

PANDAS: Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection



Overview

- What are PANDAS and PANS?
- Symptoms
- Diagnosis
- Treatment



Your Child Has Changed



Should you consider
PANDAS?
Let's talk

www.Latitudes.org

Common presentation:

- Separation anxiety, school refusal
- Sleep problems
- Worried about disasters, anxiety
- OCD – food refusal
- Rages
- Tics
- Frequent urination/bedwetting
- Sensory issues
- Change in handwriting, learning

PANS/PANDAS

Know the Signs. Know the Treatments.

Behavioral Regression

You can see the difference between the self-portrait during a PANS flare with regression and the self-portrait while the child was healing.

During Flare



In Treatment

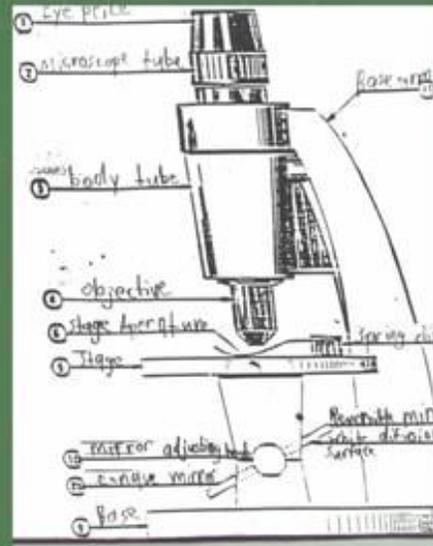


If a Child has Sudden, Acute Onset of OCD and/or Food Restriction & Multiple Neuropsychiatric Symptoms, Consider PANS/PANDAS.

Handwriting Deterioration

Prior to acute onset of PANDAS, the student could write neatly. After, handwriting becomes almost illegible and not neatly placed on the paper.

Before PANS



During Flare



Images Credit: Susan E. Swedo, M.D. Pediatrics & Developmental Neuroscience Branch NIMH, NIH Intramural Program

Diagnostic Criteria

1. Presence of OCD and/or tics
2. Age Requirement (between 3 years and puberty)
3. Acute onset and episodic (relapsing-remitting) course
4. Association with Group A Streptococcal (GAS) infection
5. Association with neurological abnormalities: hyperactivity, choreiform movements

Comorbidities: urinary frequency, mydriasis and insomnia

Not better explained by Tourette, Sydenhams Chorea, SLE, NMDI receptor or other autoimmune encephalitis

Journal of Child and Adolescent Psychopharmacology, Special Edition February 2017 (27) 1

PANDAS vs PANS

- PANDAS: disorder with specific cause and disease mechanism: postinfectious basal ganglia encephalitis
 - PANS: syndrome with a collection of behaviours, signs and symptoms without any regard for disease mechanism
- PANS TRIGGERS:
 - Mycoplasma
 - Virus: HHV6, influenza
 - Sinusitis
 - Chickenpox
 - Influenza
 - Lyme
 - Drug ingestion
 - Heavy metal poisoning
 - Pesticide poisoning

Common OCD behaviours in children with PANS

- Doorway rituals, switches
- Contamination fears
- Compulsive handwashing
- Counting/touching rituals
- Symmetry issues
- Excessive confessing

Swedo SE, Leckman JF, Rose NR (2012) From Research Subgroup to Clinical Syndrome: Modifying the PANDAS Criteria to Describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome). *Pediatr Therapeut* 2:113.

Overlap with

- Eating disorders:
 - ARFID: Avoidant/Restrictive Food Intake Disorder
 - Anorexia nervosa
 - Bulimia
- Behavioural and mood disorders:
 - Oppositional and defiant disorder
 - ADHD
 - Depression, suicidality
 - Mood swings
 - ? Autism
- Always rule out abuse: 13% of adults have a history of physical or sexual abuse



Examination findings

- Agitated and anxious child
- Tics
- Large pupils – autonomic dysfunction
- Tongue with strawberry spots
- Tonsils inflamed (microabscesses)
- Peeling fingertips and inflamed nailbeds
- Rhomberg: piano playing fingers
- Urinary frequency or accidents



PANDAS/PANS Diagnosis

- Check for group A beta haemolytic streptococcal infection: swab (throat, nose, anus), rising ASO and antiDNAse B titres; other infections, toxins
- Estimated 1% of primary school age children
- Controversy about existence of this disorder
- Just like RF and SC: some strep infections are subacute, only some serotypes are causative, not everyone gets it
- Genetic susceptibility – mild immunodeficiency
- Family history of autoimmune disorder, rheumatic fever

