1 **PANDAS & PANS**
An Integrative Approach

- Dr. Jill Crista

2 **Disclaimer**

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- Diagnostics

4 **Overview**

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

5 **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)

6 **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
-

7 **Medication Compatibility Chart**

- A living document
- Updated as new information becomes available.

8 **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.

9 **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.

10 **Integrative treatment overview**

- 1. Guard the gates
  halt T-cell migration to CNS
- 2. Immune modulation
  prevent autoimmune tendencies/gut health
- 3. Address neurotransmitter imbalance
  balance dopa & glutamate to reduce destruction
- 4. Reduce neuroinflammation/leaky BBB

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  get good stuff in and bad stuff out
- 5. Manage trauma/stress
  adrenal/nervous system burnout
- 6. Structural integrity
  chronic brain stem/cervical congestion/jaw development

11 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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14 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)

15 Integrative approach

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17 Flame Tamers

- The target is neuroinflammation, specifically the microglia.
  - Pro-resolving mediators
  - Feverfew
  - Resveratrol
  - Rosemary
  - Pine extract

18 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

19 EFAs are not created equally

- Wild vs farmed salmon
- Poorly fed fish that can't exercise = bad fat
- Fish with bad fat = humans with bad fat

20 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.

21 Feverfew

21 Feverfew

- Tanacetum parthenium ~ leaves and flowers
- Sesquiterpene lactone ~ parthenolide
  (not triterpenoid saponin/avatar)
- Anti-inflammatory and neuromodulatory effects
- “Hormone headaches”
- Ameliorates colon inflammation through regulating Treg/Th17 balance in a gut microbiota-dependent manner.
- Parthenolide inhibits the LPS-induced secretion of IL-6 and TNF-α and NF-κB nuclear translocation in microglia.
- PMID: 32373209, 33374525, 22359368

22 **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.

23 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

24 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

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.
-

25 **Rosemary**

- Rosmarinus officinalis ~ use the needle-like leaves
- Long history of use and benefits in mental health and cognition. Worn as a crown for sharp thinking.
- Rosmarinic acid inhibition of the NLRP3 inflammasome exerts antioxidant, anti-inflammatory, and neuroprotective effects
- Rosmarinic acid regulates microglial M1/M2 polarization under conditions of neuroinflammation
- Rosmarinic acid mitigates LPS-induced neuroinflammatory responses
- Inhibition of the NLRP3 inflammasome. Exerts antioxidant, anti-inflammatory, and neuroprotective effects via phase 2 enzyme induction initiated by activation of the KEAP1/NRF2 transcriptional pathway, which in turn attenuates NLRP3 activation.
- Antifungal and antimycotoxigenic activity against multiple mold species.
- PMID: 31644378, 25053064, 29318480, 35052628

26 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.

27 Pine Extract

- Multiple boreal conifer species ~ needle and bark
- Potent antioxidant and anti-inflammatory activity
- Protective against activated microglial neuroinflammation

and also T cells.

- Attenuates the release of proinflammatory cytokines in LPS-stimulated microglia in part via Inhibition of NF-κB and AP-1 activation.
- Mild antihistamine effect.
- Improves attention, learning, and memory.
- Prevents hippocampal excitotoxicity-derived memory impairment in acute stress in mouse models.
- PMID: 28642096, 26367267

28 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.

29 Integrative approach

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32 **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

33 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

34 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.

35 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

36 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

- Powder or capsule: 300 mg twice daily

- Caution:
  Best absorbed with a fatty meal or with liposomes.

37 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

38 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.
-
-

39 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

40 Nettles

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

- PMID: 37171512

41 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

42 Nettle Lemonade

- Mast cell...
- a
- PMID:

43 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

44 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.
-

45 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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50 Avatar (definition) - Ideal

- Abilities to “bend” (aka work with) all of the elements ~ air, earth, fire, water

51 **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!

52 **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)

53 **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

54 **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.

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.

55 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.

56 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

57 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

58 Chinese Skullcap benefits

- Antibacterial:
  Demonstrates inhibitory activity against Babesia duncani, and stationary phase forms of Borrelia
  Action against Mycoplasma pneumonia

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

59 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.
-

60 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

61 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

62 **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.

63 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

64 Chinese Thoroughwax benefits

- Antimicrobial, moderate activity against Streptococcus pyogenes
- Antiviral, activity against Influenza A (H1N1), more potent inhibitory activity and selectivity than the positive control, Ribavirin
- Modulates the immune system
- Significantly reduces inflammation
- Anti-histamine
- Improves attention
- Neuroprotective:
  Significant reduction in memory impairment
  Decelerates the activation of microglia and astrocytes in the hippocampus
  Preserves the morphology of neurons, reduce apoptosis and significantly inhibit amyloid-β deposition in the hippocampus
  Inhibits increased glutamate (after limbic region stimulation in rats - this stim may have increased dopamine)
- Hepatoprotective and supports detoxification
- Antispasmodic, antitussive
- Diaphoretic, antipyretic
- Analgesic
- Anti-ulcer
- PMID: 28314599, 21749378, 29956627, 28593176, 32742347, 16939901, 28293263

65 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.
-

66 **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

67 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

68 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, 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.
-

69 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

70 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

71 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:

Caution:
May cause drowsiness.
May interact with anticoagulant medication.

