

***Post Acute Infection Syndrome (PAIS):
Microbes and Mental Health
PANS/PANDAS and More***

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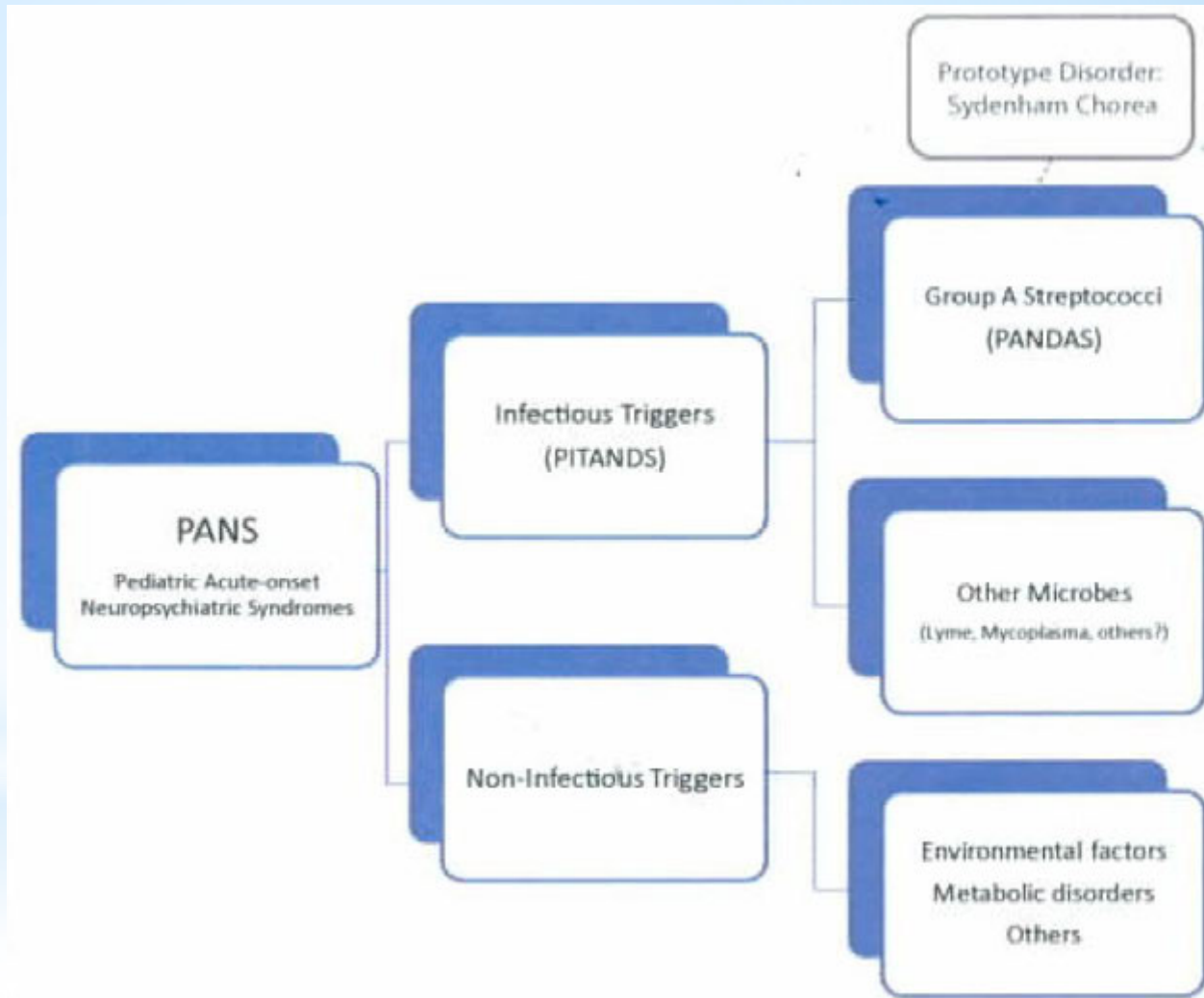
“Follow those who
seek the truth but
flee from those who
have found it.”

Vaclav Havel

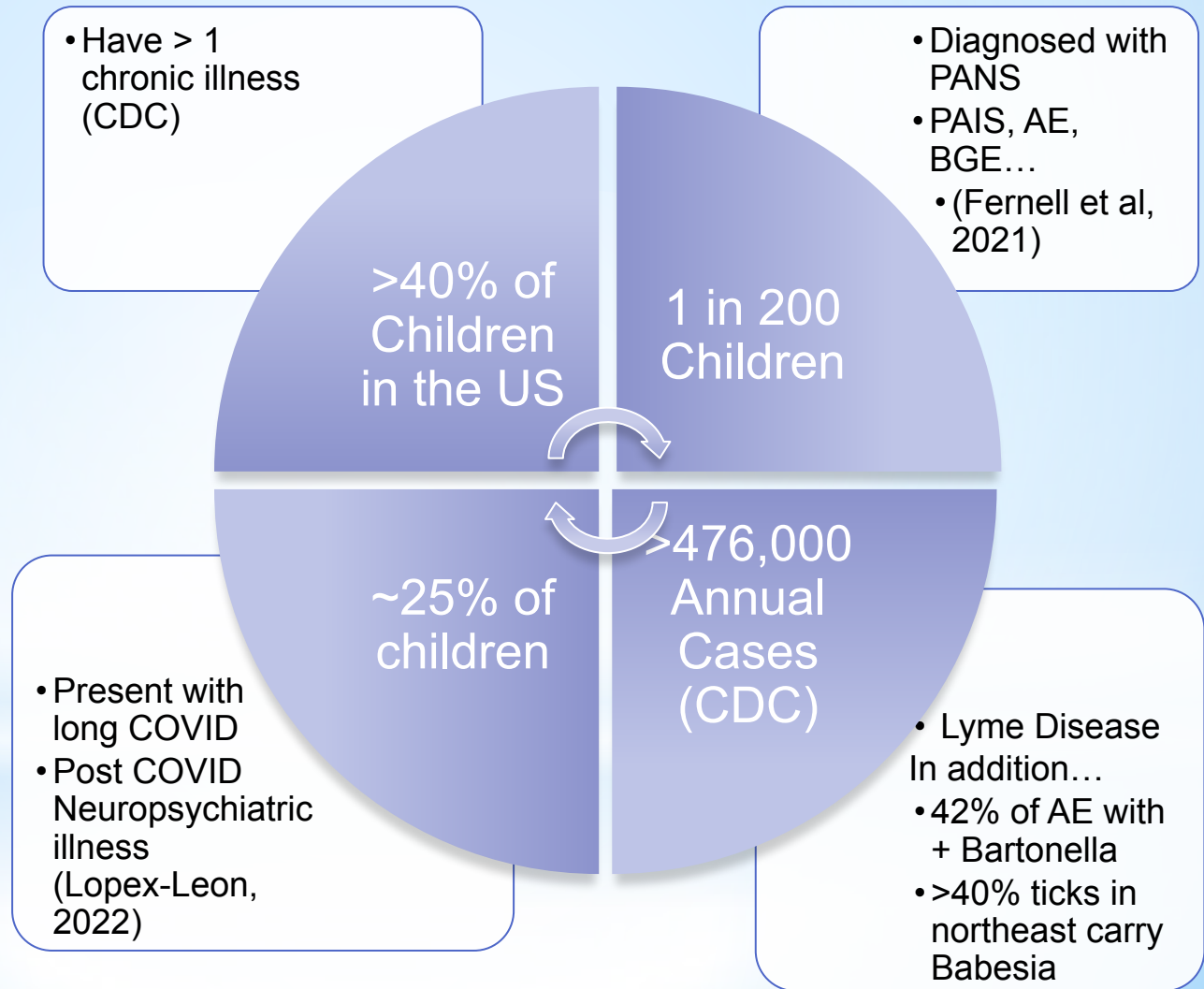


(Swedo et al, AJPpsych, 1998)

to PANS
(Swedo et al, Ped Ther, 2012)



