



Leaky Gut, Leaky Brain:

An Integrative, Evidence-Based Approach to Pediatric Neuropsychiatric Disorders

Elisa Song, MD

IHS 2024



Who I am

- Integrative pediatrician and pediatric functional medicine expert with over 20 years of experience
- Trained at Stanford, NYU School of Medicine, and UCSF Pediatrics Residency
- Additional training in functional medicine, homeopathy, acupuncture, herbal medicine, and essential oils
- Teach other practitioners pediatric functional medicine, pediatric acupuncture, and clinical homeopathy (A4M, IFM, CEDH, Academy for Pain Research, Center for Advanced Acupuncture Pediatrics)
- Created Healthy Kids Happy Kids to be a trusted online holistic pediatric resource for parents and practitioners
- Author of ***Healthy Kids, Happy Kids: An Integrative Pediatrician's Guide to Whole Child Resilience*** (coming



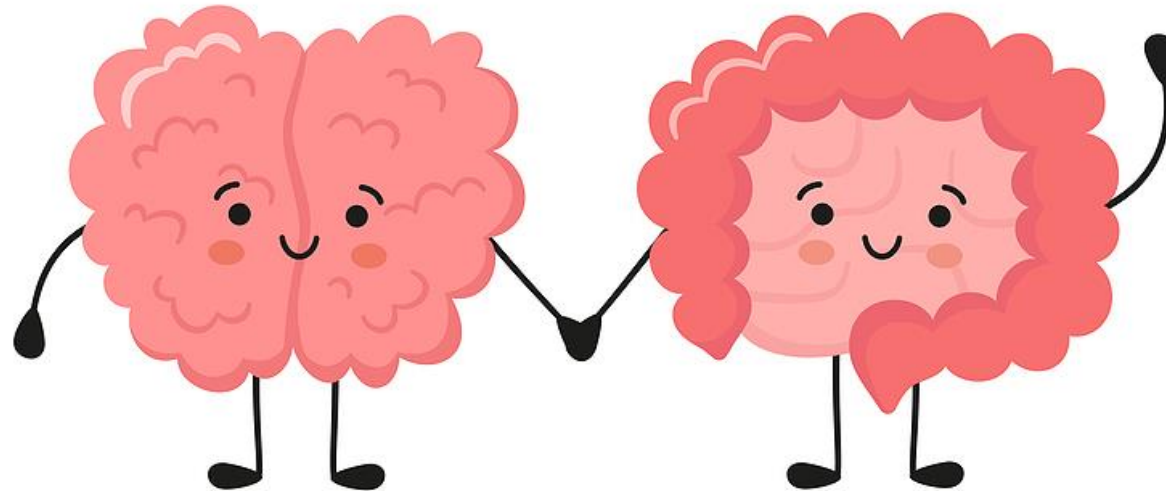


Objectives:

1. Review the pathophysiology of leaky gut and endotoxemia, and implications for leaky brain and neuropsychiatric disorders in children
2. Identify the major modern contributors to gut microbiome disruption in children
3. Develop the understanding of how to optimize gut microbiome resilience in children
4. Discuss an integrative, evidence-based approach to healing gut dysregulation, optimizing Vagus Nerve function, and restoring whole child wellness



The Developing Gut-Brain Connection



QUIZ

Who said “All disease starts in the gut”?