-

72 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

73 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

74 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.

75 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

76 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

77 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.

78 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

79 **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

80 **Integrative approach**

- Acute vs chronic presentation
- Core 4 ~
  Anti-inflammatories
  Antimicrobials
  Immune modulation
  Infection/toxicant prevention

infection/toxicant prevention

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

81 Integrative treatment overview

- 1. Guard the gates
  halt T-cell migration to CNS
- 2. Immune modulation
  prevent autoimmune tendencies/gut health
- 3. Address neurotransmitter imbalance
  balance dopa & glutamate to reduce destruction
- 4. Reduce neuroinflammation/leaky BBB
  get good stuff in and bad stuff out
- 5. Manage trauma/stress
  adrenal/nervous system burnout
- 6. Structural integrity
  chronic brain stem/cervical congestion/jaw development

82 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)

83 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

84 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

85 **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

86 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.

87 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

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

88 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.

89 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

90 Oregano

- Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
- Safe to use long term.
- Can be combined with certain Pharmaceutical Antimicrobials.
- Acute Treatment
  Glycerite: ¾ tsp, 3 times daily
  Capsule: 150 mg of 10:1 extract, 3 times daily
  Tea: 1 cup, 4 times daily (needs a minimum of 24 hours for anti-Strep effect)
- Prophylactic:
  Glycerite: ¼ tsp, once daily
  Capsule: 150 mg of 10:1 extract, once daily

- To prep the tea:
  Yield: 2 cups
  Steep 1 Tbsp dried Oregano leaves in 2 cups of boiling water for 5 minutes, covered.
  Strain, and add honey to taste. Cool to a comfortable drinking temperature.
- For the prophylactic phase, pulse, 2–3 consecutive days on, 4-5 days off
- Caution:
  Abdominal cramping, nausea, and diarrhea at higher doses or if using the oil extract.

91 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

92 Black Elderberry

- Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
- Very safe to use long term

- 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.
-

93 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

94 Licorice

- Can be combined with all Botanical Avatars to boost acute and prophylactic antibiotic therapy.
- Safe to use long term.
- Can be combined with certain Pharmaceutical Antimicrobials.
- Acute Treatment:
  Glycerite: ¾ tsp, 3 times daily
  Capsule: 300 mg, 3 times daily
  Tea: 4 cups, sipped throughout the day
- Prophylactic:
  Glycerite: ¼ tsp, 2 times daily
  Capsule: 150 mg, 2 times daily
- To prep the tea:
  Yield: 2 cups
  Prepare tea by boiling 1 teaspoon licorice root powder in 2 cups of water for 5 minutes, covered. Strain. Cool to a comfortable drinking temperature.
- Caution:
  May increase blood pressure.

95 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

96 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

- Capsule: 200 mg, 2 times daily

- Caution:
  Hypotensive, hypoglycemic

97 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

98 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

Glycerite: ½ tsp, 2 times daily

- Caution:
  Bitter flavor.
  Best suited in lower quantities for long-term dosing.

99 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

100 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.

101 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

102 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: 350 mg, 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.
-

103 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

104 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
-

105 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

106 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

107 Integrative treatment overview

- 1. Guard the gates
halt T-cell migration to CNS
- 2. Immune modulation
prevent autoimmune tendencies/gut health
- 3. Address neurotransmitter imbalance
balance dopa & glutamate to reduce destruction
- 4. Reduce neuroinflammation/leaky BBB
get good stuff in and bad stuff out
- 5. Manage trauma/stress
adrenal/nervous system burnout
- 6. Structural integrity
chronic brain stem/cervical congestion/jaw development

108 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)

109 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
-

110 Integrative treatment overview

- 1. Guard the gates
  halt T-cell migration to CNS
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  prevent autoimmune tendencies/gut health

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  get good stuff in and bad stuff out
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  adrenal/nervous system burnout
- 6. Structural integrity
  chronic brain stem/cervical congestion/jaw development

111 PANDAS/PANS Mechanism

- The way out of this brain problem
  is largely through the gut

112 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)

113 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.

114 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

115 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.

116 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

117 Vitamin A

- Fat-soluble ~
  Can bioaccumulate
  Is hepatotoxic at high levels.
  Monitor labs and dose accordingly.
- Can be super-dosed in a single dose at the first onset of viral symptoms. May cause a mild fever.
- Dose ~
  A single adult super-dose is 100,000 IU.
  Maintenance: dose via labs.
  3.33 IU per mcg.
-
-

-
-
- Use liposomal or emulsified forms for optimal absorption.
- PMID: https://ods.od.nih.gov/factsheets/VitaminA-Consumer/

118 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,

119 SCFAs and the brain

- Oral application of a mixture of the three major SCFAs acetate, propionate, and butyrate in germ-free mice, was

sufficient to restore the normal maturation process of the microglia.