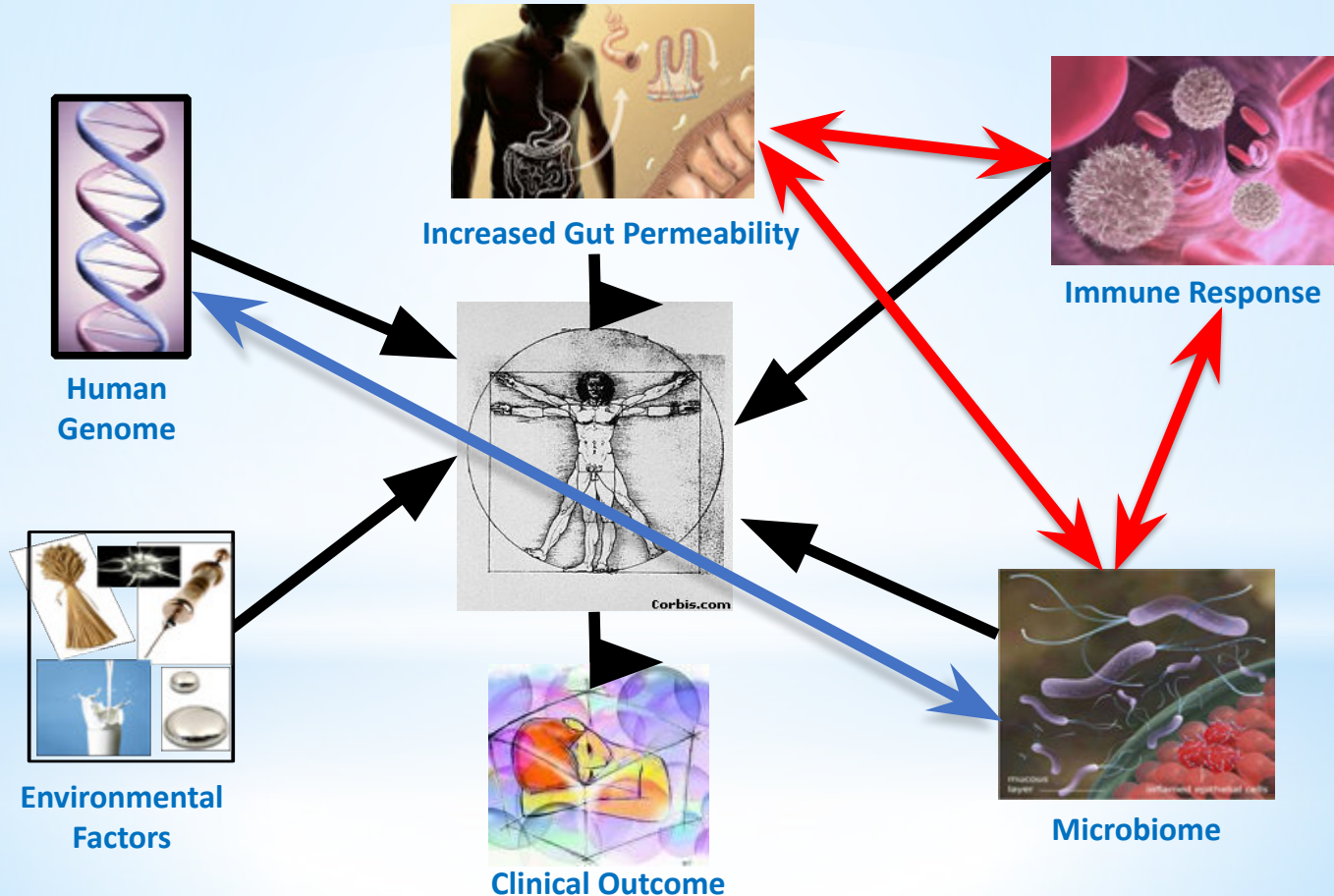
* PANS Statistics





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 asleep, 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)	Hallucinations 10%	Tics 70%

* 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) & Co-infections (Bartonella & Babesia)
- Yeast and Mold (CIRS)
- Metabolic - anesthesia, toxins, chemicals, pesticides...
- LOOK FOR:
 - History of autoimmune disorders in child &/or family
 - Preceding history
 - Infection or Febrile illness
 - Viral disease-like prodromes
 - Positive response to immunotherapy.



* Might COVID 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.

PMCID: PMC8096321

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

PMID: [33961798](#)

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

[Piero Pavone](#),^a [Manuela Ceccarelli](#),^{b,f} [Silvia Marino](#),^c [Daniela Caruso](#),^d [Raffaele Falsaperla](#),^e [Massimiliano Berretta](#),^g

[Emmanuele Venanzi Rullo](#),^g and [Giuseppe Nunnari](#)^g



- * 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

* Bartonella

- 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

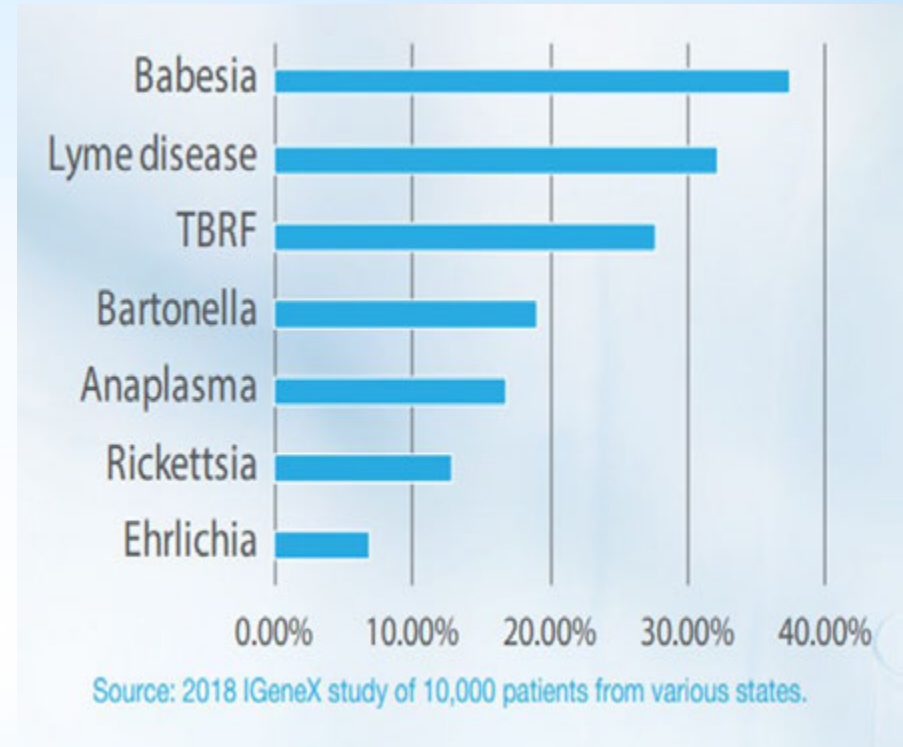


*Cases of babesiosis have increased significantly in **Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Rhode Island and Vermont.**

