PANDAS & PANS
An Integrative Approach

Dr. Jill Crista

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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

Access for 1 year

Survey

30-day money back guarantee, as long as not more than 25% of course materials have been downloaded or videos viewed.

Copyrighted course assets and equal exchange ~
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


Paradigm
Shift
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Course Outline

1. Symptoms

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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

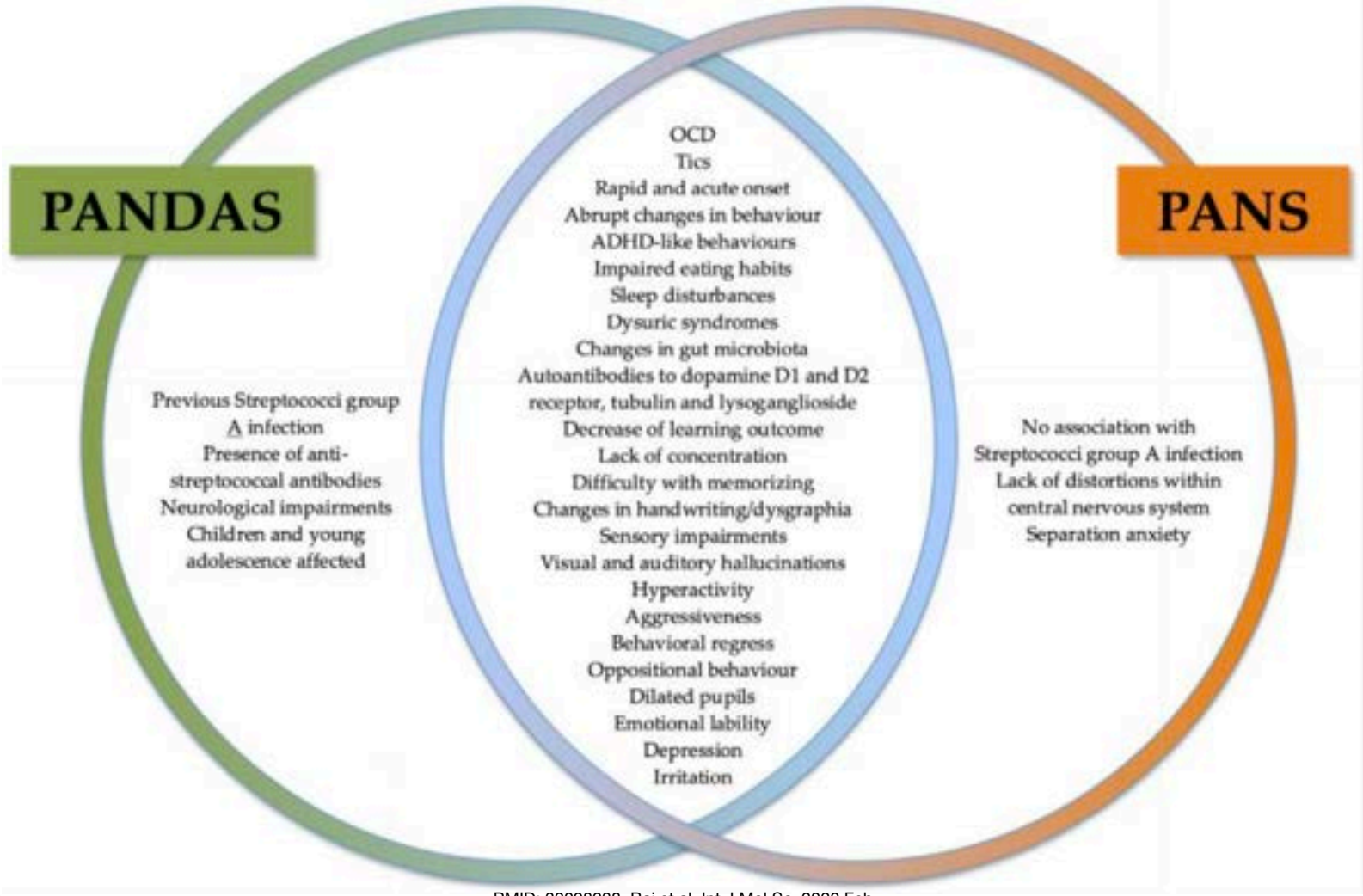
Autoimmune relapsing-remitting pattern

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



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)
- 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%)

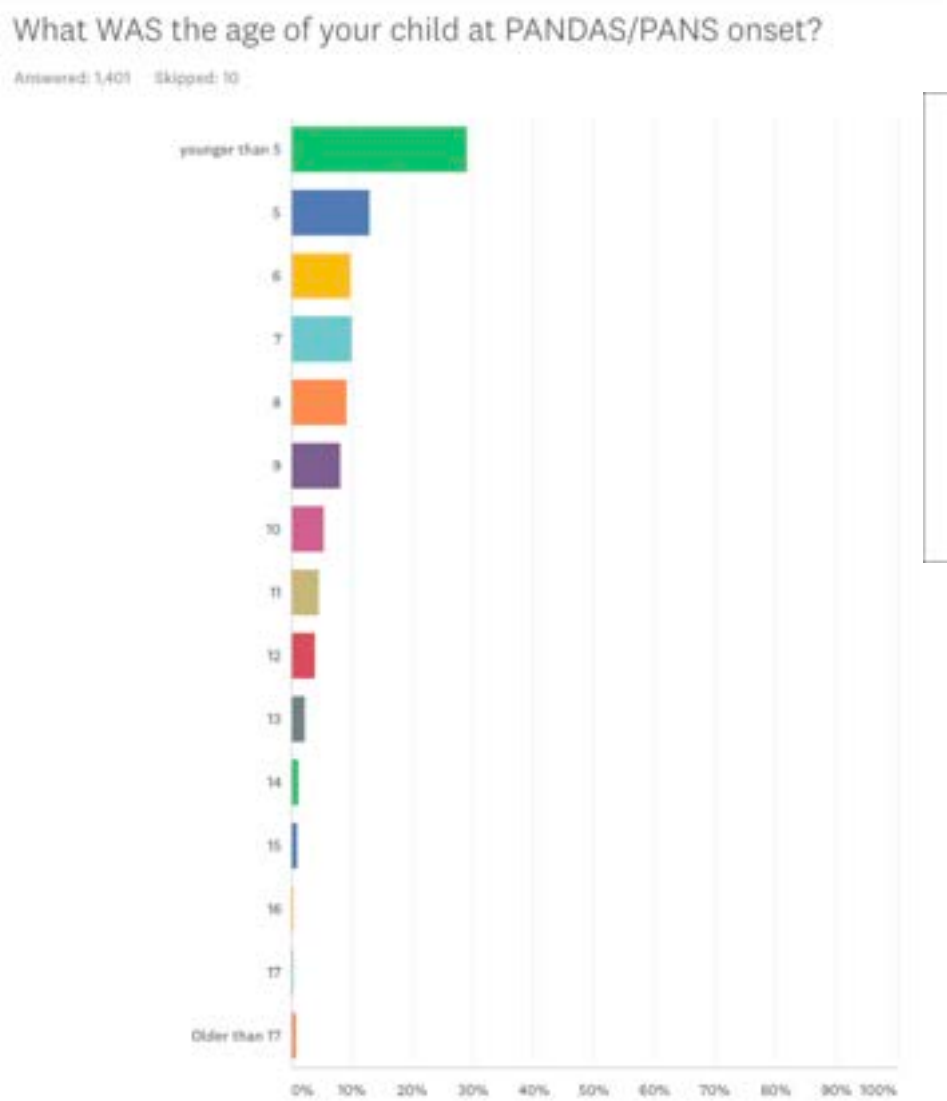
Behavioral regression (73%)

Deterioration in school (72%)

Urinary symptoms (66%)

Eating restriction (53%) [major criteria]

Frankovich, Stanford PANS clinic, presentation Neuroimmune conference May23



PANDAS Network Parent Survey Mar18

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

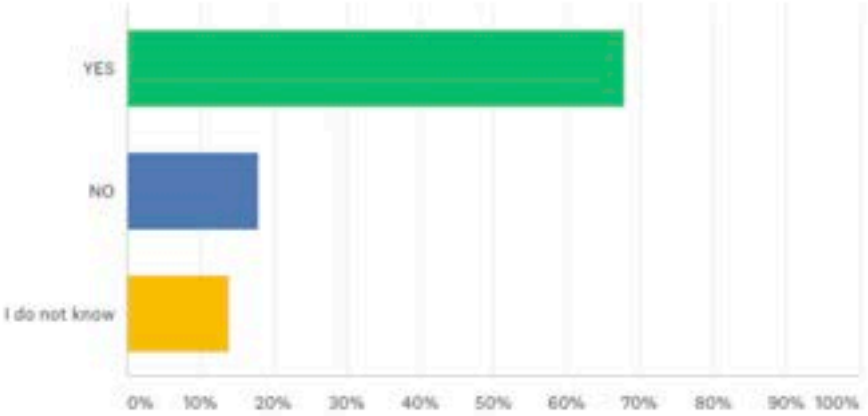
Category 4 ~ Age requirement – any, as long as pediatric

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
I do not know	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

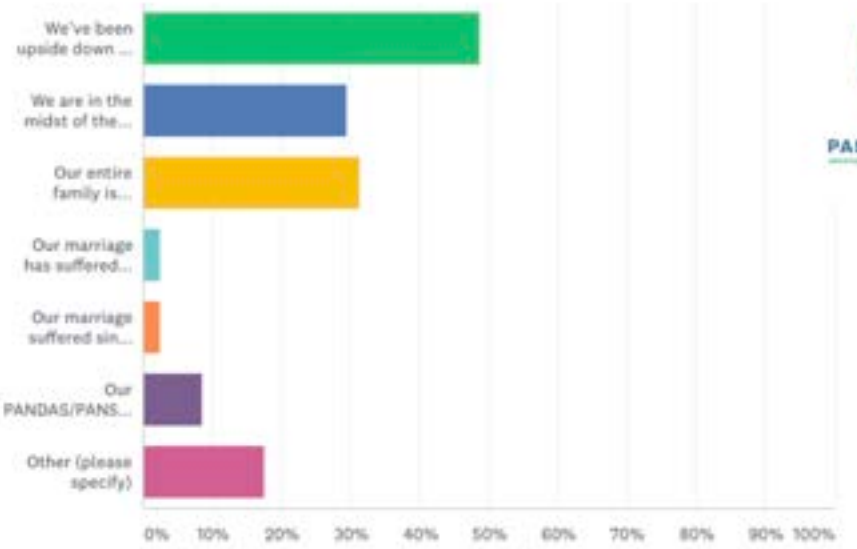
Obsessions = thoughts ~
- Often involves a silent experience of intrusive thoughts
- Intrusive thoughts interrupt normal cognition = looping/lack of focus
- Cause = neuroinflammation impeding normal brain chemistry/fxn

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.

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 Mar18


Symptoms
Next up:
Mechanisms
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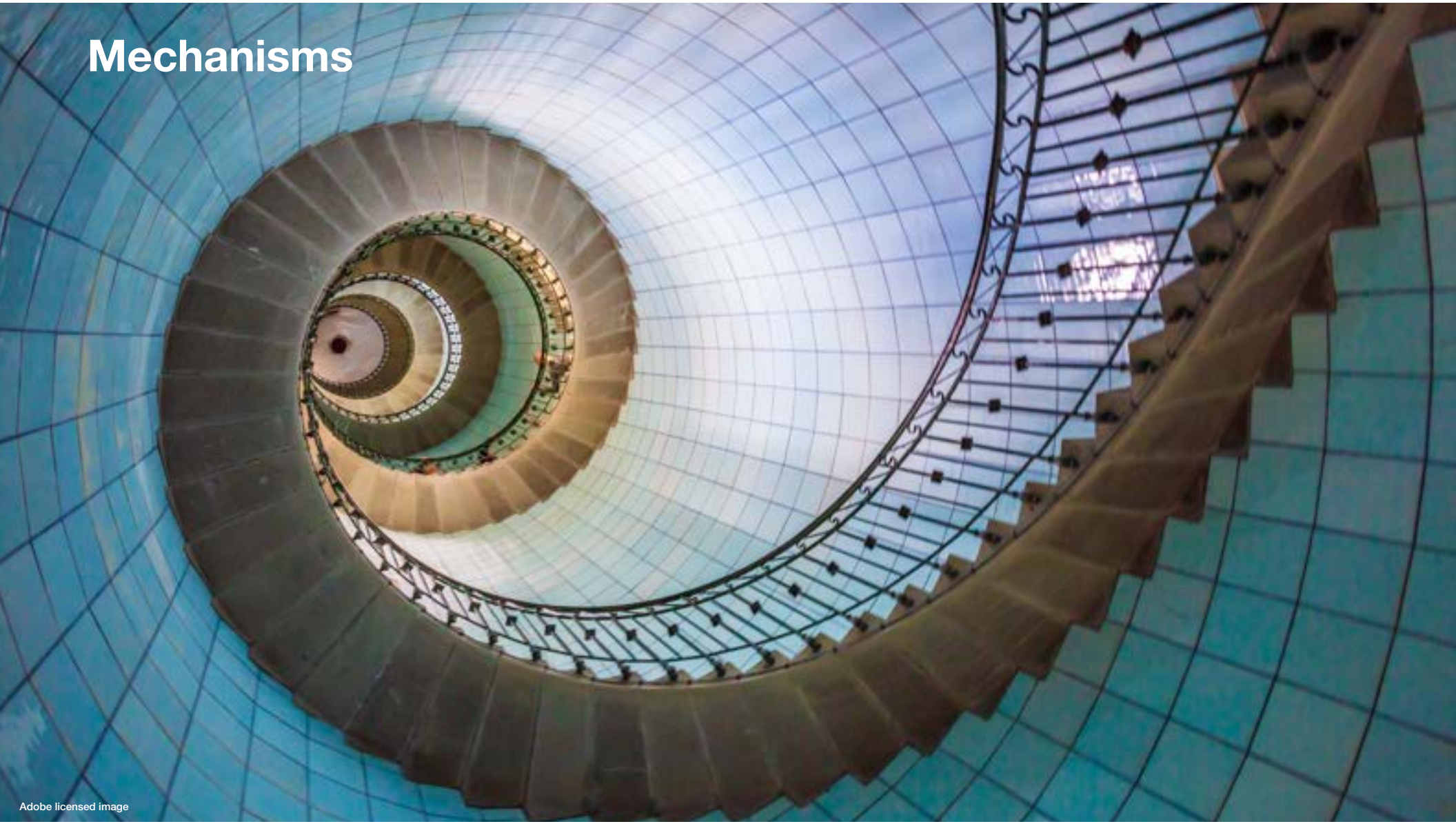
Mechanisms



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1. Symptoms
2. **Mechanisms**
3. Diagnostics
4. Conventional treatment approach
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PANDAS/PANS mechanisms

Overview of what the research tells us to date … (expect changes as our knowledge evolves)

Pre-existing immune depleted state

Microbiome alteration

T-cell mediated damage to the brain triggered by infection AND toxicants

Microglial activation → chronically “primed” neuroinflammation

Damage to dopamine receptors & cholinergic interneurons

Altered central dopamine, glutamate, ACh utilization → excitatory

Impaired innate safety systems

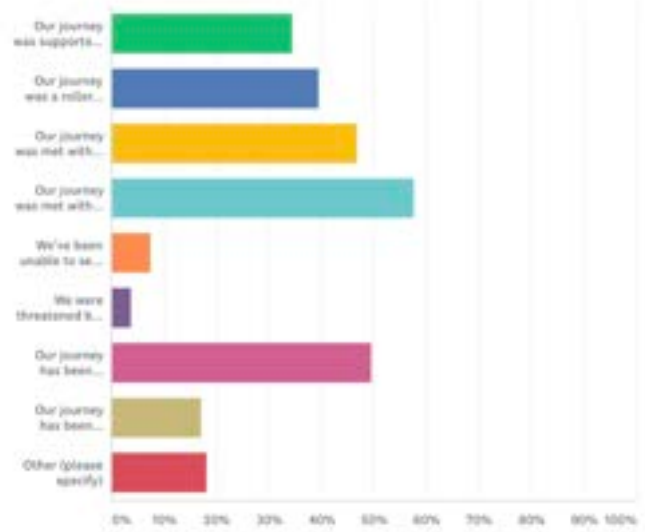
Cell danger response → limbic/vagal dysfunction

CNS structural alterations

Bad parenting!???

Humanism in Medicine: In general, which phrase(s) best reflects your journey to support your child's medical condition? (Select ALL that apply)

Answered: 1,289 Skipped: 122



ANSWER CHOICES	RESPONSES	
Our journey was supported by knowledgeable physicians with a positive attitude to help our child's medical issue.	34.52%	445
Our journey was a roller coaster ride to diagnosis, but we remain in good hands.	28.57%	370
Our journey was met with medical professionals who meant well, but were unable to help our child.	46.94%	605
Our journey was met with doubting medical professionals who made us feel like we were crazy.	57.72%	744
We've been unable to seek effective professional care due to lack of medical coverage.	7.60%	98
We were threatened by the medical professional(s) because they doubted the diagnosis of our child and forced our child into a psychiatric center against our wishes.	3.80%	49
Our journey has been supported by other families who've experienced PANDAS/PANS.	49.50%	638
Our journey has been supported by a non-profit(s) whose advice, recommendations or resources were pivotal in my child's health improvement.	17.07%	220
Other (please specify) Responses	18.15%	234
Total Respondents: 1,289		

PANDAS Network Parent Survey Mar18

*“It’s impossible to know the feeling of losing a child,
and have that child sitting right in front of you.”*

“Maybe you’re just a little tired. Try taking a nap.”

“Have you considered parenting classes?”

“You just need to be more strict.”

“Kids have tantrums.”

“Maybe she’s just a picky eater, have you tried ice cream?”

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Pre-existing immune depleted state

Top 2 negative sequela for those with immune depletion ~

1. Increased risk of infections
2. Increased risk of developing an autoimmune disorder

↑ rate of IgA deficiency in pediatric OCD compared to children with ASD and anxiety.

↑ rate of IgA deficiency in pediatric OCD compared to adults with OCD.

Dendritic cell role. May have specificity to Strep &/or nasal infection. Strep inhibits dendritic cell maturation.

PMID: 30892924, 30516814, 26417101, 19712038

Infection and risk for mental disorders

Do infections increase the risk of subsequent mental disorders during childhood and adolescence?

Population-based cohort study using Danish nationwide registers.

>1 million individuals born in Denmark between 1995 and 2012

All treated infections were identified in a time-varying manner, including severe infections requiring hospitalizations and less severe infection treated with anti-infective agents in the primary care sector.

Findings ~

Severe infections requiring hospitalizations increased the risk of hospital contacts due to mental disorders by 84% and the risk of psychotropic medication use by 42%.

Less severe infection treated with anti-infective agents increased the risks by 40% and 22%, respectively; the risks differed among specific mental disorders.

PMID: 30516814, 26417101, 19712038

Immune system of the brain

2/3 of the brain is glial (immune), 1/3 is neurons

3 glial types - microglia, astrocytes, oligodendrocytes

Microglia ~
Brain “macrophages”, scavengers
Modulate neurogenesis, influence synaptic remodeling, and regulate neuroinflammation by surveying the brain microenvironment

Astrocyte ~
Involved with glutamate and GABA activity, clean up synaptic cleft, BBB integrity

Oligodendrocyte ~
Myelinating, axonal metabolic support

Journal of Leukocyte Biology 2008, Dilger and Johnson

Innate activation

Innate I/S of brain can be activated in 4 ways ~

1. Pathogens
2. Vagal afferens pathway from enteric n.s./ hepatic projections (Kupffer cells)
3. Non-canulized pathway (inflam cytokines)- some xBBB through passive diffusion (IL-1β)
4. Pathways involving blood vessels and astrocytes (ie: heat-shock proteins)

Journal of Leukocyte Biology 2008, Dilger and Johnson

Inflammasome

Systemic inflammation shifts the brain microenvironment towards a proinflammatory state.

OCD patients had higher levels of IL-18, IL-1Ra, and TNF, compared to the healthy controls.

Blood cells of OCD patients have increased expression of NLRP3 inflammasome - an important component of the innate immune system.

Expression of genes encoding for NLRP3, caspase-1, ASC, IL-1β, IL-1RN, and TNF are significantly increased in peripheral whole blood of psychiatric patients compared to matched healthy controls.

“The findings support the inflammation hypothesis for markedly ill psychiatric patients across diagnostic groups.”

The paradigm change in mental health.

PMID: 27149601, 31786499, 36911567

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CNS structural alterations

What defines “self” vs “other”

Autoimmune = loss of tolerance to “self”

“Self” largely determined by our gut microbiome

We're **more microbe than man** - outnumbered by gut microbiome in both cell count and total DNA

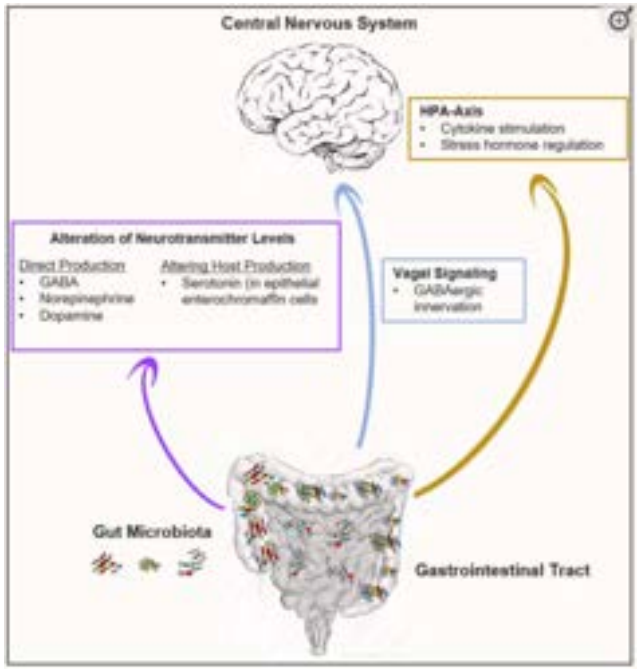
Autoimmune dzs are linked to unique microbiome composition (ie: lower Firmicutes/Bacteroidetes ratio), reduction of gut commensals, altered gut integrity

Fecal microbiota transplantation (FMT) or inoculation with specific microbes in animal models of ADs support the hypothesis that alterations of gut microbiota influence autoimmune responses and disease outcome.

Ie: changes to the gut commensals and periodontal disease have been proposed as important factors in the pathogenesis of RA

PMID: 35534624, 32731813, 32038645, 29920643

Microbiome-Gut-Brain Axis



Bidirectional crosstalk between the gut and the brain

Various afferent and efferent pathways influence Dz pathogenesis - vagus n., I/S, bacterial metabolites

Bottom up ~
Antibiotics, environmental/infectious agents, intestinal NTs/ neuromodulators, sensory vagal fibers, cytokines, metabolites all convey information to CNS about the intestinal state

Top down ~
Conversely, the HPA axis, CNS regulatory areas of satiety, and neuropeptides released from sensory nerve fibers affect the gut microbiota composition

Such interactions influence the pathogenesis of disorders where inflammation is implicated, such as mood disorder, ASD, ADHD, MS, obesity

Microbiome dysbiosis shown to affect cognitive function

PMID: 30892924, 28948967, 32130879, 35087123, 34205336, 29903615

Microbiome-microglial connection

Brain microglia not only respond to local brain signals but also input from the periphery, including the GI tract and microbiome

Microbiome plays a pivotal role in regulating brain microglial maturation and function in the brain, as well as production/consumption of NTs.

Microbial products (LPS) and microbially produced metabolites act as signalling molecules that have direct and indirect effects on the CNS and the ENS (motility)

Altered microbial composition is reported in neurological disorders with known brain microglial involvement in humans

Circadian rhythm: The composition of the gut microbiota is subject to diurnal variation and is entrained by host circadian rhythms. In turn, a diverse microbiota is essential for optimal regulation of host circadian pathways.

PMID: 30385457, 26046241, 30614568, 31478105, 29903615

Biomes, BBB, and OCD

During dysbiosis, gut-brain axis pathways are dysregulated and associated with altered permeability of the BBB and neuroinflammation

Post-prandial endotoxemia (plasma LPS) is found in approximately 1/3 of those eating Westernized diet, more common with dysbiosis

LPS caused the loss of dopaminergic neurons (in substantia nigra pars compacta) and microglia migration in a dose-dependent manner in a rat study

Imbalance in the gut and oropharyngeal microbiomes observed in OCD cases ~
Increase of bacteria from the Rikenellaceae family, associated with gut inflammation
Decrease of bacteria from the Coprococcus genus, associated with DOPAC synthesis

MS-twin study: FMT from MS-affected twin into mice promoted the dz in vivo vs FMT of twin unaffected by MS

PMID: 35087123, 33362788, 28893994, 31588712

Restricted eating

Certain gut microbiota-related compounds and food antigens can trigger the production of autoantibodies cross-reacting with appetite-regulating hormones and neurotransmitters.

Alterations in the gut microbiome and I/S may serve not only to maintain and exacerbate dysregulated eating behavior, but may serve as biomarkers of increased risk for developing an eating disorder.

Mice receiving FMT from those with anorexia nervosa (AN) displayed increased anxiety- and compulsive-like behavior relative to controls.

Conversely, case report of FMT from healthy control to pt with AN increased short chain fatty acids and serotonin, associated w normalized eating.

Increases in multiple Clostridium species belonging to the order Clostridiales.

Gastroparesis observed w neurotoxins:
mycotoxins, Borrelia spp, Bartonella, algal blooms/aquariums

PMID: 33953692, 33652962, 33546416, 31504398, 31510101

Restricted eating or self medicating?

Intermittent fasting increases microbiome diversity; significantly reduces the ratio of Firmicutes to Bacteroidetes and increases the relative abundance of Allobaculum.

Intermittent fasting attenuates LPS-induced neuroinflammation and memory impairment including enhancement of neurotrophic support.

Intermittent fasting contributes to aligned circadian rhythms through interactions with the gut microbiome.

β-hydroxybutyrate (BHB), a physiological ketone body produced by the liver in condition of fasting, low blood sugar, or carbohydrate-free (like ketogenic) diet consumption had an inhibitory effect on NLRP3-inflammasome.

Intermittent fasting attenuates LPS-induced acute lung injury in mice by modulating macrophage polarization.

PMID: 33223514, 24886300, 25686106, 36028098, 33530881

Lung microbiome effect on the brain

The lung tissue in particular has an important role in autoimmune diseases of the brain, such as MS.

There's a tight interconnection between the lung microbiota and immune reactivity in the brain.

A dysregulation in the lung microbiome significantly influenced the susceptibility of rats to developing autoimmune diseases of the CNS.

Shifting the microbiota towards LPS-enriched phyla induces a type-I-interferon-primed state in brain-resident microglial cells.

PMID: 35197636, 35417673, 35197592, 32140452, 19793773

Gut-lung-immune axis

The gut-lung axis highlights both host-microbe interactions but also microbe-microbe interactions involving inter-kingdom microbial crosstalks (ie: bacterial and fungal.)

Water-damaged buildings host biofilm, including indoor airborne bacterial endotoxin, as well as fungi, modifying the lung microbiome.

LPS endotoxin enhances the negative health effects of many mycotoxins on respiratory and gastrointestinal tissue.

Further justification for both environmental + infection management.

PMID: 35197636, 35417673, 35197592, 32140452, 19793773

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Microglial activation → chronically “primed” neuroinflammation

Damage to dopamine receptors & cholinergic interneurons

Altered central dopamine, glutamate, ACh utilization → excitatory

Impaired innate safety systems

Cell danger response → limbic/vagal dysfunction

CNS structural alterations

T-cell mediation

Intranasal infections of all types preferentially generate Th17, not just Strep

Th17 → IL17 linked to increased risk for autoimmunity

Mouse studies: glyphosate, mold mycotoxins, and mercury exposure drives increase in Th17

Pts with depressive sxs had increased amyloid proteins + fecal IL-17

Mouse studies: microbiome regulates Th17 cell-mediated depressive-like behaviors and other CNS disorders

Naïve CD4 T-cell differentiates into either T-reg or Th17 depending on the Transforming Growth Factor (TGF) 'soup flavor'

Microbiome plays a role in TGF types/quantity

PMID: 32731813, 32038645, 29510522, 29920643, 28935500, 35963408, 20049214

Strep throat becomes “Strep nose”

From throat to nose ~
GAS-pharyngitis triggers Th17 response
Formation of Abs in cervical lymphatic chain dendritic cells
In turn sends these Abs back to throat *but also the nose*

Mouse study: repeated intranasal challenge w GAS-inoculated mice promoted migration of GAS-specific Th17 cells from NALT into the brain, BBB breakdown, serum IgG deposition, microglial activation, and loss of excitatory synaptic proteins under conditions in which no viable bacteria were detected in CNS tissue.

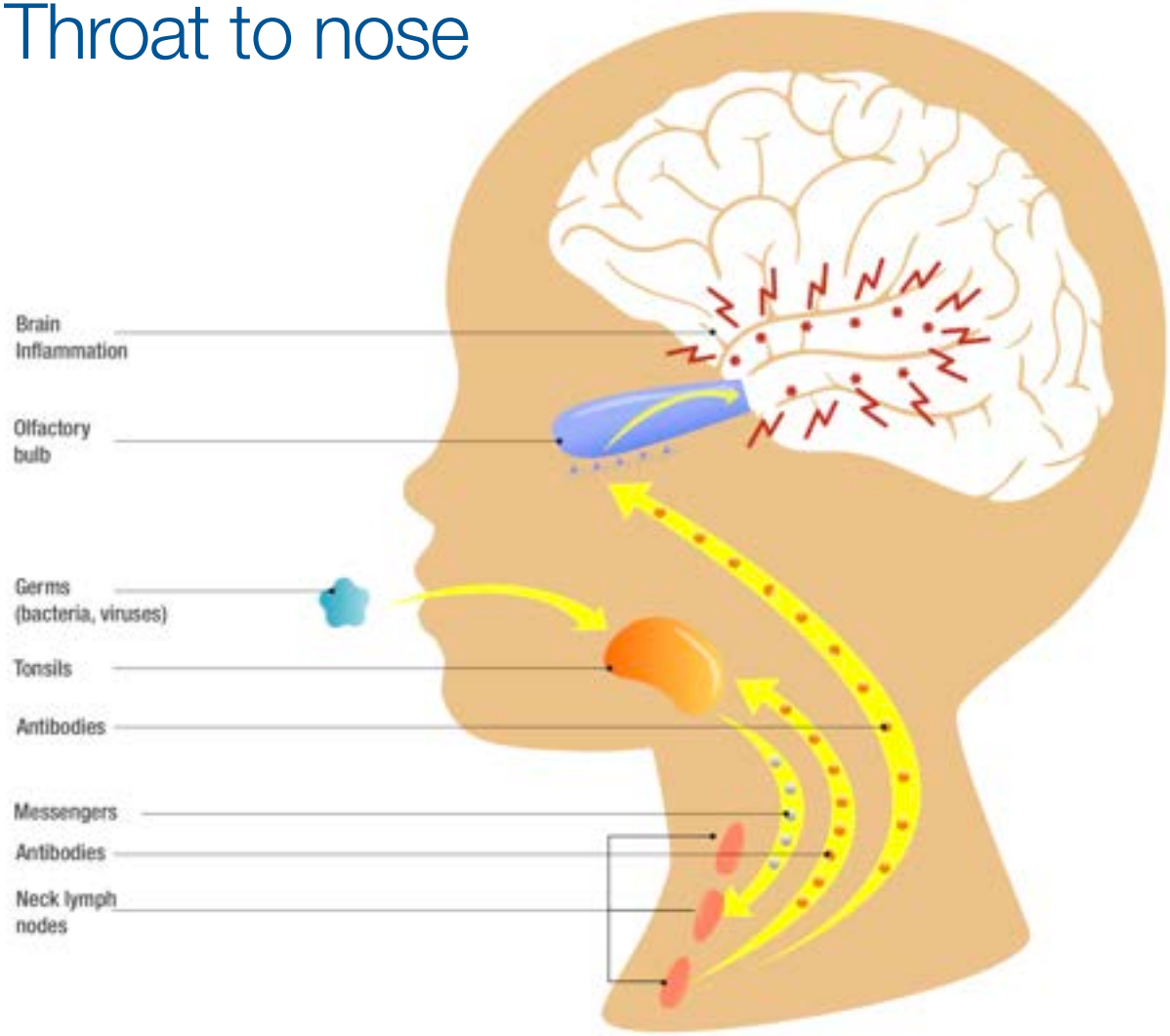
Proposed anti-GAS mimetic Abs affects DR1 & DR2 receptors, and/or cholinergic interneurons

Th1 may also play a role → strep, Herpes/EBV, H. Pylori

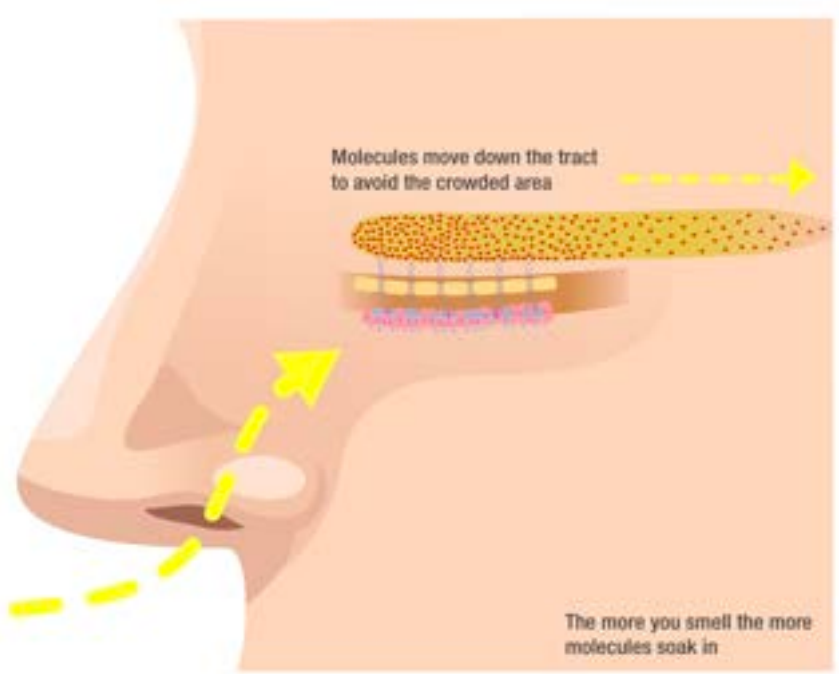
Discuss more about infectious triggers in next module

PMID: 28951419, 26657857, 26417101

Throat to nose



Olfactory access



“Smelling is a form of physical contact.”

Molecules interact with olfactory nerve terminals

Olfactory bulb void of BBB

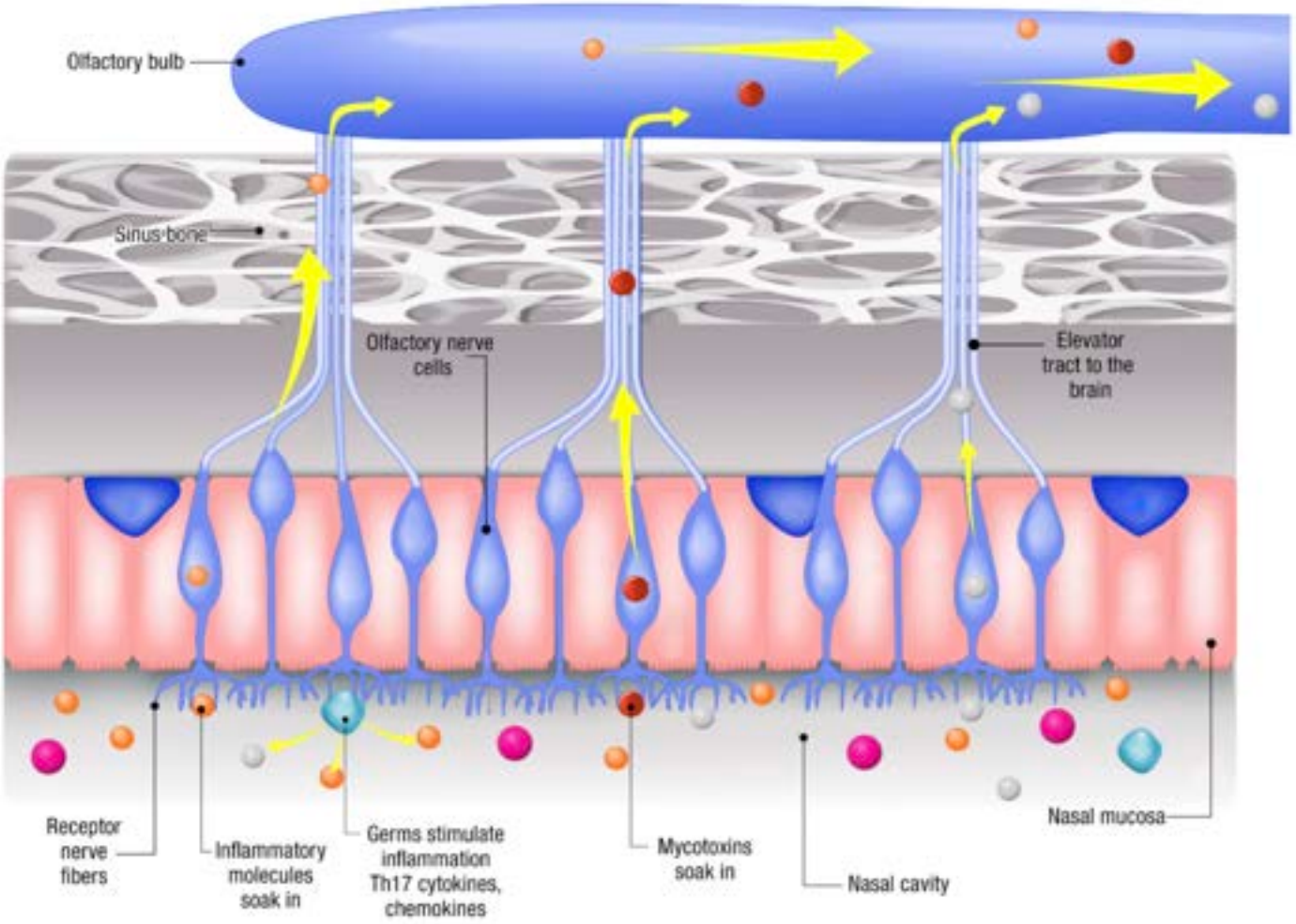
Part of limbic system

Terminates in nasal mucosa

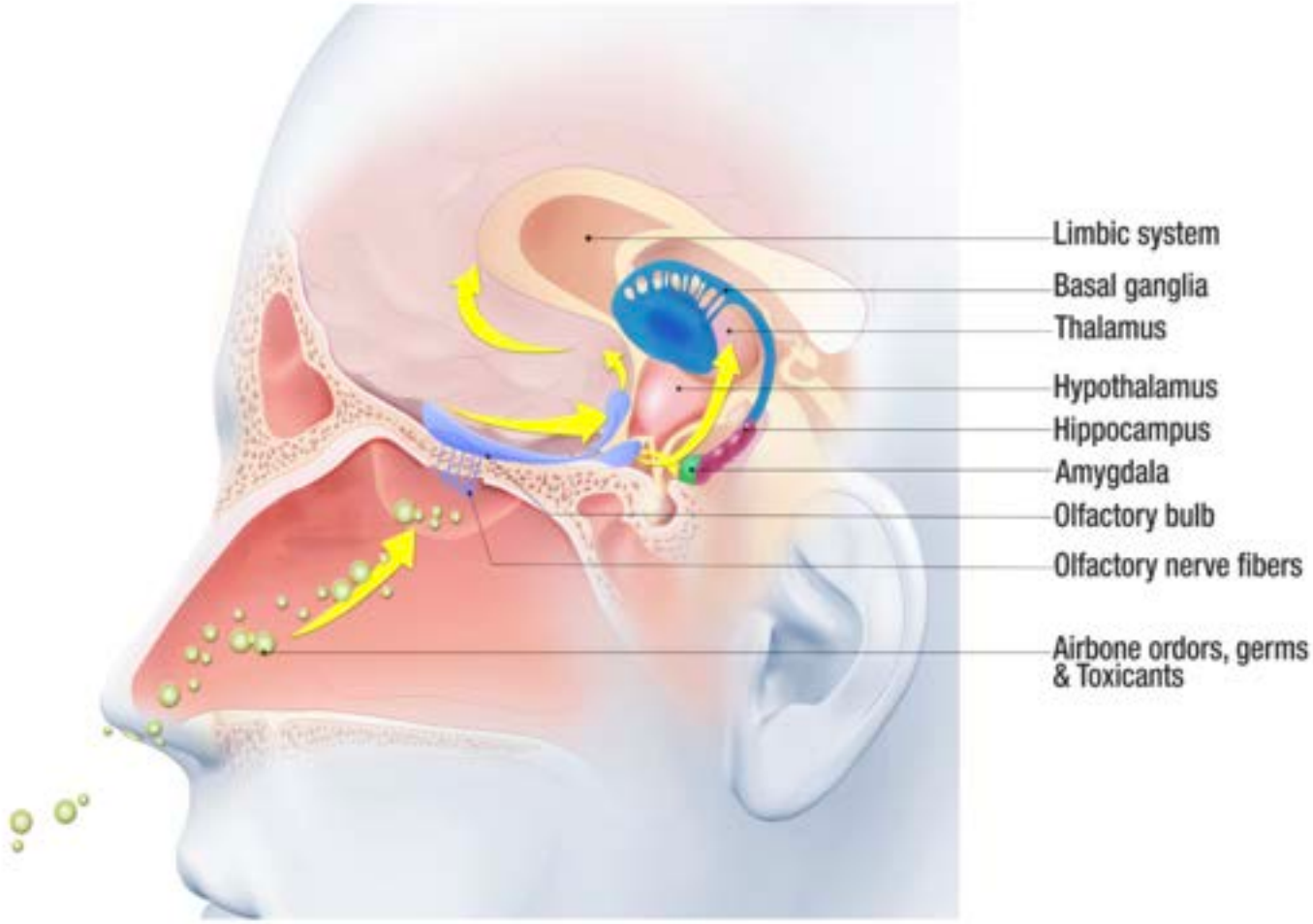
Th17 + mycotoxins uptake

Trigger microglia activation

The “elevator to the brain”



Basal ganglia



Strep antibody impacts on hypothalamus

Elevated anti-streptococcal antibodies more prevalent in patients with recent narcolepsy onset.

Narcolepsy; deficiency in hypocretin/orexin secretion from hypothalamus.

Thought to be largely genetically determined, but environmental factors were investigated based on the high discordance rate (approximately 75%) of monozygotic twins.

Retrospective, case-control study concluded that Streptococcal infections are probably a significant environmental trigger for narcolepsy.

Compared to age-matched controls, increased ASO found in 51% within 3 years of onset, compared to 19% ($P < 0.0005$) and 20% of patients with long-standing disease ($P < 0.0005$).

ASO and Anti-DNase B titers were highest close to narcolepsy onset, and decreased with disease duration.

PMID: 19725248

PANDAS/PANS mechanisms

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Pre-existing immune depleted state

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Microglial activation → chronically "primed" neuroinflammation

Damage to dopamine receptors & cholinergic interneurons

Altered central dopamine, glutamate, ACh utilization → excitatory

Impaired innate safety systems

Cell danger response → limbic/vagal dysfunction

CNS structural alterations

Microglial activation

Microglia are the brain's resident immune cells, similar to macrophages. (#monkeys)

Activated microglia are classically associated with inflammation, neuronal damage, and neurodegeneration, and often secrete inflammatory cytokines in various neuro Dzs, including Alzheimers.

Microglial activation is not always associated with inflammation. Novel roles have emerged in brain development, homeostasis, and plasticity.

Microglial dysfunction has been implicated in the onset and progression of several neurodevelopmental and neurodegenerative diseases.

Activated or "primed" microglia lose their motility projections, get stuck in place and in the more inflammatory stage (M1, aka #monkeypoo.)

Once primed, the only way out is autophagy via maturation to M2 stage.

Primed glial cells may recruit adjacent microglia and mast cells, and *remain more sensitive to systemic inflammatory responses* for the rest of that cell's lifecycle (#monkeyseemonkeydomonkeypoo.)

Contrast to tumor-associated brain macrophages (partly derived from microglia,) express M2>M1 stage.

PMID: 24487234 , 27859676, 24303218, 22632727, 28948967

Microglial dysfunction

There's evidence for microglial dysregulation and neuroinflammatory etiology in PANDAS (also OCD, Tourette's.)

Defective microglia lead to OCD behaviors [mice]~
pathological grooming, hyperanxiety, social impairment deficits

Evidence from animal studies that synaptic pruning might be altered in PANDAS, though the evidence is limited.

Additional potential contributions of microglial abnormalities beyond neuroinflammation are failures in neuroprotection, lack of support for neuronal survival.

SSRIs may reduce this effect, but in a lab-induced condition, what about wild-type with different toxicant triggers?

Reiteration: the influential role of the microbiome-microglia axis.

The role of mast cells: histamine is both a neurotransmitter and an immune modulator.
Can regulate microglia in vivo, via the H4 receptor.

PMID: 28053994, 36911567, 30385457, 29354029, 27859676

Mast cells

Reside in virtually all vascularized tissues. Differently differentiated based on recruitment trigger, location, milieu.

Secrete a wide variety of biologically active products in 50-200 granules, including diverse cytokines and growth factors, including histamine, heparin, a variety of cytokines, chondroitin sulfate, and neutral proteases.

MUCH more than, and not always, histamine, and not always degranulation.

Within 30 min releases heparin, etc but in the next 24 hours, releases cytokines and other inflammatory mediators without ever releasing histamine.

Non-redundant roles in many types of innate or adaptive immune responses, including immediate and chronic IgE-associated allergic disorders and enhancing host resistance to certain venoms, parasites, and fungi.

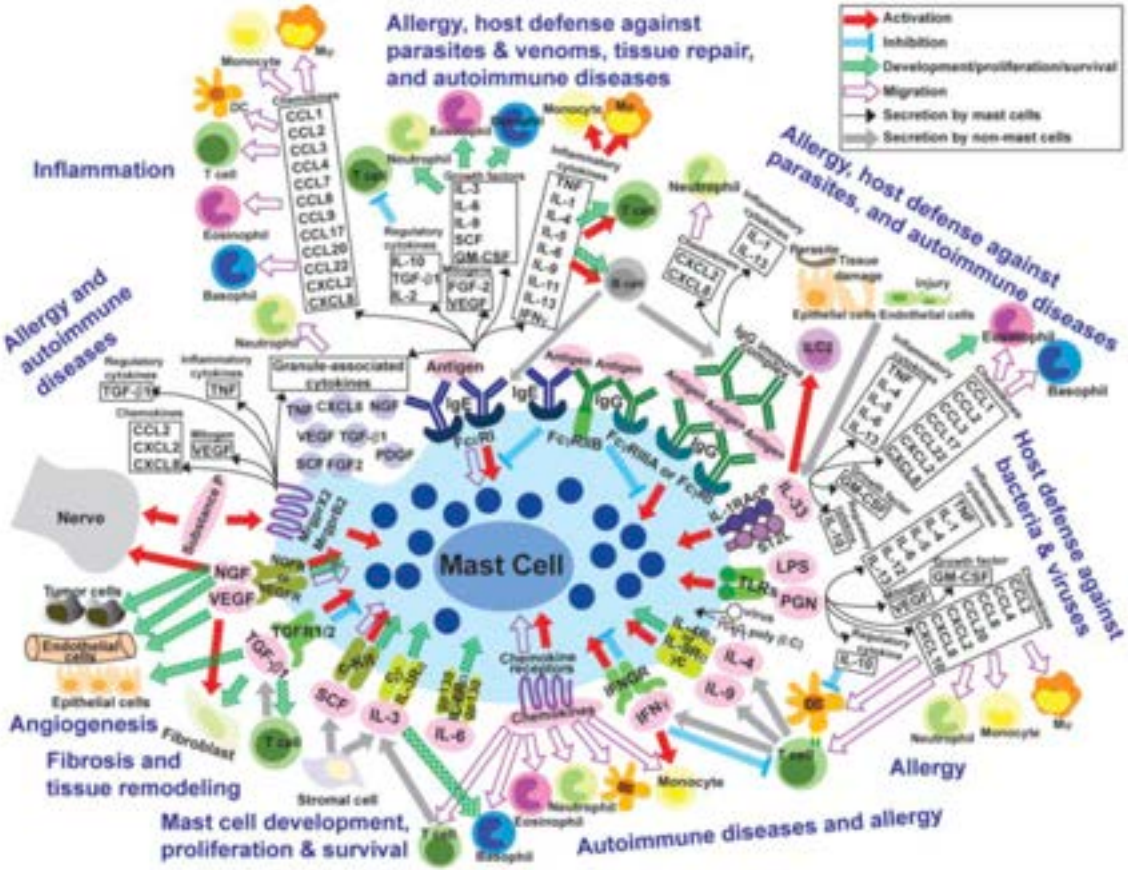
Influence many other biological processes, including responses to bacteria and virus, angiogenesis, wound healing, fibrosis, autoimmune and metabolic disorders, and cancer.

Functions reflect their ability to secrete, upon appropriate activation by a range of immune or non-immune stimuli, a broad spectrum of cytokines (including many chemokines) and growth factors, with potential autocrine, paracrine, local, and systemic effects.

“Cluster bomb” effect.

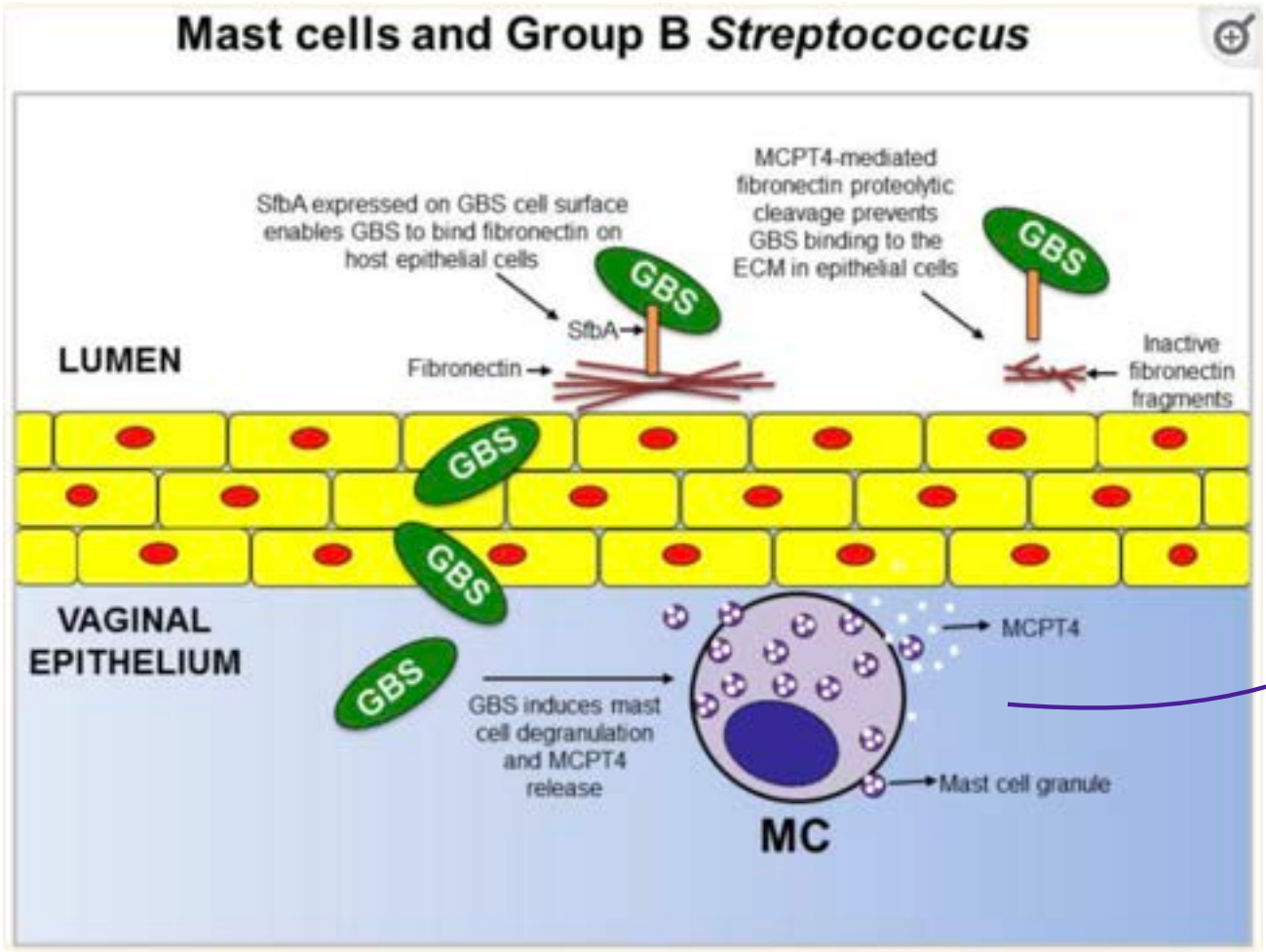
PMID: 27381299, 19527167, 19201896, 29431211

Figure 1



Highly simplified overview of the diverse stimuli and potential consequences of mast cell activation and secretion of cytokines, chemokines and growth factors

PMID: 29431212



Histamine can regulate microglia via H4

Proposed mechanism for the protective effect of MCPT4 against Group B Streptococcus (GBS) dissemination and preterm birth. MCPT4, Mast cell protease 4; MC, mast cells; SfbA, streptococcal fibronectin binding protein; ECM, extracellular matrix

PMID: 29431211

Mast cells & the gut

Dr. Theoharides - “the gateway to inflammation in the body”

“It is well established that mast cell activation can ~
- Generate epithelial and neuromuscular dysfunction
- Promote visceral hypersensitivity
- Alter motility patterns in functional gastrointestinal disorders (FGIDs), postoperative ileus, food allergy, inflammatory bowel disease.”

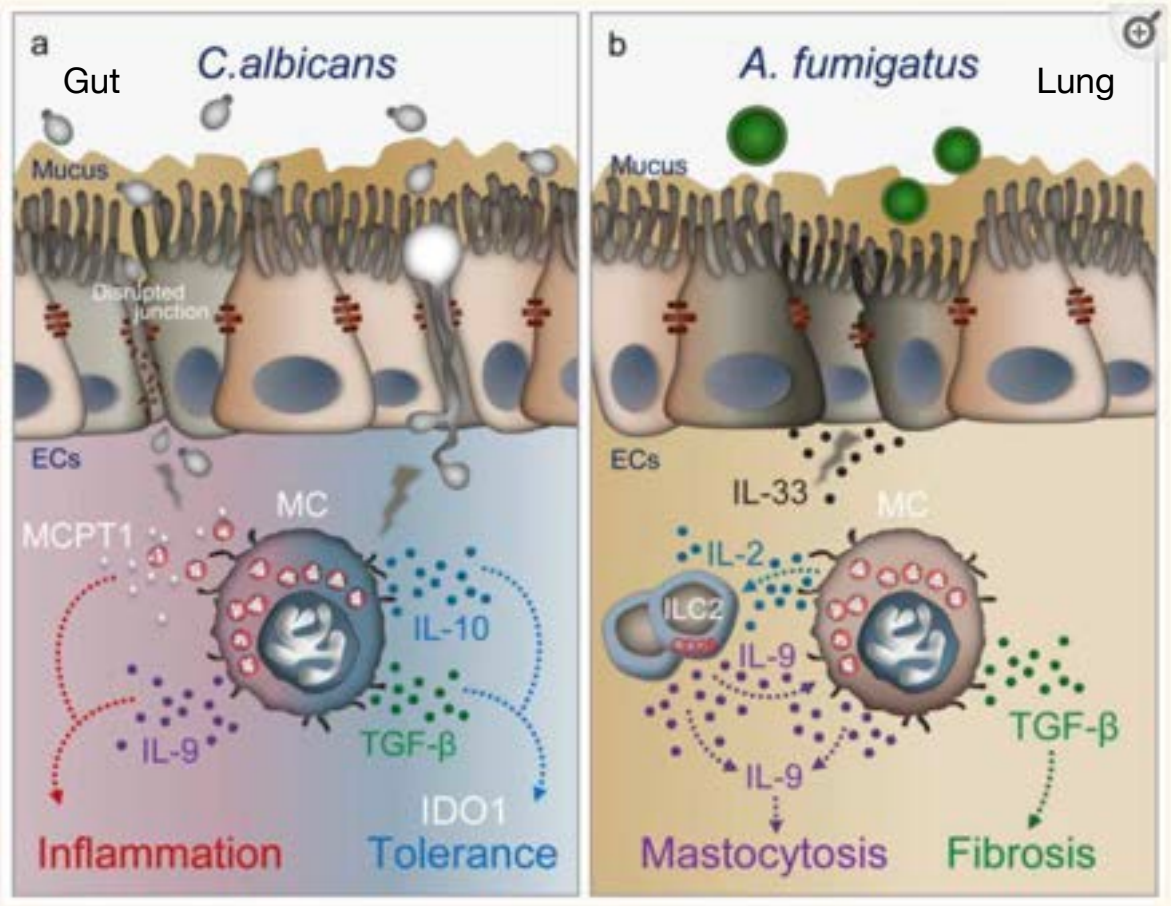
Colonic mast cell infiltration and mediator release from IBS patients, but not controls markedly enhanced the firing of mesenteric nerves, and stimulated mobilization of Ca(2+) in dorsal root ganglia neurons known to mediate nociception.

Effects were inhibited by histamine ***H(1)*** receptor blockade.

Can use biopsy from upper GI or colonoscopy. CD117 to look for mast cells. >20 mast cells significant for MCAS.

Symptoms related to eating ~
Post-prandial flushing
Post-prandial fatigue
Post-prandial brain fog
Post-prandial drop in bp
Gastroparesis
GI: heartburn, N/V, constipation, diarrhea
Food avoidances related to histamine concentration, esp left-overs

PMID: 19527167, 19201896, 29431211

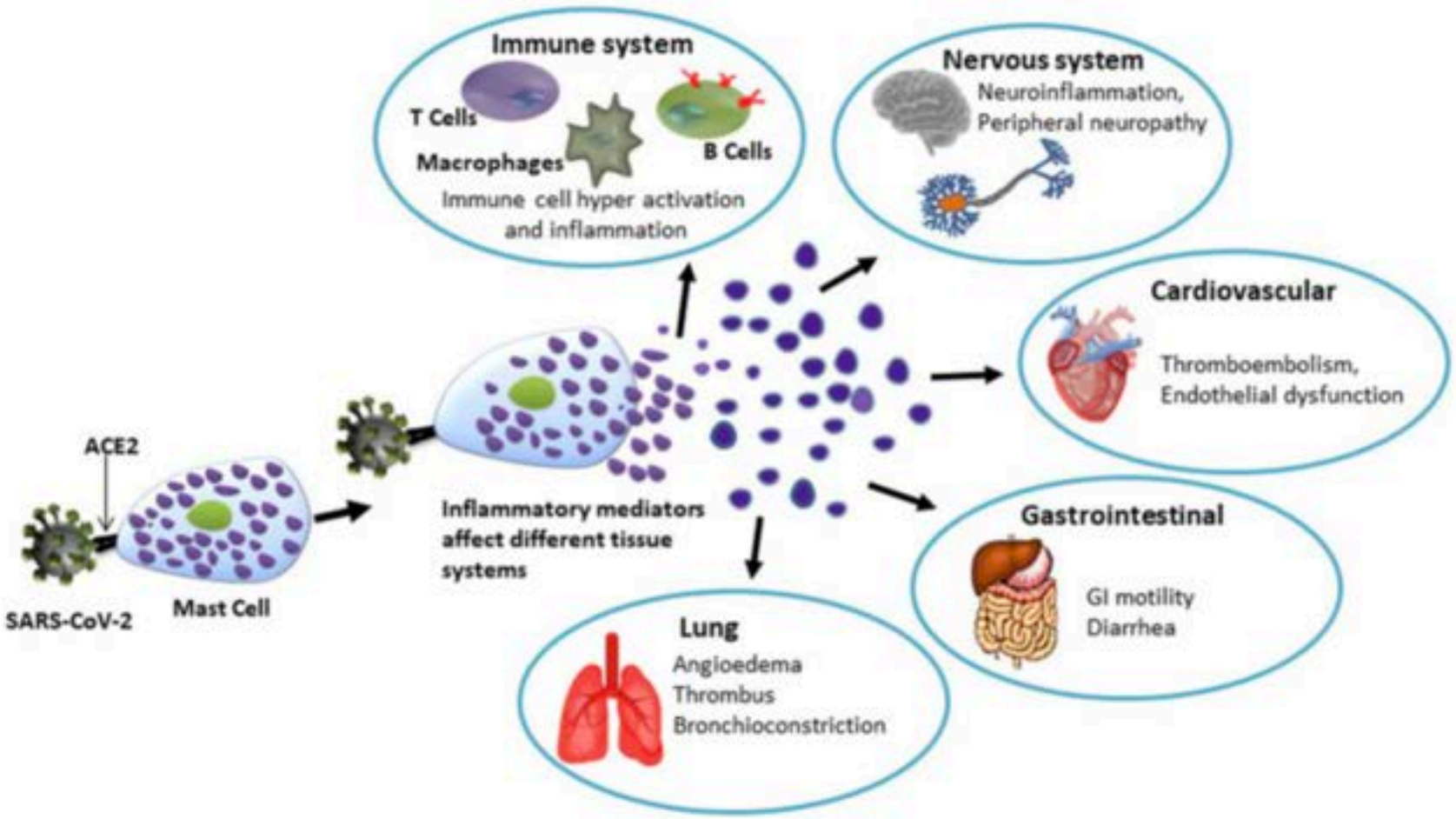


Mast cells are key players of Candida commensalism and pathogenicity at mucosal surfaces.

Empirically, increased recruitment at the stage of Evasion → Invasion of fungi.

Mold mycotoxins enhance mast cell recruitment, survival, and degranulation.

PMID: 27381299, 19527167, 19201896, 29431211



PMID: 37663654

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Dopamine receptor involvement

Dopa receptor1 & 2: posited targets of autoantibody attack, but don't forget

LPS effect:

LPS caused the loss of dopaminergic neurons (in substantia nigra pars compacta) and microglia migration in a dose-dependent manner in a rat study

Dopamine excess (possibly during flare only?)

Possible dopamine deficiency when in remission

Synaptic pruning of excitatory connections may be increased in PANDAS

Glutamate excess

Cholinergic interneuron antibody binding

PMID: 26454143, 29233751, 26866234

Cholinergic interneurons

Cholinergic interneuron (CIN) deficiency has been independently associated with tics in humans and with repetitive behavioral pathology in mice, making it a plausible locus of pathology.

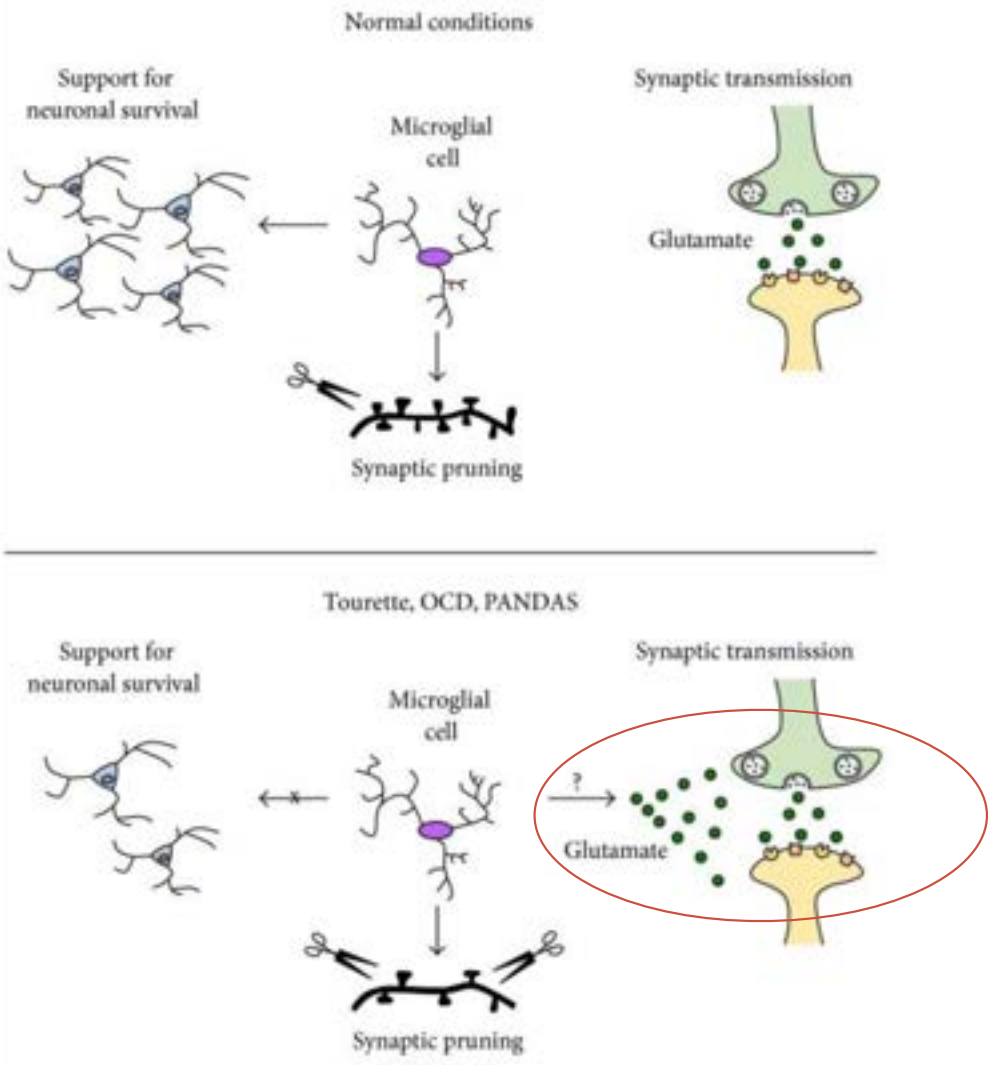
Pilot work suggests that IgG antibodies from children with PANDAS bind to cholinergic interneurons (CINs) in the striatum.

IgG from children with PANDAS bound to CINs, but not to several other neuron types, moreso than IgG from control subjects, in three independent cohorts of patients.

Post-IVIG serum had reduced IgG binding to CINs, and this reduction correlated with symptom improvement.

Baseline PANDAS sera decreased activity of striatal CINs and altered their electrophysiological responses, however post-IVIG PANDAS sera and IgG-depleted baseline sera did not alter the activity of striatal CINs.

PMID: 32539528



"Possible mechanisms of abnormal microglial functions in OCD, Tourette syndrome, and PANDAS.

Microglial cells support neuronal survival, and deficiencies in IGF-1 expressing microglia might lead to interneuronal loss (as observed in Tourette syndrome) or to abnormalities in synaptic pruning (as seen in animal models of GAS infection and excessive grooming).

Microglial dysregulation may also lead to alterations in glutamate homeostasis, a phenomenon that occurs in OCD."