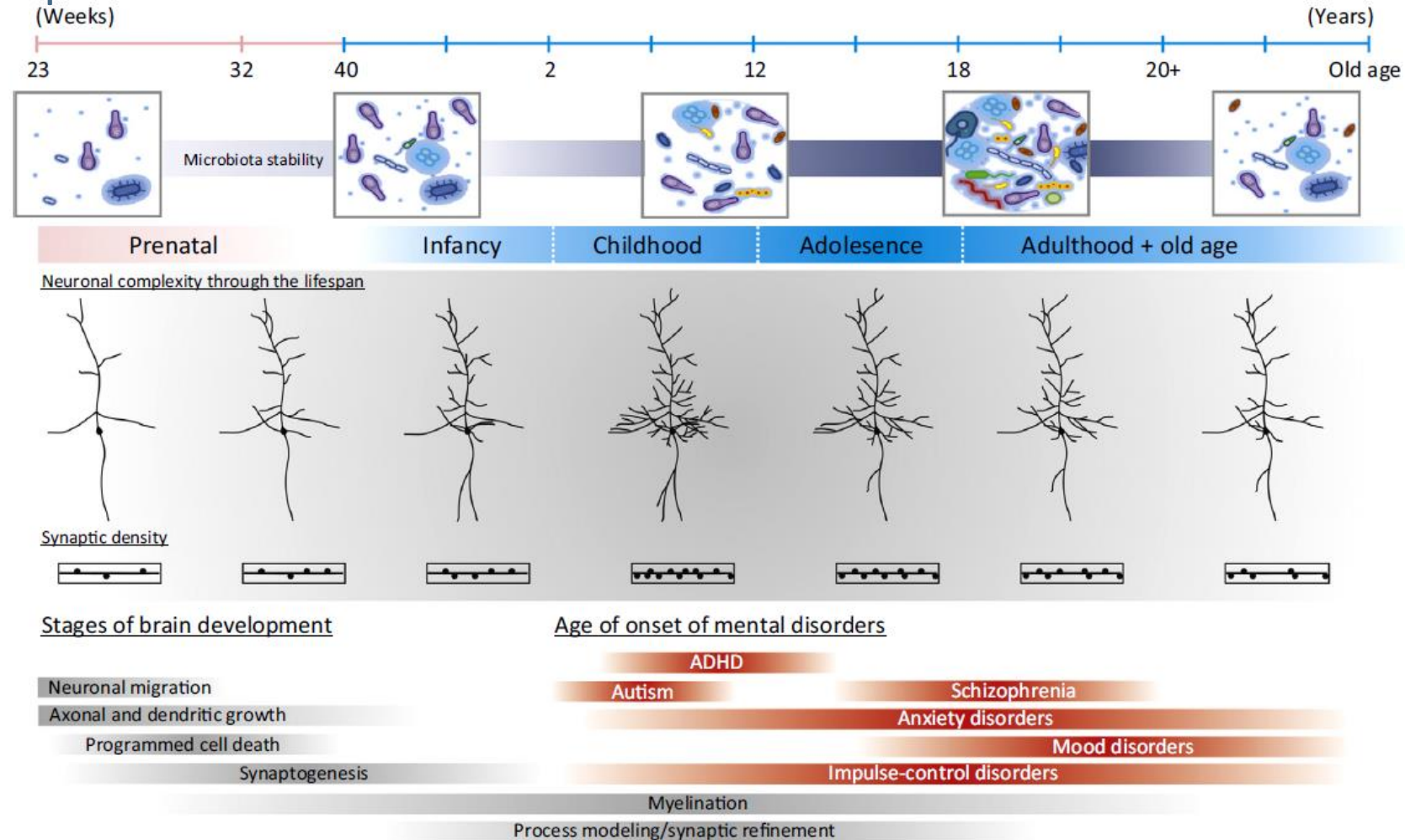


Fun Brain Facts

- Average weight of newborn brain – 370 grams (13 ounces)
- Average weight of adult brain – 3 pounds
- The newborn brain triples in size during the first year
- A child's brain reaches 90-95% of adult size by 6 years
- The adult brain has about 86-100 billion neurons with trillions of synapses
- Toddlers have almost **TWICE** the number of synapses per neuron than adults
- The brain is 60% fat
- 25% of your body's cholesterol is in your brain

Development of Gut Microbiota Occurs in **Parallel** with Neurodevelopment – Impact of Disruptions at Critical Microbial-Neural Windows

- By 2-3 years of age, there are 50% more synapses than adult brain!
- Critical windows of neurodev in infancy, adolescence, and aging correspond with rapid changes in the gut microbiome
- Disruptions during critical and dynamic periods of gut microbiota-brain development may profoundly affect bidirectional brain-gut signaling
- → increased risk of neurodev and neuropsych disorders





Early Probiotic Supplementation & Childhood Brain Disorders

- 75 infants randomized to receive *Lactobacillus rhamnosus* GG (ATCC 53103) or placebo during first 6 months of life and followed for 13 years
- Gut microbiota assessed at age of 3 weeks, 3,6,12,18, 24 mos, and 13 years
- RESULTS:
 - **At age of 13 years, ADHD or Asperger Syndrome (AS) dx'ed in 6/35 (17%) of children in placebo group (3 ADHD, 1 AS, 2 ADHD + AS), and NONE of the 40 in probiotic group (P=0.008)**
 - At 3 mos and 6 mos, children later dx'ed with ADHD or AS had significantly lower numbers of *Bifidobacterium longum* than healthy neurotypical kids
 - At 18 mos, mean number of *Bacteroides* and *Lactobacillus-Enterococcus* group bacteria lower in kids with ADHD/AS than healthy children
 - At 24 mos, mean number *Clostridium histolyticum* lower in kids with ADHD/AS
 - **At age 13, no statistically significant differences in gut microbiota composition between children with or without neuropsychiatric disorders**
 - Controlled for gender, mode of delivery, gestational age, birthweight, BF, antibiotic treatment first 6 mo of life



Early Probiotic Supplementation & Childhood Brain Disorders

- CONCLUSION:
 - ***Probiotic supplementation early in life may reduce the risk of neuropsychiatric disorder development later in childhood possibly by mechanisms not limited to gut microbiota composition***
 - ** this study originally intended to investigate probiotic supplementation for prevention of atopic eczema
 - Of note is increased incidence of atopic disease in kids with ADHD
- POSTULATION:
 - Postulated that neural pathways may be altered by the gut microbiome early in development. If such an alteration takes place at a critical moment, the sequential dysfunction of the gut-brain axis may become relatively constant into adulthood





QUIZ

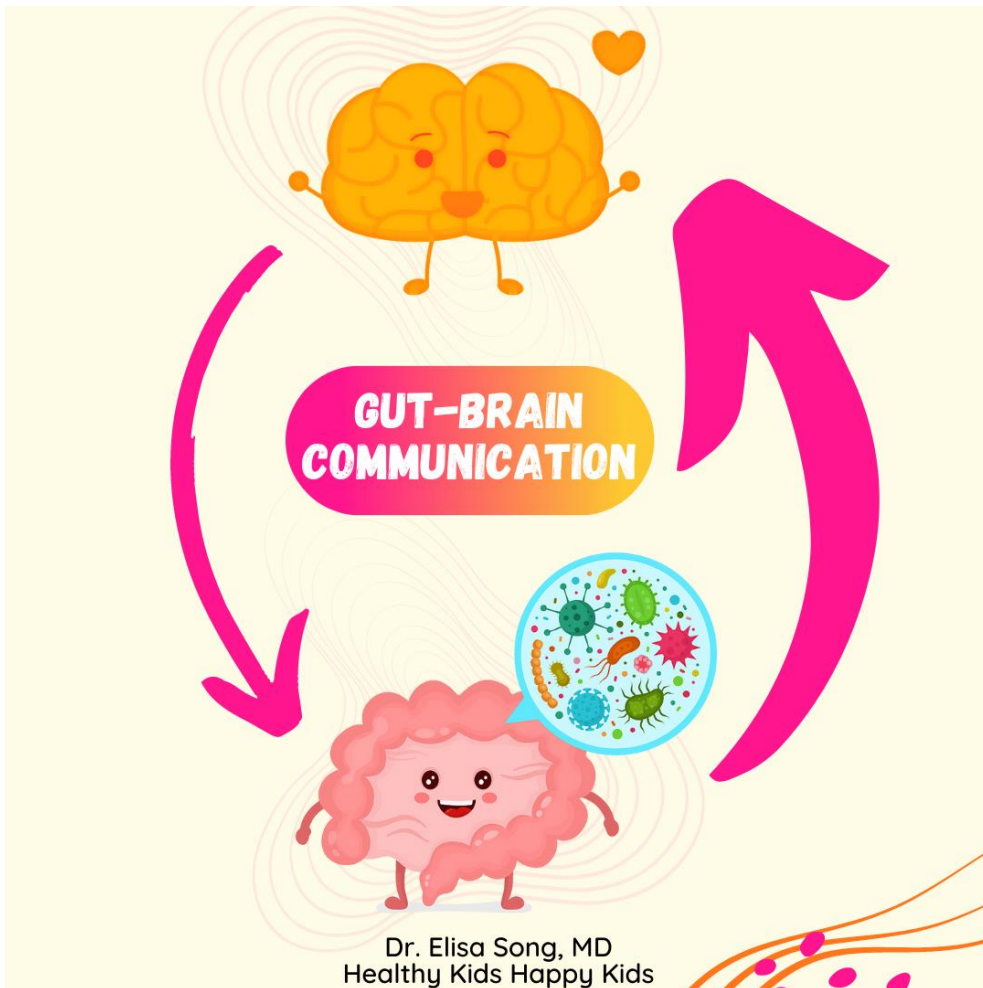
What connects the gut and the
brain?