*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/mm7211a1.htm?s_cid=mm7211a1_w



***Babesiosis**

* Babesiosis

- 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

Mold
Tick Exposures

Chemical Exposures
Pesticides
Anesthesia

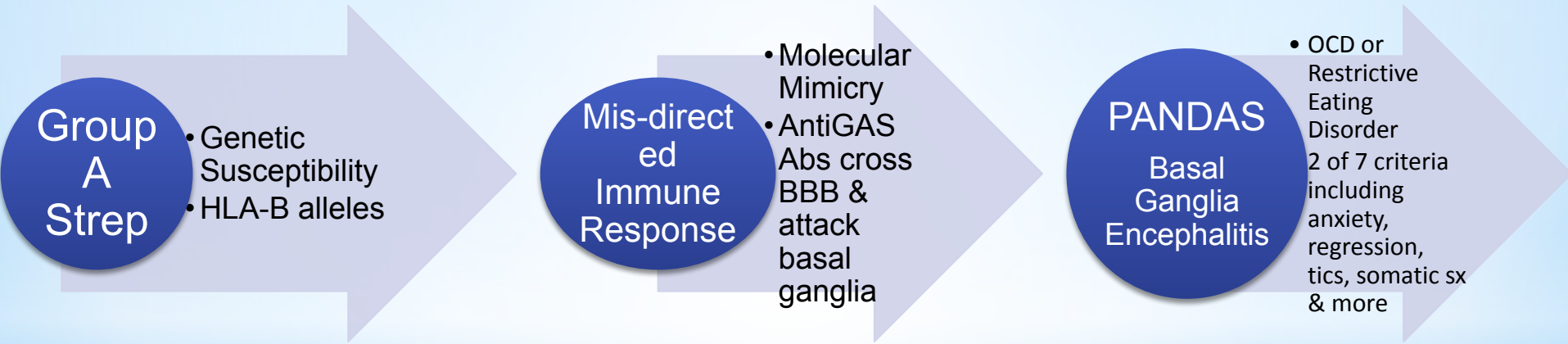
Additional Markers

Mineral & Metabolic Markers
Antioxidants
Mitochondrial Markers

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

* Etiopathogenesis for PANDAS



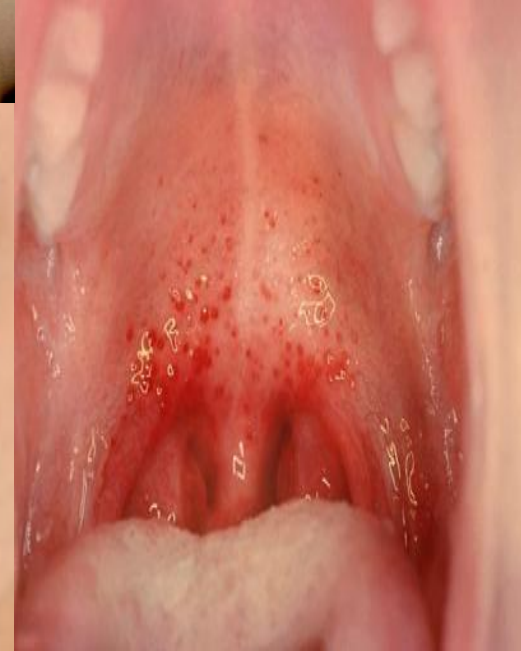
Beier K and Pratt DP, 2022

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

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

*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



© Bernard Cohen, Dermatlas: <http://www.dermatlas.org>



© Robin Stevenson, Dermatlas: <http://www.dermatlas.org>

Centers for Disease Control and Prevention, <http://phil.cdc.gov/phil/>

* Proving PANS in each child

- History and Physical Exam
 - 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 TNF-alpha, 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 :

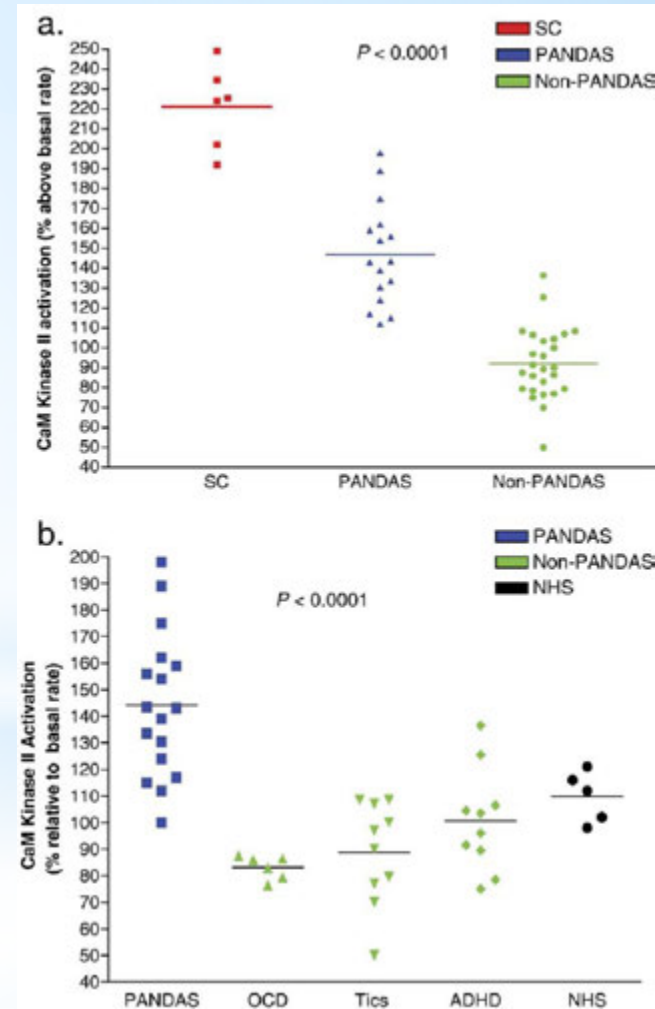
- * Mycoplasma IgG/IgM
- * Lyme and Coinfections (Bartonella, Babesia)
- * Viral markers - influenza, EBV, CMV, COVID
- * Gut dysbiosis - yeast, clostridia, parasites

Cunningham Panel

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

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

* Diagnosis





restricted intake

PANS is a clinical diagnosis requiring OCD and/or restrictive food intake...