PMID: 28053994

Neurotransmitter dysregulation

End result - increased dopa, glutamate, dysregulated ACh

Gut microbiota regulate the production, transportation, and functioning of neurotransmitters.

Persistent message “unsafe” to limbic system.

PMID: 34205336

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Cell danger response (CDR)

My thanks to Drs. Neil Nathan and Ben Lynch for “making me” learn this.

CDR is a universal response to environmental threat or injury that protects cells and hosts from harm.

Under direct control by ancient pathways in the brain that are ultimately coordinated by centers in the brainstem. (What happens if the basal ganglia is chronically inflamed?)

Expands the role of mitochondria beyond being the “powerhouse of the cell” to also being a protector and communicator of the cell status.

Mitochondria regulate the CDR (which controls innate immunity and healing), by monitoring and responding to the physical, chemical, and microbial/biological conditions within and around the cell.

Threats that exceed the cellular capacity for homeostasis trigger the CDR.

Chemical pollutants in the environment lower the threshold for CDR activation. In this way, mitochondria connect cellular health to environmental health.

Once triggered, healing cannot be completed until the the danger has been eliminated or neutralized, after which the CDR is reversed through a choreographed sequence of anti-inflammatory and regenerative pathways, and return to an updated state of readiness.

Although it’s a cellular response, CDR has the power to change human thought and behavior, child development, physical fitness and resilience.

PMID: 31877376, 23981537, 26056033

CDR “sickness behavior”/“sickness response”

When the CDR is triggered, the priorities of the organism are reset to optimize survival.

The response to danger involves an adaptive means of redirecting energy and includes ~
- Withdrawal from social contact
- Activation of innate immunity
- Decreased speech
- Fragmented sleep
- Head, muscle and abdominal aches
- Changes in the gut microbiome
- Increased sensitivity to touch, sound, and light

Similar to what many people experience when they have the flu or recovering from a serious injury.

It is the CDR that produces these familiar signs and symptoms.

Even though the term “sickness behavior” is a defined scientific term,
I prefer “sickness response”, as “behavior” can be misconstrued as a choice.

PMID: 31877376, 23981537, 26056033, 25639499

CDR in chronic illness

Abnormal persistence of the CDR lies at the heart of many chronic diseases.

CDR produces a cascade of changes in cellular electron flow, oxygen consumption, redox, membrane fluidity, lipid dynamics, bioenergetics, carbon and sulfur resource allocation, protein folding and aggregation, vitamin availability, metal homeostasis, indole, pterin, 1-carbon and polyamine metabolism, and polymer formation.

Persistent activation of CDR inhibits healing, alters metabolism and gut microbiome, impairs the collective performance of multiple organ systems, changes behavior into “sickness response”, and chronic disease results.

CDR is different from the immune response which involves activation of the immune system. Instead this is a cellular response to the danger - “batten down the hatches” of the cell while the immune system takes on the danger. Possible to have one without the other?

Metabolic memory: past encounters with stressors are stored in the form of altered mitochondrial and cellular macromolecule content, resulting in metabolic memory of the past stressors.

PMID: 31877376, 37114062

Stages of CDR

3 sequential stages, separated by quality control checkpoints, CD1, CD2, CD3. (More about these details in bonus video by Dr. Neil Nathan.)

Abnormal persistence of any phase of the CDR inhibits the healing cycle.

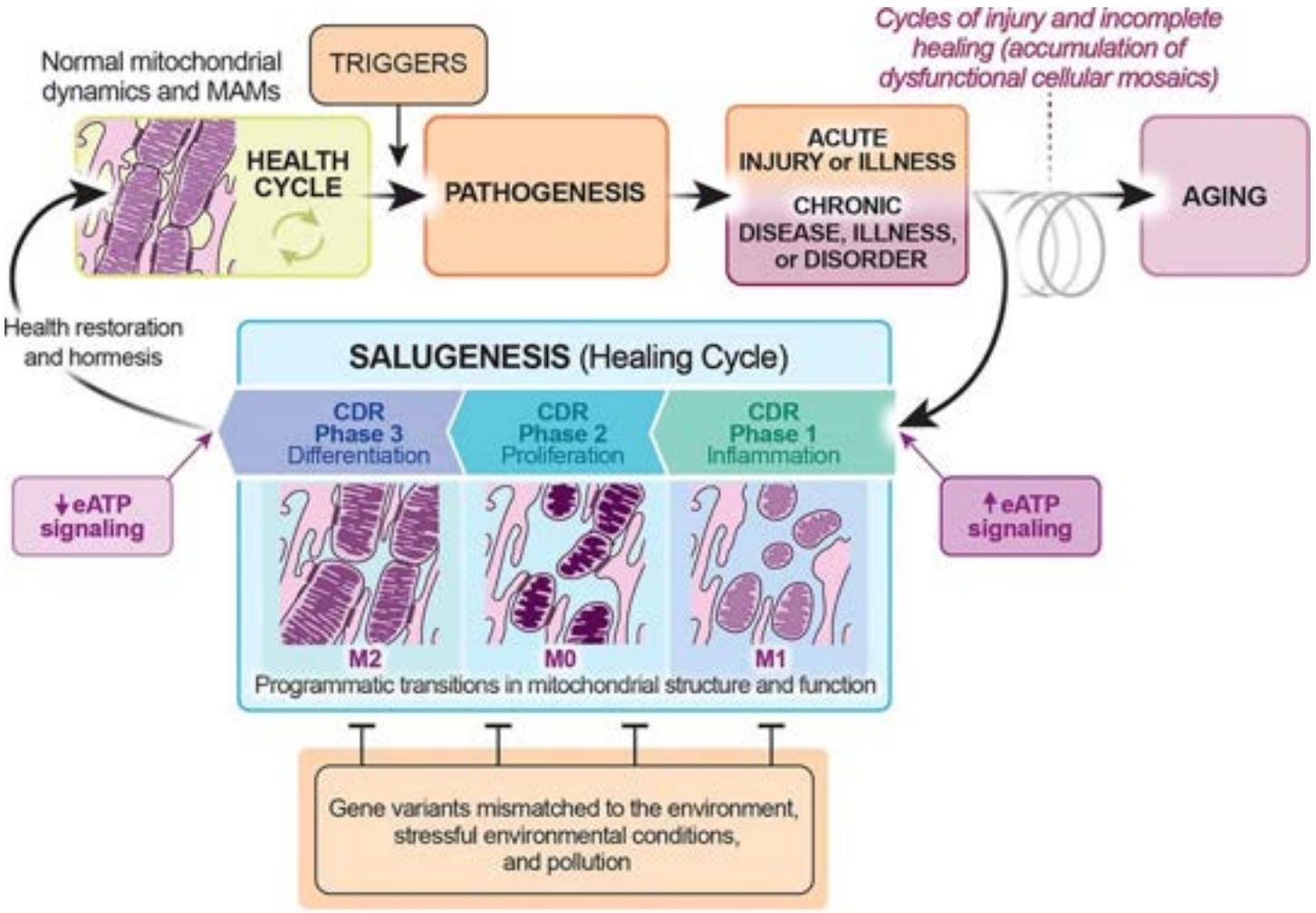
Different tissues may be at different stages of the CDR.

The importance of water: changes in mitochondrial dynamics during cell stress in tissues link increasing cytoplasmic disorder with increasing disorder of water molecules, and an increase in CDR-associated functions. (MOA structured water tx?)

The rise and fall of extracellular ATP (eATP) signaling is a key driver of the mitochondrial and metabolic reprogramming required to progress through the healing cycle.

Sphingolipid and cholesterol-enriched membrane lipid rafts act as rheostats for tuning cellular sensitivity to *purinergic signaling*.

PMID: 37120082



Abbreviation: MAMs, mitochondria-associated membranes; eATP, extracellular ATP; CDR, cell danger response. © Naviaux Lab/UCSD

PMID: 37120082

Purinergic signalling and oxidative shielding

Purinergic signalling and oxidative shielding ~
First wave of danger signals consists of the release of metabolic intermediates like ATP and ADP, Krebs cycle intermediates, oxygen, and reactive oxygen species (ROS), and is sustained by purinergic signaling (ie: ATP outside the cell as a signal of the state of the cell.)

Purinergic signalling = ATP acting as an extracellular signalling molecule (eATP).

Purinergic signalling maintains the CDR and appears to play an important role in neurodegeneration, neuroprotection and neuroregeneration.

Compelling evidence that ATP is a cotransmitter in most if not all nerves in the PNS and CNS (ie: co-released with Ach, dopa, glutamate, catecholamines.)

Additional alterations interfering with methylation, vitamin D and tryptophan metabolism, histamine and heme concentrations, lysine and P5P (pyridoxal 5-phosphate) utilization.

Antipurinergic treatments may be an effective target. (Animal models - suramin)

SARS-CoV-2 spike protein alters microglial purinergic signaling.

PMID: 31877376, 23981537, 26056033, 27573827, 23516405, 29253638, 37114062

Limbic dysregulation

More detailed and technical information, as well as treatment suggestions, can be found in the bonus video by Dr. Neil Nathan.

Limbic system in the brain gets stuck in hypervigilance.

Related to a sense of safety, or rather lack thereof.

Correlated to anxiety disorders and myofascial pain syndromes. Chronic pain and olfaction share common limbic cortical regions.

Autoimmune encephalitis describes a group of disorders characterised by symptoms of limbic and extra-limbic dysfunction occurring in association with antibodies against synaptic antigens and proteins localised on the neuronal cell surface.

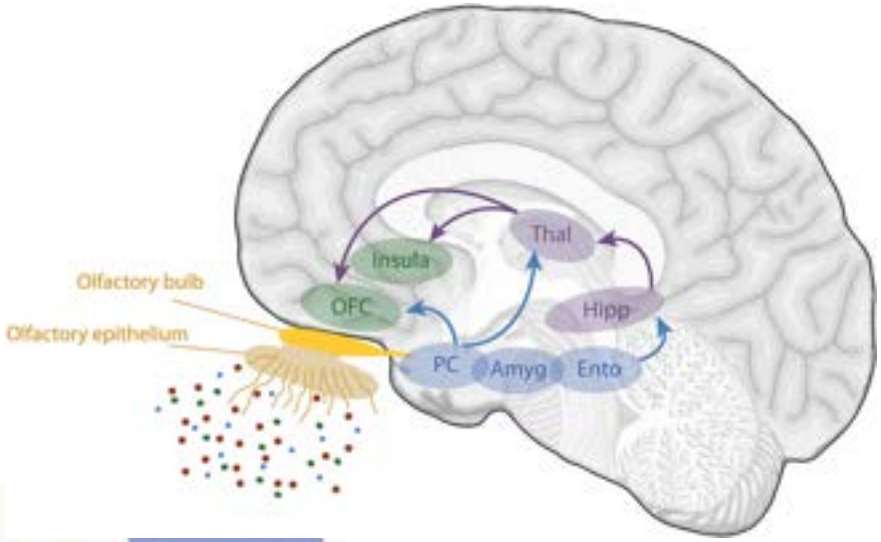
Anorexia nervosa neural roots appear to be related to dysfunctional, primarily limbic, circuits driving pathological thoughts and behaviors. Key limbic modulatory structures, such as the subcallosal cingulate and insula.

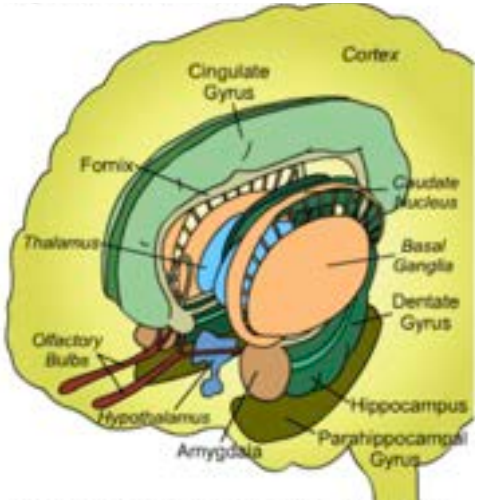
PMID: 28470168, 36307317, 25724849, 27330568, 24703713

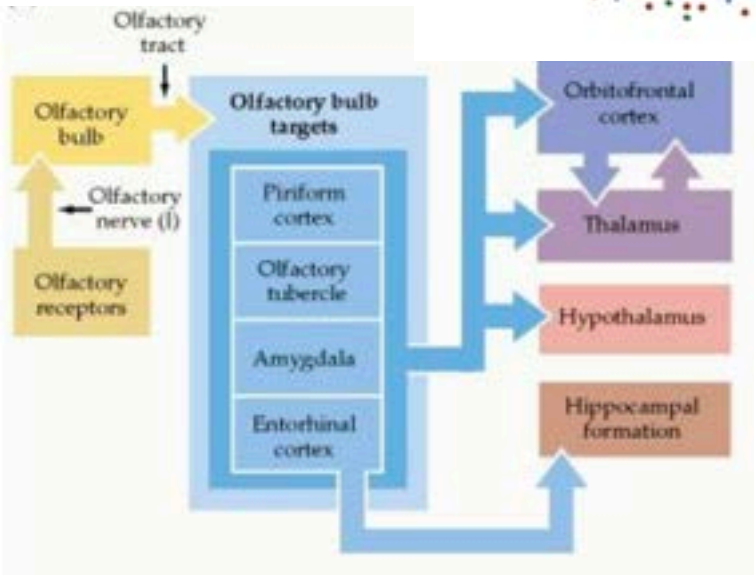
Olfactory-limbic connection

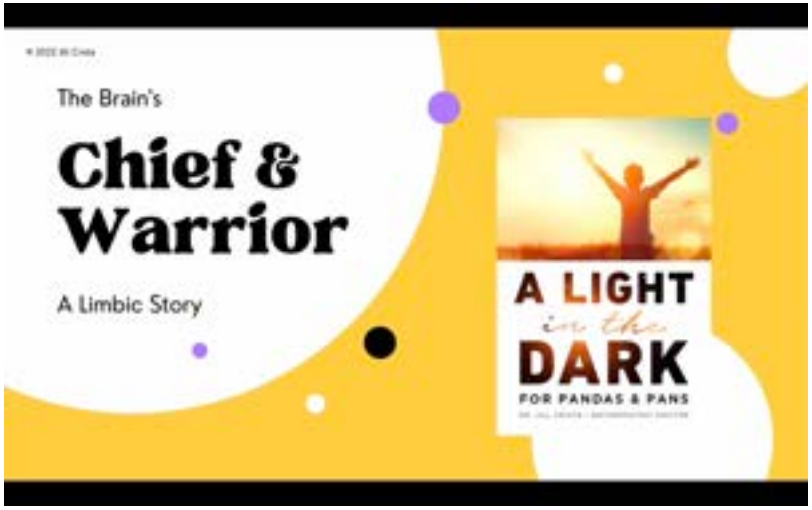
The sense able to communicate effectively to the whole limbic system is the sense of smell.

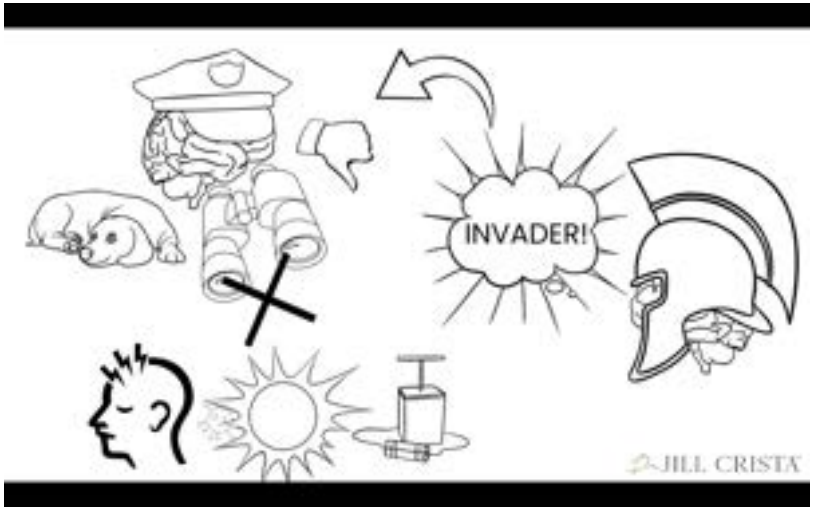
The olfactory nerve is circuitous and interacts with many different limbic centers in the brain.

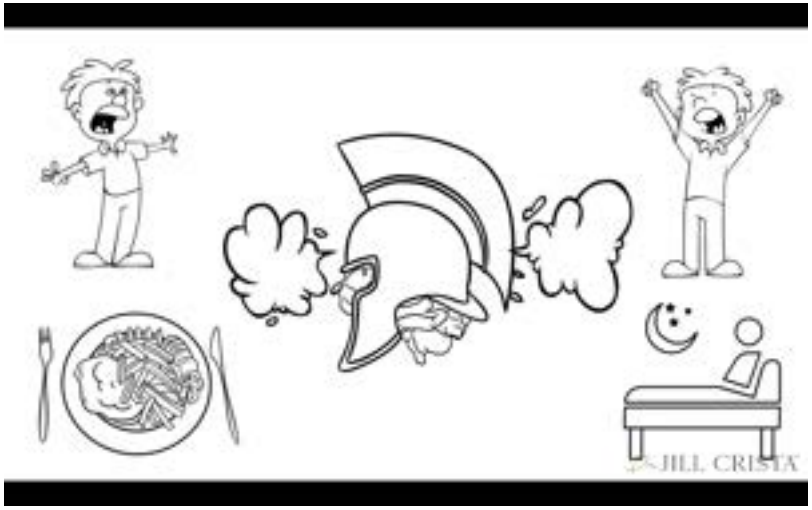


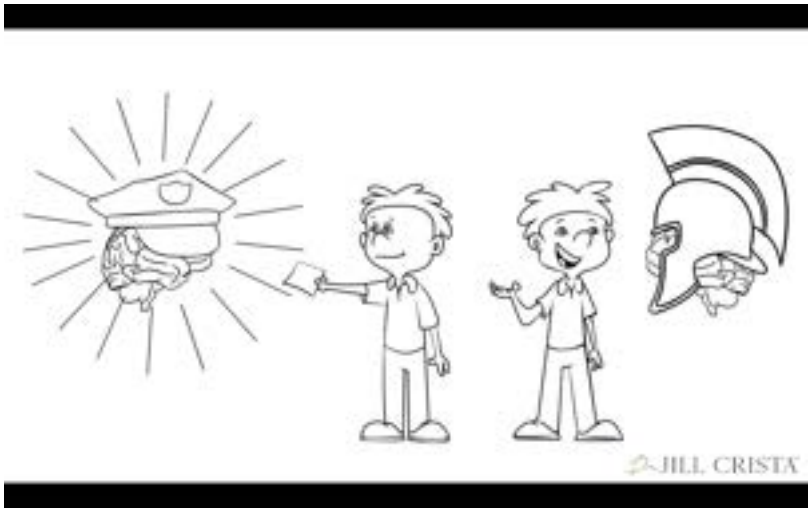












Polyvagal Theory: a science of safety

"Offers a neurophysiologic framework to consider why you act in the way you do. Actions are automatic and out of your conscious control."

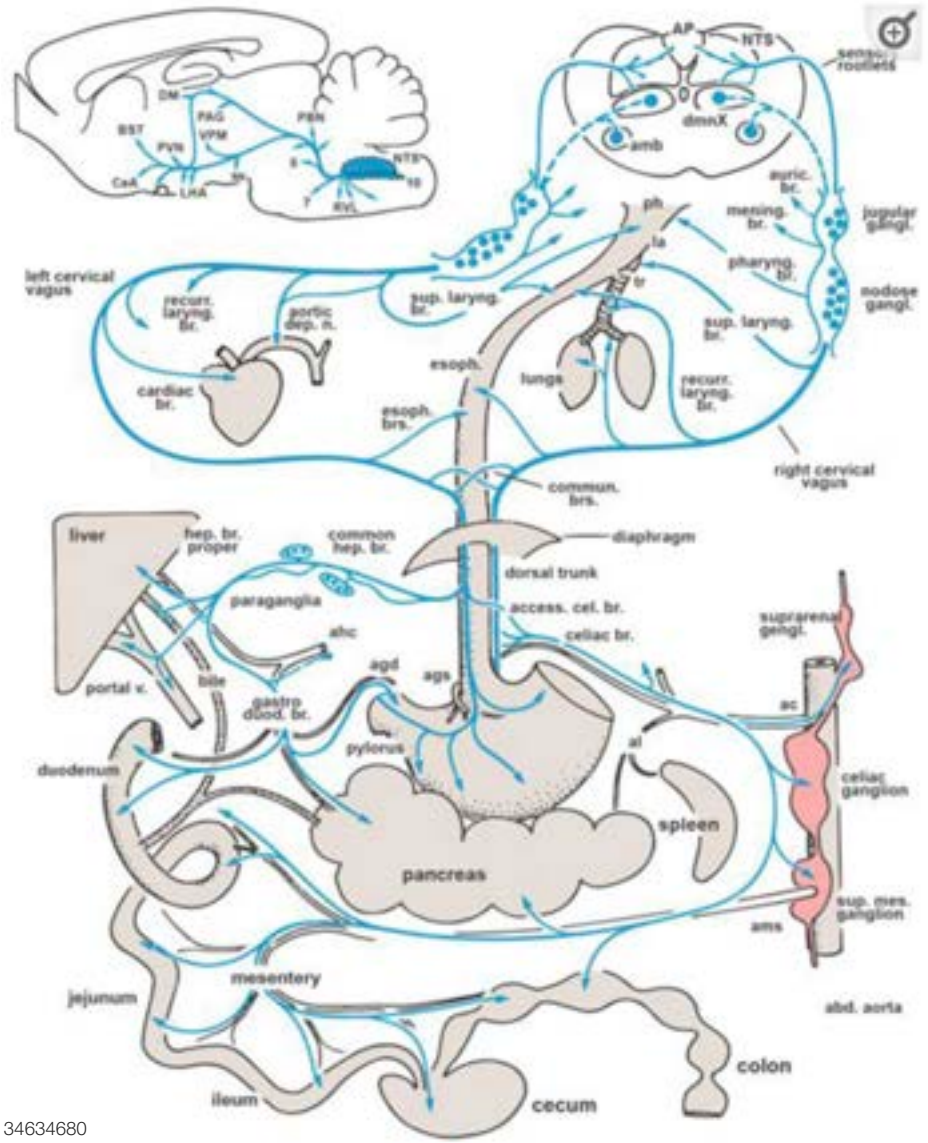
3 defining principles ~

1. The ANS has a hierarchy among which we move depending on sense of safety.
   - Ventral vagal
   - Sympathetic
   - Dorsal vagal

2. Neuroception: "safety scan". The process of your ANS unconsciously scanning for cues of safety, danger and threat. Your nervous system then uses that information to control your HR, RR, muscle tension, GI function, pain tolerance - almost every system in your body changes because your vagus nerve links them all together.

3. Co-regulation: "safer in community". Considered by PVT as a biological imperative in order to survive. Concept - your nervous system needs to be in connection with other nervous systems in order to feel both physical and psychological wellbeing.
   The key is coregulating with other nervous systems that have found their way to ventral vagal regulation.

PMID: 35645742, 30115210



PMID: 34634680

The wandering vagus nerve

Vagus (Latin meaning wander)

Extends from brain stem, along arteries, through heart, lungs, diaphragm, digestive system, liver, gallbladder, spleen, pancreas and kidneys.

The neuroception of danger in one organ is very quickly transmitted to the other organs.

Healthy individuals can freely move between each state.

Trauma survivors and those with a chronically inflamed gut/brain can get stuck in a sympathetic or dorsal vagal state.

Possible link between prenatal events with neurodevelopment and the later onset of psychiatric disorder.

Natural pattern of connection is replaced with a pattern for protection.

Polyvagal Theory Explained Simply
Lewis Psychology YouTube channel
https://www.youtube.com/watch?v=SlhFrBoEnxU

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CNS structural alterations

CNS structural alterations

Imaging studies distinguish OCD from normal controls

PANDAS children have MRI grey matter alterations in the cortex, subcortex, and cerebellum as compared to age-matched healthy controls “suggesting that the anatomical gray matter characteristics could have an immune origin.”

PANDAS children have increased striatal volumes during acute illness, as well as increased microglia activity in the striatum compared to healthy adult controls

PET study with microglia tracer examined both PANDAS and Tourette syndrome (considered noninfectious)
- Inflammation was higher and more broadly spread through the bilateral caudate and lentiform nucleus in PANDAS than in age-matched non-PANDAS Tourette syndrome
- The observed differences support the notion that PANDAS is etiologically distinct from Tourette syndrome.

Alterations extend beyond the basal ganglia to include the cortico-striato-thalamo-cortical circuit

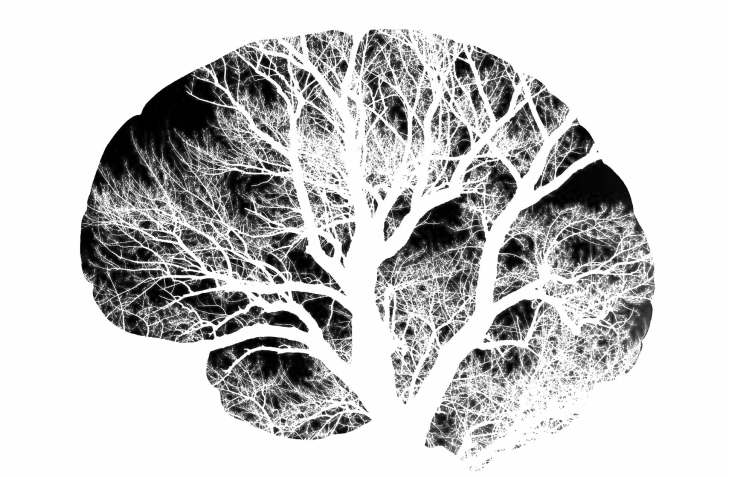
PMID: 30428956 , 28636705, 25117419, 10671403, 8768351

CNS structural alterations

"Imaging and neurological signs suggest basal ganglia inflammation

Basal ganglia exerts an inhibitory influence on motor & behavior systems.

Inflammation/autoantibodies/injury causes disinhibition and thus disrupts the normal role of the basal ganglia in governing:
- Movements
- Mood & emotion
- Behavior
- Procedural learning
- Cognition"



Frankovich, Stanford PANS clinic,
presentation Neuroimmune conference May23

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Cell danger response → limbic/vagal dysfunction

CNS structural alterations

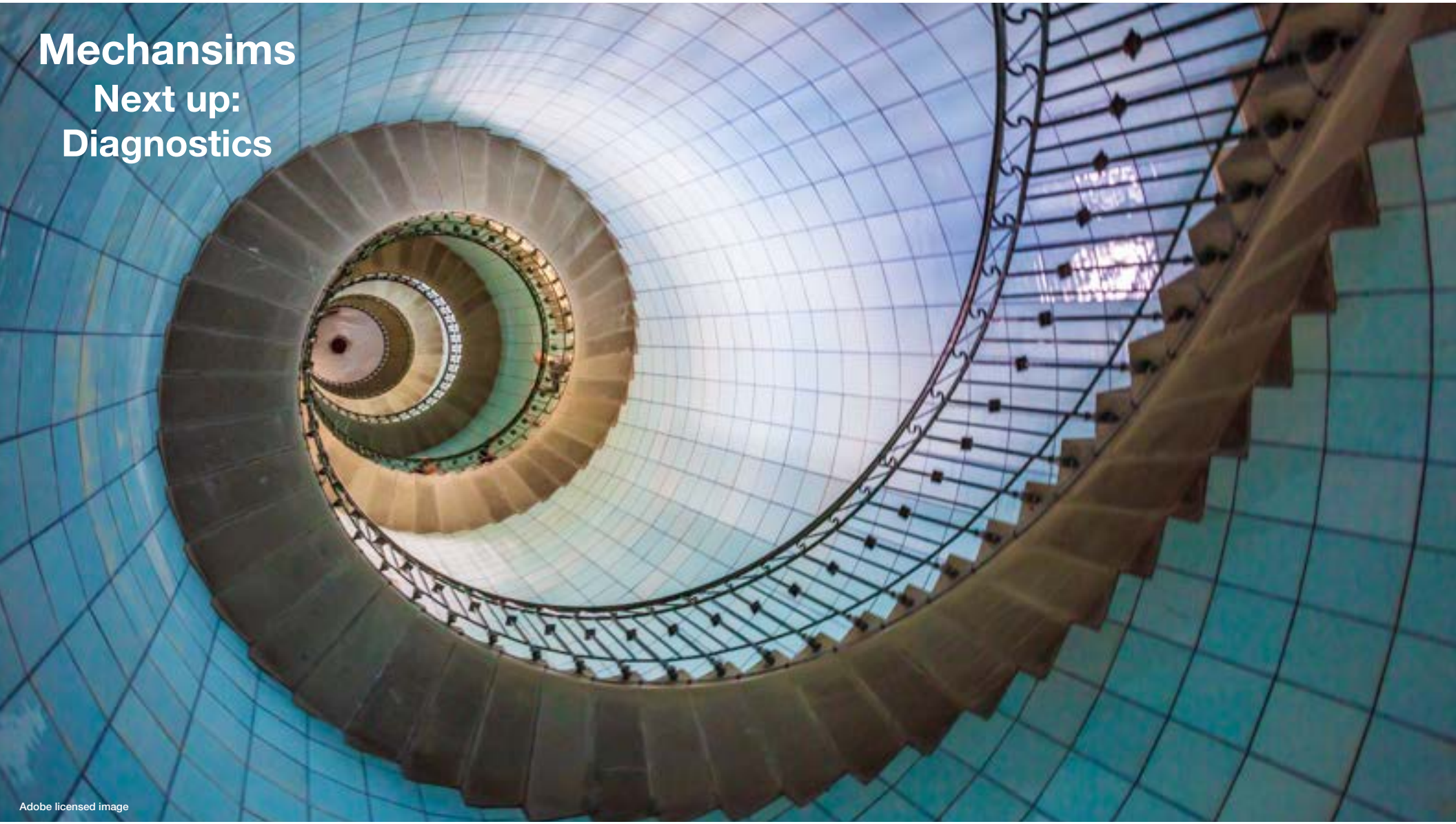
PANDAS/PANS Symptom Recap

Separation anxiety
Inability to concentrate
Urinary frequency, urgency, or urinary accidents
Handwriting deterioration
Alterations in sleep - insomnia, night terrors, inability to sleep alone
Behavioral regression
Hyper-alert appearance; enlarged pupils
Hyperactivity
Inattentiveness
Tics
Learning difficulties
Short-term memory loss
Aggression
Sensory alterations - hypersensitive or insensitive
Disordered eating
Hallucinations, rarely

Take some parenting classes??

Mechansims

Next up: Diagnostics



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PANDAS & PANS
An Integrative Approach

Dr. Jill Crista

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Diagnostics

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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

Diagnostics

Clinical diagnosis

PE and symptoms as clues

General diagnostics

Infectious triggers

Environmental triggers

Diagnostics

Reminder ~
These are

CLINICAL DIAGNOSES

If a P/P-specific test was negative, a child can still have PANDAS or PANS.

IME, we are relying too much on antibody tests to diagnose these conditions. Because many of these kids have subclinical immune deficiency, many don't have a strong enough antibody response to affect the test. This may lead to a falsely normal test.

Be mindful of the steroid effect on antibody-based labs.

Neuro P/E relevant to BGE

Burdened appearance
Dilated pupils
Hypotonia
Motor apraxia
Dyspraxia
Normal strength
Normal reflexes, not hyperactive as in Wilson's dz
Abnormal movements
Chorea
Choreiform movements, not age appropriate
Tics
Steriotypies
Ballismus
Overall rational irrationality (they realize or have insight into the abnormality)

Presented by Dr. Elizabeth Latimer
Autoimmune Encephalitis Post-Streptococcal Evaluation & Treatment Conference Oct 2019

Honor the triggers

Once the autoimmune process has started…

Environmental exposures and infections can and will flare them.

the child knows where/who is carrying something that will put them at risk

And will tell you with their behavior - honor that.

It's not pathological. It's the innate intelligence of the system at work.

Certain spaces/places may be the trigger.

Parents/siblings/caregivers may be the trigger.

Parent self care is critical in order to not be a carrier.

Additional triggers

Lose a tooth/dental visit

Puberty onset

Injury

Sunburn

Allergies

Many bug bites/spider bite

Family strife/move/loss of structure

Loss of friendships

Abuse

Symptoms with hints toward cause

Congenital Borrelia (Lyme) ~
 Atonia (reported 97% prevalence congenital Lyme by Dr. Charles Ray Jones)

Bartonella ~
 Rage/aggression

EBV ~
 Fatigue/“laziness”, chronic sore throat

Glyphosate + Mold ~
 Anxious

Glyphosate + Bartonella ~
 Persistent, non-specific abdominal pain

Mold ~
 Urinary frequency/urgency without infection, dysautnomia, PoTS

Mold + Bartonella ~
 Hypermobility

Candida ~
 Despair, suicidality

Diagnostics

Clinical diagnosis

PE and symptoms as clues

General diagnostics

Infectious triggers

Environmental triggers

General diagnostics

PANDAS/PANS (Cunningham)

Other neuro antibodies

Immune competence (IgGAME, PID, CVIDS, lymphocytes)

Imaging - Neuroquant

Food sensitivity

Sinunasal microbiologics

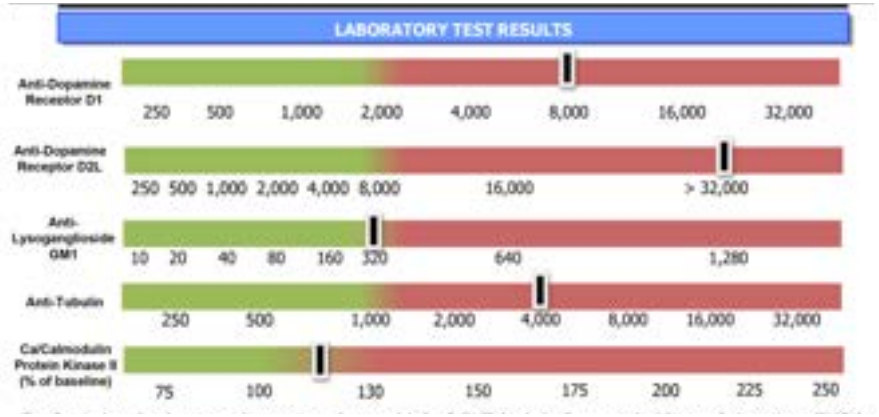
Drug metabolism

Genetic predispositions/expressions

Testing for coverage

On the horizon

Cunningham Panel ™



Considered (+) if one or more of these markers is elevated.

Suggests that neuropsych sxs may be due to an autoimmune process.

5 markers:

1. Anti-Dopamine D1 Receptor (psychosis, OCD and tics)
2. Anti-Dopamine D2L Receptor (uncontrolled motor movements, hyperactivity and impulsivity)
3. Anti-Lysoganglioside-GM1 (sleep disturbances, behavioral regression, obsessions/compulsions)
4. Anti-Tubulin (OCD-like symptoms and cognitive impairment/brain fog)
5. Calcium/calmodulin-dependent protein kinase II (CaMKII) (involuntary movements, cognitive interference, emotional lability

CaMKII is a cell stimulation assay; measures the ability of a patient's autoantibodies to stimulate the CaMKII enzyme in human brain cells. The CaMKII is involved in upregulating the production of neurotransmitters – dopa, epi, and NE.

Best suited to classic PANDAS?

Autoantibodies

Antinuclear antibodies multiplex, reflex to dsDNA, RNP, Sm, SS-A, SS-B

Demyelination Antigens ~
- Anti-tubulin IgM/IgG+IgA
- Anti-myelin basic protein IgM/IgG+IgA

BBB Disruption ~
- Anti s100b IgM/IgG+IgA (*increases with exercise)

Optical and ANS Disorders ~
- Anti-neuron specific enolase IgM/IgG+IgA

Peripheral Neuropathy ~
- Anti-GM1 IgM/IgG+IgA
- Anti-GM2 IgM/IgG+IgA

Brain Autoimmunity ~
- Anti-HSV1 IgM/IgG+IgA
- Anti-cerebellum IgM/IgG+IgA
- Anti-purkinje cell IgM/IgG+IgA
- Anti-pituitary antibodies (APA) (hypophysitis post TBI)

Immunocompetence

Quantitative IgGAME with IgG subclasses ~
Red top tube or SST? Depends on goals for testing.
Serum separator will bind some antibodies and under-report, esp in those with low Ig's.
(🙏 Dr. Paul Anderson)

NOTE that all antibody-based testing will be affected by IVIG, including other autoimmune and infection.

Lymphocyte Subset/Differential Panel ~
Offers the advantage of detecting the cell type that causes the immune defect.

3 types of lymphocytes: B, T and NK cells.
All share the same progenitor cells: hematopoietic stem cells in the bone marrow, which then give rise to multipotent progenitors, to early lymphocyte progenitors (ELP) and eventually to the differentiated progenitors of NK, B or T cells.
B and T lymphocytes are both antigen-specific lymphocytes and the main regulators of the adaptive immunity.
NK cells, in contrast, are not antigen-specific lymphocytes, thus belonging to the innate immune system.

PMID: 30248214

B cell differentiation

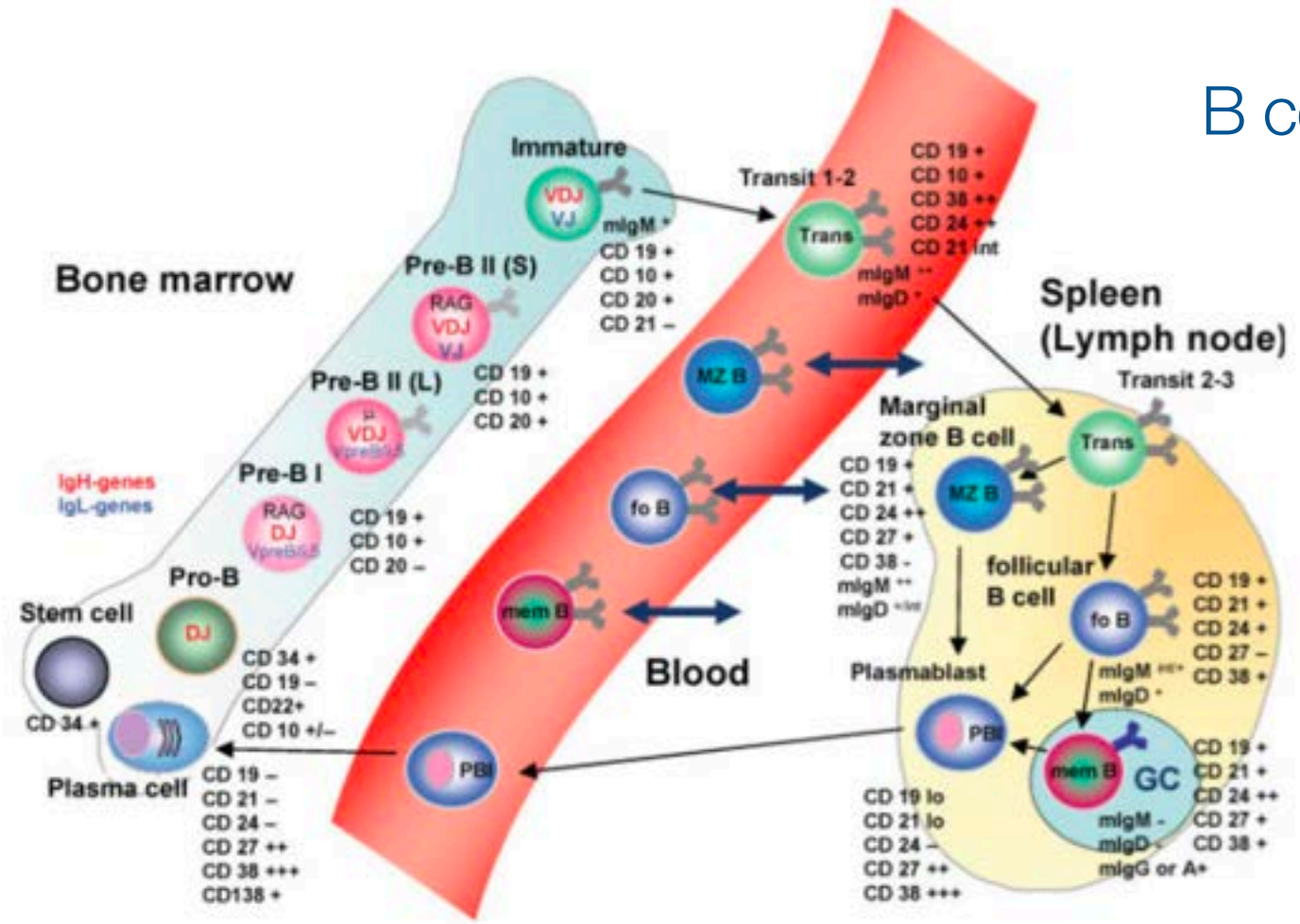


Fig. 1 The central and peripheral development and differentiation of B cells. fo B, follicular B cell; GC, germinal center B cell; mem B, memory B cell; mIg, memory immunoglobulin; MZ B, marginal zone B cell; PBl, plasmablast; Trans, Transitional B cell. Reproduced with permission from Warnatz and Schlesier.[19]

PMID: 30248214, 31694331

CD antigens, also known as cluster of differentiation, are cell surface antigens of leukocytes.

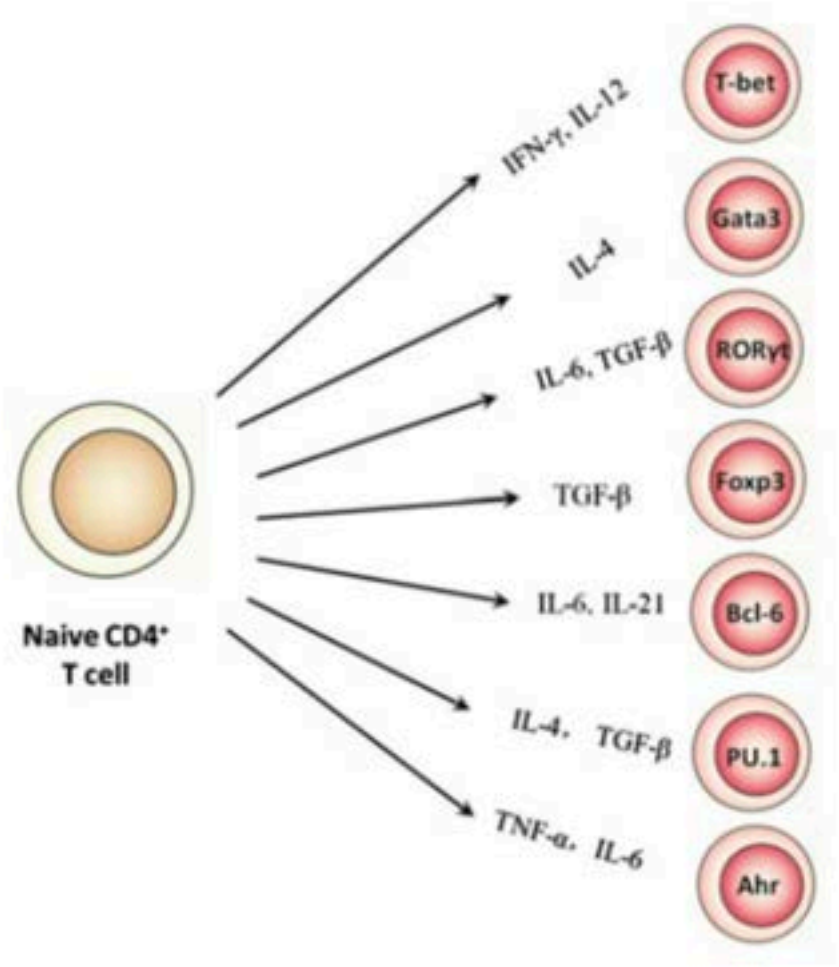
May be expressed only at certain stages of development or under certain conditions.

Some of the surface antigens are useful for delineating the cell lineage of leukocytes.

Mycotoxins dysregulate T and B cell differentiation at multiple steps —> immunosuppressive effects, such as CD27 depletion, related to multiple myeloma.

T cell differentiation

Determined by the inflammatory milieu



Th1: IFN-γ
Defense against intracellular parasites

Th2: IL-4, IL-5, IL-13
Control helminths and extracellular pathogens.
Allergic inflammation

Th17: IL-17
Defense extracellular bacteria or fungi.
Autoimmunity

Treg: TGF-β, IL-10
Immune homeostasis

Tfh: IL-21
Help B cell to make antibodies, Affinity maturation and antibody class switching

Th9: IL-9
Skin homeostasis, Tissue infalmmation.

Th22: IL-22
Tissue inflammation

PMID: 30248214

Identifying Primary Immunodeficiency

Low absolute lymphocyte count (<3,000/mm^3) suggests a cellular immunity defect and constitutes a strong indication for lymphocyte subset count (LSC).
*However, normal ALC cannot exclude such a defect.

LSC is one of the initial screening tests by general pediatrician for investigation of an immunological patient, with LSC being affected by age (Table 2 - next slide.)

Imperative to order LSC when a child presents with recurrent or opportunistic infections and the ALC is <3,000/mm^3.

Combination of good clinical examination with good interpretation of LSC will facilitate the dx of most of the common PID.

Approximately 50%–60% of all identified PID are caused by defects in antibody production. Such patients usually develop upper and lower respiratory infections, especially from encapsulated bacteria, as well as chronic GI infections from Giardia lamblia or enterobacteria.

A characteristic feature of these humoral immunity defects is the deterioration of the clinical profile after the first 6 months of life, as the levels of maternal antibodies start to recede.

PMID: 30248214

Table 2 Lymphocyte subset percentages in healthy children: Distribution by age (reproduced with permission from Shearer *et al*[18])

Subset	*n*	0–3 months Median (range)	3–6 months Median (range)	6–12 months Median (range)	1–2 years Median (range)	2–6 years Median (range)	6–12 years Median (range)	12–18 years Median (range)
3	709	73 (53–84)	66 (51–77)	65 (49–76)	65 (53–75)	66 (56–75)	69 (60–76)	73 (56–84)
19	709	15 (06–32)	25 (11–41)	24 (14–37)	25 (16–35)	21 (14–33)	18 (13–27)	14 (06–23)
16/56	784	8 (04–18)	6 (03–14)	7 (03–15)	7 (03– 15)	9 (04–17)	9 (04–17)	9 (03–22)
4	709	52 (35–64)	46 (35–56)	46 (31–56)	41 (32–51)	38 (28–47)	37 (31–47)	41 (31–52)
8	709	18 (12–28)	16 (12–23)	17 (12–24)	20 (14–30)	23 (16–30)	25 (18–35)	26 (18–35)
4/45RA/62L	805	89 (61–94)	88 (64–92)	83 (58–91)	79 (62–90)	70 (50–85)	58 (42–74)	51 (31–65)
8/45RA/62L	807	79 (56–88)	77 (53–88)	72 (47–87)	71 (46–85)	64 (42–81)	58 (39–73)	56 (42–73)
4/45RA	805	90 (64–95)	90 (77–94)	86 (64–93)	81 (63–91)	71 (53–86)	59 (46–77)	53 (33–66)
8/45RA	807	93 (80–99)	94 (85–98)	91 (75–97)	89 (71–98)	86 (69–97)	80 (63–92)	79 (61–91)
4/DR/38	805	3 (01–06)	4 (02–09)	4 (01–09)	5 (02–09)	5 (02–09)	4 (01–08)	3 (02–06)
8/DR/38	807	5 (02–17)	7 (03–16)	8 (03–25)	15 (05–30)	13 (05–29)	9 (02–20)	7 (03–18)
4/DR	805	3 (02–06)	5 (02–10)	5 (02–11)	6 (02–11)	7 (03–12)	6 (03–13)	7 (04–11)
8/DR	807	5 (02–20)	7 (03–17)	10 (04–27)	16 (06–33)	16 (07–37)	12 (06–29)	12 (05–25)
4/38	805	98 (95–99)	96 (90–98)	95 (89–97)	93 (85–97)	87 (74–94)	79 (64–86)	69 (50–79)
8/38	807	97 (89–99)	95 (83–98)	93 (78–98)	91 (73–97)	82 (52–93)	70 (42–86)	64 (33–80)
4/28	806	99 (95–100)	99 (88–100)	98 (90–100)	98 (94–100)	98 (92–99)	98 (92–100)	97 (89–100)
8/28	806	76 (54–87)	75 (43–87)	70 (42–83)	69 (49–81)	63 (42–79)	60 (42–78)	58 (39–76)
4/95	806	11 (05–21)	14 (08–21)	18 (11–34)	23 (11–39)	31 (21–45)	39 (24–53)	49 (32–66)
8/95	806	12 (02–33)	15 (06–36)	22 (08–47)	31 (07–50)	34 (12–57)	36 (10–62)	44 (15–71)
3/4/45RO	676	10 (02–22)	8 (03–16)	9 (05–18)	12 (07–20)	16 (09–26)	21 (13–30)	28 (18–38)
$3/4^{-}$/45RO	672	3 (01–09)	3 (01–07)	3 (01–08)	6 (02–12)	9 (04–16)	12 (04–21)	13 (04–23)
3/45RO	676	14 (03–31)	13 (04–24)	12 (06–25)	19 (09–31)	27 (15–41)	33 (20–46)	41 (24–57)
3^{-}/19/38	686	49 (13–75)	66 (00–82)	66 (01–78)	60 (00–79)	55 (01–70)	39 (00.60)	19 (00–57)
3^{-}/19	686	50 (14–76)	69 (00–84)	67 (01–80)	63 (00–80)	61 (02–76)	46 (00–67)	21 (00–60)

PMID: 30248214

Common Variable Immunodeficiency (CVID) in peds

Mean age at symptom onset was 18 (3-204) months.

All CVID patients with pediatric onset had decreased levels of total and memory B cells, CD4+ T cells, CD4+CD45RA+ naive T cells, and recent thymic emigrant (RTE) cells.

On the other hand, they had increases in CD8+CD45RO+ memory T cells.

Specific cellular abnormalities associated with the reduction in B and NK cells and increase in CD8+ T cells were found in patients with bronchiectasis.

In pediatric CVID patients, low serum IgA levels and decreased numbers of naive T and RTE cells were determined as risk factors for chronic diarrhea.

PMID: 31901904

Neuroquant MRI

Specialized MRI must be run at specific Neuroquant centers.
- TBAR with asymmetry
- may need to order Brain Development report b/c TBAR changes may reflect neuronal development. (Dr. Gazda)

Does not require contrast. Age- and gender-matched controls.

Normal = 40-60 percentile.

May display enlargement of the caudate.
- Blue = edema/inflammation
- Red = atrophy

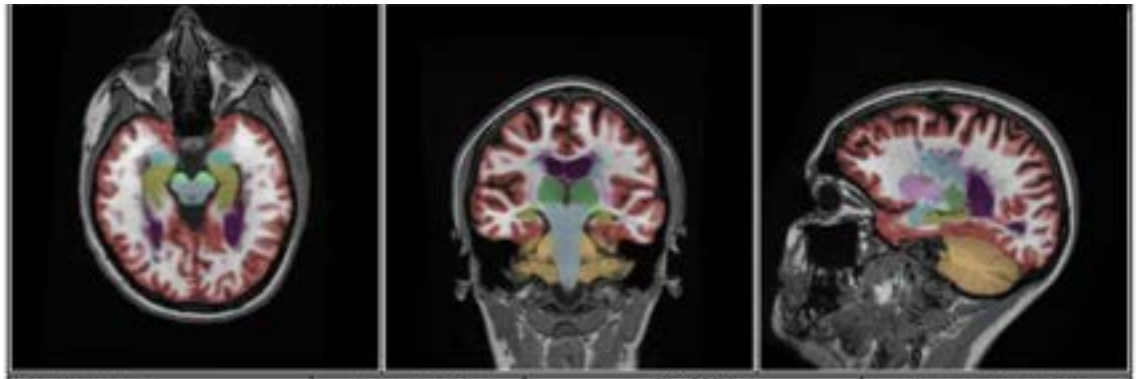
Thalamus >90% mold and Lyme. (Dr. Ackerly)

Not ideal for child with tics, as they can't remain still for imaging.

Also not ideal for sound sensitive child or child who cannot tolerate ears being covered.

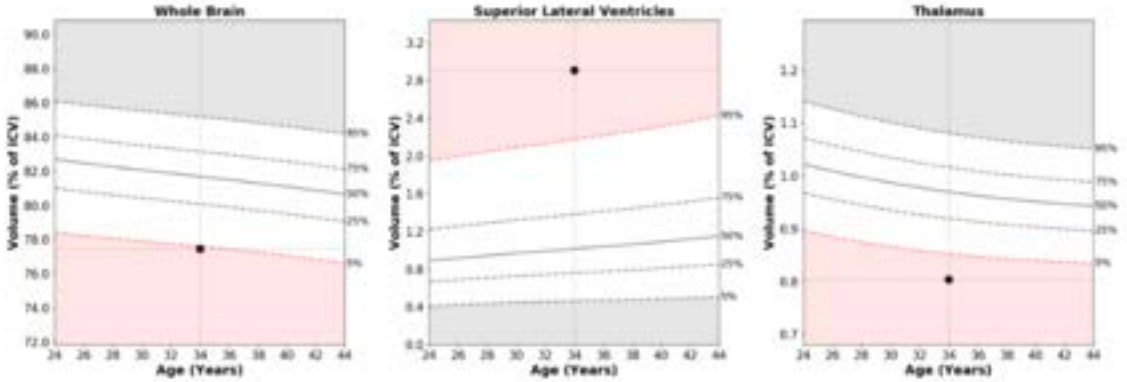
Braces/retainers will alter findings.

Neuroquant Ped Multistructure Atrophy Report

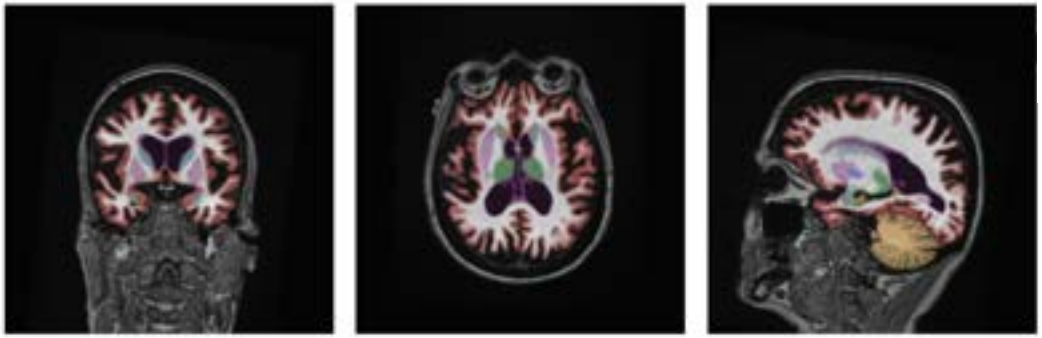


Brain Structure	Volume (cm³)	% of ICV (5%-95% Normative Percentile)	Normative Percentile
Whole Brain	1201.05	77.46 (77.59 - 85.18)	5
Superior Lateral Ventricles	45.14	2.91 (0.46 - 2.17)	99
Thalamus	12.46	0.80 (0.85 - 1.08)	1

AGE-MATCHED REFERENCE CHARTS



Neuroquant Triage Brain Atrophy Report TBAR



Brain Structure Volumes

Brain Structure	Volume (cm³)	Normative Percentile
Intracranial Volume	1433	-
Whole Brain	918	1
Forebrain Parenchyma	775	1

Brain Structure	Normative Percentiles Left	Right	Total
Cerebral White Matter	1	2	2
Cortical Gray Matter	1	1	1
Ventricle	99	99	99
Cerebral WM Hypointensities*	91	97	96
Subcortical Structures			
– Cerebellar White Matter	95	99	98
– Cerebellar Gray Matter	13	20	16
– Brainstem	-	-	3
– Thalamus	2	4	2
– Ventral Diencephalon	26	29	27
Basal Ganglia			
– Putamen	3	5	4
– Caudate	54	74	65
– Nucleus Accumbens	2	38	9
– Pallidum	1	1	1
Cingulate	55	25	35
– Anterior Cingulate	99	32	77
– Posterior Cingulate	69	85	79
– Isthmus Cingulate	1	5	1

*White matter hypointensities are abnormally low signal intensity regions within the white matter as observed on a T1-weighted MRI scan.

Color Code Key:

Pink: A tissue is below the 5th percentile OR a ventricle that is above the 95th percentile OR WM hypointensity that is above the 50th percentile.

Blue: A tissue is above the 95th percentile OR a ventricle is below the 5th

Brain Structure	Normative Percentiles Left	Right	Total
Frontal Lobe	1	1	1
– Superior Frontal	1	1	1
– Middle Frontal	9	1	1
– Inferior Frontal	14	7	7
– Lateral Orbitofrontal	1	17	2
– Medial Orbitofrontal	3	1	1
– Paracentral	1	1	1
– Primary Motor	1	1	1
Parietal Lobe	1	1	1
– Primary Sensory	1	1	1
– Medial Parietal	1	1	1
– Superior Parietal	1	1	1
– Inferior Parietal	1	1	1
– Supramarginal	1	1	1
Occipital Lobe	1	1	1
– Medial Occipital	4	1	2
– Lateral Occipital	1	1	1
Temporal Lobe	1	1	1
– Transverse Temporal + Superior Temporal	1	1	1
– Posterior Superior Temporal Sulcus	1	1	1
– Middle Temporal	1	1	1
– Inferior Temporal	1	1	1
– Fusiform	1	1	1
– Parahippocampal	23	18	17
– Entorhinal Cortex	1	1	1
– Temporal Pole	1	1	1
– Amygdala	1	1	1
– Hippocampus	1	1	1

Food sensitivities

Proteins vs Peptides

Proteins ~

Measure immune system reactivity to whole, undigested, multi-dimensional (ie: 4D) proteins.

Challenges: only detect one aspect of "the elephant in the gut"

Limited to testing the water-soluble portions of proteins, leaving out non-water-soluble peptides (ie: gluten).

Peptides ~

Measure immune system reactivity to the small, typically not water-soluble, 2D peptides created when whole proteins are digested.

Reduces cross-reactivity; increased sensitivity because peptides are highly specific to the food from which they are derived.

Antibodies to a whole protein will not recognize or bind peptides, even if those peptides are found in that whole protein.

Clinically, testing for food sensitivities at the peptide level in addition to whole protein eliminates uncertainty around food reactions.

Sinunasal microbiologics

Colonization involves a mixed microbial presence.

Marcons - yes, it's still "a thing", but other culprits are Pseudomonas and Klebsiella

Chronic rhinosinusitis patients undergoing endoscopic sinus surgery. Those with biofilm had ~
More severe disease preoperatively
Persistence of postoperative sxs
Ongoing mucosal inflammation
Increase infections

Fungal cultures inherently under-report due to inappropriate medium and duration (fast-growing species eat all the food, miss more pathogenic species.)

Dx via NGS qPCR and appropriate culturing.

Drug metabolism genetics

Ultrasensitive to psychiatric medication ~
Due to BBB integrity or genetics?

Better to know child's drug clearance *before* prescribing, especially if the effect is slower metabolism and reduced drug clearance, concentrating the drug.

Testing provides Gene-Drug interaction chart.

Also be familiar with co-enzymes that up- or down-regulate that pathway.
ie: B2, B6, NAD

Genetic predispositions/expressions

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

Metagenomics/metabolomics

The fine art of insurance coverage

Set up for IVIG coverage in case it's needed in the future (analogous to starting an IV in the ER)

don't put PANDAS or PANS Dx in chart, unless you're in a state which mandates coverage

Test IgG and IgA (plus subclasses) ~
- Using SST tubes
- Test after 3 weeks without any integrative supportive measures (test the child's true nature.)
- Test at the tail end of a steroid burst, if needed.

Also engage parent help. Bring child in every time they get sick to get it on the medical record.

Parent needs to keep school absence records, sports absence records, performance absences, etc.

Cautions ~

Zinc lozenges, silver nasal sprays, propolis throat sprays turn positive Strep tests to negative.
Diet, supplements, sleep routines, chiropractic adjustments, and all the other integrative treatments really work! We see immune numbers improve, which is great for the child, but bad for proving the need for treatment.
A hiatus helps reveal the baseline.

Pneumococcal vaccine titers are not necessary, plus may be falsely lower in kids with hypogam. Push back against insurance on this.

On the horizon?

Metagenomics: NGS qPCR of brain/CSF

Metagenomic NGS is a novel diagnostic test with the potential to revolutionize the diagnosis of pediatric meningitis and encephalitis through unbiased detection of bacteria, viruses, parasites, and fungi in cerebrospinal fluid.

"We recommend NGS should be considered as a *front-line diagnostic test in chronic and recurring presentations* and, given current sample-to-result turn-around times, as second-line in acute cases of encephalitis."

PMID: 29305150, 34951470

Diagnostics

Clinical diagnosis

PE and symptoms as clues

General diagnostics

Infectious triggers

Environmental triggers

Infectious triggers

Group A Beta-Hemolytic Streptococcus Pyogenes

Mycoplasma pneumonia

Chlamydia pneumonia

Bartonella species

Borrelia species (Lyme and Tickborne Relapsing Fever [TBRF])

Encephalitis viruses

Influenza

SARS-CoV-2

Periodontal

Streptococci

Streptococci are part of the normal human respiratory flora

Commensal and non-commensal - most are protective

Passed by respiratory droplets and saliva ~
Not considered highly transmissible on surfaces but is possible

Immunity to one strain does NOT confer immunity to any other

20 different subgroups of beta-hemolytic strep; not a homogenous population ~
Hundreds of different strains (220 M proteins x 25 T proteins)
Capsule is different for each of the Lancefield groups
Exotoxins also different

High antigenicity of Streptococcal exotoxins ~
Can turn on 20-40% of T-cells
This is how Strep doesn't need to be *in* the brain to affect the brain.

B. J. B. Wood et al. (eds.), The Genera of Lactic Acid Bacteria © Chapman & Hall 1995

Group A Strep (GAS)

GAS is the dominant respiratory pathogen ~

Accounts for 20%-40% of cases of pharyngitis in children; the remaining are caused by viruses

GAS infections ~

Strep pharyngitis, otitis media, sinusitis, skin infections (perianitis)

Colonization posited in sinuses and GI

GAS sequelae ~

Scarlet fever, cellulitis, necrotizing fasciitis, rheumatic fever, Streptococcal toxic shock syndrome, and post-Streptococcal glomerulonephritis

Strep shoots the messenger

Rewires the immune system for its survival

Unique in its abilities to ~
Direct I/S remodeling in nose/throat (possibly perianally)
Promote its own replication
Alter I/S responses

“Shoots the messenger”: GAS virulence factors modulate maturation and survival of dendritic cells (DC) aka the “delivery" cells, effects that are likely to have a critical impact on activation of innate and adaptive immune responses.

Only 6 of 24 GAS strains tested induced surface expression of MHC class II and co-stimulatory molecules consistent with DC maturation.

The majority of the strains did not promote DC maturation, and many triggered DC apoptosis.

PMID: 19712038

Strep Pharyngitis (GAS)

Symptoms ~

- Sore throat
- Pain with swallowing
- Red or swollen tonsils
- Swollen cervical lymph nodes
- Fever
- Headache
- Red petechiae or pinpoint dots on the roof of the mouth
- Angular cheilitis

Ddx ~

Viral cause. Children with Strep pharyngitis typically do not have cough, runny nose, hoarseness, mouth ulcers, or pink eye. These symptoms suggest a viral cause.

Seasonality ~

Winter & spring

Perianal Strep Dermatitis (GAS)

Symptoms ~
- Red rash around the anus with a well-defined margin
- Sore rectum or anus
- Anal pruritus
- Pain with bowel movements or when wiping
- Constipation

Ddx ~
- Candidiasis, pinworms, eczema, and contact dermatitis from soaps, detergents, and fragrances

Seasonality ~
- Winter & spring

Culture all perianal rashes AND culture to confirm successful treatment.
- Not uncommon to have pharyngeal culture neg, but perianal positive.

Skin infections: Suppurative

Impetigo - honey-colored crust, superficial - heals without scarring.

Ecthyma - deeper lesion, below dermis, indolent. Starts as a pustule and erodes to an ulcer. Often multiple lesions.

Erysipelas - raised red rash with very sharp borders. In the lymphatics of the skin. Fever and pain from skin swelling. IV Abx.

Cellulitis - border vague and irregular. Skip areas/bare areas. Painful, may not have fever. Associated with a break in skin.

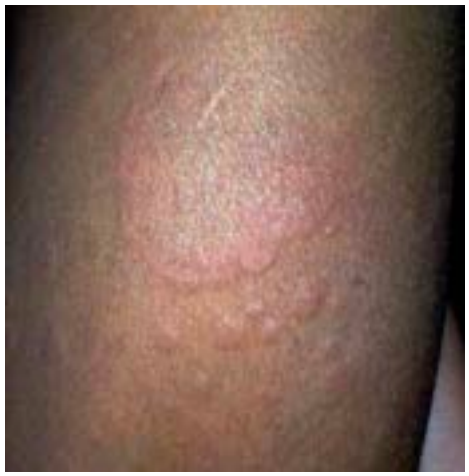
Lymphangitis - rapidly progressive infection with initial cutaneous focus but spread of infection through lymphatics.

Necrotizing fasciitis/streptococcal myositis - Streptococcal gangrene. Superficial and possibly deep layers of muscles are killed. Pain and swelling are disproportionate to everything else. Needs surgery.

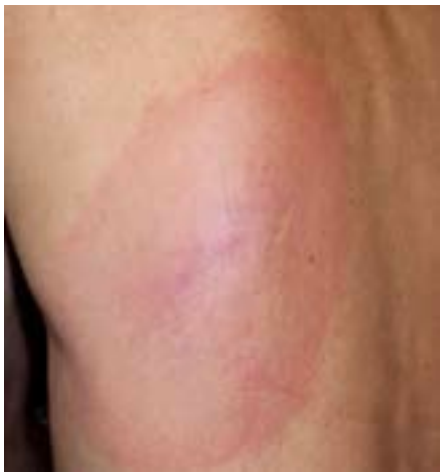
Streptococcal pupa fulminans - Skin and all structures underneath necrose. Blood vessels thrombose. + blood culture usually.

Skin: Nonsuppurative

marginatum (Strep)



migrans (Borrelia)



Sandpaper skin

Desquamation fingers/toes (also mold)

Fingernail/1˚ thumb - splinter hemorrhages

Scarlet fever: strain dependent. Diffuse erythematous rash due to the production of pyrogenic exotoxin, most commonly assoc w pharyngitis.

Scarlet fever - forms pastia's lines (bright red coloration of the creases under the arm and in the groin), strawberry tongue.

Guttate (drop-like) psoriasis.

Erythema marginatum - assoc w ARF. Rash location may change over time. Pink to red with central clearing and serpiginous (wavy) spreading edges and often are unnoticed by the patient or parent because they are painless and non-pruritic.
(distinction from Lyme erythema migrans.)