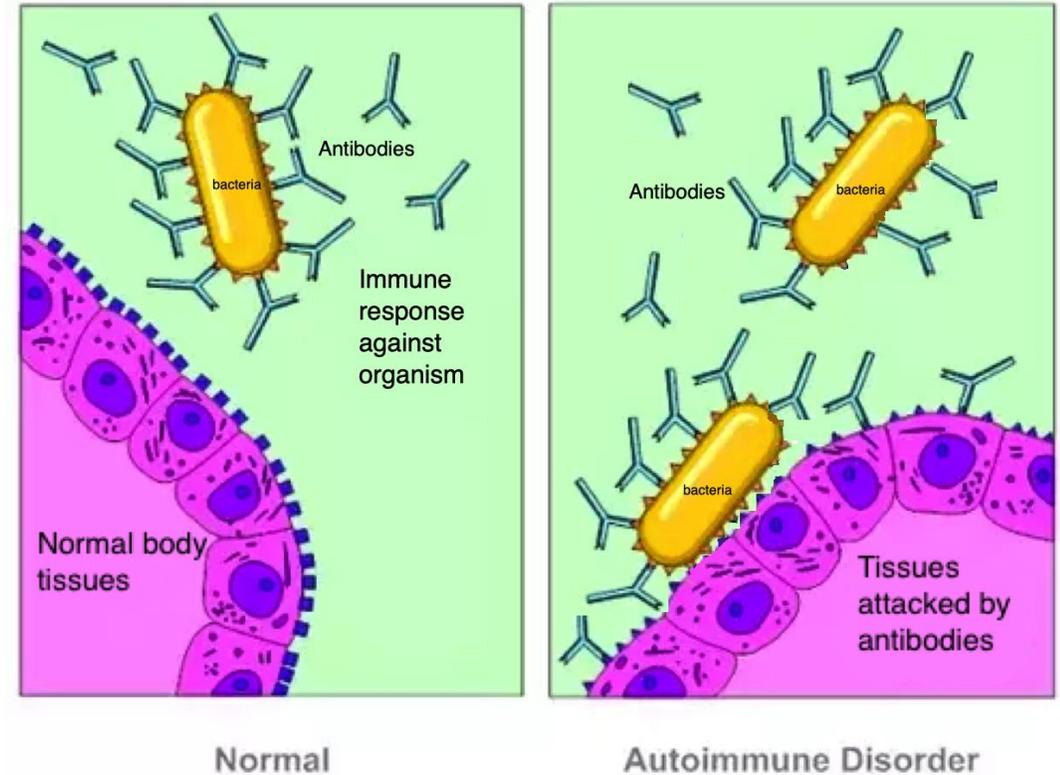
Is it always acute?

- Acute and sub-acute onset patients have similar symptoms and lab markers
- Relevance for children with diagnosis of ADHD or ASD

Jennifer Frankovich, Margo Thienemann, Jennifer Pearlstein, Amber Crable, Kayla Brown, and Kiki Chang. Multidisciplinary Clinic Dedicated to Treating Young with Pediatric Acute-Onset Neuropsychiatric Syndrome: presenting Characteristics of the First 47 Consecutive Patients. *Journal of Child and Adolescent Psychopharmacology*. 2015. (25): Issue 1

Pathophysiology

- Autoimmunity: Strep A bacterial cell wall contains molecules similar to those found in human heart, kidney, and brain tissue.
- Molecular mimicry: serum antibodies against strep cross the BBB and target basal ganglia and dysregulate basal ganglia functions
- TH17 helper cells produced in nasal cavity after recurrent strep infections move along the olfactory nerve into the olfactory bulb in the brain, break down the BBB and allow autoantibodies and TH17 cells to enter and cause neuroglia inflammation in the basal ganglia



EFFECTS OF BASAL GANGLIA INFLAMMATION

“Seeing Your First Child with PANDAS/PANS” by Margo Thienemann, MD and
The PANDAS Physicians Network Diagnostics and Therapeutics Committee

**Basal ganglia is a relay station through
which run neurons that control:**

Inflammation may cause:

