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# PANDAS & PANS An Integrative Approach

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#### Course details

7 Modules on-demand

Downloadable slides and resources mentioned are found in each Module under the Materials tab

Quizzes are at the end of the lessons where they pertain

Certificates of completion are sent for all student types

CME/CE certificates - please allow 1 week

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Survey

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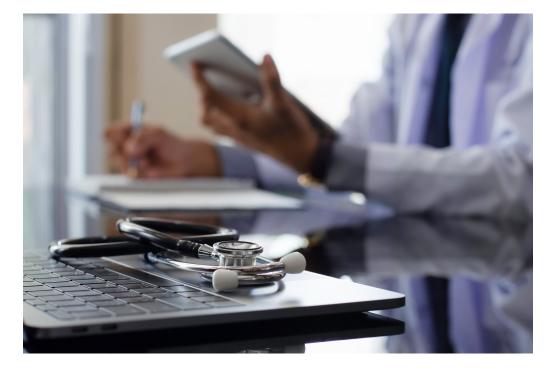
Please support my work and the voluminous hours I've spent collating my years of experience and research to put together this scientific presentation.

Please resist your healer's heart urge to share widely - even and especially if you're a parent! I understand - I've been there.

And I paid my kids' doctors with gratitude.

I ask for the same consideration.

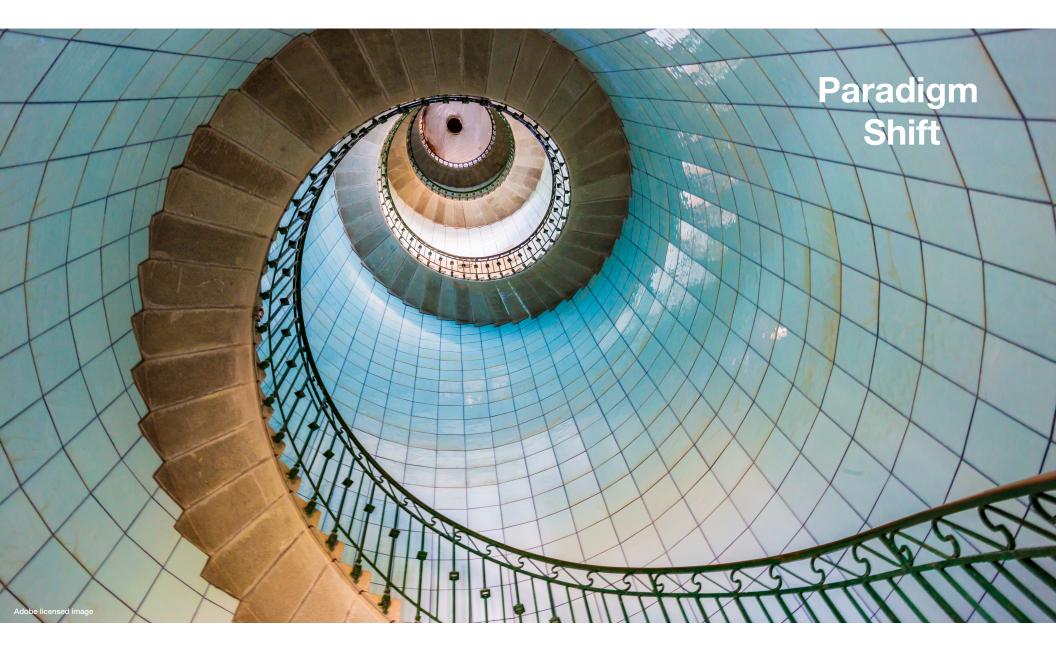


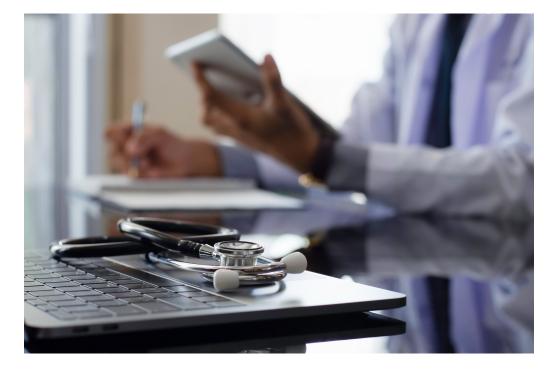


#### **Course Outline**

- 1. Symptoms
- 2. Mechanisms
- 3. Diagnostics
- 4. Conventional treatment approach
- 5. Integrative treatment approach
- 6. Recovery essentials
- 7. Cases







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# Autoimmune encephalopathies

PANDAS = pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection

PANS = pediatric acute-onset neuropsychiatric syndrome

A third category? "PLANS" or "NADAL"