...as well as two or more of the following symptoms:



OCD



emotional
lability



aggression



depression



irritability



deterioration in
school work



oppositional
behaviors



urinary
frequency



anxiety



sleep
disturbances



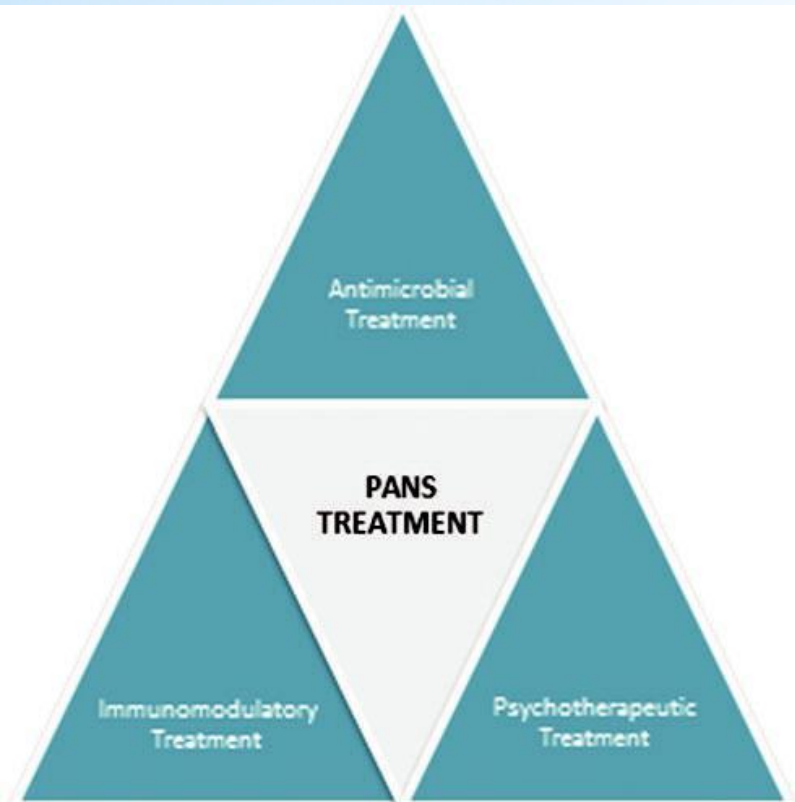
regression



sensory
abnormalities



enuresis



- *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	Therapy	Lifestyle	Adaptogens	Vit/Min/AA	Other
SSRI/SNRIs	SPACE	Breathing	Rhodiola	Magnesium	N-acetyl Cysteine
Anxiolytics	ERP (Event Response Prevention)	Mindfulness/ Meditation	Ashwagandha	Inositol	CBD/Hemp
Anti-psychotics	CBT/DBT (Dialectical Behavior Therapy)	Exercise/ Diet/Sleep	5-HTP	GABA/ Theanine	Lithium Orotate

***Treatment Options for OCD**

* OCD - N Acetyl Cysteine

- Glutathione Support - Master Antioxidant (Sulfuraphanes and Antioxidants)
 - NAC (N-Acetyl Cysteine) - Multiple studies in treatment of OCD including
 - Amino acid precursor to glutathione, helps promote detoxification.
 - Multiple studies showing the supportive effects of NAC in decreasing intrusive thoughts, anxiety, compulsive gambling, nail & skin picking, trichotillomania and promoting recovery after training, illness or stress.
 - NAC oxidizes when exposed to air so with any bottle of NAC, put each daily dose in an individualized blister pack or ziplock bag to combat this oxidation.
 - Each capsule is 600-900 mg
 - Start with 1/day or even sprinkles in children
 - Safe and effective dosing at 2400-2700 mg/day

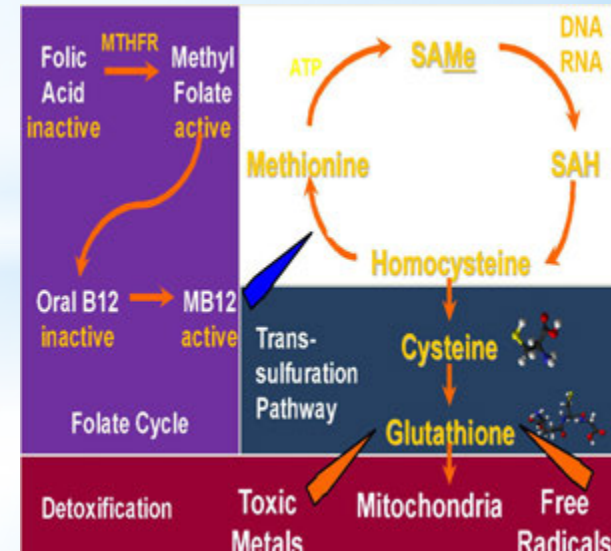
di Michele, F, Siracusano, A, Talamo, A & Niolu, C. (2018). N-Acetyl Cysteine and Vitamin D Supplementation in Treatment Resistant Obsessive-compulsive Disorder Patients: A General Review. *Current Pharmaceutical Design*, 24(17), 1832-1838.

Rodrigues-Barata, AR, Tosti, A, Rodríguez-Pichardo, A & Camacho-Martínez, F. (2012). N-acetylcysteine in the Treatment of Trichotillomania. *International Journal of Trichology*, 4(3), 176-178.

Grant, JE, Kim, SW & Odlaug, BL. (2007). N-acetyl cysteine, a glutamate-modulating agent, in the treatment of pathological gambling: a pilot study. *Biological Psychiatry*, 62(6), 652-657.

Berk, M, Jeavons, S, Dean, OM, Dodd, S, Moss, K, Gama, CS & Malhi, GS. (2009). Nail-biting stuff? The effect of N- acetyl cysteine on nail-biting. *CNS Spectrums*, 14(7), 357-360.

Grant, JE, Chamberlain, SR, Redden, SA, Leppink, EW, Odlaug, BL & Kim, SW. (2016). N-Acetylcysteine in the Treatment of Excoriation Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*, 73(5), 490-496.



* OCD

* INOSITOL (up to 18 gm/day)

* B vitamin affecting serotonin to decrease OCD, panic

- * Concerto C, Chiarenza C, Di Francesco A, Natale A, Privitera I, Rodolico A, Trovato A, Aguglia A, Fisicaro F, Pennisi M, Bella R, Petralia A, Signorelli MS, Lanza G. Neurobiology and Applications of Inositol in Psychiatry: A Narrative Review. *Curr Issues Mol Biol.* 2023 Feb 20;45(2):1762-1778. doi: 10.3390/cimb45020113. PMID: 36826058; PMCID: PMC9955821.
- * Palatnik A., Frolov K., Fux M., Benjamin J. Double-blind, controlled, crossover trial of inositol versus fluvoxamine for the treatment of panic disorder. *J. Clin. Psychopharmacol.* 2001;21:335-339. doi: 10.1097/00004714-200106000-00014.

