Demystifying PANS/PANDAS: A Functional Medicine Guide on Basal Ganglia Encephalitis

The Academy of Nutritional Medicine February 1, 2024

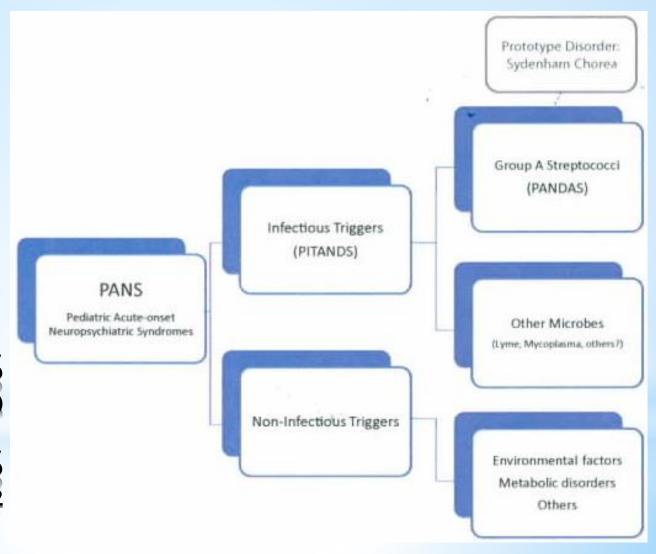
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"Follow those who seek the truth but flee from those who have found it."

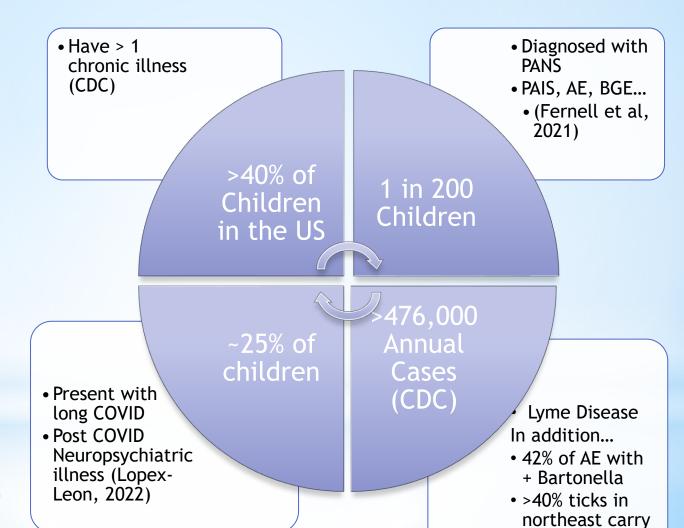
Yaclav Havel





PANDAS (Swedo et al, AJPsych, 1998)

to PANS (Swedo et al, Ped Ther, 2012

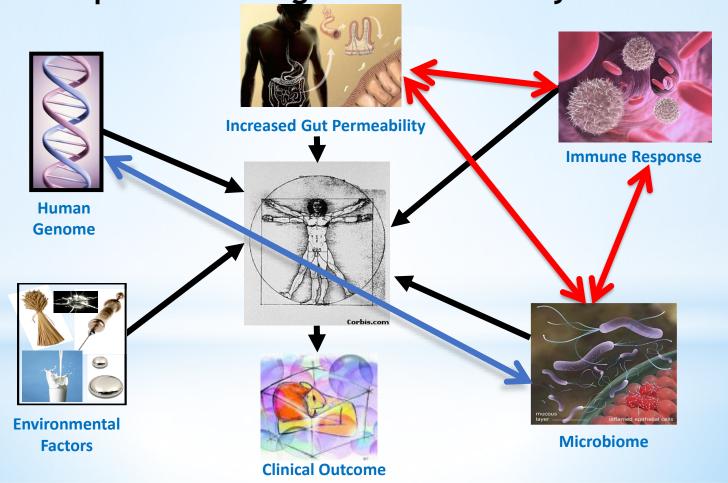


Babesia



AUTOIMMUNE DISEASE:

The Yin and Yang Between Tolerance and Immune Response Leading To Autoimmunity and Disease



Diagnostic Criteria for PANS

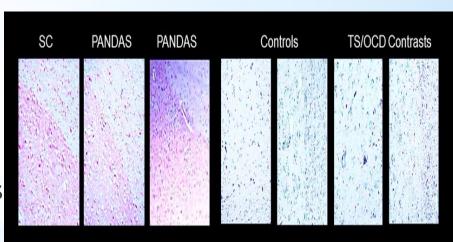
- Abrupt, dramatic onset or recurrence of OCD
- Acute-onset anorexia and/or severe, restrictive eating disorder
- Concurrent presence of neuropsychiatric sx with severe and acute onset - Two of the following
 - Separation Anxiety
 - Emotional lability
 - Behavioral/developmental regression
 - Sensory/motor abnormalities handwriting deterioration, Tics
 - Deterioration of school performance
 - Urinary symptoms (urgency, frequency, enuresis)
 - Sleep disturbance (difficulty falling aslee, REM disinhibition/restless sleep)
- Sx not better explained by another disorder (SC, SLE, TD)

Clinical observations in PANDAS/PANS

Boys:girls = 2.6:1	Family history of autoimmune disorders (64% with first degree relative with inflammatory disease)	History of persistent or repeated URIs/sinusitis
Sleep disorders (insomnia, night terrors, refusal to sleep alone) - 80%	Behavioral regression (baby talk, tantrums, play with young sibling) 98%	Urinary symptoms (frequency, urgency, enuresis) 90%
Inability to concentrate 90%	Learning difficulties 60%	Short term memory loss 60%
Hyperactivity 70%	Aggressiveness 60%	Inattentiveness 70%
Sensory modulation 40% (hypersensitivity or insensitivity)	Hyperalert appearance 80%	Handwriting deterioration 90%
Eating disorder 20% (restriction due to fear of contamination, vomiting, choking) • Toufexis 6	Hallucinations 10% et al, , JACP, 2015	Tics 70%

* Pifferential Piagnosis of PANS/PANDAS

- Sydenham chorea (acute rheumatic fever)
- Other forms of encephalitis (anti-NMDA), cerebral vasculitis
- Child abuse, sexual abuse, psychological trauma
- Toxins, medications, illicit drugs
- Tumors, strokes
- Tourette's, OCD not ACUTE
- Studies reveal that 80% of patients
- diagnosed with PANS have post-infectious
- neuroinflammation (Swedo et al, 2015)
- Neuroinflammation seen in the caudate/putamen (Kirvan et al, 2003)



* PANDAS Diagnosis
Further Neuropsychological and Other Testing

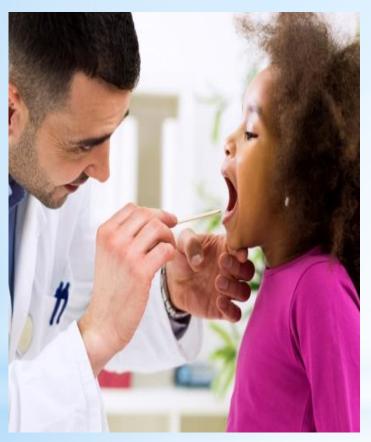
- *Margin Drift (left sided neglect)
- *Shortened attention span
- Difficulty with memory
- *Loss of math visuospatial skills
- *Dysgraphia/clumsiness
- *Patterns of executive function deficit different than those children with Tourette's
- *EEG 17% show spikes (4/42) or diffuse slowing (3/42) consistent with autoimmune encephalitis
- *Sleep study 85% show nonspecific REM motor disinhibition

(Buckley et al, NIH, J Clin Sleep Med, 2016)



* Causes and Triggers of BGE

- Group A strep throat, rectal, sinus, urinary tract, skin (Mahoney et al, J Ped Otorhinolar, 2017)
- Mycoplasma
- Viruses COVID, HSV, HHV6, EBV, CMV, others
- Lyme (Borrelia) and Lyme Co-infections (especially Bartonella & Babesia)
- Yeast and Mold (CIRS)
- Metabolic anesthesia, toxins, chemicals, pesticides...
- LOOK FOR:
 - History of autoimmune disorders in child and/or family
 - Preceding history
 - Infection or Febrile illness
 - Viral disease-like prodromes
 - Positive response to immunotherapy.



