

Connecticut PANDAS/PANS Advisory Council
Meeting Minutes

September 6, 2013



Present: Christian Andresen, Dr. Tom Moorcroft, Dr. Denis Boubolis, Lynn Johnson, Maria Synodi, Alma Hernandez, Dr. James Leckman, Dr. Robert Baltimore, Denise Sheltz
Phone attendees: Suzanne Levasseur, Vicki Kobliner, Dr. Susan Swedo,
Next meeting: Tentatively scheduled for Friday, October 11, 2013 1 pm – 3 pm

Call to order: Chris Andresen called the meeting to order at 2:05pm.

Welcome and Introduction:

Council members present and on the phone introduced themselves. Chris Andresen acknowledged other DPH staff that attended the meeting and thanked Jim Carson from the LOB for his assistance in coordinating the meeting. Chris invited members of the public to provide an email address to be put on an email list for information about the Advisory Council and mentioned the DPH webpage established for the Advisory Council (www.ct.gov/dph/PANDAS).

Overview of Public Act 13-187 and Council's charge:

Chris Andresen reviewed Public Act 13-187, which establishes an advisory council on pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS) and pediatric acute neuropsychiatric syndrome (PANS) to advise the Commissioner of Public Health on research, diagnosis, treatment, and education relating to PANDAS/PANS. The council members consist of 14 members outlined in the Act appointed by the Commissioner of Public Health, the Chairs of the Public Health Committee or their appointees, and the Commissioner or designee as an ex-officio member. The members have to elect a chairperson. A majority of the members constitutes a quorum and a majority vote of the quorum is necessary for official action. By January 1, 2014, and annually after, the council has to report to the public health committee a report of recommendations including 1) practice guidelines for diagnosis and treatment of PANDAS/PANS, 2) mechanisms to increase clinical awareness and education about PANDAS/PANS, 3) outreach to educators and parents to increase awareness of PANDAS/PANS, and 4) development of a network of experts on the diagnosis and treatment of PANDAS/PANS to assist in education and outreach.

PANDAS/PANS overview:

Chris Andresen gave an overview of PANDAS and PANS. PANDAS is a subset of children/adolescents who have obsessive-compulsive disorder (OCD) or tic disorders in whom symptoms worsen following streptococcal infections. PANDAS is a subset of PANS, which are cases of acute onset of OCD in children, not necessarily associated with strep infections. The theory behind PANDAS is that it is an autoimmune reaction that is triggered by a strep infection. It is important to note that all cases of OCD do not

equal PANDAS, and not all cases of strep equal PANDAS. There is a lot of conflicting information about the condition. Additionally, there are not a lot of providers who diagnose or treat PANDAS/PANS. Treatment for PANDAS/PANS is limited. There is agreement that a strep infection should be treated with antibiotics. According to the NIMH website, treatment for OCD is usually cognitive behavioral therapy and/or selective serotonin reuptake inhibitors (SSRIs), but they are not always effective and SSRIs can have adverse reactions. The University of Florida and Mass General are currently researching long-term antibiotics use as a treatment, currently not yet recommended due to a lack of research in its use for the PANDAS/PANS population. There are some promising preliminary findings for intravenous immunoglobulin (IVIG), which is potentially beneficial for PANDAS, but the data are limited and the research was a small study and has not yet been confirmed with other studies. Dr. Jim Leckman from Yale is currently leading a formal clinical trial for the use of IVIG. An interim analysis of the study will be completed in the near future according to Dr. Leckman.

Lynn Johnson added that the reason we need this advisory committee is because there is conflicting information out there and not enough information, and people are easily misled. She stated that we want to be able to make sure people in Connecticut find accurate and proper information. Lynn added that it is important to consider the timing of treatments like cognitive behavioral therapy when looking at its effectiveness in treating PANDAS, and that it is important that the group can start to shape information so people get accurate information.