Mood and emotion

OCD, Mood lability, Anxiety

Behavior

OCD, Rage, Developmental regression

Procedural learning

Handwriting changes, Clumsiness

Motor Movements

Tics, Choreiform Movements

Cognition

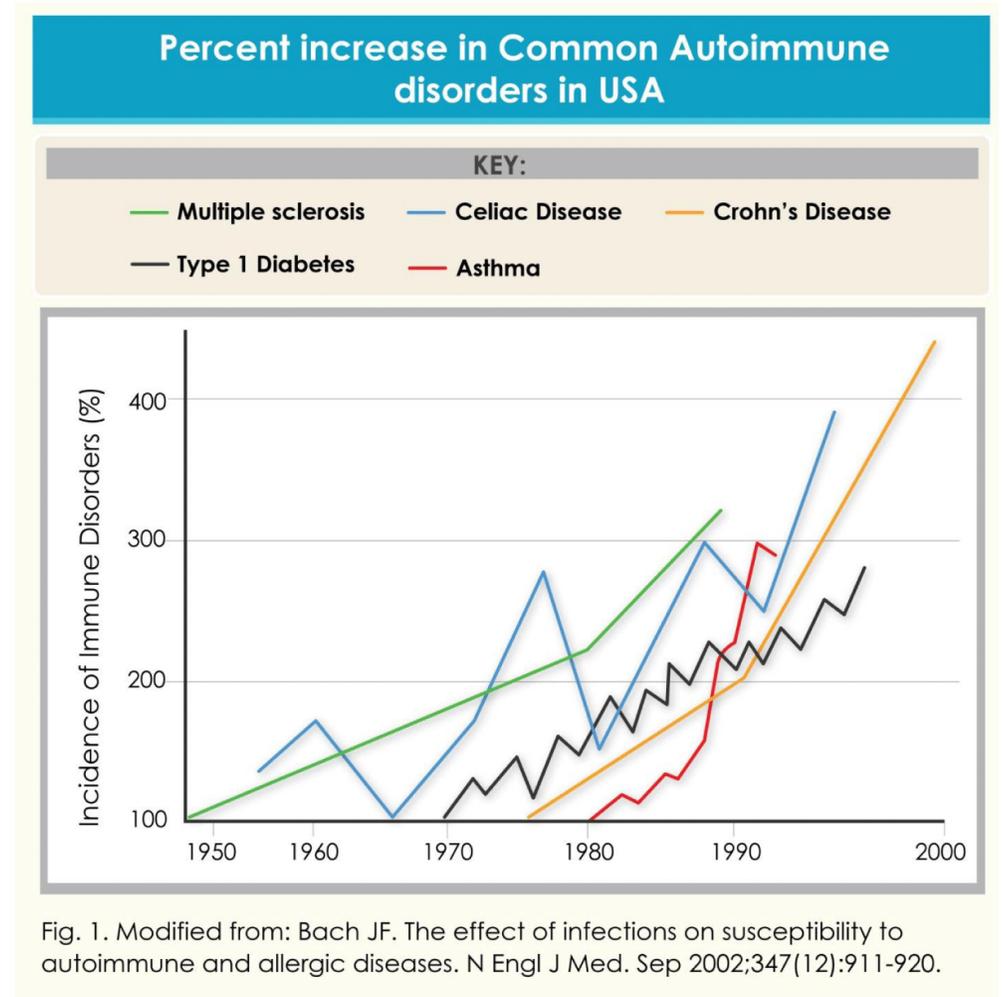
**Slow processing speed, Memory issues
specific Sensory learning deficits
(often Math)**