- 600 million cases of acute pharyngitis annually (Dewyer et al, 2020)
- * Untreated strep throat leads to serious post-streptococcal complications, such as Rheumatic Fever, Glomerulonephritis
- Sydenham Chorea is a manifestation of Rheumatic Fever
 - *Occurs in up to 40% of patients with RF
 - *Most prevalent form of chorea movements in children
 - Chorea & choreiform movements are due to the development of antibody attack of the basal ganglia

* Group & Beta-hemolytic Strep

Epub 2012 Jan 14.



Brain, Behavior, and Immunity

Volume 99, January 2022, Pages 281-288



[Mycoplasma pneumoniae encephalitis associated with basal ganglia necrosis]

[Article in French]

N El Hafidi ¹, B Allouch, F Benbrahim, M Chellaoui, C El Mahraoui

Affiliations + expand

PMID: 22244792 DOI: 10.1016/j.neurol.2011.01.023

Abstract

Introduction: Severe central nervous system diseases, such as encephalitis, have been reported in association with Mycoplasma pneumoniae infections.

Case report: A previously healthy 5-year-old boy presented with an atypical pneumonia; he rapidly developed encephalitis revealed by lethargy, generalized status epilepticus. MRI showed abnormal signals in the basal ganglia, typical of bilateral striatal necrosis. Serologic tests for M. pneumoniae were positive, the child recovered almost completely.

Conclusion: M. pneumoniae infection should be considered in all cases of acute encephalopathy; yet the pathogenesis of the disorder is unknown and the treatment uncertain.

Mycoplasma pneumoniae IgG positivity is associated with tic severity in chronic tic disorders

Jaana Schnell ^{a, 1}, Molly Bond ^{b, 1}, Natalie Moll ^c, Elif Weidinger ^a, Bianka Burger ^d, Rod Bond ^e, Andrea Dietrich ^f, Pieter J. Hoekstra ^f, Anette Schrag ^g, Davide Martino ^{h, i}, the EMTICS collaborative group, Markus Schwarz ^c, Ute-Christiane Meier ^{c, j}, Norbert Müller ^a A

Infectious pathogens may represent an environmental risk factor for chronic tic

Abstract

disorders (CTD). This cross-sectional study aimed to determine whether Mycoplasma pneumoniae (M. pneumoniae) IgG positivity is associated with the presence or severity of tics. We compared M. pneumoniae IgG positivity across three groups: children and adolescents (3–16 years) with \underline{CTD} (CTD group; n=302); siblings (3–10 years) of people with CTD who developed tics within a seven-year follow-up period (tic onset group; n=51); siblings (4–10 years) who did not develop tics within the study period and were ≥10-years-old at their last assessment (unaffected group; n=88). The relationship between M. pneumoniae IgG positivity and the presence and severity of tics was analysed using multilevel models controlling for site, family relatedness, sex, age, presence of comorbid obsessivecompulsive and/or attention-deficit/hyperactivity disorder and use of psychotropic medication. M. pneumoniae IgG positivity was not associated with the presence of CTD, or the first onset of tics as compared to siblings who remained unaffected. M. pneumoniae IgG positivity was associated with a higher tic severity score within the CTD group (β = 2.64, s.e. = 1.15, p = 0.02). It is possible that M. pneumoniae infection influences tic severity in CTD or, that having more severe tics, increases the risk of infection. However, it is more likely that the association observed in this study reflects a propensity toward enhanced immune responses in people with CTD and that, rather than a causal relationship, infection and greater tic severity are indirectly linked via shared underlying immune mechanisms.



OVID Post-inflammatory Syndromes Help in Decreasing Controversy?

SARS-CoV-2 is not unique in its ability to cause post-acute sequelae; certain acute infections have long been associated with an unexplained chronic disability in a

minority of patients.

- The relatively similar symptom profiles of individual PAISs, irrespective of the infectious agent, as well as the overlap of clinical features suggest the potential involvement of a common etiopathogenesis.
- PAISs, including post-acute sequelae of SARS-CoV-2 infection (PASC)require continued biomedical research

Lancet Child Adolesc Health. 2021 Jun; 5(6): e19-e21.

Published online 2021 May 4. doi: 10.1016/S2352-4642(21)00135-8

SARS-CoV-2 related paediatric acute-onset neuropsychiatric syndrome

Piero Pavone, a Manuela Ceccarelli, b, Silvia Marino, Daniela Caruso, Raffaele Falsaperla, Massimiliano Berretta, Piero Pavone, a Manuela Ceccarelli, D, Silvia Marino, Daniela Caruso, Raffaele Falsaperla, Massimiliano Berretta, Piero Pavone, a Manuela Ceccarelli, D, Silvia Marino, Daniela Caruso, Raffaele Falsaperla, A Massimiliano Berretta, Piero Pavone, a Manuela Ceccarelli, D, Silvia Marino, Daniela Caruso, Raffaele Falsaperla, A Massimiliano Berretta, Piero Pavone, A Manuela Ceccarelli, D, Silvia Marino, Daniela Caruso, Raffaele Falsaperla, A Massimiliano Berretta, Piero Pavone, A Manuela Ceccarelli, D, Silvia Marino, D Daniela Caruso, Raffaele Falsaperla, A Massimiliano Berretta, Piero Pavone, Piero Pa

PMCID: PMC8096321

PMID: 33961798

Emmanuele Venanzi Rullo, ⁹ and Giuseppe Nunnari⁹

Choutka, J., Jansari, V., Hornig, M. et al. Unexplained post-acute infection syndromes. Nat Med 28,

911-923 (2022). https://doi.org/10.1038/s41591-022-01810-6



- * Flu-like symptoms
- * Neck pain
- * Joint pain
- * Nerve pain
- * Peripheral neuropathy
- * Vertigo
- * Headaches
- * Cardiac symptoms
- * Brain Fog
- * Anxiety and Depression
- * Cognitive Impairments

*Lyme Disease - Borreliosis

Review > Psychiatr Clin North Am. 1998 Sep;21(3):693-703, viii.

doi: 10.1016/s0193-953x(05)70032-0.

The underdiagnosis of neuropsychiatric Lyme disease in children and adults

B A Fallon ¹, J M Kochevar, A Gaito, J A Nields

Affiliations + expand

PMID: 9774805 DOI: 10.1016/s0193-953x(05)70032-0

Free article

Abstract

Lyme Disease has been called "The New Great Imitator," a replacement for that old "great imitator" neurosyphilis. This article reviews the numerous psychiatric and neurologic presentations found in adults and children. It then reviews the features of Lyme Disease, which makes it almost uniquely hard to diagnose, including the complexity and unreliability of serologic tests. Clinical examples follow that illustrate those presentations of this disease that mimic attention deficit hyperactivity disorder (ADHD), depression, and multiple sclerosis.

Neuropsychiatric Borreliosis

PMCID: PMC7884317

PMID: 33603684

Front Psychiatry, 2021; 12: 505941.

Published online 2021 Feb 2. doi: 10.3389/fpsyt.2021.505941

Case Report: PANDAS and Persistent Lyme Disease With Neuropsychiatric Symptoms:

Treatment, Resolution, and Recovery

Amy Cross, Denis Bouboulis, Craig Shimasaki, and Charles Ray Jones³

- Muscle and Joint pains
- Headaches
- Fatigue & Brain Fog
 - Impaired executive function
 - Slow processing speed
- Migratory neuropathy
- Migratory fasciculations
- Rage and Aggression
- Constant and daily "flare"
- Anxiety, depression, OCD
- Foot/heel pain
- Striae
 - Do not follow dermal lines
 - Blanch





Infectious and Autoimmune Causes of Encephalitis in Children

Timothy A. Erickson, PhD, MSPH, Abf Eyal Muscal, MD, MS, & Flor M. Munoz, MD, Timothy Lotze, MD, Rodrigo Hasbun, MD, Eric Brown, PhD, Kristy O. Murray, DVM, PhD 4

BACKGROUND AND OBJECTIVES: Encephalitis can result in neurologic morbidity and mortality in children. Newly recognized infectious and noninfectious causes of encephalitis have become increasingly important over the past decade.