The Vagus Nerve: The Gut-Brain Superhighway

- BI-DIRECTIONAL communication between the gut and the brain via the VAGUS NERVE
 - Gut microbiome directly influences our emotions, moods and behavior, AND vice versa → 2-way street
- 80-90% of the communication occurs FROM the gut TO the brain!
- Enteric glia very similar to CNS astrocytes
 - Enteric nervous system can live without the brain, but the brain CANNOT live without the enteric nervous system
- Which really is the “second brain” vs. the “first brain”?





Gut Microbiome-Neurotransmitter Connection

- Gut microbes produce hormones and neurotransmitters identical to those produced by humans.
 - *Lactobacillus* species produce acetylcholine and GABA
 - *Bifidobacterium* species produce GABA;
 - *Escherichia* produce norepinephrine, serotonin and dopamine;
 - *Streptococcus* and *Enterococcus* produce serotonin; and
 - *Bacillus* species produce norepinephrine and dopamine
- 90% of our serotonin is made by our gut microbiota
- 50% of our dopamine is made by our gut microbiota
- Our gut microbiome produces 400X melatonin than our pineal gland



When Something Goes Wrong

The Epidemic of Pediatric Neuropsychiatric Disorders

QUIZ

Nearly 1 in **XXX** children has a
chronic condition.



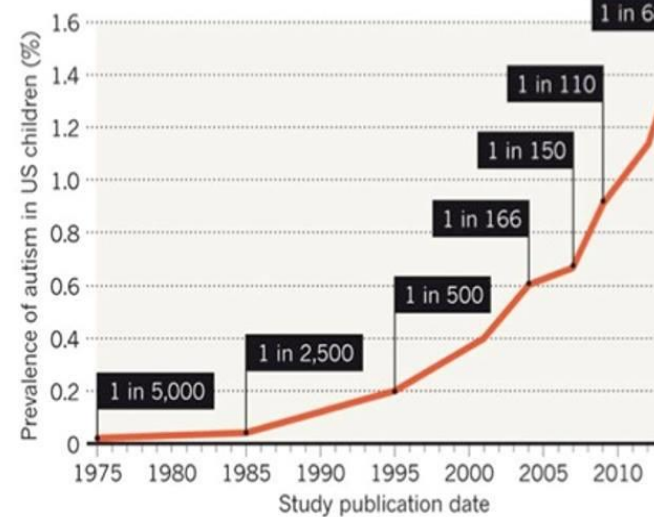
The Rise Autism

- Autism rates are skyrocketing
- 2023 CDC surveillance data: 1 in 36 children has autism spectrum disorder
 - 1 in 44 in 2018
- 4X more common among boys than girls
- 1 in 43 in Maryland
- 1 in 22 in California

• <https://www.cdc.gov/media/releases/2023/p0323-autism.html>

AUTISM DIAGNOSES RISING

Almost 1.5% of US children are now diagnosed with autism, according to data from 11 regions in the United States.