Sensory

**Sensitivity to light, sounds, smells,
tastes, textures**

Why so much PANDAS

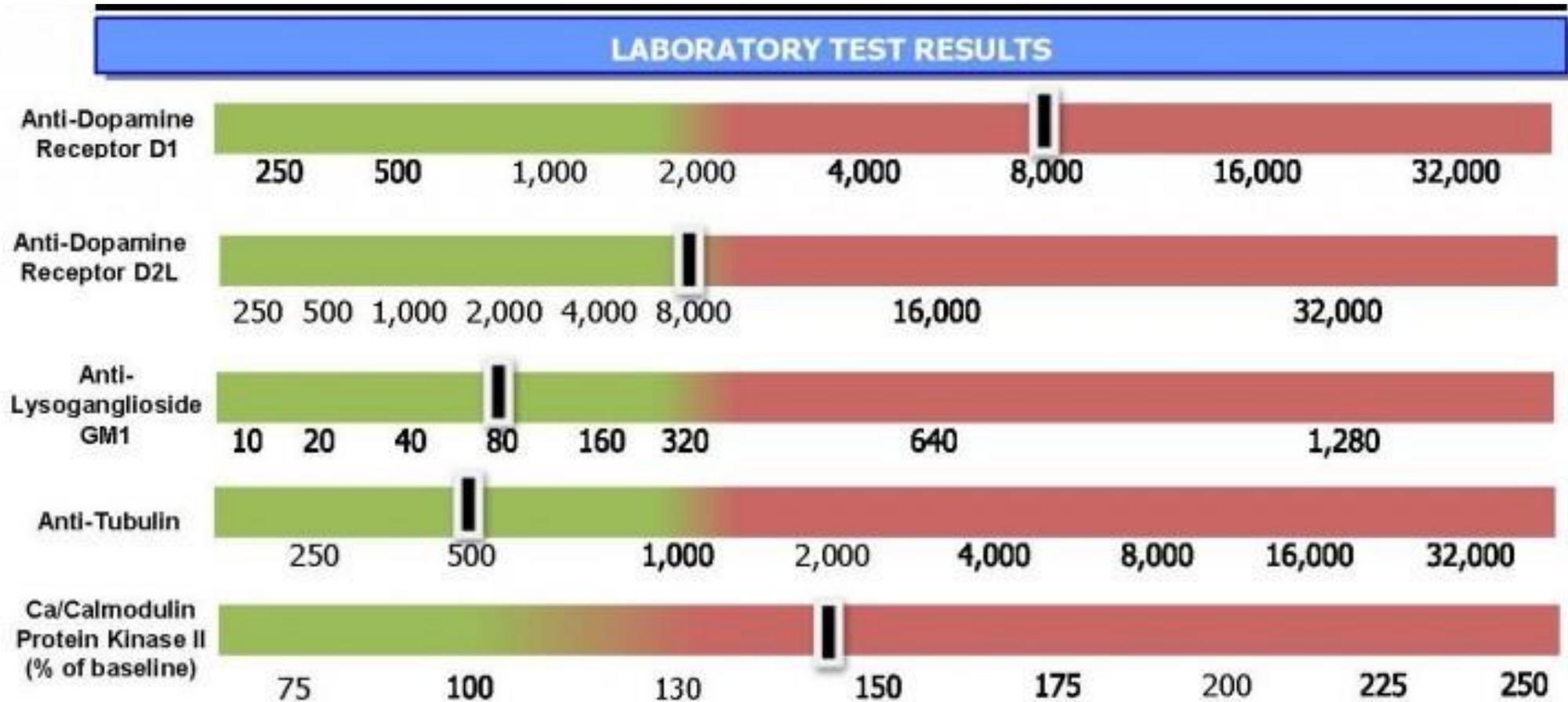
- Auto-immune diseases are all on the rise
- Hygiene, Vitamin D, nutrition, microbiome depletion
- Antibiotic use increases carrier status
- Increased rate of exposure - crowding
- Increased awareness – often misdiagnosed as Tourette syndrome, psychosis



Laboratory tests

- Throat, nasal, anal swab
- ASOT, anti DNase B
- Full blood count
- CRP
- Vitamin D
- Ferritin
- Liver function: AST/ALT ratio
- Renal function: bicarb
- ? Zinc, selenium
- ANA
- Immunoglobulins
- Mycoplasma serology
- HHV6, influenza
- Cunningham panel?

Cunningham Panel



Treatment guidelines for PANS/PANDAS

- **Reduce inflammation:** trial of nurofen 3 days; 5 day burst of steroids
- **Treat infection:** Bacterial: Augmentin, Pen VK or Azithromycin for 3-4 weeks. Change if not better after 2 weeks. Viral: acyclovir.
- **Treat anxiety/OCD:** SSRI (side effects)
- **Treat immune activation:** IVIG, plasmapheresis

Treatment - integrative

- **Alternatives to antibiotics:** Taiga, Berberine, Usnea, oregano; vitamin C and A
- **Boost immune system and reduce inflammation:** anti-inflammatory diet, vitamin D, zinc, curcumin, omega 3 (SPM), quercetin,
- **Protect/modulate microbiome:** probiotics (e coli; d lactate free)
- **For OCD/tics:** magnesium, NAC, Glutathione, inositol, 5 HTP
- **Calming:** Gaba, glycine (Gaba promoter), lithium orotate, Adaptogens, CBD