METHODS: We retrospectively reviewed medical records from pediatric patients in Houston diagnosed with encephalitis in both an urban and rural catchment area between 2010 and 2017. We conducted an investigation to understand the etiology, clinical characteristics, and diagnostic testing practices in this population.

RESULTS: We evaluated 231 patients who met the case definition of encephalitis, among which 42% had no recognized etiology. Among those with an identified etiology, the most common were infectious (73; 31%), including viral (n = 51; 22%), with the most frequent being West Nile virus (WNV; n = 12), and bacterial (n = 19; 8%), with the most frequent being *Bartonella henselae* (n = 7). Among cases of autoimmune encephalitis (n = 60; 26%), the most frequent cause was anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis (n = 31). Autoimmune causes were seen more commonly in female (P < .01) patients. Testing for herpes simplex virus and enterovirus was nearly universal; testing for anti-NMDAR encephalitis, WNV, and *Bartonella* was less common.

CONCLUSIONS: WNV was the most common infectious cause of encephalitis in our pediatric population despite lower testing frequency for WNV than herpes simplex virus or enterovirus. Increasing testing for anti-NMDAR encephalitis resulted in frequent identification of cases. Increased awareness and testing for WNV and *Bartonella* would likely result in more identified causes of pediatric encephalitis. Earlier etiologic diagnosis of encephalitides may lead to improve clinical outcomes.



abstract

<u>J Cent Nerv Syst Dis.</u> 2019; 11: 1179573519832014.

Published online 2019 Mar 18. doi: 10.1177/1179573519832014

PMID: 30911227

PMCID: PMC6423671

Bartonella henselae Bloodstream Infection in a Boy With Pediatric Acute-Onset Neuropsychiatric Syndrome

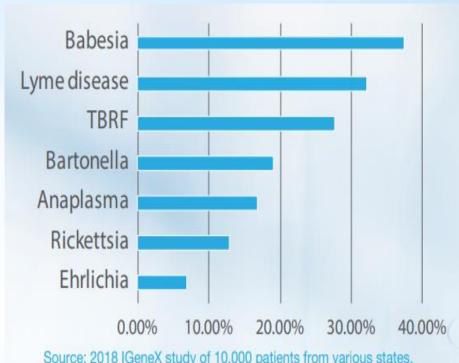
Edward B Breitschwerdt, ¹ Rosalie Greenberg, ² Ricardo G Maggi, ¹ B Robert Mozayeni, ³ Allen Lewis, ⁴ and Julie M Bradley, ¹

* Cases of babesiosis have increased significantly in Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Rhode Island and Vermont.

* This is only counting *B. microti* cases. The dominant *Babesia* sp. in deer ticks is *B*. odocoilei and it's infecting humans at a much, much higher rate than B. microti.

* B. odocoilei is much more sophisticated parasite and does not cause the typical acute babesiosis syndrome but produces chronic babesiosis with variable levels and kinds of symptomatology.

https://www.cdc.gov/mmwr/volumes/72/wr/m m7211a1.htm?s_cid=mm7211a1_w



Source: 2018 IGeneX study of 10,000 patients from various states.



- Chronic Symptoms
 - Unrelenting headache (especially head pressure)
 - Paresthesias and dysautonomia
 - Night sweats
 - Rib and bone pain
 - Cough and Air Hunger
 - Encephalopathy, anxiety
 - Myalgias and arthralgias
 - Brain fog, depression, insomnia
 - Gastrointestinal symptoms





Environmental Exposures

Additional Markers

Mold Tick Exposures Mineral & Metabolic Markers

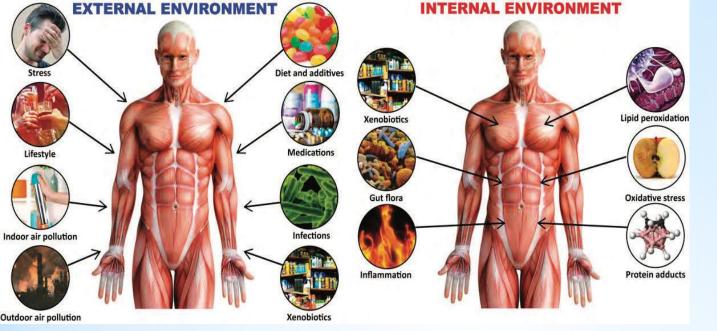
Antioxidants

Mitochondrial Markers

Chemical Exposures
Pesticides
Anesthesia

Thyroid Antibodies
Folate Receptor Antibodies (FRAT)
Celiac Panel, HLA, Food Allergies/Sensitivities
COVID Antibodies

- Chronic Inflammatory Response Syndrome -> genetic predisposition to an environmental trigger, most commonly mold or Lyme disease.
- With CIRS, biotoxins and microbes induce immune system production of inflammatory cytokines and persistent inflammation. What should be a warming campfire of immune reaction becomes a devastating wildfire of inflammation.
- The most common symptoms include:
 - Electric shock sensations
 - Ice pick or lightening bolt pains
 - Pulsing or vibrating sensations (especially down spine)
- Other symptoms can include:
 - Fatigue, weakness
 - Memory, concentration and executive function problems
 - Headaches, Vertigo and lightheadedness
 - Muscle aches, cramping, joint pains, unusual skin sensitivity
 - Hypersensitivity to light, blurred vision, burning eyes
 - Cough, chronic congestion, sinus and asthma-like illnesses, shortness of breath
 - Chronic GI complaints cramping, nausea, diarrhea
 - Thirst, appetite swings, body temperature irregularities and night sweats





- Genetics play a part in the pathophysiology of autoimmune disorders
- Environmental factors have a greater role
- The solution is to detect the trigger, remove it from the environment or diet, then repair the damage to the individual's body and health.

Vojdani, A.; Vojdani, E. The Role of Exposomes in the Pathophysiology of Autoimmune Diseases I: Toxic Chemicals and Food. *Pathophysiology* **2021**, *28*, 513-543. https://doi.org/10.3390/pathophysiology28040034

* Etiopathogenesis for PANDAS

Group A Genetic Susceptibility Strep • HLA-B alleles Misdirected
Immune
Response

• Molecular
Mimicry
• AntiGAS
Abs cross
BBB &
attack
basal
ganglia

PANDAS

Basal
Ganglia
Encephalitis

Restrict
Eating
Disorde
2 of 7 cr
includin
anxiety,
regressi
tics, son

OCD or
 Restrictive
 Eating
 Disorder
 2 of 7 criteria
 including
 anxiety,
 regression,
 tics, somatic sx
 & more

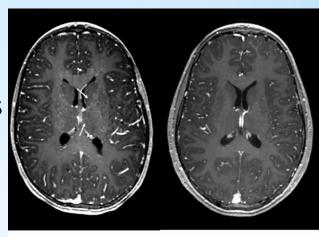
Beier K and Pratt DP, 2022

Dr. Dritan Agalliu: Looking at the Brains of PANDAS/PANS Children: How Peripheral

Infection Triggers Brain Inflammation: https://www.pandasppn.org/agalliu/#webinar

Evidence that PANS/PANDAS exists

- High rate autoimmunity in 1st degree relatives
- Strong association with HLA-B alleles
 - Associated with vasculitis (Frankovich, 2016)
- High rate of autoimmune signs/biomarkers
- Auto-antibody profiles similar to SC
 - Cam Kinase (Brimberg et al, Neuropsychopharm, 2012)
- Animal models of basal ganglia inflammatory response (Lotan et al, Brain, Behav & Immun, 2014)
- Evidence of autoantibodies in basal ganglia and strep specific Th17 cells in animal models (Dileepan et al, J Clin Invest 2015)
- Imaging data showing inflammation and activated microglia in basal ganglia in patients with PANS/PANDAS
- Patient response to immunomodulatory therapy



Lenticulostriate Vasculitis

Normai



*Most important Biomarker

*HISTORY!