PMID: 27051572; Steere, A., Strle, F., Wormser, G. et al. Lyme borreliosis. Nat Rev Dis Primers 2, 16090 (2016). https://doi.org/10.1038/nrdp.2016.90

Other exposures

Strep “carriers” ~
Check parent/siblings tonsils
Often child’s are small and parents/siblings are enlarged or boggy (may also be EBV)
Check skin infections of other family members

Pets ~
Animals cannot get infected by Strep as it’s strictly a human pathogen
Transfer via saliva from licking carrier’s face or skin infection

Probiotics ~
Until we know which peptide or protein induces an immune reaction, I recommend
avoiding Strep-based probiotics

Neonatal (Group B)

Group B Streptococcus

Debated the degree to which Group B Strep in mom before birth contributed to the development of PANDAS, but doctors specializing in PANDAS have reported a correlation.

Vaginal swab culture

Why worry about Strep in PANS?

Strep is kryptonite in kids with PANDAS -and- PANS

Even though it may not have been the triggering infection, Strep can trigger flares in PANS.

Strep detection

Culture culture culture ~

Antibody response is more complex than previously understood. A negative rapid strep test can still be culture positive. F/U negative rapid with culture.

Rapid strep tests ~

Very high specificity (98-99%) = very few false positives.
However, sensitivity lower (90-95%) = greater chance of false negatives.
Package insert recommends F/U negative tests with a culture.
Lawsuits against docs who didn't F/U with culture, missed Strep, and serious sequelae.

Cochrane Database Systematic Review 2016 ~

Out of 100 children with strep throat:
86 would be correctly detected with the rapid test
14 would be missed and not receive antibiotic treatment

Is clinical over-reliance in rapid strep tests a contributing factor for the rise in PANDAS/PANS?

PMID: 27374000

Additional Strep labs

Anti-DNase B - repeat in 2–6 weeks for antibody rise or fall
Note: not anti-human DNA. DNase B or Deoxyribonuclease B is an antigen produced by group A streptococci which contributes to Strep's pathogenicity.

ASO - repeat in 2–6 weeks for antibody rise or fall ~
Significant prevalence of seronegative ASO (Dr. Cleary)

Streptozyme - similar to Anti-DNase B.

How to test others if not your patient? (harder since EMR)

Mycoplasma pneumonia

Look for it, and look again, and again. It's ubiquitous and often asymptomatic or only mild illness.

Shares many of the same skills as Strep in evading the I/S and affecting the brain. Second most favorite places to play in the body are brain and CNS.

Can cause encephalitis. CNS complications are seen more so in kids. Just like Strep, certain proteins on Mycoplasma mimic brain tissue.

Been shown to be able to persist in an intracellular environment. Antibiotic resistance issues.

Do not develop lifelong immunity to Mycoplasma.

More common in the winter and is estimated to be much more common than previously understood.

A super-spreader: takes up to 3 weeks before symptoms develop and is shed from the respiratory tract for many weeks after symptom abatement.
Equates to **up to 6 weeks of potential transmissibility with one infection**.

Sometimes, Mycoplasma's main hideout is the tonsils. For children whose tonsils have become Mycoplasma reservoirs, removing the tonsils may be helpful.

Mycoplasma pneumonia symptoms

Symptoms of respiratory Mycoplasma in children under 5:

- Watery eyes
- Runny nose or sneezing
- Sore throat
- Digestive changes such as diarrhea or vomiting

Symptoms of respiratory Mycoplasma in children 5 years or older:

- Feel tired
- Low-grade fever
- Sore throat
- May have a headache
- Slowly worsening dry cough that may last for weeks

The cough is normally dry. Even though it commonly takes weeks for the cough to go away, it should stay dry. If the cough becomes productive, and is accompanied by worsening fever or chills, or feeling SOB, r/o “walking pneumonia”.

Mycoplasma may cause other non-lung symptoms, such as achy muscles and joints, skin rashes, heart symptoms, liver inflammation, and eye symptoms such as pink eye and anterior uveitis.

Also mimics RBCs and can lead to hemolytic anemia. May be mistaken for Babesia, which infects RBCs and causes many of the same circulatory symptoms.

Mycoplasma detection

IgG may or may not be positive with a positive IgM.

IgM remains positive much longer than other microbes, so can be a false positive.

Confirm IgM+ via immunofluorescence (Mayo) - titers vary wildly by the moment.

T-cell option

Chlamydia pneumonia

Respiratory infection, not the STI Chlamydia trachomatis.

Obligate intracellular bacteria that infects the respiratory epithelial tissue and may play a role in chronic inflammatory dzs.

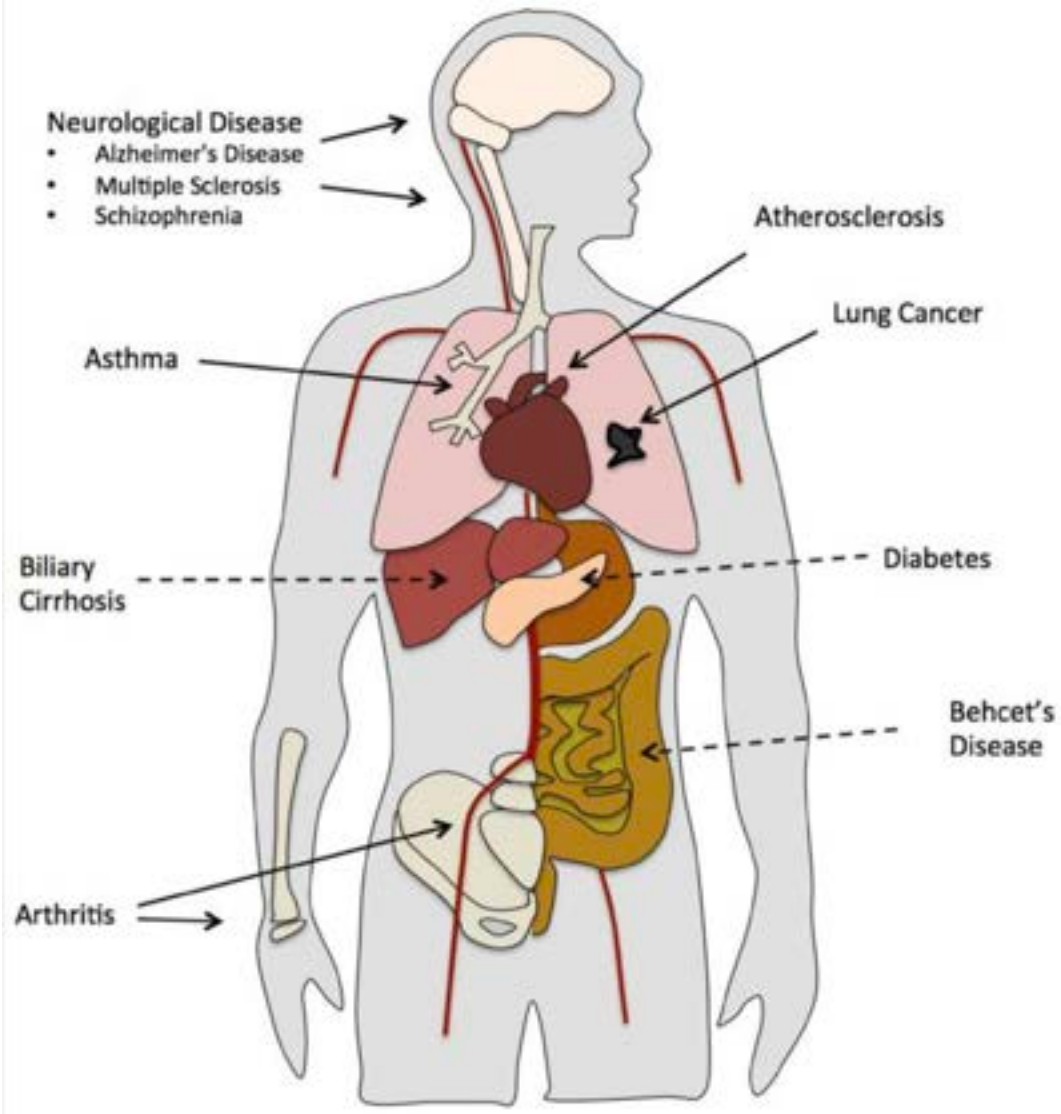
Majority of individuals are exposed throughout their lifetimes with an antibody prevalence of 50% by age 20 and 80% by 60–70 years old.

Predominantly asymptomatic or mild, but can result in the development of acute upper and lower respiratory illness including bronchitis, pharyngitis, sinusitis, and pneumonia/community-acquired pneumonia.

CNS can also be a target.

Co-infection of C. pneumoniae and M. pneumoniae with SARS-CoV-2 is associated with more severe features.

PMID: 30687565, 23218799, 11371760, 33482238



C. pneumonia

May contribute to a range of inflammatory diseases.

Dissemination from the lung throughout the body can possibly lead to atherosclerosis, arthritis, as well as neurological diseases, such as Alzheimer's, MS, and schizophrenia.

May also be associated with biliary cirrhosis, diabetes, and Behcet's disease.

C. pneumonia detection

T-cell

Chronic infection is somewhat more difficult to determine and requires the detection of persistent IgG levels, which is complicated by the fact that IgG has a half-life of weeks to months and may therefore be present for some time following acute infection.

It has been proposed that IgA levels may provide a better indication of chronic infection, but according to Dowell et al., the use of IgG and A serological markers alone should not be used.

Identification of C. pneumoniae messenger RNA (mRNA) by PCR can also be used to determine whether C. pneumoniae is in a metabolically activated state.

PCR detects presence within tissues (ie: tonsils.)

PMID: 8665464, 11462186

Bartonella spp

Include a number of different species, which are growing in number as detection improves.

Transmitted through flea bites, tick bites, and scratches or bites from an infected animal. Vertical transmission during pregnancy.

Best known as cat scratch fever, but that's misleading.
- A scratch isn't required (vector bite).
- Not just cats - also dogs, rabbits, and many other pets such as hamsters and gerbils.

Can disperse far and wide in the body, and can migrate in and out of the blood. This causes a relapsing-remitting pattern, making it quite difficult to discern between a chronic Bartonella infection and a PANDAS or PANS flare.

Each species causes a slightly different symptom picture, which makes diagnosis difficult. There are commonalities based on favorite tissues to infect, those being the brain, nervous system, and connective tissue, especially collagen.

Bartonella

Formerly, considered an issue only for those with severe immune compromise.

New research is supporting what many of us working with P/P kids have found—it's far more common and often chronic. May even be "asymptomatic", but with the rising prevalence of anxiety and hypermobility in kids, one wonders about that.

Anxiety is the most common brain-related symptom with Bartonella, as well as neuropathies. We also see mood swings that can be quite drastic and seemingly unprovoked. These may present as out-of-control anger and rage events.

Regarding connective tissue, research suggests that Bartonella impairs collagen synthesis and repair. (So does mold.) This mechanism accounts for the "Bartonella stretch marks."

This collagen-interrupting effect is why many cases of hypermobility are due to undetected, chronic Bartonella in kids and teens living in moldy environments.

We worry about Bartonella's effect on the connective tissue of our hardest-working tissues, such as the eyes and the heart, where it can weaken and infect the heart valves.

Acute cases typically fit the classic s/sxs, but chronic Bartonellosis is missed frequently due to the variance in how it presents in different children.

Acute Bartonella spp

Fever

Ice-pick pains, especially of the ear

Skin rashes or nodules

Stretch marks that don’t blanch

Extremely enlarged lymph nodes

Anger or rage events

Hemolytic anemia

Joint pain

Uveitis

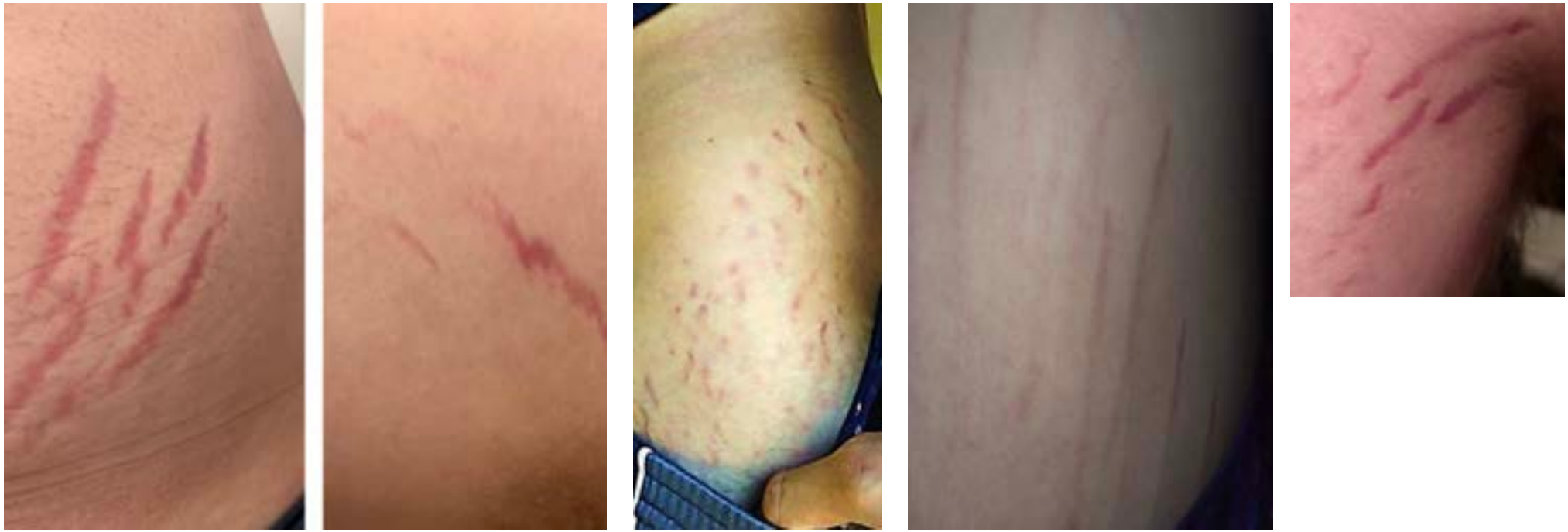
Neuroretinitis

Encephalitis

Endocarditis

Bartonella: Cutaneous lesion presentation depends on strain. “Bart striae” or non-blanching stretch marks.

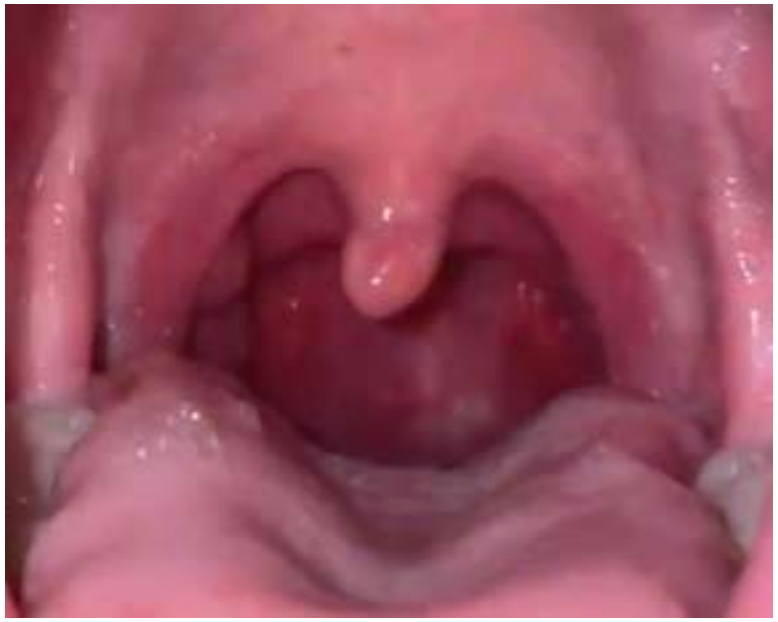
PMID: 33291688

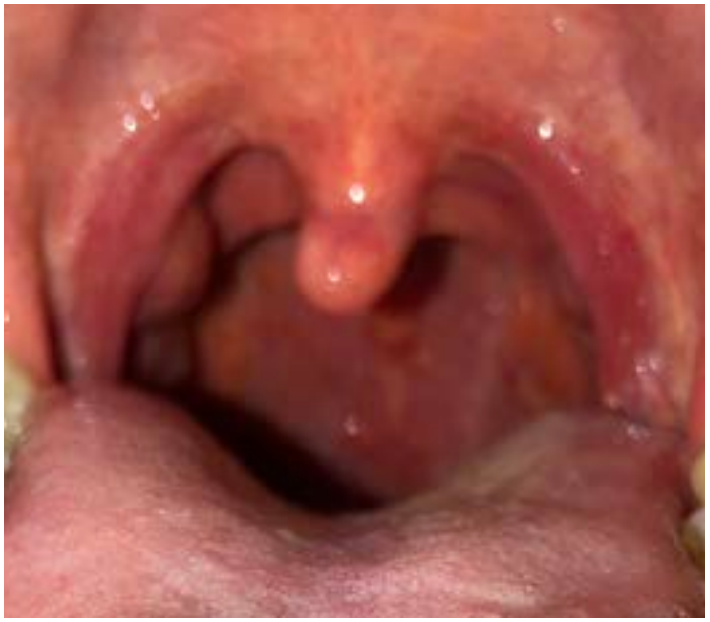


Chronic Bartonella spp

Anxiety
Mood swings
Memory problems
Fatigue
Low-grade fever
Headache, migraine
Eyes sensitive to light
Red crescents at the back of the throat that come and go
Generalized ear or throat pain
Occasional problems with swallowing
Crawling sensation on skin
Nerve zinging, vibration, or pain
Hypercoagulability
Generalized lymphatic stagnation
Gastritis, reflux
Heart palpitations with or without chest pain
Hypermobility
Migrating joint and muscle pain
Injuries slow to heal
Plantar fasciitis, worse on first steps in the morning

Bartonella throat crescents





Bartonella diagnostics

Acceptable to treat based on a presumptive diagnosis.

Famously difficult to detect due to their migratory pattern from the blood into tissues, evading the I/S.

IFA, PCR, T-cell

“ILADS folklore” - draw between 2-4pm

May provoke with homeopathics for 1 week prior.

Borrelia

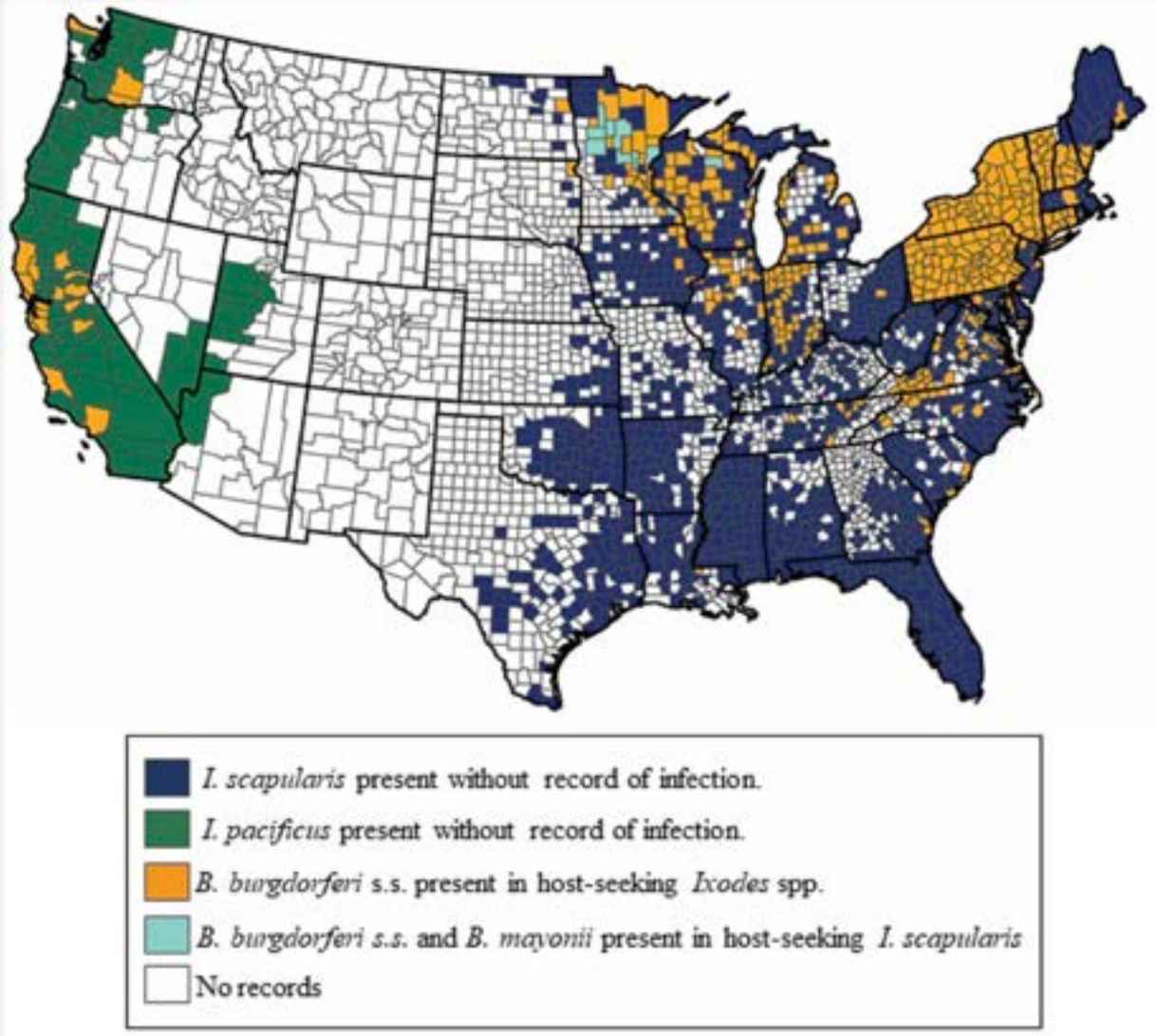
Ticks that transmit Lyme Disease reported in 48.6% of US counties (Ixodes scapularis and pacificus)

Technically refers to Borrelia burgdorferi sensu lato
- Encompasses 18 known species
- (ex: B. burgdorferi sensu stricto, afzelii, garinii, mayonii, californiensis, japonica, andersonii, lusitaniae, bissettii, spielmanii)
- The most human pathogenic species to date (N of equator) ~
  - B. burgdorferi sensu stricto (US & Europe)
  - B. afzelii, garinii (Europe & Asia)

Tick-borne relapsing fever Borrelia (TBRF) ~
- B. hermsii, turicatae, parkeri, miyamotoi

Louse-borne relapsing fever Borrelia (LBRF) ~
- B. recurrentis

Coinfection is the norm, not the exception ~
- Bartonella, Babesia, Anaplasma, Ehrlichia, Powassan, Franciscella (Tularemia), Rickettsia (RMSF), Q Fever, etc



Prevention is Key

Attractors ~

- CO_2 is the tick attractor.
- Also pheromones from Lyme carriers.
- Certain mosquito-attracting (flavi)virus-induced skin volatiles:
  - Acetophenone, a volatile compound that is predominantly produced by the skin microbiota, is enriched in the volatiles from the infected hosts to potently stimulate mosquito olfaction for attractiveness.
  - An effect partially combatted by Vitamin A.

Defense ~

- Treated clothing
- Essential oil - lemon eucalyptus, yarrow (acaricidal); reapply often (min hourly)
- Coming inside: clothes stripped and in hot dryer x 10 min
- Tape roll pets
- Tick tubes around outdoor spaces

PMID: 35777355, 36905473

“Never had a tick bite” “Not outdoorsy”

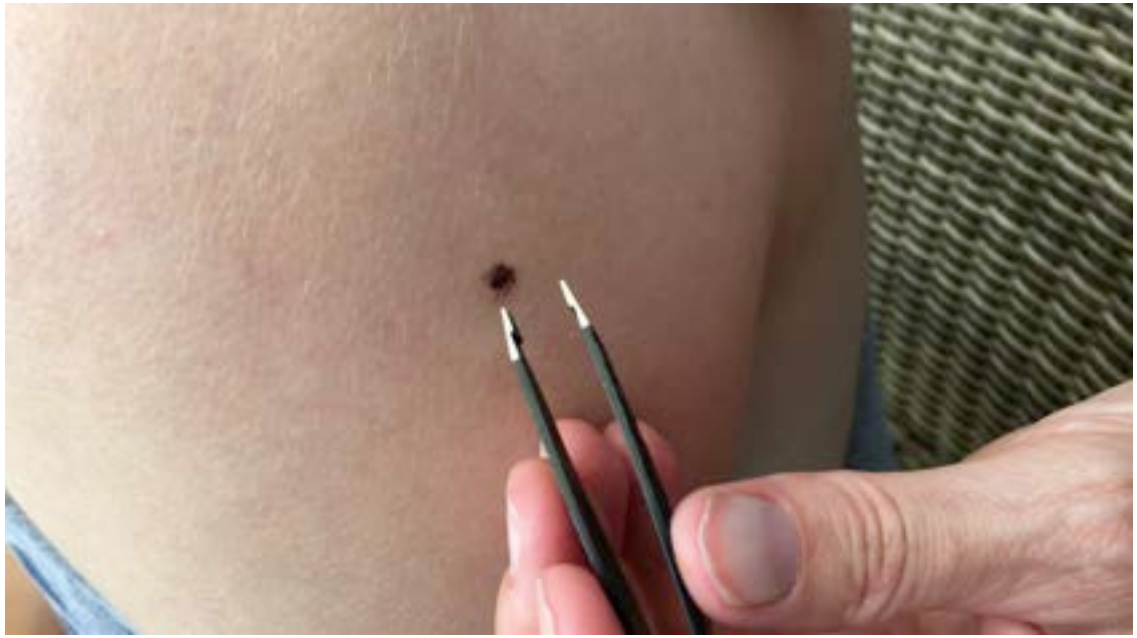
Tick saliva contains an anesthetic

Also anticoagulant and immunosuppressive substances

Provides a localized environment at the site of the bite to evade detection — enhancing infection

Soft-sided ticks (TBRF) are “snackers” — may self-detach and find new host, won't necessarily engorge

Migratory birds carry ticks anywhere the bird can go (even Home depot)



Tweezer removal method.
YouTube & https://drcrista.com/2018-5-26-lyme-the-best-way-to-remove-a-tick/

Lyme: How To Make A Poultice To Extract Embedded Tick Head

Found A Tick

Ledum 30c Homeopathic

Remove with Tweezers & Apply Poultice

Check Incidence Maps

Non-Lyme Endemic Area

Save Tick for Testing
(Check testing algorithm)

Lyme Endemic Area

Send Tick for Testing

Call Lyme Literate Doctor

Begin Antimicrobial Treatments
(Prophylactic)

Monitor for Symptoms

If Symptoms Develop, Begin Treatment Immediately

Wait for Tick Test Results
(Upgrade if Needed)

4 - 6 Weeks Later - Get Tested for Lyme Disease

Symptoms

Headache
Fever
Malaise
Lethargy
Fatigue
Aches / Flu
Stiff Neck
Joint Pain
Muscle Pain

Enlarged Lymph Nodes

Maybe Rash

Monitor for 6 weeks

Dr JILL CRISTA™

Design by Dr. Christina Carew

Tick bite management

Save the tick - moistened paper towel inside ziploc x 2. Freezer.

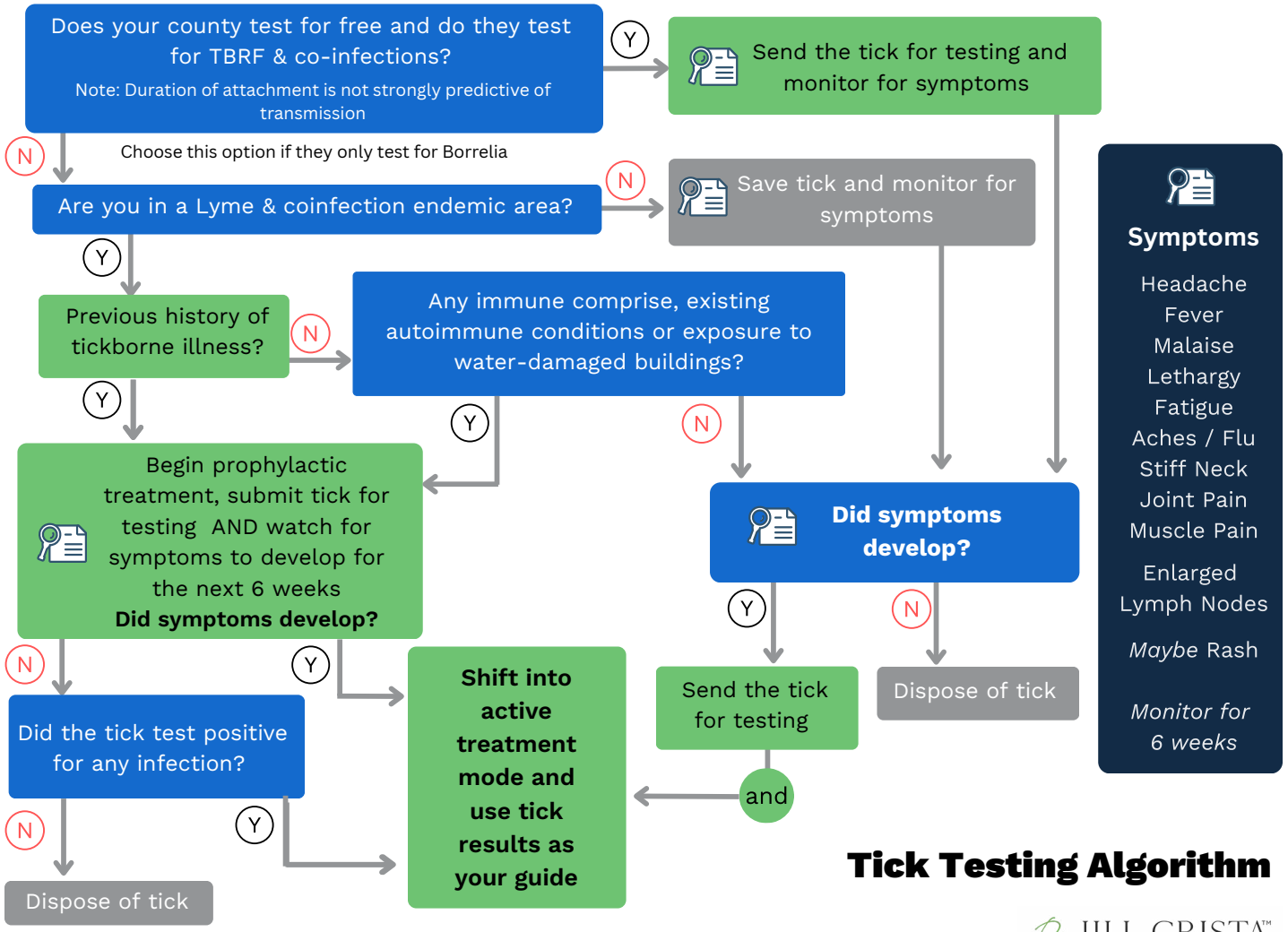
Treat bite area (tick feces) - andrographis tincture (Dr. Chesney), povidone iodine.

Snap a pic of the bite area immediately and then every day after for 10days.

Histamine reaction vs EM rash ~

EM has increased erythema at farthest edge from bite
Either may expand irregularly
Called “Erythema migrans” not “erythema in scopum” (target)
so “migration” is the unique feature

Submit tick for testing - algorithm.



Tick Testing Algorithm

Tick tests can be falsely negative. Treat the patient and not the lab. Use symptoms as a guide if negative.

Design by Dr. Christina Carew

Dr JILL CRISTA™

Acute Borrelia spp “Lyme”

Onset from 1 day to 1 month after bite.

Tick saliva induces migration of Borrelia into the blood stream, and out of stationary phase.

* if symptomatic at day 1, consider a possible reactivated persistent Borreliosis, treat as acute Lyme+

Influenza-like illness ~
Low-grade fever (co-infxn higher), headache, stiff neck, malaise/ lethargy, joint pn, muscle pn, localized L/A

Sick within a day, also consider:
Powassan virus - transmitted in 15 minutes
Anaplasma/ehrlichia

Early disseminated

Onset weeks to months after bite.

Early disseminated Lyme can occur even if no acute sxs.

Areas ~

- HT - carditis, A-V block
- Neurological - cranial/peripheral neuropathy
- M/S - migratory arthralgias
- Eye - all the “itis”s - uveitis keynote, retinal tears
- Skin/lymphatics
- Liver/kidney - LFTs, proteinuria

Late or “chronic” Lyme

Onset months to years after tick bite.

Can also occur w/o any prior sxs.

Dr. Horowitz’s Lyme/MSIDS Questionnaire is the premiere sx list.

May have never felt well since, or triggered by stressor (mold, MVA, surgery, dental, mental/emotional, pregnancy, puberty, menopause, etc)

Correlated with extreme morbidity.

Chronic progressive multisystem illness in:

- M/S
- Neuro
- Skin - acrodermatitis chronica atrophicans (European)
- Hormone

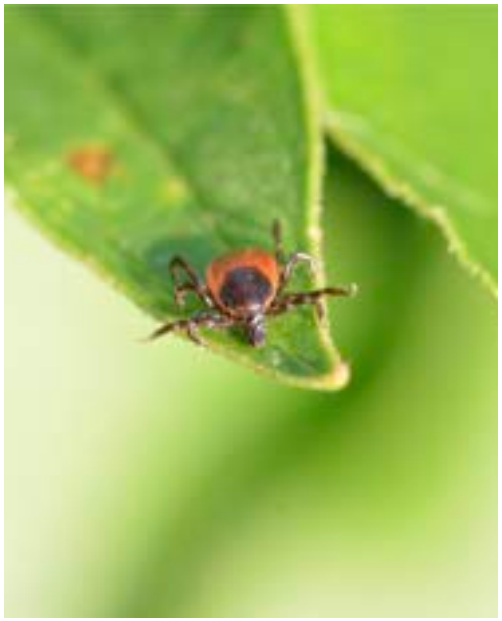
Non-Lyme Borrelia - TBRF

Tick-borne relapsing fever

Transmission - soft-sided ticks (don't engorge, they "snack" and may move hosts,) lice, fleas, possible spider bites

Tests negative on Lyme disease tests.

In Children - Early Lyme



Early Lyme disease:

- Fever
- Fatigue
- Flu-like illness, including achiness and malaise
- Headache
- Stiff neck
- Swollen lymph nodes
- Weakness or numbness in one side of face, or develops paralysis
- Spreading red rash or target rash (less than half of cases)
- Muscle and/or joint pain that migrates around the body
- Swollen joints
- Carditis or inflammation of the heart

In Children: Early TBRF

Early Tickborne Relapsing Fever:

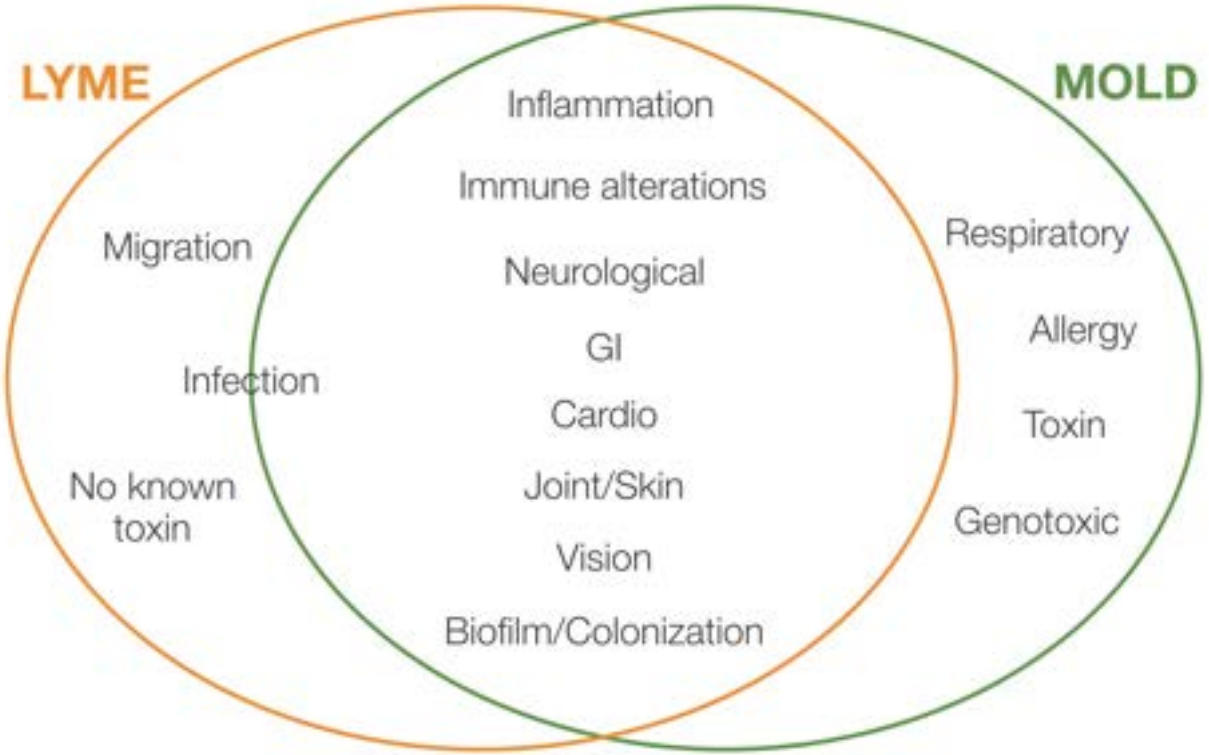
- High fever, chills
- Headache
- Muscle and joint aches
- Fever relapses and lasts for about 3 days
- Rarely a rash

In Children - Persistent/Chronic Borrelia

Persistent or chronic Lyme disease or Tickborne Relapsing Fever:

- Fatigue
- Brain fog
- Problems remembering new learning
- Child avoids play or friends
- Mood changes, depression, anxiety
- Insomnia
- Headaches
- Frequently changing vision
- Rashes that come and go
- Nerve pain, numbness, tingling, or random hot or cold feeling
- Heart palpitations
- Digestive problems
- Muscle and/or joint pain that migrates around the body
- Frequent musculoskeletal injuries
- Generalized heightened body pain

The Great Imitators



Understanding Symptoms

Borrelia OSPs bind to the glycosaminoglycan (GAG) chains of host proteoglycans, binding promotes tissue colonization

Gravitates to ECM and other areas rich in GAG nutrients ~
- Endothelial glycocalyx
- Tubules of the teeth (peg teeth = congenital)
- Eyes
- Joints
- Cardiac nerve bundles
- CNS
- Neuromuscular junctions (fibromyalgia TPs, congenital atonia)
- GB

Migrates (as seen in rash)

Unilateral (ie: Bell's palsy)

PMID: 29116038

Take-Aways

"Lyme" has become an umbrella term used to describe many iterations of tick-borne infections
- different infections/combinations of infections
- different stages/states

2-tier reflex to WB missing an inordinate number of cases

ER/Urgent care labs too early to detect

Clinical diagnosis is sufficient to initiate Tx

Known tick bite is not required to Dx

Rash is not required to Dx

Tx for 7-10 days is not sufficient

Delayed onset of Tx is correlated to worse outcomes

"Post treatment Lyme syndrome" is an erroneous Dx. IME culprit is surviving bacteria, but is blamed on the immune system gone awry

"Antibiotic refractory" - a research term - IME from undertreated and/or missed acute Dz → widely disseminated, genetically savvy bacteria (more later)

Reportable Dz - if they'll accept it (my story of Advanced Labs culture +)

Vertical transmission has been reported, positive cord blood and culture positive neonate

Borrelia Testing

Culture-enhanced PCR

Draw between 2-4pm - better chance of catching migrating spirochete

Alternate for suppressed pt: provocation with deep tissue massage from immediately prior to up to ~4-6 hrs before draw

Off ALL antimicrobials (including herbal) of all kinds for the culture to be reliable (one dose GSE turned negative)

Itraconazole will affect this test. It acts on an ergosterol biosynthesis pathway that Borrelia uses to defend itself.

Food-based antifungals in small amounts are likely okay, but be cautious of the stronger ones that also work against bacteria such as garlic, onions, thyme, oregano.

Borrelia Testing

Immunoblot > WB
- Band 31 highly correlated with autoimmune sequelae

T-cell - best choice for hypogammaglobulinemia pts but limited by the strains tested, and potentially weaker reaction to Borrelia than co-infections.

Phage -
- Good for immunocompromised patients (hypogam+mold reduced T-cell)
- Reactive for bacteria (Borrelia), not nec for parasites (Babesia)

Provoke with Lyme Nosode ~
- 10 drops under tongue daily, 2wks prior
- Administer away from anything by mouth for 15 minutes before and after the dose

*Reminder - positive test NOT required for Dx or Tx

Encephalitis Viruses

VIRUS	CONDITION	TRANSMISSION
Herpes Simplex 1	Cold sores	Oral contact
Herpes Simplex 2	Genital herpes	Genital contact
Epstein-Barr	Mononucleosis	Direct saliva contact
Varicella Zoster	Chicken pox and shingles	Airborne
Human Herpes 6	Sixth disease	Saliva Congenital possible
Coxsackie B	Hand, foot, and mouth	Respiratory droplets Direct contact Contact with infected feces
Parvovirus B19	Fifth disease	Respiratory secretions Congenital
West Nile	West Nile fever	Mosquito bite
Chikungunya	Fever, joint pain	Mosquito bite

- Predilection for the brain
- Can induce neuroinflammation even with mild infections
- Flare may occur weeks after infection

children

MDPI

Review

PANDAS/PANS in the COVID-19 Age: Autoimmunity and Epstein–Barr Virus Reactivation as Trigger Agents?

Stefano Pallanti [1,2,*] and Michele Di Ponzio [3]

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Abstract: COVID-19 impacted the entire world's population, frequently resulting in long-lasting neuropsychiatric complications. Furthermore, social distancing, lockdowns and fear for one's personal health worsen individual psychological wellbeing, especially in children and adolescents. Herein, we discuss the results of studies that specifically reported data about the impact of the COVID-19 pandemic or infection on children with Pediatric Acute-Onset Neuropsychiatric Disorders (PANS). Furthermore, we present the cases of five adolescents with PANS whose symptomatology increased following SARS-CoV-2 infection. What emerged from this study was that COVID-19 resulted in the exacerbation of obsessions, tics, anxiety and mood symptoms and decreased wellbeing. Moreover, new symptoms, as well as new PANS cases, are reported to have arisen after COVID-19 infection. Here, we hypothesize that the pathogenic mechanisms of silent viruses, such as the Epstein–Barr virus, are related to neuroinflammation, immune responses and reactivation, with additional roles played by social-isolation-related inflammatory processes. The discussion of PANS, which represents a model of immune-mediated neuropsychiatric manifestations, is particularly relevant, with the aim of uncovering the mechanisms that lead to neuropsychiatric Post-Acute COVID-19 Syndrome (PACS). Prospects for future studies and treatment implications are discussed.

check for updates

Citation: Pallanti, S.; Di Ponzio, M.

Early antigen (EA) - add-on

Chronic/reactivated pattern ~
- VCA-IgG - pos
- VCA-IgM - neg
- EA-IgG - pos
- EBV-NA - highly pos
- (if 3-4x positive, consider chronic/reactivated)

vs Past infection pattern ~
- EA - neg
- NA - lower pos

Influenza

Very commonly reported cause of PANS and flares by parents.

Influenza symptoms:

- Fatigue
- Fever
- Chills
- Cough
- Sore throat
- Runny or stuffy nose
- muscle or body aches
- Headaches
- Less commonly, vomiting and diarrhea

Monitor for secondary bacterial infections - sinus, ear, lung, pneumonia

If child is reporting fever sxs with no rise in temp ~

- Concern for CDR1, innate immunodeficiency (mold/NK cell fxn)
- Increased risk factor for autoimmune activity

Mold mycotoxin exposure makes flu worse

frontiers in Immunology

ORIGINAL RESEARCH
published: 04 October 2018
doi: 10.3389/fimmu.2018.02297

Aflatoxin B_1 Promotes Influenza Replication and Increases Virus Related Lung Damage via Activation of TLR4 Signaling

Yuhang Sun[1,2], Jiarui Su[1,2], Zixuan Liu[1,2], Dandan Liu[1,2], Fang Gan[1,2], Xingxiang Chen[1,2] and Kehe Huang[1,2]*

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Cellular Physiology and Biochemistry

Cell Physiol Biochem 2018;49:1151-1167
DOI: 10.1159/000493294
Published online: 6 September, 2018
Accepted: 28 August, 2018

Original Paper

Low-Level Aflatoxin B_1 Promotes Influenza Infection and Modulates a Switch in Macrophage Polarization from M1 to M2

Yuhang Sun[a,b] Zixuan Liu[a,b] Dandan Liu[a,b] Jin Chen[a,c] Fang Gan[a,b] Kehe Huang[a,b]

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Low level exposure ~

Promotes infection

Increases inflammatory responses

Immune organ damage

Induce a switch in alveolar macrophage polarization from M1 to M2

Confer poorer outcomes in SIV-infected in mice

SARS-CoV-2

Multiple entry routes into the brain - olfactory bulb, thalamus, and brain stem may be infected through a trans-synaptic transfer of the virus. Additional vagal nerve delivery via dendritic cells.

Induces release of chemokines, cytokines, and inflammatory signals to the BBB and infects the astrocytes, which causes neuroinflammation and neuron death; neurodegenerative implications.

Pathogenic effect on the CNS with specific impact on the **midbrain dopamine neurons which abundantly express ACE-2 receptors**.

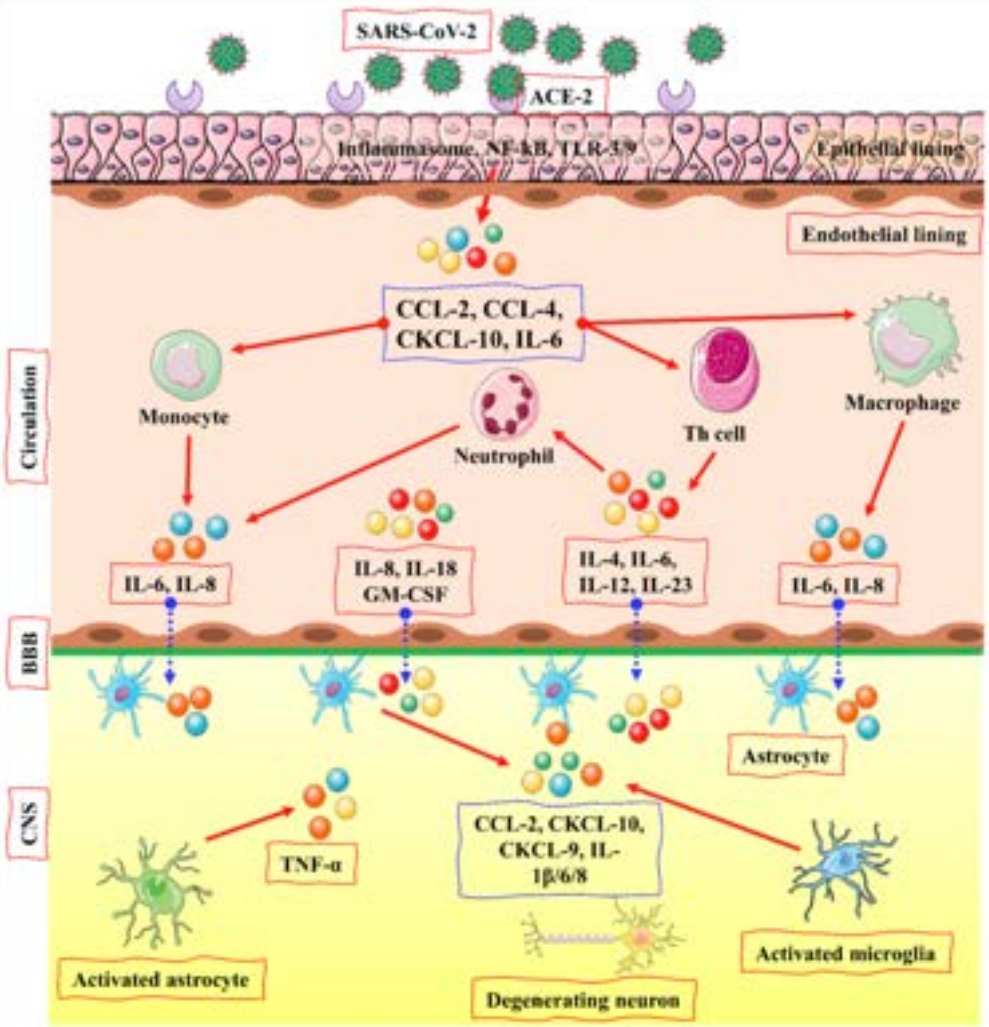
Spike protein can reach different brain regions, irrespective of viral brain replication. Can itself cause BBB dysfunction and damage neurons either directly, or via activation of brain mast cells and microglia and the release of various neuroinflammatory molecules.

Spike protein alters microglial purinergic signaling in vitro, may potentiate the Cell Danger Response.

Published case report examined adolescents who acutely developed new OCD, neuropsychiatric, and motor dysfunction symptoms consistent with PANS, having a temporal correlation, 2 weeks after a diagnosis of Covid-19.

“Highly likely that neural autoantibody production is facilitated by SARS-CoV-2 infection…”

PMID: 35601258, 36899824, 33158605, 33936086, 37114062, 37606433, 35883527, 33748620, 35390636



Cytokine cascade

Entry in the brain via ACE2 (abundantly expressed in midbrain.)

TLR or NF-κB signaling activate the pro-inflammatory self-defense inflammasome after viral attachment.

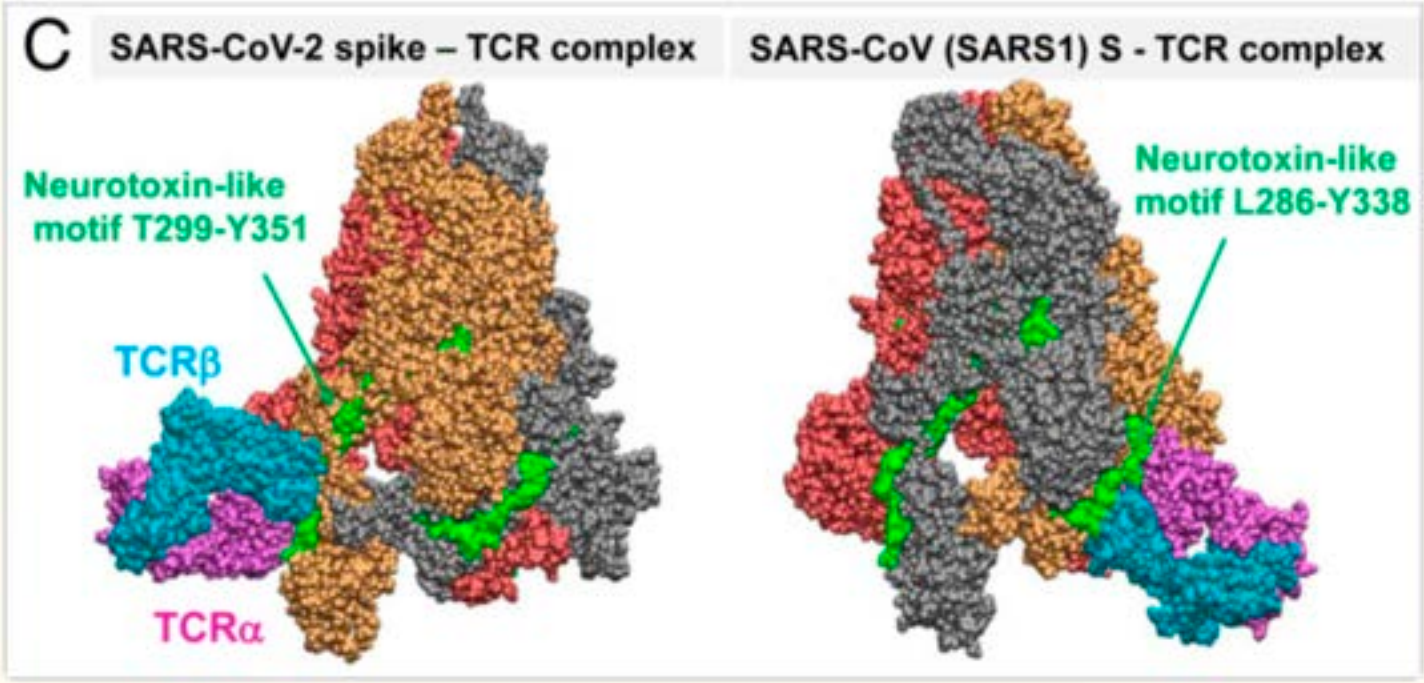
Pro-inflammatory feedback loop activates CNS immune cells, astrocytes and microglia, which induce IL-1, IL-6, TNF- α, and IL-8.

Several CNS-related illnesses are linked with elevated levels of these inflammatory cytokines.

Neurotoxic components

"Superantigenic" neurotoxin-like motif exhibits a high tendency to bind T-cell receptors.

PMID: 32989130 (Oct 2020)



Periodontal infections

A major under-recognized contributor to PANDAS/PANS and neuroinflammation.

ID via qPCR Next-Generation Sequencing. Also tests for resistance in strains.

Dentist or periodontist collects a small amount of fluid from an infected pocket in the gums, as well as a saliva sample.

Avoid ozone for 1 week prior to sample collection as it's a potent antimicrobial.

Treatments using ozone are well-tolerated by P/P ~

Multiple published case studies using ozone gas to treat "untreatable" periodontal conditions (3-4 month nightly rinse.)

Some evidence (15-day trial) ozone rinse is not as effective against gingivitis as commonly used chemicals (chlorhexidine) but is a viable alternative for chemically-sensitive. Need a longer duration study - empirically quite effective.

PMID: 36570588, 32594645

Infectious triggers

Group A Beta-Hemolytic Streptococcus Pyogenes

Mycoplasma pneumonia

Chlamydia pneumonia

Bartonella species

Borrelia species (Lyme and Tickborne Relapsing Fever [TBRF])

Encephalitis viruses

Influenza

SARS-CoV-2

Periodontal

Diagnostics

Clinical diagnosis

PE and symptoms as clues

General diagnostics

Infectious triggers

Environmental triggers

Environmental triggers

Top 7 from my clinical practice ~

1. Herbicides
2. Mold
3. EMFs
4. Mercury
5. Pesticides
6. Vaccine adjuvants

(Food dyes get a dis-honorable mention)

Commonality? All are neurotoxins and immunotoxins.

Glyphosate (Roundup)

Genetically modify crops to be “roundup ready”.

Allows the GM plant to survive the mechanism of the chemical.

But not just for killing weeds anymore!

Additionally used as a desiccant for non-GMO grains, spraying enough to kill the greenery via desiccation for easier harvest of grains, equating to higher than approved levels just before harvest.

Increases incidence of Fusarium mold infestation in storage.

“Coherent and compelling evidence that glyphosate and glyphosate-based formulations are a cause of non-Hodgkin lymphoma (NHL) in humans exposed to these agents.”

Successful legal case linking exposure to NHL resulted in it being quietly taken off the market for residential use.

Commercial use allowed to continue!

PMID: 34052177, 31342895

No human effects?

Affects shikimate pathway - not found in human cells but is utilized by our gut microbiome

Reduces gut immunity and confuses the definition of “self”, increasing the incidence of autoimmunity via Th17 and mast cell infiltration

Salmonella and Clostridia are resistant to it

Glyphosate-induced intestinal dysbiosis impacts CNS, in emotional, neurological and neurodegenerative disorders

In mice, low-level “subchronic” exposure increased anxiety and depressive-like behaviors

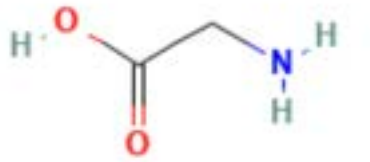
Low-level exposure linked to gut dysplasia

Animal studies, low-level maternal glyphosate exposure linked to increased incidence of ASD

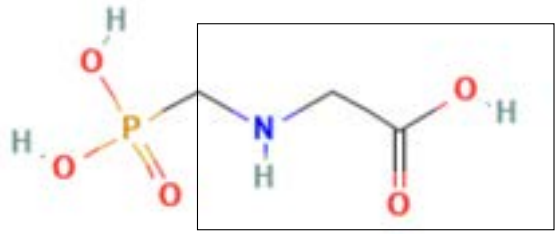
PMID: 31442459, 29635013, 20012598, 28848410, 32398374

Glycine backbone

Gly-cine



Gly-phosate



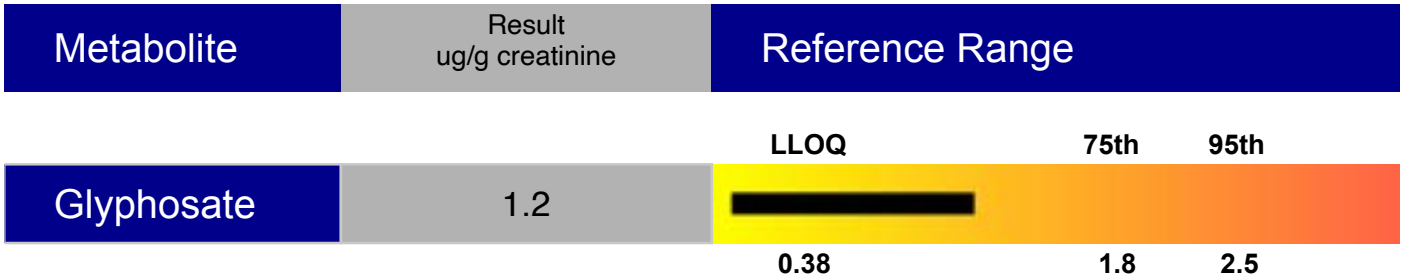
Core of the molecule is glycine
∴ may displace glycine metabolically

Impacts ~
Neurotransmitter (calming NT)
Glutathione (one of the AAs)
Glycine membrane channels (leading to channelopathies)

Possible fertility impacts ~
alters testicular morphology and testosterone levels

Glyphosate urine test

Glyphosate Profile



Atrazine - “pre-emergent” herbicide

Endocrine disrupting chemical with neuroendocrine/epigenetic toxicity.

Targets hypothalamus-pituitary-gonadal (HPG) axis.

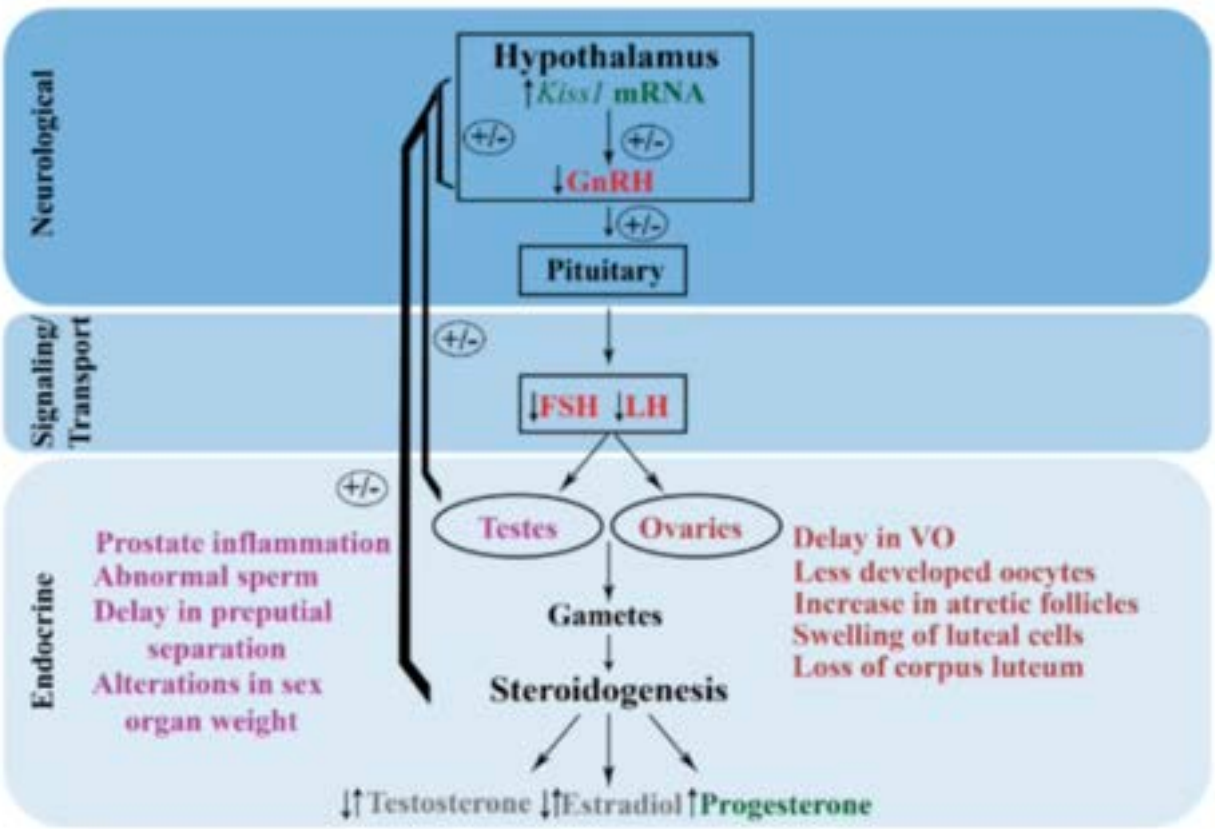
Frogs: low exposure males become females, high exposure males can procreate.

Evidence of crosstalk between systems affected by Atrazine exposure, causing widespread dysfunction and leading to changes in behavior, even with no direct link to the hypothalamus.

EU banned Atrazine use in 2003 recognizing the health risks of Atrazine exposure as a public health concern with no way to contain contamination of drinking water.

Yet, the US recently reapproved Atrazine's use in the fall of 2020.

PMID: 27413107, 35410624



Histological and morphological alterations in the ovaries and testes are observed; dependent on duration of exposure and dose.

Green = increases

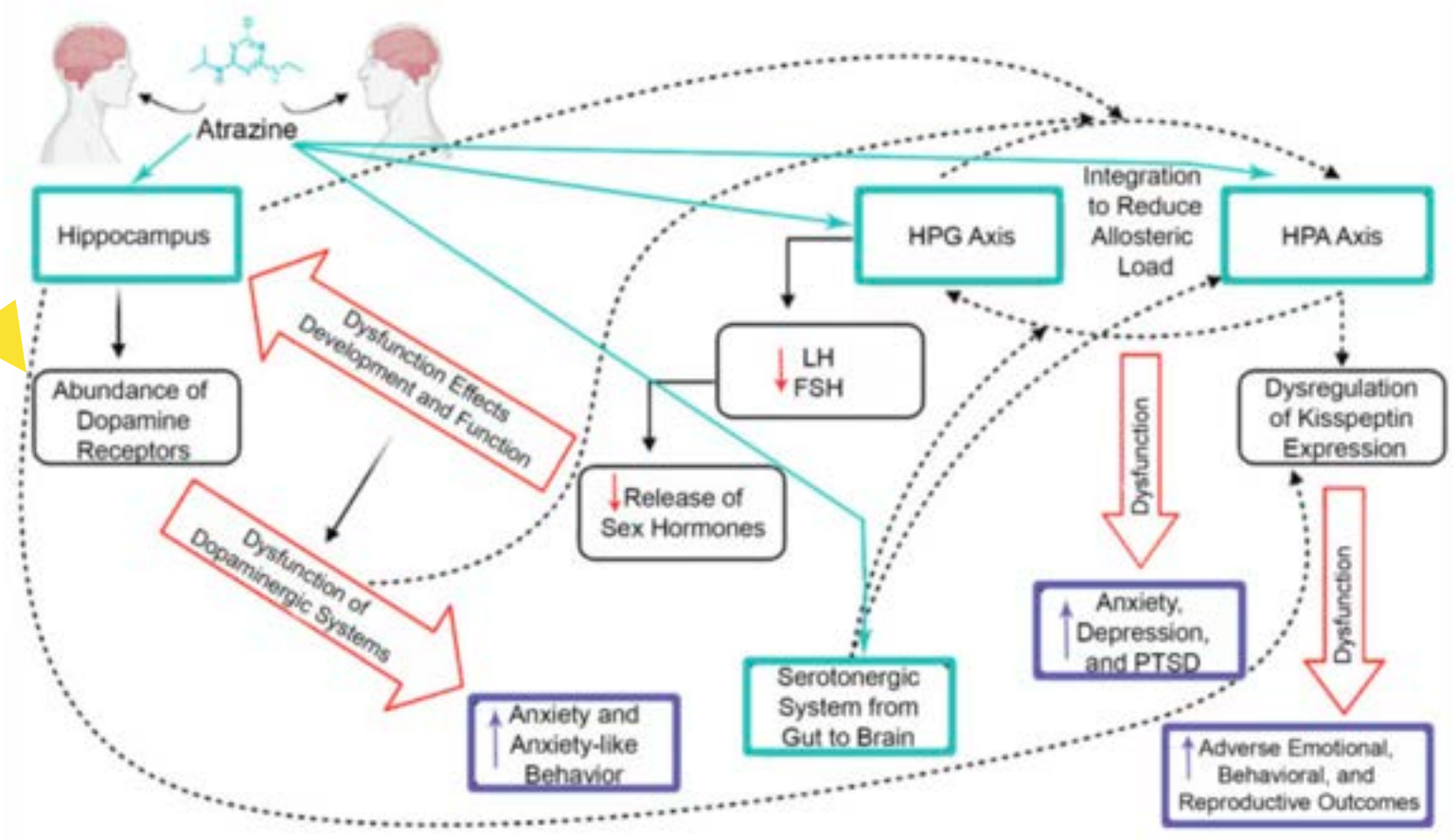
Pink = reductions

Grey indicates that both increases and reductions are reported

Effects in males are in purple

Alterations in females are in red (VO: vaginal opening)

PMID: 28713818



Abundance of DRs → dysfunction of dopaminergic systems → ↑anxiety/anxiety-like behavior
Might destruction of DRs be a compensatory reaction to Atrazine exposure?