Autoimmune encephalitis (AE) found to be as common as infectious encephalitis (Mayo Clinic 2018)

Antecedent state: immune depletion

Autoimmune trigger: INFECTIONS &/or TOXICANTS

Target tissues depend on specific type of AE

PANDAS/PANS/BGE ~ brain stem/basal ganglia, GI, kidneys (theorized)



#### Overview

Incidence: Lacking large population data, however roughly estimated as 1 in 200-250 children

Prevalence: males>females 2.6:1

FHx: autoimmune disease

Autoimmune relapsing-remitting pattern

Average 3 month pattern

Challenge of mgmt: Wax: flare/natural progression or new exposure? Wane: treatment effect or natural remission?

Some variation PANDAS vs PANS

Different diagnostic criteria



#### **PANDAS**

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NATUROPATHIC

Previous Streptococci group <u>A</u> infection Presence of antistreptococcal antibodies Neurological impairments Children and young adolescence affected

OCD Tics Rapid and acute onset Abrupt changes in behaviour ADHD-like behaviours Impaired eating habits Sleep disturbances Dysuric syndromes Changes in gut microbiota Autoantibodies to dopamine D1 and D2 receptor, tubulin and lysoganglioside Decrease of learning outcome Lack of concentration Difficulty with memorizing Changes in handwriting/dysgraphia Sensory impairments Visual and auditory hallucinations Hyperactivity Aggressiveness Behavioral regress Oppositional behaviour Dilated pupils **Emotional lability** Depression Irritation

No association with Streptococci group A infection Lack of distortions within central nervous system Separation anxiety

PANS

PMID: 32098238. Baj et al, Int J Mol Sc. 2020 Feb

Rea, I et al. Front Neurol. 2021 "Our findings confirm a clear clinical difference between PANDAS and PANS."

#### Clinically Observed Symptoms: PANS/PANDAS

Separation anxiety (98%) Inability to concentrate (90%) Urinary frequency, urgency, or urinary accidents (90%) Handwriting deterioration (90%) Alterations in sleep - insomnia, night terrors, inability to sleep alone (80%) Behavioral regression Hyper-alert appearance; enlarged pupils (80%) Hyperactivity, inattentiveness (70%) Tics (70%) Learning difficulties (60%) Short-term memory loss (60%) Aggression (60%) Sensory alterations - hypersensitive or insensitive (40%) History of repeat UTIs or sinusitis Disordered eating (20%) Hallucinations (10%)



Clinical observations O'Hara/Wells presentation WNDA Annual Conference 2021

#### PANS Phenotype (n=43)

#### Anxiety 43 (100)

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NATUROPATHIC

Panic/Somatica 15 (35) Generalized anxiety disorder (GAD) 20 (47) Separation anxiety disorder (SAD) 33 (77) Social phobia 12 (28) School avoidancea 20 (47) Mood and behavioral symptoms 43 (100) Emotional lability and/or increased irritability 43 (100) Anxious/Depressed 19 (46) Withdrawal/Depression 10 (24) Somatic complaints 9 (22) Social problems 2 (5) Thought problems 21 (51) Attention problems 8 (20) Rule-breaking behavior 3 (7) Aggressive behavior 12 (29) Suicidality (n=33) 10 (30) Behavioral regression 36 (84) Deterioration in school performance 36 (88) Sleep disturbance 36 (84) Tics 30 (70) Simple 30 (70) Complex 12 (28) Sensory abnormalities 26 (61)

Urinary problems 24 (56) Frequent urination (pollakiuria) 19 (44) Enuresis 11 (26) Handwriting deterioration; 7–14 years (n=30) 17 (57) Food restriction 20 (47) ADHD diagnosis 20 (47) Inattention 11 (26) Impulsivity/hyperactivity 14 (33) Oppositionality 11 (26) Irrational thinking and/or psychotic symptoms 12 (28) Visual hallucinations 5 (12) Olfactory hallucinations 4 (9) Auditory hallucinations 3 (7) Mydriasis 10 (23) Choreiform movements 9 (21) Anorexia (not caused by PANS-OCD) 5 (12) Visuospatial/Motor impairment (n=42) 28 (67) Obsessive compulsive symptoms Harm to self and/or others 39 (91) Ordering and/or arranging, symmetry 30 (70) Contamination 29 (67) Sexual and/or religious 16 (37) Collecting and/or hoarding 14 (32)