J Child Adolesc Psychopharmacol. 2019 May 29. doi: 10.1089/cap.2018.0151. [Epub ahead of print]

Clinical-Serological Characterization and Treatment Outcome of a Large Cohort of Italian Children with Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection and Pediatric Acute Neuropsychiatric Syndrome.

Lepri G1, Rigante D2,3, Bellando Randone S1, Meini A4, Ferrari A4, Tarantino G2, Cunningham MW5, Falcini F1.

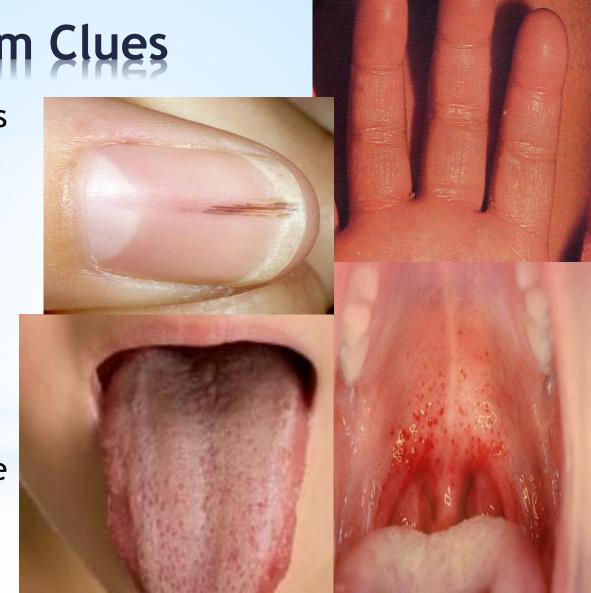
Author information

Abstract

Objective: Pediatric autoimmune neuropsychiatric disorder associated with Streptococcus pyogenes infection (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS) are emerging immune-mediated encephalopathies characterized by sudden onset of seemingly inexplicable complex neuropsychiatric symptoms, including obsessions, compulsions, and heterogeneous tics, which occur in children. Main goal of this study was to report our experience in a large cohort of Italian children affected by either PANDAS or PANS and treated long term with an antibiotic regimen similar to that used for acute rheumatic fever. Patients and Methods: The clinical charts of a cohort of 371 consecutive Italian children, 345 with PANDAS (93.0%) and 26 with PANS (7.0%), were retrospectively evaluated. Antistreptococcal, antinuclear antibodies, and serologic evaluation for a group of common autoantibodies and microbial agents were also assessed. A strict differential diagnosis with other autoimmune diseases displaying neuropsychiatric manifestations was performed. Results: Antistreptolysin O and anti-DNase B antibody titers were tested and were positive in all PANDAS subjects, but negative in PANS. Anti-Mycoplasma pneumoniae antibodies and anti-Epstein-Barr virus Nuclear Antigen antibodies were found positive in 11 (42.3%) and 5 (19.2%) patients with PANS, respectively. Among PANDAS cases, a clear streptococcal infection was clinically evident at the onset of neurological symptoms in only 74 patients (21.4%), whereas the relationship with Streptococcus pyogenes was confirmed by serologic tests in the other 271 (78.6%). All patients fulfilling the diagnostic criteria for PANDAS (n = 345) received amoxicillin/clavulanic acid for 10-21 days at diagnosis, while those who were diagnosed with PANS (n = 26) received treatment according to the causative agent. Thereafter, all PANDAS/PANS patients received prophylaxis with benzathine benzylpenicillin for an overall period of at least 5 years to prevent subsequent potential streptococcal infections. To date, 75.0% of PANDAS patients (n = 258) have shown an improvement of neurologic symptoms, mainly observed within 3-5 months of treatment for PANDAS cases, while 88.4% of PANS patients (n = 23) have improved after 6-12 months. Infection-related relapses of neurologic manifestations were observed in both PANDAS and PANS patients (n = 167 out of 371; 45% of the total cohort) in the long term. Conclusions: Our study has confirmed the usefulness of the preliminary diagnostic criteria for PANDAS and PANS, revealing also the importance of early diagnosis to reduce the risk of evolution toward disabling chronic neurologic sequelae. Longterm antibiotic prophylaxis has resulted in a substantial benefit to reduce neurological symptoms for the majority of PANDAS and PANS patients over a 7-year period.

* Physical Exam Clues

- Choreiform Movements
- Strep (PANDAS)
 - Red anal ring
 - Peeling fingers
 - Tongue
 - Palate petechiae
 - Damaged nail bed vasculature



- Erythema Migrans
- Striae that blanches
- Swollen/tender glands
- Tender sinus palpation
- Whiteness on tongue
- Positive Woods Lamp

* Physical Exam Clues



History and Physical Exam

- Proving PANS in each child
- Clinical Diagnosis of ABRUPT onset symptoms
- Choreiform movements (piano playing fingers)
- Evidence of infection/inflammation
- Culture of possible infectious sites strep and viral cultures
- Culture of Tonsils and Adenoids (surface/core) at time of T & A
- Tonsillectomy as treatment (Demesh et al, JAMA 2015)
 - Discordance between surface and core bacterial isolates (Internat J Ped Otorhinolar, 1987)
 - Significantly different concentrations of cytokines (as compared with tissue removed due to obstructive sleep apnea (PANDAS - high TNFalpha, low IL8, IL10 & IL12))

(Walls et al. 2016; Parker-Athill et al, JCAP, 2015)

- Laboratory evidence DO NOT TREAT TITERS
 - Inflammatory markers CRP, ESR, ANA > 56 % + (Cox et al, JACP, 2015)

Laboratory evidence

Strep markers- ASO, anti DNaseB Ab

- * 6-8 weeks for rise in titers post infection
- * These antibodies only mean that the child has had a previous strep infection
- * It does NOT mean the child has PANDAS
- * ~40% of children with documented GAS infections do

NOT show a rise in titers

Other infectious markers:

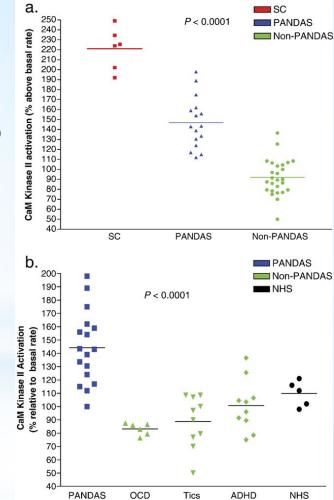
- * Mycoplasma IgG/IgM
- * Lyme and Coinfections (Bartonella, Babesia)
- * Viral markers influenza, EBV, CMV, COVID
- * Gut dysbiosis yeast, clostridia, parasites

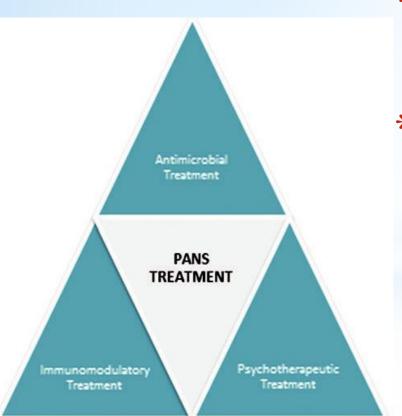
Cunningham Panel

Testing may be helpful when child in a flare or not classical clinical picture

Camkinase, antineuronal Ab (Fallon et al., 2020)







- *Treating the symptoms including supportive interventions (CBT, supplements, psychoactive medications)
- *Removing the source of the inflammation treating with antimicrobials
- *Treating immune disturbances with immunomodulatory and/or anti-inflammatory interventions