PMID: 34564358

Atrazine urine test

Organophosphate pesticides

Test Name (mcg/g)	In Control	Moderate	High	Current Level	Previous Level 10/29/2021
Diethyldithiophosphate (DEDTP)	≤0.20	0.21–0.48	≥0.49	0.02	4.19
Dimethyldithiophosphate (DMDTP)	≤0.80	0.81–5.08	≥5.09	0.29	5.75
Diethylthiophosphate (DETP)	≤0.70	0.71–2.76	≥2.77	0.17	7.49
Dimethylphosphate (DMP)	≤5.20	5.21–37.19	≥37.20	0.19	3.11
Diethylphosphate (DEP)	≤0.80	0.81–12.59	≥12.60	0.76	3.50
Dimethylthiophosphate (DMTP)	≤4.60	4.61–29.20	≥29.21	4.20	9.82
Atrazine	≤0.02	0.03–0.05	≥0.06	<0.01	7.16
Atrazine mercapturate	≤0.03	0.04–0.06	≥0.07	0.03	7.04


Adobe licensed video

MOLD

Natural function of fungi is to compost and recycle

Excrete 1° and 2° metabolites ~ inhaled, ingested, and dermally absorbed

1° metabolites ~ necessary for survival aldehydes, alcohols, odors, digestive enzymes, and structural elements (ie: beta-glucans)

2° metabolites ~ competitive antimicrobials, mycotoxins (energetically expensive for the mold to make)

Mold is tenacious

Moisture ~ 1° element for growth,
2° is organic substrate

Obvious or visible water not necessary

Relative humidity above 50% promotes growth

Grows on WD surface within 24-48 hours

Difficult to kill ~ any intact spore is dormant,
not dead (a dead spore is a fragment)

Spore formation and release increases more
when drying than when wet
(survival of species)

More than “spore illness”

Spores

IgE | Allergic rhinitis, asthma, hypersensitivity pneumonitis (CDC)
Non-IgE | Non-IgE mediated Asthma exacerbation (CDC)
Infection | Aspergillosis (CDC)
Mast cell | Recruitment, degranulation, enhanced survival

Fragments

“Mold-othelioma”

Other Mould Dangers

Chemicals | VOCs, aldehydes, alcohols, MPA
Mycotoxins | Colonization

Biofilm

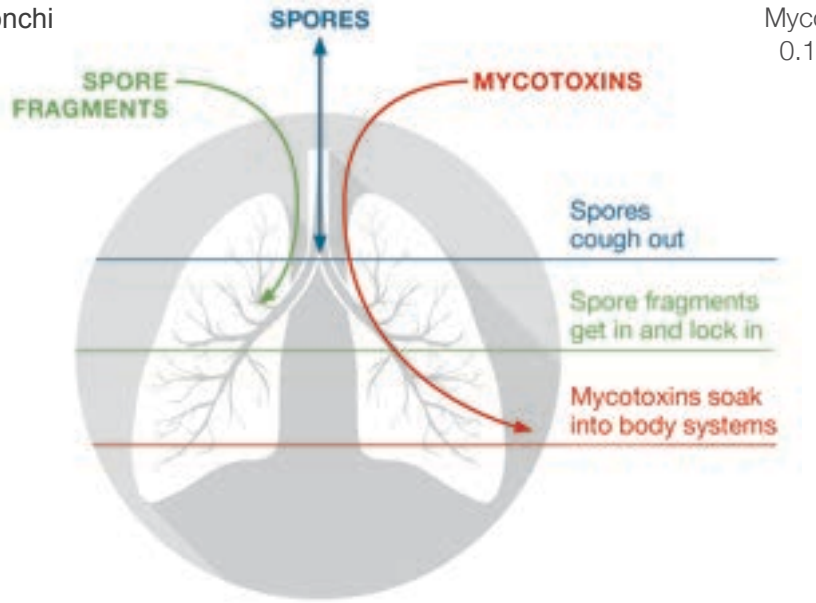
Water-damage=increased microbial diversity (ie: actinomycetes, endotoxin)
Quorum behavior

PMID: 24368325, 20537281, 24368325, 23710148

Respiratory system vs Mold

Respiratory System

>7m Nasal
5-7m Pharynx
3-5m Trachea
3-5m 1° Bronchi
2-3m 2° Bronchi
1-2m Terminal bronchi
<1m Alveoli



Mold

Spores-
Cladosporium 3-5m
Aspergillus 2-5m
Penicillium 1-5m
Fragments-
1-2m
Mycotoxins-
0.1m

Mycotoxins

Aflatoxin
Aspergillus flavus, A. parasiticus

Chaetoglobosin A,C
Chaetomium globosum

Citrinin
Aspergillus, Penicillium, Monascus

Enniatin B_1
Fusarium spp

Gliotoxin
Aspergillus fumigatus, Candida spp

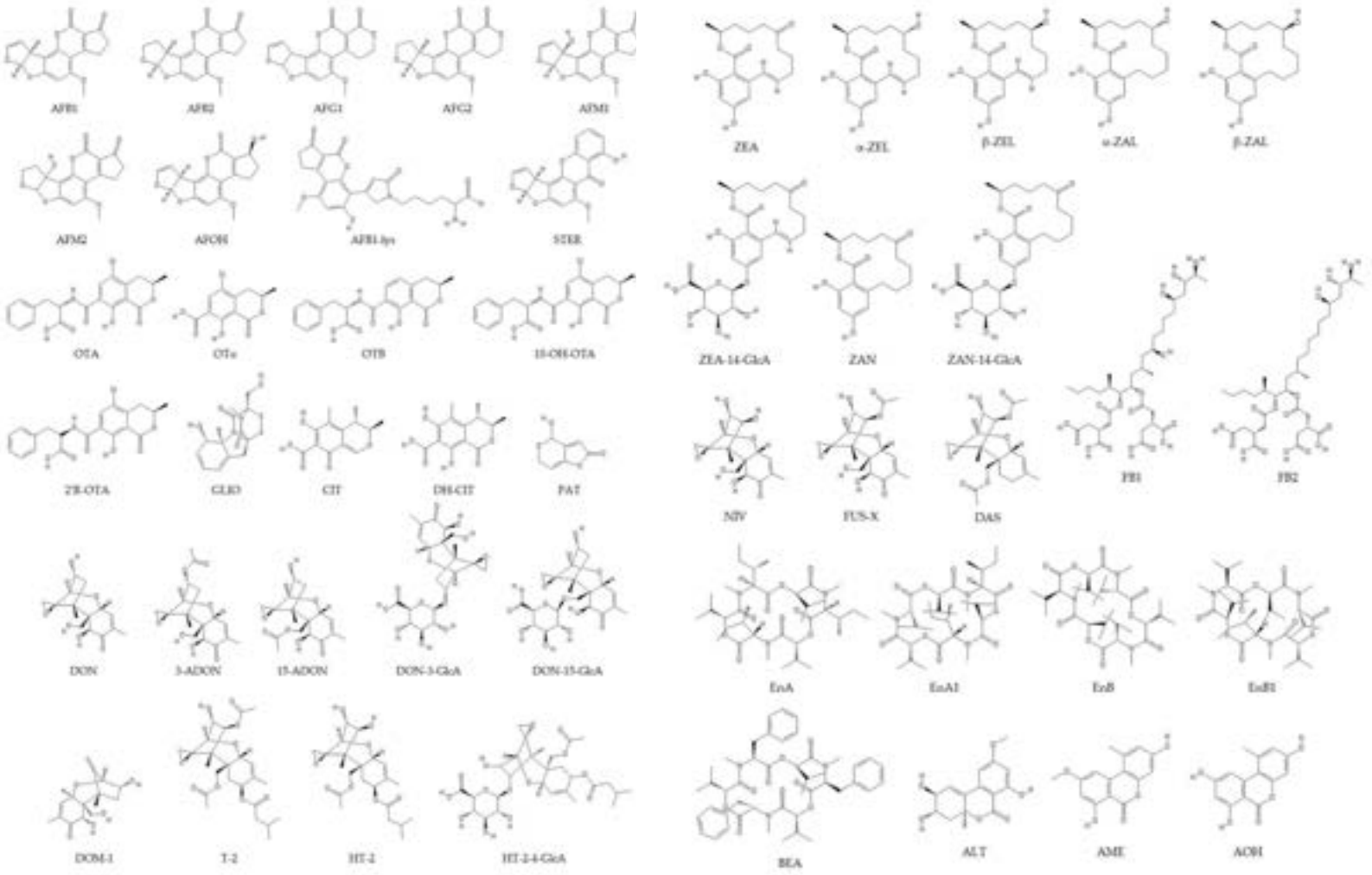
Ochratoxin A
A. ochraceus, A. niger, Penicillium verrucosum, P. nordicum, P. chrysogenum

Patulin
Aspergillus spp, Penicillium spp, Mucor, Fusarium spp

Sterigmatocystin
Precursor of Aflatoxin, A. versicolor

Trichothecenes (Roridin, Verrucarin, Nivalenol, Deoxynivalenol, Diacetoxyscirpenol, Satratoxin)
Stachybotrys chartarum, Trichoderma viride, Fusarium spp, Myrothecium

Zearalenone
Fusarium spp



PMID 32121036

Mycotoxin health impacts summarized

Lipophilic

Immunotoxic

Neurotoxic

Alimentary toxic

Dermatoxic

Nephrotoxic

Hepatotoxic

Hepatocarcinogenic

Genotoxic

Teratogenic

Carcinogenic

PMID: 26474839, 27178040, 25449202,12221236, 26600019

Comparative Study > J Assoc Off Anal Chem. 1983 Nov;66(6):1485-99.

Analysis for Fusarium toxins in various samples implicated in biological warfare in Southeast Asia

C J Mirocha, R A Pawlosky, K Chatterjee, S Watson, W Hayes

PMID: 6643363

Abstract

Samples of leaves, water, cereal grains, soil, and yellow powder as well as blood, urine, and body tissues from chemical warfare victims were analyzed for Fusarium toxins by using gas chromatography and mass spectrometry. The leaves, water, and yellow powder samples contained various combinations of T-2 toxin, diacetoxyscirpenol, deoxynivalenol, nivalenol, and zearalenone in concentrations ranging from trace (1.0 ppb) amounts to 143 ppm. These trichothecenes do not occur naturally on the substrates described and were correlated with the so-called "yellow rain" chemical attacks against Hmong people in Southeast Asia. Analysis of leaves, soil, water, and cereals collected in areas adjacent to but apart from the area where chemical attacks had been staged did not contain any Fusarium toxins. Moreover, T-2 and HT-2 toxins were found in human blood, urine, and body tissues (heart, esophagus, kidney, lung, and large intestine) of alleged victims. In addition, diacetoxyscirpenol was found in the kidney of one person who had died.

Mycotoxins have a long history of use as a biological warfare weapon.

"Yellow rain" T-2 toxin use against the Hmong people in Southeast Asia.

So, yes, they affect everyone.

Multisystem Multisymptom

More common than not that each person in an exposure environment has a completely different presentation.

Every living being is affected.

Depends on type of mould, presence of mycotoxins, duration and dose of exposure, and individual susceptibility.

CATEGORY 1:

GENERAL:
- ☐ Fatigue that doesn't otherwise make sense
- ☐ Trouble sleeping
- ☐ Worse after eating
- ☐ Worse after exercise
- ☐ Increased thirst
- ☐ Stubborn weight gain
- ☐ Anemia

SENSITIVITY:
- ☐ Bothered by tags and seams on clothing
- ☐ Chemical sensitivities
- ☐ Sensitive to light, sound, or touch

HEAD/MIND:
- ☐ Slowed thinking or brain fog
- ☐ Unsettled feeling, unquieted mind, overwhelm
- ☐ Headaches
- ☐ Dizziness, vertigo, or drunken feeling
- ☐ Unexplained mood changes, anxiety, or depression

EENT:
- ☐ Allergies/hay fever year-round
- ☐ Eye irritation
- ☐ Dark circles under eyes
- ☐ Floaters in your vision
- ☐ Vision blurry, frequently changes, or difficulty reading
- ☐ Sneezing or persistent runny nose
- ☐ Acute sense of smell for mold
- ☐ Recent sinusitis
- ☐ Ears feel plugged or clogged
- ☐ Itchy or sore ear canals
- ☐ Sores in the mouth
- ☐ Post-nasal drip or frequent throat clearing
- ☐ Chronically sore throat
- ☐ Coated tongue

RESPIRATORY:
- ☐ Easily irritated lungs
- ☐ Episodic cough
- ☐ Shortness of breath, air hunger, or yawn/sigh often

CARDIOVASCULAR:
- ☐ Easy bruising
- ☐ Heart palpitations
- ☐ Lower extremity edema
- ☐ Protruding veins on limbs

DIGESTIVE:
- ☐ Nausea
- ☐ Bloated abdomen or flatulence
- ☐ Unexplained change in digestion/bowels
- ☐ Recent change in appetite
- ☐ Crave carbs, sweets, or alcohol

GENITOURINARY:
- ☐ Overactive bladder
- ☐ Bladder infections

SKIN:
- ☐ Skin rash, redness or flushing

IMMUNE:
- ☐ Frequent infections or delayed recovery from colds

MUSCULOSKELETAL:
- ☐ Increased body pain

Total CATEGORY 1 boxes checked : _____

0 - 4 symptoms =	Score 0
5 - 7 symptoms =	Score 1
8 - 10 symptoms =	Score 2
11+ symptoms =	Score 3

ENTER CATEGORY 1 SCORE : _____

CATEGORY 2:

GENERAL:
- ☐ Voice sounds nasally
- ☐ Frequent or strong static shocks
- ☐ Histamine intolerance
- ☐ Non-obstructive sleep apnea
- ☐ React poorly to musty spaces

SENSITIVITY:
- ☐ Sensitivity to EMFs

HEAD/MIND:
- ☐ Migraines
- ☐ Difficulty thinking clearly or memory loss
- ☐ Confusion or disorientation

EENT:
- ☐ Allergies are not well-controlled by medication
- ☐ Chronic sinusitis
- ☐ Nose bleeds
- ☐ Ear ringing or ear pain that's new or worsening

RESPIRATORY:
- ☐ Asthma or wheezing
- ☐ Chronic cough
- ☐ Burning lungs

CARDIOVASCULAR:
- ☐ Episodes of fast heart beat
- ☐ Chest pain
- ☐ Low platelets

DIGESTIVE:
- ☐ Increased food sensitivities
- ☐ Frequent vomiting
- ☐ Irritable bowel or alternating constipation/diarrhea
- ☐ Digestive ulcer or blood in the stool
- ☐ Celiac or non-celiac intestinal disease
- ☐ Fatty liver
- ☐ Liver pain or swelling

GENITOURINARY:
- ☐ Unexplained menstrual changes
- ☐ Bacterial vaginosis
- ☐ Kidney pain or swelling

SKIN:
- ☐ Itchy or burning skin
- ☐ Peeling or sloughing skin
- ☐ Raynaud's syndrome
- ☐ Eczema or psoriasis

IMMUNE:
- ☐ Epstein-Barr virus activation

MUSCULOSKELETAL:
- ☐ Slow reflexes
- ☐ Balance issues or incoordination
- ☐ Joints easily injured
- ☐ New or worsening nerve pain, numbness or tingling
- ☐ Muscle weakness or spasm

Total CATEGORY 2 boxes checked : _____

0 - 2 symptoms =	Score 0
3 - 5 symptoms =	Score 1
6 - 8 symptoms =	Score 2
9+ symptoms =	Score 3

ENTER CATEGORY 2 SCORE : _____

CATEGORY 3:

GENERAL:

- ☐ Current exposure to mold
- ☐ Previous exposure to damp, musty or water-damaged building any time in your life
- ☐ Mold allergy
- ☐ Abnormal reaction to medications or supplements
- ☐ Autism or sensory processing disorde
- ☐ Chronic fatigue syndrome
- ☐ Chronic inflammatory response syndrome (CIRS) or positive Shoemaker tests

SENSITIVITY:

- ☐ Feeling of an internal vibration

HEAD/MIND:

- ☐ Dysautonomia or Postural Tachycardia Syndrome (PoTS)
- ☐ Dementia

EENT:

- ☐ Daily use of sinus spray, sinus prescription, or Neti pot
- ☐ Nasal polyps
- ☐ Sinus surgery at any time in your life
- ☐ Hearing loss
- ☐ MARCoNS
- ☐ Oral thrush

RESPIRATORY

- ☐ Asthma that's difficult to control with medication
- ☐ Lung scarring or nodules
- ☐ Pulmonary Edema
- ☐ Idiopathic Pulmonary Fibrosis
- ☐ Respiratory distress or Idiopathic pneumonitis
- ☐ Lung cancer

CARDIOVASCULAR:

- ☐ Arrhythmia
- ☐ Coagulation abnormalities
- ☐ Arteriovenous abnormality
- ☐ Churg Strauss Syndrome

DIGESTIVE:

- ☐ Peanut allergy
- ☐ Cyclical vomiting syndrome
- ☐ Eosinophilic esophagitis
- ☐ Non-alcoholic steatohepatitis (NASH)
- ☐ Hepatocellular carcinoma or other liver cancer

GENITOURINARY:

- ☐ Infertility
- ☐ Chronic pelvic pain
- ☐ Interstitial cystitis
- ☐ History of kidney stones
- ☐ Reduced GFR (glomerular filtration rate)
- ☐ IgA nephropathy, nephrotic syndrome, nephritis, or other kidney disease
- ☐ Kidney cancer

SKIN:

- ☐ Recurrent yeast infections or fungal skin infections, including athlete's foot, jock itch or yeast vaginitis
- ☐ Erythema nodosum
- ☐ Toenail fungus

IMMUNE:

- ☐ Autoimmunity
- ☐ Mast cell activation syndrome (MCAS)
- ☐ Aspergillosis, current or history of
- ☐ Previous or current cancer diagnosis, not otherwise specified
- ☐ Aplastic anemia
- ☐ Sarcoidosis

MUSCULOSKELETAL:

- ☐ Hypermobility or Ehlers-Danlos syndrome
- ☐ Tremors or tics
- ☐ Difficulty walking

Total CATEGORY 3 boxes checked : _____

Score 1 for each box checked.

Total items checked and the Category Score will be the same for this category.

ENTER CATEGORY 3 SCORE : _____

TOTAL MOLD RISK RESULTS

Gather your Category Scores from the 3 previous categories.

CATEGORY 1 SCORE: _____
CATEGORY 2 SCORE: _____
CATEGORY 3 SCORE: _____

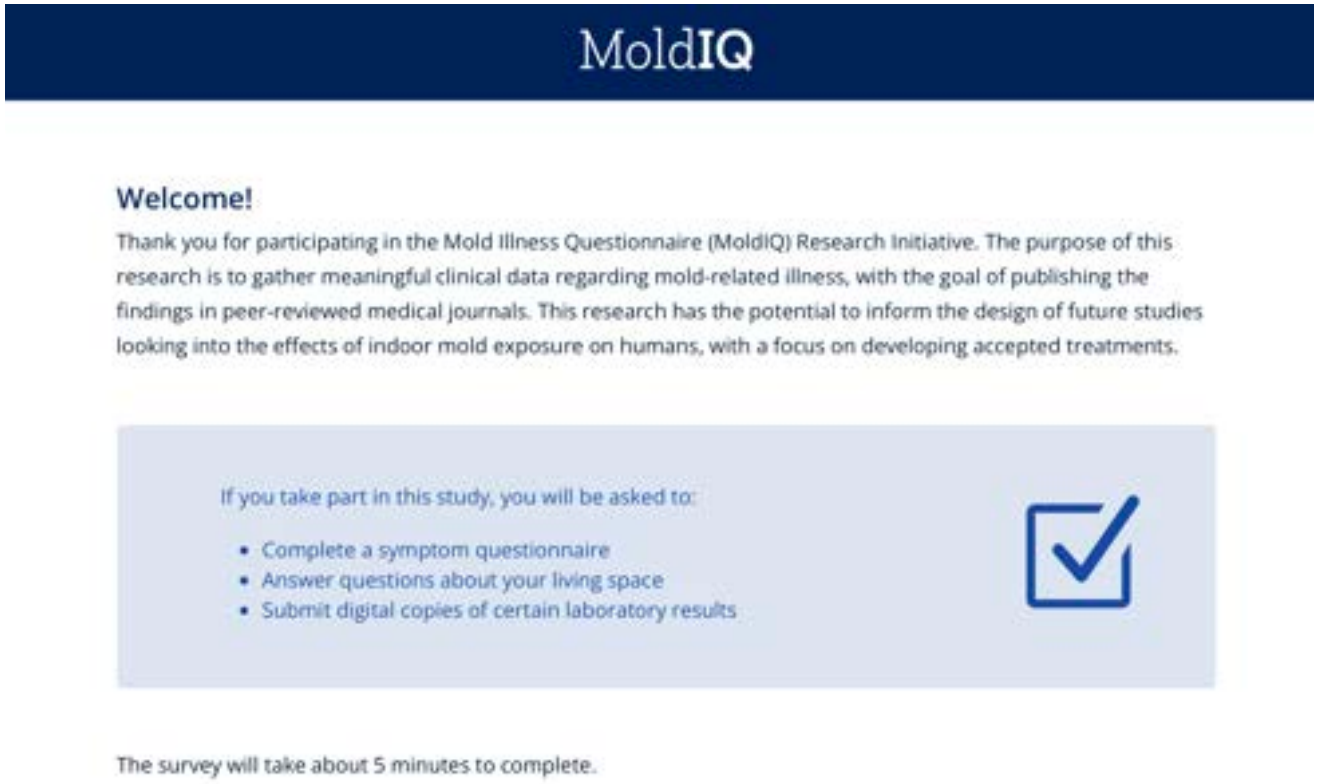
Add Category Scores together to calculate your total mold risk.

TOTAL MOLD RISK_____

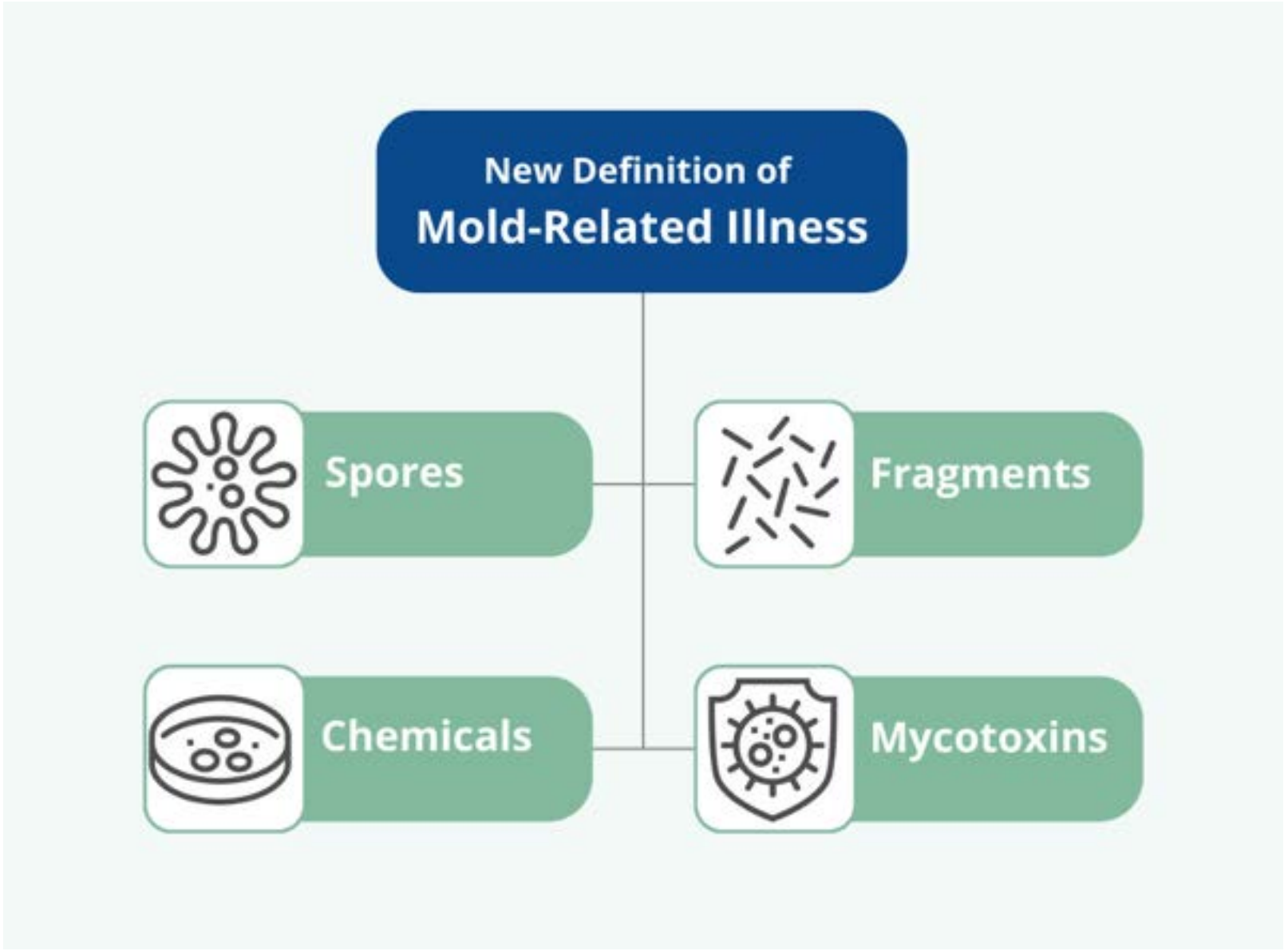
0 - 4 = Not Likely Mold-Related Illness
5 - 9 = Possible Mold-Related Illness
10+ = Probable Mold- or Biotoxin-Related Illness

OTHER THINGS TO CONSIDER:
Lyme Disease, MSIDS, Tick-Borne Co-Infections (Use HOROWITZ MSIDS-LYME QUESTIONNAIRE)
Other environmental toxins (IE: glyphosate, mercury, lead, PM2.5, VOCs, etc.)
Intestinal parasites
Chronic viral syndromes or other stealth infections
Food sensitivities
CVIDS or immunodeficiency syndromes

Research Study



MoldIQ.org



What Explains Symptom Persistence?

Occupational studies ~
- Coin flip: ~50/50 persister/recovered
- Do they stay symptomatic out of the building?
- **likely different stats for home exposure*

CFS study ~
- Normal controls: +fungus, -mycotoxins
- CFS pts from WDB: +fungus, +mycotoxins

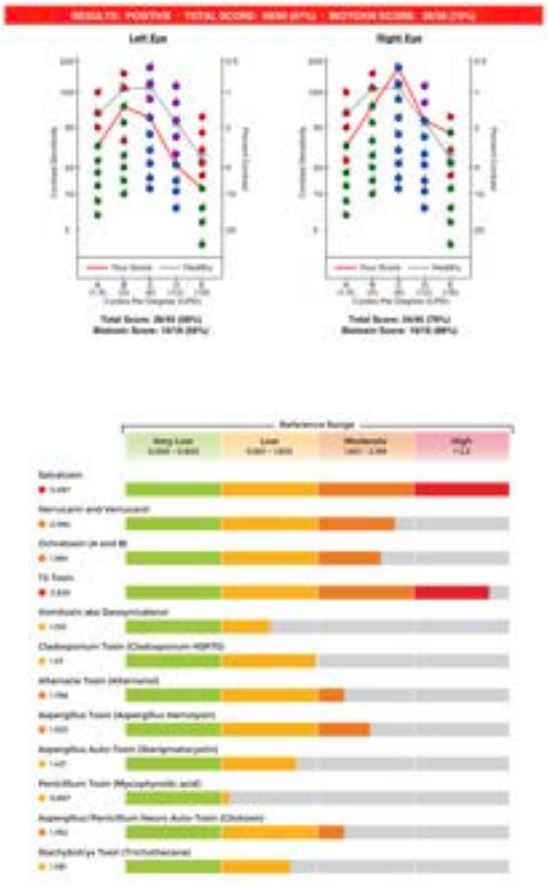
Damp or WDB exposure is the key

Mould is the trigger

Colonization is the result

PMID: 23580077 Brewer et al, Detection of mycotoxins in patients with chronic fatigue syndrome

Mold Assessments



Direct Tests ~
Urine mycotoxin (LC-MS method)
Stool microbial assay +yeasts

Indirect Tests ~
Visual Contrast Sensitivity (vcstest.com)
Serum IgE/G *mycotoxin* antibody
IgE/G mold spore antibody (standard)
Urine mycotoxin (ELISA method)
CBC:
  ↓WBC, relative lymphopenia
  ↑NLR, microcytic anemia
Vit D (↓25-OH and ↑1,25)
Liver function - esp ↑GGT
↓NK cell *function* with ↓ or normal NK cell total
↑MMP-9 (mast cell correlate)
Organic Acids Urine Test
NeuroQuant (1˚ neuro sxs)

Electrosmog

Dr JILL CRISTA
NATUROPATHIC DOCTOR

eEMFs

Electromagnetic frequency radiation (external) - the invisible toxin of our time.

Emitted from mobile phones, Wi-Fi, Bluetooth devices, smart meters, microwave ovens, many electrical devices, power and transmission lines, and wiring problems *involving bad grounding*.

Thermal effects: increase BBB permeability to macromolecules.

Main action is non-thermal via voltage-gated ion channels leading to channelopathies: oxidative stress, sperm/testicular damage, neuropsych effects including EEG changes, apoptosis, cellular DNA damage, endocrine changes, and calcium overload.

Behavioral studies have particularly concentrated on the effects of eEMFs on learning, memory, anxiety, and locomotion.

Study in adolescents: change in memory performance over 1 year was strongly negatively associated with eEMF dose.

PMID: 26474271, 31463749, 20550949, 29573716, 26300312

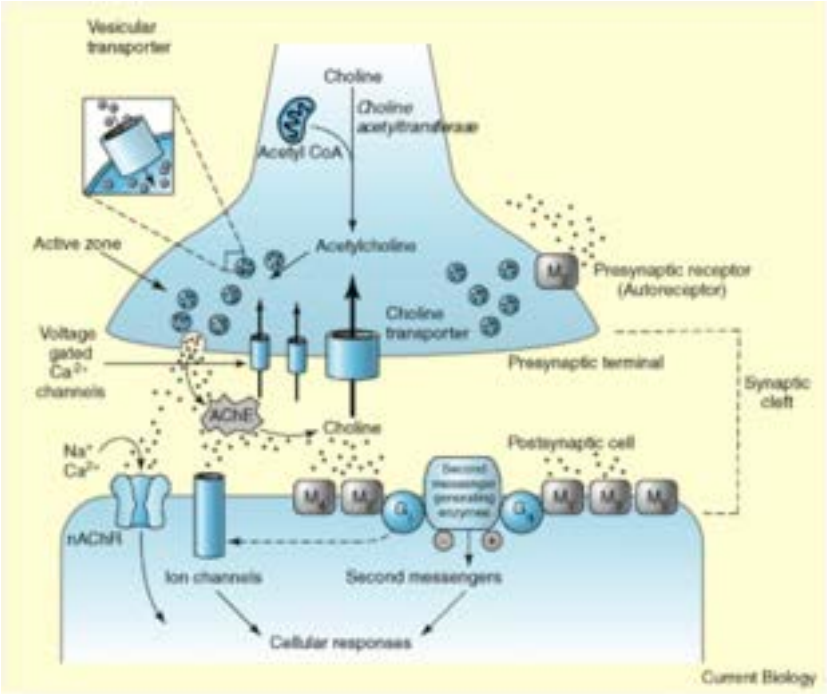
Voltage-gated channelopathies

Synaptic vesicles in the presynaptic terminal contain a high density of voltage-gated Ca2+ channels.

When an action potential arrives at the distal end of the axon – the presynaptic terminals – the inrush of positive charge activates voltage-sensitive Ca2+ channels.

Ca2+ entry then initiates the release of NTs into the synaptic cleft.

When NTs, such as ACh or glutamate, activate cation (for example Na+ or Ca2+) channels, and are thus depolarizing, they can be described as excitatory.



PMID: 15753022

eEMFs

Signs ~

EEG changes consistent with voltage-gated calcium channel activation

Symptoms ~

Sleep disturbance/insomnia
Headache
Depression/depressive symptoms
Fatigue/tiredness
Dysesthesia
Concentration/attention dysfunction
Memory changes
Dizziness
Irritability
Loss of appetite/body weight
Restlessness/anxiety
Nausea
Skin burning/tingling/dermographism

Screen reliance

Only safe space for many P/P kids is virtual spaces

Virtual school often required

Screen addiction common (dopamine)

eEMF Blocking ~
Lap pads, sleep canopies

eEMF Grounding ~
Nature!, grounding mats

eEMF Discharging ~
Movement (produces non-polarized internal or iEMFs)

eEMF Diagnostics

Test spaces, no known “body” test at this time.

Guard sleep space the most.

Resources:

Building Biology Institute (buildingbiologyinstitute.org)

EMF Analysis (emfanalysis.com)

Environmental Health Trust (ehtrust.org)

Physicians for Safe Technology (mdsafetech.org)

Tech Wellness (techwellness.com)

*Beware of over-reliance on EMF protection gadgets.
Reduction of exposure is the best mitigation measure.

Mercury

WHO March 2017 ~

- Considered by WHO as 1 of the top 10 chemicals or groups of chemicals **of major public health concern**.
- Even small exposure amounts may cause serious health problems, and is a threat to the development of the child in utero and early in life.
- May have toxic effects on the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes.

Comparison of typical exposures versus regulatory safety standards suggests that many people receive unsafe exposures.

1 in 6 women have mercury levels high enough to create a neurologic risk for their children.

Norway was the first country that banned the use of mercury in all products in 2008 including dental amalgam, followed by Sweden and Denmark.

2018: the EU banned the use of dental amalgam for children under 15 and for pregnant/nursing women.

PMID: 34941760, 24420334

Mercury sources

Organic ~

Methylmercury - fish/water contamination from coal-fired power plants

Ethylmercury (Thimerosal) - vaccine adjuvant, preservative (ie: contact lens solutions)

Inorganic/elemental ~

-“Silver” dental amalgams (about 50% mercury).

-Dentists like its malleability and hardness as compared to other materials.

-Continuously release elemental mercury vapor.

-Amalgam surface area that exceeds the safe level of airborne mercury in the intraoral cavity:

Adult: >0.8 surface of a tooth

Child: >0.6 surface of a tooth

- ∴ **more than one small filling is harmful to a child’s health**

PMID: 21782213, 34941760

Mercury sources

Household Hazardous Waste

- Average amalgam filling - 1000mg
- Thermometers - 500mg
- Barometers
- Electronics
  - LCD screens/monitors
  - Laptop screen shutoffs
- Antiques; jewelry, clocks, glass/mirrors
- Old appliances & vehicle switches
- Medical
  - Preservative - eye, nasal, skin, injections
  - Skin ointments (hemorrhoid cream)
  - Antiseptics (Mercurochrome)
  - Pharmaceuticals (diuretics)
  - BP cuffs
- Some batteries
- Fluorescent lightbulbs - 4mg
- Food ~
  - Seafood: 1 can tuna - 15-60 mcg
  - High-fructose corn syrup
- Flu shot - 25 mcg per 0.5-mL dose

Dental mercury amalgams in children

Evidence of safety of dental mercury amalgams in children has been based on 2 key studies from 2006 known as the Children's Amalgam Trials; followed >500 children each over 5/7 years.

Both studies found no difference in neurobehavioral outcomes between the amalgam group and the composite (non-amalgam) group—although in both trials the amalgam group showed a statistically significant increase in urinary mercury levels.

These two studies, in addition to being widely cited in the literature, are cited by the FDA and the ADA as providing evidence for the safety of amalgam.

However, a 2011 reanalysis suggests harm, and >boys with common genetic variants.
-Reanalysis used an exposure metric based on amalgam size and years of exposure
-Found a significant association between amalgam and the porphyrin biomarkers for mercury-related enzyme blockage

"Dental amalgams are a significant
chronic contributor to mercury body burden."

PMID: 24420334, 21053054

Dental amalgams disperse

Mercury doesn't stay in the tooth!

A study quantifying the excretion and distribution of mercury in biological samples after dental amalgams found ~
-Concentrations of Hg in the biological samples of those with amalgams were found 6-8 times higher than the non-amalgam users (control).
-Spike in Hg in RBCs, plasma, and urine on 1st day of filling, but not in hair or nails.
-Accumulation in hair and nails by day 12, but reduced in RBCs, plasma, and urine.

Mercury levels in the blood, urine or other biomarkers do not reflect the mercury load in critical organs.

Gestational mercury exposure ~
-Gestational exposure in infants of mothers who did not consume fish, had an elevated risk of URIs requiring a doctor visit.
-Alterations in both T cells and gene expression in placenta at birth.

Amalgams continuously release elemental mercury vapor (up to 20 micrograms per day.)
Odorless and tasteless.
Primarily absorbed in lungs where it can disperse widely, even xBBB.

PMID: 27464660, 30743244, 34129869

Exposure estimates

Organic mercury is more genotoxic than inorganic/elemental, yet “Amalgam-related Hg exposure [which is inorganic/elemental form] exceeds that from fish or other sources for the majority of the population.”

The highest allowable average mercury concentration in fish per serving when eating 1 serving per week = 0.46 µg/g

Whereas, estimates of Hg exposure from amalgam fillings “based on the least conservative of the scenarios evaluated, it was estimated that some 67.2 million Americans would exceed the Hg dose associated with the reference exposure level (REL) of 0.3 µg/cubic meter of air established by the EPA.”

Exposure estimates are consistent with previous estimates presented by Health Canada, and amount to 0.2-0.4 µg/day per amalgam-filled tooth *surface*, or 0.5-1 µg/day per amalgam-filled *tooth*, depending on age/other factors.

PMID: 21782213, 34941760

Dentists and dental hygienists

Study of dentists in Iran found that the mean of the mercury level in the urine, nail, and blood was higher than the standard of the WHO.

"So, in accordance with Article 10 of the European Union Regulations (EUR), in the context of the Minamata Convention (MC) on Dental Amalgam (DA), in order to avoid the dangers of mercury exposure in dentists, it is necessary for Iran and other countries to approve laws and to implement a national plan to reduce mercury levels and replace the appropriate materials."

"Numerous studies have reported neurobehavioural effects in dental personnel occupationally exposed to *chronic low levels* of mercury (Hg)."
- elevation of amyloid protein expression, deterioration of microtubules and increase or inhibition of transmitter release at motor nerve terminal endings.
- neurodegenerative diseases such as Alzheimer's, MS and mood disorders.
- idiopathic disturbances in motor functions, cognitive skills and affective reactions.

PMID: 33312669, 30589214

Amalgams vs fish

Reference Dose of safety - *level of exposure that is reasonably certain to be without appreciable risk for a population exposed over a long period of time.*

EPA set RfD for methylmercury consumption in women of childbearing age (and their fetuses). No other population of defined, not even children.
Reference Dose = 0.1 mcg/kg/day methylmercury. [45 lb child = 2 mcg/day]

Amount of elemental mercury vapor from one amalgam filling =
1 surface = up to 20 mcg/day.
The lower the body weight, the more increased the concentration.

"Throughout the world, efforts are underway to phase down or eliminate the use of mercury dental amalgam." (PMID 24420334) Yet there are no RfDs set for amalgams in the US, not even for those with lower body weight.

**I acknowledge this is comparing different forms of mercury and so may have different health/absorption/accumulation effects*

Mercury health impacts

Neuro ~

As vapor: can xBBB and lipid cell membranes, and can be accumulated into the cells in its inorganic forms.
Methylmercury can xBBB and placental barriers, causing serious damage in the CNS.
Animal studies: motor and cognitive impairment and neural loss.

Nephrotoxic.

Oral microbiome ~

Marked differences in the composition of the oral microbiome, associated with dental decay, found with even low concentrations of salivary mercury.

Gut ~

Gut connection to neurotoxicity: Healthy intestinal microbiota demethylates MeHg and promotes excretion through feces.
But in so doing, it impacts the gut microbiota and metabolites related to gut-brain interactions.
Induces changes of intestinal microbial community structure which induces changes to regulating neuron activity.
Elemental Hg induces archaea (methanogens) conversion to methylmercury in vitro.

PMID: 29777524, 32887894, 31918252, 33242089

Mercury, mast cells, and histamine

Mercury induces histamine release from basophils.

Mercury induces inflammatory mediator release from mast cells, specifically VEGF and IL-6.

Animal models:
- Induces a Th-2-dominated autoimmune syndrome with tissue injury in the form of a vasculitis and arthritis.
- Sensitizes mast cells for mediator release and interleukin-4 expression.
- Impacts mast cell survival.

Links to autoimmunity, disruption to BBB and subsequent neuroinflammation.

PMID: 20222982, 11222498, 19604304, 22103852, 9492216

Oral galvanism

Electromotive forces and electrical currents discharged from a tooth when two or more dissimilar metals coexist in the mouth (i.e. as used to make the “amalgam”.)

Interact with salivary electrolytes, worse acidic saliva.

Also occurs with contact between occluding metallic restorations.

Can be measured (biological dentist): the threshold for pathological values of 5 microA for galvanic currents and 100 mV for galvanic voltage.

A long-lasting influence (>15 hours) of galvanism can, in sensitive and genetically susceptible individuals, influence lymphocyte proliferation and surface molecule expression.

“After removal of the electro-active restorations, both the contents of metals in saliva and galvanic currents decreased in comparison with the levels before the treatment.”

German study concluded that the removal of dental amalgam leads to “the permanent improvement of various chronic complaints in a relevant number of patients in various trials.”

PMIID: 14917837, 15789284, 19178813, 15451237, 16804514

Mercury s/sxs

Symptoms are variable and nonspecific. Neuropsych sxs have high cross-over with P/P.

Poor resistance to infection, especially to yeast and yeast overgrowths.

Anxiety, depression, “mercurial mood”, irritability, suspicious, impulsive

Memory problems, incoordination, movement abnormalities, a sense of internal vibration, paresthesias particularly of the hands and feet

Neuromuscular junction: fasciculations, tremors

Halitosis, excessive salivation, metallic or salty taste, aphthous ulcers, tongue or tooth shocks, sensitive teeth, frequent dental caries, gingivitis, gums bleed easily, burning mouth syndrome, acute or chronic pharyngitis, perioral rashes

Night sweats, over-sensitivity to changes in temperature (think thermometer) and environments

Intestinal Methanogen Overgrowth (IMO), IBS

Urinary frequency, kidney conditions

Increased allergic and mast cell related conditions

Increased fasting blood glucose

Increased risk for autoimmune conditions, esp Hashimoto’s

**Tip: for toxic metals, look up homeopathic materia medica for complete list of sxs*

Mercury diagnostics

Due to rapid dispersal from plasma into tissue, and tissue accumulation, blood reference ranges are often not reliable indicators of health impact.

Blood ~

May apply to organic sources (diet and injected)
If positive, consider active/very recent exposure
>1.8 mcg/L associated with risk of Thyroglobulin Ab (Hashimoto's)
Normal does not rule out low-grade chronic exposure or tissue accumulation.

Urine ~

May apply to elemental sources (amalgam vapor)
Both pre- and post-provoked may be helpful
Why provoke? Assess chelating agent efficacy
Elevated unprovoked urine levels (95th percentile) considered significant for exposure.
*Abstain from eating fish/taking fish oil supplements for 1 wk prior to sample collection.

Correlated to higher levels of fasting glucose.

Empirically, also correlated to chronic Candida/yeast burden.

Toxic Metals; urine

TOXIC METALS		RESULT µg/g Creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	1.6	< 15	
Antimony	(Sb)	0.074	< 0.18	
Arsenic	(As)	12	< 40	
Barium	(Ba)	0.88	< 5	
Beryllium	(Be)	<dl	< 0.10	
Bismuth	(Bi)	0.091	< 0.8	
Cadmium	(Cd)	0.35	< 0.6	
Cesium	(Cs)	11	< 9	
Gadolinium	(Gd)	<dl	< 0.5	
Lead	(Pb)	2.1	< 1.1	
Mercury	(Hg)	0.55	< 0.8	
Nickel	(Ni)	7.7	< 4	
Palladium	(Pd)	<dl	< 0.2	
Platinum	(Pt)	<dl	< 0.1	
Tellurium	(Te)	<dl	< 0.2	
Thallium	(Tl)	2.2	< 0.4	
Thorium	(Th)	<dl	< 0.007	
Tin	(Sn)	0.19	< 3	
Tungsten	(W)	<dl	< 0.4	
Uranium	(U)	<dl	< 0.03	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	32.5	35 – 240	

Pesticides (Insecticides)

Notoriously persistent chemicals in the tissues of mammals, especially those higher up the food chain.

The dose makes the poison, or does it?
Chronic low-level exposure more detrimental than a single poisoning event.

Neurotoxins ~
The issue comes when the molecular target is shared by non-target species.
Critical need for improved translation from animal models to humans.

Pesticides such as organophosphates are linked to increased risk of neurological dz and dysfunction in humans, including chronic organophosphate-induced neuropsychiatric disorders in a time and dosage dependent manner.

Easily absorbed: inhalation, any cutaneous/mucocutaneous, ingestion.

PMID: 31197504, 21402100, 30144465, 35439576

Pesticides (Insecticides)

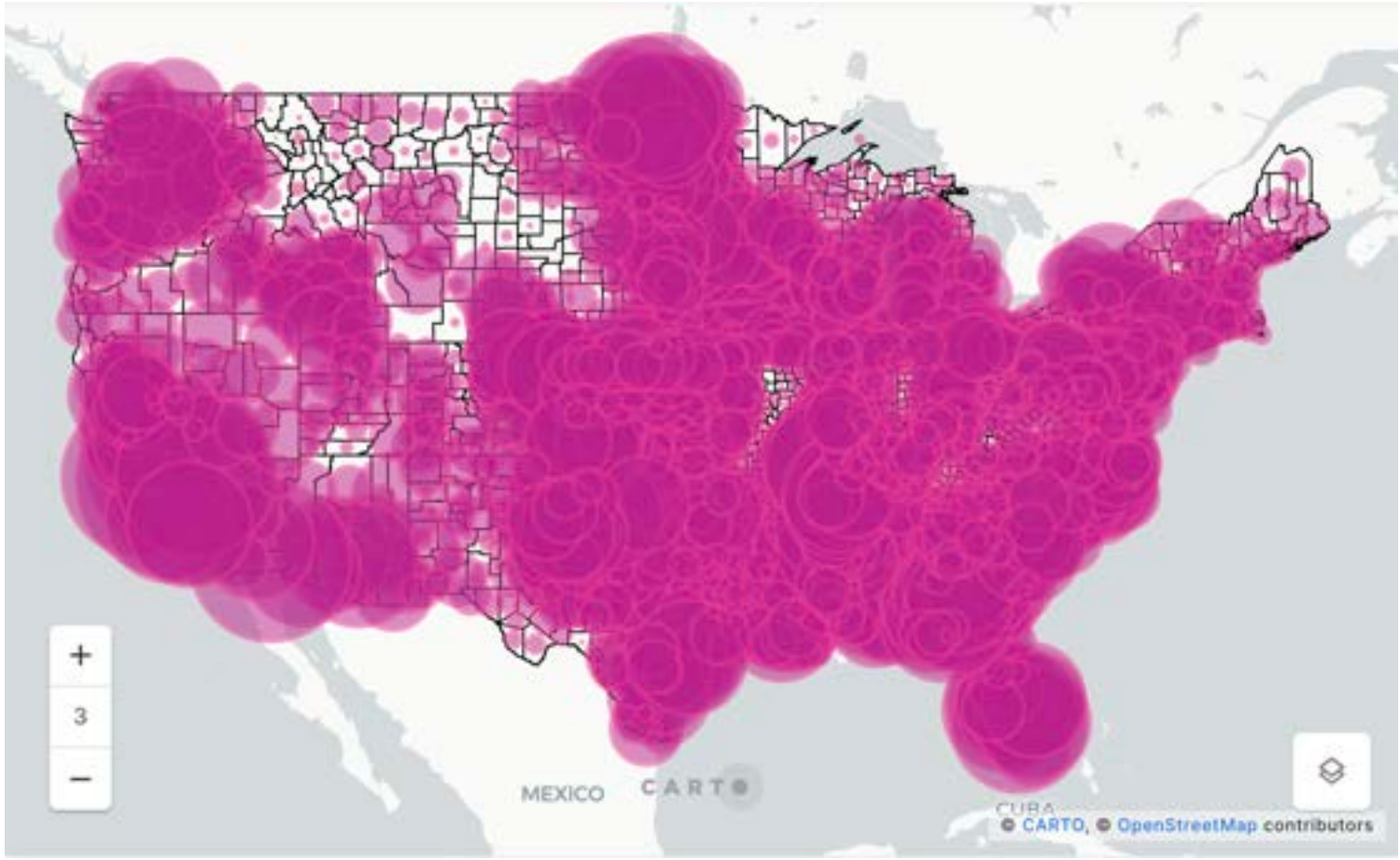
Exert neurotoxicity primarily through the inhibition of acetylcholinesterase (AChE).
Leads to a buildup of ACh in the synapse, and hyperstimulation of cholinergic receptors in the CNS/PNS. Acute poisoning “cholinergic crisis”.

Dopaminergic neuronal cells ~
Significantly alter dopaminergic neurochemistry.
Additive/synergistic effects of different pesticides that act on different targets within the dopaminergic system.
Promote severe ox stress, mainly due to mitochondrial dysfunction, accompanied by significant upregulation and activation of caspases, thereby leading to apoptosis.

In vivo: damaged brain mitochondria marked by significantly reduced levels of catalase, glutathione (GSH) and superoxide dismutase (SOD), and increased lipid peroxidation.

PMID: 31197504, 21402100, 30144465

Organophosphate use in the US



https://earthjustice.org/feature/organophosphate-pesticides-united-states#:~:text=Organophosphate%20Pesticides,-Learn%20about%2017%20of%20the

Pesticide urine test

Organophosphate pesticides

Test Name (mcg/g)	In Control	Moderate	High	Current Level	Previous Level 10/29/2021
Diethyldithiophosphate (DEDTP)	≤0.20	0.21–0.48	≥0.49	0.02	4.19
Dimethyldithiophosphate (DMDTP)	≤0.80	0.81–5.08	≥5.09	0.29	5.75
Diethylthiophosphate (DETP)	≤0.70	0.71–2.76	≥2.77	0.17	7.49
Dimethylphosphate (DMP)	≤5.20	5.21–37.19	≥37.20	0.19	3.11
Diethylphosphate (DEP)	≤0.80	0.81–12.59	≥12.60	0.76	3.50
Dimethylthiophosphate (DMTP)	≤4.60	4.61–29.20	≥29.21	4.20	9.82
Atrazine	≤0.02	0.03–0.05	≥0.06	<0.01	7.16
Atrazine mercapturate	≤0.03	0.04–0.06	≥0.07	0.03	7.04

Vaccines

🙏 Please allow me to preface this section with a humble admittance that I exist in extreme uncertainty about this subject, and I am far from being an expert.

What I am is a “curious digger”, a clinician researcher.

I’m presenting my understanding as of this moment, which is simply my own understanding.

I welcome scientific dialogue and hope we can, together, advance our collective understanding.

I invite you to remain curious, and promise that I will too.

Risk of prevention vs infection

In my PANDAS/PANS patient population, vaccines have consistently induced flares, *but obviously so have infections.*

How to counsel parents on each of the 72+ vaccinations to fulfill the childhood vaccination schedule?

What is the risk ratio of infection:vaccination for each?

Problematic situation:
No data on PANDAS/PANS kids.

Even more problematic:
In fact, there's no placebo-controlled data in healthy children either!

Wait, . . . what!?

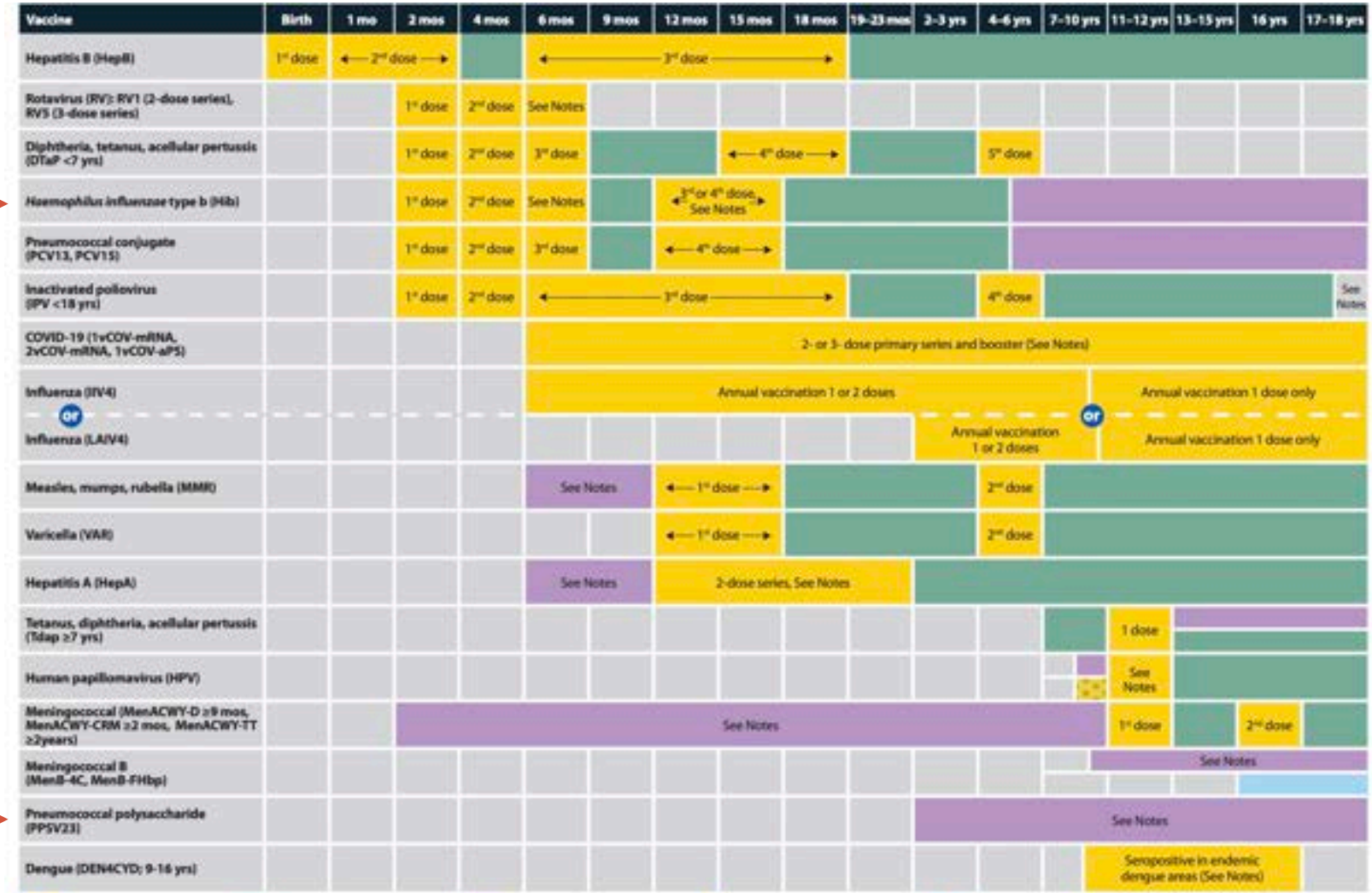
Vaccine safety

NO single childhood vaccine or combination of childhood vaccines has been tested against non-vaccinated controls in clinical trials, *ever*.

Only a few have been studied against “controls" but the “controls” were either ~
- the adjuvants, rather than inert placebo. (ie: PedvaxHIB) By design, adjuvants are intended to evoke an immune response.
- other experimental vaccines (ie: Pneumonia: compared against an experimental meningitis vaccine that has never been approved, and to this day is still not approved. Yet the vaccine was not only approved for licensure, it became the “control” for the next generation pneumococcal vaccine trial.)

CDC’s own definition of placebo from their website ~
“Placebo: A substance or treatment **that has no effect on living beings**, usually used as a comparison to vaccine or medicine in clinical trials.”
https://www.cdc.gov/vaccines/terms/glossary.html#P

These “controls" do not meet the definition of placebo-controlled.



Vaccine adjuvants

NO vaccine adjuvants have been tested as single agents *or* in any combination against placebo controls to show that they're safe to be injected into children, *ever.*

FDA recommends Aluminum not to exceed 5 mcg/kg/day parenterally.

Children get an estimate of 622 mcg/kg of Aluminum in the CDC schedule (average of 4mg per child).

A recent paper found a 4-fold increase in the incidence of childhood asthma per 1mg Aluminum. This **increases the risk of asthma by a factor of 16** (4mg x 4-fold increase).
(Read the raw data, not the the abstract. I have provided access to the full study in your course materials.)

Strictly economically speaking, in 2007, the US economic burden of asthma was estimated at $56 billion. (I struggled to find a more recent estimate.)

PMID: 36180331, 22477831

More details on Aluminum and asthma study

Exclusion criteria and stratification by eczema diagnosis:
From an initial population of 398,191 children, 15,036 (3.8%) did not meet inclusion criteria, 30,976 (7.8%) had vaccine-related exclusions, and 25,188 (6.3%) were excluded due to asthma diagnosed prior to age 24 months. The final study cohort comprised 326,991 children, among whom 14,337 (4.4%) were diagnosed with eczema before age 12 months.

The incidence rate of asthma appeared to increase with increasing levels of aluminum exposure in the eczema and no eczema cohorts.

Among children with eczema after adjustment for covariates, cumulative vaccine-associated aluminum was positively associated with persistent asthma (adjusted hazard ratio [aHR] 1.26 per 1 mg increase in aluminum, 95% CI 1.07, 1.49).

For children with eczema, the mean and median cumulative vaccine-associated aluminum were 4.07 mg (SD 0.60), and 4.18 mg (IQR 3.97, 4.43), respectively.
For children without eczema, the mean and median were 3.98 mg (SD 0.72) and 4.18 mg (IQR 3.93, 4.43), respectively.

PMID: 36180331

Mercury controversy

Claim: Methylmercury (found in fish) and ethylmercury (thimerosal as sodium ethylmercurithiosalicylate) have different health effects…?
They're both organic form. Studies?

2016 industry flyer - "Thimerosal use is still permitted in multi dose vaccines and contact lens solutions at concentrations of up to *100 and 70* ***mg****/kg respectively*."
*mg, not mcg

CDC's National Immunization Program statement in 2004 - "…thimerosal-free vaccine costs more than the thimerosal-containing vaccine—about $12 versus $8.50 per dose."

*https://assets.thermofisher.com/TFS-Assets/CMD/Application-Notes/AN-43141-ICP-MS-Mercury-Contact-Lens-Solution-AN43141-EN.pdf

Ethylmercury on the mind

Thimerosal-derived ethylmercury is a mitochondrial toxin in human astrocytes; inhibits mitochondrial respiration with concurrent increases in the formation of ROS.

Cell studies provide evidence for the passive and active transport across the BBB.

Animal and clinical studies specifically examined whether mercury accumulates in the brain after exposure to ethylmercury-containing compounds (thiosalicylate) or Thimerosal.

The results indicate that ethylmercury-containing compounds are **actively transported across membranes** by the L (leucine-preferring)-amino acid transport (LAT) system, **the same as methylmercury-containing compounds**.

Further, 22 studies from 1971 to 2019 show that exposure to ethylmercury-containing compounds (intravenously, intraperitoneally, topically, subcutaneously, intramuscularly, or intranasally administered) **results in accumulation of mercury in the brain**.

In total, these studies indicate that ethylmercury-containing compounds and Thimerosal readily cross the BBB, convert, for the most part, to highly toxic inorganic mercury-containing compounds, which significantly and persistently bind to tissues in the brain, **even in the absence of concurrent detectable blood mercury levels**.

PMID: 31841767, 22811707

Vaccine efficacy

NO vaccination on the childhood schedule has been tested for *efficacy* against non-vaccinated controls in clinical trials - *ever.*

Do childhood vaccinations actually protect from the disease they're targeted against? How could we know? It's never been tested in a clinical trial.

Duration of non-placebo "controlled" trials from which vaccines have been licensed track for an average of 4-5 days. (Ie: Hep B)

What about long-term health outcomes?

Human and animal data suggest vaccine adjuvants increase the risk of developing an autoimmune disease, including RA, SLE, Sjögren syndrome, autoimmune thyroiditis and antiphospholipid syndrome.

PMID: 26275795, 27417999

Vaccine efficacy

The full extent of inquiry is *one* retrospective analysis by Dr. Paul Thomas of over 11,000 children born into his pediatric practice, where he had a statistically significant cohort of his patients who's parents decided to forgo vaccination and those who vaccinated their children - providing a treatment group and a control group.

Among the vaccinated, 25.16% had a family history of autoimmunity, whereas among the unvaccinated, 31% had the same characteristic.

The Quality Assurance Analysis showed ~

> Vaccinated children had 4-5x more health issues than the unvaccinated children, including allergic conditions, asthma, neurodevelopmental conditions such as ADHD, and infectious diseases, including those for which they were vaccinated against.

*these results were using his vaccine-friendly plan, which staggers vaccinations to reduce immune aggravation and allow for clearing of adjuvants.

This paper was retracted and to this date there's been no discernible reason why.

PMID: 33266457

PMID: 33266457

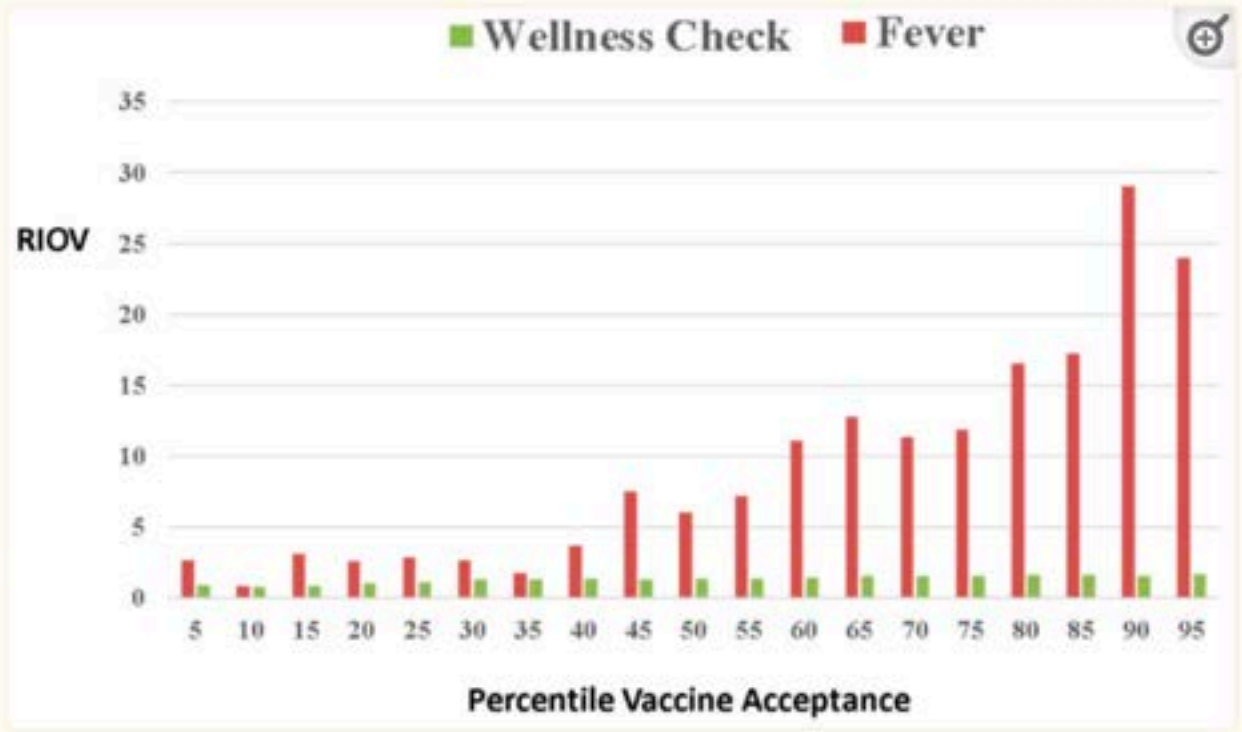
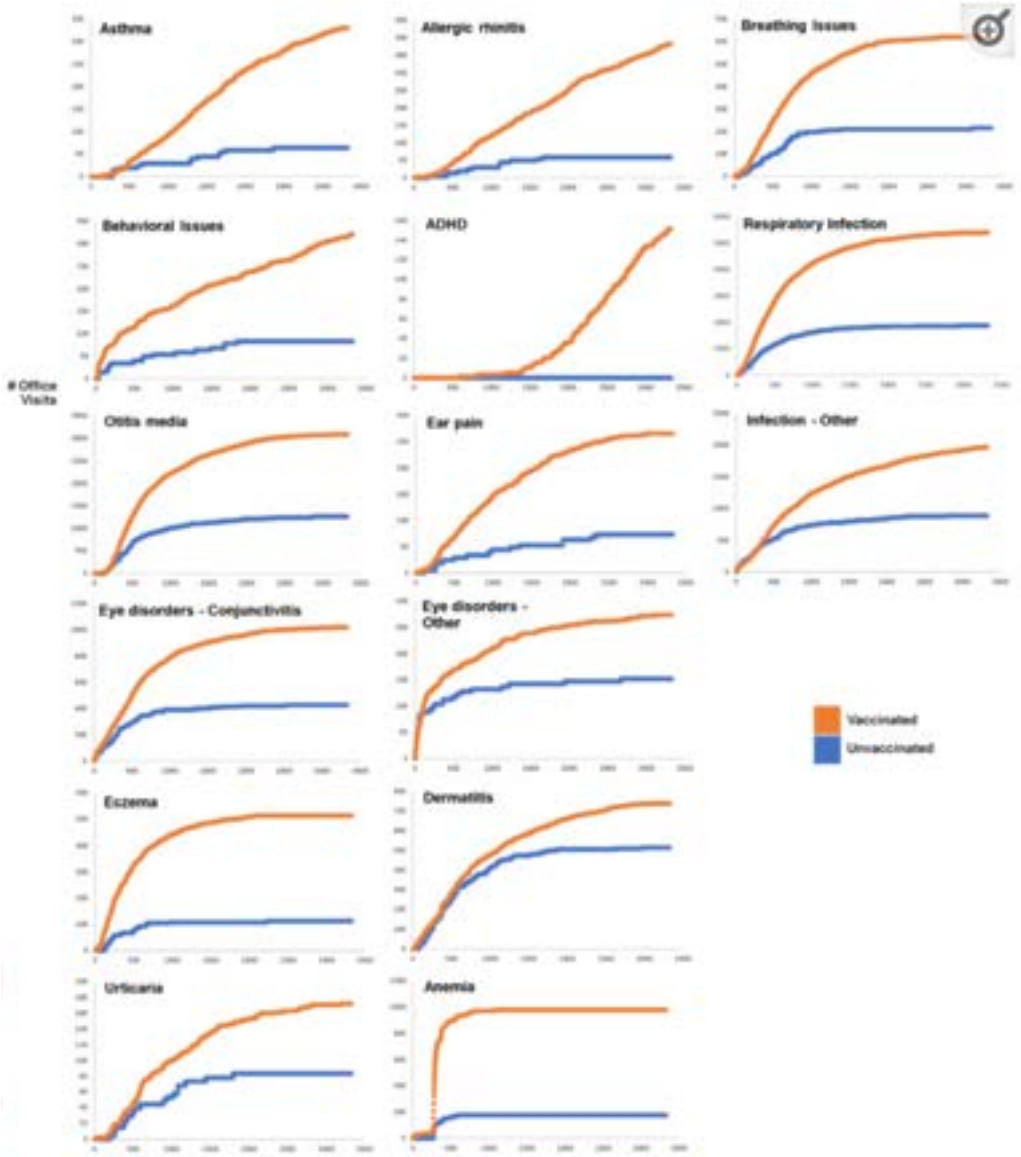


Figure 3

Relative Incidence of Office Visit (RIOV) percentile vaccinated vs. unvaccinated design of analysis: power decreases from left to right; thus, a stable trend (increase or decrease) becomes noteworthy. The data shown are for the Relative Incidence of Office Visits (RIOVs) to average incidence ratio of billed office visits related to fever in the vaccinated compared to the unvaccinated (OV_V/OV_{UV}) conditions and for "Well Child" visit on the right. For all the clinical conditions studied, RIOV reflects the total number of billed office visits per condition per group, reflecting the total disease burden on the group and the population that it represents.

PMID: 33266457



Published Reanalysis

Dr. Thomas's paper was retracted based on the complaint of one person—after it had passed peer review, was published, and had been read by over 250,000 people.

"His complaint hinged on the supposition — unsupported by any data —that vaccinated children made their scheduled HCVs more regularly than unvaccinated, implying that those unkept appointments led to fewer diagnose.

We show, here, new data from the same practice that the opposite is true.

