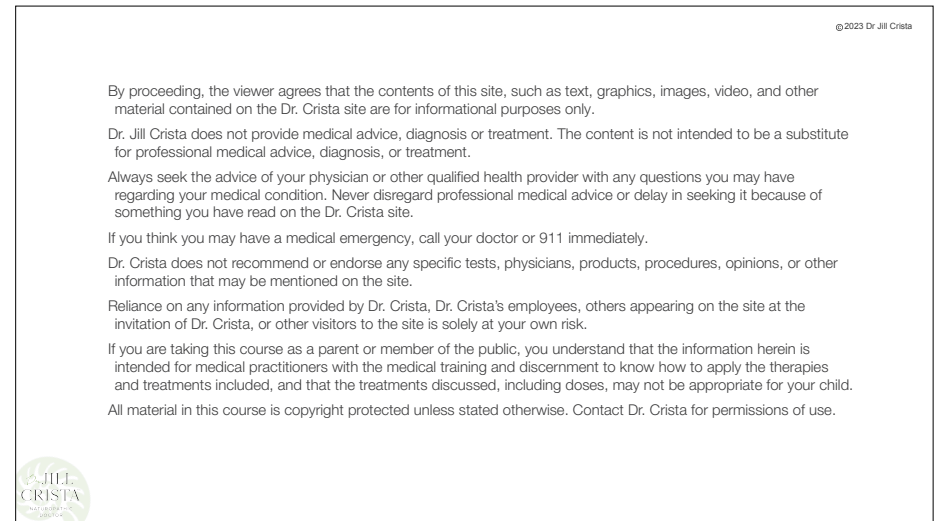
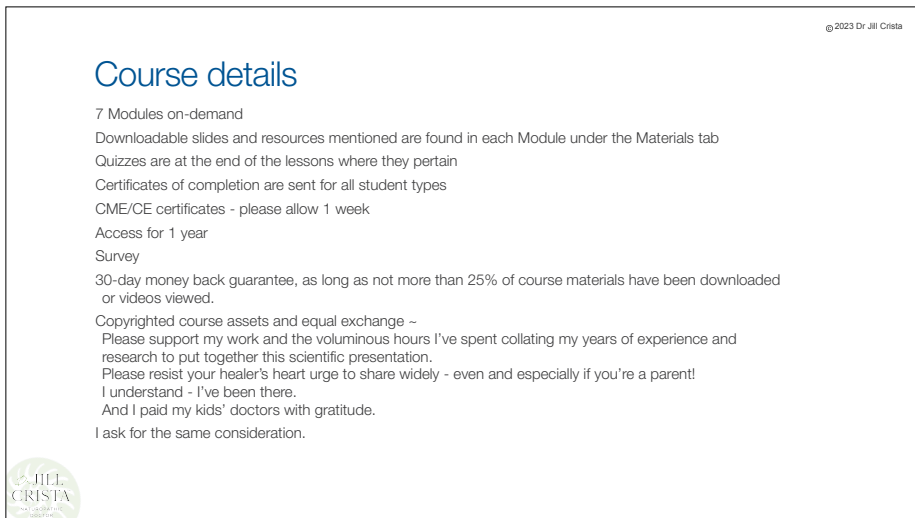