Three modes of intervention

Swedo et al, J Child Adol Psychopharm, 2017

* TREATMENT FOR SYMPTOMS

OCD

Tics

Anxiety

Aggression Irritability

Sleep Disturbances

Eating Disorders



- Medications (SSRIs)
 - Low dose with slow titration
 (Coffey, J Child Adol Psychopharm, 2007)
 - NAC (N-Acetyl Cysteine)
 - •Multiple studies in treatment of OCD (Oliver et al, Clin Psychopharm Neurosci, 2015)
- Herbal Adaptogens Ashwagandha (Withania somnifera)
 Comparable efficacy in mice models to fluoxetine (Asian Pac J Trop Med, 2012)
- * INOSITOL (up to 18 gm/day) B vitamin affecting serotonin to decrease OCD (Palatnik et al, J Clin Psychopharm, 2001)
 - CBD (Hemp Oil) Cannabidiol
 - * Reverses mCPP-induced marble burying in mice
 - * Nardo et al, 2013; Delana et al, Psychopharm, 2012
- Lithium Orotate (O'Donnell et al, Eur Neuropsychopharm, 2003)
- * GABA Modulates glutamate; significantly higher in OCD subjects' CSF (Pittenger et al, 2011)
- Mindfulness (Hansteded et al, J Nerv Ment Dis, 2008)
- Exercise (Otto et al Oxford Univ Press, 2011)



* Medications

- * Beta blockers (Propranolol)
- * Alpha blockers (Clonidine, Guanfacine)
- * Anxiolytics (Lorazepam)
- * Others (Amantadine)

* 5-HTP

- * Precursor to serotonin and melatonin biosynthesis
- * 5-HTP significantly reduced the reaction to the panic trigger, number of panic attacks, panic symptom score, and subjective anxiety, when compared to placebo (Schruers et al,2002)

* MAGNESIUM

* Magnesium insufficiency associated with anxiety, depression, PTSD, ADHD, and bipolar. (Botturi et al, 2020)

* B6

* Increases inhibitory GABAergic neural influences and reduced selfreported anxiety in young adults (Field et al, 2022)

* LEMON BALM

* Lemon balm significantly improved mean anxiety and depression scores compared with the placebo, particularly in acute settings (Ghazizadeh et al, 2021)

* SAFFRON

* Reduced depression scores and improved social relationships and decreased in heart rate variability during exposure of a stressor (Jackson et al, 2021)

* LAVENDER

- * Inhalation shown to significantly reduce anxiety levels (Donelli et al, 2019)
- * 6-week-intake of lavender oil capsule was shown to be as effective as lorazepam in adults with GAD (Woelk and Schlafke, 2010)

*ANXIETY



- * L-MTHF (if MTHFR mutation OR CFD)
- * Meditation
- * Exercise
- * Cognitive Behavioral Therapy (CBT)



- Others as listed for Anxiety, OCD (ex: CBD, NAC, GABA, Adaptogens)
- Magnesium
 - Insufficiency -> musculoskeletal pain, constipation, and heightened sense of anxiety (Xue, W., You, J., Su, Y., & Wang, Q. (2019). The Effect of Magnesium Deficiency on Neurological Disorders: A Narrative Review Article. Iranian journal of public health, 48(3), 379-387.)
 - Form Citrate, oxide, glycinate, threonate, Epsom Salt baths, etc.
- Pharmaceuticals
 - Antihypertensives Propranolol, Guanfacine, Clonidine (Qasaymeh, M. M., & Mink, J. W. (2006). New treatments for tic disorders. Current treatment options in neurology, 8(6), 465-473)
 - Neuroleptics Risperidone, Pimozide, Aripiprazole (Eddy CM, Rickards HE, Cavanna AE. Treatment strategies for tics in Tourette syndrome. *Ther Adv Neurol Disord*. 2011;4(1):25-45)
 - Anticonvulsants Levetiracetam, Lamotrigine (Martínez-Granero MA, García-Pérez A, Montañes F. Levetiracetam as an alternative therapy for Tourette syndrome. Neuropsychiatr Dis Treat. 2010;6:309-316)
 - Others SSRIs, Movement disorder meds- Tetrabenazine (Porta, M., Sassi, M., Cavallazzi, M., Fornari, M., Brambilla, A., & Servello, D. (2008). Tourette's syndrome and role of tetrabenazine: review and personal experience. Clinical drug investigation, 28(7), 443-459)
- Therapy, Counter Tics, Acupuncture & physical medicine, Meditation & Mindfulness, Diet & Exercise

J Clin Sleep Med. 2016 Jul 15;12(7):1027-32. doi: 10.5664/jcsm.5942.

Rapid Eye Movement Sleep Abnormalities in Children with Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS).

Gaughan T1, Buckley A1, Hommer R1, Grant P1, Williams K2, Leckman JF3, Swedo SE1.

Author information

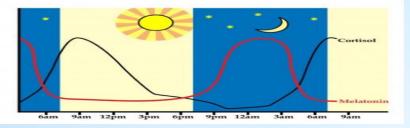
Abstract

STUDY OBJECTIVES: Polysomnographic investigation of sleep architecture in children presenting with pediatric acute-onset neuropsychiatric syndrome (PANS).

METHODS: Fifteen consecutive subjects meeting criteria for PANS (mean age = 7.2 y; range 3-10 y) underwent single-night full polysomnography (PSG) read by a pediatric neurologist.

RESULTS: Thirteen of 15 subjects (87%) had abnormalities detected with PSG. Twelve of 15 had evidence of rapid eye movement (REM) sleep motor disinhibition, as characterized by excessive movement, laughing, hand stereotypies, moaning, or the continuation of periodic limb movements during sleep (PLMS) into REM sleep.

CONCLUSIONS: This study shows various forms of REM sleep motor disinhibition present in a population of children with PANS.



* SLEEP DISTURBANCES

***** MELATONIN

* Helpful for sleep disorders and other associated neurological disorders (Esposito et al, 2019)

* 5-HTP

* 5-HTP modulate arousal level; induce long-term improvement of sleep terrors (Bruni et al, 2004)

* MAGNESIUM

- * Improves sleep quality and restless leg syndrome
- * Increases GABA and is an NMDA antagonist (Schwalfenberg and Genuis, 2017)

*GABA + L-THEANINE

* Improves sleep onset and increased sleep duration (Kim et al, 2019)

***VALERIAN ROOT**

- * Constituents have sedative and sleep-enhancing properties (Fernandez et al, 2004)
- * Inhibits excess activity in the amygdala (Fernandez et al, 2004)
- * Decreases OCD (Pakseresht et al, 2011)

RESTRICTIONS

*ZINC

- * Zinc mediates food intake and appetite by influencing the expression of Hypothalamic Neuropeptide Y (Levenson, 2003)
- *Increasing PROTEIN in diet (i.e. protein powders)
- *MCT OIL
- *Digestive bitters
 - * Ginger
 - * Gentian
 - * Anise

Case Reports > J Child Adolesc Psychopharmacol. 2015 Feb;25(1):48-56.

doi: 10.1089/cap.2014.0063. Epub 2014 Oct 20.

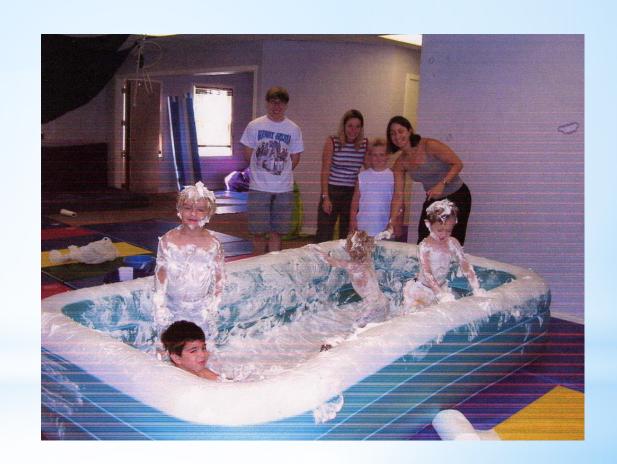
Disordered eating and food restrictions in children with PANDAS/PANS

Megan D Toufexis 1, Rebecca Hommer, Diana M Gerardi, Paul Grant, Leah Rothschild, Precilla D'Souza, Kyle Williams, James Leckman, Susan E Swedo, Tanya K Murphy



What lies behind us and what lies before us are small matters compared to what lies within us.

