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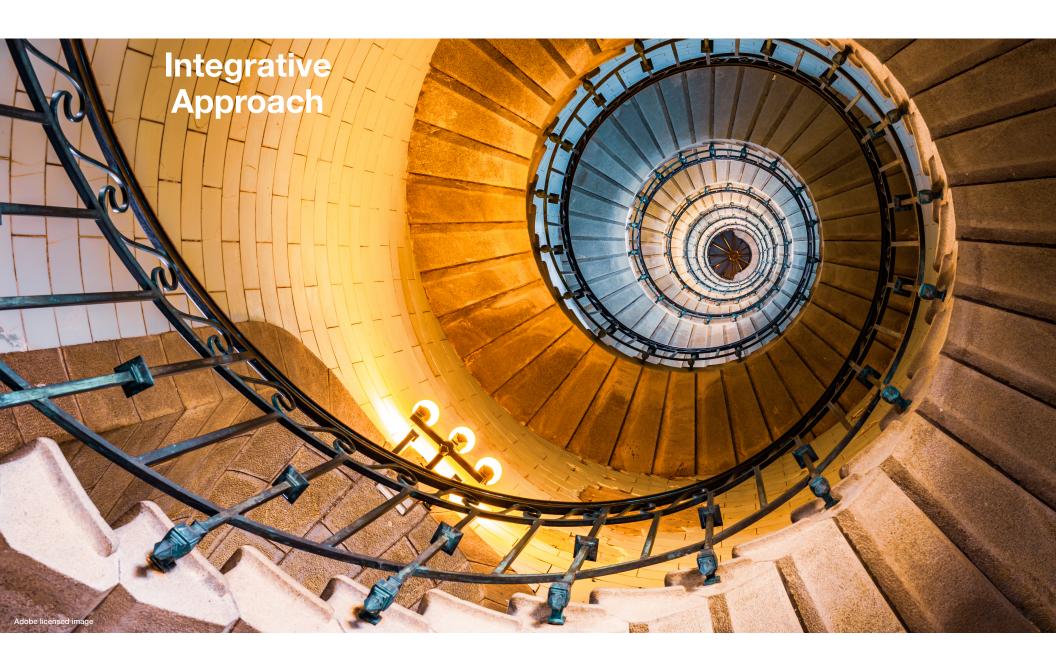
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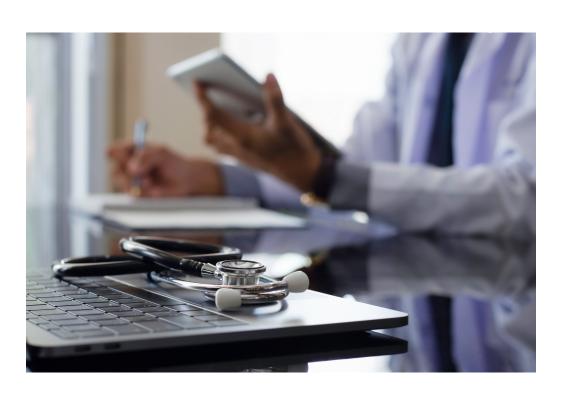
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## **Course Outline**