We have shown, using a variety of exhaustive methods, that the anonymous reader's concerns that led to the retraction of Lyons-Weiler and Thomas (2020) were unfounded. …we conclude that the paper was wrongfully retracted…"

SOURCE: James Lyons-Weiler PhD and Russell L. Blaylock, MD. *Revisiting Excess Diagnoses of Illnesses and Conditions in Children Whose Parents Provided Informed Permission to Vaccinate Them*, International Journal of Vaccine Theory, Practice, and Research. September 26, 2022 p. 603. https://doi.org/10.56098/ijvtpr.v2i2.

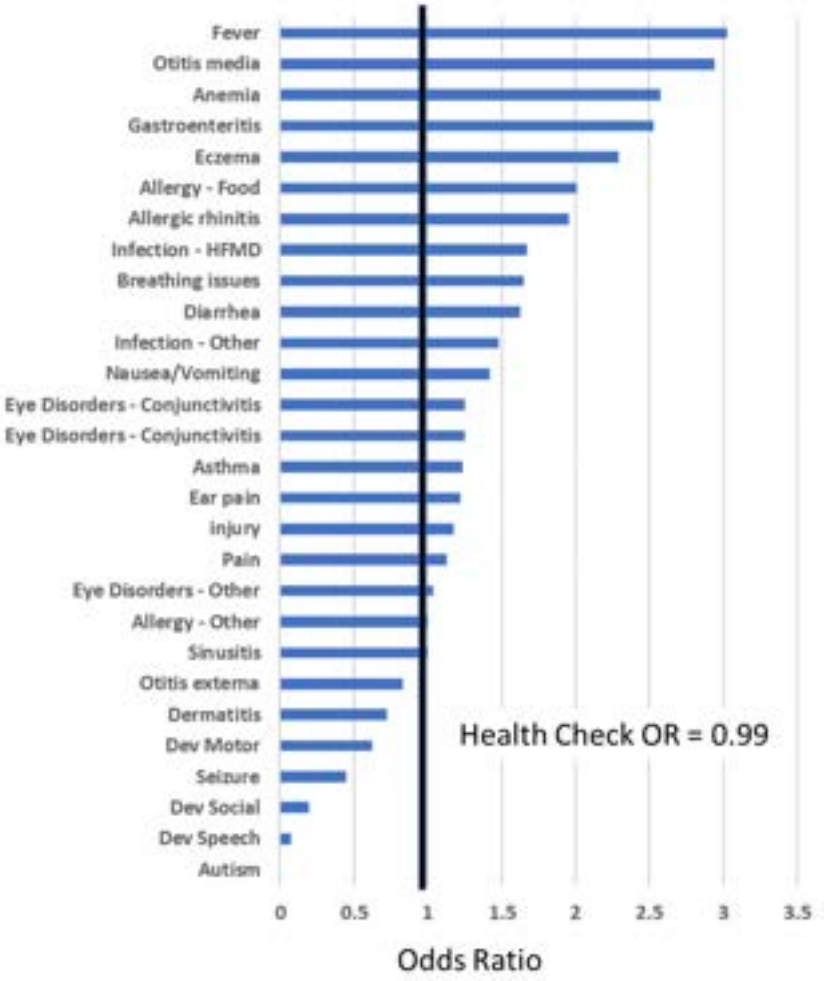


Figure 4. Odds ratio of office visits for specific health issues in the comparison of 561 unvaccinated and 561 vaccinated patients in the matched analysis.

When the data for vaccinated versus unvaccinated children are examined, the critic's claim is exactly reversed.

Relative Risk and Odds Ratios sustain and augment the original report. Additional office visits, beyond scheduled HCVs, are quantified, controlling for variation in kept HCVs and age/days of care.

Estimates of Health Care Incidence (HCI) show that visits above regular HCVs increase due to vaccination by 2.56 to 4.98 additional office visits for vaccine-related health issues per unit increase in vaccination per year.

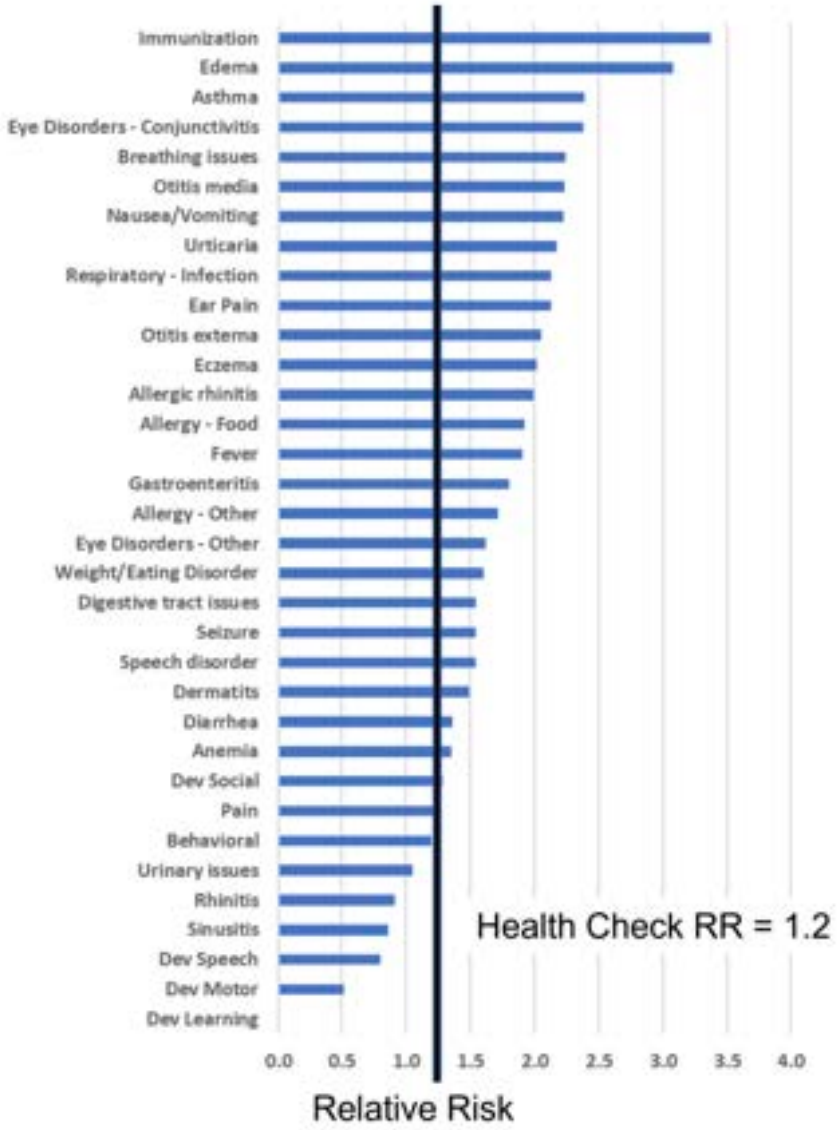


Figure 7. The age-matched effects of vaccine cessation. High Relative Risk values denote increased risk of a given health outcome in patients receiving more vaccines in the older age group (>1,500 days of age). The black bar shows the Relative Risk of HCV between these groups as a baseline.

Additionally, the comparison of the High- and Low-vaccinated patients aged 1,500 days or more shows that vaccine cessation leads to a reduction in many conditions (thus the increased relative risk in the vaccinated patients;[.]"

1 study. 1 reanalysis.

Why hasn't this been repeated?

Does volunteer reporting work?

VAERS put in place by the CDC to monitor vaccine safety; voluntary, complaints about time it takes to submit a report.

So HHS commissioned the Agency for Healthcare Research and Quality (AHRQ) for a pilot project with Harvard researchers to use machine learning to facilitate detection and clinician reporting of vaccine adverse events directly into VAERS. Goal: improve completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system.

EHR from all ambulatory care encounters in a large multi-specialty practice. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care Dx codes, lab tests, and prescriptions were evaluated for values suggestive of an adverse event.

Protocol was reviewed in advance by the CDC's Clinical Immunization Safety Assessment (CISA) Network.

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) Report, PI: Lazarus, 2010

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients. 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals.

Of these doses, 35,570 possible reactions that fit the criteria of an adverse event were identified (2.6 percent of vaccinations.) Equates to an average of 1 in 37 vaccines given. (At the time, CDC was reporting the occurrence of 1 in 1 million.)

This is an average of 1.3 events per clinician, per month.

Found that fewer than 1% of vaccine injuries reported to doctors and recorded by an encounter within 30 days were actually being reported on VAERS. The VAERS system is underreporting more than 99% of adverse events.

These data were presented at the 2009 AMIA conference.

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) Report, PI: Lazarus, 2010

Conclusion

"Low reporting rates preclude or slow the identification of "problem" drugs and vaccines that endanger public health. New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting: reporting is not part of clinicians' usual workflow, takes time, and is duplicative. Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs."

Response? CDC shut down the pilot project.

Researchers: "the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation."

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) Report, PI: Lazarus, 2010

Timing and ethics

Once a vaccine is licensed, it is considered unethical to conduct a placebo-controlled clinical trial, as you'd be denying the child the standard of care . . .
*even though licensure was granted without a placebo-controlled clinical trial.

We are in a pickle:
How do we weigh the risk of infection against vaccination with limited data in kids with neurological autoimmunity.
How do we stratify which child's immune system will go too far?

In fairness, many of the herbs and other natural treatments that I'll be teaching about have never been tested against placebo controls. I'm fully aware that natural is not the same thing as safe.

Weighing the risks

Doctor, did you know that because the CDC hasn't done the appropriate research, the determination of whether any vaccination is *safe* or *effective* for your patient, or whether it increases their risk for developing allergies, asthma, ADHD, autoimmunity, or even the very infection it's intended to treat, **is being left up to you?**

> *"We need more investment in vaccine safety science,"*
> *Heidi Larson, Director, WHO Vaccine Confidence Project*

Ultimately it's the parent's decision, with "informed-as-much-as-possible-with-limited-data" consent.

Parents are beginning to sue doctors since they can't get compensation for injury or death from the pharmaceutical companies for anything classified as a "vaccine" (per 1986 The National Childhood Vaccine Injury Act.)

Did you know you were being asked to take on that much personal medicolegal risk?

https://aaronsiri.substack.com/p/clinical-trial-to-license-rotateq

Coverage

This is the parent's responsibility. Do not allow abdication of the responsibility to you. However, do your duty to inform as much as possible.

Require parents to sign a consent form for either decision; vaccinate or not. Consider each vaccine separately.

Copy the entire package insert and require that the parent read it before signing your consent form ~
Federal Regulatory Code
-Pre-2006 approved: § 201.80 “The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved.”
https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-201/subpart-C/section-201.80
-After 2006: § 314.70 “To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter;”
https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314/subpart-B/section-314.70

Consent form includes, but not limited to ~
-The risk of the getting the infection (sxs, severity, duration)
-Have a check box where the parent attests
“_X_ I have read the vaccine package insert for ____”
“_X_ I understand that this vaccine has not been compared for safety or efficacy against true placebo-control in clinical trials, nor has it been compared against non-vaccinated children in a clinical trial.”
-Make sure parents are aware that therefore it’s impossible to provide a true “informed consent”.

Check your malpractice coverage for vaccine injury and injury from not vaccinating.

Mitigating vaccine reactions

Many parents choose to vaccinate.

Alternate schedule - one at a time, separate by weeks
Pro - allows for I/S response resolution/adjuvant detox between, know what immunization is easier/harder on child, doesn't overwhelm I/S or toxicities
Con - more needle sticks/doctor visits, increased chance of losing to follow-up

Preservative-free or low preservative option (only addresses thimerosal)

Prep with homeopathy ~
Ledum 30c - 3 pellets under tongue 15-30min before injection
Thuja 30c - 3 pellets under tongue right after injection, and repeat immediately if any neuro sxs arise

Glutathione ~
450mg bid the day before, the day of, and day after injection

AVOID acetaminophen! (depletes glutathione)

Environmental triggers

Top 7 from my clinical practice ~

1. Herbicides
2. Mold
3. EMFs
4. Mercury
5. Pesticides
6. Vaccine adjuvants

(Food dyes get a dis-honorable mention)

Commonality: all are neurotoxins and immunotoxins.

Diagnostics

Clinical diagnosis

PE and symptoms as clues

General diagnostics

Infectious triggers

Environmental triggers

Kid in a bubble?

Natural for parents to want to protect their child.

Soften your perspective, and…

LISTEN to the child's behaviors!

Prognosis

Do they grow out of it? In my practice, not without treatment.

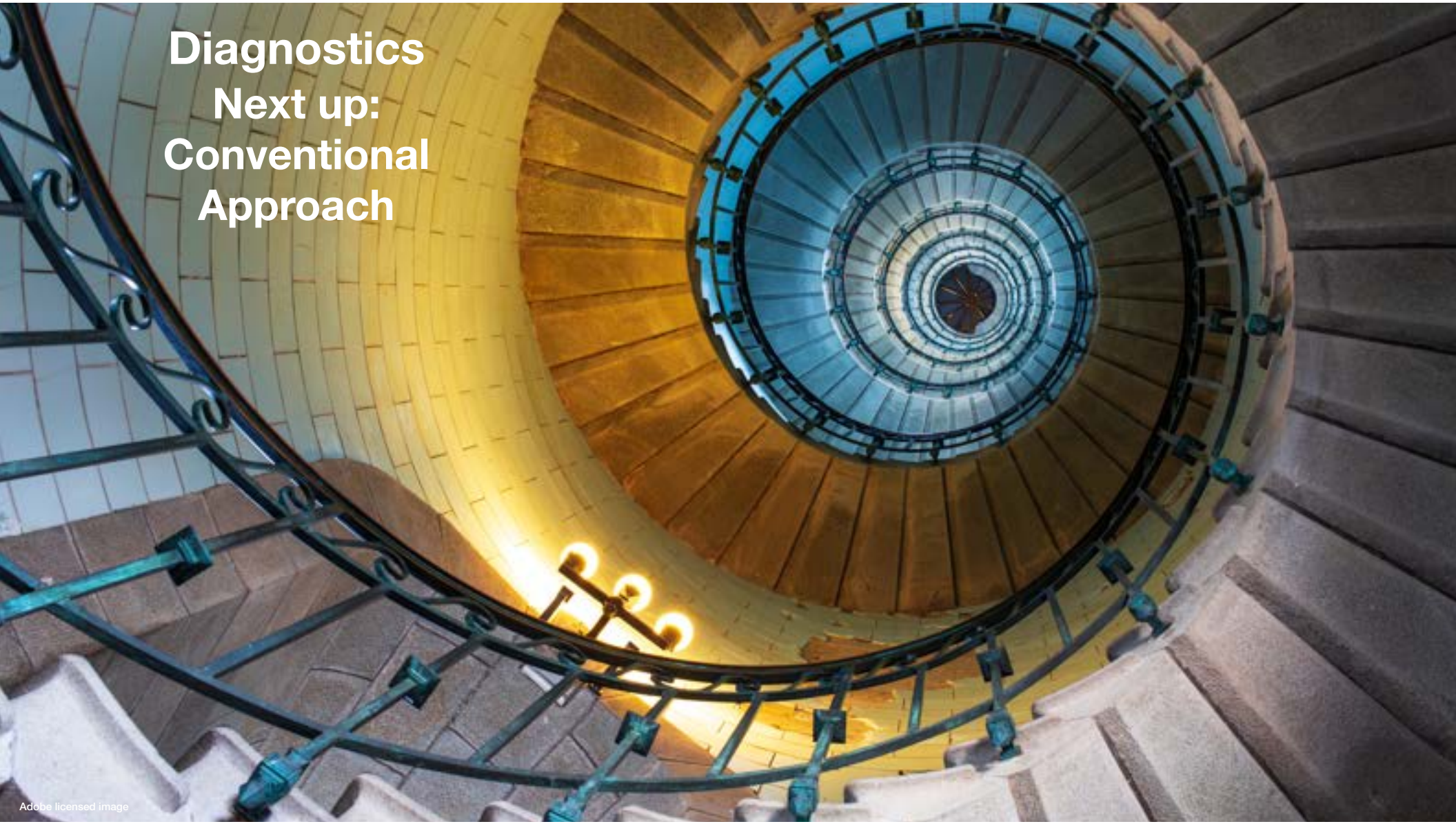
Seem better outwardly, as they learn how to cope better/not disturb others = extreme inward suffering with outward “norm’ing”.

Some improvement even without treatment after the hormone swings of puberty calm down.

Most can get back to life but must prioritize health/minimize environmental and infectious exposures.

With adequate treatment, most grow into independently-living adults with careers, hobbies, relationships, etc.

Diagnostics Next up: Conventional Approach



PANDAS & PANS
An Integrative Approach

Dr. Jill Crista

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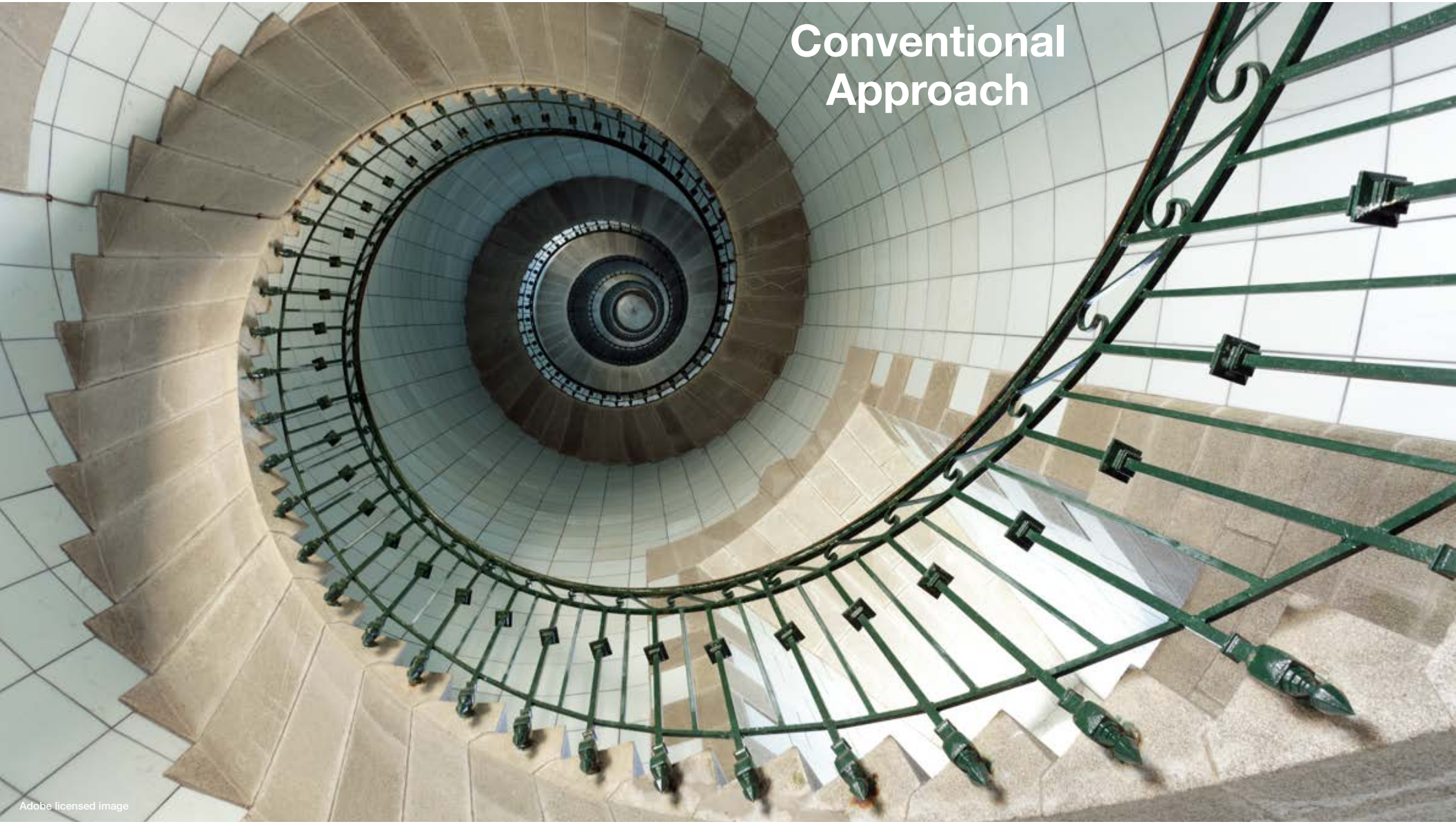
Conventional
Approach
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Course Outline

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

Conventional management

1. Control inflammation
   NSAIDs, steroids
2. Prevent/treat infection
   Prophylactic Abx + perianal Strep tx
3. Remove reservoirs of infection
   Tonsillectomy
4. Correct neurotransmitters
   SSRIs/SNRIs
5. Manage behaviors
   CBT
6. Immune modulation
   IVIG, Rituximab, CellCept, Plasmapheresis

Flowchart from PANDAS Physician Network website

Control inflammation

Ibuprofen ~

NSAID. MOA: non-selective inhibitor of cyclooxygenase (COX) which is required for the synthesis of prostaglandins via the arachidonic acid pathway.

Trial period/flare management

10mg/kg bid-tid x 2 weeks.

Maintenance dose varies (Naproxyn may be used for maintenance.)

Tell parents this is intended as prescription strength, may not match OTC dosing, so watch closely for s/e's

S/E - nausea, reflux, bloating, tinnitus, edema, and stomach, intestinal or unusual bleeding

If significant improvement from trial dose, then you know that "taming the flame" is an important target of tx.
Variety of options other than, or used with, NSAIDs

Control inflammation

Corticosteroids ~

Dexamethasone. MOA: glucocorticoids modulate the inflammatory response by repressing the expression of pro-inflammatory cytokines by immune cells.
C/I - hypersensitivity to dexamethasone, uncontrolled infection, systemic fungal infection
S/E - thrush, acne, increased risk of infection, dyspepsia, insomnia, wt gain, h/a, htn, hyperglycemia, confusion/amnesia, vertigo, growth stunting, bone loss, bruising, muscle atrophy

Oral Burst/Taper ~ PANDAS Physician Network

Oral prednisone 2 mg/kg for 1 week
-then taper to 1 mg/kg the second week
-0.5 mg/kg the third week
-0.5 mg/kg QOD for the final week
The maximal initial starting dose is 60 mg per day.
Am dosing and/or before 3pm to mitigate problems with sleeping

Per Stanford PANS clinic “for autoantibody-mediated encephalitis, NSAIDS and oral steroids often won’t come close.”

IV: 3mg/kg/d by continuous IV infusion x 3d/mo x 6mo
Follow with Rituximab or Cellcept (mycophenolic acid/mold derivative)

Prevent infection

Prophylactic Antibiotics ~
- Triggering event is long gone
- GABHStrep is target = “cell wall” beta-lactam antibiotics
- ex: Penicillins, Cephalosporins, Cephamycins
- Per some specialists, dose *really* matters, don’t go too low
  - Ie: Augmentin (875mg amoxicillin + 125mg clavulanate) bid
  - Clavulanate - also beta-lactamase inhibitor
  - S/E - diarrhea, candida, liver/kidney toxicity

Per Stanford PANS Clinic, to keep in remission ~
- IM Penicillin (long-acting) q2-3 weeks
- Even if were compliant on oral AB
- Sydenham’s chorea similarity
- More fitting for PANDAS than PANS?

PMID: 33728634 2021 Cochrane Review. Different antibiotic treatments for Group A Streptococcal pharyngitis.

Perianal Strep

Commonly persistent. Tonsils/gut serve as co-infected reservoirs.

Studies show that treating all the potential reservoir locations, rather than just a topical cream, is most effective.

Topical silver sulfadiazine or pharmaceutical antibiotics *Along* with oral antimicrobials, until there's no sign of infection on culture.

ALWAYS re-culture to make certain is eradicated.

PMID: 30627524

Antimicrobial sources

Many are derived from mold, some are actual mycotoxins
- Compare to enviro testing (if available) before prescribing
- Will affect susceptibility and side-effects if use same source Rx as environment.

Penicillium
- Penicillin, amoxicillin

Acremonium
- *Cephalosporins

Actinomycetes/actinobacteria
- Tetracyclines, macrolides, aminoglycosides, rifamycins

Actinobacteria
- Ivermectin

Side-effects as mold clues

Penicillin

Allergy - IgE-mediated pruritus, rash, GI
Correlated with exposure to environmental Penicillium

"IgE-mediated allergy wanes over time, with 80% of patients becoming tolerant after a decade."…why? tolerance or move?

"Cross-reactivity between penicillin and cephalosporin drugs occurs in only about 2% of cases."

+penicillin skin testing, high-risk anaphylactic cases, +spores

∴ Low- to moderate-risk missed w skin testing, +mycotoxins

PMID: 30644987, 405332

Side-effects as mold clues

Tetracyclines

S/E - photophobia
Correlated with mold exposure
Vitamins A & D deficiency also correlated,
common in mold-exposed patients,
esp if being treated with LT Rx binders

PMID: 14650691, 26269110

Side-effects as mold clues

Macrolides

S/E - Tinnitus
Correlated with mold exposure
Neurotoxic. “First pass" effect at the sinuses
Cavernous sinus - many nerve pass-throughs
Internal carotid artery, abducens nerve (cranial nerve VI)
Cranial nerves III, IV, V1, V2, (oculomotor, trochlear, ophthalmic, and maxillary)

S/E - Cholestatic hepatitis
Inflam/congestion of bile ducts also correl with mold exposure

Remove reservoirs of infection

Tonsils and sinuses can become reservoirs of infection.

Much scientific debate about tonsillectomy. In a survey conducted by the PANDAS Physician Network, parents reported anecdotal evidence that tonsillectomy may have benefit.

IME some benefit, and some don't. Leaves parents conflicted over whether surgery is the right decision.

Where I've seen clear benefit of tonsillectomy are in the children with a specific combination of factors:

- Free of perianal Strep, verified by culture.
- Been dairy free for more than 6 weeks. (Common cause of enlarged, chronically infected tonsils.)
- Free of cavities or dental infections.
- Gut microbiome has been addressed.
- Tonsils have been aggressively tx'd, yet remain large, boggy, cryptic, and may form tonsilloliths.
- Tonsils are large enough to cause snoring or obstructive sleep apnea.

Tonsillectomy in these cases reduces infection and recurrence of autoimmune flares, and improves sleep.

Culture or NGS-PCR test the removed tissue.

- If + for biofilm species, must be treated or may persist in other tissues/sinuses.
- Prevotella - Gram neg anaerobe - most commonly found by Dr. Trifiletti.
- Also commonly find Pseudomonas and Klebsiella.

PANDAS Physician Network Website: Tonsillectomy

"While there have been no published research on the effect of tonsillectomy on PANS or PANDAS patients, there has been unpublished findings and anecdotal evidence that show tonsillectomy may have benefit. ***Many PANS/PANDAS patients have damaged or cryptic tonsils, but the potential benefit of tonsillectomy is not limited to patients with those tonsil characteristics*.**

In an unpublished research study done at Georgetown Medical Center, PANDAS patients had their tonsils removed, analyzed, and the children subsequently tracked for over six months. The tonsils relative to non-PANDAS patients had many pathogens, most prominent being staphylococcus (staph). ***Streptococcus pyogenes was not found in PANDAS patients but was present in non-PANDAS controls***. Other notable pathogens included MRSA, E. coli, Pseudomonas and Serratia marcens. ***The absence of Streptococcus in the PANDAS cohort suggests that once the patient has been "sensitized" other pathogens can induce neurologic symptoms in susceptible patients.***

In addition, the ***tonsils belonging to PANDAS patients contained elevated levels of TH17***, indicating a consistent immune response to the pathogens lodged within the tonsils. TH17 has been found in animal PANDAS research to be a potential agent for opening the blood brain barrier, allowing inflammation in targeted regions of the brain.

The Georgetown study and physician experience indicates that removal of the tonsils can provide remission of PANS and PANDAS symptoms for some patients. There is no marker to determine which patient a tonsillectomy will result in remission of PANS/PANDAS symptoms.

A clear benefit of tonsillectomy that was found in the Georgetown study and further observed by practitioners who see many PANS/PANDAS patients, is that ***those PANS/PANDAS cases that have undergone tonsillectomy, have a significantly lower chance of recurrence post-immunotherapy such as IVIG*.** Since immunotherapy suppresses the potential cause of basal ganglia encephalitis and in some cases like IVIG "reboots" the immune response, then removing a consistent infectious trigger housed within the tonsil or removing a repository for new pathogen agitators would most likely be beneficial."

What factors lead to the benefit?

2016 Review by Windfuhr. *Tonsillectomy remains a questionable option for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS).*

"The positive outcome after TE as reported in case studies may be influenced by the postoperative medication and is not supported by the results of large-scale studies. In the light of the considerable postoperative morbidity rate, it appears wise to indicate TE for PANDAS only in supervised clinical studies."

Options to address sinus and tonsil health is covered in the next module.

PMID: 28025607

Correct neurotransmitters

SSRIs/SNRIs
- Ultra low dose required (consistent with toxin-based syndromes)
- Postulate that flare increases permeability of BBB
- Equates to “sprinkles” of typical initial dose, ie: 1/8-1/4 normal dose
  - ex: 6.25mg sertraline, 2mg fluoxetine
- Tendency to increase dose bc not responding = miss therapeutic window
- Often will cut dose rather than increase
- Also must account for normal wax/wane of dz

Must weigh the costs to the brain living in torture vs S/Es of Rx
- “Never belittle the history” & “assess for safety” (behaviors/nourishment)
- Views rage attacks as “defensive aggression” ie: cornered animal
- Often won’t remember bc “no one’s home” during the event
- Safety for all is imperative. Monitor triggers (hunger, fatigue, infection risk)
- Dr. Margot Thienemann, Stanford PANS Clinic
- *Recommend Stanford CME she offers: 1st steps when you meet w PANDAS/ PANS pt

EMDR - helpful also for parents who are perpetually in dread, waiting for next flare

Manage behaviors

CBT ~
Cognitive-Behavioral Therapy
My bias - worsens limbic imbalance
False ‘belief’ or wiring? Or are they reacting to triggers we haven’t yet identified.
Highlights the need for paradigm shift - recognize trauma-induced vs physiologically-induced behaviors
I encourage a middle ground - honor the sensory input and tamper the reaction.
Utilize CBT or other like measures with modification to help the child gain skills.

MCBT more fitting

CBT is best for the parents!

Cautionary Tale

Intravenous Immunoglobulin Therapy (IVIG)

Not every child with PANDAS or PANS needs this to recover.

Hesselmark et al, cohort of Swedish patients: Antibiotics and IVIG were rated as the most successful treatments by participants and were associated with higher patient satisfaction.

The purpose is suppression of Ig production, resulting in loss of autoantibodies/memory cells.

Dose and route of administration are paramount.
Dose: 1.5-2 g/kg given over 2 days given IV [note: dose typo in my book]

Needs to be high dose to accomplish suppression. SQ cannot hit the peak plasma level required for suppression.

Requires repetition to maintain the suppression - IME q 4-8 weeks. The “one and done” has not been durable.

Insurance often pressures you to use the typical supportive dose or SQ. This is NOT recommended. Can flare autoimmunity.

Must check IgA w subclasses (as well as IgG w subclasses) to choose IVIG brand. Some include IgA (risk of thrombosis if not also IgA deficient.)

I suggest referring to collaborative Allergist/Immunologist for administration. Home health services are available, but I don’t recommend this if you don’t have the specialty, and especially not for the first few rounds.

PMID: 31009235

IVIG supportive care

IVIG side effects ~

Occur on days of infusion + a few days following.
Low-grade fever, headache, flushing, itching, back pain, increased blood pressure, and fatigue.
May also see a temporary autoimmune thyroiditis, which tends to go away once the child is done with treatments after 6-9 mo's.

S/E management ~

Diphenhydramine, ibuprofen on infusion days + few days following.
May use IV glutathione push or steroids to prevent severe headaches.
Write on the order *SLOW INFUSION RATE* ~ 6-8 hours per day: many AEs can be prevented.
Home health nurses will go faster if not stipulated every time.

Many side effects can be prevented with 3 simple things ~

IV hydration - 500 mL hydration IV bag just before the IVIG
Slow drip rate
Glutathione

IVIG genetic prognostics?

Is it possible to screen for who will respond best to IVIG and who might respond better using it as step therapy to Rituximab or Plasmapheresis?

Empirically, best responders have genetic snp of Fcγ Receptors. Could Ig senescence be a contributing factor for persistence?

2010 Review: “Possible mechanisms of action of IVIg in autoimmune and inflammatory diseases are: *intact Fc-dependent blockage of IgG* (as in ITP), inhibition of membrane attack complexes (C5b-C9) and activated components C3b and C4b (as in Kawasaki's disease), and anti-idiotypes against autoantibodies (as in acquired hemophilia due to autoantibodies against factor VIII). IVIg also contains various cytokines and natural antibodies that may act against pathogens, altered molecules, cells, autoreactive B cell clones, and tumors.”

PMID: 19590986

Immune modulation

Rituximab ~

Humanized chimeric anti-CD20 monoclonal antibody, which is expressed on the surface of pre-B and mature B-lymphocytes. After binding to CD20, rituximab mediates B-cell lysis.

“we still do not fully understand the mechanisms of action … Direct signaling, complement dependent cellular cytotoxicity and antibody dependent cellular cytotoxicity all appear to play a role.”

Plasmapheresis ~ **Ochratoxin**

“Blood cleaning” procedure - child’s blood is removed through IV catheter and processed by a plasmapheresis machine, which spins it to separate the formed elements (RBCs, WBCs, platelets) from the plasma. The plasma is removed and replaced with equal volumes of albumin. The albumin is mixed with the child’s blood components and returned to his body through a second IV catheter. Multiple procedures are needed, often requires insertion of a central line. Carries significant, but manageable risks, it should be done only in pediatric apheresis centers.

PMID: 20350658. Other Sources: PANDAS Physician Network, Journal of Child and Adolescent PsychopharmacologyVol. 25, No. 1


Conventional Approach
Next up: Integrative Approach
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Integrative Approach

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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

Programmed bias

Bring awareness to your medical programming

May be triggered by the sheer accessibility of the things presented in this section

Accessible has been labeled “simplistic” “ineffectual” “dangerous”

By who? By those standing to gain from the separation

“Doctor as guru” (dependence) over “doctor as teacher” (empowerment)

It’s okay to put some trust in nature!

Your grandmother’s grandmother did - and you are living proof of that trust

You are not just “part of nature”, you are nature

… and so is your patient

(and you will never be without a job)

Integrative approach

Acute vs chronic presentation

Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials

Medication Compatibility Chart

	Anthelmintic	Antibiotic B-Lactams	Antibiotic Macrolides	Antibiotic Tetracyclines	Antifungal	Antifungal Triazoles	Antihistamine H1	Antihistamine H2
	Ivermectin, Mebendazole, Praziquantel	Amoxicillin, Penicillin, Cefuroxime, Cephalexin	Azithromycin, Clarithromycin, Erythromycin	Doxycycline, Minocycline	Nystatin	Fluconazole, Itraconazole	Cetirizine, Diphenhydramine, Ketotifen, Loratadine	Cimetidine, Famotidine
Black elderberry	😐	😐	😐	😐	😐	😐	😐	😐
Black walnut	🚫	✍️	✍️	✍️	✍️	✍️	😐	😐
BPC-157 peptide	👍	👍	👍	👍	👍	👍	😐	👍
Brahmi	😐	😐	😐	😐	😐	😐	😐	😐
Butyrate	😐	😐	😐	😐	😐	😐	😐	😐
Chinese skullcap	–	–	–	–	–	–	😐	😐
Cryptolepis	–	–	–	–	–	–	–	–
DAO (diamine oxidase)	😐	😐	😐	😐	😐	😐	👍	👍
Echinacea	😐	😐	😐	🕒 4h	😐	😐	😐	😐
Feverfew	😐	😐	😐	😐	😐	😐	😐	😐
Glycine	😐	😐	😐	😐	😐	😐	😐	😐
Gotu kola	😐	😐	😐	😐	😐	😐	😐	😐
Immunoglobulins (oral)	👍	👍	👍	👍	👍	👍	👍	👍
Inositol	😀	😀	😀	😀	😀	😀	😀	😀
Japanese knotweed	–	–	–	–	–	–	–	–
Licorice	😐	✍️	✍️	✍️	😐	😐	😐	😐
Lithium (low dose)	😀	😀	✍️	✍️	😀	✍️	✍️	✍️
Luteolin	😀	😀	😀	😀	😀	😀	👍	👍
Magnolia	😐	😐	😐	😐	😐	😐	😐	😐
Oregano	😐	😐	😐	😐	😐	😐	😐	😐
Oregon grape	😐	😐	😐	😐	😐	😐	😐	😐

KEY:
Beneficial to co-administer 👍
No negative interaction 😀
Evidence suggests low risk of interactions 😐
No data (–)
Some interaction if taken at the same time, separate dose by time indicated 🕒
Some interaction, dose adjustment may be needed ✍️
Do not use together without your doctor's guidance 🚫

SOURCES:
NIH, Office of Dietary Supplements, Health Professional Fact Sheet: https://ods.od.nih.gov/factsheets/list-all/#
Indiana University Department of Medicine Clinical Pharmacology, Drug Interactions Flockhart Table ™: https://drug-interactions.medicine.iu.edu/MainTable.aspx
Herb, Nutrient, and Drug Interactions by Mitchell Bebel Stargrove, Jonathan Treasure, Dwight L. McKee
Botanical Safety Handbook by American Herbal Products Association
Herb Contraindications & Drug Interactions by Francis Brinker, ND

DISCLAIMER:
*This table does not apply to women who are pregnant or nursing.
*This content is health information and not intended as personal medical advice. Viewing it does not establish a doctor-patient relationship. It is not intended to diagnose, treat, cure or prevent any disease or medical condition. The information discussed is not intended to replace the advice of your healthcare provider. Reliance on information provided by Dr. Jill Crista, employees, or others appearing at the invitation of Dr. Crista is solely at your own risk.

A living document

Updated as new information becomes available.

Adjust doses for children

All doses will be given as adult doses for continuity.

Adjust by weight using Clark's Rule for ages 2-17.

Clark's Rule:

First, divide the child's weight in pounds by 150 (or the child's weight in kilograms by 68.)

Find the fraction or decimal, whichever makes it easier to make sense of liquid vs capsule.

Then multiply the fraction or decimal by the typical adult dose to find the child's dose.

Getting herbs into kids

Ask parents: savory vs sweet, hot vs cold, texture issues, time of day

Forms: teas, glycerites, powders, mixed/cooked into food, popsicles, chews

Mixers: honey, black strap molasses, coconut, butter, nut butters, ranch dressing, ketchup, mustard, spaghetti sauce, curry, salsa, teriyaki, broth

Chasers: pickle juice, chai

First few doses (this is my sneakiest tip): Fry an onion 5 min prior. Aroma boosts stomach acid & primes the body for bitter. Once this positive association is set, subsequent dosing goes easier.

Have multiple options to plan ahead for refusals - they will happen!
It's natural.

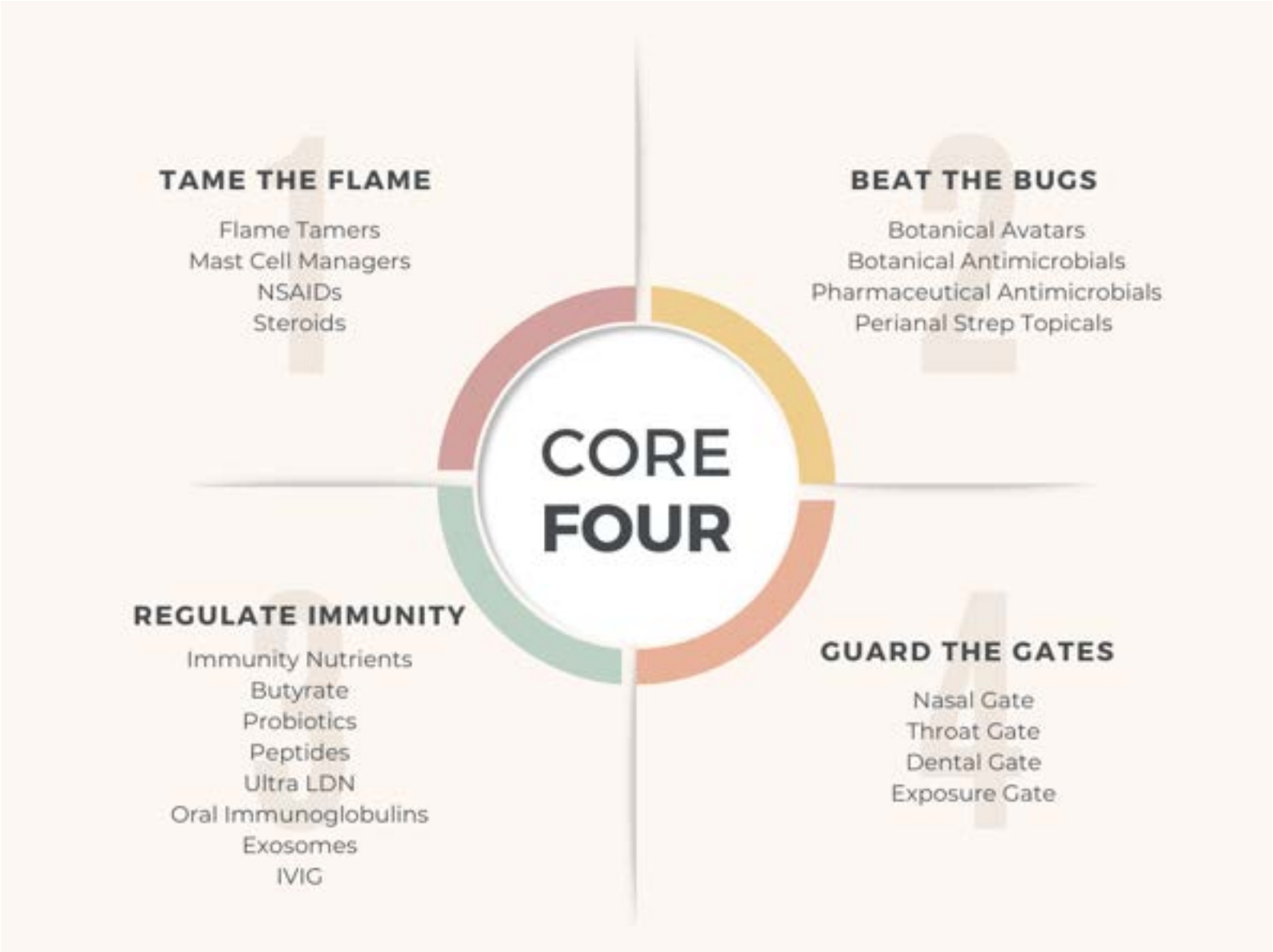
Acute vs Chronic

Important to identify at what stage the patient is presenting.

Different level of intervention for acute vs chronic.

Acute - don’t mess around! These kids take their own lives.

- Conventional approach + Core 4 - Infection/toxicant prevention (Guard the Gates)



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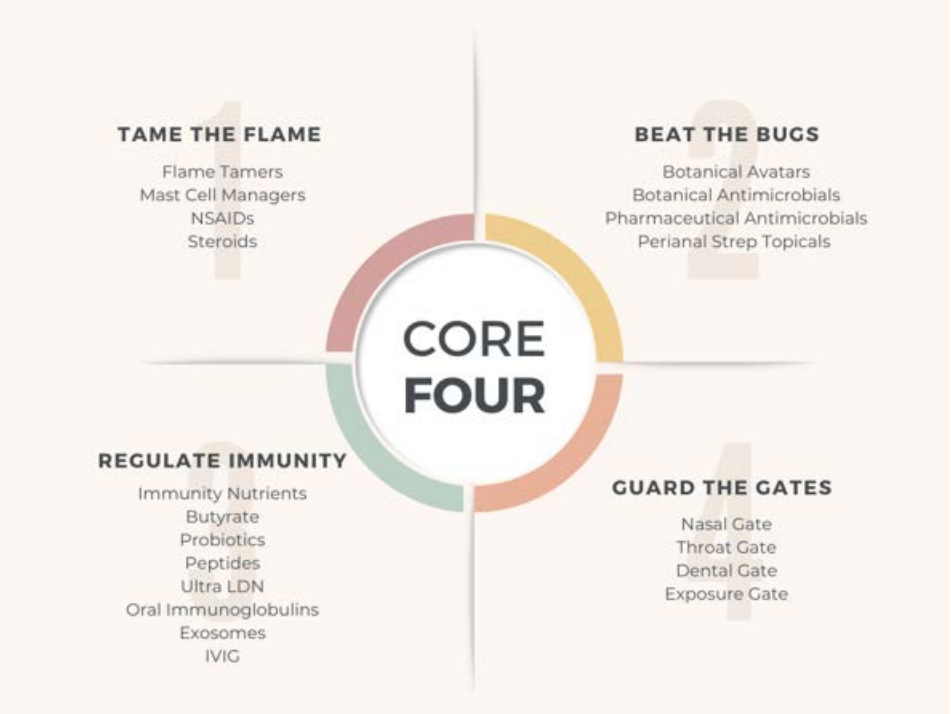

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Add Core immune modulation.

Choose 2 methods for each of the Nasal, Throat, and Dental gates.

Explore various ways to close the Exposure Gate, starting with hand-washing (family/caregivers), removing glyphosate and mold, reducing infection exposures.

Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Integrative approach

Acute vs chronic presentation

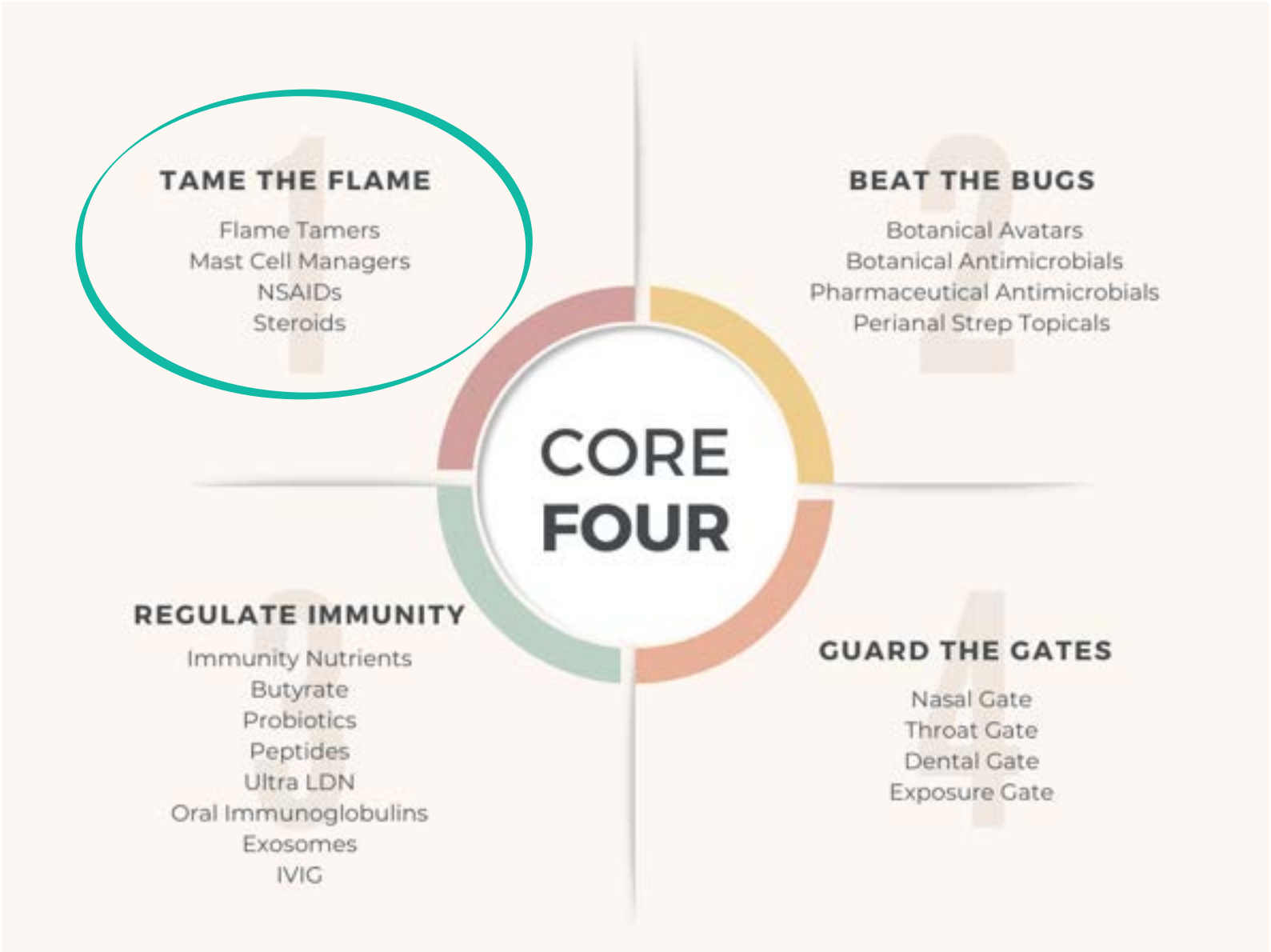
Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials



Flame Tamers

The target is neuroinflammation, specifically the microglia.

- Pro-resolving mediators
- Feverfew
- Resveratrol
- Rosemary
- Pine extract

Pro-resolving mediators

Also referred to as specialized pro-resolving mediators (SPMs) ~

18-hydroxyeicosapentaenoic acid
17-hydroxydocosahexaenoic acid
14-hydroxydocosahexaenoic acid

The most anti-inflammatory aspect of fish oils - not just “rebranded” fish oil.

Resolve inflammation rather than suppress the inflammatory process.

Helpful in inflammatory processes that become self-perpetuating and pathogenic; CIRS, MCAS, and autoimmune diseases such as PANDAS/PANS.

Reduce neuroinflammation and microglial activation.

PMID: 34822458, 28483532, 33486004

Wild vs farmed salmon

Poorly fed fish that can't exercise = bad fat

Fish with bad fat = humans with bad fat

Read between the lines

Pro-resolving mediators

Quells inflammation from dental plaque buildup (many PANDAS/PANS kids are behind on dental care.)

A method to increase EFAs for histamine-sensitive children.

Especially helpful for a child who's had a concussion or has concomitant ASD with head banging.

Works well in combination with almost every supplement, herb, and medication

Daily:

Capsule: 500 mg daily

Flare:

Capsule: 1000 mg twice daily

Caution:

May interact with anticoagulant medication.

Feverfew

Tanacetum parthenium ~ leaves and flowers

Sesquiterpene lactone ~ parthenolide
(not triterpenoid saponin/avatar)

Anti-inflammatory and neuromodulatory effects

“Hormone headaches”

Ameliorates colon inflammation through regulating Treg/Th17 balance in a gut microbiota-dependent manner.

Parthenolide inhibits the LPS-induced secretion of IL-6 and TNF-α and NF-κB nuclear translocation in microglia.

PMID: 32373209, 33374525, 22359368

Feverfew

For appetite-improving effect, use 30 minutes before meals. Combines well with Gotu kola.
Effect is dose dependent. Before abandoning this herb, try a higher dose.

Daily:

Tea: 1 cup twice daily
Glycerite: ½ tsp twice daily
Capsules: 350 mg twice daily

Flare:

Tea: 2 cups up to four times daily
Glycerite: 1 tsp up to four times daily
Capsules: 700 mg up to four times daily

To prep the tea:

Yield: 2 cups
Prepare tea by steeping 1 Tbsp dried Feverfew leaves and flowers in 2 cups of boiling water for 5 minutes, covered. Strain and add honey to taste. Cool to a comfortable drinking temperature.

Caution:

May cause allergic reaction in those with ragweed allergies.
May interact with anticoagulant medication.

Resveratrol

NLRP3 inflammasome is implicated in OCD, psych disorders ~
Resveratrol regulates microglia M1/M2 polarization in conditions of neuroinflammatory injury.
Suppresses the NLRP3 inflammasome pathways in microglia.

Resveratrol inhibits NLRP3 inflammasome activation by preserving mitochondrial integrity and augmenting autophagy.

Specific mycotoxin protective effects ~
Attenuation of intestinal inflammation and oxidative damage linked to the alteration of gut microbiota and butyrate from mycotoxins.

Attenuates allergic asthma and reduces DNA damage in bronchial epithelia, as well as enhancing NK cell cytotoxicity.

Combats known mycotoxin mechanisms, for example, by activating the Nrf-2 pathway and alleviating Nf-kappa-B neuroinflammation.

Reduces achiness and neuropathic pain.

PMID: 25535911, 34739715, 34130737, 28268115, 28283884, 30619345, 32186748, 31035454, 27316789, 31090224, 33770763

Resveratrol

Usually easy to get kids to take the liquid, tastes sweet.

Studies suggest a minimum therapeutic dose for mycotoxin exposure of 1 gram daily to meet the desired plasma concentration.

Daily:

Liquid or capsule: 500 mg daily

Flare:

Liquid or capsule: 500 mg three times daily

Caution:

May cause low blood pressure at high doses.

Rosemary

Rosmarinus officinalis ~ use the needle-like leaves

Long history of use and benefits in mental health and cognition. Worn as a crown for sharp thinking.

Rosmarinic acid inhibition of the NLRP3 inflammasome exerts antioxidant, anti-inflammatory, and neuroprotective effects

Rosmarinic acid regulates microglial M1/M2 polarization under conditions of neuroinflammation

Rosmarinic acid mitigates LPS-induced neuroinflammatory responses

Inhibition of the NLRP3 inflammasome. Exerts antioxidant, anti-inflammatory, and neuroprotective effects via phase 2 enzyme induction initiated by activation of the KEAP1/NRF2 transcriptional pathway, which in turn attenuates NLRP3 activation.

Antifungal and antimycotoxigenic activity against multiple mold species.

PMID: 31644378, 25053064, 29318480, 35052628

Rosemary

Crosses the BBB. Aroma induces brain calming and mood lightening effect.

For appetite-improving effect, use 30 minutes before meals

Daily:

- Tea: ½ cup twice daily
- Glycerite: ¼ tsp twice daily
- Capsules: 350 mg daily

Flare:

- Tea: 1 cup three times daily
- Glycerite: ½ tsp three times daily
- Capsules: 700 mg three times daily

To prep the tea:

- Yield: 2 cups
- Prepare tea by steeping 1 Tbsp dried Rosemary leaves in 2 cups of boiling water for 5 minutes, covered. Strain, and add honey to taste. Cool to a comfortable drinking temperature.

Also consider essential oil topical applications

Caution:

- May cause dry eyes and mouth.
- Children sensitive to phenols may tolerate the tea best.
- May lower blood sugar and iron absorption at high doses.
- May interact with anticoagulant medications.

Pine Extract

Multiple boreal conifer species ~ needle and bark

Potent antioxidant and anti-inflammatory activity

Protective against activated microglial neuroinflammation and also T cells.

Attenuates the release of proinflammatory cytokines in LPS-stimulated microglia in part via Inhibition of NF-κB and AP-1 activation.

Mild antihistamine effect.

Improves attention, learning, and memory.

Prevents hippocampal excitotoxicity-derived memory impairment in acute stress in mouse models.

PMID: 28642096, 26367267

Pine Extract

Pycnogenol® is an extract from pine bark.
Taiga is from pine needles.

Daily:
- Pine bark extract capsule: 100 mg daily
- Pine needle extract capsule: 320 mg daily

Flare:
- Pine bark extract capsule: 200 mg twice daily
- Pine needle extract capsule: 320 mg twice daily

Caution:
- Overpowering taste. May cause a bad taste in the mouth at high doses.
- May cause nausea at high doses.

Integrative approach

Acute vs chronic presentation

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- Anti-inflammatories
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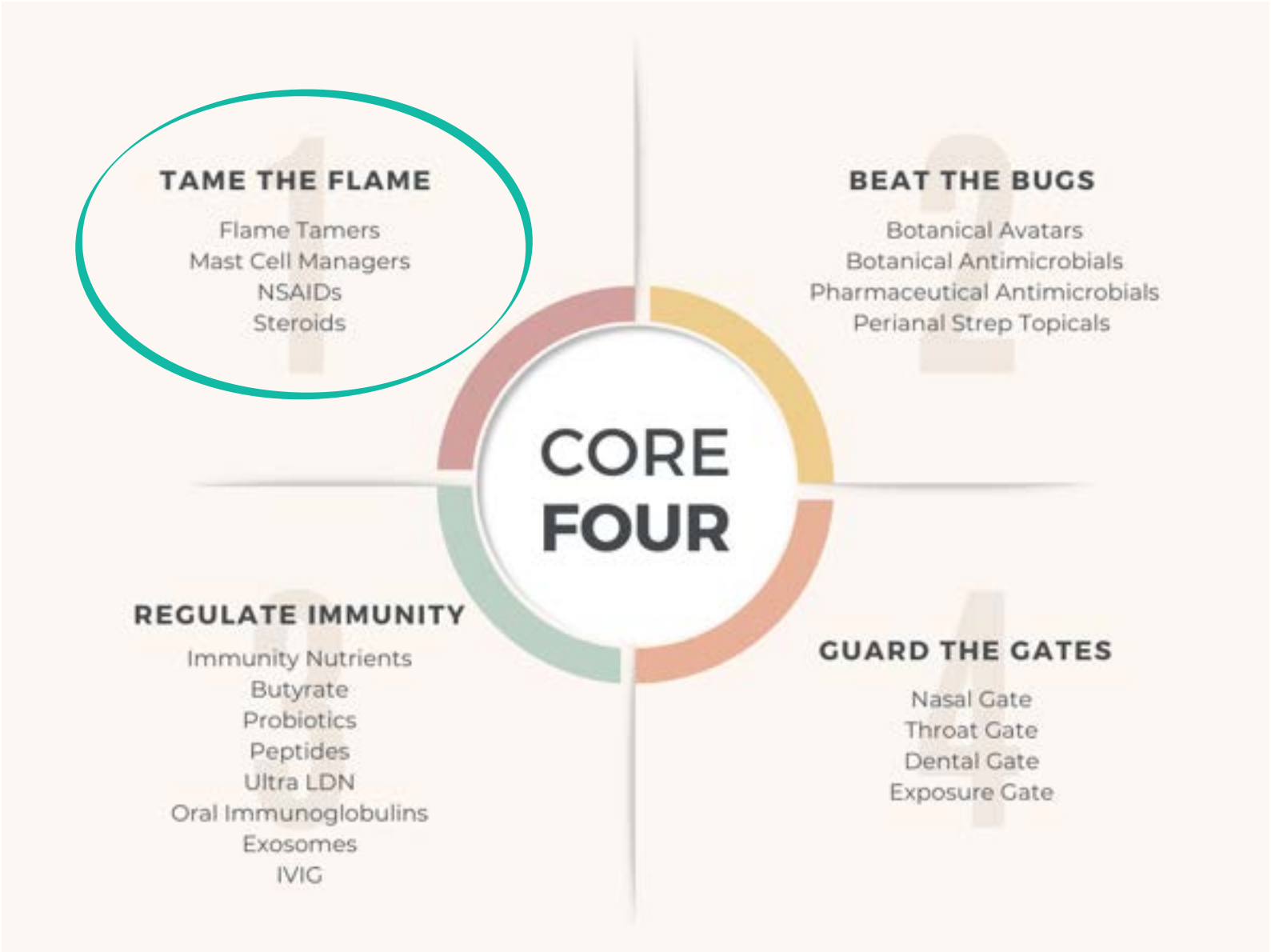

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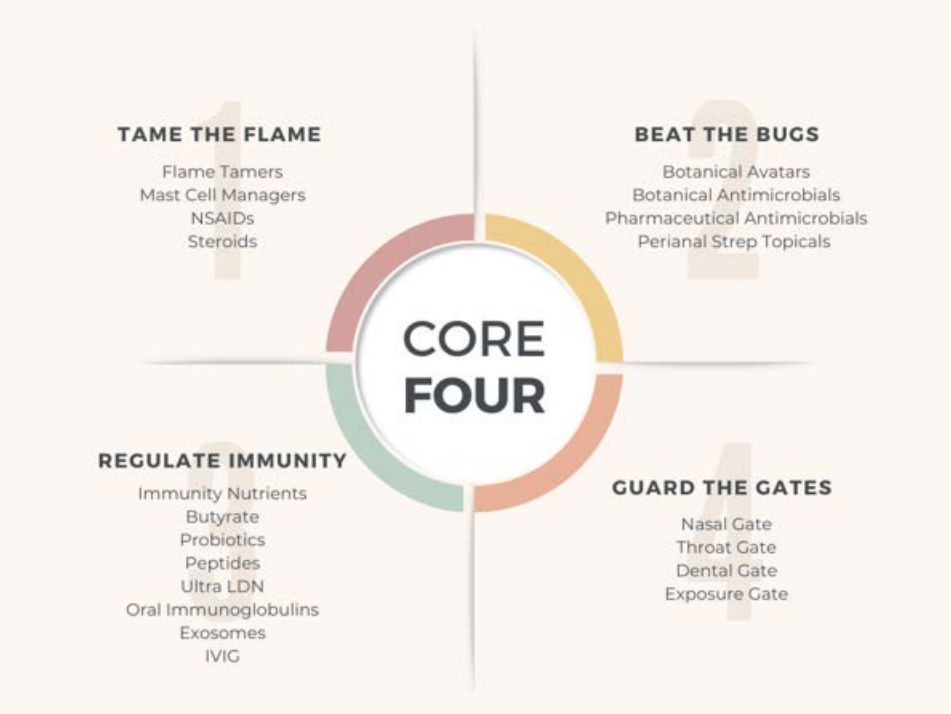

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Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Mast cell managers

Mast cells are a major player in the “flare potential” of a child with PANDAS or PANS.

The more mast cells that are recruited, the easier it is to trigger them.

Preventing mast cells from being recruited and triggered is the focus.

- Vitamin C
- PEA
- Quercetin and Luteolin
- Nettles
- Perilla
- DAO
- Antihistamine Medications

Vitamin C

Mast cell stabilizer; attenuates degranulation by inhibiting peroxidation of membrane phospholipids.

Acts as a scavenger of free radicals, involved in collagen synthesis, detoxification, and is also required for the synthesis of several hormones and neurotransmitters.

In humans, vitamin C reduces the duration of common cold symptoms, even if its effect is not clear.

Supplementation improves the function of the human immune system, such as antimicrobial and NK cell activities, lymphocyte proliferation, chemotaxis and delayed-type hypersensitivity.

Vitamin C depletion has been correlated with histaminemia which has been shown to *damage endothelial-dependent vasodilation*.

PMID: 35781358, 23830380

Vitamin C

Many kids are low in this basic vitamin! Before adding pharmaceutical antihistamines, first optimize Vitamin C status.

I prefer liposomal Vitamin C for kids with PANDAS and PANS.

Daily:
- Liposomal liquid: 1,000 mg daily

Flare:
- Liposomal liquid: 1,000 mg up to five times daily

Caution:
- May cause diarrhea at high doses.
- May falsely elevate glucose labs.

*synergism with vitamin E, B6.

Kale has 76% more Vitamin C than Lemon

PEA - palmitoylethanolamide

Made naturally endogenously in our brains as a neuroprotector, especially during transient hypoxia and episodes of low blood sugar.

The main protective mechanism is to prevent mast cell degranulation.

Some activity in resolution of inflammation.

Unfortunately, PEA gets depleted from microglial activation. The result being that kids with PANDAS/PANS don't have this tried-and-true way to shut down mast cells.

The inflammation begets more inflammation. Supplementing this nutrient stops the cycle, and can reduce pain.

Cell study research suggests neuroprotective activity against Covid.

PMID: 33917573, 33636368, 27423516, 26055231

PEA

PEA is made from phenylalanine, which is found in diet beverages. One tip that a child needs this supplement is if he's craving artificially sweetened drinks.

There's some evidence that this nutrient works best when combined with luteolin (next section).

Daily:

Powder or capsule: 300 mg twice daily

Flare:

Powder or capsule: 600 mg twice daily

Caution:

Best absorbed with a fatty meal or with liposomes.

Quercetin & Luteolin

"Vitamin yellow" ~ neon yellow antioxidant bioflavonoids

Mast cell stabilizers;
- Anti-inflammatory and antipruritic effects
- More effective than cromolyn in blocking human mast cell cytokine release

Hinders microglial activation to alleviate neurotoxicity via the interplay between NLRP3 inflammasome and mitophagy.

Regulatory effects on M1/M2 macrophage polarization and oxidative/antioxidative balance.

GI protective ~ anti-inflammatory, preserves the length of intestinal villi and mucosal thickness, increases the production of butyrate, improves gut dysbiosis in antibiotic-treated mice.

Preserves oral cavity health by mitigating inflammation and microbial dysbiosis.

Cytoprotective against mold mycotoxins.

PMID: 35010945, 34082381, 30799996, 27423516, 22470478, 24382176, 32845255, 34899728, 26802676, 26134454, 25532488

Quercetin & Luteolin

I've found that liposomal forms are the fastest acting.

Daily:

Liposomal liquid or capsule: 300 mg twice daily

Flare:

Liposomal liquid or capsule: 600 mg up to four times daily

Caution:

May be an issue for kids who don't tolerate phenols.
In those cases, I use low-phenol forms.

Nettles

Urtica dioica ~ leaves (mast cell), root, seed

Rich in quercetin, rutin, and ellagic acid.

Shown to possess antioxidant, hypotensive, anti-inflammatory, anti-diabetic, analgesic, antioxidant and antiproliferative properties.