OMEGA 3 fatty acids

Keratosis pilaris, bumpy, dry skin on upper arms: low EFA



Modulate immune system: SPM

Specialized Pro-resolving lipid Mediators

- Active resolution process of inflammation in the body
- New classes of small, local acting endogenous biological factors that act like local hormones with brief action
- Made from precursors of omega 3 fatty acids
- Prevent excessive inflammation and promote removal of microbes and apoptotic cells
- Resolve inflammation and return to tissue homeostasis

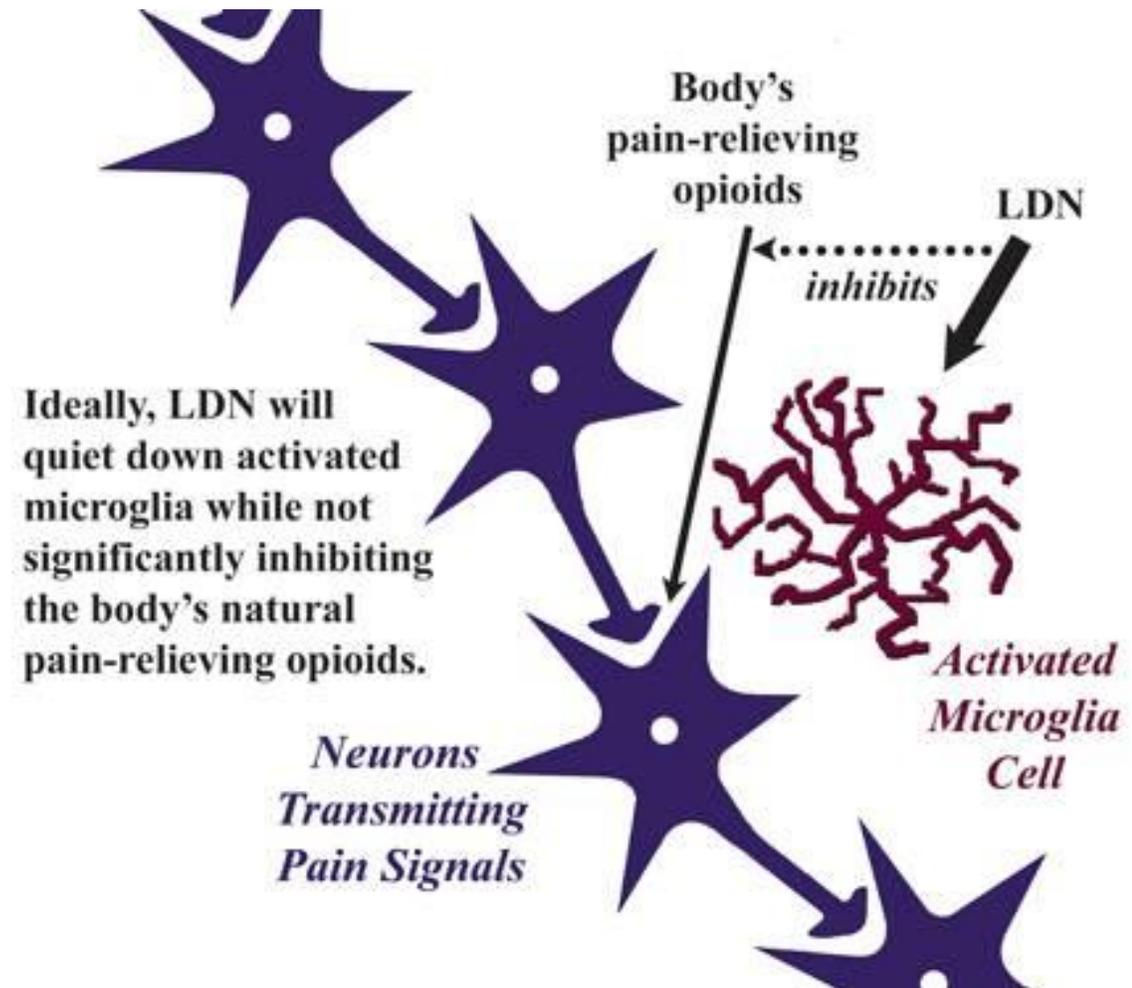


Low zinc:
almost the norm in NZ and Australia



Modulate immune system: LDN

- LDN: Low dose naltrexone 1-3mg given at night
- Opioid antagonist
- At low dose: rather than blocking opioid receptors, can block non-opioid receptors (Toll-like receptor 4) on brain microglial cells
- potent anti-inflammatory effect
- Cave sleep problems



Further Treatment Considerations: Mind

- Positive parenting and care: Triple P
- Mindfulness - Smiling Mind App
- Breathing training
- Nature therapy – green prescription
- Didactic behavioural therapy or CBT
- Support groups for parents, child and siblings
- Work with schools on PANDAS/PANS education
- Osteopathy, chiropractic, acupressure, neurofeedback...