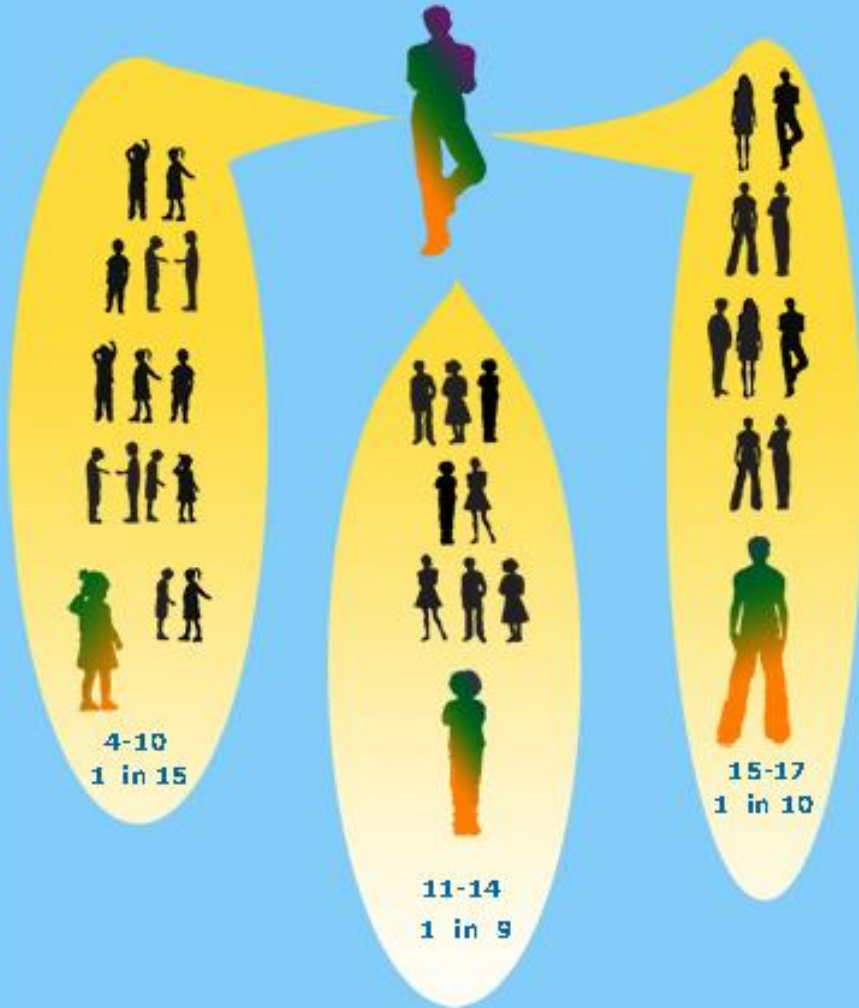
*2033
1 in 4

Assuming
continued 13%
annual growth
rate.

*K. Weintraub, Nature 479, Nov. 3 2011, 22-24.

Estimates of 1 in 4 by 2033 are based on a projected annual growth rate of 13%; MIT Scientist Stephanie Seneff has estimated that 1 in 2 children will have autism by 2025

Children Currently Diagnosed with ADHD
Ages Ranging from 4-17

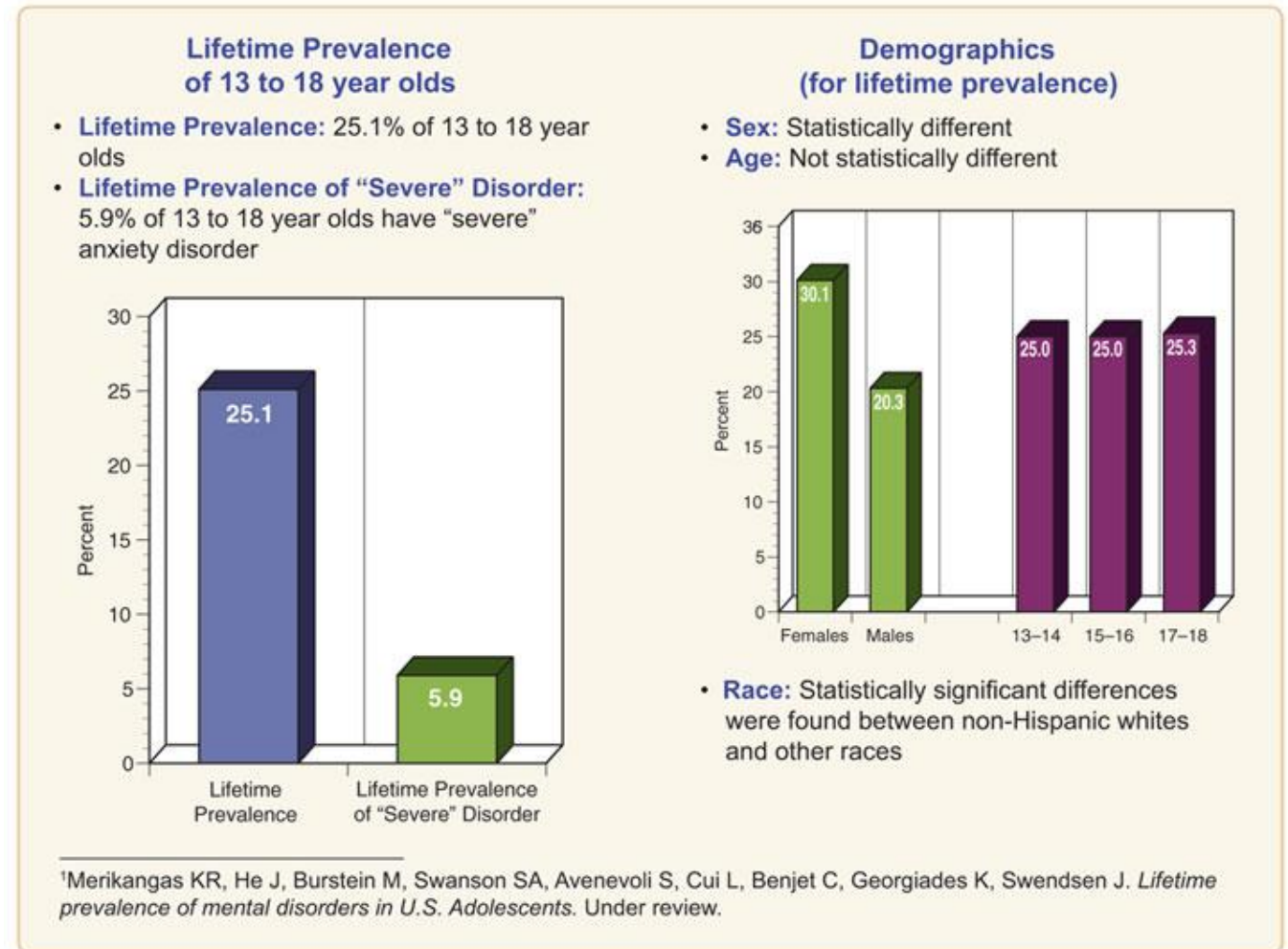


The Rise in ADHD

- ADHD data from 2016-2019 (CDC)
- 6 million children (9.8% or 1 in 10 children 3–17 years) has ADHD:
 - 3-5 years: 2% (1 in 20)
 - 6-11 years: 10% (1 in 10)
 - 12-17 years: 13% (1 in 8)
- Co-morbidities are common
 - 1 in 2 also have behavior/conduct problem
 - 3 in 10 also have anxiety
 - <https://www.cdc.gov/ncbddd/adhd/data.html>