- 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**

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	Modication Compatibility Criait							
	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	*	*	*	-00-	*		*	.₩
Black walnut	0	<u></u>	<u></u>	<u> </u>	<u></u>	<u></u>	*	÷
BPC-157 peptide	de la	uls.	de la	de	ulg	de	*	de la companya della companya della companya de la companya della
Brahmi	*	*	*	*	*	*	*	÷
Butyrate	*	*	*	-\$-	*	÷		÷
Chinese skullcap	_	_	_	_	_	_	*	.₩
Cryptolepis	_	_	_	_	_	_	_	_
DAO (diamine oxidase)	*	*	*	÷	*	÷	de	4
Echinacea	*	*	*		*	*	*	*
Feverfew	*	*	*	*	*	÷	*	*
Glycine	*	*	*	-\$-	*	*	*	<b>.</b>
Gotu kola	*	*	*	÷	*	÷	*	*
Immunoglobulins (oral)	ale .	de	de	de	ale	de	de	de
Inositol	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	•
Japanese knotweed	_	_	_	_	_	_	_	_
Licorice	*	<u></u>	<u></u>	<u> </u>	*	*	*	<b>.</b>
Lithium (low dose)	<u> </u>	<u> </u>	<u></u>	<u> </u>	<u> </u>	<u> </u>	<u></u>	<u></u>
Luteolin	<u> </u>	<u> </u>	<u> </u>	<u>@</u>	<u> </u>	<u>@</u>	de	de
Magnolia	*	*	*	<b>\$</b>	*	*	*	*
Oregano	*	*	*	*	*	*	*	*
Oregon grape	*	*	*	-Q:	*	.⇔	*	*

A living document Updated as new

information becomes available.

Beneficial to co-administer 🝁

No negative interaction <sup>(1)</sup>

Evidence suggests low risk of interactions 🌣

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 S

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 1<sup>th</sup> 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

This table does not apply to women who are pregnant or nursing.

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# 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.



#### TAME THE FLAME

Reduce autoimmune damage, microglial activation, and mast cell infiltration

#### **BEAT THE BUGS**

Prophylactic and active treatment of existing infections

# CORE **FOUR**

#### **REGULATE IMMUNITY**

Bolster the immune system and increase beneficial microbiota of the gut microbiome

#### **GUARD THE GATES**

Prevent exposures to respirable and dental infections and toxicants



## 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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#### TAME THE FLAME

Flame Tamers Mast Cell Managers NSAIDs Steroids

#### **BEAT THE BUGS**

Botanical Avatars Botanical Antimicrobials Pharmaceutical Antimicrobials Perianal Strep Topicals

# CORE **FOUR**

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes

IVIG

#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



# Putting It Together

TAME THE FLAME **BEAT THE BUGS** Flame Tamers **Botanical Avatars** Mast Cell Managers **Botanical Antimicrobials NSAIDs** Pharmaceutical Antimicrobials Steroids Perianal Strep Topicals CORE **FOUR** REGULATE IMMUNITY **GUARD THE GATES Immunity Nutrients** Butyrate Nasal Gate **Probiotics** Throat Gate Peptides Dental Gate Ultra LDN **Exposure Gate** Oral Immunoglobulins Exosomes IVIG

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** 

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## 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



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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"



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 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-kB 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

Core 4 ~

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#### TAME THE FLAME

Flame Tamers
Mast Cell Managers
NSAIDs
Steroids

#### **BEAT THE BUGS**

Botanical Avatars Botanical Antimicrobials Pharmaceutical Antimicrobials Perianal Strep Topicals

# CORE **FOUR**

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes

IVIG

#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



# 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)



# 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.

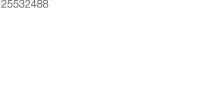
GI protective ~ anti-inflammatory, preserves the length of intestinal villi and mucosal thickness, increases the production of butyrate, improves gut dysbiosis in antibiotic-treated mice.

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





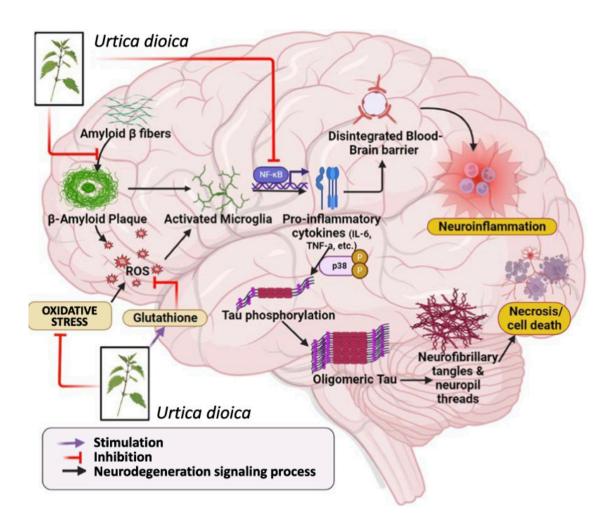




Fig. 2 Potential neuroprotective mechanism of action of U. dioica and of its components PMID: 37171512

## 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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Steroids

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# CORE FOUR

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes

IVIG

### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



# Putting It Together

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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.