Gut flora transfers anxiety



Collins S et al. The adoptive transfer of behavioral phenotype via the intestinal microbiota: experimental evidence and clinical implications. *Current Opinion in Microbiology*. 2013;16 (3) 240-245,

Environmental toxins and anxiety

- Organic solvents, benzene
 - Dry-cleaning, paint thinners, pesticides, nail polish
- Methyl Chloride in swimming pools
- Mould
- Heavy metals
 - Aluminium, arsenic, **lead**, manganese, **mercury**
 - Brown JS. Psychiatric Issues in Toxic Exposures. 2007 Psychiatr Clin N Am 30 837-854.



Recurrences

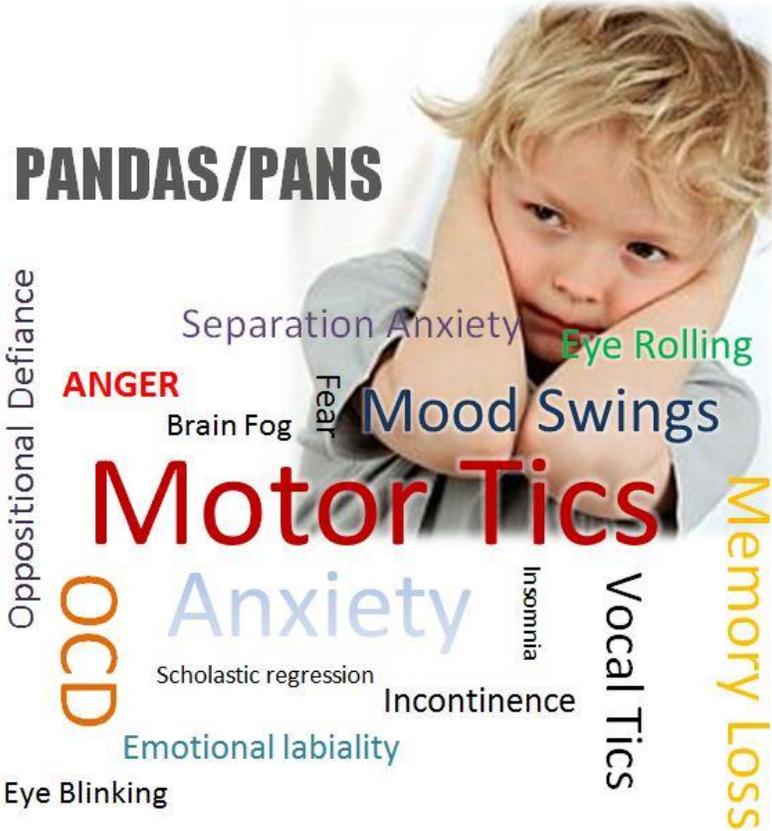
- Exposure to strep/virus carriers – swab the family
- Seasonal: allergies
- Environmental: toxic exposures
- Stress
- Emergency kit: restart treatment that worked previously
 - Nurofen/steroids
 - Antibiotics
- Consider prophylactic antibiotics
- Microbascesses: Tonsillectomy?

Summary

- **Trial of anti-inflammatory tx:** nurofen, steroids
- **Identify the trigger** so you know what to treat
 - Swabs or blood test for streptococcal antibodies
 - If negative test further
 - EBV, HHV-6, HHV 1+2, Mycoplasma pneumonia, EBV, Parvo B-19, Coxsackie A+B, CMV, measles, mumps, rubella
- **Treat the trigger to get the titers back to normal:**
 - antibiotics?, herbs – Taiga; antivirals?, vitamin A
- **Reduce inflammation**
 - Diet. Vitamin D, Omega 3/SPM, zinc, curcumin, quercetin, NAC; avoid toxic exposure
- **Calming anxiety and tics:**
 - Magnesium, NAC, CBD oil
 - Adaptogens Ashwaganda (herbal Valium), Rhodiola reduce adrenal stress
- **Modulate immune system**
 - LDN
 - IVIG