The Rise in Childhood Mental Health Disorders

- Anxiety
 - 1 in 4 13-18 year-olds has an anxiety disorder
 - 1 in 15 has a “severe” anxiety disorder
- Depression
 - 1 in 10-15 teens has depression
- Any mental disorder 13-18 years
 - 46% - ALMOST 1 IN 2!!!
- The pandemic has created a mental health EMERGENCY in kids (and adults)



Leading Causes of Death in the United States (2016)

Data Courtesy of CDC

	Select Age Groups							
Rank	10-14	15-24	25-34	35-44	45-54	55-64	65+	All Ages
1	Unintentional Injury 847	Unintentional Injury 13,895	Unintentional Injury 23,984	Unintentional Injury 20,975	Malignant Neoplasms 41,291	Malignant Neoplasms 116,364	Heart Disease 507,118	Heart Disease 635,260
2	Suicide 436	Suicide 5,723	Suicide 7,366	Malignant Neoplasms 10,903	Heart Disease 34,027	Heart Disease 78,610	Malignant Neoplasms 422,927	Malignant Neoplasms 598,038
3	Malignant Neoplasms 431	Homicide 5,172	Homicide 5,376	Heart Disease 10,477	Unintentional Injury 23,377	Unintentional Injury 21,860	CLRD 131,002	Unintentional Injury 161,374
4	Homicide 147	Malignant Neoplasms 1,431	Malignant Neoplasms 3,791	Suicide 7,030	Suicide 8,437	CLRD 17,810	Cerebro-vascular 121,630	CLRD 154,596
5	Congenital Anomalies 146	Heart Disease 949	Heart Disease 3,445	Homicide 3,369	Liver Disease 8,364	Diabetes Mellitus 14,251	Alzheimer's Disease 114,883	Cerebro-vascular 142,142
6	Heart Disease 111	Congenital Anomalies 388	Liver Disease 925	Liver Disease 2,851	Diabetes Mellitus 6,267	Liver Disease 13,448	Diabetes Mellitus 56,452	Alzheimer's Disease 116,103
7	CLRD 75	Diabetes Mellitus 211	Diabetes Mellitus 792	Diabetes Mellitus 2,049	Cerebro-vascular 5,353	Cerebro-vascular 12,310	Unintentional Injury 53,141	Diabetes Mellitus 80,058
8	Cerebro-vascular 50	CLRD 206	Cerebro-vascular 575	Cerebro-vascular 1,851	CLRD 4,307	Suicide 7,759	Influenza & Pneumonia 42,479	Influenza & Pneumonia 51,537
9	Influenza & Pneumonia 39	Influenza & Pneumonia 189	HIV 546	HIV 971	Septicemia 2,472	Septicemia 5,941	Nephritis 41,095	Nephritis 50,046
10	Septicemia 31	Complicated Pregnancy 184	Complicated Pregnancy 472	Septicemia 897	Homicide 2,152	Nephritis 5,650	Septicemia 30,405	Suicide 44,965

BEFORE the pandemic:

- Suicide is the 2nd leading cause of death for 10-24 year olds (after unintentional injury)
- 27X more teens die of suicide than influenza
- 136 reported suicides in 5-9 year olds 2001-2021
 - Likely an undercount
- In 2019:
 - Suicide was the 8th leading cause of death in children 5-11 years
 - COVID-19 would have been the 10th

Ruch DA, Heck KM, Sheftall AH, et al. Characteristics and Precipitating Circumstances of Suicide Among Children Aged 5 to 11 Years in the United States, 2013-2017. JAMA Netw Open. 2021;4(7):e2115683. Published 2021 Jul 1. doi:10.1001/jamanetworkopen.2021.1568
 ©Elisa Song, MD – Healthy Kids Happy Kids 2024

QUIZ

Since the pandemic, 1 in **XXX** teen girls has seriously thought of suicide?