2012 CT Legislative activity related to PANDAS/PANS:

Chris Andresen described a document that was created through funding the Connecticut Legislature allocated last year for the PANDAS Resource Network to conduct a study on PANDAS. The document, A Comprehensive Analysis of Research on the Diagnoses and Treatment for Pediatric Autoimmune Neuropsychiatric Disorder (PANDAS/PANS), was completed in February of 2013. Chris shared the recommendations from the report as a starting point for discussion among the group. Recommendations in the report include the development of: clinical and public awareness programs, effective epidemiological studies in Connecticut, outcome studies of clinical intervention strategies, and clinical effectiveness studies of cognitive behavior therapy and SSRI therapy. It also recommends establishing a liaison with the National Institute of Mental Health (NIMH) and Centers for Disease Control and Prevention (CDC) to help develop science-based guidelines for identification and treatment of PANDAS/PANS and establishing a “blue ribbon” panel of experts to draft practice guidelines. Finally the analysis recommends developing a liaison between government, community, clinical stakeholders and insurance industries to develop practice guidelines.

Discussion:

Dr. Robert Baltimore described how the infectious disease providers and the Academy of Pediatrics have not embraced the PANDAS diagnosis. There is concern about the

linkage to streptococcus among infectious disease providers including streptococcus experts.

Chris Andresen acknowledged the controversy around this diagnosis and that the public health community is very concerned about the prudent use of antibiotics and the problem of antibiotic resistance.

Lynn Johnson added that she works with many families impacted by the condition and they agree there is a need for better research and diagnostic tools. Based on the Academy of Pediatrics response to legislation related to PANDAS in CT, she would rather have a child try antibiotics first before going into long term psychiatric track for treatment. She added that the goal of this committee is to come together with people who embrace and understand PANDAS to move legislation forward. She expressed that she did not want to see this committee become an experience where we spend the majority of the time teaching and training a few members of the committee who might not be as educated in the disorder as they need to be.

Dr. Swedo said that she agrees with Dr. Baltimore about the cautions that should be employed about extending this post-infectious disorder to other things, but that she disagrees with his view on the connection between strep and OCD. She described a number of studies linking OCD and Sydenham Chorea.

Dr. Cunningham described the overlap of cross-reactive anti-streptococcal antibodies between PANDAS and Sydenham Chorea and related studies she has done in this area.

Dr. Swedo added other information about these studies and then stated that she felt the role as an advisory council should focus on 1) educating folks about the difference between Sydenham Chorea and PANS/PANDAS, 2) Making sure everybody remembers that not all strep is PANDAS and neither is all OCD, and 3) describing the differences in clinical presentation between PANS/PANDAS and other OCD and tic disorders.

Chris Andresen offered that the group might want to discuss it will work together, to meet, and to share information. He also encouraged some of the non-medical people at the table to speak up.

Lynn Johnson added that she agreed with Drs. Cunningham and Swedo that we need to educate to make accurate diagnoses and how doctors sometimes will often only test for strep and if it's negative will rule out PANDAS when that might not be the case.

Dr. Bouboulis added that PANDAS is a clinical diagnosis and cannot be readily made solely through strep test.

Lynn Johnson shared the difficulty in diagnosis her own daughter's strep and the number of tests that needed to be done to finally diagnose it.

Dr. Baltimore added that he agrees with Dr. Bouboulis on the importance of how we consider strep titers and described research by Dr. Leckman that demonstrated that strep titers bounce up and down in a normal population over time.

Dr. Leckman discussed how he recognizes fully that acute onset OCD does occur, however he believes that some of the data out there is on children who do not actually have PANDAS. He acknowledged that earlier there was not the specificity needed to accurately identify cases. However, it has been clear in doing his clinical research with NIMH that acute onset OCD and other symptoms do happen. He is hopeful that biomarkers that are more helpful in diagnosing cases will be identified through the clinical trial. He hopes to be able to present preliminary data in early 2014.

Lynn Johnson described the challenges in diagnosing her daughter with strep because she is among the group of people that do not show a rise in titers when tested. She described how it wasn't until her daughter and entire family were treated for strep that they saw improvements in her tics. Ultimately IVIG treatment stopped her tics. Lynn acknowledged the doctors and scientists that worked with her family through this.

Chris Andresen asked if anyone in the group had any questions. He asked about the terms used to describe these conditions and the difference between PANS & PANDAS.