Ameliorates allergy symptoms and lowers skin irritability ~
- Antihistaminic; antagonist and negative agonist activity against the H1 receptor
- Mast cell stabilizing; inhibition of mast cell tryptase preventing degranulation and release of a host of pro-inflammatory mediators
- inhibits prostaglandin formation through inhibition of central enzymes in pro-inflammatory pathways COX-1, COX-2, and Hematopoietic Prostaglandin D2 synthase (HPGDS)

Neuroprotective ~
- Improves memory function and cognition
- Reduces chronic stress-related dysfunctions of the CNS in animal models
- Positive effects on microvasculature

PMID: 37171512, 35399803, 29844782, 19140159

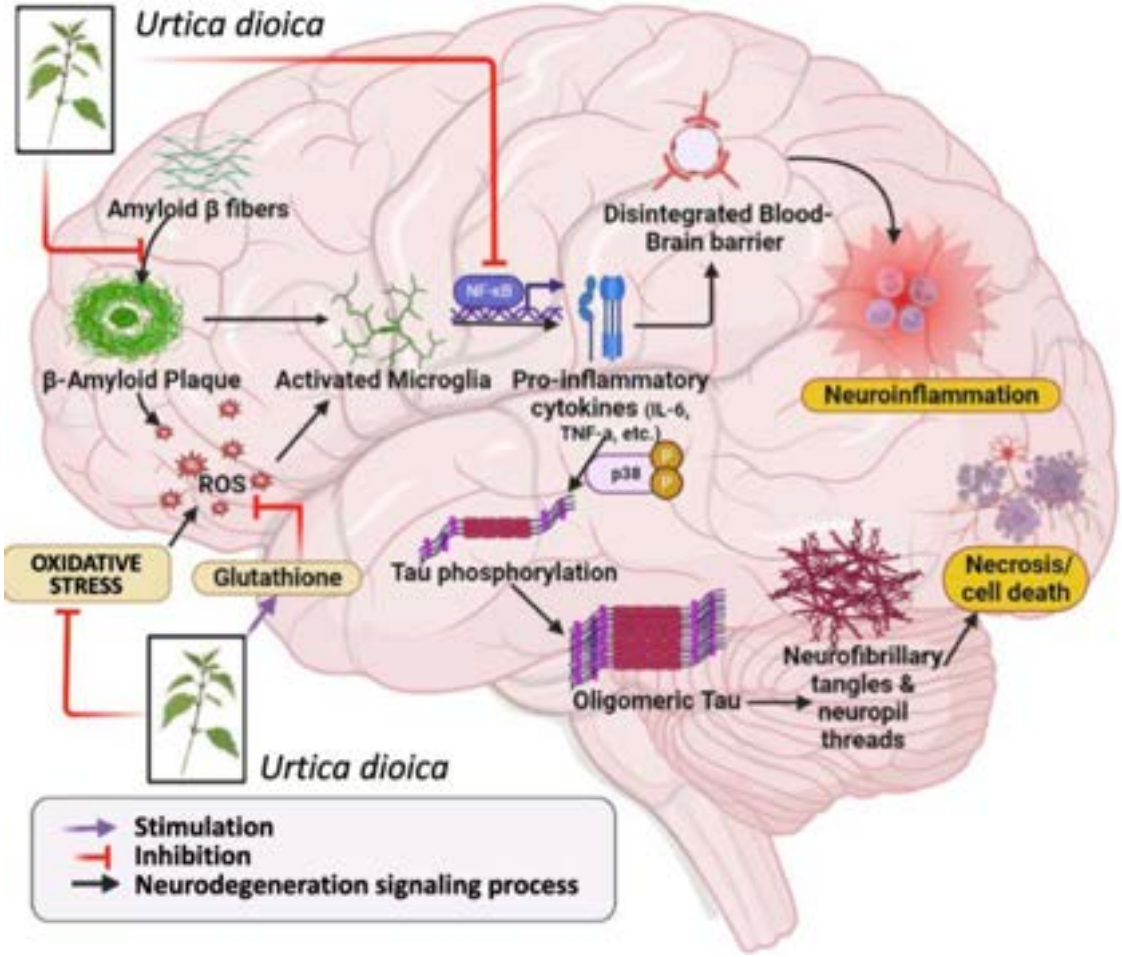


Fig. 2 Potential neuroprotective mechanism of action of U. dioica and of its components

PMID: 37171512

Nettles

Used as a staple green in many indigenous diets. Very safe to use as food and in higher doses than many herbs.

Randomized, double-blind, placebo-controlled, clinical trial using 150mg qid x 1mo reduced IFN-γ levels but no significant difference in allergic rhinitis over control.
(Not high enough dose, short duration, and/or the control “green matter” was also beneficial.)

Daily:
- Glycerite: 2 tsp twice daily
- Capsule: 600 mg twice daily

Flare:
- Glycerite: 2 tsp up to four times daily
- Capsule: 600 mg up to four times daily

Caution:
- Fresh plant will sting; cook or dry, or handle with gloves
- Source of oxalates

PMID: 29844782

Nettle Lemonade

Perilla

Perilla frutescens ~ leaves and seeds

Rich in luteolin.

Inhibitory effect of mast cell-mediated immediate-type allergic reactions *in vivo.*

Potently suppresses IgE-mediated immediate hypersensitivity reactions.

Attenuates airway inflammation.

Inhibits NLRP3 inflammasome assembly, reduced the excessive accumulation of ROS, leading to reduced inflammation.

Protective effect of Nrf2-ARE activator on dopaminergic neuronal loss in a Parkinson's disease model.

Additional antimicrobial properties; inhibits several virulence attributes of C. albicans including biofilm formation and yeast-to-hyphal transition.

PMID: 35058774, 28167258, 27986566, 24871572, 10946827, 36978975, 36302165, 32822688

Perilla

Anti-histaminic effects are dose dependent. If you've tried this herb at a lower dose and didn't get the desired effects, try increasing the dose.

Daily:

Glycerite: ½ tsp twice daily
Capsule: 150 mg twice daily

Flare:

Glycerite: 1 tsp up to three times daily
Capsule: 300 mg up to three times daily

Caution:

May cause rare allergic reactions if applied on the skin.

DAO

Diamine oxidase (DAO) is an enzyme that breaks down histamine in the gut.

Excessive mast cell histamine release and/or high histamine diets may deplete this enzyme.

Genetic snps affect production.

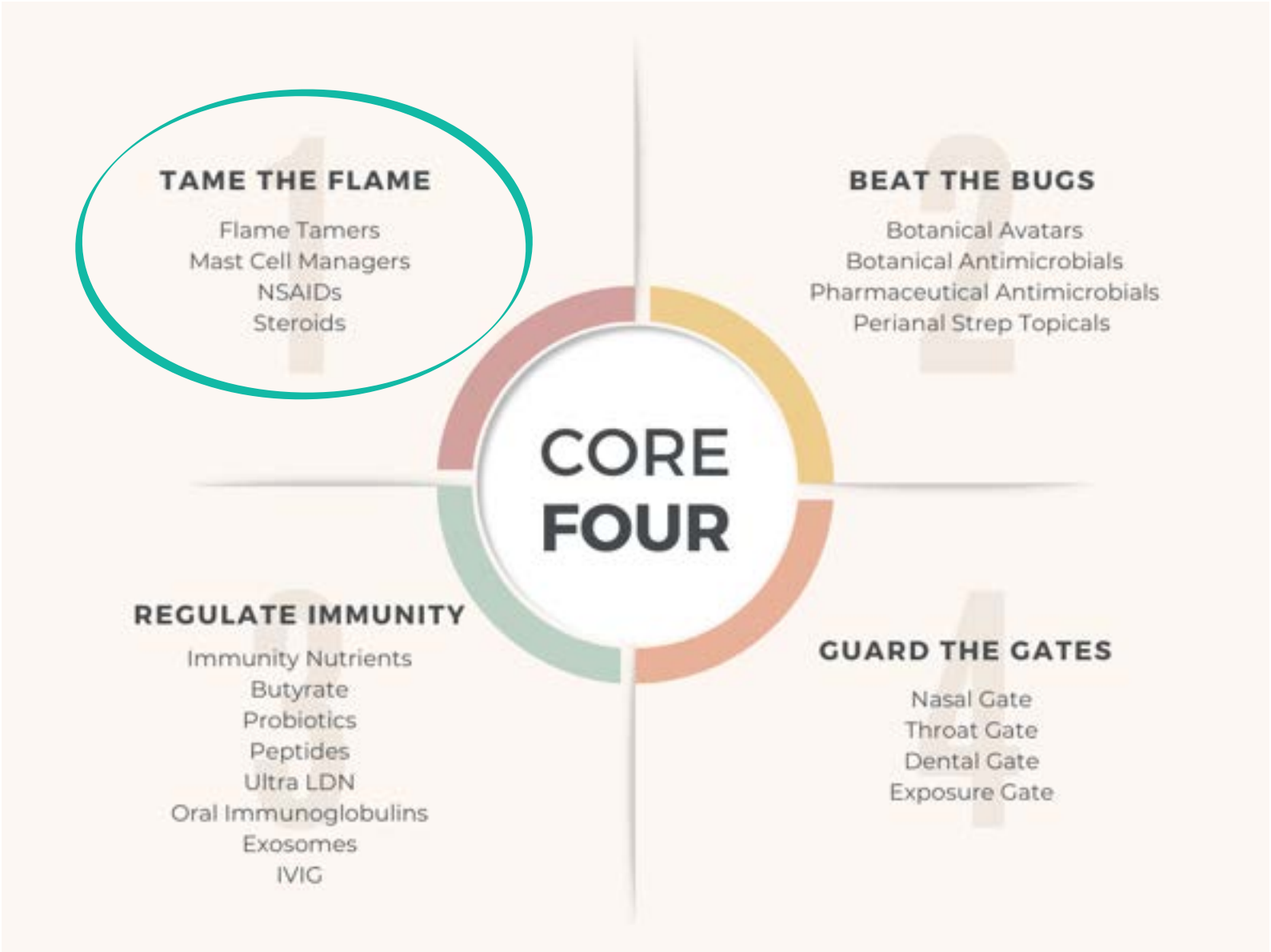
Gut-brain axis ~ gut-brain histamine activates microglia.

While a low-histamine diet can make a huge difference in a child's overall histamine load, sometimes his enzyme system could use a little help.

Daily:
Capsule: 10,000 HDU up to 15 minutes before largest meal

Flare:
Capsule: 10,000 HDU up to 15 minutes before every meal

Caution:
Pork sourced - allergy, religious abstention



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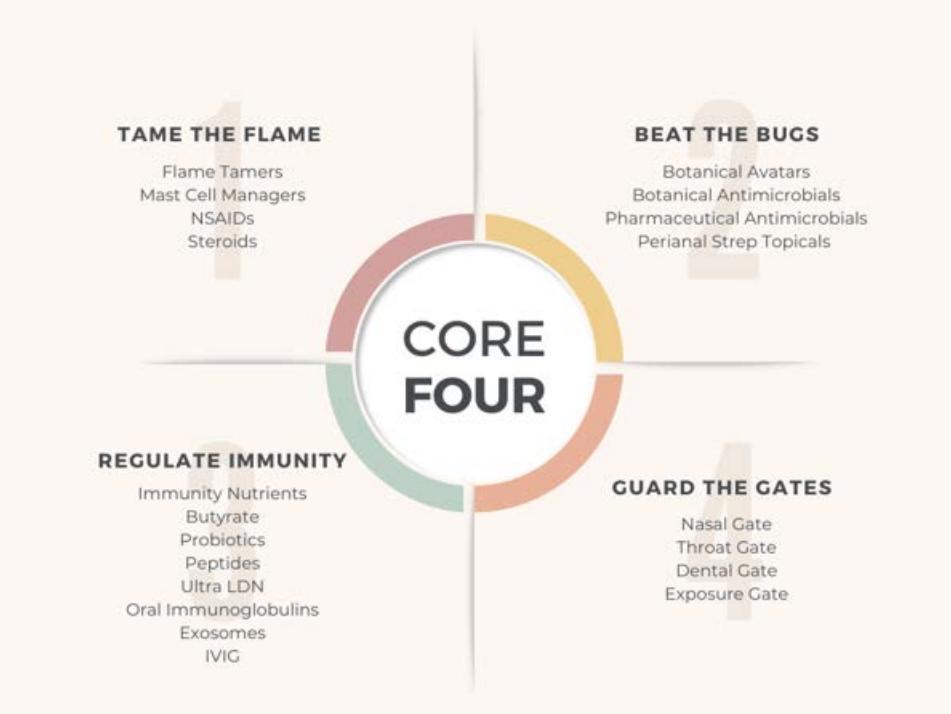

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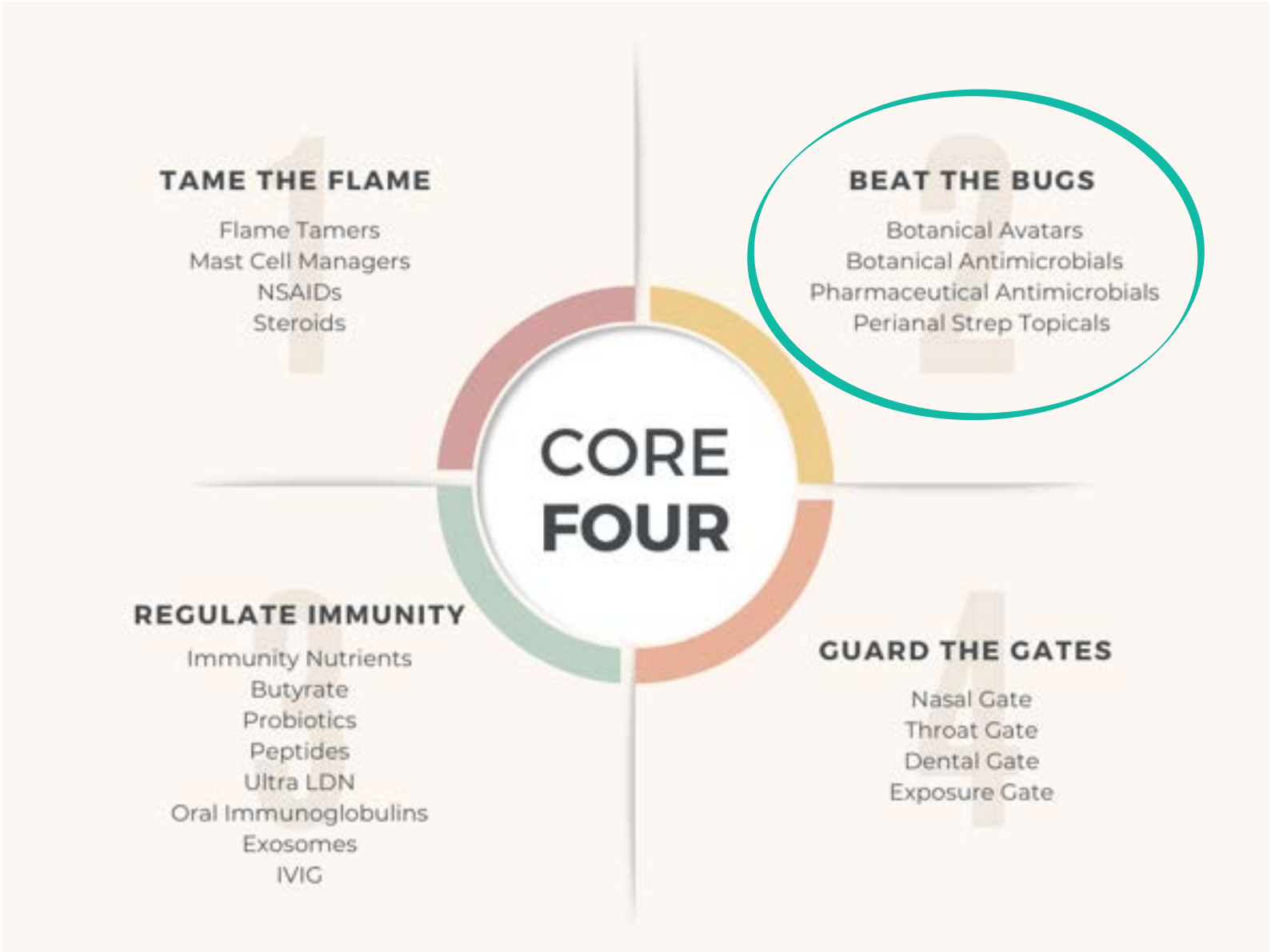


Avatar (definition) - Ideal

Abilities to “bend” (aka work with) all of the elements ~
air, earth, fire, water

In an ideal world

An ideal remedy for PANDAS and PANS would do the following:

- Serve as a broad-spectrum antimicrobial
- Modulate the immune system
- Neutralize neuroinflammation
- Act as an antioxidant for the brain and nervous system
- Reduce dopamine and glutamate
- Normalize acetylcholine
- Boost GABA (gamma-aminobutyric acid) and serotonin
- Heal the gut
- Foster a healthy microbiome

Oh, if only there was one treatment that hit all those marks!

Botanical Avatars

Ideal medicinal botanicals for PANDAS and PANS because they hit each of the previous points AND they're antimicrobial.

I use at least one of these herbs as the foundation of treatment, to which all other methods are added if needed.

- Chinese Skullcap (Scutellaria baicalensis)
- Oregon Grape (Berberis aquifolium)
- Thorough-wax (Bupleurum species)
- Brahmi (Bacopa monnieri)
- Magnolia (Magnolia species)
- Silk Tree (Albizia julibrissin)
- Gotu Kola (Centella asiatica)

For the herb nerds

∴ Look for triterpenoid saponins

Tie that binds

Lipophilic ~ nervous system, intracellular, mitochondria

Immune modulation

Steroidal in nature (anti neuroinflammatory)

Restore neurotransmitter imbalance

Antioxidant

Restore programmed pruning

Avatar how-to

I often combine 2 or 3 of these herbs, depending on the specific benefits I'm seeking for the child.

To safely combine them, I adjust the dose by half if using 2 of these herbs at once, or by a third if using 3 at once.

In the acute flare phase, I commonly add Botanical Antimicrobials (see the next section). While Botanical Antimicrobials may be better antimicrobials, they don't have the full spectrum of mechanisms needed in PANDAS/PANS. We need a Botanical Avatar base.

For the prophylactic phase, the Botanical Avatars are often enough to prevent infection and gain ground on healing the gut and the brain.

Working with botanicals successfully

Herbs aren't drugs. We dose them differently.

The keys to success with herbal medicine treatments are to use a strong enough dose, dose frequently, and work around the taste factor.

Weak doses and repeating too infrequently are common reasons for herbal failures.

For tips on using herbal medicines with kids, see the "Getting Herbs into Kids" slide.

Adult doses are given as a standard. See the "Dose Adjustment for Children" slide.

Botanical cautions

Worsens neurotransmitter imbalance and/or depersonalization risk

If it's good for Parkinson's research first to understand why/how.

Who makes my "bad-atar" list?
dopaminergic

Turmeric, boswellia, schisandra, lemon balm, passionflower, kava,
plus many 'calming' herbs due to effect on dopa

May be useful after a flare if child hits bottom/despair

And now for some PANS/PANDAS Avatars…

PMID: 20513244

Chinese Skullcap

Scutellaria baicalensis ~ root

Triterpenoid saponin ~ wogonoside

Flavonoid rich ~ antioxidant

Personality ~ as if perfectly prepped to handle the rocky inner world of a child with PANDAS or PANS, this herb grows best in rocky terrain.

This is different from North American skullcap, or Scutellaria lateriflora, which has been used for millennia by Native Americans for nervous disorders and inflammatory ailments. The Chinese variant is slightly more specific to PANDAS and PANS.

Not only is it a good bug killer, Chinese skullcap is soothing to the nervous system, usually without causing drowsiness. It can be given before school or other times that provoke anxiety, yet require focus.

Because of its ability to regulate the T cell balance, I choose this Avatar for kids who also have allergies.

PMID: 33224253, 31236960, 29143798, 27730005, 27845861, 22196758, 28859441

Chinese Skullcap benefits

Antibacterial:
- Demonstrates inhibitory activity against Babesia duncani, and stationary phase forms of Borrelia
- Action against Mycoplasma pneumonia

Antiviral

Reduces anxiety

Purinergic G protein-coupled receptor (GPCR) antagonist: helpful in turning off purinergic signaling to address CDR

Protects the brain and nervous system:
- Protects against dopamine neurotoxicity
- Inhibits LPS-stimulated microglia
- Significantly reduces secretion of inflammatory cytokines from stimulated microglia

Reduces inflammation

Regulates immune Th1/Th2 balance

Improves intestinal barrier function

Modulates gut microbiota for more beneficial species

Nephroprotective

PMID: 33224253, 31236960, 29143798, 27730005, 27845861, 22196758, 28859441

Chinese Skullcap dosing

Chinese skullcap can be used for acute and prophylactic antibiotic therapy. It's safe to use long term. If needed, it can be combined with Botanical Antimicrobials and certain Pharmaceutical Antimicrobials. (See the Medication Compatibility Chart in the appendix.)

The glycerite has a mildly bitter aftertaste. Nothing that a little xylitol gum can't overcome.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily with food
Capsule: 870 mg, 3 times daily with food

Prophylactic:

Glycerite: ½ tsp, 2 times daily with food
Capsule: 435 mg, 2 times daily with food

Caution:

Rarely, kids may get too relaxed to focus on school with Chinese skullcap.
May drop blood sugar or cause stomach upset. Take with food.

Oregon Grape

Berberis aquifolium ~ root

Triterpenoid saponins ~ stigmasterol glucoside

Broad-spectrum antimicrobial

Personality ~ happiest on misty days with partial sun in soil rich in humus. (A positive response to humic acid may be a hint that this herb is indicated.)

Oregon grape has more specific activity against Strep than Chinese skullcap. As with Chinese skullcap, it also protects and heals the brain changes seen with P/P.

Oregon grape helps with kids whose moods change drastically with blood sugar dips. It's also a nice match for kids with digestive issues, such as leaky gut, food allergies, and belly pain.

Also consider Barberry (Berberis vulgaris), Goldenseal (Hydrastis canadensis) which have very similar activity.

PMID: 31981716, 29232416, 28656094, 23840629, 26616870, 28403947, 27898425

Oregon Grape benefits

Broad-spectrum antibacterial, moderate activity against Streptococcus pyogenes

Antiparasitic

Protects the brain and nervous system:
- Inhibits the release of glutamate in nerve terminals
- Protects against glutamate-induced neural cell injury
  - ↓ ROS gen, lipid peroxidation, DNA fragmentation, while improving glutathione content + SOD activity in glutamate-injured cells
- Reduces neuroinflammation
- Improves repair in glutamate-injured cells
- Antagonist at both dopamine D1/D2 receptors

Reduces inflammation

Reduces histamine

Balances unstable blood sugar

Promotes the gut microbiota to produce butyrate, leading to increased energy metabolism

PMID: 31981716, 29232416, 28656094, 23840629, 26616870, 28403947, 27898425

Oregon Grape dosing

Oregon grape can be used for both acute and prophylactic antibiotic therapy. In many cases, its antimicrobial activity is strong enough to be used solo, without having to combine with a Botanical Antimicrobial. It's safe to use long term. If needed, it can be combined with certain Pharmaceutical Antimicrobials. (See the Medication Compatibility Chart in the appendix.)

When combined with oral antibiotics, the butyrate stimulating effect is negated, so I add supplemental butyrate.

The glycerite is bitter, which may take more than xylitol gum to overcome.

Acute Treatment:
- Glycerite: 1 tsp, 3 times daily
- Capsule: 500 mg, 3 times daily

Prophylactic:
- Glycerite: ½ tsp, 2 times daily
- Capsule: 250 mg, 2 times daily

Caution:
- Bitter flavor.
- May cause digestive upset.
- May alter the gut microbiome if used in high doses for long periods.

Chinese Thoroughwax

Bupleurum spp ~ root

Triterpenoid saponins ~ saikosaponins, buddlejasaponin, sandrosaponins

Multiple species researched - B. falcatum, marginatum

Personality ~ This plant has a unique characteristic where the stem seems to pierce the leaf and grow right through it. In other words, rather than flow around the leaf, it barrels straight through, taking the harder route. Also could be seen that the leaf “flows around” the stem.

Thorough-wax has been used for thousands of years in Asia. The American species can be found in and around Glacier National Park. It’s the primary ingredient in a Chinese formula called “free and easy wanderer.”

Significant anti-inflammatory activity, antioxidant, anti-histaminic, analgesic

Alleviates symptoms of ADHD

PMID: 28314599, 21749378, 29956627, 28593176, 32742347, 16939901, 28293263, 24438177

Chinese Thoroughwax benefits

Antimicrobial, moderate activity against Streptococcus pyogenes

Antiviral, activity against Influenza A (H1N1), more potent inhibitory activity and selectivity than the positive control, Ribavirin

Modulates the immune system

Significantly reduces inflammation

Anti-histamine

Improves attention

Neuroprotective:
- Significant reduction in memory impairment
- Decelerates the activation of microglia and astrocytes in the hippocampus
- Preserves the morphology of neurons, reduce apoptosis and significantly inhibit amyloid-β deposition in the hippocampus
- Inhibits increased glutamate (after limbic region stimulation in rats - this stim may have increased dopamine)

Hepatoprotective and supports detoxification

Antispasmodic, antitussive

Diaphoretic, antipyretic

Analgesic

Anti-ulcer

PMID: 28314599, 21749378, 29956627, 28593176, 32742347, 16939901, 28293263

Chinese Thoroughwax dosing

Due to its long history of use in traditional Chinese formulas, it's rather difficult to find Thorough-wax on its own in capsule form. I use the glycerite to make sure I'm not getting other herbs by default in a formula. It has a mild flavor most kids don't mind. It pairs well with maple syrup if masking is needed.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily

Caution:

May increase dopamine in some kids, so proceed cautiously. Start with half the dose and slowly increase, watching for signs of agitation.

Leaves a prickly feeling in the mouth and throat. This is normal and goes away on its own.

Brahmi

Bacopa monnieri ~ whole plant

Triterpene saponins ~ bacosides, brahminosides

Personality ~ This water-loving herb grows in ponds, wetlands, and generally mucky areas. It's a match for anything "boggy," such as boggy tonsils and boggy brains. I use this with the child whose brain feels waterlogged, yet inflamed—a unique combination of dampness and heat.

Brahmi's use goes back centuries in traditional Ayurvedic medicine, where it's touted as a brain tonic and cognitive aid. That claim is bearing out as scientists find multiple nootropic compounds.

I think of Brahmi as a "chill" agent. Kids often feel the change in inflammation, saying their brains don't feel as swollen. It helps sharpen the mind and reduces pain. It's a nice choice before school.

Useful for kids restricting food, as it protects the brain during hypoglycemic episodes.

PMID: 27473605, 28583132, 23772955, 23975094, 23975094, 29676230, 25884228

Brahmi benefits

Antibacterial, mild, activity against pathogenic Staphylococcus aureus

Antifungal, mild

Antioxidant

Increases cerebral blood flow

Inhibits inflammatory pathways in the brain
- Inhibits the release of inflammatory cytokines from microglial cells
- Inhibits enzymes associated with inflammation in the brain

Neurotransmitter modulation (acetylcholine, serotonin, dopamine)

Preservation of dopamine D1/D2 receptors

Protects the brain in low blood sugar states

Reduces neuropathic pain ~ allodynia and hyperalgesia

Hepatoprotective

PMID: 27473605, 28583132, 23772955, 23975094, 23975094, 29676230, 25884228

Brahmi dosing

Brahmi needs to be combined with Botanical Antimicrobials for acute and prophylactic antibiotic therapy. It's safe to use long term. If needed, it can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily
Capsule, powder: 650 mg, 3 times daily
Capsule, extract: 350 mg, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily
Capsule, powder: 650 mg, 1 time daily
Capsule, extract: 350 mg,1 time daily

Caution:

May cause dry mouth, tummy cramps, and diarrhea at too high of doses.

Magnolia

Magnolia spp ~ flowers and bark

Triterpenoid saponin ~ germacranolides, parthenolide

Personality ~ As one of the oldest species of trees on the planet, this Avatar is a nice match for the child who's an "old soul." Folklore tells that the bark may be chewed to kick a tobacco habit. This may have to do with how easily it crosses the blood-brain barrier. I find it helpful for teens who can't kick screen time habits.

Magnolia is protective and regenerative to the brain and nervous system. It has a relaxing effect and helps to normalize our response to stress. It's especially useful for the child who gets completely maxed out by the stress of daily life, resulting in anxiety and depression.

PMID: 24062717, 25953946, 17879752, 29627576, 34400262, 34362632, 32664494

Magnolia benefits

Antimicrobial, mild

Antidepressant, anxiolytic

Neuroprotective:
- Crosses BBB easily, wide range of activity
- Reduces neuroinflammation
- Protects the NMDA (N-methyl-D-aspartate) receptor
- Neurotrophic
- Inhibits dopamine biosynthesis

Antispasmodic, improves asthma symptoms

Antithrombotic (caution low platelets)

Hepatoprotective
- Regulates GI hormones and metabolism
- Protects the intestinal lining
- Fosters beneficial microbiome species

PMID: 24062717, 25953946, 17879752, 29627576, 34400262, 34362632, 32664494

Magnolia dosing

Magnolia can be used for prophylactic antibiotic therapy. It's often combined with Botanical Antimicrobials in the acute phase. This Avatar may not be suited for long-term use in certain situations. If needed, it can be combined with Botanical Antibiotics and select Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily
Capsule: 500 mg, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily
Capsule: 250 mg, 2 times daily

Caution:

May cause drowsiness.
May interact with anticoagulant medication.

Silk Tree

Albizia julibrissin ~ flowers and bark

Triterpenoid saponins ~ hehuanoside, julibroside, etc

Personality ~ referred to as “the sleep tree” and also “happiness bark.”
Its leaves slightly close or wilt at night, which tells us how to match it.
It’s the perfect remedy for the child or teen who drags through the day, then lights up at night when they should be sleeping.

Also called the Mimosa tree, which is a little misleading. Be careful to use the correct herb: Albizia.
There’s another commonly used herb, called Mimosa pudica. Same word “mimosa” but a different herb.

Silk tree provides uplifting calm. One little guy I worked with said it took the static out of his brain. It has a mood-stabilizing effect that neutralizes the brain chemistry imbalances we often see with PANDAS and PANS.

Mild sedative effects - not necessarily one for the morning.
However, children with intense anxiety early in the day may benefit.

PMID: 12127229, 24884469, 28764915, 34303280, 33550033, 31057652, 32278761

Silk Tree benefits

Antimicrobial, mild

Antifungal, antiparasitic, mild

Immune modulation

Reduces inflammation

Nootropic, memory retention

Engages the parasympathetic nervous system

Stabilizes the mood

Brain healing nootropic:
- Boosts serotonin
- Reduces dopamine
- Suppresses LPS-induced microglia activation
- Pro-apoptotic (microglial pruning)

Anticonvulsant

Antioxidant

Mild sedative and relaxation effects

Antipyretic

PMID: 12127229, 24884469, 28764915, 34303280, 33550033, 31057652, 32278761

Silk Tree dosing

Mild antimicrobial activity and cleans up cellular debris. I usually combine this with Botanical Antimicrobials.

Silk tree can be used for prophylactic antibiotic therapy. It's often combined with Botanical Antimicrobials in the acute phase. It's safe to use long term. If needed, it can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily, best later in the day
Capsule: 500 mg, 3 times daily, best later in the day

Prophylactic:

Glycerite: ½ tsp, at bedtime
Capsule: 500 mg, at bedtime

Caution:

May cause drowsiness.

Boost effect with NAGs.

Gotu Kola

Centella asiatica ~ leaves

Triterpenoid saponins ~ centellosides (asiaticosides, centellosides, brahminosides, madecassosides, etc)

Personality ~ known as the herb of enlightenment. Eaten as a leafy green in many parts of Asia and is said to restore vigor.

As a powerful antioxidant, it leads to generalized reduced inflammation—from the brain to the gut to the joints. As a tonic to the brain and nervous system, it minimizes the impacts of excessive worry and chronic stress.

I use it mostly as a tea before meals to reduce food refusal. Crosses BBB within 5-15 minutes. Drinking the tea before the meal protects the brain from post-prandial spikes in endotoxin.

Especially helpful for kids with digestive issues, food sensitivities, and leaky gut, where eating exposes their brains to increased endotoxins.

PMID: 30516814, 29354820, 26848139, 22001429, 33022343, 33039960, 29436598

Gotu Kola benefits

Neuroprotective - xBBB in 5-15 min

Antibacterial, mild

Antiviral, mild

Antifungal, mild

Neuroprotective:
- Preserves glutathione
- Protects against dopamine/glutamate neurotoxicity
- Reduces LPS-induced microglia activation

Restores mucosal barrier and gut microbiota homeostasis

Antioxidant - ↓ oxidative stress comparable to vit C/GSH

Reduces joint pain

Improves locomotor dysfunction

PMID: 30516814, 29354820, 26848139, 22001429, 33022343, 33039960, 29436598

Gotu Kola dosing

Gotu kola is best combined with additional Botanical Antimicrobials for acute and prophylactic antibiotic therapy. It's very safe to use long term. If needed, it can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily
Capsule: 400 mg, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily
Capsule: 200 mg, 2 times daily

To prep for meals:

Tea: 1–2 cups 10–15 minutes before eating
The tea has a slight musky spice flavor.

Prepare tea by steeping 1 Tbsp dried Gotu kola leaves in 2 cups of boiling water for 5 minutes. Strain, and add honey to taste. Cool to a comfortable drinking temperature.

Caution:

May increase skin sensitivity to sunlight.

Astragalus

Triterpenoid saponin ~ astragaloside

Immune modulation

Antimicrobial

Attenuates progression of autoimmune encephalomyelitis:
- Remarkably modulate T cell differentiation in CNS
- ↓ BBB leakage
- Reduce ROS production by up-regulation of T-SOD → GSH
- Reduce neuroinflammation by inhibition inflammatory cytokines

Neurotrophic:
- Differentiates neural stem cells
- Restoration of dopaminergic neurons

Dose: 500mg-1gram qd-bid

PMID: 29481521, 27725851, 25150364

Panax Ginseng

Triterpenoid saponins - ginsenosides

Immune modulation

Neuroprotective ~ attenuates dopamine-induced apoptosis

Suppress intracellular oxidative stress

Stabilize excitable cells

Regulate voltage-gated ion channels (Ca, Na,K, Cl)
& ligand-gated ion channels (GABAA, 5HT, nicotinic ACh, NMDA)

*Mixed data on dopamine effects, caution during flares

Used mostly as nasal spray in P/P (ginsenosides)

PMID: 12877931, 24678300, 28412215

Integrative approach

Acute vs chronic presentation

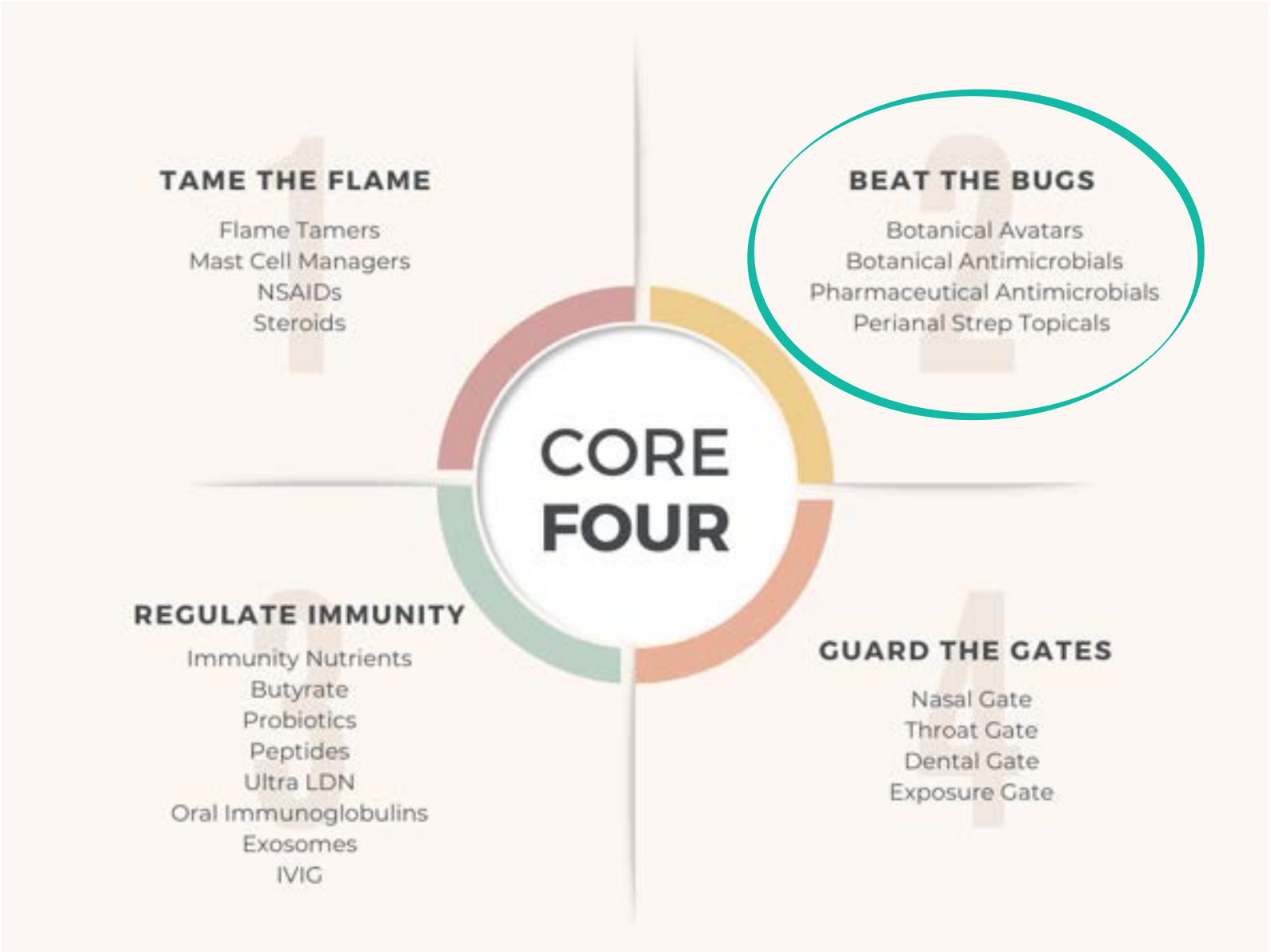
Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

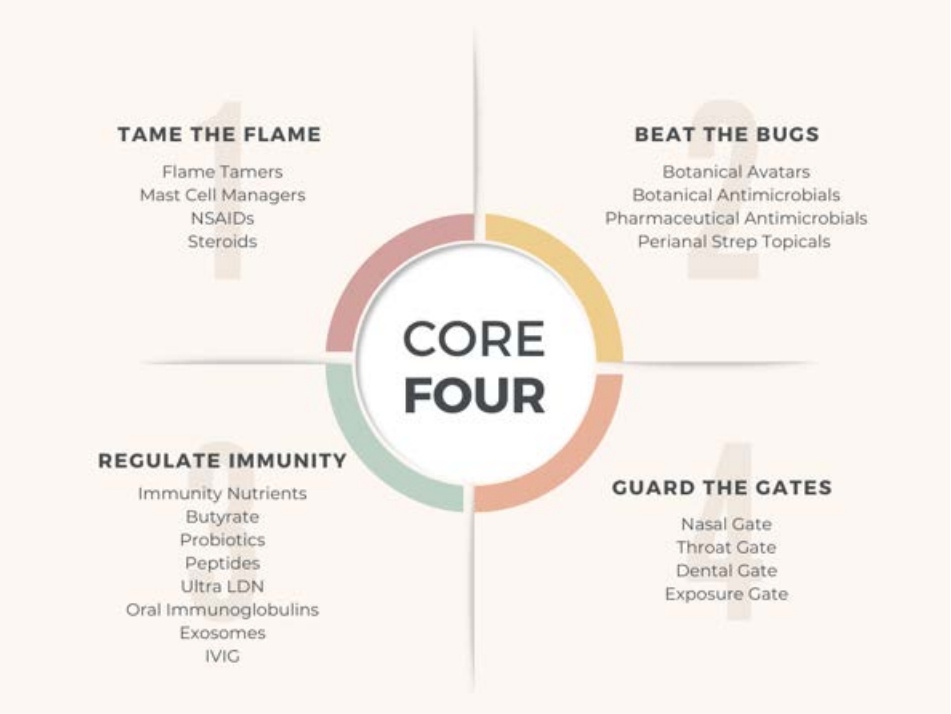
Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials



Putting It Together



Select 1 Flame Tamer and 1 Mast Cell Manager.

Choose the 1 or 2 Botanical Avatars that fit the child.

Add 1 Botanical Antimicrobial to fit the child's current infection load.

Optimize Vitamin D.

Add Core immune modulation.

Choose 2 methods for each of the Nasal, Throat, and Dental gates.

Explore various ways to close the Exposure Gate, starting with hand-washing (family/caregivers), removing glyphosate and mold, reducing infection exposures.

Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Botanical Antimicrobials

Botanical antimicrobials typically have multiple mechanisms and action against multiple microbes. I've classified them by their strongest action, but their activity likely is broader spectrum, depending on the herb. These are safe to use with children old enough to eat solid food.

Antibacterial:

Strep: Echinacea, Thyme, Oregano
Staph: Thyme, Echinacea, Oregano
E. Coli: Thyme, Oregano
Mycoplasma pneumonia: Chinese skullcap
Pseudomonas: Thyme, Oregano
Bartonella: Cryptolepis, Japanese knotweed
Borrelia: Cryptolepis, Japanese knotweed, Black walnut
Babesia duncani: Cryptolepis, Japanese knotweed

Botanical Antimicrobials (continued)

Antiviral:
Coronaviruses*: Black elderberry, Licorice, Olive leaf
Adenovirus: Black elderberry
Rhinovirus: Black elderberry
Influenza: Black elderberry, Licorice, Thyme, Echinacea, Japanese knotweed
Herpes family (EBV, Chickenpox/Shingles): Licorice, Black elderberry, Thyme, Oregano

Antiparasitic: Black walnut, Neem

Antifungal: Thyme, Oregano, Rosemary, Sage

Thyme

Thymus vulgaris - leaves

Broad-spectrum antibacterial ~
Streptococcus pyogenes, Staphylococcus aureus,
Escherichia coli, Salmonella Typhimurium, Pseudomonas aeruginosa

Antiviral ~
Influenza, Herpes viruses

Antifungal ~
Candida (multidrug resistant), Aspergillus, Trichophyton

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.

Safe to use long term.

Can be combined with certain Pharmaceutical Antimicrobials.

May spare a child from having to take additional antifungals during antibiotic therapy.

PMID: 34579365, 33212200, 33176697, 32512899, 31359292

Thyme

Acute Treatment:
Glycerite: ¾ tsp, 3 times daily
Capsule: 350 mg, 3 times daily
Tea: 1 cup, 4 times daily

Prophylactic:
Glycerite: ¼ tsp, 2 times daily
Capsule: 175 mg, 2 times daily

To prep the tea:
Yield: 2 cups
Prepare tea by steeping 1 Tbsp dried Thyme leaves in 2 cups of boiling water for 5 minutes, covered.
Strain, and add honey to taste. Cool to a comfortable drinking temperature.

Caution:
Thyme tea and glycerite may cause temporary tingling in the mouth.

Echinacea

Echinacea spp - root

Antibacterial ~
Streptococcus pyogenes, Staphylococcus aureus

Antiviral ~ Influenza

Echinacea reduces overall recurrence and severity of respiratory infections and is very safe to use with children.

Meta-analysis of randomized-controlled Echinacea trials reported that Echinacea "potently lowers the risk of recurrent respiratory infections and complications thereof."

Seems to help the most susceptible individuals the most.

In children with recurrent tonsillitis, Echinacea can be combined with Azithromycin to boost its efficacy.

PMID: 32487336, 20036523, 25784510

Echinacea

Echinacea can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Very safe to use long term.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:
Glycerite: 1 tsp, 3 times daily
Capsule: 1000 mg, 2 times daily

Prophylactic:
Glycerite: ½ tsp, 2 times daily
Capsule: 500 mg, 2 times daily

Caution:
May cause temporary tingling in the mouth.

Oregano

Origanum vulgare - leaves

Antibacterial ~
Streptococcus pyogenes, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa

Antiviral ~ Herpes viruses

Antifungal ~Candida species, Trichophyton species, Microsporum species

Potent, broad-spectrum antimicrobial herb, effective against many drug-resistant species, including fungi.

Prevents Strep biofilm. For chronic tonsillitis due to Strep, tea form is best.

Option for patients with concomitant SIBO.

Like Thyme, Oregano may spare a child from having to take additional antifungals during antibiotic therapy.

PMID: 31450579, 30792999, 29452197, 25631514

Oregano

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Safe to use long term.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment
- Glycerite: ¾ tsp, 3 times daily
- Capsule: 150 mg of 10:1 extract, 3 times daily
- Tea: 1 cup, 4 times daily (needs a minimum of 24 hours for anti-Strep effect)

Prophylactic:
- Glycerite: ¼ tsp, once daily
- Capsule: 150 mg of 10:1 extract, once daily

To prep the tea:
- Yield: 2 cups
- Steep 1 Tbsp dried Oregano leaves in 2 cups of boiling water for 5 minutes, covered.
- Strain, and add honey to taste. Cool to a comfortable drinking temperature.

For the prophylactic phase, pulse, 2–3 consecutive days on, 4-5 days off

Caution:
- Abdominal cramping, nausea, and diarrhea at higher doses or if using the oil extract.

Black Elderberry

Sambucus nigra - flowers and berries

Antibacterial ~
Streptococcus pyogenes, mild

Antiviral ~
Influenza, Common cold Coronavirus, Adenovirus, Rhinovirus

Reduces the duration and symptoms of the common cold and influenza, such as fever, pain, congestion, and cough.

Reduced duration and severity equate to reduced inflammation. High in antioxidant bioflavonoids, which further reduces inflammation.

Meta-analysis of RCTs poses it as a “a potentially safer alternative to prescription drugs for routine cases of the common cold and influenza.” I have found this to be true in practice.

PMID: 30670267, 27023596, 21352539, PMC7347422

Black Elderberry

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Very safe to use long term.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:
Glycerite or Syrup: 1 tsp, 3 times daily
Capsule: 500 mg, 3 times daily

Prophylactic:
Glycerite or Syrup: ½ tsp, 2 times daily
Capsule: 250 mg, 2 times daily

Caution:
Black elderberry syrup may contain added sweetener.
May stain teeth if taken immediately after using a whitening agent.

Licorice

Glycyrrhiza glabra - root

Antibacterial ~
Mild—Escherichia coli, Staphylococcus aureus, Enterococcus faecalis, Pseudomonas species, Salmonella paratyphi

Antiviral ~
Herpes viruses (EBV, HSV I/II, CMV, Zoster), Influenza, Hepatitis viruses

Antiparasitic ~ Mild—Babesia, Plasmodium species

Soothing expectorant and anti-inflammatory. Sipping the tea eases a sore, scratchy throat.

Preliminary research on using Licorice for SARS-CoV-2 due to positive previous research on SARS viruses.

Traditional Chinese medicine - used for viral infections of the liver. Good for children exposed to mycotoxins which are hepatotoxic, such as Aflatoxin.

PMID: 34579633, 32106571, PMC7808814

Licorice

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Safe to use long term.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:
- Glycerite: ¾ tsp, 3 times daily
- Capsule: 300 mg, 3 times daily
- Tea: 4 cups, sipped throughout the day

Prophylactic:
- Glycerite: ¼ tsp, 2 times daily
- Capsule: 150 mg, 2 times daily

To prep the tea:
- Yield: 2 cups
- Prepare tea by boiling 1 teaspoon licorice root powder in 2 cups of water for 5 minutes, covered. Strain. Cool to a comfortable drinking temperature.

Caution:
- May increase blood pressure.

Olive leaf

Olea europaea

Rich in phenolic compounds with antimicrobial, anti-inflammatory, anti-oxidant, analgesic, antipyretic, immunomodulatory, and antithrombotic activities.

SARS-CoV-2 ~

Randomized, triple-blinded clinical trial in hospitalized Covid-19 pts - improved the clinical status of the patients and decrease the length of hospitalization.
Data suggest by modulating the expression of SOD2, NF-kB and also ACE2 and TMPRSS2, whose expression is required for SARS-CoV-2 virus entry.
Anti-inflammatory effect on senescent and small airway epithelial cells.
"…great benefit in the control of associated inflammatory cytokine storm and disseminated intravascular coagulation (DIC) in COVID-19 patients."

Activity against several infectious agents, namely herpes simplex type 1 (HSV-1), Epstein Barr virus (EBV), gram positive bacteria (Bacillus cereus, B. subtilis and Staphylococcus aureus), gram negative bacteria (Pseudomonas aeruginosa, Escherichia coli and Klebsiella pneumoniae) and fungi (Candida albicans and Cryptococcus neoformans);
activity against Acyclovir-resistant HSV.

PMID: 37627504, 35496299, 36319585, 36899824, 34200316, 32050880, 34834807, 17873849

Olive leaf

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.

Safe to use long term.

Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily

Capsule: 500 mg, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily

Capsule: 250 mg, 2 times daily

Caution:

Hypotensive, hypoglycemic

Cryptolepis

Cryptolepis sanguinolenta - root

Ghanaian quinine;
bitter root tea traditionally used for malaria
"chambered charm" "strong blood"

Antibacterial ~
Borrelia species
Bartonella species

Antiparasitic ~Babesia duncani

Activity against both the growing and non-growing forms of Borrelia, Bartonella, and at least one species of Babesia.

PMID: 33763384, 32154254, 29750083

Cryptolepis

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.

Safe to use long term in lower prophylactic doses.

Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:

Glycerite: 1 tsp, 3 times daily

Prophylactic:

Glycerite: ½ tsp, 2 times daily

Caution:

Bitter flavor.

Best suited in lower quantities for long-term dosing.

Japanese Knotweed

Polygonum cuspidatum - root

Antibacterial ~
Borrelia species, Bartonella species

Antiviral ~ Influenza

Antiparasitic ~ Babesia duncani

Invasive weed with the tenacity and vigor of bamboo.

Rich in resveratrol; anodyne, anti-inflammatory properties.

Similar to Cryptolepis, Japanese knotweed has activity against both growing and non-growing forms.

PMID: 34719206, 33763384, 32154254, 25658356

Japanese Knotweed

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Safe to use long term.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:
Glycerite: 1 tsp, 3 times daily
Capsule: 600 mg, 3 times daily

Prophylactic:
Glycerite: ½ tsp, 2 times daily
Capsule: 300 mg, 2 times daily

Caution:
May interact with anticoagulant medication.

Black Walnut

Juglans nigra - green outer flesh of the nut, leaves, bark

Antibacterial ~
Borrelia species, oral Staphylococcus aureus (mild)

Antiparasitic ~ Acanthamoeba

Best known for its purgative properties. Long history of use in expelling parasites.

While we might believe that expelling parasites would harm the gut microbiome, Black walnut helps to increase microbiome diversity and reduces Th17.

Black walnut also has activity against growing and dormant Borrelia.

It can be safely combined with the other two herbs that specialize in this, Cryptolepis and Japanese knotweed.

PMID: 33915494, 32154254, 27816681, 26358271

Black Walnut

Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
Best used in short-term or pulsed long-term doses.
Can be combined with certain Pharmaceutical Antimicrobials.

Acute Treatment:
Glycerite: ¼ tsp, 3 times daily
Capsule: 250 mg, 3 times daily

Prophylactic:
Glycerite: 1/8 tsp, 2 times daily
Capsule: 125 mg, 2 times daily

Caution:
May cause digestive upset, cramping, and diarrhea.
Best used in short-term or pulsed long-term dosing, 1 week on, 2 weeks off.

Antimicrobial implications

Pharmaceutical antibiotics have a negative effect on the gut microbiome, affecting its diversity and function - an effect we don't see with botanical antimicrobials.

Antibiotics impact microglia function, modulate microglia-synapse interaction.

Correlation with antibiotic use and depression, amongst other neuroinflammatory disorders such as Parkinson's and Alzheimer's.

Fungal overgrowth, worsened in colonized mold-sick pt

When needed, support microbiome+microglia via probiotics & SCFAs

PMID: 34685628, 33513791, 31791704

Using Pharmaceuticals Functionally

5 critical discernment points relating to Pharmaceutical Antimicrobials:

- Determining when they're needed
- Dose, delivery, and duration
- Persister infections and resistance factors
- Gut microbiome impact
- Fungal overgrowth

Utility of long-term antibiotic prophylaxis?

"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.

Long-term 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."

Retrospective analysis.

No control group.

PMID: 31140830

Antimicrobial combinations

Combining certain herbs with Rx reduces impact and resistance

Oregon grape root preserves SCFA production

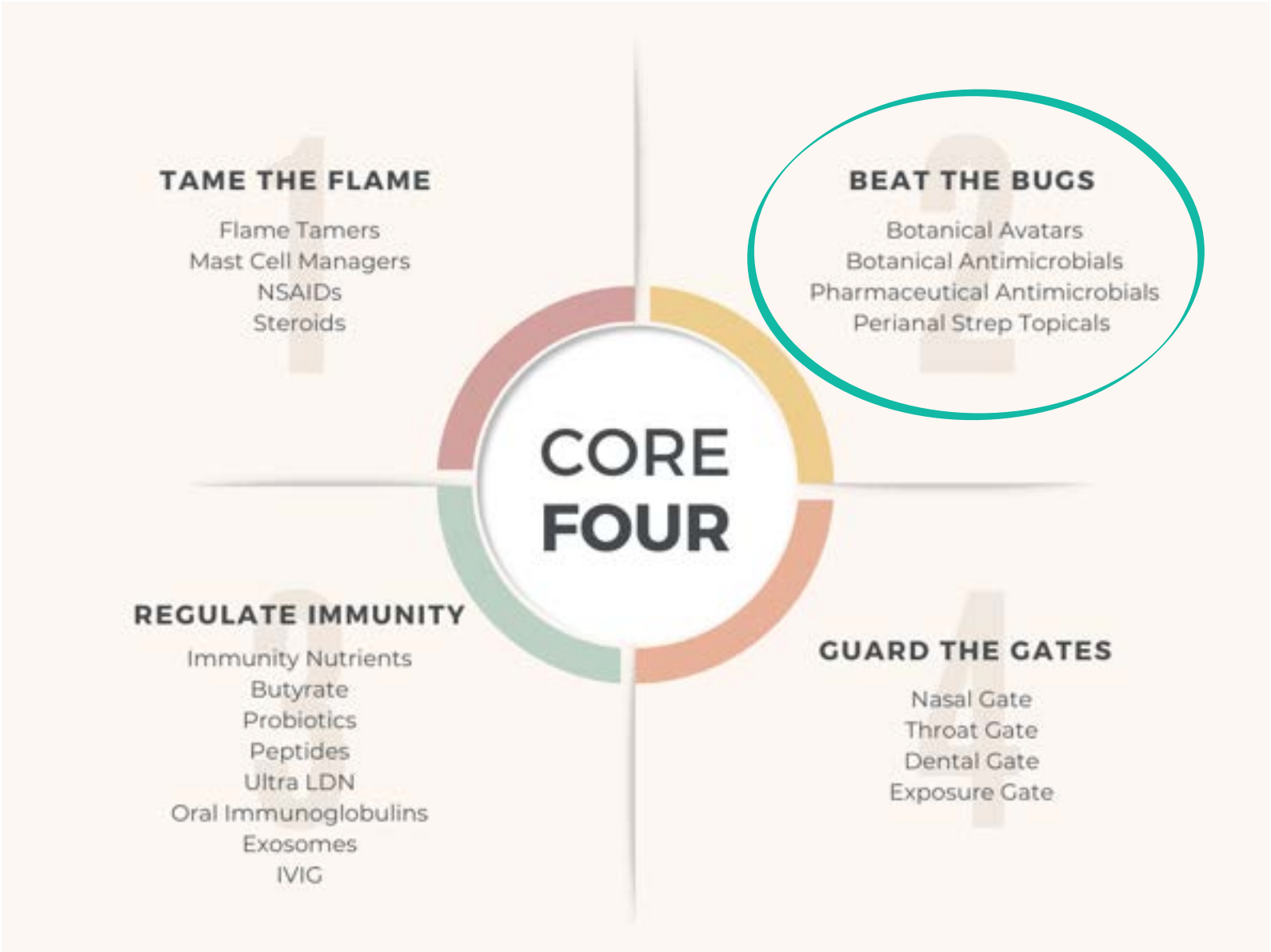
Oregano combine safely w fluconazole & cipro ~

↓drug resistance

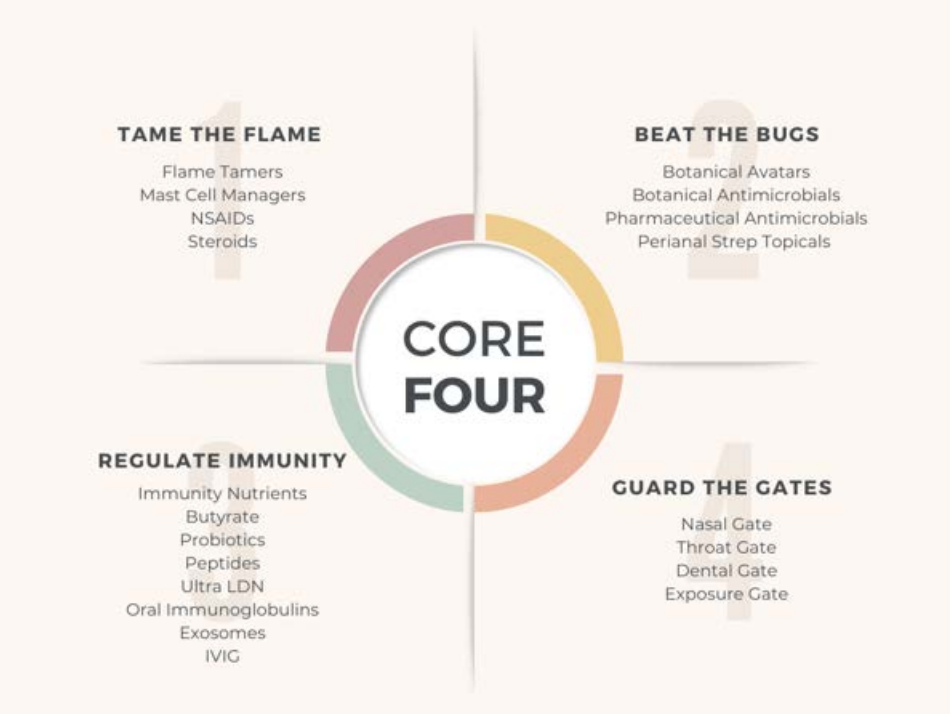
↓free-rad formation+S/E

Meta-analysis of 17 trials, over 1400 children and adolescents ~
Combinations w Chinese herbal formulas improved tx efficacy for Mycoplasma pneumonia (built around Chinese skullcap)
Reduced overall symptoms and duration
Improved lung X-ray findings
Yet didn't increase adverse events

PMID: 25364204, 32028237, 34177587



Putting It Together



Select 1 Flame Tamer and 1 Mast Cell Manager.

Choose the 1 or 2 Botanical Avatars that fit the child.

Add 1 Botanical Antimicrobial to fit the child's current infection load.

Optimize Vitamin D.

Add Core immune modulation.

Choose 2 methods for each of the Nasal, Throat, and Dental gates.

Explore various ways to close the Exposure Gate, starting with hand-washing (family/caregivers), removing glyphosate and mold, reducing infection exposures.

Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Integrative approach

Acute vs chronic presentation

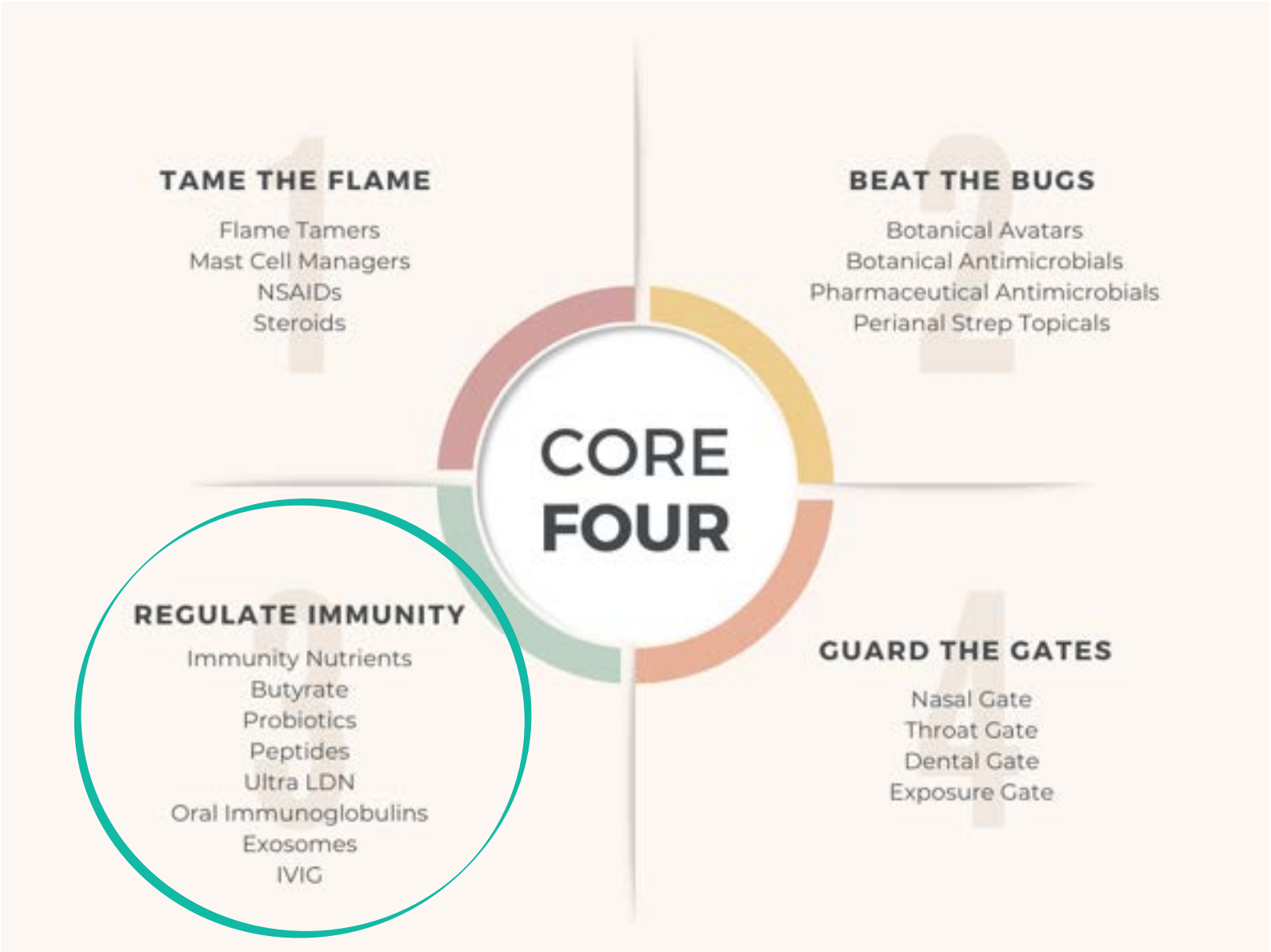
Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

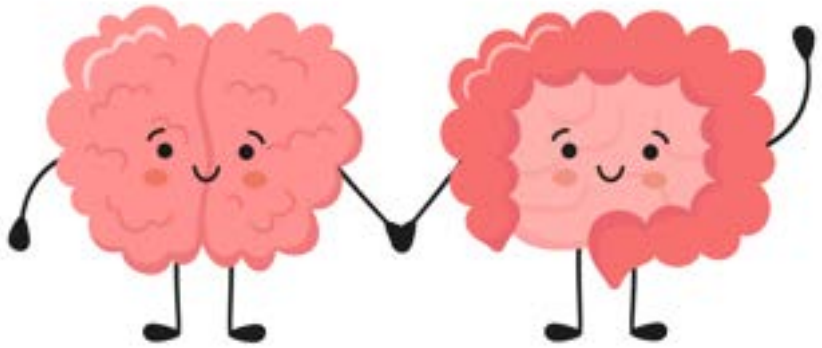
Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials



The way out of this brain problem is largely through the gut



Regulate Immunity

Immune modulation is the goal of this Core section.
Improves autoimmunity vs worsening it (outmoded concept)

- Immunity Nutrients
- Butyrate
- Probiotics
- Fecal Microbiota Transplant (FMT)
- Helminth Therapy
- Oral Immunoglobulins
- Peptides
- Ultra-Low-Dose Naltrexone (ULDN)
- Exosomes
- Intravenous Immunoglobulins (IVIG)

Immunity Nutrients

"Seasoned chicken" is my goofy acronym for the immunity nutrients that get depleted in autoimmune disease: SEAZnDCK.

Nutritional support for 2-3 days at the first signs of infection:

Selenium: 200 mcg twice daily

Vitamin E: 800 IU

Vitamin A: 50,000 IU

Zinc: 30 mg twice daily (*take with food to prevent nausea)

Vitamin D: 50,000 IU

Vitamin C: 2,000 mg every 2 hours up to 10,000 mg
(*may cause loose stool at high doses)

Vitamin K: 400 mcg

Some can be used longer term with your oversight.

IV is an option for kids struggling with food refusal or swallowing issues.

Vitamin D

Role in both innate & adaptive immunity ~
T-cell regulator
Upregulates monocyte genes

Study looking at gut microbiota and Strep, kids with PANDAS had a significant deficiency in Vitamin D as compared to normal controls.

Adequate Vitamin D reduces acute respiratory tract infections and severity in children, including Influenza, and possibly Covid.

In a randomized clinical trial for Covid, a single high-dose of vitamin D was compared against a single low-dose in adults at a high risk. The high dose offered statistically significant protection, even with just a single dose.

Vit D receptor in intestine & kidney significantly down-modulated after mycotoxin exposure.

Promote lung tissue repair in *particle-induced pulmonary injury*.

PMID: 32038645, 33371905, 32847594, 20219962, 30698894, 25483621, 25912039, 26404359,18569389

Vitamin “sunshine”

Fat-soluble ~
Can bioaccumulate
Monitor labs

I typically dose to meet specific lab values for at least 3 months in order upregulate receptors ~
60–90 ng/mL
150–225 nmol/L

Use liposomal or emulsified forms for optimal absorption.

Vitamin A

Critical for many biological processes including the maintenance and modulation of immunity, and the homeostasis of epithelium and mucosa.

Affects cell integrity, cytokine production, innate immune cell activation, antigen presentation, and lymphocyte trafficking to mucosal surfaces.

Has been reported to influence the gut microbiota composition and diversity.

Vitamin A deficiency results in the imbalanced production of inflammatory and immunomodulatory cytokines, intestinal inflammation, weakened mucosal barrier functions, and disruption of the gut microbiome.

Infections decrease the intestinal absorption of Vitamin A, thereby contributing to secondary deficiency.

Vitamin A deficiency is associated with more severe and persistent Mycoplasma pneumonia infections.

2022 Cochrane Database Systematic Review confirmed that Vitamin A supplementation is associated with a clinically meaningful reduction in morbidity and mortality in children.

PMID: 36501067, 32175413, 35294044

Vitamin A

Fat-soluble ~
- Can bioaccumulate
- Is hepatotoxic at high levels.
- Monitor labs and dose accordingly.

Can be super-dosed in a single dose at the first onset of viral symptoms. May cause a mild fever.

Dose ~
- A single adult super-dose is 100,000 IU.
- Maintenance: dose via labs.
- 3.33 IU per mcg.

Ages	Upper Limit
Birth to 12 months	600 mcg
Children 1–3 years	600 mcg
Children 4–8 years	900 mcg
Children 9–13 years	1,700 mcg
Teens 14–18 years	2,800 mcg
Adults 19 years and older	3,000 mcg

Use liposomal or emulsified forms for optimal absorption.

PMID: https://ods.od.nih.gov/factsheets/VitaminA-Consumer/

Butyrate

Short-chain fatty acid (SCFA) produced by beneficial microbiome that nourishes enterocytes.

Butyrate benefits ~

- Calms the microglia (#monkeys)
- Stimulates brain repair
- Balances brain chemistry
- Gives the brain mitochondria a boost
- Impacts the gut-brain-immune axis

"…we hypothesise that butyrate and other volatile SCFAs produced by microbes may be involved in regulating the impact of the microbiome on behaviour including social communication."

Some antibiotics halt the manufacture of Butyrate in the microbiome.

Botanical antimicrobials don't seem to have this same effect. In fact, most of them stimulate Butyrate, as in the case of Oregon grape.

PMID: 27346602,

SCFAs and the brain

Oral application of a mixture of the three major SCFAs acetate, propionate, and butyrate in germ-free mice, was sufficient to restore the normal maturation process of the microglia.

SCFAs can modulate neurotransmitters, like glutamate, glutamine, GABA, and neurotrophic factors.