Emerson



* PANS/PANDAS - TREATMENT

Antibiotics

- IM Bicillin (> 60 lbs 1.2 million units-perhaps monthly)
- Penicillin, Amoxicillin-Clavulanate, Azithromycin, Clarithromycin, Cephalexin, Cefadroxil, Clindamycin (Shulman et al, Clin Inf Dis, 2012)
- Azithromycin (EKG for diagnosis of prolonged QT interval)
 - Advantages Activity against Mycoplasma & Immunomodulatory (Obregon et al, Neuropsych, 2012; Murphy et al, J Antimicrob Chemoth, 2008)
 - Disadvantages Regional resistance (Silva-Costa, Exper Rev Anti Infec Ther, 2012)
- * Randomized Trial of CEFDINIR vs Placebo Cefdinir group with significant improvement in tics and OCD over placebo group

(Murphy et al. J of Child & Adol Psychopharm, 2015)

 Double Blinded Randomized Placebo-Controlled Pilot Study of Azithromycin in Youth with Acute-onset OCD

(Murphy et al, J Child Adol Psychopharm, 2017)

Antibiotic Prophylaxis with Penicillin or Azithromycin



* ANTIMICROBIAL HERBS FOR STREP

- * Usnea
 - *Activity against strep species (Abachi et al, 2016)
- * Taiga Pine needle extract
 - *Antimicrobial/antifungal activity (Lee et al, 2005)
- * Berberine (Goldenseal)
 - * Berberine sulfate blocks adherence of Streptococcus pyogenes to epithelial cells, fibronectin, hexadecane (Sun D et al, 1988)
- *Oregano Oil
 - * Antimicrobial activity of carvacrol against erythromycinresistant Group A Streptococci (Magi et al. 2015)
- * Neem
 - * Neem extract effective against four Streptococcus species responsible for causing dental caries (Chava et al., 2012).

* ANTIMICROBIAL INTERVENTIONS FOR MYCOPLASMA

- *Azithromycin first
- *Berberine/Goldenseal
- *Houttuynia
- *Isatis
- *Colloidal Silver
- *Rotation of:
 - *Cat's claw & Campsiandra
 - * Alternate with Otoba bark and Stevia every 2 weeks
 - *Take 1 ½ days (3 doses) off in between changes



(Arjoon et al, BMC Complement Altern Med, 2012)

* Vitamin A

- * Inhibits murine norovirus replication and modulates gut microbiome specifically Lactobacillus (Lee and Ko, 2016)
- * High dose may aid in protective immune response to COVID-19 (Midha et al, 2021)
- * Vitamin D
 - * Modulates both the adaptive and innate immune system (Bui et al, 2021)
 - * Vitamin D deficiency risk factor for increased symptom severity and mortality with COVID (Brenner et al, 2020)
- * Vitamin C
- * Stimulates neutrophil migration to infection site, enhances phagocytosis & microbial killing (Carr and Maggini, 2017)

 * L-Lysine
 - * Amino acid that decreases viral replication and inhibits viral yield (Melano et al, 2021)
- * Monolaurin
 - * Inactivates viruses by disintegrating the viral envelope(Hierholzer and Kabara, 1982)
 - * Circulating monolaurin was higher in protected subjects suggesting a potential defensive role against SARS-CoV-2
- * Olive Leaf
- * Prevents virus shedding, budding, and assembly of cell membranes
- * Lemon Balm
 - * Inhibits virus replication (Pourghanbari et al, 2016)
- * Implement acute viral protocols at onset of viral illnesses
 - * i.e vitamin A, D, Zinc, L-lysine, etc)

infection (Barberis et al, 2021)

ANTIVIRAL INTERVENTION

ANDREH WHO? Name_ Bavrillo Princip of the Black Hand Gungl FINATI: taxal he arch DUKO Franz Fredmand WHAT? The assassination 1 GROUP OF WHEN? June 28,1914 COUNTRAING WE pphorfu WHERE? Sarajevo, Bosnia AtiONIALSM & PRICE IN YOUR DWN Because the Black-HAND GAND WHY? COUMRY wanted to kill World War I Guses

- *Multiple Antibiotics
 - *Cystic/Persistor
 - * Metronidazole
 - * Tinidazole
 - *Cell wall agents
 - * Penicillins
 - *Cephalosporins
 - *Intracellular
 - *Tetracyclines
 - *Macrolides
- * Duration
 - Weeks? Months? Longer?
- *May require multiple courses of tx
- *Use of BIOFILM Busters
- *Role of herbal interventions

Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani

Yumin Zhang¹, Hector Alvarez-Manzo¹, Jacob Leone², Sunjya Schweig³ and Ying Zhang^{4*}

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*Treatment of Lyme
& Co-Infections



- Inhibits the cytokine cascade initiated by Bartonella
- Active against stationary phase nongrowing B. henselae and against log phase growing B. henselae

BERBERINE

henselae (Li et al., 2019) **CRYPTOLEPIS**

- Active against stationary phase nongrowing B. henselae and against log phase growing B. henselae
- Ma et al., 2020

ARTEMISIA

- Against stationary phase of Borrelia burgdorferi (Feng et al, 2020)
- Reduces memory impairment when combined with IV ceftriaxone in Lyme patients (Puri et al, 2017)

GRAPEFRUITSEED EXTRACT

In vitro activity against spirochetes & cysts of Borrelia (Brorson and Brorson, 200)

STEVIA

Efficacy of leaf against all forms High activity against stationary phase B. of Borrelia burgdorferi and ~40% efficacy in reducing attached biofilm mass (Theophilus et al., 2015)

CATS CLAW

Decreased symptoms of Lyme; 85% of patients re-tested neg (Cowden et al, 2003) 2 week Rotation of:

Cat's Claw, Stevia & Otoba Bark

Then Cat's Claw, Campsiandra & Stevia

Take 1 ½ days (3 doses) off in between changes

Shor SM, Schweig SK. The Use of Natural Bioactive Nutraceuticals in the Management of Tick-Borne Illnesses. *Microorganisms*. 2023; 11(7):1759. https://doi.org/10.3390/microorganisms11071759



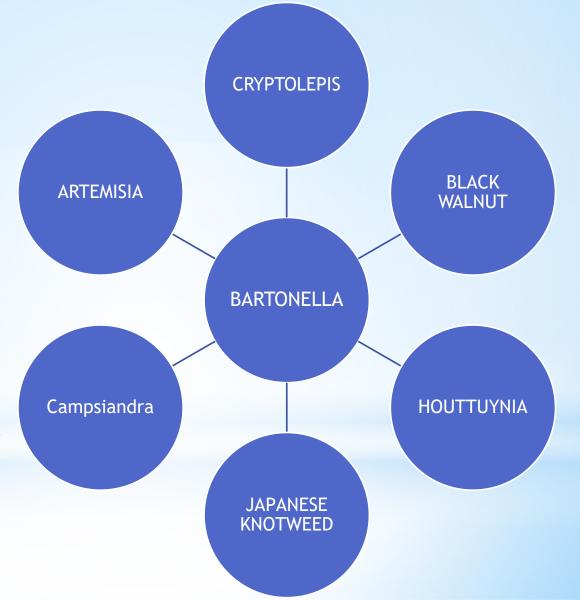
* Japanese Knotweed

Houttynia with
Campsiandra & add
Stevia for biofilm and
persistors

If above does not work, add Cryptolepis

Cheslock MA, Embers ME. Human Bartonellosis: An Underappreciated Public Health Problem? Trop Med Infect Dis. 2019 Apr 19;4(2):69. doi: 10.3390/tropicalmed4020069.

PMID: 31010191; PMCID: PMC6630881.