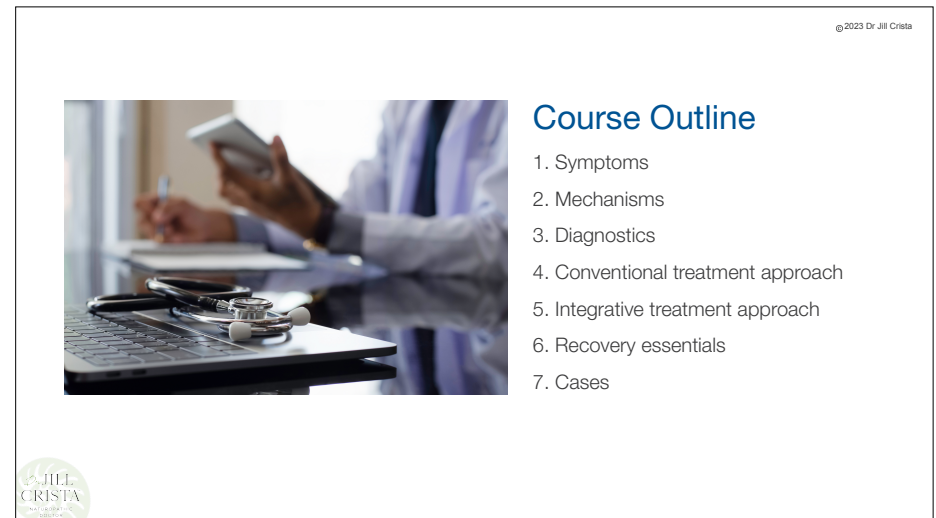
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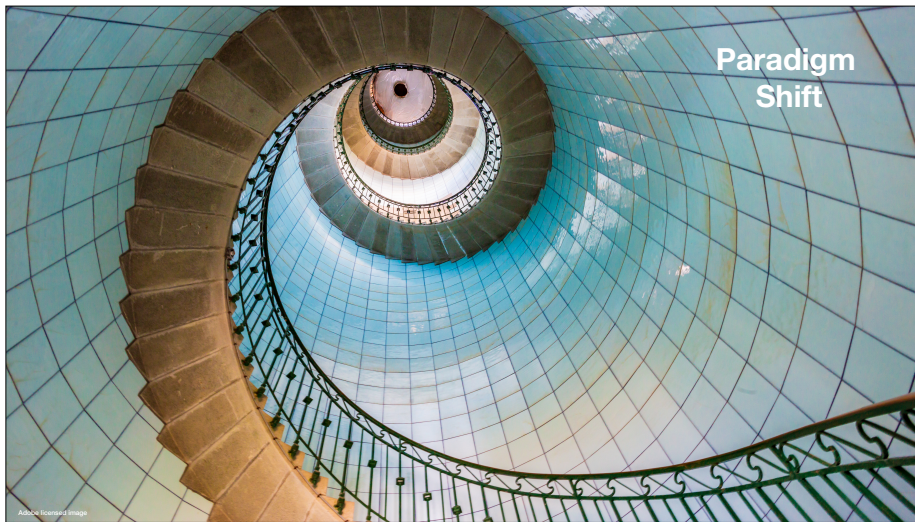
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Paradigm Shift

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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)

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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

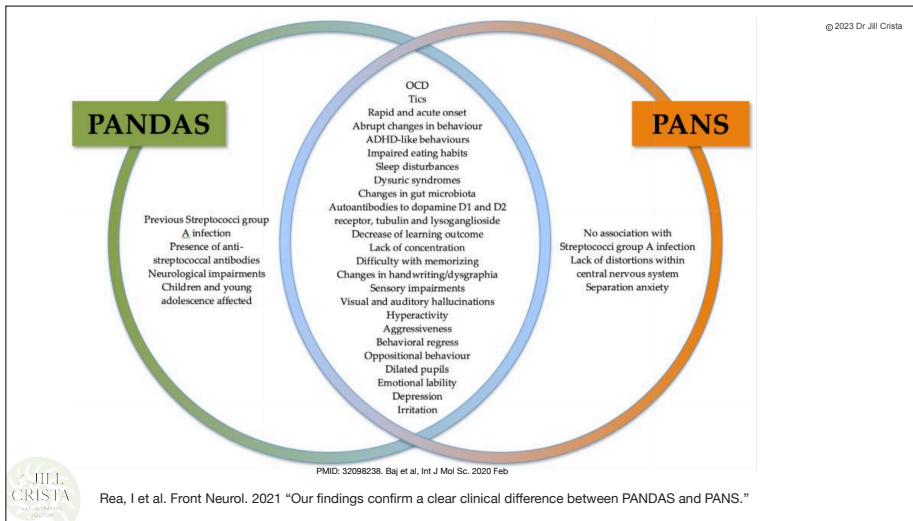
Challenge of mgmt:
Wax: flare/natural progression or new exposure?
Wane: treatment effect or natural remission?

Some variation PANDAS vs PANS

Different diagnostic criteria

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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

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PANS Phenotype (n=43)

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<p>Anxiety 43 (100)</p> <ul style="list-style-type: none"> Panic/Somatica 15 (35) Generalized anxiety disorder (GAD) 20 (47) Separation anxiety disorder (SAD) 33 (77) Social phobia 12 (28) School avoidanca 20 (47) <p>Mood and behavioral symptoms 43 (100)</p> <ul style="list-style-type: none"> 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) <p>Deterioration in school performance 36 (88)</p> <p>Sleep disturbance 36 (84)</p> <p>Tics 30 (70)</p> <ul style="list-style-type: none"> Simple 30 (70) Complex 12 (28) <p>Sensory abnormalities 26 (61)</p>	<p>Urinary problems 24 (56)</p> <ul style="list-style-type: none"> Frequent urination (pollakiuria) 19 (44) Enuresis 11 (26) <p>Handwriting deterioration; 7-14 years (n=30) 17 (57)</p> <p>Food restriction 20 (47)</p> <ul style="list-style-type: none"> 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) <p>Obsessive compulsive symptoms</p> <ul style="list-style-type: none"> 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.