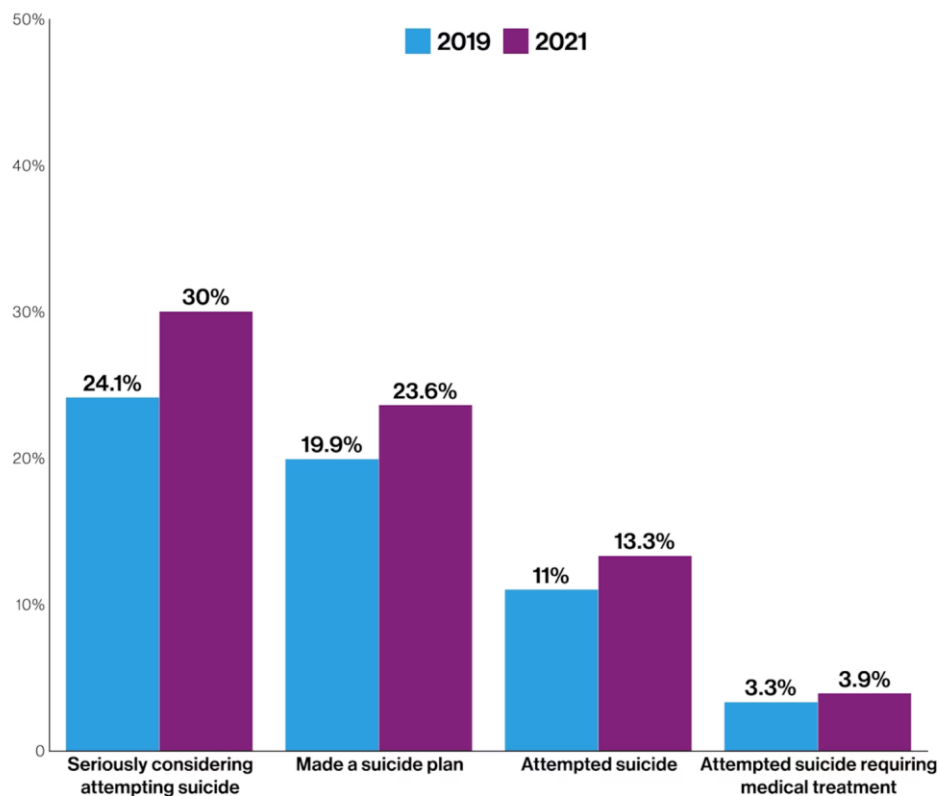




Since the Pandemic: The Rise in Childhood Suicide

U.S. Teen Girls Experiencing Suicidal Thoughts and Behaviors

2019-2021



- Seriously thought of suicide: **1 in 3 teen girls**
- Made a suicide plan: **~ 1 in 4**
- Attempted suicide: **> 1 in 10**
- Died by suicide: **TOO MANY**

• https://www.cdc.gov/healthyyouth/data/yrbs/yrbs_data_summary_and_trends.htm

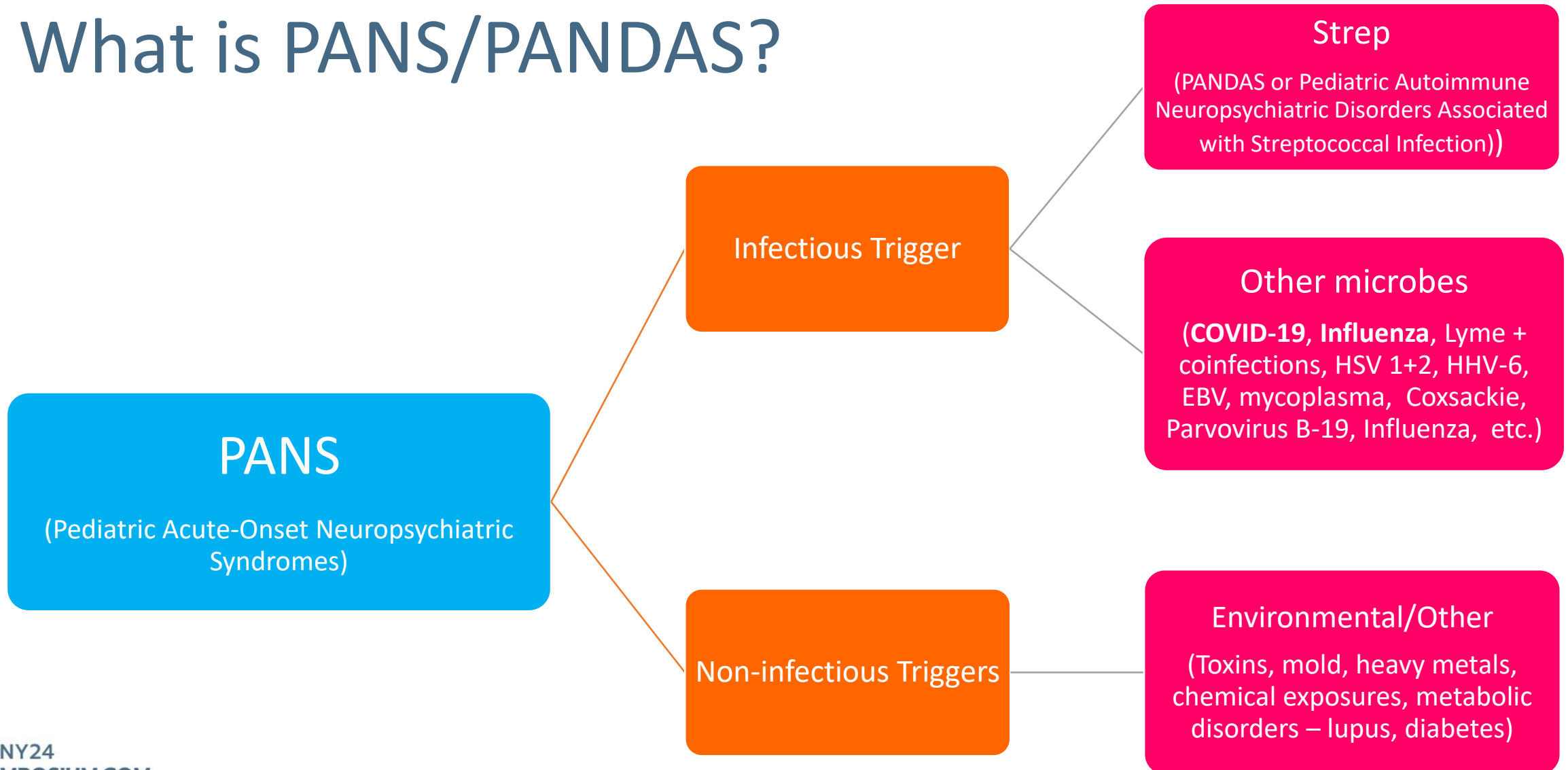


The Rise in PANS/PANDAS

- At least 1 in 200 US children has PANS/PANDAS
- As many as 1 in 4 kids with OCD and tic disorders (like Tourette syndrome) may have PANDAS
 - www.pandasnetwork.org
- For more info, check out my 2-part interview for Fx Medicine Australia
 - <https://www.fxmedicine.com.au/content/integrative-paediatrics-pandas-part-1-dr-elisa-song>
 - <https://www.fxmedicine.com.au/content/integrative-paediatrics-pandas-part-2-dr-elisa-song>
- And my interview with Dr. Kara Fitzgerald on New Frontiers in Functional Medicine
 - <https://www.drkarafitzgerald.com/2019/07/13/functional-medicine-pediatrician-dr-elisa-song-pans-pandas-dx-treatment/>



What is PANS/PANDAS?