Dr. Bouboulis clarified that PANDAS is a prototype condition and that PANS describes that autoimmune response to infectious triggers. Dr. Bouboulis feels that it's important that every child diagnosed with OCD, anxiety or a tic disorder to be evaluated for an autoimmune condition. He sees many children who were misdiagnosed in his practice and placed on psychotropics when they may have an underlying infection. He also described how sometimes when he speaks to parents, it seems like many of them have had neuropsychiatric symptoms exacerbated with infections but never diagnosed.

Lynn Johnson spoke of how she has been a PANDAS advocate for 4 years. In the last 3.5 months she has been working full time with Dr. Bouboulis in a clinical setting and has seen amazing results and lives changed. Lynn mentioned that Lyme disease is often missed clinically as a missing piece in these children and that many doctors are not educated in Lyme and don't know how to effectively diagnose and treat it.

Dr. Bransfield (on phone) discussed research correlations between autoimmunity including Lyme disease and the relationship to severity of autistic symptoms. Many labs do not test for the bands he's identified in studies he has done.

Dr. Leckman discussed how registries may be a way to track patients over time and that there is much more to learn about neuroinflammation and the role it plays in autoimmunity.

Dr. Swedo described a parent-founded registry that has expanded to include physicians and researchers as a way to begin to understand the entirety of the clinical presentation and to understand how broad the syndrome is. Dr. Leckman asked that Dr. Swedo forward the information on the registry to Chris to distribute to the group.

Representative Srinivasan said that this is an extremely complex issue and that research is important and critical. We should have short term and long term goals. Research takes years, but what do we do in the interim. We should educate providers and the public on the acute onset of OCD in the meantime.

Dr. Bouboulis said that the first order of business should be practice parameters for doctors and others to properly identify the condition and make referrals, and also to have a registry.

Lynn Johnson agrees on short term goals to educate physicians clinically while research is moving forward. People are still sick while this research is going on and there needs to be protections for doctors that treat PANDAS since it is controversial. Lynn said a short term goal should be to put forth legislation to protect doctors who treat PANDAS as doctors who treat Lyme are protected.

Chris Andresen opened the discussion to non-council members.

Renee Bryan (parent) shared that it is important to identify individuals seeing children to ensure children are sent in the right direction for care.

Lynn Johnson added that money could be saved if first responders are educated to identify the condition. She described some parents' experiences with PANDAS and how much money could have been saved had a diagnosis been made earlier.

Paula Renna (parent) described the importance of short term goals for parents that are dealing with this and described her experience with her child not being diagnosed with PANDAS by a pediatrician and being directed to mental health care.

Dr. Nick Bennett (Medical Director, Infectious Diseases & Immunology at CCMC) suggested that the group move forward with science-based evidence. If the group is going to make practice and legislative recommendations, they need to be backed up with science. He shared concerns that children are being labeled with PANDAS who have something else. There is a risk of inappropriate antibiotic use and IVIG. Based on current scientific knowledge, he is not convinced that IVIG is the answer. He also

described himself as the doctor at his facility that prescribes more IVIG for children than anyone else.

Lynn Johnson countered that she is convinced that her daughter has been cured by IVIG because she has been symptom free for four years and that checking for an infectious cause prior to psychotropic treatment would be preferable to most parents.

Dr. Bouboulis added that he agreed with Dr. Bennett that we do not want to over treat with antibiotics or use IVIG inappropriately, but there is evidence that a lot of these kids have a post infectious or infectious autoimmune encephalopathy. He doesn't know the numbers, but based on the phone calls his office gets daily, there are more than we realize. This is an area where more research needs to be done. He added that most children respond well to antibiotics and do not need IVIG. He feels it's a tragedy if kids who are experiencing something infectious are not treated and go on lifelong psychiatric drugs and treatment, including the possibility of institutionalization.

Dr. Baltimore added to Dr. Bennett's comments regarding the question of anecdotes. A provider may see benefits in patients going from one drug to another, but may not see failures. Drs. Bennett and Baltimore see a large number of people seeking additional medical care because they've been treated for PANDAS or chronic Lyme but do not have them and are not benefitting from the treatment, and are looking for something else. He described that this is why the level of science recommended for deciding what is a beneficial therapy is a placebo controlled trial. There are no placebo controlled trials that show that the treatments being advocated for are beneficial. Multiple studies have shown that people with so-called chronic Lyme disease have not benefitted. This cannot be seen in an office practice, only through collaborative placebo controlled trials. Statistics require reasonable numbers of people being tested before you can say there is a benefit. He added that he would like the level of conversation about this issue to go beyond anecdotes.