Propionate and butyrate can influence the cell signaling system via modification of the intracellular potassium levels, and regulate the expression levels of tryptophan 5-hydroxylase 1, involved in the synthesis of serotonin, and tyrosine hydroxylase, which is involved in the biosynthesis of dopamine, adrenaline, and noradrenaline.

In mouse models of Parkinson's, oral and IV sodium phenylbutyrate was found to protect the loss of dopaminergic neurons and improve motor function.

PMID: 33362788, 21902286, 21372141, 22723850

Butyrate

The challenge is taste. Parents often mask with ranch dressing (dairy or nondairy) and/or vanilla to mask the flavor.

Butyrate is quite effective when administered as an enema as well. Sometimes that little nugget of information is motivation for a kid to opt for plugging their nose and getting it down.

Daily:
Powder, liquid or capsule: 375 mg twice daily with food

Flare:
Powder, liquid or capsule: 500 mg three times daily with food

Caution:
Tastes like rotten eggs.
May cause reflux. Best taken with food.

IV:
Sodium phenylbutyrate. (Requires training.)

Post biotics

The “peristaltic wave” of the future.

Different concept than probiotics which have the goal of increasing the biota, post-biotics are the metabolites of a healthy biota, affecting the milieu.

Expanding: “you are the sum of the company you keep”
To: “you are the sum *of the products* of the company you keep”

Freeze-dried, sterilized, non-viable processed stool from healthy donor.

Careful screening of donors ~
Breastfed, vaginal birth, minimal if any antibiotics (<5), no Hx anxiety/depression
30+ plant-based foods per week (diversity of diet = diversity of microbiome)

Much more than SCFAs (lipids, AAs, bile acids, peptides, nucleotides, etc) yet has SCFAs in optimal ratios 60:20:20 acetate:butyrate:proprionate.

Empirical data showing ox stress benefit. No human studies as of yet.

Dose: “dusting” up to 1/4 cap to start.
Maintenance -1/d. Flare tx - up to 2 bid.

Probiotics

Multiple studies have shown improvement in depression, anxiety, OCD, and the perception of stress.

Anxiety or eating disorders ~

Review article: pts with generalized anxiety or eating disorders (anorexia nervosa, bulimia nervosa, and binge-eating disorders) show a specific profile of gut microbiota. This imbalance can be partially restored after a single or multi-strain probiotic supplementation.

Fears ~

Mouse model: probiotic tx after fear conditioning inhibited microglial activation and had similar therapeutic effects as the microglial cell repopulation.

Conclusions: Probiotic tx after fear conditioning might promote long-term fear extinction which could be associated with the mitigation of synaptic pruning of activated microglial cells;

Probiotics may be applicable as therapeutic strategy to inhibit microglial activation and treat fear-related disorders.

PMID: 31144383, 34022177, 28868181

Probiotic strains

Psychobiotics ~

Bifidobacterium adolescentis produces GABA

Lactobacillus plantarum JYLP-326 relieves anxiety, depression, and insomnia

Lactobacillus gasseri CP2305 (postbiotic) significantly reduced of State Trait Anxiety Inventory (STAI)-trait scores (6 month trial)

Sleep ~

Lactobacillus casei Shirota YIT9029, LcS suppresses sleep latency and increased sleep intensity (in healthy adults)

Histamine friendly ~

Bifidobacterium infantis, B. bifidum, B. longum, B. lactis, B. breve

Lactobacillus salivarius, L. plantarum

Avoid *L. reuteri 6475*

Mold mycotoxins ~

Lactobacillus plantarum C88/MON03, L. rhamnosus GAF01

L. casei strain Shirota

PMID: 32839473, 37033942, 28443383, 33652962, 18544899, 22384111, 28129335, 24738739, 23030351, 21816119

Spore-based probiotics

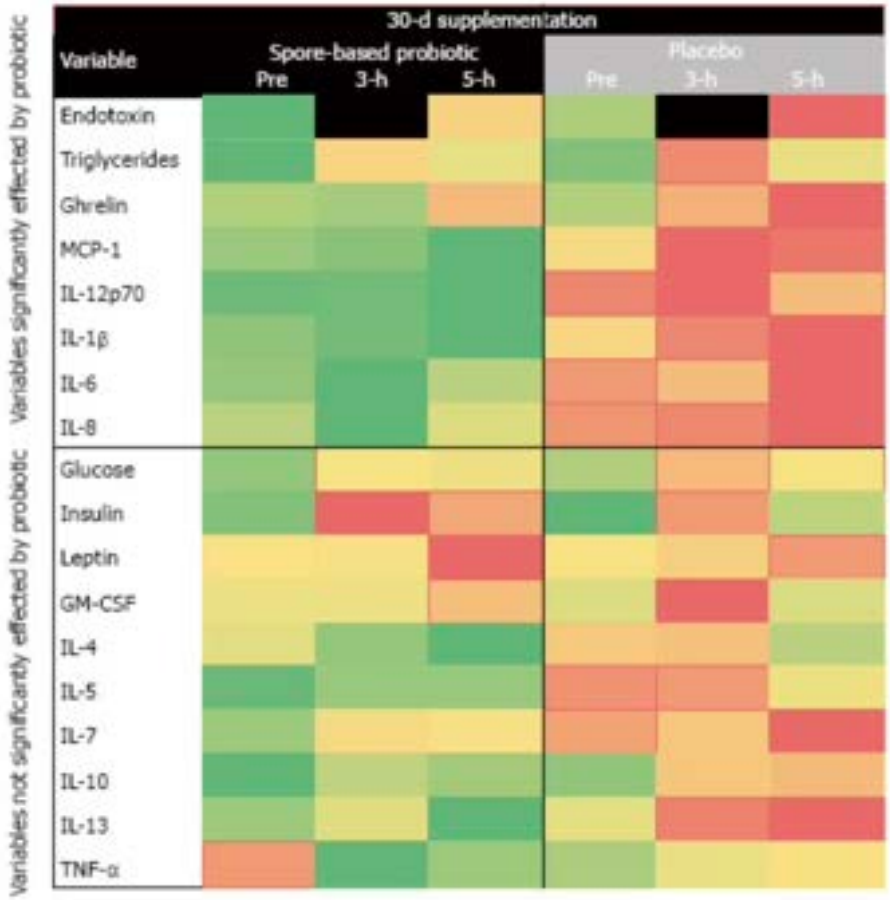
Spore-based probiotic study ~

Healthy men and women (n = 75) screened for post-prandial dietary endotoxemia. Subjects whose serum endotoxin concentration increased by at least 5-fold from pre-meal levels at 5-h post-prandial were considered "responders" and randomized to receive either placebo or tx.

Given spore-based probiotic supplement for 30d [Bacillus indicus (HU36), Bacillus subtilis (HU58), Bacillus coagulans, and Bacillus licheniformis, and Bacillus clausii]

Oral spore-based probiotic supplementation was associated with 42% reduction of post-prandial dietary endotoxin & significant post-prandial reductions in inflammatory markers IL-1β, IL-12p70, and ghrelin.

PMID: 31144383, 34022177, 28868181



Variables were divided into those that demonstrated a significant (upper panel) and those that did not (lower panel) have a significant probiotic effect. Responses were coded a lower (green to yellow) or higher (yellow to red) compared to baseline. An unchanged (yellow) response was also identified. PMID: 28868181

Probiotic dosing tips for P/P kids

For multi-strain, introduce one strain at a time and watch for 2 weeks.

Postbiotics and spore-based probiotic ~
Dose: start VERY low, die-off common. 1 capsule over 1-2 weeks, then 1 capsule over 4-7 days, then 1 capsule over 2 days, until maintenance dose of 1/day.

Use supplemental pro/postbiotics with prescription antibiotics for prevention of Clostridia.

Avoid/Cautions ~
Avoid Streptococcus strains
Caution with prebiotics (fungal overgrowth)

Fecal microbiota transplant (FMT)

Empirical reports of success

Both the donor and recipient gut milieu seems to matter

Safety: Safety trial: Human RCT using FMT from lean donor in obese, metabolically uncompromised patients
Led to sustained changes in the intestinal microbiome and bile acid profiles that were similar to those of the lean donor.
No changes in BMI at week 8.
Imho - duration too short, dose mb too low, but was found to be safe.

Precedent: Huntington's dz: neurodegenerative disorder which also involves psychiatric, cognitive and motor sxs (possible genetic role in P/P)
Mouse study: wild-type donor FMT positively modulated cognitive outcomes, particularly in females.

Efficacy: Emerging evidence supports the possibility that controlling inflammation in the recipient intestine might facilitate engraftment by reducing host immune system pressure on the newly transferred microbiota.

PMID: 31301451, 33907321, 36035436, 35854629

HDCs / Helminth therapy

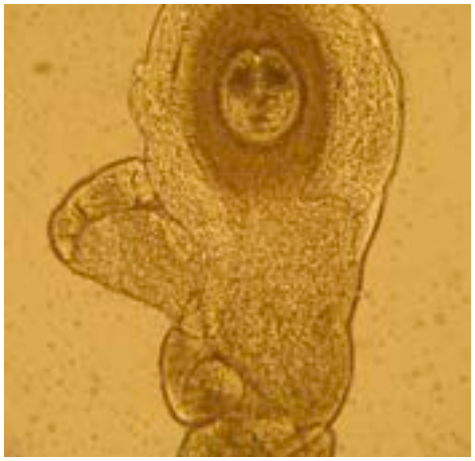


Photo courtesy of
https://biomerestoration.com/hdc/

HDCs ~
- Hymenolepis diminuta cysticercoids (rat tapeworm cysticerci)
- Part of normal flora in many non-industrialized areas.
- From grain beetles; eaten unknowingly in food supply.
- Remain in lumen; low risk of colonization in human; intermediary host required.

Helminth secretome ~
- Excretory/secretory products
- Helminth derived miRNAs are delivered in exosomes.
- Exosomes are internalized by immune host cells; exert the expansion of Treg cells, resulting in the control of inflammation.

PMID: 28484453, 25712154, 27297184

Effect on host immune cells

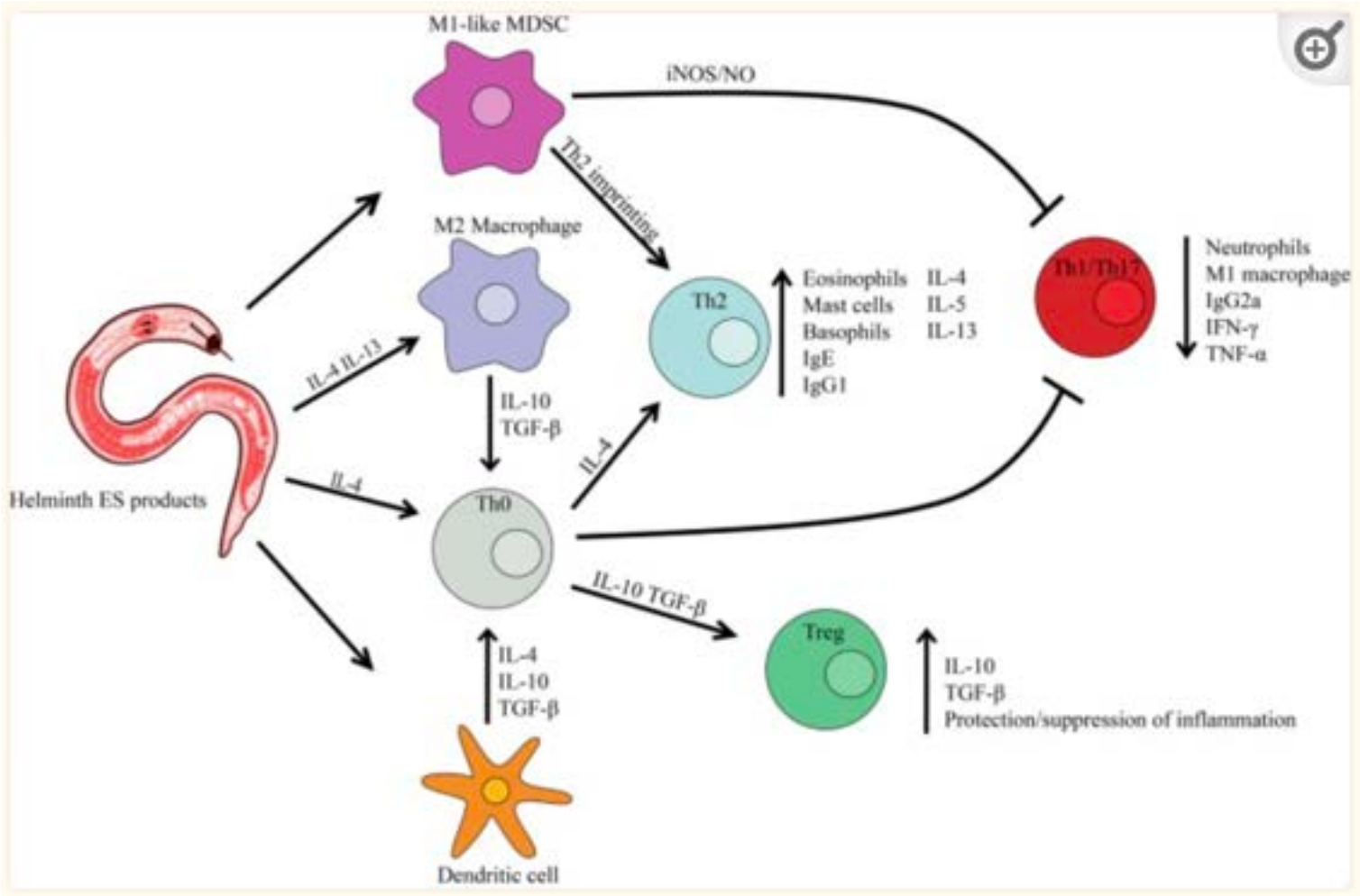
Polarization toward Th2 response (preventing Th1 or Th17 immune response) characterized by Th2 cytokines.

Differentiation of macrophages toward the M2 phenotype, resulting in a Th2 immune response.

Prevent dendritic cell synthesis of pro-inflammatory cytokines and promote the production of immunoregulatory molecules such as IL-10 and TGFβ.
Induces regulatory T cell (Treg) phenotype, promoting the protection/suppression of inflammation produced by a Th1 autoimmune disease.

Myeloid-derived suppressor cells (MDSC) function as immunoregulators, producing reactive oxygen/nitrogen species that inhibit the function of T cells.

PMID: 28484453, 25712154



HDCs / Helminth therapy

HDC Oral Dose ~

Start low and titrate slowly. May temporarily increase neuro sxs. May induce mast cells/increase IgE and histamine.
Target dose: ~1ml po every 3 weeks x 3 mo min, then reassess.
May be mixed in room-temp or cool liquid but must contain fat and drink the whole amount.

Helminth-derived peptides ~ on the horizon.

Safety ~

Slight risk with helminths of infection. Avoid if child is constipated (less than 1 BM/day) or taking immunosuppressive medications.
Helminth-derived peptides vs actual helminths alleviates concerns associated with live infection in kids with immune depletion.

PMID: 28484453, 25712154

Oral Immunoglobulins

Resilience factors. Sourced from colostrum.

May or may not improve lab immunoglobulin numbers, but have an immune-modulating effect clinically - reduced susceptibility to GI and respiratory infections, and shorten recovery times.

Oral immunoglobulins don't seem to aggravate or flare the autoimmunity like subcutaneous immunoglobulins can.

Ideally supplement as Colostrum in order to be closer to its natural whole food form ~ Colostrum supplementation has been shown to protect against side effects of antibiotics, anti-inflammatory drugs and steroids, and psychophysical stress.

Immunoglobulins are also available as a supplement.

Colostrum is easy to get into kids - tastes like a milkshake.

Bovine-free alternatives available.

PMID: 34444709, 27100711, 37189633

Oral Immunoglobulins

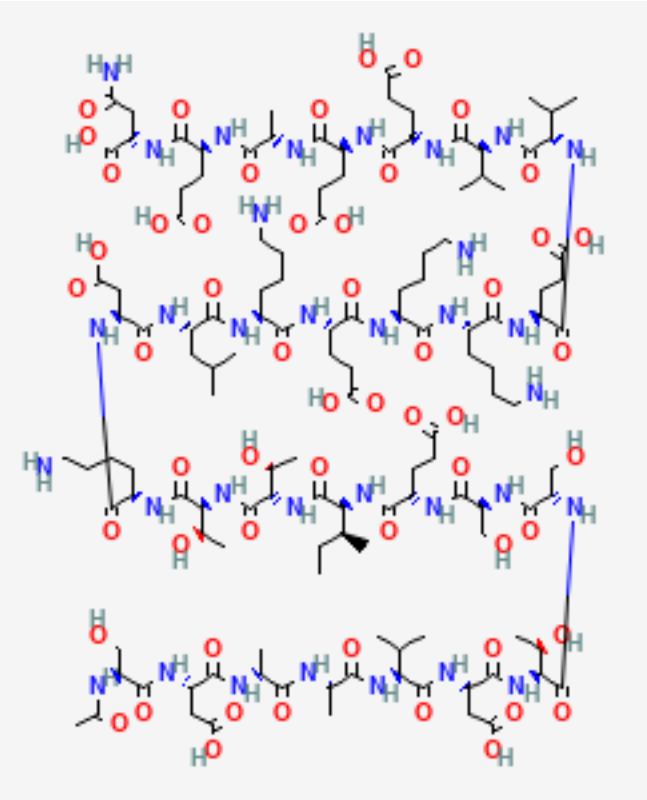
Unlike the Immunity Nutrients, withhold Oral Immunoglobulins during an active infection as it can cause more mucous—it's doing its job, but that can cause more discomfort to an already snotty kid.

Rx:
EnteraGam (serum-derived bovine Ig): 1 packet bid

Daily:
Colostrum powder, chew, or capsule: 1,500 mg twice daily
IgG capsule: 500 mg twice daily

Caution:
May increase mucous during acute respiratory illnesses.
Low risk of worsening constipation.

Peptides



Protein messengers ~

Depending on the peptide, can turn the immune system either up or down.

Send different types of messages to different types of tissue.

In PANDAS and PANS, we focus on the gut-brain-immune messages.

Body Protection Compound (BPC), Thymosin Beta, Cerebrolysin

Body Protection Compound (BPC) peptide

Gastric peptide intended to maintain gut barrier protection from infections that aren't cleared by stomach acid, with additional wide beneficial effect, both peripherally and centrally.

Gut-brain axis ~ anxiolytic, anticonvulsive, antidepressant effects

Animals: brain neuronal damages were resolved as well as disturbed memory, locomotion, and coordination.

Counteracts encephalopathies; counteracts dopamine disturbances (dopamine receptors blockade, receptors super sensitivity development, or receptor activation, over-release, nigrostriatal damage, vesicles depletion); inflammation reduction; nerve recovery.

Empirically reduces tics.

Anti-inflammatory; heals wounds, tendon injuries, muscle healing and function recovery.

Add this peptide with children taking NSAIDs. (Reduced stomach lesions and encephalopathy.)

Being studied as potential COVID-19 treatment.

PMID: 34380875, 34798584, 29134359, 37242459

Body Protection Compound (BPC)

Dissolves easily in water, so can be used in children who don't swallow pills.
Acts fairly quickly.

Daily:
Powder or capsule: 500 mcg once daily

Flare:
Powder or capsule: 500 mcg twice daily

Caution:
May increase mucous production.
May induce a low-grade fever after the first few doses.

Thymosin Beta 4

Activity is similar to the nasal peptide Thymosin Alpha-1 to be discussed in the next section.

Neuroprotective and fortifies the BBB.

Animal studies suggest a reparative role in a range of encephalopathies.

Appears to use a cholinergic pathway to force defective microglia into autophagy.

Reduces food sensitivities by fortifying the gut wall barrier integrity.

Particularly useful for children exposed to molds that affect the myocardium. Assists with myocardial tissue regeneration.

Use the 4-fragment to concentrate the active fragment.

May use freeze-dried thymus gland for a more “whole food” version of this supplement.

Being studied as potential COVID-19 treatment.

PMID: 34335970, 33967626, 31877278, 30552633

Thymosin Beta 4

Dissolves easily in water, so can be used in children who don't swallow pills.

Daily:
TB4-FRAG+ powder or capsule: 150 mcg once daily

Flare:
TB4-FRAG+ powder or capsule: 150 mcg twice daily

Caution:
May increase mucous production.
May induce a low-grade fever after the first few doses.

Cerebrolysin

Modified version of the IV peptide for oral administration; little longer duration to see the effects seen IV.

Reduces neuroinflammation and improves vascular changes in the brain.

Human and animal studies suggest benefit in headaches, migraines, post-concussion, stroke, and other vascular and neurodegenerative changes in the brain. I have found it to also be helpful in PANDAS/PANS.

Typically, it takes about 2 weeks to see any changes, and longer term dosing has been beneficial to reduce the frequency of flares, despite exposures and triggering events.

Specially-formulated capsules can be opened and stirred into cool or room temp fluids.

Pork sourced; stronger taste than the milk-shake taste of BPC.

PMID: 33515100, 29752991

Cerebrolysin

Dissolves easily in water, so can be used in children who don't swallow pills. ("pork" taste.)

Daily:

Powder or capsule: 100 mg once daily

Caution:

May induce transient headache
May increase mucous production.
May induce a low-grade fever after the first few doses.

Ultra-Low-Dose Naltrexone (ULDN)

ULDN manages autoimmunity aspect.

Structure almost identical to endogenous endorphins. High affinity binding to mu opiate receptor. Receptor antagonist. Short acting.

Low dose has long-term effect of up-regulating endorphin receptors, results in pain relief esp of neuropathic pain, anti-inflammatory effects, improved immunity.

Reduces neuroinflammation via an immunometabolic modulatory role on the microglia and mast cells.

Attenuates learning and memory disturbances with associated neuroinflammation.

Over time, improved sleep, reduced pain, reduced flares, and improved autoimmune markers.

Not the doses used for treatment of substance use disorder in this application.

PMID: 34445130, 32905811, 29885638

ULDN: Off-label use

Compounding pharmacy.

It works best over a long period of time. 6-9 months for full effect. Duration of tx often more than a year.

Low-dose (2.0-4.5mg) and ultra-low-dose (0.1-1.5mg). Due to BBB permeability in kids with P/P, I've found that the ultra-low-dose formulation is much better tolerated.

Usually given hs.
*Give first doses in the morning on a day when the child can sleep, if needed.
Initially, may induce nightmares. Give it in am and then shift it to nighttime after 3-7 days.

Caution ~
May reduce sensitivity to novocaine and other pain medications. Compensate with a slightly increased dose of the pain medication.
Have parents alert dentist and oral surgeon if child needs dental work or oral surgery.
Also alert any doctors involved in managing pain.

Exosomes

Mesenchymal stem cell-derived (MSC) Exosomes are on the cutting edge of cell-free stem-cell-based therapies for PANDAS and PANS.
Source is important (umbilical cord mesenchymal stem cells).

Immunomodulatory and regenerative properties.

Act like a messenger guardian over the microglia. Result is decreased neuroinflammation and autoimmune activity.

Empirically, observe clinical improvement and normalization of autoantibody markers.

Cell studies: mechanisms ~
Reduce pro-inflammatory Th1, Th17 cytokines, and IL-6, IL-12p70, IL-17AF, IL-22.
Upregulate T-regs.
Dampen LPS-induced expression of inflammation-related genes by microglia.

Activity on enterocytes ~
Animal studies: involved in intestinal epithelial integrity.

PMID: 31117376, 30898154, 36751776, 37440921,

Exosome administration

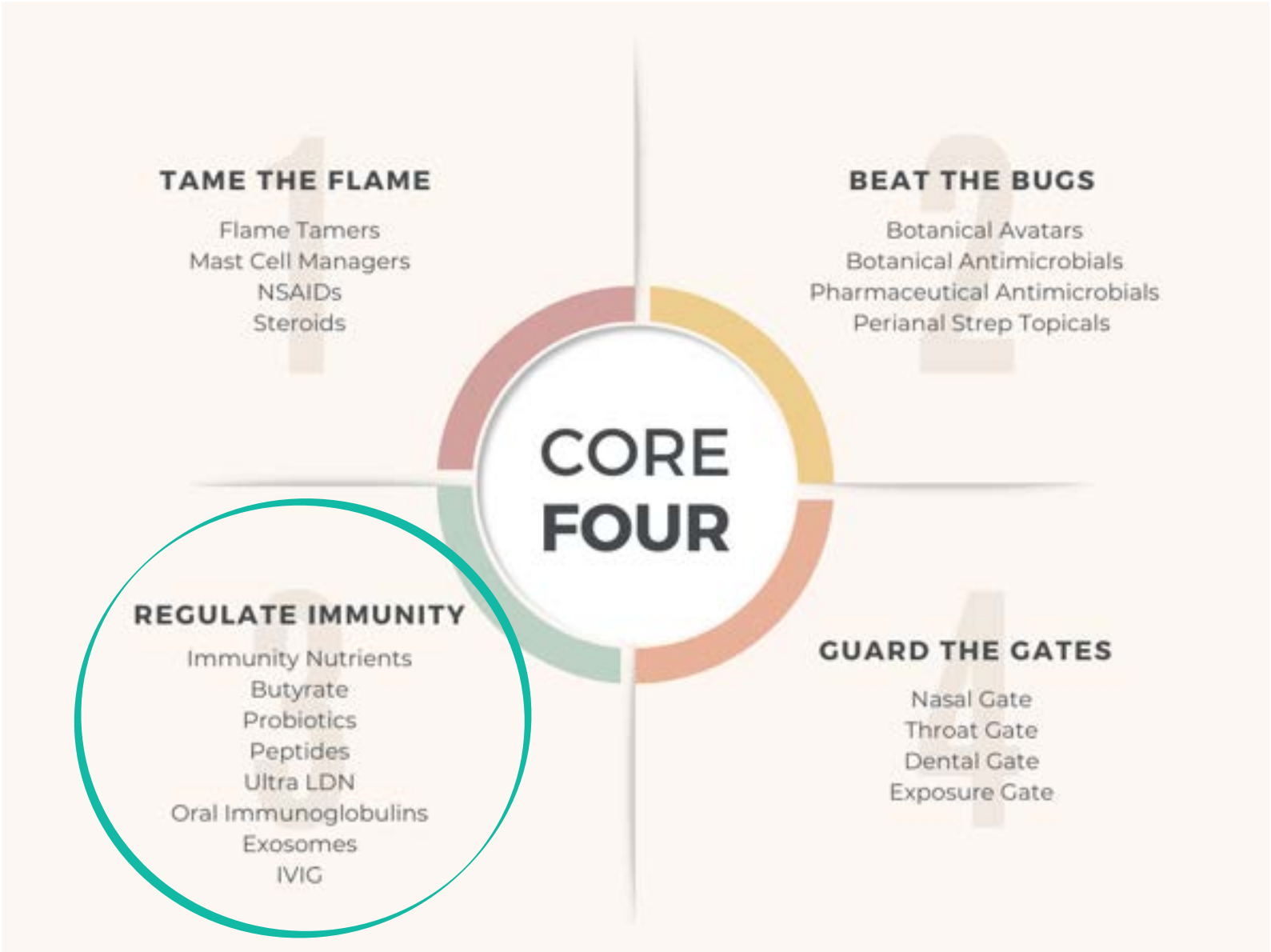
IV administration - specialized training beyond course scope.

The origin of the Exosomes is of extreme importance. Some can be inflammatory.
Use mesenchymal stem cell-derived exosomes with PANDAS/PANS.

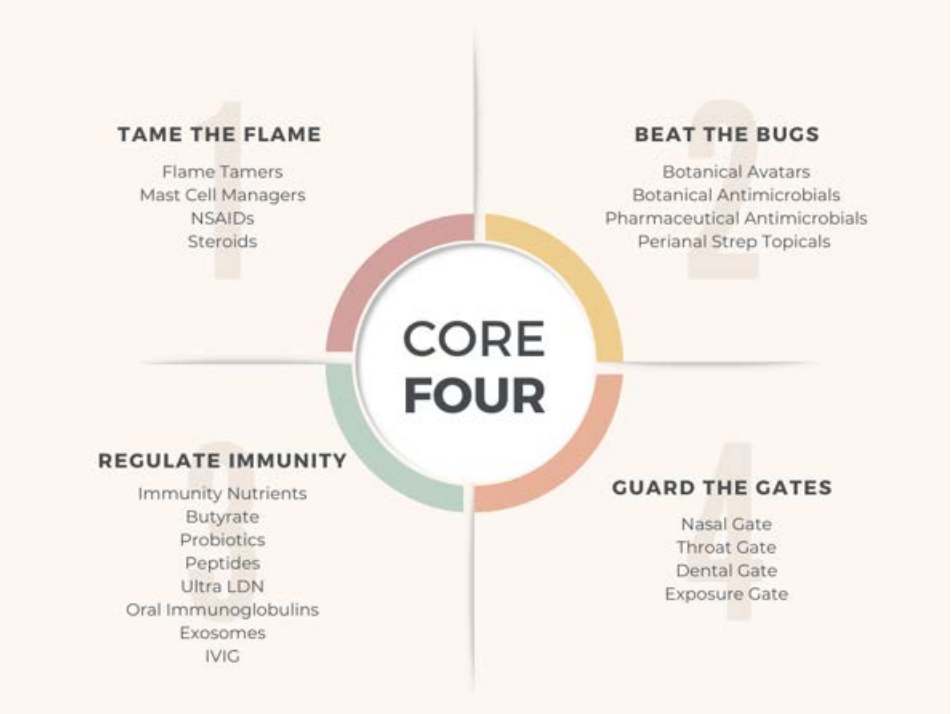
Still considered an experimental therapy.

Cautions ~
Risk of inducing inflammation, even if the perfect sourcing was used.
Risk of seizure.

Possible future nasal applications ~
Rat model: Intranasally administered exosomes reached the brain and reduced microglia-mediated neuroinflammation in rats with perinatal brain injury.



Putting It Together



Select 1 Flame Tamer and 1 Mast Cell Manager.

Choose the 1 or 2 Botanical Avatars that fit the child.

Add 1 Botanical Antimicrobial to fit the child's current infection load.

Optimize Vitamin D.

Add Core immune modulation.

Choose 2 methods for each of the Nasal, Throat, and Dental gates.

Explore various ways to close the Exposure Gate, starting with hand-washing (family/caregivers), removing glyphosate and mold, reducing infection exposures.

Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Integrative approach

Acute vs chronic presentation

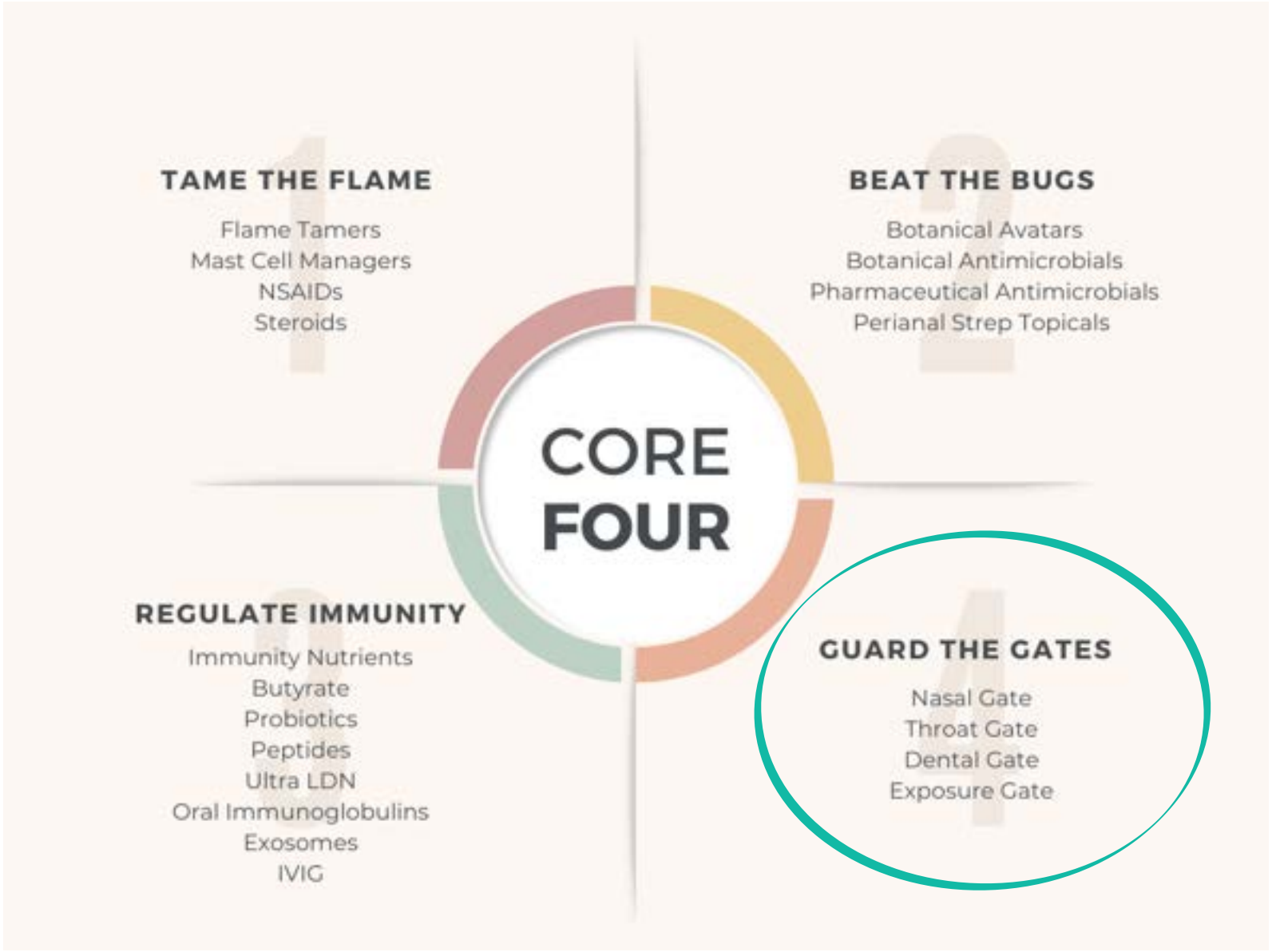
Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials



Nasal Gate

A strong Nasal Gate minimizes infection and brain inflammation.

Reminder: infections of the throat also affect the nose. When the nose is triggered, neuroinflammatory chemicals get an “elevator ride” via the olfactory bulb to the limbic system. Inhaled mold mycotoxins can as well.

Nasal mucosa traps germs and dissolves toxins, and the cilia sweep the border clean. But microbes and inhaled toxins paralyze the cilia.

- Topical Nitric Oxide
- Nasal Probiotics
- Steam Inhalation
- Nasal Photobiomodulation
- Intranasal Colloidal Silver
- Intranasal Propolis
- Aromatherapy/Essential Oils
- Thymosin Alpha-1 Intranasal

Nasal Nitric Oxide

Mucosal Nitric oxide (NO) ~

Protective surface chemical made by our respiratory passages.

Noxious to germs. When released, NO temporarily sanitizes the region against microbes, including Strep species, Influenza, and SARS-CoV-2.

Also has the potential to disperse biofilm and make microbes more susceptible to antibiotic therapy.

Inducible via humming ~

Empirically, the level of nasal microbial contamination is correlated to the frequency of vocal tics.

Administer via NO nasal spray, as needed.

PMID: 33992687, 27378676, 26856845, 23562771, 23547821

Nasal Probiotics

Supports the sinubiome by enhancing diversity.

Certain strains play a protective role against pathogens and restore weak barriers in the nasal and sinus tissue.

Lactobacillus sakei ~

Folkloric use: snort the juice from fermented kimchi to ward off infection.
Modulates allergic Th2 responses enhancing Treg generation.

Lactobacillus casei ~

Restores airway epithelial integrity in CRS pts with nasal polyps.

PMID: 34212544, 30154801, 22972842

Nasal Probiotics

Easy on kids and can be used in very young children.

Mix the probiotic powder in water and swab the nostrils, then sniff.
Safe to swallow if a sniff was too vigorous.

Use qd to bid. Easy to add to the end of the tooth brushing routine.

A helpful tip: L. sakei is used to cure meats. A child who craves cured meats may be needing nasal barrier help.

Steam Inhalation

Certain herbs' antimicrobial oils become more potent once they're in steam form.

Steam can access hard-to-reach sinus tissue to clear congestion, ease allergies, soothe irritated passages.

Many common kitchen herbs, such as **oregano, thyme, basil, rosemary, and sage**, become superpowers once they're steamed. These herbs can also be made into tea to be gargled for sore throats.

Some parents worry that tenting a towel over an anxious child's head would only increase anxiety, but I hear over and over again from kids that they feel calmer under the towel.

Handout in resources for Thyme, substitute any herb above.
How-to video on my website.

PMID: 34770961, 29452197

Thyme Steam Inhalation

Many common kitchen herbs, such as thyme, oregano, basil, rosemary, and sage, become superpowers once they're steamed. Essential oils are released in the steam that excel at killing microbes and mold.

The steam can get far back into the hard to reach places in the sinus cavities, and is safe for children.

Thyme is used in this recipe for its antiviral, anti-fungal and antibacterial properties. It's effective against a broad spectrum of pathogens, while also neutralizing mold's ability to make mycotoxins to fight back and defend itself.

SUPPLIES

Large bowl or pot
Large light-weight towel (large enough to create a "tent" over the bowl)

INGREDIENTS

2-3 cups boiling water
Thyme: (choose one)
- 5-10 drops of Thyme essential oil, or
- 2-3 tablespoons dried Thyme, or
- ½ - ¾ ounces fresh Thyme

DIRECTIONS

1. Fill large pot/bowl with boiling water
2. Depending on the form of Thyme used:
   Drop 5-10 drops of Thyme essential oil into the bowl, if using; or
   Stir in dried Thyme and steep for 5 minutes, if using; or
   Drop in the fresh Thyme and steep for a few minutes until leaves wilt and turn dark green, if using.
3. Lean your head over the bowl close enough to feel the steam, cover your head with the towel and create a tent to trap the steam. Be careful to not get to close to the water for the risk of burning your skin.
4. Inhale through your nose, exhale through your mouth. Continue for 5-10 minutes or until congestion, sore throat, headache, and/or lung issues subside.

Repeat as needed.

*May irritate eyes. Close eyes to reduce eye irritation.

Check out the How To video on my website DrCrista.com.

Nasal Photobiomodulation

Intranasal Photobiomodulation (i-PBMT); red light (~660nm)

Published case presentation paper ~

20 patients, treated with bid dosing, 10 seconds per nostril x10 consecutive days.
100% of patients experienced improvement in overall Total Nasal Symptom Score.
Of those patients, 40% brought their Total Nasal Symptom Score down to 0.

Locally reduces mast cell degranulation, eicosanoids, and Th2 cytokines in animal models of allergic rhinitis.

Evidence shows that nostril-based i-PBMT improves blood rheology and cerebral blood flow; has potential as a novel approach for neurorehabilitation.

Doses tend to be device dependent based on wavelength. Cut duration by 1/4 - 1/2 for children.

*Not yet FDA approved, but available for personal use.

PMID: 37312188 , 34731332, 31812948

Intranasal Silver

Historically, stored well water in a silver pitcher or bucket, or at the very least, put a silver ladle in a water container or eat with “silver”ware to stave off infection. Today, silver ions are used to coat tubing to keep water microbe-free.

Antimicrobial ~
Escherichia coli, Staphylococcus aureus, and Streptococcus pyogenes.
Considerable antifungal activity against fluconazole resistant Candida albicans.
Particularly effective against P. aeruginosa in planktonic and biofilm forms.
Activity against Staphylococcus aureus biofilms.

Good safety profiles. No toxic effects on primary human nasal epithelial cells in vitro.

Used for children who get Strep easily and frequently or those with recalcitrant CRS.

For young children, colloidal silver liquid can be swabbed inside the nose daily.

For teens and older children who can tolerate nasal sprays,
this can be administered as a nasal pump spray.

PMID: 34653555, 29696011, 24431107, 33690064, 28530184

Intranasal Propolis

Antimicrobial, anti-allergic/anti-histamine, anti-asthmatic, immunomodulatory, anti-inflammatory. Created by honeybees-protects hives from microbial invasion.

Bactericidal, virucidal, fungicidal.

Pilot study in 40 children (2-12yo) with acute rhinitis and common cold ~
Propolis nasal spray tid.
After 7 days there was a significant decrease of sxs.
Majority of the sample reported no sxs by day 7 with resolution of sxs occurring day 4.
Additionally, there was no need for supplementary treatment.

SARS-CoV-2 study suggested it may inhibit viral spike fusion in host cells, viral-host interactions that trigger the cytokine storm, and viral replication.

Gentle to the nasal tissue.

Sweet aftertaste and is very acceptable to children who don't tolerate stronger nasal sprays.

PMID: 29254297, 33793885, 33669054

Aromatherapy/Essential Oils

Essential oils are reliable broad-spectrum antimicrobials with a long tradition of safe use.

They are the concentrated volatile oils of plants. It takes about 1,000 plants to extract 1 ounce of essential oil, which means they are STRONG.

Knowing their strength, we need to take precautions to use them safely with kids, while still preserving their antimicrobial properties.

Essential oil treatments need to be repeated frequently in order to be effective. This often leads families to go with diffusers, which keep a constant dose in the air.

PMID: 33212200, 32512899, 30187508, 29977171, 25522803, 25532297, 25550774, 17972131

Antimicrobial essential oils

Ajowan
Basil
Bee Balm
Cinnamon
Eucalyptus
Lemon
Oregano
Pine
Rosemary
Sage
Sweet Annie
Tea Tree
Thyme
Wormwood
Black Zira (easier to find in the Middle East, Africa)

PMID: 33212200, 32512899, 30187508, 29977171, 25522803, 25532297, 25550774, 17972131

Aromatherapy techniques

Essential oil diffusers can be used in a child's bedroom throughout the night.

I prefer the old-school version with the sticks. Add 1 ounce of essential oil to a bottle with a narrow mouth, then add three to four bamboo sticks. Flip the sticks whenever the scent gets faint. Refill once the sticks are dry.

Diffusers that use water can encourage mold growth by increasing the humidity in the room. Dry diffusers are available, but warn parents that they may emit eEMFs, make sure they're not near the bed.

Essential oil inhalation sticks are great on the go, and pretty popular with teens. They can be used many times throughout the day and when a child feels like they were exposed.

If diffusers and inhalation sticks don't work, try the cotton ball technique. Add 10–20 drops of essential oil to four cotton balls and stuff them into the four corners of your child's pillow case for treatment while sleeping.

It's important to let children pick the essential oils that they want to use.

Children are often attracted to the essential oil that provide the most protection.

Essential oils can be combined into a blend as well.

Thymosin Alpha-1 Intranasal

Thymus gland derived peptide that's long been recognized for modifying, enhancing, and restoring immune function.

Antibacterial and antiviral properties. Stimulates immune cell activity to prevent infection.

Mucosal barrier protection. Promotes wound healing of irritated or damaged sinonasal tissue.

Prevents the excessive activation of T cells.

Nov 2020 article in Clinical Infectious Disease: Reversed T-cell exhaustion and recovered immune reconstitution during SARS-CoV-2 infection.

Nasal spray up to bid.

Caution:

Best used between flares to strengthen sinunasal barrier and prevent infection.
May cause aggravation during a flare due to immune-activating effect,
but reduces flare frequency overall.

PMID: 33362999, 32442287

Integrative approach

Acute vs chronic presentation

Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials

Throat Gate

Throat infections are the nexus of this brain problem.
Guarding the Throat Gate is key to protecting the brain.

- Herbal Gargles
- Throat Sprays
- Carrot Poultice
- Reservoirs of Infection

Herbal Gargles

Before antibiotics, people would regularly gargle with antiseptic rinses of salts or iodine, but also the herbs thyme, mint, and clove to prevent infection.

While saltwater gargles can be soothing for a sore throat and reduce tonsil size, saltwater itself doesn't seem to have enough punch to beat a throat infection. Herbal teas added to the saltwater mix incorporates the infection fighting aspect.

Antimicrobial herbal teas can be made from familiar, friendly herbs such as cinnamon, cloves, licorice, bay leaves, oregano, thyme, basil, rosemary, sage.

Honey is also one of my favorite antimicrobials. Pots of honey were excavated from Egyptian tombs completely preserved, unspoiled, and germ free. I often add a dab of honey to the saltwater herb gargles.

Children instinctively know that these help. They tend to ask for them after a suspected exposure.

I've seen herb gargles reduce handwashing frequency, anxiety, tics, and food refusal.

PMID: 31450579

Sage Tea Gargle

Sage is a miracle plant with many medicinal properties. One of its lesser known talents is to soothe a sore throat. Simply drinking a cup of Sage tea can soothe an irritated throat, a common tool used by clergy and singers.

You can increase its medicinal activity against viruses and fungi by gargling it before swallowing. Gargling helps to move lymph from sore and swollen lymph nodes.

This humble kitchen herb is perfect for those affected by mold who are prone to sore throats and swollen lymph nodes, especially when the seasons change.

Supplies

Tea strainer
Tea pot or tea cup
Plate or lid

Ingredients

1 cup boiling water
1 tablespoon packed chopped/torn fresh Sage, or
1 teaspoon dried Sage, or
3/4 teaspoon powdered Sage

Directions

1. Fill tea strainer with Sage.
2. Fill tea pot or tea cup with boiling water.
3. Place tea strainer filled with Sage in boiling water and cover with a plate or lid.
4. Steep for five to ten minutes.
5. Remove tea strainer from cup.
6. Cool tea to a comfortable temperature to gargle/drink.
7. Gargle with tea for 5-10 seconds and then swallow tea. Repeat until you have gargled and swallowed the entire cup of tea.

Repeat as needed.

Check out the How To video on my website DrCrista.com.

Throat Sprays

Initiate throat sprays as a topical pain reliever and antimicrobial when there's an active sore throat—the sooner the better. Often soothes a sore throat enough to allow a child to get some sleep.

Propolis ~

- As per earlier, antimicrobial, anti-allergy, anti-inflammatory activity.
- Combined with antimicrobial drugs to reduce drug resistance.
- Can stop a sore throat on contact. Instantly. No joke.
- Pungent flavor on the tongue.

Berberine-containing herbs ~

- Goldenseal contains the anti-inflammatory antimicrobial berberine.

In a perfect world, we'd use a throat spray with both propolis and goldenseal.

Warn parents, this combo is strong tasting.

- Fruit snack chasers are often needed.

PMID: 28914244, 21524711, 34903790

Carrot Poultice

Cold carrot compress is a simple way to resolve infection and lymphadenopathy without asking a sore, scratchy throat to swallow anything. The sooner it's used at the first signs of a sore throat, the more effective it will be.

Natural source of beta-carotene. Use a cold carrot to bring more blood to the area.

Our skin is like a sponge. Adding natural beta-carotene to the skin allows it to soak into the capillaries of our skin and join the local bloodstream. There it can be converted to Vitamin A, a favorite fuel for the immune cells.

Remember that the neck lymph nodes are the connecting lymph highway, linking the throat to the nose. And that once something triggers the nose, brain-inflaming chemicals get a direct elevator ride to the brain. **We can stop this train at the neck with a carrot poultice.**

Children may notice a little flushing of the skin during and after the poultice. That's normal and nothing to worry about. It will resolve on its own.

Cold Carrot Poultice

If your child does come down with a sore throat, a cold carrot compress is a simple way to knock it back, without asking that sore, scratchy throat to swallow anything. The sooner it's used at the first signs of a sore throat, the more effective it will be.

Carrots are a natural source of beta-carotene, a precursor to a potent immune-fighting vitamin, vitamin A. Our skin is like a sponge. Adding natural beta-carotene to the skin allows it to soak into the capillaries of our skin and join the local bloodstream. There it can be converted to Vitamin A, a favorite fuel for immune cells.

SUPPLIES

Winter scarf
Paring knife
1.5 feet of cheesecloth (ideally) or paper towel
Vegetable grater

INGREDIENTS

2 medium carrots, chilled

(Note: Putting the poultice on while it's cold will encourage more blood flow to the area as your child's body tries to warm the chilly spots. This helps absorb more nutrients and disperse inflammation.)

DIRECTIONS

1. Moisten cheesecloth or paper towel, and lay out lengthwise.
2. Chop off the top ends of the cold carrots, then grate directly onto cheesecloth or paper towel in two piles, 4-6 inches from each other.
3. Fold over lengthwise to make a neck wrap.
4. Wrap while still cold around child's neck, placing carrot piles over neck lymph nodes.
5. Wrap the scarf around the child's neck to keep the poultice in place and hold in warmth.
6. Keep wrapped until very warm to the touch, usually 20 minutes.

Dr. JILL CRISTA

Reservoirs of Infection

Keep the tonsils clear of infection by ~

- Clearing perianal Strep
- No Strep carriers around the child
- Manage sinus colonization if present
- Prevent “bogginess” of the tissue

Salt water gargle (desiccant)

Homeopathic tonsil formulas ~

- “Like cures like”: compounds used in nanoparticle amounts that in toxic amounts cause tonsillar hypertrophy, inflammation, and reduced immune responses, for instance.

Oral photobiomodulation (red light) ~

- Empirically, stimulates tissue repair in boggy, ineffectual tonsils.
- Cell culture: enhances M2 macrophage polarization properties of tonsil-derived mesenchymal stem cells.

PMID: 37579650, 31873066

Integrative approach

Acute vs chronic presentation

Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials

Dental Gate

The gut and the sinuses aren't the only ones with their own unique microbiome. The mouth has one too. The healthier the oral microbiome, the healthier our teeth.

- Mercury and Nitrous Oxide Avoidance
- Prophylactic Antimicrobials
- Xylitol
- Biofilm
- Structural Realignment

Avoidance of common dental practices

Very common for parents to report a dental procedure as the preceding event before a flare.
Was it the potential infection exposure, or toxicity, or structural alignment issues? Or all of the above?

NO “silver” fillings/mercury.

NO root canals.

NO Nitrous oxide “laughing” gas ~
- Avoid use in children.
- Can inhibit major enzymatic pathways.
- Repeated exposure may lead to neurologic damage.
- Animal studies in several species have shown that it can be associated with apoptosis in the developing brain.
- Accentuates B12 deficiency in those with MTHFR gene mutation.
- Symptoms may not appear until days to weeks after exposure.

PMID: 18458554, 17683399, 23731042

Amalgam removal

Only use a trained biological dentist if removal is needed. This takes special training and detox support for the child. (next slide)

Without training, the removal can become a second serious exposure.

Appropriate removal involves separate source of filtered air for the child to breath to reduce vapor exposure, filtered suctioning to protect the child and dentist/ staff, dental dams to reduce swallowing, etc.

~International Academy of Oral Medicine & Toxicology (iaomt.org)

Mercury

Chelation for accumulated mercury is beyond the scope of this course.
***can mobilize and redistribute in the brain, so please get training!
MULTIPLE additional natural substances to treat toxicity. PMID: 31762676

For oral exposures, especially surrounding amalgam removal, **bind with Maitake (Grifola frondosa) liquid extract** (or capsules for kids who can swallow caps).

Rat model: Accelerated the decline of blood mercury level, which fell precipitously by 50% on the second day. Also promoted elimination of the burden of mercury in the liver and kidneys.

Dose ~ Pre-dose the day before removal, day of removal, and for 4-7 days following removal, based on symptoms/amount of amalgam removed.
Extract - 1 full dropper tid.
Capsules - 500mg tid.
(Yes even for mold-affected. This is temporary.)

PMID: 30514871, 31762676

More support for amalgam removal

Support the 3 routes of detoxification/removal ~

Thiols: Glutathione 450mg, NAC 500mg, or ALA 300mg x 4-7 days.
MeHg is excreted in the bile as a glutathione conjugate and then undergoes enterohepatic recycling, with reabsorption of some of the MeHg from the intestine. MeHg is transferred from plasma proteins to the low molecular weight thiols glutathione and cysteine.

Orange-colored bioflavonoids: Luteolin 100mg *pre-treatment + 4-7 days following.
Inhibits thimerosal-induced VEGF release from human mast cells.
In plasma, most methylmercury (about 99%) is bound to albumin, complexing with the free sulfhydryl group of a terminal cysteinyl residue. Bioflavs assist transfer.

Postbiotics: Postbiotic oral fecal transplant 1 capsule bid x 4-7 days.
Demethylation occurs predominantly in the intestinal tract.

Reminder: “After removal of the electro-active restorations, both the contents of metals in saliva and galvanic currents decreased in comparison with the levels before the treatment.”

PMID: 21244751, 16804514

Prophylactic antimicrobials

Pathogenic Strep can act like kryptonite to a P/P kid.

Even healthy oral microbiomes host a little pathogenic Strep, which can migrate into the blood stream during the procedure.

Prophylactic antibiotics with dental procedures are highly recommended.

Knowing the impact of pharmaceutical antibiotics on the gut microbiome, I often use herbal medicines containing berberine, such as Oregon grape, and/or butyrate, to support the microbiome/gut wall, but it depends on the needs of the child and the child's susceptibility.

Xylitol

Xylitol has direct anti-Strep activity and prevents plaque.

Triple-blinded randomized-controlled field trial.
Children were instructed to chew xylitol gum for 5 minutes bid after meals for a month. Those chewing xylitol gum had a reduction in Streptococcus mutans, a cavity former.

Randomized-controlled trial to determine whether oral xylitol could reduce bloodstream infections from mouth germs in children undergoing stem cell transplant.
Xylitol was so clearly beneficial, the study was stopped early to publish their findings more quickly, and so they could institute the practice for all stem cell transplant children. Even the matched controls in the healthy arm of the study who received the xylitol had improved microbial diversity—a finding associated with better oral health.

Xylitol is an easy add-on in kids and teens with PANDAS or PANS because it's added to many commercially available products. You can find it as a toothpaste, mouthwash, and as a treat—gum.

PMID: 32600259, 30127194

Biofilm

Dental plaque is the best example of a biofilm. Regular dental cleanings stay ahead of the plaque, or biofilm. However, due to fears, many P/P kids fall behind on dental cleanings.

Preventing biofilm ~

- Regular dental cleanings
- Xylitol
- Herbs such as clove, oregano, tea tree, and thyme (also prevent yeast overgrowth.)
- Clove oil is also effective against Pseudomonas (fishy odor to their breath.)
- Propolis

Xylitol, propolis, and the herbs just mentioned have been added to commercially available toothpastes, making it very easy to rotate into regular daily routines.

Alternate xylitol toothpaste with an herbal biofilm-busting toothpaste.

- Use one in the morning and the other in the evening.

PMID: 24031950, 30607063

Structural realignment

CranioSacral therapy (CST) after dental appointments ~

Long periods of time with a child's mouth wide open is not only unnatural, it's especially hard on kids with basal ganglia encephalitis.
The degree of swelling at the base of their brain affects glymphatic flow.
When the mouth is held open for an extended period of time in a kid with a swollen brain, their cranial bones will adjust to relieve the pressure.
The result is compressed glymphatic drainage, increase in intracranial pressure, and worsening of tics and neuropsychiatric symptoms.

As a preventive, structural realignment is a *necessary* second step after any dental procedure.

Look for someone trained in CST by the Upledger Institute.

I recommend families schedule the CST on the same day if possible.
More and more dentists are offering this in their offices.

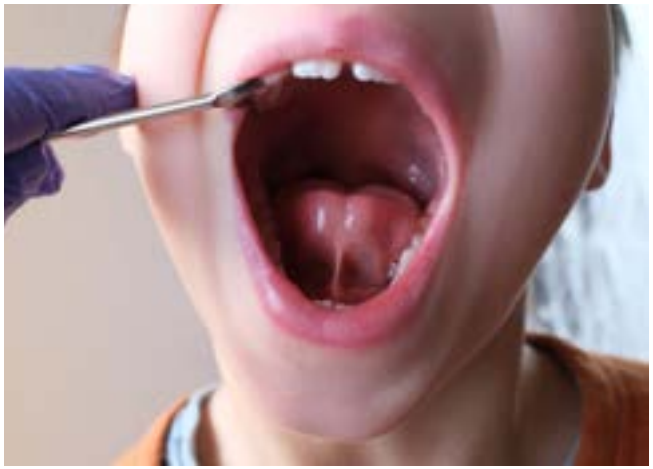
Airway issues

Multiple factors ~ enlarged tonsils, tongue tie, narrow palate, “lazy” tongue, sinus colonization.

Signs of an airway issue ~
Sleep disturbance, unrefreshed sleep, mouth breathing during sleep, snoring, apnea, headache, allergic facies/narrow face, high bp.

Work with biologic dentist to address oral/ structural causes. Narrow palate commonly needs palatal expansion (ie: via ALF appliance.) Manage tongue tie.

Taping is a “bandaid” for mouth breathing.
I’m not a fan. It closes down the airway.
Must address the structural reasons.



Recap work flow for parents

Recap regular dental appointments ~

- Start prophylactic antibiotics the day before procedure
- No silly gas
- No mercury
- Structural alignment afterwards

Recap amalgam removal ~

- Start prophylactic antibiotics the day before procedure
- Start Maitake the day before removal and continue for 4-7 days following removal, based on symptoms/amount of amalgam removed.
- No silly gas
- No mercury
- Structural alignment afterwards

Integrative approach

Acute vs chronic presentation

Core 4 ~

- Anti-inflammatories
- Antimicrobials
- Immune modulation
- Infection/toxicant prevention

Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

- Recovery Essentials

Exposure Gate

Exposures involve both infections and toxicants.

- Respiratory Infections
- Tick-Borne Infections
- Environmental Exposures
- Footbaths
- Glycine

Minimize infection exposure

Respiratory infections ~

- Wash hands! And regularly wipe down surfaces touched by hands.
- Repeated handwashing is a sign this is needed by others.
- Monitor those in contact with the child for Strep.

Tickborne ~

- Pretreated clothing, essential oils, tape rollers, tick tubes, clothes in hot dryer, no outdoor pets in the bed.

Environmental exposures

eEMFs ~

- Don’t appear to accumulate, so the goal is to continue to minimize exposure.
- Protect sleep - sleep sanctuary (canopies)
- Mitigate device exposure (grounding mats, blocking pads)
- Some benefit from a reset of their cellular calcium channels (see the Footbath treatment next.)

Mold ~

- Avoidance sufficient for about half.
- Others need treatment for both respiratory and non-respiratory sequelae.

Glyphosate, channelopathies, and ionic foot baths

Channelopathies, or “clogged” voltage-gated channels. *Different than molecular tollways. Frequency vs chemistry.

Common causes: glyphosate, mold mycotoxins, heavy metals, eEMFs, and excess histamine - possibly also Covid spike protein.

Different kinds of channel disruptors require different ways to bump it out of the cell membrane. The brief on-off polarization during an ionic footbath allows the cell to clean things up from channels related to electrical frequency rather than molecular tollways.

Electrical current delivered via a pad in a bucket of water that the child rests his feet on. The pad emits a biocompatible frequency to create a field of ionization. This ionized field helps to draw oppositely charged particles from ion channels, opens voltage-gated channels, and stimulates an ion flux across cell membranes.
In simple terms, it causes a brief “cell membrane skin” wash.

The color of the water

The water will turn interesting colors. While technicians may attribute different colors to different maladies, I haven't found a direct correlation. I think these claims lead to the discounting of the treatment.

Some also discount this treatment because the water will turn colors even if there aren't any feet in the bucket. *Of course it will.* Polarizing will affect the ions in the water. If anything, this only further proves the MOA.

Protocol ~

For the best effect, treat daily x 3 consecutive days. Take 1-4 days off. On the days off, the child takes an electrolyte formula throughout the day and glycine at bedtime (see the next section, "Glycine"). This pattern can be repeated until glyphosate labs normalize.

May be too intense for some kids. Start with 1 tx and watch for 1 week, then increase.

Improved sxs related to immunity, digestion, and neuropsych.

Glycine to bump glyphosate

Amino acid at the base of the glyphosate molecule.

Glycine ~

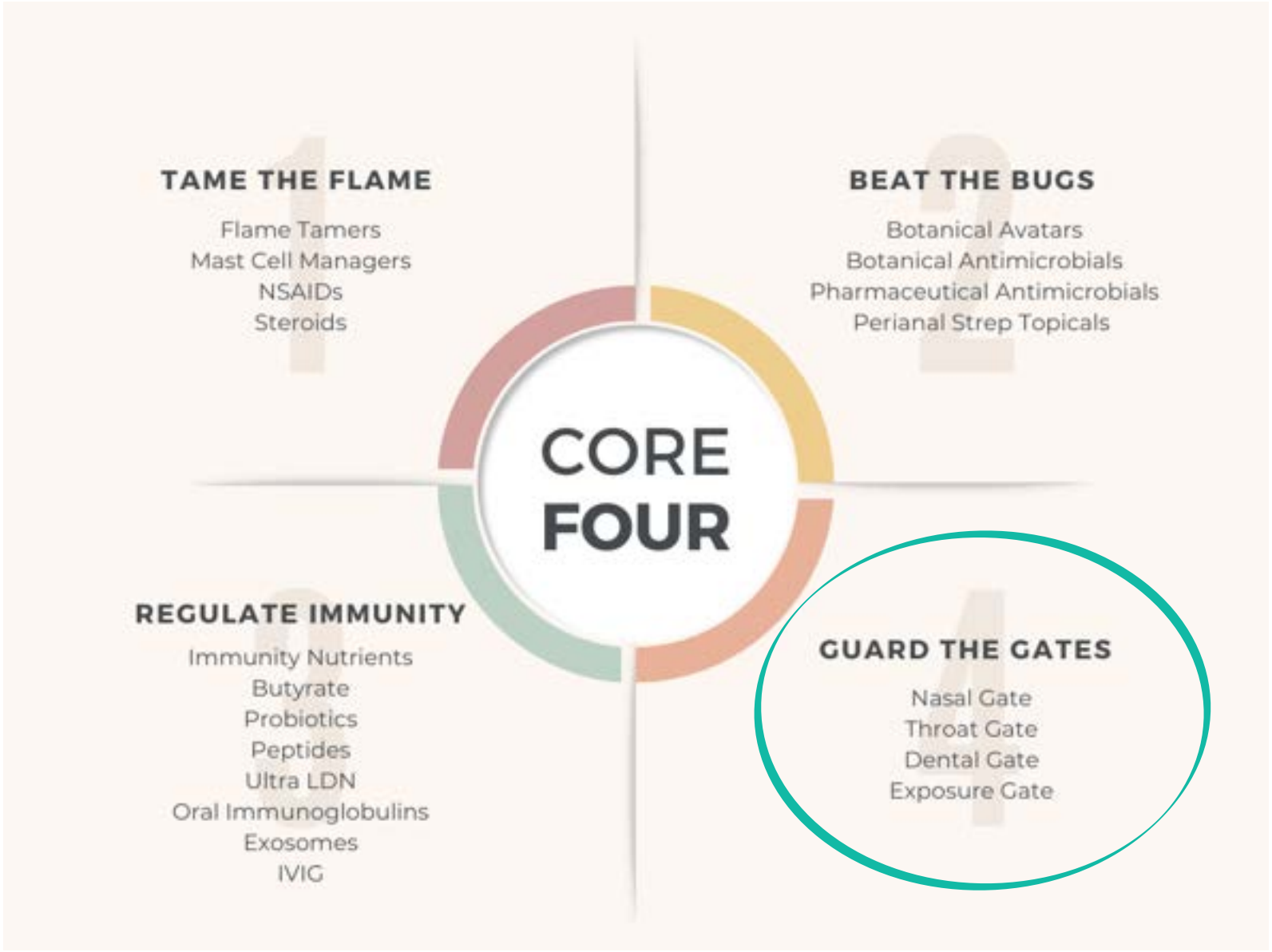
- Inhibitory neurotransmitter
- One of the 3 amino acids that make up glutathione.

Researchers think glyphosate displacing glycine. Goal is to out-compete glycine receptors with more of the glycine form that we want—pure glycine.

Pure glycine has a long history of safe use in kids with anxiety. Sweet on the tongue.

Dosing strategies ~

- Powdered can be placed under the tongue for an immediate anxiolytic effect. Start with a few granules - can cause spaciness and in rare cases is stimulating.
- Up to 1 gram can added to water to be sipped over time.
- Glycine is fast-acting and short-lived.
- Aids sleep-onset insomnia.



Integrative approach

Acute vs chronic presentation

Core 4 ~

- Anti-inflammatories
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- Immune modulation
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Treatment cautions

Then, once out of acute, and in order to prevent/heal, use tools in the next module -

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Treatment cautions

An autoimmune brain works differently than all other brain conditions.

"Good for the brain" doesn't mean it's good for a child with PANDAS or PANS. In fact, it may cause harm.

Different MOA than children with Autism or garden-variety OCD.

Counterintuitive reaction to commonly used substances for stress, brain health, and sleep.

The "Caution" supplements aren't absolute NOs because of the wax and wane pattern of the condition. While they have excess excitatory brain chemistry during flare, between flares, excitatory brain chemistry may tank.

That's when to consider a short-term fix with these supplements.

Be mindful.

Supplement cautions

Avoid ~

Avoid probiotics with Strep strains until we know peptide or protein the I/S is reacting to.

Caution ~

Prebiotics: Often cause gas, bloating, and fungal overgrowth.
Glutamine: Amplifies excitatory brain chemistry, such as glutamate.
NAC: Increases the release of glutamate, an excitatory brain chemical.
Citicoline: Increases dopamine synthesis and inhibits dopamine uptake, leading to further excess of excitatory brain chemistry.
Caffeine: Induces dopamine and glutamate release.
Melatonin: May affect puberty in prepubescent children at higher doses. Use with caution and at lower doses if needed.
Cannabis/CBD/CBG: May cause depersonalization in kids with P/P (remember, an autoimmune brain works differently—imagine an “entourage effect” happening to an obsessive thought.) Also has a mixed effect on dopamine. Extremely dose and form dependent. If used, select only pharmaceutical grade.

Caution Dopaminergics

I generally stay away from the following herbs with PANDAS/PANS kids since we have so many other effective options.

These herbs tend to increase excitatory brain chemistry, especially dopamine (dopaminergic) by either encouraging more dopamine production or reducing its breakdown.

I use caution with the following herbs, and usually avoid their use in PANDAS/PANS:

- Turmeric
- Boswelia
- Schisandra
- Lemon Balm
- Passionflower
- Hops
- Kava kava
- Black cohosh
- Chaste tree berry
- St. Johns Wort

Noni (Morinda) - biphasic effect on dopamine (additional antipsychotic effects:

- attenuates dopa excess at low daily dose
- dopa agonist at high doses

Med Cautions

Disulfiram

Hypomania and psychosis have been reported. Probable Dopamine agonism.

Metabolites ~

Diethyldithiocarbamate (DDC) and its metabolite carbon disulfide (CS2).
DDC chelates copper which impairs the activity of dopamine beta-hydroxylase, which then catalyzes the metabolism of dopa to NE, which causes depletion of presynaptic NE and accumulation of dopamine.

Depletion of NE may also contribute to hypotension in POTS.

~ 2 weeks for full clearance of the drug.

Copper supplementation may alleviate.

Med Cautions

Methylene blue

Commonly used to correct the CDR effects on mitochondria.

Not indicated for P/P kids due to dopaminergic effects; specifically decreases anterior pituitary D2 receptor number with a corresponding reduction in its affinity - insomnia, agitation.

Especially do not combine with SSRIs/SSNRIs - may lead to serotonin syndrome, which may be life-threatening ~
Confusion, agitation, rapid heart rate or changes in blood pressure, fever, nausea, vomiting, diarrhea, muscles spasms, and hallucinations.