QUIZ

There are diagnostic bloodtests for
PANS/PANDAS

True / False



Diagnostic Criteria

PANS is defined by the following criteria:

Abrupt, dramatic onset of OCD or severely restricted food intake; symptoms are not better explained by a known neurologic or medical disorder; and the addition of at least 2 of the “accompanying” symptoms:

- Anxiety
- Emotional lability and/or depression
- Irritability, aggression and/or severely oppositional behaviors
- Behavioral (developmental) regression
- Deterioration in school performance
- Sensory or motor abnormalities
- Somatic signs including sleep disturbances, enuresis or urinary frequency

The onset of PANS may start with infectious agents other than strep. It also includes onset from environmental triggers or immune dysfunction.

PANDAS is defined by the following criteria:

Clinical diagnosis of PANDAS includes 5 criteria:

- Presence of significant obsessions, compulsions and/or tics
- Abrupt onset of symptoms or a relapsing-remitting course of symptom severity
- Prepubertal onset
- Association with streptococcal infection
- Association with other neuropsychiatric symptoms (includes any of the PANS “accompanying” symptoms)

**PANS/PANDAS remains a
CLINICAL diagnosis**
(what about PANS that does not present
“dramatically”?)



Post-COVID Pediatric Neuropsychiatric Problems & Multi-System Inflammatory Syndrome in Children

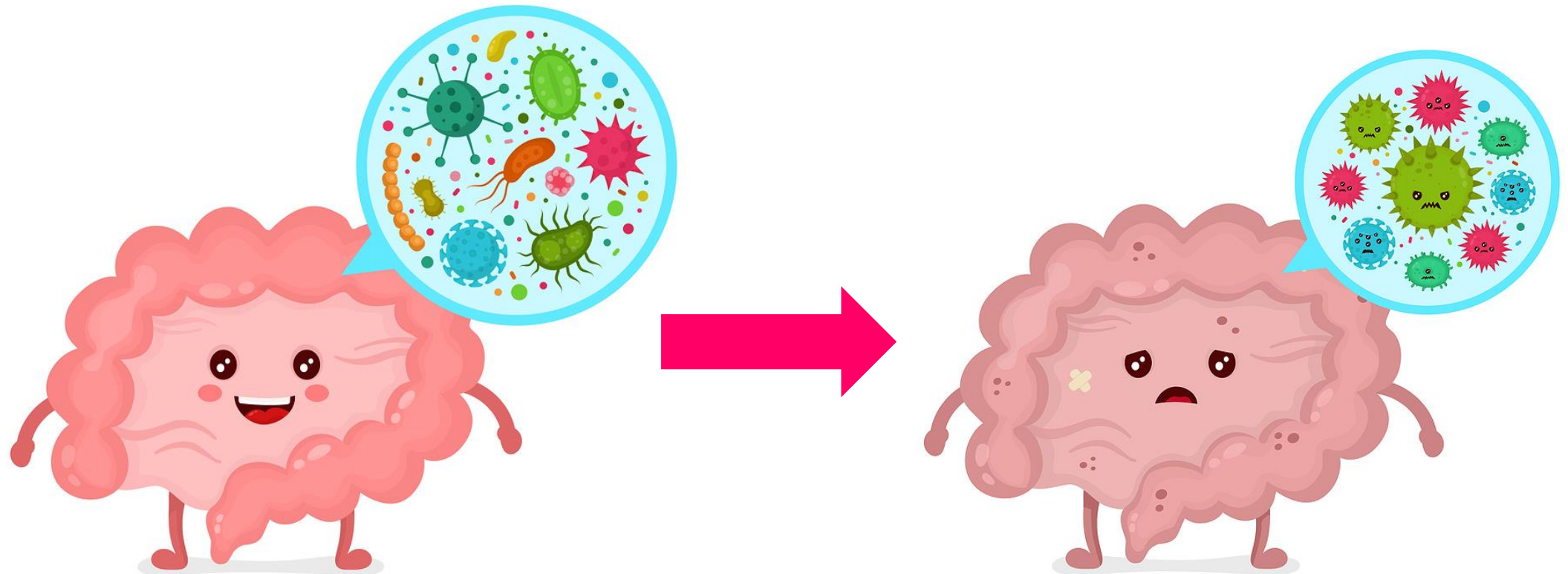
- Post-COVID neurologic and psychiatric problems
 - COVID-19 can trigger PANS
 - Pavone P, Ceccarelli M, Marino S, et al. SARS-CoV-2 related paediatric acute-onset neuropsychiatric syndrome. Lancet Child Adolesc Health. 2021;5(6):e19-e21. doi:10.1016/S2352-4642(21)00135-8
 - Efe A. SARS-CoV-2/COVID-19 associated pediatric acute-onset neuropsychiatric syndrome a case report of female twin adolescents. Psychiatry Res Case Rep. 2022;1(2):100074. doi:10.1016/j.psycr.2022.100074
 - Antineuronal antibodies (similar to PANS patients) found in children with COVID-19 and neuropsychiatry symptoms
 - Bartley CM, Johns C, Ngo TT, et al. Anti-SARS-CoV-2 and Autoantibody Profiles in the Cerebrospinal Fluid of 3 Teenaged Patients With COVID-19 and Subacute Neuropsychiatric Symptoms. JAMA Neurol. 2021;78(12):1503-1509. doi:10.1001/jamaneurol.2021.3821
- MIS-C: Multisystem Inflammatory Syndrome in Children
 - Associated with neuropsychiatric symptoms
 - Enner S, Shah YD, Ali A, et al. Patients Diagnosed with Multisystem Inflammatory Syndrome in Children Have Persistent Neurologic, Sleep, and Psychiatric Symptoms After Hospitalization. J Child Neurol. 2022;37(5):426-433. doi:10.1177/08830738221075924