- SCFAs can modulate neurotransmitters, like glutamate, glutamine, GABA, and neurotrophic factors.
- Propionate and butyrate can influence the cell signaling system via modification of the intracellular potassium levels, and regulate the expression levels of tryptophan 5-hydroxylase 1, involved in the synthesis of serotonin, and tyrosine hydroxylase, which is involved in the biosynthesis of dopamine, adrenaline, and noradrenaline.
- In mouse models of Parkinson's, oral and IV sodium phenylbutyrate was found to protect the loss of dopaminergic neurons and improve motor function.
- PMID: 33362788, 21902286, 21372141, 22723850

120 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.)

121 Postbiotics

- 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.

122 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

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

123 Probiotic strains

- Psychobiotics ~
  Bifidobacterium adolescentis produces GABA
  Lactobacillus plantarum JYLP-326 relieves anxiety, depression, and insomnia
  Lactobacillus gasseri CP2305 (postbiotic) significantly reduced of State Trait Anxiety Inventory (STAI)-trait scores (6 month trial)

- Sleep ~
  Lactobacillus casei Shirota YIT9029, LcS suppresses sleep latency and increased sleep intensity (in healthy adults)

- Histamine friendly ~
  Bifidobacterium infantis, B. bifidum, B. longum, B. lactis, B. breve
  Lactobacillus salivarius, L. plantarum
  Avoid L. reuteri 6475

- Mold mycotoxins ~
  Lactobacillus plantarum C88/MON03, L. rhamnosus GAF01
  L. casei strain Shirota

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

124 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

125 Probiotics

- 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

126 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

Avoid Streptococcus strains
Caution with prebiotics (fungal overgrowth)

127 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

128 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

129 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

130 Oral Immunoglobulins

131 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

132 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

133 Oral Immunoglobulins

- Unlike the Immunity Nutrients, withhold Oral Immunoglobulins during an active infection as it can cause more mucous—it's doing its job, but that can cause more discomfort to an already snotty kid.

- Rx:
  EnteraGam (serum-derived bovine Ig): 1 packet bid
- Daily:
  Colostrum powder, chew, or capsule: 1,500 mg twice daily
  IgG capsule: 500 mg twice daily
- Caution:
  May increase mucous during acute respiratory illnesses.
  Low risk of worsening constipation.
-

134 Peptides

- Protein messengers ~
  Depending on the peptide, can turn the immune system either up or down.
  Send different types of messages to different types of tissue.
- In PANDAS and PANS, we focus on the gut-brain-immune messages.
- Body Protection Compound (BPC), Thymosin Beta, Cerebrolysin

135 Body Protection Compound (BPC) peptide

- Gastric peptide intended to maintain gut barrier protection from infections that aren’t cleared by stomach acid, with additional wide beneficial effect, both peripherally and centrally.
- Gut-brain axis ~ anxiolytic, anticonvulsive, antidepressant effects
- Animals: brain neuronal damages were resolved as well as disturbed memory, locomotion, and coordination.
- Counteracts encephalopathies; counteracts dopamine disturbances (dopamine receptors blockade, receptors super sensitivity development, or receptor activation, over-release, nigrostriatal damage, vesicles depletion); inflammation reduction; nerve recovery.

- Empirically reduces tics.
- Anti-inflammatory; heals wounds, tendon injuries, muscle healing and function recovery.
- Add this peptide with children taking NSAIDs. (Reduced stomach lesions and encephalopathy.)
- Being studied as potential COVID-19 treatment.
- PMID: 34380875, 34798584, 29134359, 37242459

136 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.
-

137 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

138 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.
-

139 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

140 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.

141 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

142 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

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.

143 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,

144 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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  chronic brain stem/cervical congestion/jaw development

146 **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)

147 **Integrative approach**

- Acute vs chronic presentation
- Core 4 ~
  Anti-inflammatories
  Antimicrobials
  Immune modulation
  Infection/toxicant prevention

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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148 Integrative treatment overview

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149 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

150 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

151 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

152 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.

153 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

154 Thyme steam inhalation instructions

- Thyme Steam Inhalation
-
- SUPPLIES
- Large bowl or pot
- Large lightweight towel
-
- INGREDIENTS
- 2–3 cups boiling water
- 5–10 drops of Thyme essential oil, or
- 2–3 tablespoons dried Thyme, or
- 1/2–3/4 ounce fresh Thyme
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- DIRECTIONS
- Fill large pot/bowl with boiling water.
- Depending on Thyme source:
- Drop 5–10 drops of Thyme essential oil into the bowl.
- Stir in dried Thyme, and steep for 5 minutes.
- Drop in the fresh Thyme, and steep for a few minutes until leaves wilt and turn dark green.
- Lean your head over the bowl close enough to feel the steam, cover your head with the towel, and create a tent to