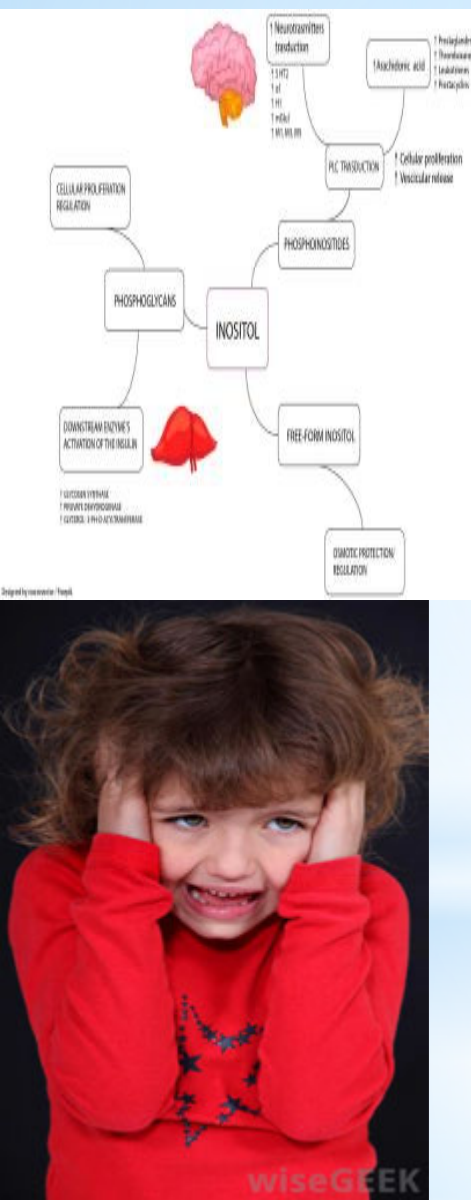
* Ashwagandha (*Withania somnifera*)

- Decreases stress and anxiety
- Improves quality of life, sleep quality & sleep onset
- Comparable efficacy in mice models to fluoxetine

- Kelgane SB, Salve J, Sampara P, Debnath K. Efficacy and Tolerability of Ashwagandha Root Extract in the Elderly for Improvement of General Well-being and Sleep: A Prospective, Randomized, Double-blind, Placebo-controlled Study. *Cureus.* 2020 Feb 23;12(2):e7083. doi: 10.7759/cureus.7083. PMID: 32226684; PMCID: PMC7096075.
- Kaurav BP, Wanjari MM, Chandekar A, Chauhan NS, Upmanyu N. Influence of *Withania somnifera* on obsessive compulsive disorder in mice. *Asian Pac J Trop Med.* 2012 May;5(5):380-4. doi: 10.1016/S1995-7645(12)60063-7. PMID: 22546655.

* Lithium Orotate - Low dose with superior BBB uptake

- * Pacholko AG, Bekar LK. Lithium orotate: A superior option for lithium therapy? *Brain Behav.* 2021 Aug;11(8):e2262. doi: 10.1002/brb3.2262. Epub 2021 Jul 1. PMID: 34196467; PMCID: PMC8413749.
- * Hamstra SI, Roy BD, Tiidus P, MacNeil AJ, Klentrou P, MacPherson REK, Fajardo VA. Beyond its Psychiatric Use: The Benefits of Low-dose Lithium Supplementation. *Curr Neuropharmacol.* 2023;21(4):891-910. doi: 10.2174/1570159X20666220302151224. PMID: 35236261; PMCID: PMC10227915.



* 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 (Schruiers 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 self-reported 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)

* ANXIETY



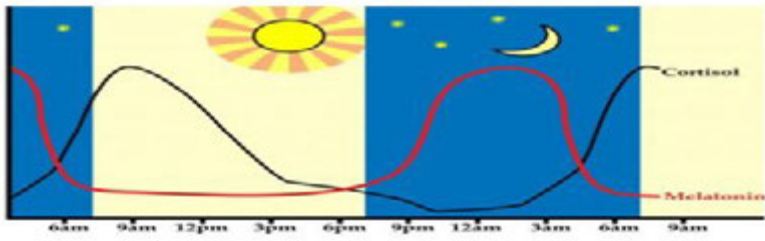
* L-MTHF/Folinic Acid (if MTHFR mutation OR CFD)

Wells L, O'Hara N, Frye RE, Hullavard N, Smith E. Folate Receptor Alpha Autoantibodies in the Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) Population. J Pers Med. 2024 Jan 31;14(2):166. doi: 10.3390/jpm14020166. PMID: 38392599

* Treating Tics

- 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)
- Cognitive Behavioral Therapy, Counter Tics, Acupuncture & physical medicine, Meditation & Mindfulness, Diet & Exercise

* SLEEP DISTURBANCES



* MELATONIN

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

* 5-HTP

- * Modulates 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)

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 yr; range 3-10 yr) 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.

FOOD 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 Toufexis¹, 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

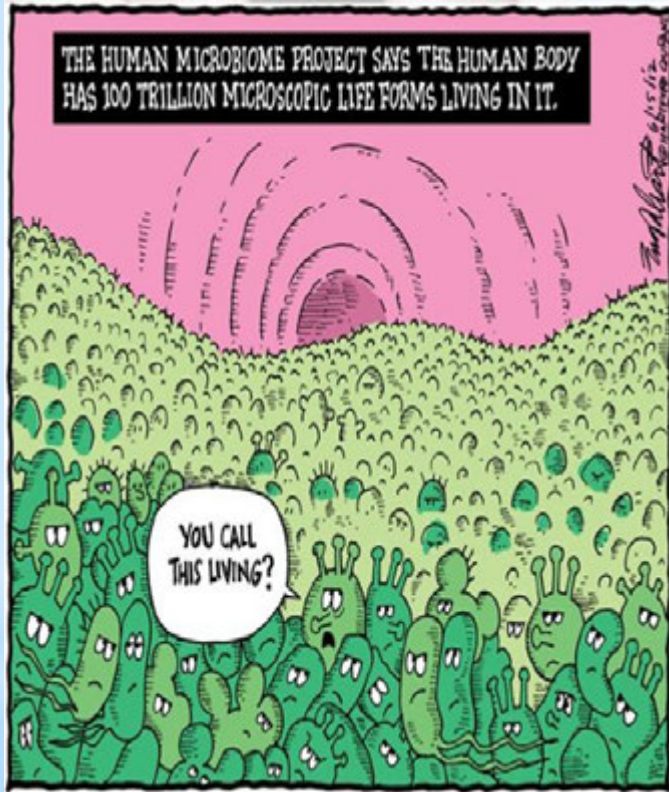


* PANS/PANDAS – TREATMENT

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 erythromycin-resistant 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 infection (Barberis et al, 2021)

- * **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)

* **ANTIVIRAL INTERVENTIONS**

- * Multiple Antibiotics
 - * Cystic/Persister
 - * 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



JAPANESE KNOTWEED

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

BERBERINE

- High activity against stationary phase *B. henselae* (Li et al., 2019)

CRYPTOLEPIS

- Active against stationary phase non-growing *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, 2007)

STEVIA

- Efficacy of leaf against all forms 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)