Lynn Johnson added that she is proud to be from the first state in the country that passed legislation requiring doctors who conduct traditional tests for Lyme to tell patients that a negative test does not mean a patient does not have Lyme disease. She added that we do know without a doubt that the serology does not work and is not accurate. A patient has the right to seek further treatment through a clinical diagnosis. CDC recognizes Lyme disease as a clinical diagnosis. Lynn stated that she believes we need more research, but as a short term goal need first responders educated. If doctors are educated better about how to diagnose this disorder clinically while researchers are working to find serology that works, lives will be saved. She shared that if her pediatrician knew in 2006 that PANDAS existed, her family would not have experienced what it has. Children need to be treated now in a clinical setting with a clinical diagnosis. We have enough knowledge to know this exists, it just needs fine tuning.

Dr. Moorcroft echoed what others said around the table. He agrees that improved testing and biomarker will be great as we move forward. However there are people who are sick today. Similar to Dr. Baltimore, he sees patients that come to him misdiagnosed and seeking other treatments. He also has patients that he treats, the treatments don't work, and they seek other treatments elsewhere. This is a reality of practicing medicine. In cases where the evidence is poor, like PANDAS and chronic Lyme disease, he suggests a shared decision making model and bringing in other opinions. There is a need to empower physicians and others in the front lines to have conversations to promote clinical diagnosis and evaluation. He described reaching out to other physicians with opposite opinions to his to keep him an honest clinician and that this model should be promoted.

Sally Young (parent) described how her children with PANDAS have done well on IVIG. Regarding discussion about anecdotal evidence, we need to listen to patients and what's going on and therefore go with a clinical diagnosis.

Dr. Bennett added to Dr. Moorcroft's comments about collaboration and described how doctors often have patients with elusive diagnoses who do better on antibiotics but we are not sure what is actually going on. In some of these cases, there are antibiotics that are not active against strep and should not need to be used. He described how his program has collaborated with the Psychiatry program to better define and diagnose children with these symptoms. Addressing this condition involves collaboration.

Dr. Leckman concurred that we do not have all the evidence we need. He is convinced that many cases he sees diagnosed are not actually PANDAS or PANS. There are some patients who have shown a remarkable improvement to sham IVIG, a positive placebo response. We need to see what the data show and articulate those findings. He is hopeful there will be enough research in the near future where we would be in a better position where it would make sense to develop some guidelines for the practicing community. The education part is something we can do earlier. We need to find out who these children are and to collect better information to guide future practice.

Dr. Swedo added that early detection and prompt treatment of strep infection has been successful in reducing neuropsychiatric symptoms and that perhaps we should step back a level. We should inform providers about the clinical presentation of PANDAS and suggest checking the throat for strep. It is important to detect strep early and to treat, and that she is not talking about anything outside current standards of care.

Lynn Johnson agreed with what Dr. Swedo said and that we are just asking that if there is an acute onset of neuropsychiatric symptoms that infectious triggers are considered. She has seen anecdotally that the longer the children have had this disorder, the harder it is to treat. It is imperative to get them at first acute onset of symptoms that can usually be remedied by the right dose of antibiotics at the right time.

Dr. Leckman shared his clinical experience that there are some children who show neuropsychiatric symptom improvement after a dose of antibiotics that reemerge after they are stopped. This is enough anecdotal evidence to begin another course that may lead to prophylactic treatment if symptoms reemerge. It is not clear whether the results related to antibiotic effectiveness or anti-inflammatory properties in some of these antibiotics may be causing the improvement.

Lynn Johnson described her daughter's case with increasing antibiotic dose and changing treatments to see symptom improvement. She also described one of her initial interactions with a provider who suggested her daughter was being abused and put her on psych medications. Her daughter was unable to eat, go to school, etc. It wasn't until a trial use of antibiotics that symptoms improved. We need to educate first responders; there aren't enough practitioners educated to treat this or who feel they can safely practice without scrutiny. We will get attacked. A short term goal should be to build awareness and protect physicians.