PMID: 19760660

Med Cautions

First generation antihistamine

An often missed drug incompatibility SSRIs/SSNRIs with some older generation antihistamines that are available OTC.

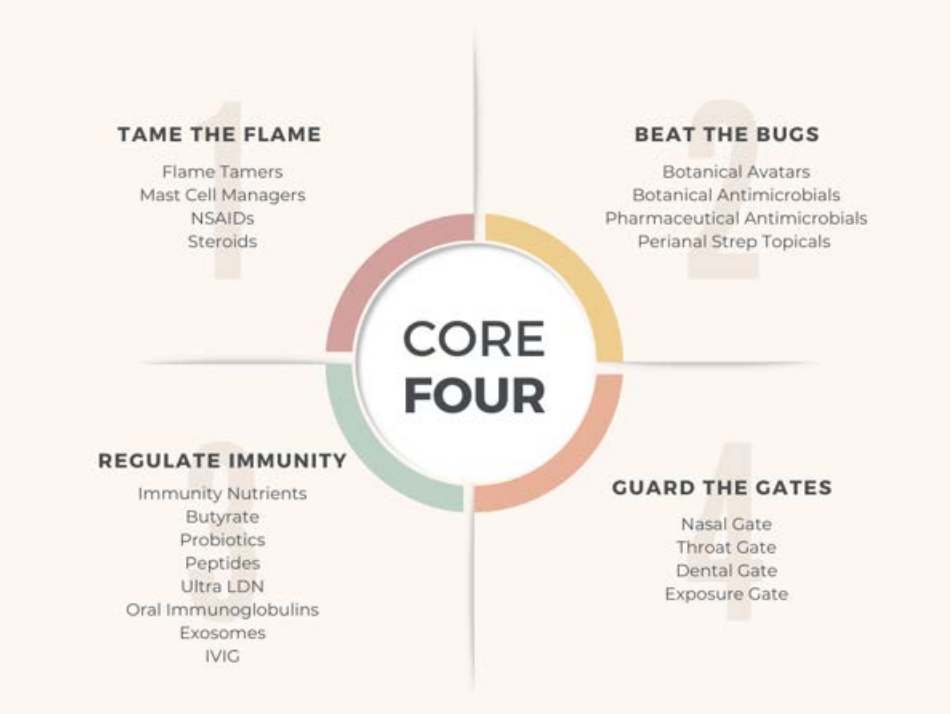
These older drugs are also selective serotonin-reuptake inhibitors, the same mechanism as SSRIs and SSNRIs.

Be cautious of the cough suppressant dextromethorphan and the antihistamine chlorpheniramine with SSRIs and SSNRIs.

Combining these can cause serotonin syndrome, with symptoms of confusion, agitation, rapid heart rate or changes in blood pressure, fever, nausea, vomiting, diarrhea, muscles spasms, and hallucinations.

This may be life-threatening.

Putting It Together



Select 1 Flame Tamer and 1 Mast Cell Manager.

Choose the 1 or 2 Botanical Avatars that fit the child.

Add 1 Botanical Antimicrobial to fit the child's current infection load.

Optimize Vitamin D.

Add Core immune modulation.

Choose 2 methods for each of the Nasal, Throat, and Dental gates.

Explore various ways to close the Exposure Gate, starting with hand-washing (family/caregivers), removing glyphosate and mold, reducing infection exposures.

Assess after 4 weeks, add more support/tweak and/or Rx if needed to any Core area.

(Acute - conventional approach + Guard Gates)

Working the steps

The steps may be done all at once if a child is in crisis.

Ideal: add one thing at a time every 3–4 days to assess (+) or (-) reactions.

Work this plan for a few months, tweaking as needed. Can feel like whack-a-mole for the first 3–6 months, and that's normal.

Expect modifications ~

If histamine turns out to be the main barrier, increase Mast Cell Managers.
If infections keep raising their ugly head, boost antimicrobial support.
If mood, food restriction, or self-harm are a concern, go all out on Taming the Flame while working with a psychiatrist to tweak that part of the plan.

Goal is to stabilize through 2–3 cycles, then wean back to only a few supplements, and eventually use most things on an "as-needed" bases.

Long-term success plan

In this for the long haul.

Expect refusals. It's normal, and actually a good sign they're starting to click in to the world of reality. Unfortunately, the first place children tend to practice this rediscovered skill is with their parents.

Understand that this moment is about the child reclaiming a sense of control, so set it up for success from the beginning. Give the child control over remedy choice—not whether he will take it, but which one he will take.

Start from the beginning by having two options for each item. The child gets to take control over which of the remedies he'd like to take that day. "Do you want this one or this one today?" Set the pattern. It isn't an option to refuse all remedies, only "which" remedy.

When you hear, "I'm not taking that." Be ready with, "Okay, it looks like you're choosing this one instead." And if you still hear, "I'm not taking that either," you're equipped with the knowledge that the hidden goal is control. State that he has a choice.: "It's your choice, this one or this one. Which one do you want? It's in your hands."

And if all else fails, I don't judge parents if they bribe. I did.


Integrative Approach
Next up: Recovery Essentials
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PANDAS & PANS
An Integrative Approach

Dr. Jill Crista

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Recovery
Essentials
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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

Recovery Essentials

Structure

Brain food

Peace of Mind

Dream Team

Structure

Routine Calm

Structural Alignment

Structured Breath

Structure of Movement

Structured Water

Necessity of Nature

Routine calm

Chronobiology: circadian rhythm rebalance - moving with the tide of biology rather than against it.

Routine is a gift to the adrenals, which govern immunity, inflammation, and blood sugar fuel to the brain.

Wake, eat, move, and sleep around the same times each day.

Morning -

- Get outside immediately after waking, before 8am ideal
- Use full-spectrum daylight lightbulbs before 3pm, not after

Timing of meals

Evening -

- Turn lights down
- Turn temp down

Sleep rule “2 before 12”.

PMID: 32130879 When Rhythms Meet the Blues: Circadian Interactions with the Microbiota-Gut-Brain Axis

Structural alignment

Physical structure is something that needs to be constantly realigned in a kid with P/P.

The constant pressure of BGE changes the alignment of the cranial bones, and restricts blood flow in and waste products out.

When the cranial bones are out of alignment, the brain's lymphatics can't drain. The brain's function is also impaired, especially the cranial nerves which govern our senses.

Cervical congestion is also observed.

Also address oral palate narrowing/jaw development/tongue placement - holistic dentist

CST after every dentist visit. Sustained jaw opening amplifies the improper alignment.

Glymphatics drain the brain ~
Dr. Bredesen's latest findings - sleep on side for maximal glymphatic drainage.

Breath

In its protective wisdom, the body adjusted its systems to under-breathe. The brain tells the respiratory system to breathe only enough to survive, not thrive. Why?

Germs and toxins carried in the air may have a free “elevator ride to the brain” via the olfactory nerve.

Many kids need to be taught breathing techniques to resuscitate natural breathing instincts.

Additionally, terror of their thoughts commonly over-rules natural autonomic respiratory rates (sympathetic state.)

Adequate belly breathing engages the vagus nerve. Most kids with P/P hold their bellies too tight to engage their vagus nerve.

Better if exhale is longer than the inhale. Children can hum to help lengthen the exhale.

Breathing techniques can be learned in calm times to prep for crisis moments, and as a quick part of the pre-meal routine to prep the body for eating.

Make breath part of the scheduled structure.

We're made to move

Improved cognitive effects from short bouts of movement (ie: walk to school, recess).

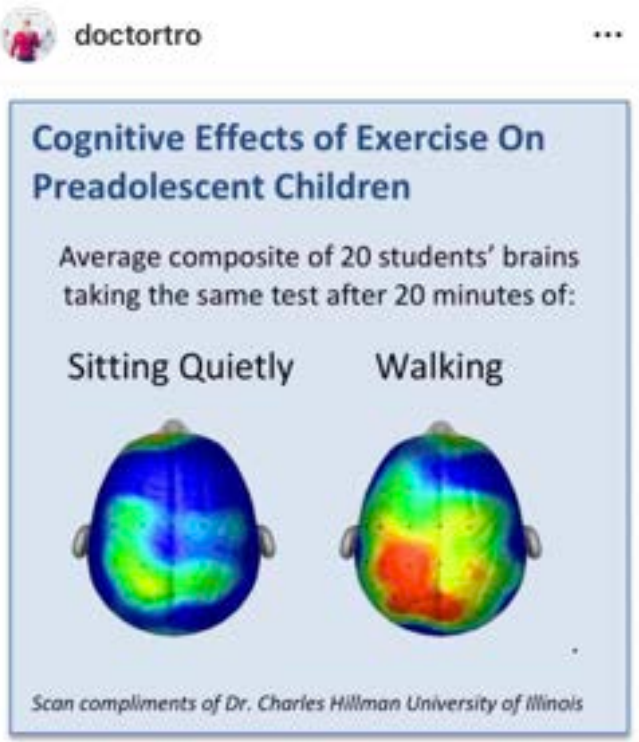
Physical activity has a positive effect on attention.

Additional improvement in academic performance and executive functions (inhibition, working memory, cognitive flexibility and planning.)

Physical exercise inhibits inflammation and microglial activation via neuroprotective myokines.

Exercise facilitates the M1-to-M2 polarization of microglia by enhancing autophagy via the BDNF/AKT/mTOR pathway (in neuropathic pain model.)

Association of calf muscle pump stimulation with sleep quality.



PMID: 19356688, 29054748, 36288601, 31324021, 27686225

Structured water

Water is water is water, right!? Wrong.

A special phase of water (aka the fourth phase or exclusion zone/EZ water) is ordered and acquires features that are different from bulk or liquid water.

The transition of ordered EZ water to bulk water serves as an important trigger of many cellular physiological functions, and in turn cellular health.

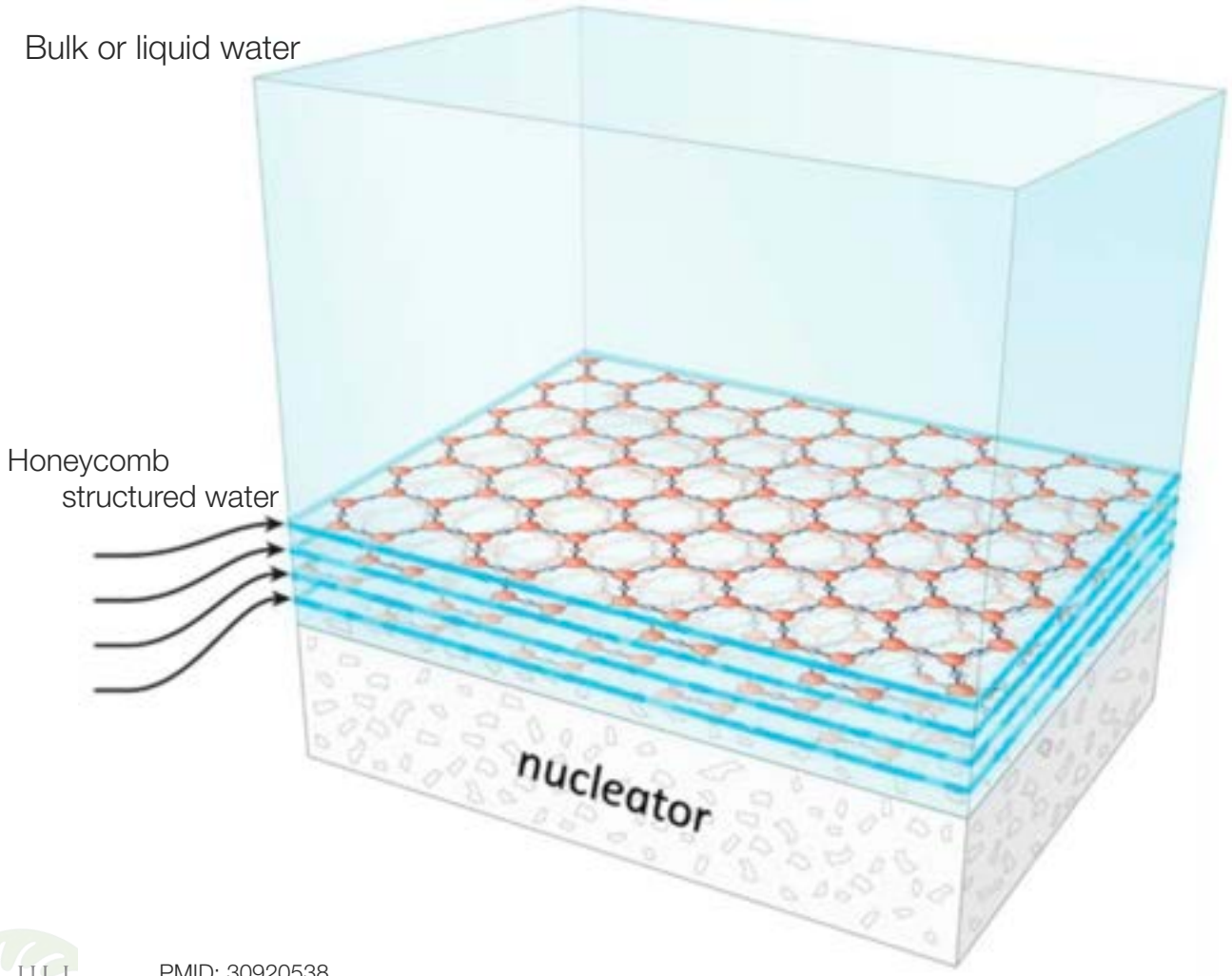
Maintains a unique electrical charge (our battery) and helps conduct the electrical impulses of the brain and nervous system, as well as drive a “current” within our blood vessels, taking the workload off the heart as a pump.

Referred to as exclusion zone water because the structure of the water creates a hydrogel of pure water in the form of H3O2, which not only creates a selectively polarized internal and surface charge, it also excludes colloidal and molecular solutes from extensive regions next to the hydrophilic surface.

Hydrogel water-to-solid ratios sometimes reach tens of thousands to one. *Yet can hold a frequency.*

In nature water becomes structured as it bounces, falls, and squeezes through limestone. We make it intrinsically the same way, by simply moving (ie: rebounder.)

PMID: 30920538, 32708867, 30202249



PMID: 30920538

Agents known to enhance biological function (ie: coconut water, holy basil, turmeric) result in EZ expansion.

Whereas glyphosate considerably diminishes EZ size.

However, while the expansion effect of the health-promoting agents was observed over a wide range of concentrations, excessive doses ultimately reduced EZ size.

PMID: 30202249

Nature is a necessity

Shinrin-yoku or forest bathing/forest medicine = appreciation with all 5 senses.

Increases NK activity, the number of NK cells, and the intracellular levels of anti-cancer proteins.

Reduces BP and HR.

Reduces stress hormones, such as urinary adrenaline and noradrenaline and salivary/serum cortisol.

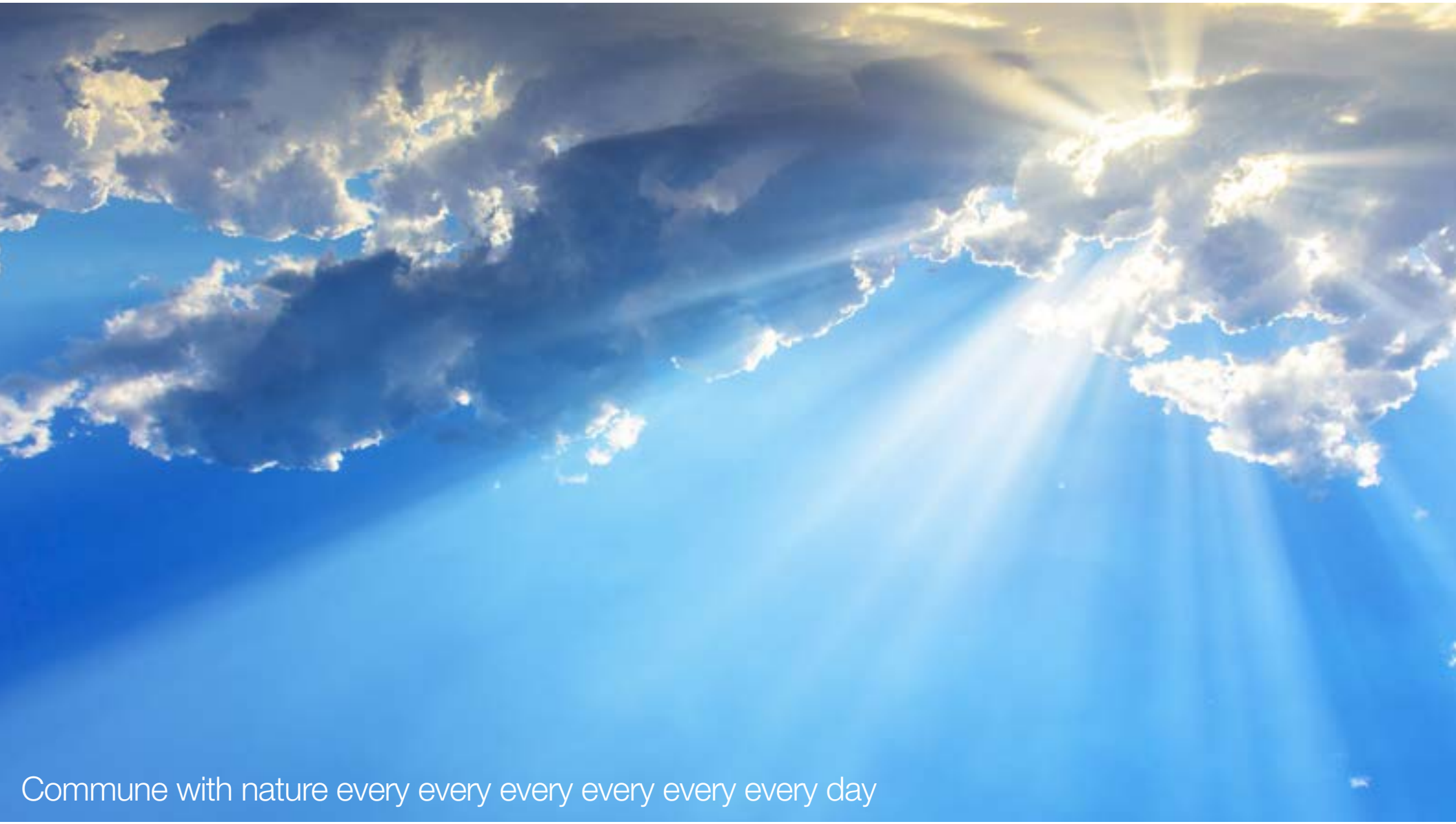
Increases the activity of parasympathetic nerves and reduces the activity of sympathetic nerves to stabilize the balance of autonomic nervous system.

Improves sleep.

Increases the levels of serum adiponectin and dehydroepiandrosterone sulfate.

Reduces the scores for anxiety, depression, anger, fatigue, and confusion, and increases the score for vigor, showing preventive effects on depression.

May have preventive effect on COVID-19 by boosting immune function and by reducing mental stress.


Commune with nature every every every every every every day

Recovery Essentials

Structure

Brain food

Peace of Mind

Dream Team

Brain Food

Organic matters most

Additional dietary considerations

Disordered eating

Joy seeking


Organic!

Additional dietary considerations

Are there additional dietary considerations? Certainly!

*****BUT be cautious of creating issues around food/eating!*****

Diet high in antioxidants are not only beneficial for mental health, they're also protective against pesticides, insecticides, mycotoxins.

Good fats reduce inflammation and nourish nervous system.

Sufficient B-vitamins as psychobiotics.

Sufficient protein prevents blood sugar sweeps. Aim for 1g/kg body weight.

Be mindful of histamine.

Dr. Kharrazian: possibility of food cross-reactivity to cerebellar, myelin basic protein, streptococcus - dairy, eggs.

Timing may be more important than content (intermittent fasting data from earlier - benefits to microbiome-gut-brain axis)

PMID: 32358751, 32340112, 30904906

Extra-virgin olive oil (EVOO)

RCT: 30 pts with impaired fasting glucose (common in food-restrictive kids), receive a lunch with or without **10 g (2¼ tsp) EVOO**.

Markers measured before, 60 and 120 min after lunch:
Serum LPS, Apo-B48, markers of oxidative stress [oxidized LDL (oxLDL) and soluble Nox2-derived peptide (sNox2-dp), a marker of nicotinamide-adenine-dinucleotide-phosphate oxidase isoform Nox2 activation], and plasma polyphenols.

Gut-derived LPSs increase post-prandial oxidative stress via Nox2 activation in patients with impaired fasting glucose tolerance.

At 120 min, LPS (β - 15.73, $p < 0.001$), Apo-B48 (β - 0.14, $p = 0.004$), sNox2-dp (β - 5.47, $p = 0.030$), and oxLDL (β - 42.80, $p < 0.001$) significantly differed between the two treatment groups.

EVOO administration significantly mitigated post-prandial oxidative stress-related inflammation, potentially triggered by LPS.

PMID: 29766292

B-vitamins and the biome

B-vitamins function as psychobiotics.

Are obligate cofactors and co-enzymes for many aspects of the nervous system.

Primary source-diet (we can't synthesize), secondary-microbiome.

Important cofactors mediating multiple metabolic pathways in humans, esp liver detox, neurological health, and I/S surveillance and homeostasis.

Involvement as psychobiotics in brain energetic metabolism (kynurenines/tryptophan pathway) for neurological functions.

Studies exhibit malfunctioning related to deficiency.

Microbiome made up of B-producers and B-consumers.

**B-consumer biome is in competition with our cells for these nutrients.

Can be administered orally or as IM/IV if the child has leaky gut or is restricting food. (Parenting tip: mentioning this option has helped parents get their child to take their B's.)

PMID: 36583209, 36271691, 31058161

B fulfilled

I start with Vitamin B2, Riboflavin ~
Nourishes the brain and nerves, and it has the lowest possibility of causing any kind of reaction.
Typical therapeutic dose is 50 mg daily.

Next, I add Vitamin B6, Pyridoxine ~
High dopamine can deplete Vitamin B6. When this vitamin is low, the brain chemistry shifts to the more excitatory brain chemical glutamate.
Typical therapeutic dose is 100 mg daily.

If a child is struggling with fatigue or nerve tingling, I optimize Vitamin B12, Cobalamin ~
Especially needed if a child has had heavy exposure to silly gas or weed killer. Silly gas forces this vitamin into its inactive form. Glyphosate, the chemical in weed killer, can impair the area of the intestines where we absorb Vitamin B12.
Typical therapeutic dose is 1,000 mcg daily.

In kids who've been exposed to mold, I optimize Vitamin B1, Thiamine ~
Molds emit alcohols that can chew through this vitamin very quickly. Since mold mycotoxins are stored in the fat and cause the most problems there, I use the fat-soluble form called Benfotiamine.
Typical therapeutic dose is 150 mg daily.

Bs may cause nausea, impedes sleep if taken too late in the day.

Histamine

One area where a child might benefit from temporary dietary restrictions, especially if mold exposed.

Histamine intolerance is a very common reason for disordered eating, small appetites, and reactions after eating.

Histamine reactions can happen soon after eating and include ~

Irritability
Redness or flushing
Pruritus
Allergic reactions
Headache
Reflux, nausea or indigestion
Joint pain
Worsening asthma soon after eating

High histamine foods to avoid

Leftovers

Packaged and processed foods

Fermented foods

Aged cheeses

Cured meats

Fruit and citrus juices (except lemon)

Strawberries

Spinach

Raw tomatoes

Vinegar

Soured foods

Fish (flash frozen salmon is okay)

Bone broth

Collagen (also feeds Bartonella)

Disordered eating

By asking why a child isn't eating, we may be able to point to an area of intervention.
Ask why, don't assume.

Fear of Choking ~
Swallowing involves an intricate interplay of nerves and muscles, run right through the area of inflammation in the brain of a P/P kid.
If a child fears choking, it's quite likely a valid fear.
To help kids swallow with more ease, take measures that are used with post-stroke patients, such as puréeing food and adding thickeners to liquids.
This fear gets better as inflammation reduces.

Fear of Contamination ~
Tells you his gates are being breached.
Add measures to Guard the Gates, ie: spices high in Strep-killing essential oils to support the sense of safety in the limbic system to allow a kid to eat.
Add cinnamon to sweet foods, or thyme and oregano to savory foods. Even smelling the essential oils may be enough to give green light to eat.

Disordered eating mechanisms

Histamine Intolerance ~

Feeling sick or fluey soon after eating is classic histamine intolerance.
In these cases, kids will simply avoid feeling bad by not eating. The reactions can be so bad that hunger feels like the least bad option.
Add Mast Cell Stabilizers, such as Perilla and Quercetin/Luteolin, or antihistamine medication 15–20 minutes before eating, while following a low-histamine diet may help.

Mental Health Flare ~

Having mental health flares after eating is a sign that the gut microbiome is disrupted.
Gut-derived exotoxin agitation of the microglia can flare any of the neuropsychiatric symptoms.
The Botanical Avatars Gotu kola and Chinese skullcap reduce gut-derived inflammatory endotoxins such as LPS (lipopolysaccharide), as do Flame Tamers Feverfew and Rosemary. Any or all of these glycerites may be taken 15 minutes before meals to prevent microglial activation.

Disordered eating mechanisms

Belly Pain ~

While you're working on fostering a beneficial microbiome, you may need to soothe an achy belly. Hot or cold teas of mint and ginger not only reduce pain but also inflammation. These are easy additions to mealtimes.

Aloe juice is also soothing, gives the gut immunity a boost, acts as a binder, and comes conveniently as single-serving bottled juices for when you're on-the-go.

Eating-Related Trauma ~

Sometimes the eating issue has been so severe in the past, there's now a lot of "energy" around it. Parents become hyper-aware of intake, and kids can feel it. Kids feel this as pressure and trauma.

Trauma can shut down the vagus nerve.

Humming can turn it back on. Humming stimulates the vagus nerve to induce a feeling of calm and relaxation, and turns on digestion. A happy vagus nerve tells the body it's safe to eat.

Hum for 5-10 minutes before the mealtime. It doesn't have to be constant. Maybe he hums along to a favorite song or as part of a breathing technique. Either way, hum.

Fry an Onion!

Joy seeking

"The web of laughter" ~
Laughter interacts with several frontal and limbic regions, including cingulate, orbitofrontal, medial prefrontal and anterior insular regions involved in interoception, emotion, social reward and motor behaviour.

Humor therapy has been shown to be effective in improving depression and anxiety in those with health problems.

PMID: 36126672, 37340873

Joy is basic nourishment

Play, stories, music, art, dance, sports, animals, games, curiosity, friends, food, photography, creating, unplanned time, jumping on the bed, etc.

Recovery Essentials

Structure

Brain food

Peace of Mind

Dream Team

Peace of Mind

Avoid talking it into being

Mindfulness

Limbic & Vagal

Treat yeast

Neural nutritional support

Homeopathy

Nasal ginsenosides

Addiction

Prisoners in their own minds

Even after the worst of it passes, these children find themselves continuously looking over their shoulder, expecting and waiting for the mind torture to happen again.

The physical change to their brains traumatizes their mental-emotional state.

The images and obsessions playing in a child's mind are frightening, grotesque, and unnerving.

It isn't uncommon for a child to believe her parent has been replaced by an imposter or to have a "daymare" of killing her pet, sibling, teacher, or you—or even harming herself.

It's important to understand the level of trauma a P/P child is living with every day, 24-7.

Mindfulness

For long-term recovery into adulthood, kids with P/P need mental health skills and support. Many of my patients who are now young adults are thriving with this skillset.

Virtual mindfulness resources available for kids, teens, and young adults recovering from P/P, especially those unable to leave their bedrooms.

Interactive practices, mediations, and even online retreats.

Compared to higher-force interventions such as IVIG, you might be thinking, “why bother?” While it might seem too “fluffy”, I can report from working with families that Mindfulness saved the day in more instances than I can count.

Teens often report that the Mindfulness recordings helped their parents also chill out, and that was the medicine needed at the moment.

With practice, Mindfulness can become a stabilizing presence in a child’s *and* parent’s life.

Avoid talking it into being

*Trigger warning to psychologists, psychiatrists, counselors, social workers.

Talking about an intrusive thought will take it from thinking to being. From thought to reality.

Neuroscience is showing that our brains can't tell the difference between concentrated thought and reality. In studies on exercise, people who did concentrated visioning of themselves exercising every day for a half hour, grew muscle on par with those who had actually exercised for a half hour.

Be cautious of growing these unwanted thoughts by talking about them. Their compulsions manage their obsessions. Temporarily, consider letting the compulsions fly. They are a healing salve on the scary thoughts.

Let your child determine the timing. I have seen children who were forced into counseling or prodded to talk about their visions become very unstable and a danger to themselves.

Tame your own curiosity.

Later, after the storm of brain inflammation passes, kids probably will need to talk . . . a lot, and to professionals.

P/P brains are different than externally traumatized brains

I'm not recommending to avoid counseling or psychiatry. They're a key part of the Dream Team (next).

I'm suggesting that you ask that member of your Dream Team to avoid talking the visions into reality with your child. They must contain their academic curiosity and do what's best for the child.

Trauma from PANDAS/PANS is different than historical trauma, because the trauma is happening right now.

The child is IN the war.

We wouldn't sit a child down who's in the middle of a war zone and ask her to rehash the horrific events of that day. We'd spend the time praising her for her strength, reassuring her that it will get better, and consoling her suffering.

There are plenty of other things to talk about. And talking about other things keeps her mental highways open to more flexible thought.

Acknowledge that I'm not trained in psychology or psychiatry. I'm speaking from many heart-wrenching experiences. And if you'd like to understand more, check out Dr. Joe Dispenza's work.

So what CAN you do?

What would you rather think about?

Prompt by parents (and you if handling this part of the Dream Team.)

Will have to do so over and over and over and over again. This very powerful question was taught to me by my mentor and seasoned clinical psychologist, Jan Engels-Smith.

“What would you rather think about?”

Of course if they could, they would be thinking about puppies and unicorns. But their inflamed brains pressure the negative thoughts, compulsions, and visions.

Ask, ask, and ask again. Go ahead. Be annoying. Be a broken record on repeat.

Repeating “what would you rather think about?” keeps the wiring fluid.

They will get mad at everyone for continuously asking. Do it anyway.

Eventually, they’ll start to ask it to themselves.

Limbic retraining with Aromatherapy

Utilizes the olfactory route to effect change in the limbic system.

Mechanisms ~

First-order neurons transmit the odor-evoked response to the olfactory bulb.

In the olfactory bulb, the axons of mitral cells (a) and some tufted cells (secondary neurons) form the olfactory tract.

The axons of some mitral cells or lateral branches enter the anterior olfactory nucleus and pass to the contralateral olfactory bulb.

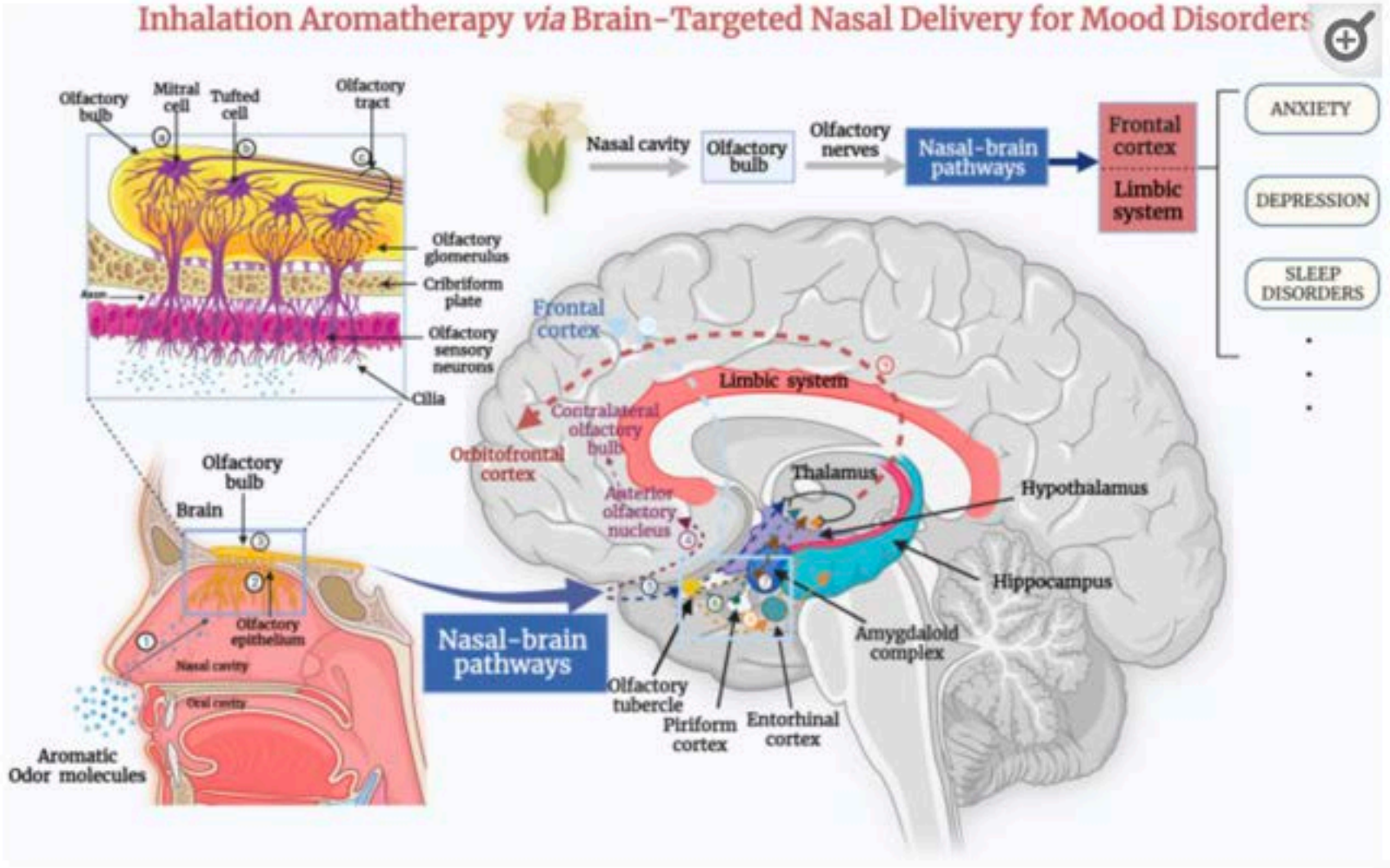
Additional secondary neurons enter the olfactory striatum (medial, lateral, and medial) and then project to central olfactory areas, including the olfactory tubercle, piriform cortex, amygdala, and the entorhinal cortex.

The entorhinal cortex partially transmits to the hippocampus. Eventually, the central olfactory-area signals are transmitted through the thalamus to the orbitofrontal cortex.

An additional olfactory signaling pathway passes directly from the central olfactory area to the prefrontal cortex.

These impulses induce the release of neurotransmitters such as serotonin or endorphin, which act as a “bridge” between nerves and other bodily systems.

PMID: 35496310, 23531112, 30525233, 33411049, 31604545



PMID: 35496310

Limbic retraining

Aromatherapies that have a calming effect and assist in limbic retraining are:

Lavender
Blue tansy
Lemon balm
Bergamot
German chamomile
Black spruce

Use high-quality oils free of pesticides and solvents and store them in glass containers.
Much fewer side-effects than psychotropic drugs.

Additional aids: limbic retraining programs, frequency-specific microcurrent, homeopathy, prayer, and many other modalities available.

PMID: 35496310

Cell danger response

Dr. Naviaux's ground-breaking work using anti-purinergics (suramin - a P2-purinoceptor antagonist) to re-establish cellular safety signals. Suramin Autism Treatment-1 (SAT-1) trial.

Double-blind, placebo-controlled, translational pilot study to examine the safety and activity of low-dose suramin in children with ASD.

Ten male subjects with ASD, ages 5-14 years, were matched by age, IQ, and autism severity into five pairs, then randomized to receive a single, IV infusion of suramin (20 mg/kg) or saline.

75% of the pathways that were altered by suramin in children with ASD were also altered in the mouse models.

Autism Diagnostic Observation Schedule-2 (ADOS-2) comparison scores improved in the suramin group and did not change in the placebo group.

Expressive One-Word Picture Vocabulary Test (EOWPVT) scores did not change.

Secondary outcomes also showed improvements in language, social interaction, and decreased restricted or repetitive behaviors.

Not an approved use in US. It's been used to treat African sleeping sickness (trypanosomiasis) for over 100 years, and remains on the WHO list of essential medications.

No data on PANDAS/PANS.

PMID: 23516405, 28695149

Targeting **P2 receptors in purinergic signaling**: a new strategy of active ingredients in traditional Chinese **herbals** for diseases treatment

PMID: 33751327

Botanical anti-purinergics for CDR

Botanicals that target P2 receptors in purinergic signaling “exhibit superior pharmacological activities on diversified P2R channels.”

Botanical Avatars ~
- Chinese skullcap (Scutellaria baicalensis)
- Astragalus
- Ginsengs

Botanical Antimicrobials ~
- Japanese knotweed

Red sage - Salvia miltiorrhiza (Dan shen)

Sweet Annie - Artemisia annua (Qinghao)

Rhubarb - Rheum palmatum (Dahuang)

Ligusticum walliichi (Chuan xiong) (may be called Sichuan lovage root)

Gardenia jasminoides Ellis (Zhizi)

Ginger - cholinergic activity as well

PMID: 29795391, 33751327, 27002391, 25752193, 32441354

Vagus nerve stimulation

"When the CDR is chronically activated, the coordination between the two limbs of the vagus nerve is disrupted."

Humming, laughing, gargling, vocalizing, belly breathing.

Safe and Sound Protocol - suitable for children. Listening with headphones. Non-invasive acoustic vagus nerve stimulator and builds sense of safety. Can be delivered in-clinic or remotely.

Transcutaneous vagal nerve stimulation (tVNS) - may alter the functions of the limbo-cortical and peripheral networks underlying the hyperarousal component of PTSD and thus improve patient health and well-being. Suitable for children with refractory epilepsy. P/P kids?

PMID: 28824913

Yeast is a mental beast

Animal models: C. albican infection aggravates neuroinflammation via CNS dissemination and local induction of encephalitogenic cytokines.

Clinical pearl ~

If things are going sideways, make sure the child doesn't have yeast overgrowth. Yeast overgrowth is often missed, and it predictably messes with a child's mental game.

If found, treat it aggressively and for longer than you think is needed. Die-off symptoms after initiating antifungal therapies are diagnostic.

Many Candida strains are resistant to current medications. Combining herbs, such as garlic, with the medications can reduce resistance.

PMID: 34901093, 28584446, 25969836

Neural support

DHA ~ (Docosahexaenoic acid)

Helpful with mold exposure. Protects the brain, nervous system, and eyes from mycotoxin effects.
Therapeutic dose is up to 3 grams daily until symptoms reduce, then maintenance dose of 500 mg daily.
Vegetarian sources from algae.

PQQ ~ (Pyrroloquinoline quinine)

CoQ's cousin. Improved function of the mitochondria, heart, and brain.
Helps with learning, memory, and reduction of brain fatigue.
Protects the brain from the damage of excess excitatory NTs during flares.
Nourishing the brain with PQQ during a flare can prevent the post-flare exhaustion.
Therapeutic dose is 20 mg daily.

Phosphatidylserine ~

Important for proper brain function. Gets used up in kids with P/P. Phosphatidylserine blocks excessive amounts of excitatory brain chemistry.
Repairs and prunes neuronal circuits, thereby keeping a focus on desired nerve tracts to reduce brain chaos. Results in improved focus and better sleep.
Therapeutic dose is 100 mg in the morning and 200 mg before bed. In rare cases, it can initially cause insomnia while the low tank is filling.

PMID: 23686346, 24755484, 34585770, 32657463

Inositol

Though not technically a B-vitamin, it's often referred to as Vitamin B8.

Particularly helpful for severe OCD and tics, especially where sleep is a struggle.

Typically use the myo-inositol form.

Therapeutic dose is much higher than other B-vitamins at 3,500 mg taken bid.
Powdered form very well tolerated.

PMID: 21352883, 32215361

Low-dose lithium

Lithium is a natural element. Stigmatized due to high dose Rx use for bipolar disorder and mania.

Can be toxic in high doses. Must be monitored with regular blood testing. But the low-dose version can be used safely OTC for mood stabilization in kids with P/P.

Low dose has subtle mood-elevating effect, anti-neuroinflammatory effects, and lesser known mitochondrial activation effects (CDR).

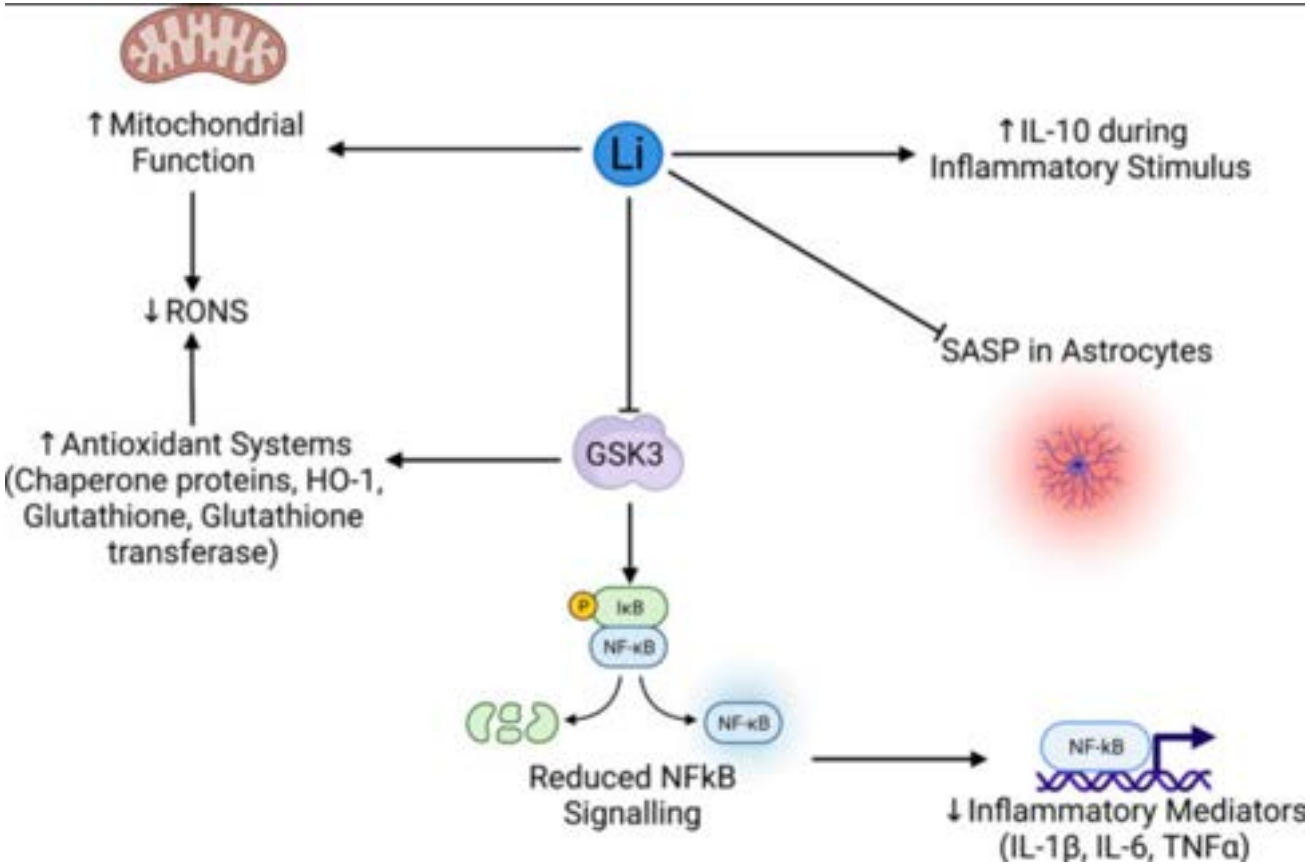
Pool story: Changing nothing else with their child's regimen, a family changed their pool chemicals to a mineral blend based around lithium. Within days, their child became stable and a pleasure to be around. Nearly a month after the pool had to be winterized, she relapsed. We tried low-dose lithium, and the stable child returned.

A systematic review reported that across studies, LDL was reported to be safe.

A*dult* therapeutic low-dose is 10 mg taken twice daily, best taken earlier in the day.

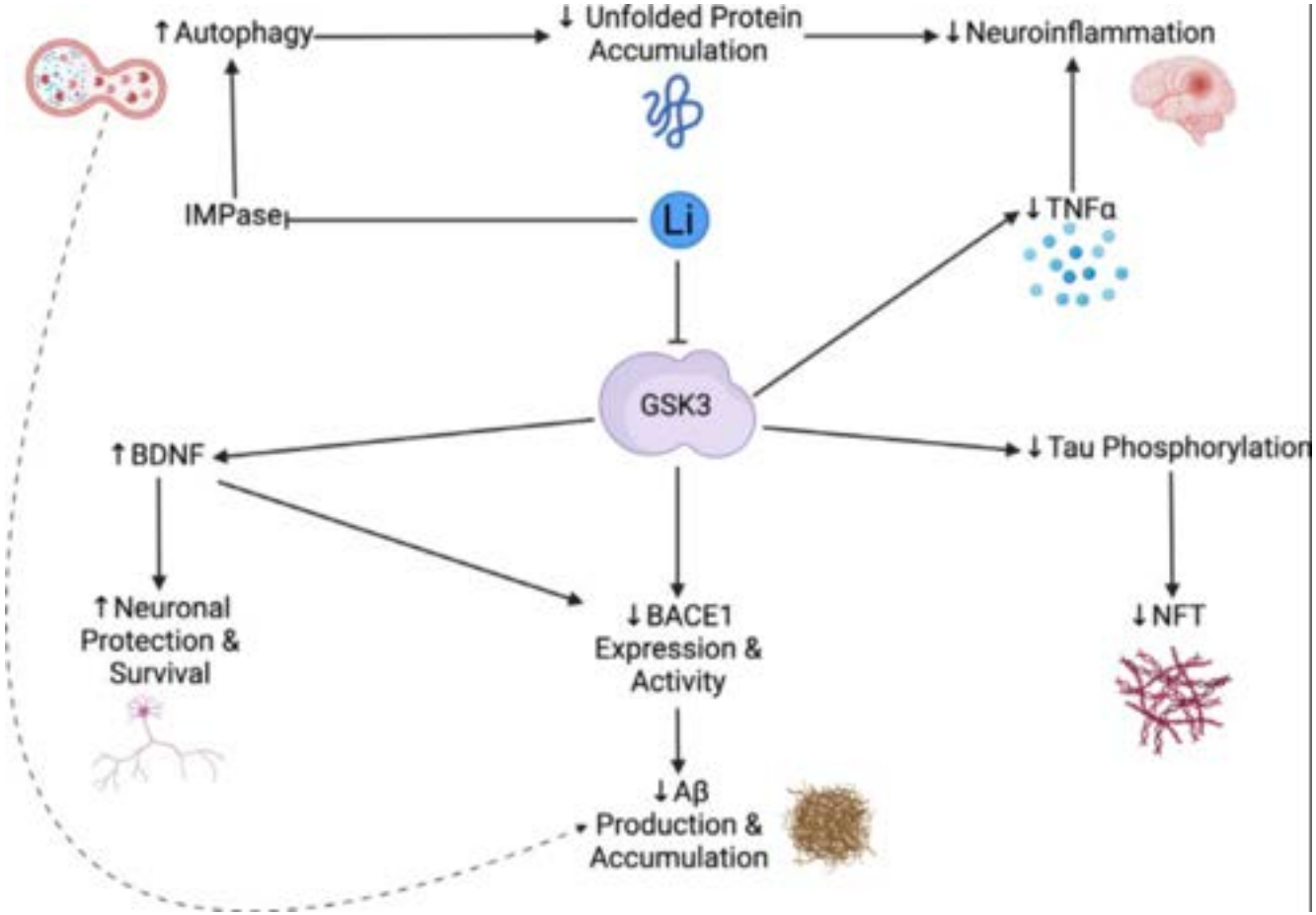
One caution with Lithium is that it has a litany of drug interactions, even in low doses. Check the Medication Compatibility Chart.

PMID: 35236261, 36436738



Lithium increases mitochondrial function, reduces inflammation, and protects the BBB

PMID: 35236261



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Lithium reduces neuroinflammation and induces BDNF

Homeopathy

Homeopathy uses the principles of “like cures like” and the “law of minimum dose.”

The principle of “like cures like” states that a substance, which in large doses would cause similar symptoms to the patient, is then administered in minute amounts to treat the same symptoms. Hence like cures like.

The “law of minimum dose” says that the more minute the amount of a substance, the greater will be its therapeutic effect.

“It’s as if we give the body a red herring reason that it’s upset, so it has something to organize a response around. In other words, we tell the body it isn’t mad at brain cells, it’s actually mad at the remedy. And since it’s in such a small dose, the body gets to be successful, and fully resolve the issue. This is very calming to a body, and a brain.”

List in handouts - not an exhaustive list but a place to start.

Extremely easy and safe to use with kids of all age. Can be administered on sugar pellets or in a little sip of water held in the mouth for 30 seconds. I usually use the 30c OTC potency with P/P kids.

To prevent “discharging” the remedy, here are some guidelines:

Storage: Do not expose to cell phone or microwave radiation, or full-strength essential oils
Pellets: Do not touch them before popping them under your child’s tongue
Liquid: Use a glass cup only

Nasal ginsenosides

The “hope hit.” May be used if there’s a mood or energy crash after a flare. Nasal spray is fast acting.

Compounded blend of ginseng extracts and nicotinamide riboside. Ginsenosides from ginseng are the very parts that make a Botanical Avatar work so well, the triterpenoid saponins.

Ginsenosides protect the brain from excess excitatory brain chemicals, reduce microglial activation, and restore normal brain neuron function.

Has an effect on the same ion channels affected by glyphosate. Is a perfect follow-up nasal spray for kids who play outdoor sports on chemically-sprayed fields.

Healing to tissues. The more it’s used, the less it’s needed.

Cautions ~

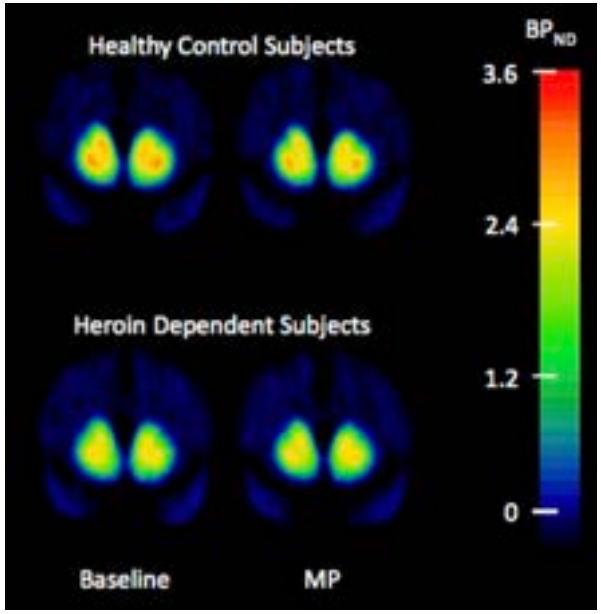
In some children, this has a very stimulating effect. Start by using it in the morning only, with the lowest dose, and in only one nostril to test it out.

Some compounding pharmacies combine this with methylcobalamin. If a child has methylation issues, skip or substitute with hydroxocobalamin.

PMID: 28412215, 24678300

Addiction

Dopamine receptors



Extremely high risk of addiction based on chemistry and structural changes in the brain.

Chicken or egg?

PET imaging studies have shown that addiction to a number of substances of abuse is associated with a decrease in dopamine D(2/3) receptor binding and decreased presynaptic dopamine release in the striatum.

Not just substances - screens/gaming, gambling, high-risk behaviors, etc.

If opiate, encourage appropriate MAT tx, ie: buproprion treatment. If trained properly, can be done in your office (if not addiction or psychiatric clinic, bypasses some FDA reporting/charting requirement.)

PMID: 22015315

Recovery Essentials

Structure

Brain food

Peace of Mind

Dream Team

Dream Team

Beliefs

Parent, caregiver, and sibling support

Medical support village

Yes, their world gets smaller

False belief ~
smaller = less support

Parents need to be given permission to rewrite that belief.

Their child can have disruptive behaviors AND they can be supported.

Parents, caregivers, and siblings

Check on how they're doing. Like, really…how.

Spend time in the appointment on them and developing their support plan.

Set up the Dream Team (the medical support team) for the sick child, but don't forget the other members of the family.

Siblings are often missed collateral damage. Have suffered a "death loss", and chaos, and loss of parents. Discuss with the parents about sibling support.

Excellent book for siblings by Dr. Lindsey Wells ~
"Super Sam! and the battle against PANS/PANDAS"

It takes a medical support village

Naturopathic/Functional Medicine Doctor

Allergist/Immunologist

Neurologist

Psychologist/Psychiatrist

Nutritionist

PANDAS/PANS-Aware Dentist

CranioSacral Therapist

School Nurse

Homeopathic Practitioner

Spiritual/Energetic Practitioner

Intention of collaboration

Setting the intention for collaboration among the healthcare Dream Team members STARTS WITH YOU.

Be mindful of unintentionally putting the parents in the middle of a difference of opinion of practitioners.

Pick up the phone/video and have a real conversation with the other practitioner.

Collaboration doesn't require agreement, but does require mutual respect and humility.

No standard of care due to lack of clinical trials. "Our review highlights the need for a comprehensive algorithm…" - meaning that none of us has "the only way".

Collaboration is essential for the child's recovery and trust.

Trusted practitioners become valuable allies in the child's life as he grows into adulthood.

PMID: 37251418


Recovery
Essentials
Next up:
Cases
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PANDAS & PANS
An Integrative Approach

Dr. Jill Crista

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Cases

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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**

Success Plan

Set your parents up for success from the beginning. Like it or not, they're in this for the long haul.

Expect the child/teen to refuse treatment. It's normal, and actually a good sign - starting to take their power back, click in to the world of reality. And unfortunately, the first place children tend to practice this rediscovered skill is with their parent.

Refusal moments are the child reclaiming a sense of control.

Give the child control over remedy choice—not whether he will take it, but which one he will take.

Start from the beginning—have 2 options for each item. The child gets to take control via choice. "Do you want this one or this one today?" Set the pattern. It isn't an option to refuse all remedies, only "which" remedy.

When you hear, "I'm not taking that." Be ready with, "Okay, it looks like you're choosing this one instead." And if you still hear, "I'm not taking that either," you're equipped with the knowledge that the hidden goal is control. State that he has a choice.: "It's your choice, this one or this one. Which one do you want? It's in your hands."

And if all else fails, I never judge if they bribe. I did.

Core 4 Variety

Four different PANDAS/PANS kids from my practice, named for the biggest pain point for the child:
Anxious, Starved, Insomniac, and Strep-Magnet.

Each are different in how I chose the specific Cores of treatment.

I often add extra nutrients such as the things in Recovery Essentials, but these display how to apply the Core 4.

Anytime you see individual glycerites listed, they usually were mixed together whenever they could be dosed at the same time. That allows parents to focus on getting one remedy down rather than five.

Anxious

Anxious had compulsions that made learning and socializing difficult.

Very concerned about infection exposure. (Sign of low immunity and breeched barriers.)

Focused on remedies that reduced anxiety and brightened the mind.

The herb combination is a daytime combination and not suited for bedtime, unless noted.

Mixed the herbal glycerites and divided in half, flavoring each with his chosen flavors—one mint and one ginger. (Build in the control over choice.)

Dosed by weight at Flare dose until fears calmed + 2-3 weeks.

Tame the Flame:

Flame Tamer: Resolvins in the morning, Rosemary (added as glycerite to the Avatar formula taken in the morning, at lunch and after school/before dinner.)
Mast Cell Managers: Vitamin C (anytime of day), PEA in the morning.

Anxious, cont

Beat the Bugs:

Botanical Avatars: Brahmi, Thorough-wax, Gotu kola
Botanical Antimicrobial: Japanese knotweed
(Mix above as a glycerite to take in the morning, at lunch, and after school/before dinner.)
Black elderberry syrup after dinner.

Regulate Immunity:

Vitamins A + D weekly
Butyrate after dinner (Self-conscious of “fart breath”, so took it at night.)

Guard the Gates:

Nasal essential oil inhalation stick every morning on the way to school, repeat whenever he feared exposure.
Nasal probiotic swab every evening after brushing teeth.
Sage tea gargle after brushing teeth in the morning. (Parents made a batch every week and kept refrigerated. A ½ cup was taken out the night before and set by the bathroom sink.)
Switch to xylitol toothpaste.

Starved

Starved had a fear of choking, feeling like she couldn't swallow correctly.

She was hungry but couldn't eat.

She'd also have histamine flares after eating, so many of her remedies were taken 15 minutes before eating.

Also added blended soups, ground up meats, and used thickeners for fluids to help her swallow.

Had a persistent Strep presence which turned out to be due to perianal Strep and mold exposure. Once addressed, her eating difficulties went away.

Tame the Flame:

Flame Tamers: Feverfew and Rosemary added to glycerite and taken 15 minutes before eating.

Mast Cell Managers: Liposomal Quercetin/Luteolin, DAO taken 15 minutes before eating.

Starved, cont

Beat the Bugs:

Botanical Avatars: Gotu kola, Chinese skullcap, Oregon grape, Brahmi taken 15 minutes before eating.

Botanical Antimicrobials: Oregano, Licorice, Black walnut pulsed on the weekends.

Perianal Strep: Topical silver cream qd.

Regulate Immunity:

Butyrate, Colostrum and Peptides mixed together and taken in the morning and night.

Guard the Gates:

Nasal propolis spray twice daily.

Propolis throat spray twice daily. (Gargles are hard for kids with swallowing difficulties. Their choking fear amplifies. It's kinder to use sprays.)

Switch to Dentalcidin toothpaste.

Insomniac

This poor guy could NOT sleep. Anytime someone in the house got a little sniffle, he'd be up all night.

Focused his formulas on afternoon and nighttime dosing, with a little extra antiviral kick.

Tame the Flame:

Flame Tamers: Resolvins, Feverfew (added to above glycerite formula)
Mast Cell Manager: Vitamin C

Beat the Bugs:

Botanical Avatars: Silk tree, Chinese skullcap, Oregon grape, Magnolia taken at 4pm and 6pm, and added 9pm if still awake.
Botanical Antimicrobials: Licorice tea in the morning.

Insomniac, cont

Regulate Immunity:

Vitamins A + D weekly.

SEAZnDCK whenever someone else at home was sick.

Guard the Gates:

Nasal colloidal silver in the morning.

Thyme steam inhalation as part of the bedtime routine. (He found this very relaxing. Parents made 1 gallon once per week, pour out enough for the steam, and microwave it in the bowl to be used for the steam treatment.)

Switch to Myrrh toothpaste.

Strep Magnet

The name explains it all. This was a very sick boy. He wasn't able to attend school or soccer after PANDAS/PANS hit. An example of how to combine naturopathic medicine with antibiotics and IVIG.

Severe compulsions, mood issues, and tics, as well as trouble eating and sleeping. Due to pretty hefty environmental exposures from weed killer on his soccer field and mold in his home, we needed to begin with a heavier medical intervention.

Tame the Flame:

Flame Tamers: Vitamin C, Resolvins, Feverfew (higher as steroids wore off).
Mast Cell Managers: Quercetin/Luteolin
NSAIDs: Ibuprofen on a 2-week suppressive course, then prn.

Beat the Bugs:

Botanical Avatars: Oregon grape in the morning with Augmentin, Silk tree in the evening with Augmentin.
Botanical Antimicrobials: Thyme twice daily added to each glycerite below for Strep and fungal overgrowth.
Pharmaceutical Antimicrobials: Augmentin 875 mg twice daily. Itraconazole pulsed.

Strep Magnet, cont

Regulate Immunity:

- Vitamin D: Daily dosing for more stable protection.
- Butyrate (to compensate for lowering effect from Augmentin): Twice daily with Augmentin.
- Probiotics: Once daily away from Augmentin by 1 hour.
- Peptide - BPC 157: Twice daily.
- Ultra-Low-Dose Naltrexone: Taken in the evening.
- IVIG: 1.5–2.0 g/kg over 2 consecutive days, every 6 weeks. Co-administered IV steroids, diphenhydramine, and ibuprofen.

Guard the Gates:

- Colloidal silver nasal spray in the morning.
- Nasal probiotic swab in the evening after brushing teeth.
- Switch to Dentalcidin toothpaste.

Strep Magnet, cont

He also benefitted from an ultra-low dose of sertraline. Later, we found he had Bartonella, so we added Cryptolepis twice daily at the same time as the Augmentin. Once Bartonella was addressed, he no longer required the sertraline.

I'm happy to report that this boy is now a man. He has graduated from technical college and is enjoying independent living with a little extra support from his parents when needed.

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7. Cases

Integrating Therapeutics → Family Bliss!

Neuroimmune Foundation
neuroimmune.org

Northwest PANDAS/PANS Network
nwppn.org

PANDAS Canada
pandascanada.wixsite.com/pandascanada

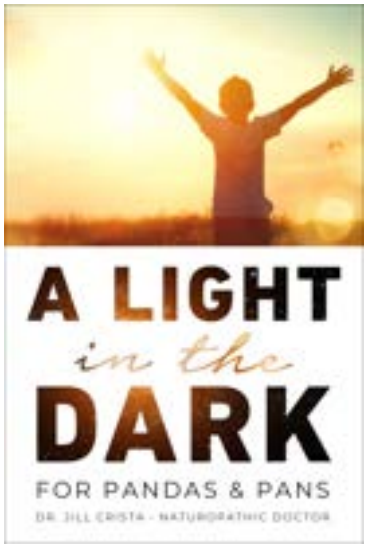
PANDAS Italia
pandasitalia.it

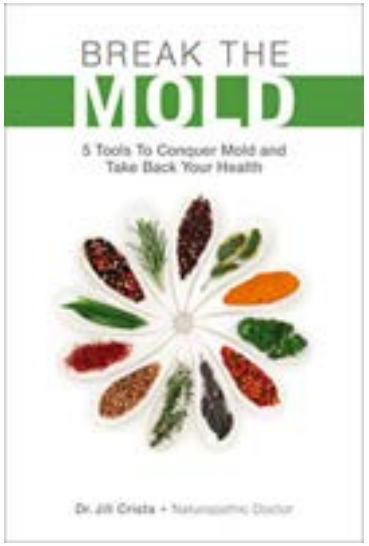
PANDAS Physicians Network (parent version available)
pandasppn.org and pandasnetwork.org

PANS PANDAS UK
panspandasuk.org

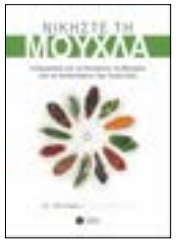
SANE (PANDAS Sweden)
sane.nu

Books





Greek



Chinese

Polish

German

Education

For the public ~

For medical practitioners ~

Prerequisite training for our mentorship is the basic training via the mentorship or my mold certification course (accessible on my website.)

Email askdrnathan@gmail.com for details.

Other books & trainings ~

Neuroimmune.org

MAPS conference

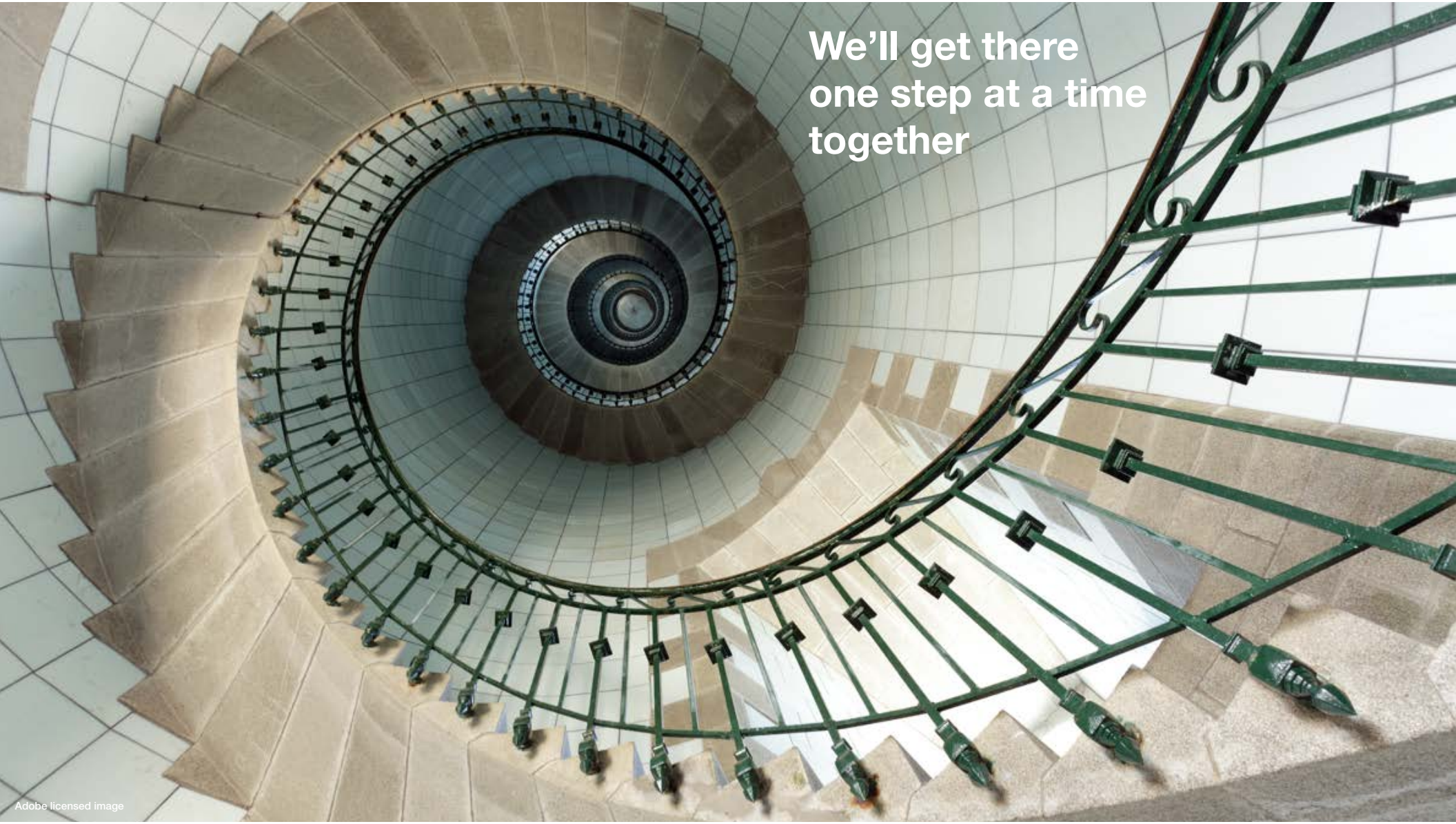
PANDAS Physician Network conferences

Mentorship with Dr. Nancy O'Hara

Book by Dr. Nancy O'Hara
Demystifying PANS/PANDAS

Book by Dr. Kenneth Bock
Brain Inflamed

Book by Dr. Angelica Lemke
Healing Complex Children with Homeopathy


We’ll get there
one step at a time
together
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Vierge Lighthouse in Brittany

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