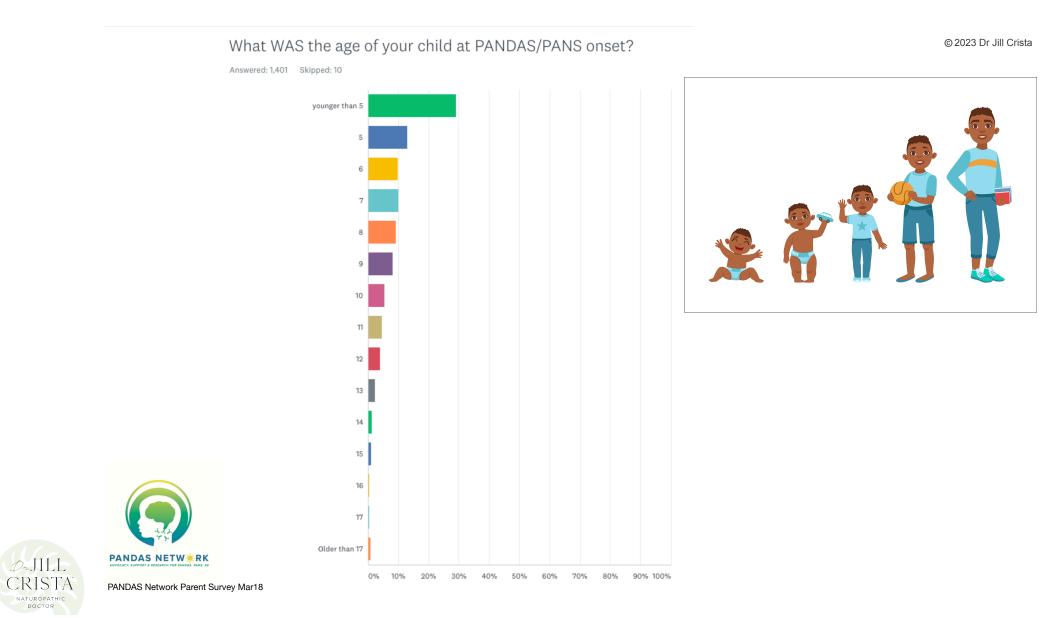
PMID: 25314221. Murphy et al, J Child Adolesc Psychopharmacol. 2015. Dr. Tanya Murphy questionnaire. Symptom headings were proposed core PANS diagnostic criteria symptoms.

## Stanford PANS Clinic Cohort (n=220)

Anxiety (97%) Sensory amplification (97%) Sleep issues (93%) - Insomnia, nightmares, restless sleep, reverse cycling, REM motor disinhibition = REM Behavior Disorder (RBD) Obsessions & compulsions (92%) [major criteria] Mood disorder (92%) Irritability/aggression (90%) Behavioral regression (73%) Deterioration in school (72%) Urinary symptoms (66%) Eating restriction (53%) [major criteria]



Frankovich, Stanford PANS clinic, presentation Neuroimmune conference May23



#### PANDAS Dx Criteria

Category 1 ~Presence of OCD (compulsions) and/or tics, particularly multiple, complex or unusual tics [must be severe enough to meet criteria for OCD or a tic disorder and interfere with the patient's ability to function at pre-illness levels]

Category 2 ~Age Requirement [first evidence between 3yo and puberty]

Category 3 ~Acute onset and/or episodic (relapsing-remitting) course [with abrupt, dramatic, debilitating exacerbations of existing symptoms, at which time the symptoms seem to "explode" in severity]

Category 4 ~ Association with Group A Streptococcal (GAS) infection [evidence of GAS infection found without apparent pharyngitis]

Category 5 ~ Association with Neurological Abnormalities [abnormal results on neurological examination. Motoric hyperactivity and adventitious movements such as choreiform movements or tics are particularly common]

Comorbidities ~ anorexia, urinary frequency, mydriasis, insomnia, abd pain boys>girls

PMID: 28989283



## PANS Dx Criteria

Category 1 ~ An abrupt, acute, dramatic onset of obsessive-compulsive disorder or eating restriction

[many treating docs see a nuanced acute onset, owing to congenitally acquired infxns]

Category 2 ~ 2 co-morbid symptoms (also sudden onset):

1. Anxiety (commonly severe separation anxiety)

2. Sensory dysregulation (light, sound, and/or pain) or motor abnormalities (handwriting deterioration, piano fingers, tics, or motoric hyperactivity)

- 3. Behavioral (developmental) regression
- 4. Deterioration in cognitive functioning (school performance)
- 5. Mood disorder (emotional lability, depression, irritability, rage)
- 6. Urinary symptoms (polyuria, urge, enuresis)
- 7. Severe sleep disturbances

[most have 5-6 co-morbid symptoms]

Category 3 ~ Symptoms not better explained by a known neurologic or medical disorder

Category 4 ~ Age requirement – any, as long as pediatric

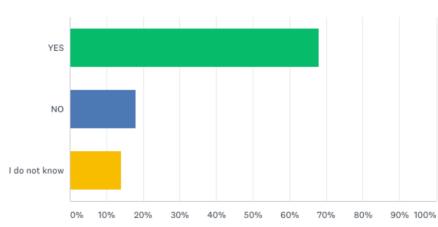
Comorbidities ~ mydriasis, generalized abdominal pain



PMID: 28989283

# In hindsight, did your child display any subtle or early manifestations of symptoms within 6 months of the ACUTE ONSET of PANDAS/PANS symptoms?