Dr. Bouboulis shared Dr. Leckman's experience of treating patients, even for a few months with antibiotics, and seeing symptoms reoccur. He asked infectious disease doctors how long it takes to treat strep.

Dr. Baltimore responded that there is much knowledge about treating strep pharyngitis and that 5 days is not enough. People do better at 10 days and there is extinction of the strep. People who still have strep after 10 days are considered carriers. American Academy of Pediatrics does not recommend retesting for strep after 10 days since those people would be considered carriers.

Lynn Johnson brought up the issue of viral triggers for these conditions and that antibiotics do not treat viruses. She described her daughter's experience after contracting Epstein Barr Virus which triggered a serious exacerbation of her PANS. We need to look at how we treat inflammation of the brain. She also described cases of bacterial or viral triggered anorexia nervosa where people have died from the condition.

Chris Andresen suggested that since there are not a lot of council members at this first meeting that we postpone the vote until the next meeting. He said he would put out an email soliciting potential chairs and vote at the next meeting. Chris will also send out an electronic meeting schedule survey to schedule the next meeting. Chris suggested the end of September and members suggested early October. Chris asked people to email him ideas for how to structure work moving forward and that meetings can be held in locations other than the LOB.

Lynn Johnson added that she is looking forward to getting a chair on board and whether we are going to vote via email or at the next meeting.

Chris said that if people are comfortable voting by email, and the group responded they were comfortable with that. Chris will solicit nominees and each who accepts will write a blurb about themselves for members to review and then vote if that worked for them. He then opened the discussion up to the floor again.

Joanne Sloane (school nurse) said it is important that educators, school nurses, etc. are educated about PANDAS/PANS. She said we need to be able to work with diagnosed children and how we can help them while they are in school if they are able to attend. We need to know what school nurses can do to help students maintain their education.

Chris Andresen referenced a study that said community clinicians are more likely to diagnose the condition than specialists and we need to keep in mind that we do not want this diagnosed inappropriately. Dr. Bouboulis said that practice guidelines will help prevent inappropriate diagnosis.

Lynn Johnson said it's safe for general practitioners to suggest symptoms may be PANDAS/PANS and refer to a specialist. However, if that specialist is a neurologist or psychiatrist who does not understand the condition based on their experience they may hesitate to test and treat.

Renee Bryan added that we want doctors to feel safe to treat, but parents also need to feel safe bringing children to other practitioners. If a parent is comfortable with a diagnosis and treatment is working, she does not want to be dealing with doctors competing over whether the condition exists or dealing with repercussions if doctors feel the diagnosis and treatment is inappropriate.

Lynn Johnson discussed while there is no CPT code or official diagnosis for PANDAS, there are hundreds of diseases like that. She said that PANDAS is extremely common, but rarely diagnosed. They have seen patients who went to emergency departments and their children were taken away because they mention PANDAS. They deal with the repercussions from insurance companies. Dr. Bouboulis is one of the few doctors specializing and treating this condition and it is challenging to fight for payment. One of the long term goals should be to work with insurance companies on outcome studies that can show the savings they'd see.

Dr. Bennett clarified that he does believe in PANDAS and that he has seen children who respond to treatment. He has also seen kids who have PANDAS-related symptoms and a positive strep test where a doctor immediately assumes it's PANDAS. We need to educate properly to avoid children being unnecessarily referred for the condition. We need to figure out how to best define, understand, and treat the condition and not put the cart before the horse.

Lynn Johnson, Dr. Bouboulis and Dr. Bennett discussed viral triggers that require clinical diagnosis as well as atypical presentations that can make proper diagnosis difficult.

Heather Punska (parent) thanked the group for its work and shared that she and her husband are working on legislation in Massachusetts.

Lynn Johnson added the when she polls their community 50% have more than one child with PANDAS and that perhaps there is a genetic predisposition or environmental factors we are unaware of contributing to this.

Meeting was adjourned.

Video of meeting available at: <http://www.ctn.state.ct.us/ctnplayer.asp?odID=9381>