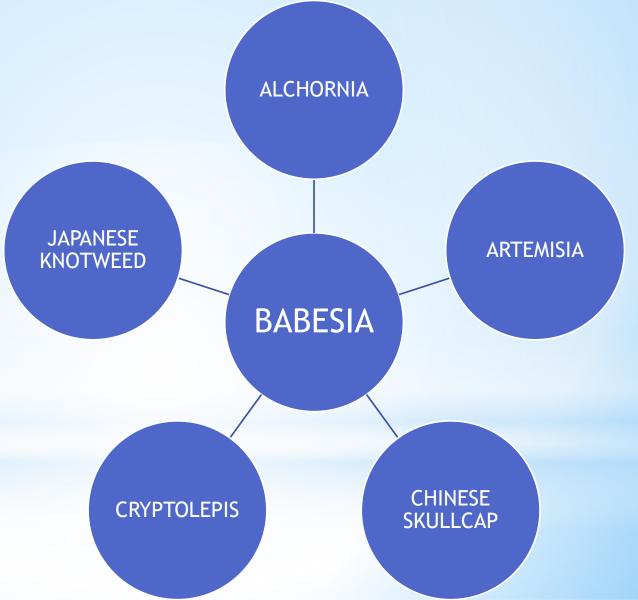


* Atovaquone & Azithromycin

Cryptolepis and Cat's Claw

As well as
Artemisia PULSING
around new and
full moons

Abraham A, et al. Establishment of a continuous *in vitro* culture of *Babesia duncani* in human erythrocytes reveals unusually high tolerance to recommended therapies. J Biol Chem. 2018 Dec 28;293(52):19974-19981. doi: 10.1074/jbc.AC118.005771. Epub 2018 Nov 21. PMID: 30463941.





PANS/PANDAS - Immune Modulators

- * Probiotics and Prebiotics
 - * Lactobacillus, Bifidobacterium, Bacillius
 - * Saccharomyces Boulardii



* Modulation of inflammatory reactions, lowering triglycerides, nerve transmission

* Aloe

* Anti-oxidant properties to decrease ROS (Landmead et al, 2004)

* Curcumin

* Efficacy of curcumin, and a saffron/curcumin combination for the treatment of major depression: A randomized, double-blind, placebo-controlled study (Lopresti et al, 2017)

* SPM

- * Immunomodulation, anti-inflammatory, anti-histamine benefits
- * Regulate macrophage infiltration and cytokine production in SARS-CoV2 and promote a pro-resolving macrophage phenotype (Balta et al, 2021)



* CBD Oil

* suppression of cytokines and chemokines at inflammatory sites and upregulation of FoxP3⁺ regulatory T cells (Nagarkatti et al, 2009)

- MAST CELL MEDIATED DISORDERS/MAST CELL Activation
- Antihistamines (Cetirizine, Diphenhydramine, Hydroxyzine)
- Antihistamines with anti-eosinophilic action (Ketotifen)
- Antihistamines with anti-serotonin action (Cyproheptadine)
- Flavonoids (luteolin, quercetin of high purity)
 - * Potent mast cell stabilizer inhibits release of histamine & inflammatory mediators

* Prevents excessive release of histamine (Chuenkityanaon et

- al. Int J Toxicology 2010; 29(4): 418-424)

 Antileukotrienes (Montelukast)
- Cromolyn sodium (Gastrocrom)

Observational Study > J Child Adolesc Psychopharmacol. 2017 Sep;27(7):619-628.

doi: 10.1089/cap.2016.0193. Epub 2017 Jul 11.

Effect of Early and Prophylactic Nonsteroidal Anti-Inflammatory Drugs on Flare Duration in Pediatric

Acute-Onset Neuropsychiatric Syndrome: An Observational Study of Patients Followed by an Academic Community-Based Pediatric Acute-Onset

Kayla D Brown $^{1\ 2}$, Cristan Farmer 3 , G Mark Freeman Jr $^{2\ 4}$, Ellen J Spartz $^{1\ 2}$, Bahare Farhadian 2 , Margo Thienemann $^{2\ 5}$, Jennifer Frankovich $^{1\ 2}$

Neuropsychiatric Syndrome Clinic

* Additional

MCMD

* Treatment - Immune Modulators

Steroids (oral vs IV; length of course depends on symptom severity)

- Short burst therapeutic & diagnostic
- Temporary fix in some
- Transient worsening typical

Helminth Therapy

(www.biomerestoration.com)

IVIG

Maddle-share 2040 A-405440 440 day and sales 2040 Feb 204

Helminth therapy for autism under gut-brain axis- hypothesis.

Arroyo-López C1

Author information

Abstract

Autism is a neurodevelopmental disease included within Autism Syndrome Disorder (ASD) spectrum. ASD has been linked to a series of genes that play a role in immune response function and patients with autism, commonly suffer from immune-related comorbidities. Despite the complex pathophysiology of autism, Gut-brain axis is gaining strength in the understanding of several neurological disorders. In addition, recent publications have shown the correlation between immune dysfunctions, gut microbiota and brain with the behavioral alterations and comorbid symptoms found in autism. Gut-brain axis acts as the "second brain", in a communication network established between neural, endocrine and the immunological systems. On the other hand, Hygiene Hypothesis suggests that the increase in the incidence of autoimmune diseases in the modern world can be attributed to the decrease of exposure to infectious agents, as parasitic nematodes. Helminths induce modulatory and protective effects against several inflammatory disorders, maintaining gastrointestinal homeostasis and modulating brain functions. Helminthic therapy has been previously performed in diseases such as ulcerative colitis, Cronn's disease, diabetes, multiple sclerosis, asthma, rheumatoid arthritis, and food allergies. Considering gut-brain axis, Hygiene Hypothesis, and the modulatory effects of helminths I hypothesized that a treatment with Trichuris suis soluble products represents a feasible holistic treatment for autism, and the key for the development of novel treatments. Preclinical studies are required to test this hypothesis.

- No improvements in sham IVIG group; significant decrease in OCD severity in IVIG and plasmaphoresis groups after 1 month (Perlmutter et al, Lancet, 1999; Williams et al. J of Amer Acad of Child & Adol Psychiatry, 2016)
- One to six month course in moderate-severe of 1.5-2 gm/kg (Frankovich et al, J Child Adol Psychopharm, 2017)
- Plasmophoresis severe-extreme disease (Dalmau et al, Lancet Neuro, 2011; Latimer et al. J of Child & Adol Psychopharm, 2015)
- Rituximab deteriorating, moderate-extreme disease & previous responsiveness & autoimmunity (Chang et al, J Child Adol Psychopharm, 2015)

- Adenotonsillectomy
 - Retrospective analysis No difference in Sx severity or strep Ab (Pavone etal, lint J Immunopath Pharm, 2014; Murphy et al, Ped Inf Dis J, 2013)
 - Use with Sleep Apnea & frequent GAS as per general population (Baugh et al, Otolaryngol Head Neck Surg, 2011)
- Vitamin D
 - Assoc increased frequency infections (Thornton et al, Ped Inf Dis J, 2013)
 - Downregulate autoimmune processes (Rolf et al, Ann N Y acad Sci, 2014)
- IBUPROFEN/NSAID (Spartz et al, J Child Adol Psychopharm, 2017)
- ALKALINIZATION
- XYLITOL
- PROBIOTICS
 - BLIS K12



Vitamin D Deficiency in Obsessive-Compulsive Disorder Patients with Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections: A Case Control Study.

Celik G¹, Taş D², Tahiroğlu A¹, Avci A¹, Yüksel B³, Çam P². Author information

Abstract

Noro Psikiyatr Ars. 2016 Mar;53(1):33-37. doi: 10.5152/npa.2015.8763. Epub 2016 Mar 1.