Answered: 1,401 Skipped: 10





ANSWER CHOICES	▼ RESPONSES	*
✓ YES	67.95%	952
✓ NO	18.06%	253
<ul> <li>I do not know</li> </ul>	13.99%	196
TOTAL		1,401



PANDAS Network Parent Survey Mar18



## **Differential Diagnoses**

Obsessive-compulsive disorder (non-PANDAS/PANS)

Tourette syndrome

Sydenham's chorea (acute rheumatic fever)

Abuse and/or trauma

Other encephalidities (AE, NMDA-R)

Medications, recreational drugs

Post-concussive autoimmune hypophysitis

Tumor

Cerebral vasculitis, autoimmune vasculitis, Behcet's syndrome (Herpes?)

And of course, myriad unrecognized contributing environmental and infectious factors (ie: novel viruses)



## PANDAS or SC?

Is PANDAS actually Sydenham's chorea 2.0?

Both are the result of a Strep infection.

Both conditions have OCD sxs and involuntary or unpredictable movements as part of their dx criteria.

May have ID'd what distinguishes them - different Strep proteins may lead more to one than the other, but it remains a diagnostic challenge.

About 1/3 with PANDAS or OCD have the choreiform movements seen in SC.

SC may cause more severe OCD symptoms, while also resolving sooner than PANDAS.

Be mindful of this close look-alike. SC is a common sx of rheumatic fever and therefore may require treatment strategies for RF.

PMID: 25301689



# Distinguishing from other AEs

Distinguish by symptomatology that's missing.

IE: NMDA-R AE

-seizures

-myoclonus

-coma

-focal neurological signs



#### Genetic Predisposition?

PANS: HLA alleles:

HLA-B 38, 52, 55

My own observations:

Snps related to IgG: Fcγ Receptors Snps related to NTs: COMT, MAOA Snps related to detox: Phase I: CYP1A2, CYP1B1, CYP3A4 (mold) Phase II: GSTM1, MTHFR, SUOX Snps related to histamine: DAO



# OCD in children

Obsessive-compulsive uncoupling

Obsessions = thoughts ~ Often involves a silent experience of intrusive thoughts Intrusive thoughts interrupt normal cognition = looping/lack of focus Cause = neuroinflammation impeding normal brain chemistry/fxn

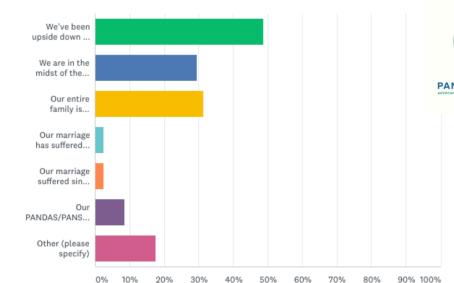
Compulsions = behaviors ~ Involves a sense of lack of control Take control of what they can

\*By listening to these with an investigative mind, they often point to the causal issue.

- controlling adherence to routines/everyone else must as well adrenals
- avoidance of certain people strep carriers
- food avoidance digesting increases LPS, neurological dysphagia
- must look left or bad things a need for craniosacral re-alignment
- hand-washing fear of further infection/need for immunomodulation



#### Describe the CURRENT state of your family life during or post PANDAS.







#### ANSWER CHOICES ▼ RESPONSES ▼ We've been upside down and sideways, but we are stable now. 48.79% 627 ▼ We are in the midst of the roller coaster and don't see an end in sight. 29.57% 380 - Our entire family is suffering, and our other children are feeling the effects as much as our PANDAS/PANS child. 31.36% 403 ▼ Our marriage has suffered. We are in the process of separation. 31 2.41% Our marriage suffered since the onset of our child's PANDAS/PANS, and we have since divorced. 2.57% 33 ▼ Our PANDAS/PANS journey was not the only factor of our current family dynamic. 8.56% 110 Other (please specify) Responses 17.59% 226 Total Respondents: 1,285

PANDAS Network Parent Survey Mar18

Answered: 1,285 Skipped: 126



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