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(Acute - conventional approach + Guard Gates)



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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- $\beta$  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





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#### TAME THE FLAME

Flame Tamers
Mast Cell Managers
NSAIDs
Steroids

#### **BEAT THE BUGS**

Botanical Avatars Botanical Antimicrobials Pharmaceutical Antimicrobials Perianal Strep Topicals

# CORE FOUR

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes
IVIG

#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



## 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: 1/4 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: 1/4 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.





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### 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



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#### TAME THE FLAME

Flame Tamers
Mast Cell Managers
NSAIDs
Steroids

#### **BEAT THE BUGS**

Botanical Avatars Botanical Antimicrobials Pharmaceutical Antimicrobials Perianal Strep Topicals

# CORE FOUR

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes

IVIG

#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



## 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





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#### TAME THE FLAME

Flame Tamers
Mast Cell Managers
NSAIDs
Steroids

#### **BEAT THE BUGS**

Botanical Avatars Botanical Antimicrobials Pharmaceutical Antimicrobials Perianal Strep Topicals

# CORE **FOUR**

#### **REGULATE IMMUNITY**

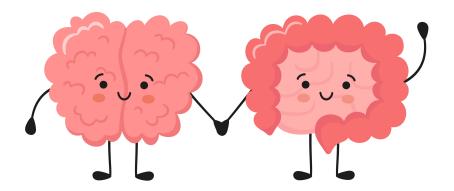
Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes
IVIG

#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



# 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.

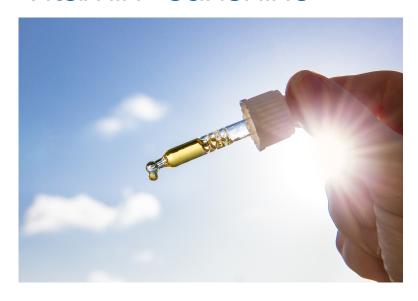
Vit D receptor in intestine & kidney significantly down-modulated after mycotoxin exposure.

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.





A single adult super-dose is 100,000 IU.

Maintenance: dose via labs. 3.33 IU per mcg.

Ages	<b>Upper Limit</b>
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 5hydroxylase 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

On JILL
CRISTA"
NATUROPATHIC
DOCTOR

PMID: 32839473, 37033942, 28443383, 33652962, 18544899, 22384111, 28129335, 24738739, 23030351, 21816119

# Spore-based probiotics

Spore-based probiotic study ~

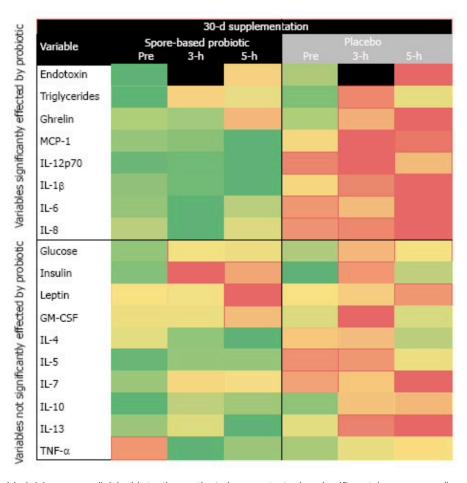
Healthy men and women (n = 75) screened for post-prandial dietary endotoxemia. Subjects whose serum endotoxin concentration increased by at least 5-fold from pre-meal levels at 5-h post-prandial were considered "responders" and randomized to receive either placebo or tx.

