate group of expert clinicians for critical review and comment. The members of the three workgroups and the expert review panels include the following:

Dritan Agalliu (Columbia University)
David Brick (NYU Langone Medical Center)
Kiki Chang (Stanford University)
Michael Cooperstock (Univ Missouri)
Madeleine Cunningham (Univ Oklahoma)
Michael Daines (Univ Arizona)
Josephine Elia (DuPont Hosp for Children)
Jenny Frankovich (Stanford Univ)
Hayley Gans (Stanford Univ)
Jay Giedd (UCSD)
Earl Harley (Georgetown)
Rebecca Hommer (NIMH)
Cynthia Kapphahn (Stanford Univ)
Elizabeth Latimer (Georgetown Univ)
James Leckman (Yale Univ)
Tanya K Murphy (Univ South Florida)
Sydney Rice (Univ Arizona)
Terence Sanger (USC)
Michael Sherman (Univ Missouri)
Susan Swedo (NIMH)
Wendy Vargas (Columbia Univ)
Kyle Williams (MGH/Harvard Univ)

Gail Bernstein (Univ Minnesota)
Reuven Bromberg (Miami Children's)
Harry Chugani (DuPont Hosp. for Children)
Dan Coury (Nationwide Children's Hosp.)
Tyler Cutforth (Columbia Univ)
Russell Dale (Univ New South Wales, Australia)
Bahare Farhadian (Stanford Univ)
Robert Fryer (Columbia Univ)
Daniel Geller (MGH/Harvard Univ)
Paul Grant (NIMH)
Joseph Hernandez (Stanford Univ)
Mady Hornig (Columbia Univ)
Miro Kovacevic (Loyola Univ)
Bryan King (UCSF)
Eyal Muscal (Baylor Univ)
Mark Pasternack (MGH/Harvard Univ)
Alan Rosenberg (Univ Saskatchewan)
Richard Shaw (Stanford Univ)
Janell Sherr (Stanford Univ)
Margo Thienemann (Stanford Univ)
Theresa Willet (Stanford Univ)
Yujuan Zhang (Tufts Univ)

The 44 contributors represent 23 different academic institutions from across the US, Canada and Australia, and include not only clinicians with expertise in the diagnosis and treatment of PANS/PANDAS, but also experts in the fields of child psychiatry, pediatrics, infectious diseases, microbiology, neurology, neuroimmunology, immunology and rheumatology. The contributing authors and all members of the PANS/PANDAS Clinical Research Consortium unanimously approved the final sets of guidelines. Thus, the guidelines truly represent a national standard of care, and the use of IVIG for moderate-severe PANS/PANDAS has been endorsed as a "best practice" by clinicians from all across the US and beyond.

Susan E. Swedo, M.D.
Chair, PANS/PANDAS Clinical Research Consortium

*References:*

[1]Kalman B. Autoimmune Encephalitides: A broadening field of treatable conditions. Neurologist 22(1):1-13, January 2017

[2]Williams KA, Swedo SE. Post-infectious autoimmune disorders: Sydenham's chorea, PANDAS and beyond. Brain Res 1617:144-54, 2015.

[3]Garvey MA, Snider LA, Leitman SF, Werden R, Swedo SE. Treatment of Sydenham's chorea with intravenous immunoglobulin, plasma exchange or prednisone. J Child Neurol 20:424-429, 2005.

[4]Perlmutter SJ, Leitman SF, Garvey MA et al. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. Lancet 354:1153-1158, 1999.

[5]Williams KA, Swedo SE, Farmer CA et al. Randomized, controlled trial of intravenous immunoglobulin for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). J Am Acad Child Adolesc Psychiatry 55(10):860-867, 2016.

[6]Swedo SE, Frankovich J, Murphy TK. Treatment of pediatric acute-onset neuropsychiatric syndrome (PANS). J Child Adolesc Psychopharmacology, In press, 2017.

[7]Frankovich J, Swedo SE, Murphy TK. Clinical management of pediatric acute-onset neuropsychiatric syndrome (PANS): Part II – Use of immunomodulatory therapies. J Child Adolesc Psychopharmacology, In press, 2017.

*Attachment* - Excerpts from "Treatment of PANS"[6] and "Use of immunomodulatory therapies"[7]