Further Considerations

- Food sensitivities/leaky gut
- Methylation defects
- Mitochondrial dysfunction
- Thyroid and adrenal dysfunction
- Environmental toxin testing



Pandasnetwork.org

Pandasppn.org

Pandas Physicians Network





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Children's **HEALTH** A^{to} Z



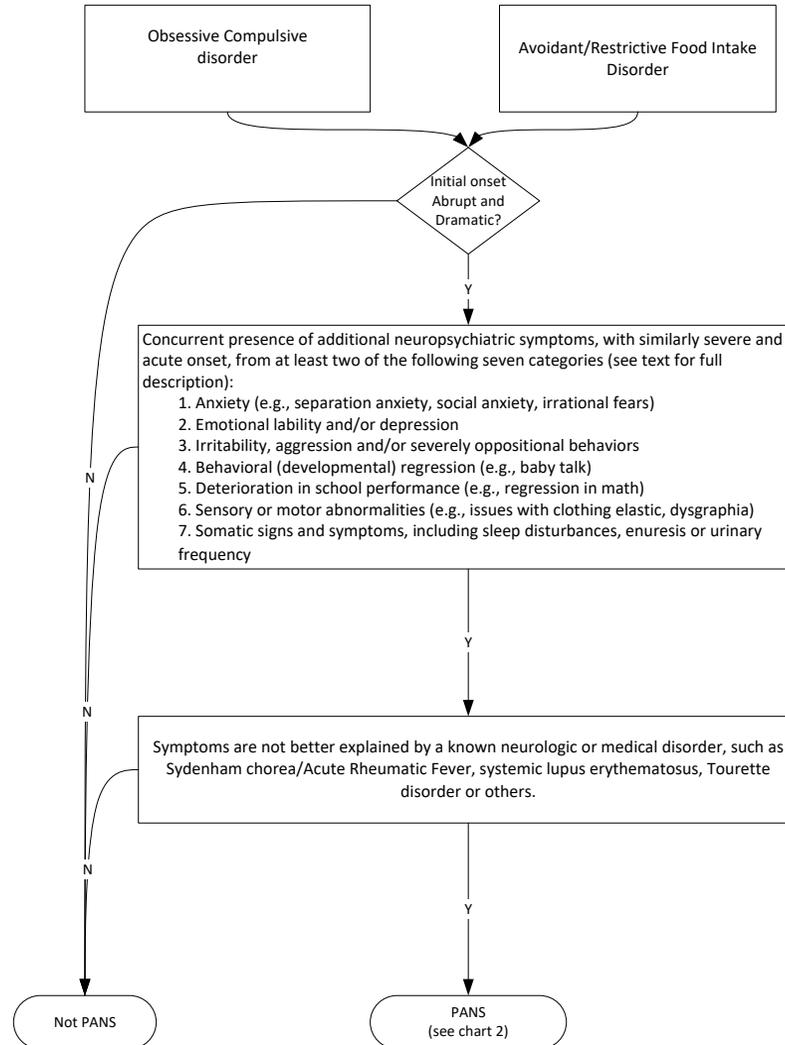
*Help
your child
get better
and stay well
naturally*

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PANDAS FLOW CHART



Common Obsessive Compulsive symptoms in children are:

- Doorway rituals
- Contamination fears
- Compulsive hand washing
- Counting/Touching ritual
- Symmetry issues
- Excessive confessing