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

#### 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



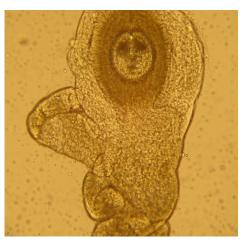


Photo courtesy of https://biomerestoration.com/hdc/

### Effect on host immune cells

Polarization toward Th2 response (preventing Th1 or Th17 immune response) characterized by Th2 cytokines.

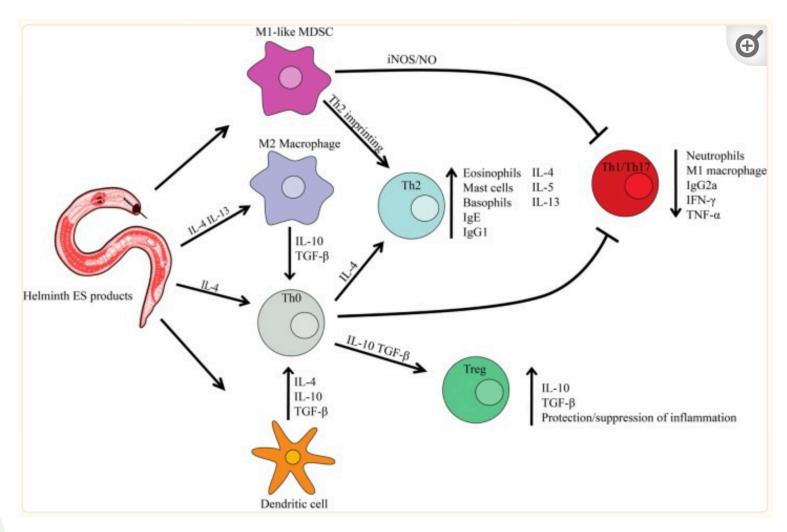
Differentiation of macrophages toward the M2 phenotype, resulting in a Th2 immune response.

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 lg): 1 packet bid

#### Daily:

Colostrum powder, chew, or capsule: 1,500 mg twice daily

IgG capsule: 500 mg twice daily

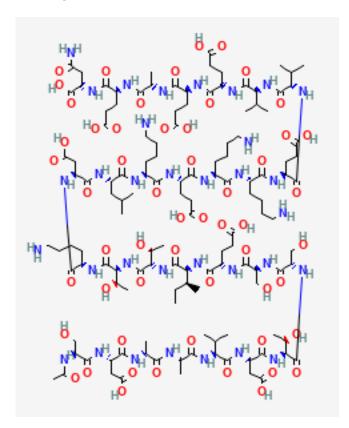
#### Caution:

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-brainimmune 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.





# 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.



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Steroids

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Botanical Antimicrobials
Pharmaceutical Antimicrobials
Perianal Strep Topicals

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# 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





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Perianal Strep Topicals

# CORE **FOUR**

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
Exosomes

IVIG

### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



### **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



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#### 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
- 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.

- 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 neede

\*May irritate eyes. Close eyes to reduce eye irritation.

Check out the How To video on my website DrCrista.com.

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### 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.

On JILL
CRISTA
NATUROPATHIC
DOCTOR

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.



# 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.

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# 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.

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### 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

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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.



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# **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

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# 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

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# **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.



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#### TAME THE FLAME

Flame Tamers
Mast Cell Managers
NSAIDs
Steroids

#### **BEAT THE BUGS**

Botanical Avatars
Botanical Antimicrobials
Pharmaceutical Antimicrobials
Perianal Strep Topicals

# CORE **FOUR**

#### **REGULATE IMMUNITY**

Immunity Nutrients
Butyrate
Probiotics
Peptides
Ultra LDN
Oral Immunoglobulins
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#### **GUARD THE GATES**

Nasal Gate Throat Gate Dental Gate Exposure Gate



# Integrative approach

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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.