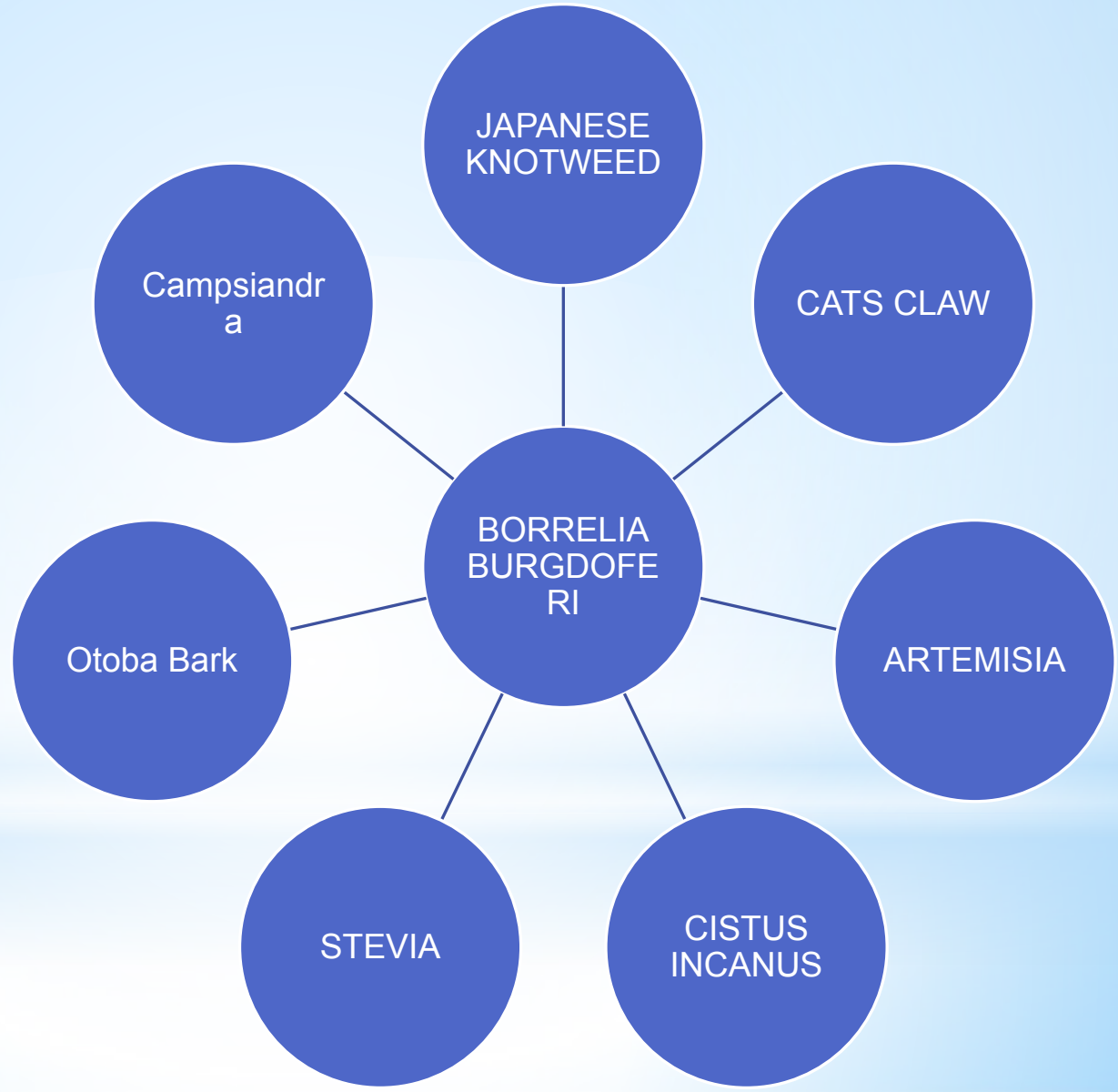
* **2 week Rotation of:**

**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/microorga
nisms11071759](https://doi.org/10.3390/microorganisms11071759)