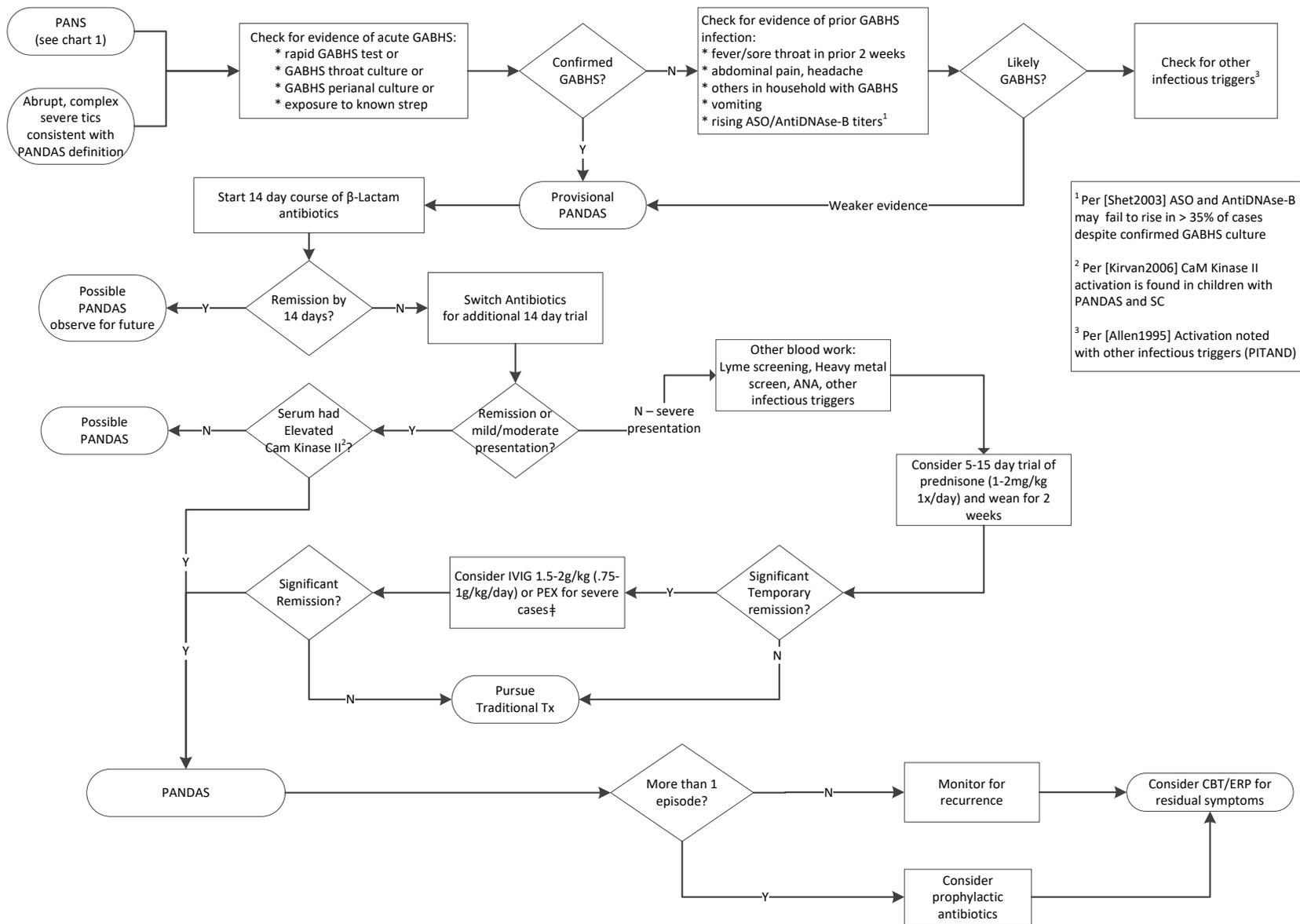
To be considered for PANS, the child must meet the DSM 5 criteria for OCD or be diagnosed with avoidant or restrictive food intake disorder.

Abrupt and dramatic onset is defined as significant behavioral change that is typically isolated to a particular day or week. Typical presentation has a shift of >16 pts in CYBOC scores. Unlike traditional OCD or ED, many parents can name the time/day when onset occurs in their child

In children, daytime urinary frequency (with no apparent UTI) is a common first clinical complaint.

The diagnostic work-up of patients suspected of PANS must be comprehensive enough to rule out these and other relevant disorders. The nature of the co-occurring symptoms will dictate the necessary assessments, which may include MRI scan, lumbar puncture, electroencephalogram or other diagnostic tests.

Swedo SE, Leckman JF, Rose NR. [From research subgroup to clinical syndrome: modifying the PANDAS criteria to describe PANS \(pediatric acute-onset neuropsychiatric syndrome\)](http://dx.doi.org/10.4172/2161-0665.1000113). Pediatrics & Therapeutics 2012, 2:2. On-line article available at: <http://dx.doi.org/10.4172/2161-0665.1000113>



¹ Per [Shet2003] ASO and AntiDNase-B may fail to rise in > 35% of cases despite confirmed GABHS culture

² Per [Kirvan2006] CaM Kinase II activation is found in children with PANDAS and SC

³ Per [Allen1995] Activation noted with other infectious triggers (PITAND)