INTRODUCTION: Previous studies have indicated that vitamin D deficiency is common in psychiatric patients, particularly in those with

neuropsychiatric disorders such as autism and schizophrenia. Vitamin D is an important neurosteroid hormone and immunomodulatory agent that also has bone metabolic effects. There has been an increasing interest in immune-related neuropsychiatric symptoms that are triggered by group A beta-hemolytic streptococcal infections. In this study, we aimed to compare the serum levels of vitamin D between obsessivecompulsive disorder (OCD) patients with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)

and control subjects. METHODS: Thirty-three OCD patients with PANDAS and 20 healthy controls were enrolled in the study. Serum 25-hydroxyvitamin D (25-(OH) D), calcium, phosphorus, alkaline phosphatase, and parathormone levels of the two groups were compared. Serum 25-(OH) D levels of <15 ng/mL were classified as vitamin D deficiency. The children's Yale-Brown Obsessive Compulsive Scale (YBOCS) and Clinical Global

Impression (CGI) were used to assess the severity of OCD symptoms. RESULTS: There was no significant difference in serum 25-(OH) D levels between the patient and control groups. However, vitamin D deficiency was significantly more frequent in the patient group than in the control group (48.5% vs. 20.0%; p=0.038). Moreover, OCD patients with vitamin D deficiency had higher rates of comorbid ADHD than those without vitamin D deficiency (87.5% vs. 52.6%; p=0.027). While serum phosphorus levels were negatively correlated with age as well as alkaline phosphatase and ASO levels, they were positively correlated with the YBOCS total score and global severity score. Serum parathormone levels were positively correlated with the YBOCS total

score, compulsion score, obsession score, and global severity score. CONCLUSION: This study supports the hypothesis that an association between vitamin D metabolism and PANDAS-related OCD exists. We suggest that biochemical parameters predicting metabolic bone diseases are more common in PANDAS patients. There is a need for

prospective studies to show a clear association between PANDAS and bone metabolic turnover based on autoimmune mechanisms.

enrolled to be treated daily for 90 days with a slow-release tablet for oral use, containing no less than 1 billion colony-forming units/tablet of S.

MATERIALS AND METHODS: We enrolled 61 children with a diagnosis of recurrent oral streptococcal disorders. Thirty-one of them were

pharyngotonsillitis in children. Di Pierro F¹, Colombo M², Zanvit A³, Risso P⁴, Rottoli AS⁵. Author information

Use of Streptococcus salivarius K12 in the prevention of streptococcal and viral

Abstract

BACKGROUND: Streptococcus salivarius K12 is an oral probiotic strain releasing two lantibiotics (salivaricin A2 and salivaricin B) that antagonize the growth of S. pyogenes, the most important bacterial cause of pharyngeal infections in humans also affected by episodes of acute otitis media. S. salivarius K12 successfully colonizes the oral cavity, and is endowed with an excellent safety profile. We tested its preventive role in reducing the incidence of both streptococcal and viral pharyngitis and/or tonsillitis in children.

Drug Healthc Patient Saf. 2014 Feb 13;6:15-20. doi: 10.2147/DHPS.S59665. eCollection 2014.

antipyretic therapy and days of absence from school or work.

salivarius K12 (Bactoblis®), and the remaining 30 served as the untreated control group. During treatment, they were all examined for streptococcal infection. Twenty children (ten per group) were also assessed in terms of viral infection. Secondary end points in both groups were the number of days under antibiotic and antipyretic therapy and the number of days off school (children) and off work (parents). RESULTS: The 30 children who completed the 90-day trial with Bactoblis® showed a significant reduction in their episodes of streptococcal pharyngeal infection (>90%), as calculated by comparing the infection rates of the previous year. No difference was observed in the control group. The treated group showed a significant decrease in the incidence (80%) of oral viral infections. Again, there was no difference in the control group. With regard to secondary end points, the number of days under antibiotic treatment of the treated and control groups were 30

and 900 respectively, days under antipyretic treatment 16 and 228, days of absence from school 16 and 228, and days of absence from work 16 and 228. The product was well tolerated by the subjects, with no side effects, and only one individual reported bad product palatability and dropped out. CONCLUSION: Prophylactic administration of S. salivarius K12 to children with a history of recurrent oral streptococcal disease resulted in a considerable reduction of episodes of both streptococcal and viral infections and reduced the number of days under antibiotic and/or



* You & Your Patient Can Do This!

- One step, one child at a time
- Consider mentoring drohara.com/mentoring
- Consider membership drohara.com/membership
 - Discount code for conference attendees
 - Short videos
 - Longer lectures
 - Live & recorded Q & As with experts in the field
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 - For members only

* How Can I Po This?



Nancy O'Hara, MD, MPH, FAAP

PEDIATRIC NEUROBEHAVIORAL HEALT

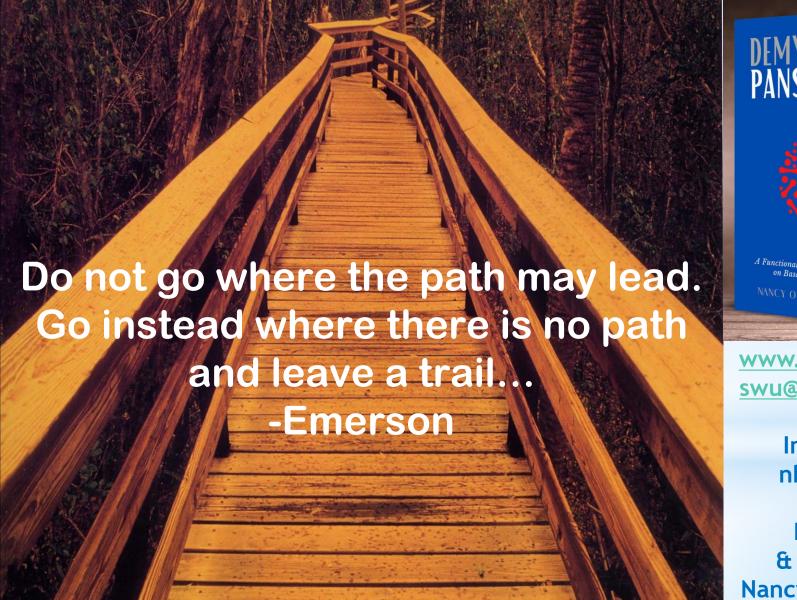
* PANS/PANDAS Recap

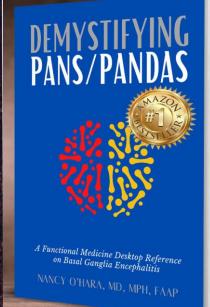
- Clinical diagnosis confirmed (or not) by laboratory evidence
- Complete medical & psychiatric history and physical exam
- Cultures and blood testing
 - Strep titers (ASO, antiDNaseB antibody), Mycoplasma IgG and IgM
 - Appropriate Borrelia, Bartonella, Babesia suspicion and testing
 - Immune markers (ANA, CRP, ESR, thyroid antibodies, immunoglobulins including subclasses, strep pneumococcal serotypes)
 - Urine organic acids & mitochondrial, metabolic, antioxidant markers as warranted
- Neuropsychological testing as necessary, warranted, able
- Additional testing depending on presentation (CSF, MRI, EEG, EKG, polysomography) Chang et al, J Child Adol Psychopharm, 2015
- Use treatment as diagnostic tool as well as therapeutic intervention (antimicrobials, steroids, immunotherapy, diet, emotional support)



Closing Reminders

- Pediatric Post Infectious Syndromes leading to autoimmune encephalitis, including PANS/PANDAS, is a CLINICAL DIAGNOSIS
- Think PANS/PANDAS with ACUTE ONSET of symptoms (tics, OCD, anxiety)
- Don't forget about Bartonella, Borrelia and more
- Treatment plan should include the 3-pronged approach
 - Antimicrobial interventions
 - Immunomodulatory interventions
 - Symptom support including CBT
- Decrease the severity, frequency, and duration of flares in a relapsing and remitting course of disease; Earlier Dx & Tx = Better Outcomes
- Treatment is a marathon and not a sprint, but things will get better
 - Create fluid access in and out of services
 - Be a partner with the family; Don't let anyone blame the child





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