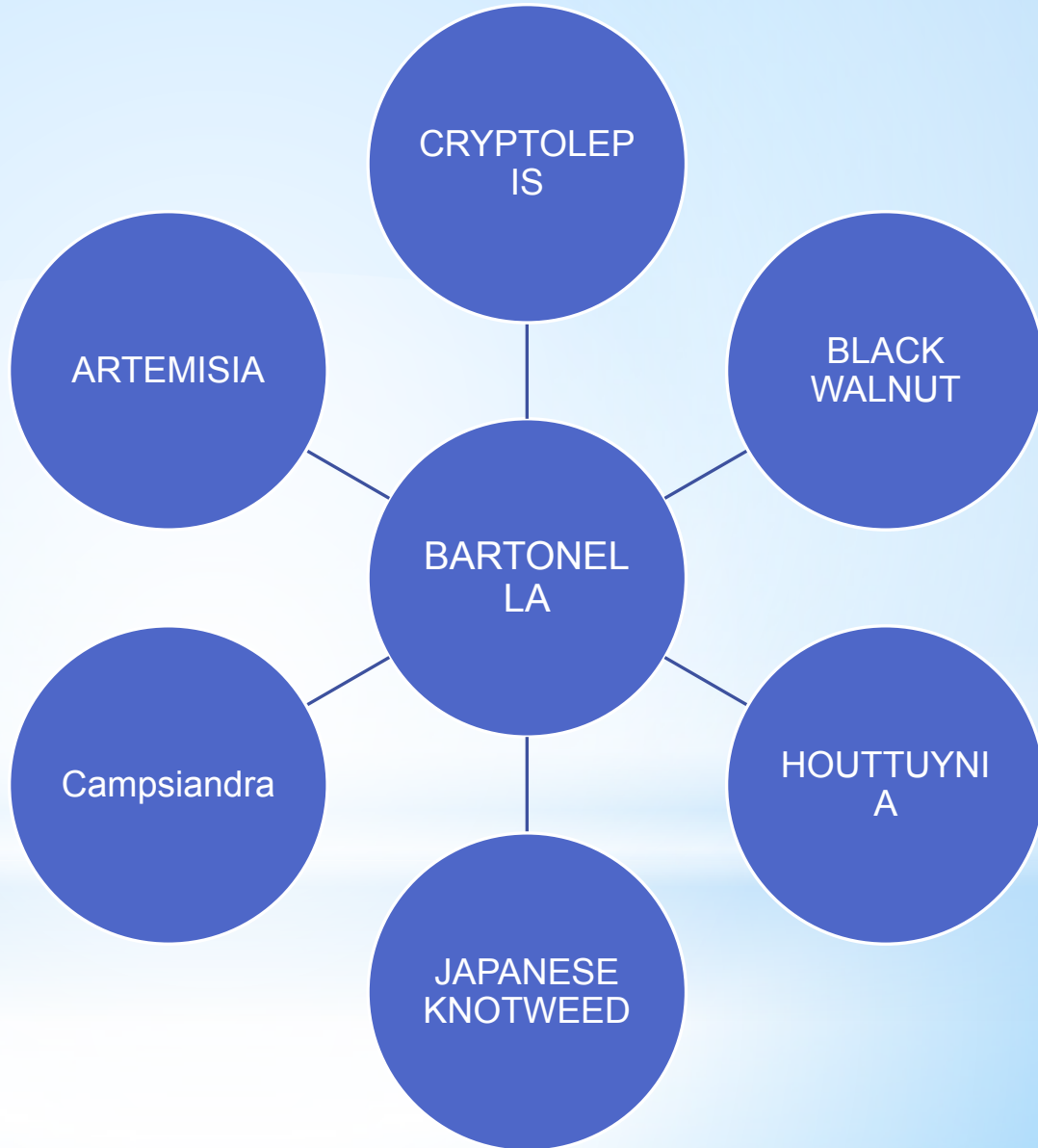


*Japanese Knotweed

**Houttynia with
Campsandra & 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.

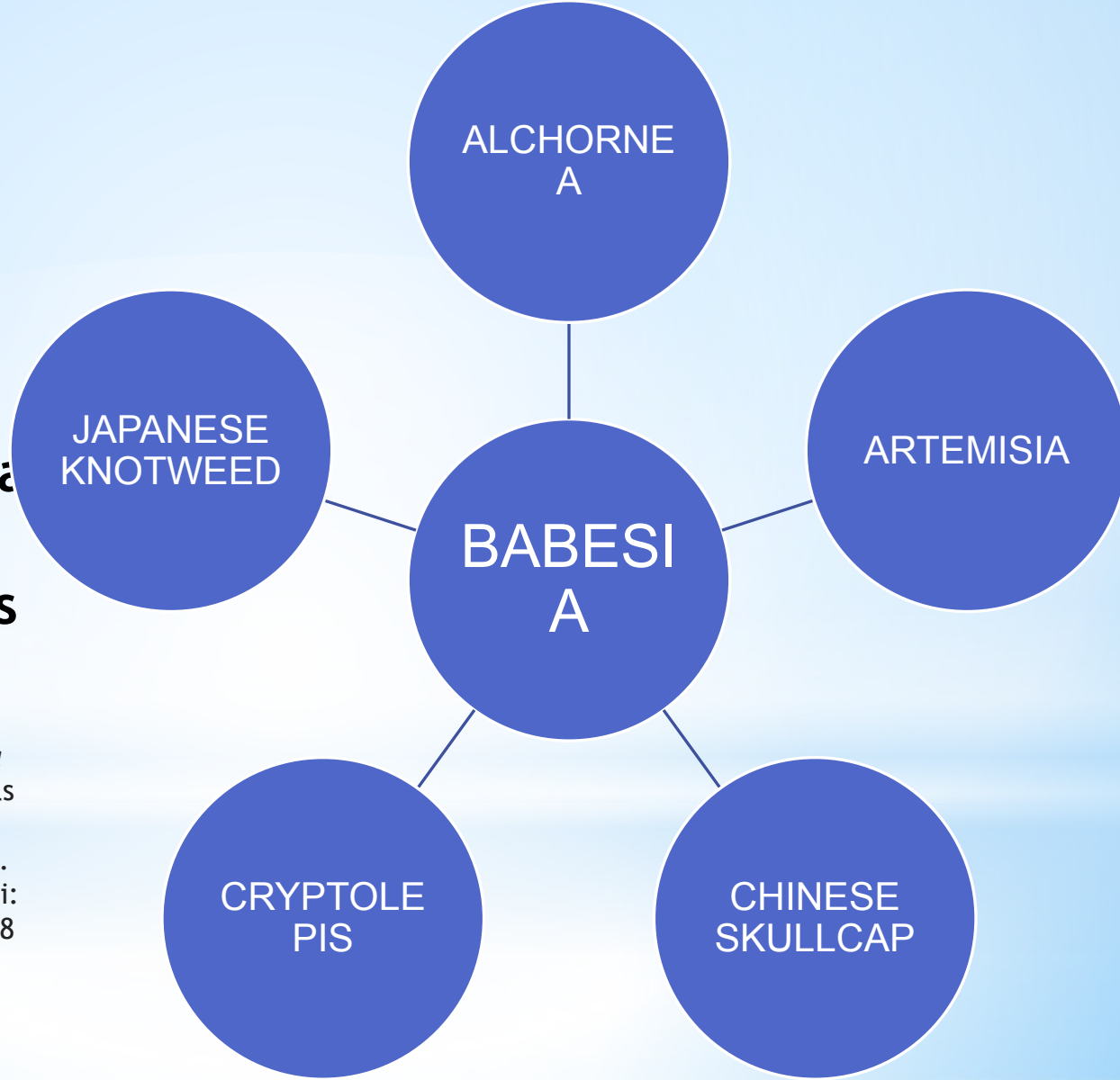


* Atovaquone & Azithromycin

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, Bacillus
- * Saccharomyces Boulardii

* Essential Fatty Acids-Omega 3 (EPA/DHA) & 6 (GLA) - Belluzzi et al, 1996

- * 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)



* EGCG

- * Inhibits inflammatory cytokines -TNF-alpha, IL-6, IL-8, VEGF (Menegazzi et al, 2020)
- * Protective to the mitochondria

* Medicinal Mushrooms

- * **Cordyceps** - study revealed that mice infected with streptococcus pyogenes and treated with cordyceps did not have bacterial dissemination as seen in control group (Holliday J and Cleaver M, 2004)
- * **Lion's Mane** - increases immune system in the intestines (Sheng et al, 2017)
- * **Reishi** - increase Th1 cytokine activity and downregulate th2 (Guggenheim et al, 2014)



* Additional Immune Support

- Ibuprofen
- Low Dose Naltrexone (LDN topically or orally)
- 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 Neuropsychiatric Syndrome Clinic

Kayla D Brown^{1 2}, Cristan Farmer³, G Mark Freeman Jr^{2 4}, Ellen J Spartz^{1 2}, Bahare Farhadian², Margo Thienemann^{2 5}, Jennifer Frankovich^{1 2}

*** Additional
Immunomodulators &
MCMD**

* Treatment - Immune Modulators

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

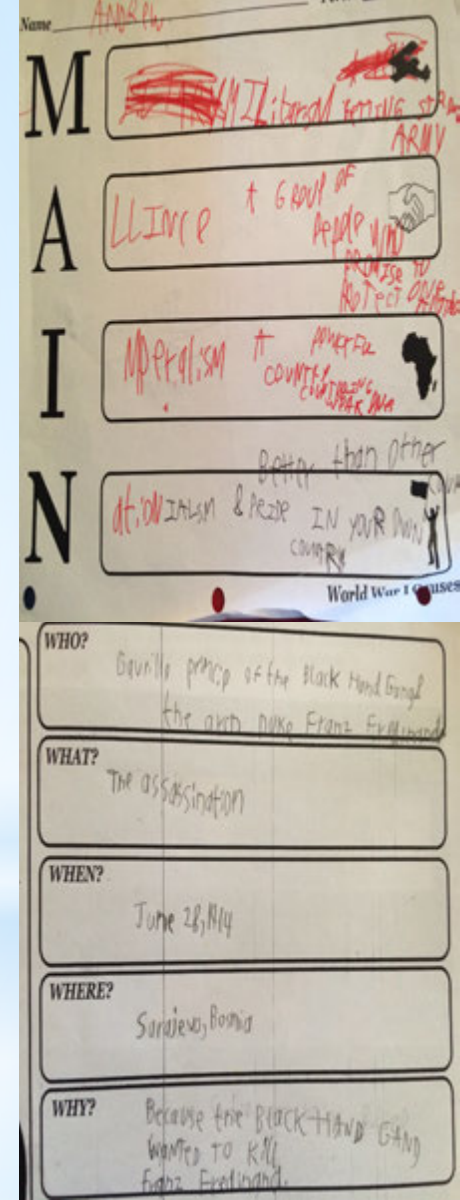
- Short burst - therapeutic & diagnostic
- Temporary fix in some
- Transient worsening typical