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Stanford PANS Clinic Cohort (n=220)

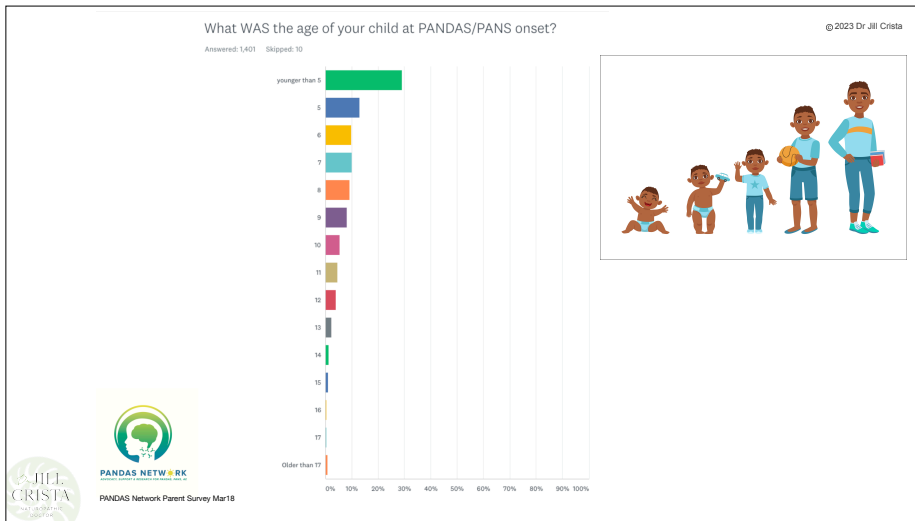
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- Anxiety (97%)
- Sensory amplification (97%)
- Sleep issues (93%)
 - Insomnia, nightmares, restless sleep, reverse cycling, REM motor disinhibition = REM Behavior Disorder (RBD)
- Obsessions & compulsions (92%) [major criteria]
- Mood disorder (92%)
- 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

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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

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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]

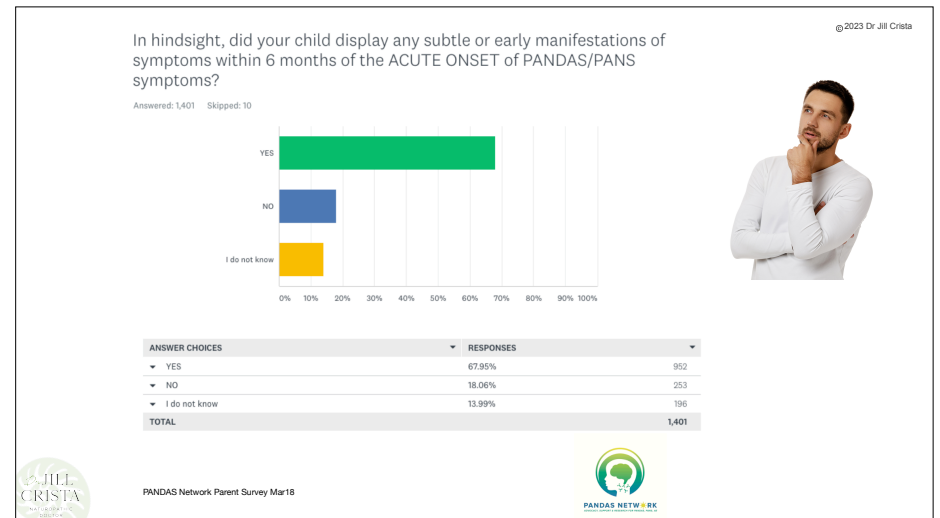
Category 3 ~ Symptoms not better explained by a known neurologic or medical disorder

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

Comorbidities ~ mydriasis, generalized abdominal pain

PMID: 28989283

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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 sx's 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

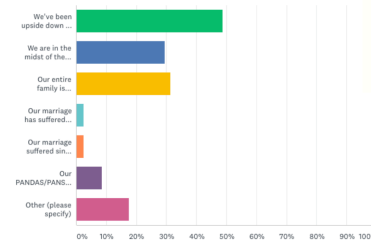
*By listening to these with an investigative mind, they often point to the causal issue.

- 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.

Answered: 1,285 Skipped: 126



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.	2.41% 31
▼ 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 Mar'18