IVIg

- No improvements in sham IVIg group; significant decrease in OCD severity in IVIg and plasmapheresis 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)

Plasmapheresis - 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 et al, Int 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

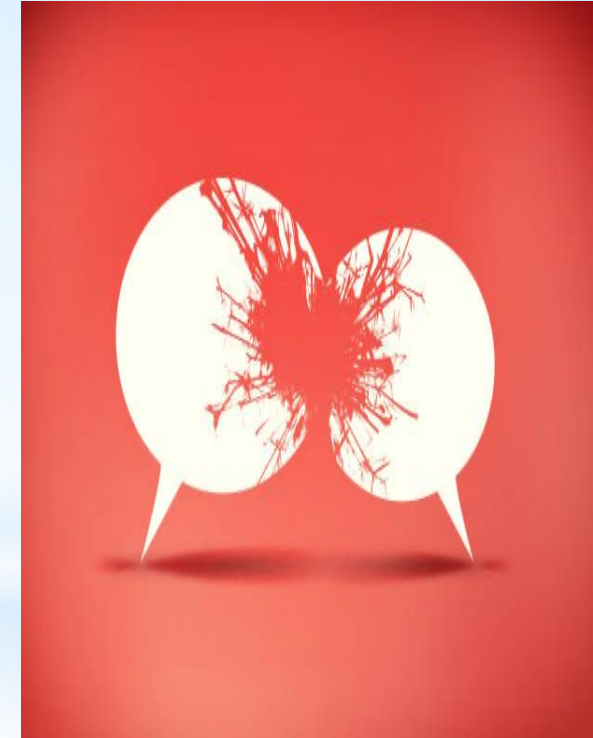
PANDAS – Other Treatment Options



* You
Can Do
This!

* So Why All The Controversy?

- 79% of pediatricians will treat presumed Strep with antibiotics without a positive culture.
- Timing of strep infection or exposure
- If child is treated with Amoxicillin several times in their lifetime and then is suspected of having PANDAS and treated with Amoxicillin alone might not help the symptoms, as the child may now be resistant to Amoxicillin
- Multiple studies but small number of prospective studies exist
- Kitschy and overused acronym
- Autoimmune disease with multiple triggers



- * Clinical suspicion
 - * Behavioral changes (OCD, tics, anxiety) & More
 - * Handwriting changes
 - * Somatic symptoms
 - * After strep infection
 - * With strep exposure
- * Possible Physical exam findings
 - * Choreiform movements
 - * Handwriting changes
- * Response to immunomodulatory interventions



*** So How Do I Know
It's PANDAS?**



- * Initial course 3-4 weeks

- * Improvement

- * Wean to prophylaxis

- * Herbs? Azithromycin?

- * Without improvement

- * Change antimicrobial

- * Reassess

- * What have I missed?

- * **Length of Treatment**

- * Ibuprofen
- * Turmeric
- * Acute Viral Protocol (Vitamins A & D, Zinc, Lysine)
- * Further immune support (what helped before)
- * Figure out the trigger and treat accordingly
 - * Exposure to strep (culture child even if without throat symptoms)
 - * Exposure to viruses including COVID
 - * Tick bite or endemic area exposure
 - * Mold or water damage
 - * Teething or dental procedures
- * Breathe - your stress/parent stress increases child's symptoms

*Treatment of Acute Flares

- One step, one child at a time
- Podcast - *Demystifying PANS/PANDAS*
- Consider mentoring - drohara.com/mentoring
- Consider membership - drohara.com/membership
 - Discount codes In May & October
 - Short videos
 - Longer lectures
 - Live & recorded Q & As with experts in the field
 - Monthly live and recorded teachings
 - Resource section

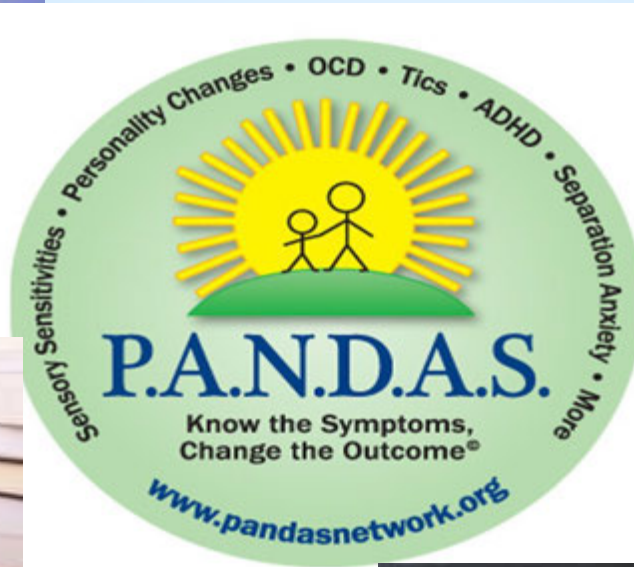
* How Can I Do This?



Nancy O'Hara, MD, MPH, FAAP
PEDIATRIC NEUROBEHAVIORAL HEALTH

* PANS/PANDAS Recap

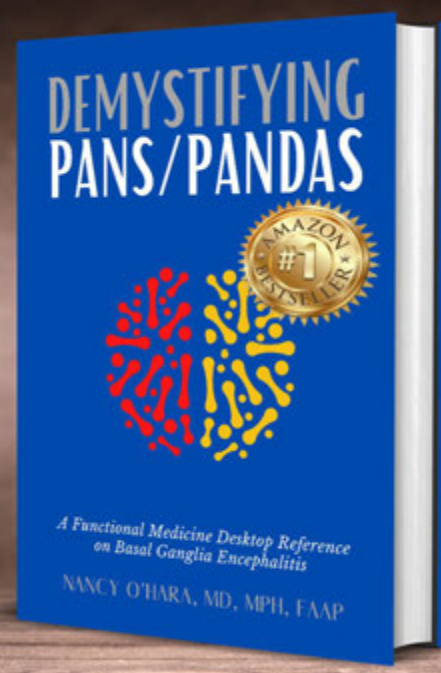
- Clinical diagnosis confirmed (or not) by laboratory evidence
- Complete medical & psychiatric history and physical exam
- Cultures and blood testing
 - Strep titers (ASO, antiDNaseB antibody), Mycoplasma IgG and IgM
 - Appropriate Borrelia, Bartonella, Babesia suspicion and testing
 - Immune markers (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, polysomnography) Chang et al, J Child Adol Psychopharm, 2015
- Use treatment as diagnostic tool as well as therapeutic intervention (antimicrobials, nutraceuticals, immunotherapy, diet, therapeutic 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
 - Don't let anyone blame the child; find someone to partner with you & your child

Do not go where the path may lead.
Go instead where there is no path
and leave a trail...
-Emerson



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