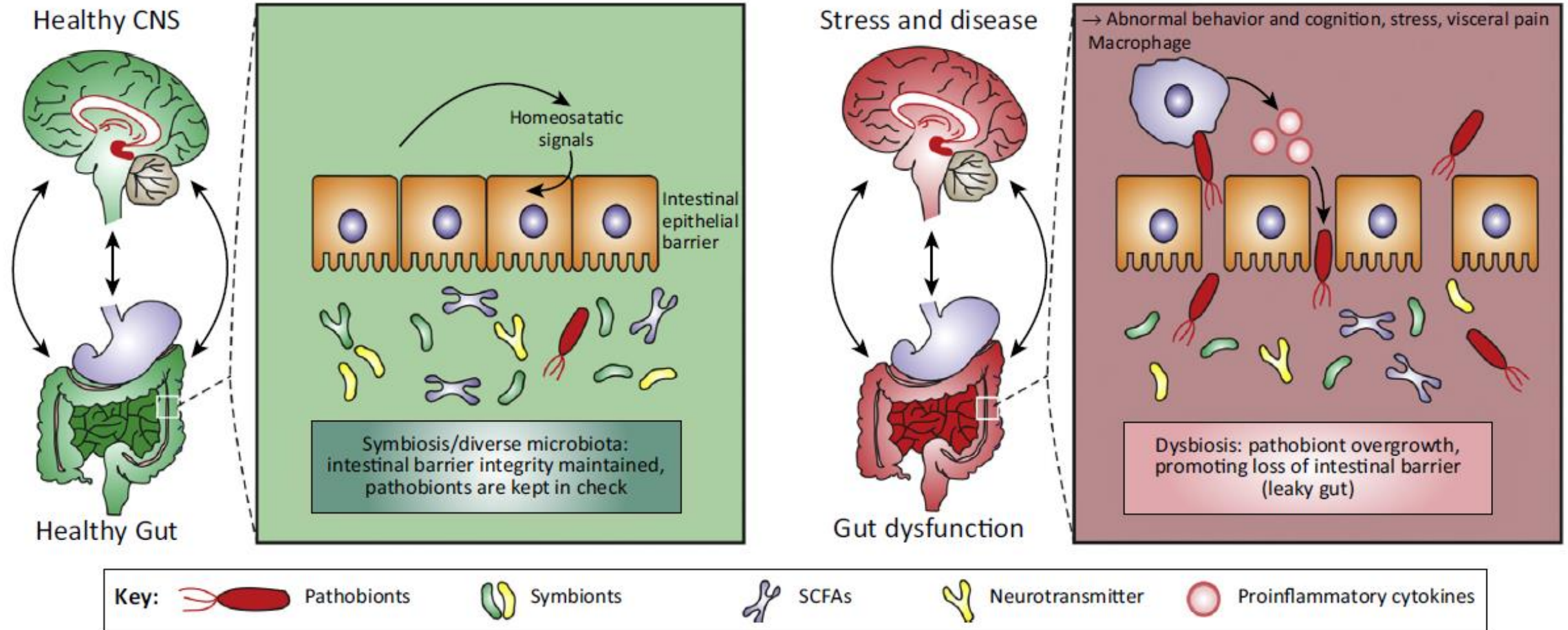
What's Going on?

Gut-Brain Dysfunction in Our Kids

When the Gut Microbiome is Disrupted → Gut Dysbiosis, Leaky Gut, Metabolic Endotoxemia



Microbiota-Gut-Brain Axis In Health & Disease



TRENDS in Molecular Medicine



Gut Dysbiosis & Mental Health Disorders

- Several studies have shown altered gut microbiota and gut dysbiosis in patients with mental health disorders
 - Chen Z et al. Comparative metaproteomics analysis shows altered fecal microbiota signatures in patients with major depressive disorder. [Neuroreport](#). 2018 Mar 21;29(5):417-425.
 - Aizawa E et al. Possible association of Bifidobacterium and Lactobacillus in the gut microbiota of patients with major depressive disorder. [J Affect Disord](#). 2016 Sep 15;202:254-7. doi: 10.1016/j.jad.2016.05.038.
 - Gareau MG et al. Bacterial infection causes stress-induced memory dysfunction in mice. [Gut](#). 2011 Mar;60(3):307-17. doi: 10.1136/gut.2009.202515.
 - ...



QUIZ

Just one round of antibiotics before 2 years of age can increase the risk of mental health disorders later in childhood/adolescence by **XXX%**?





Early Exposure to Antibiotics & Risk for Neuropsychiatric Disorders

- Antibiotic use in childhood and the brain
 - Antibiotic use during the first 2 years of life may increase the risk of mental health concerns later in childhood or adolescence by **up to 50%** - including sleep disorders, ADHD, mood and anxiety disorders, and other behavioral concerns
- Study population: All births in Finland between 1996 and 2012, 1 million births, studied for **antibiotic drug exposure: mothers during pregnancy and the children the first two postnatal years.**
 - RESULT: 10–50% increased risks of childhood-onset sleep disorders, ADHD, conduct disorder, mood and anxiety disorders, and other behavioral and emotional disorders
 - **Strongest risk for antibiotic exposure BEFORE 6 months of age**
 - Lavebratt C, Yang LL, Giacobini M, et al. Early exposure to antibiotic drugs and risk for psychiatric disorders: a population-based study. Transl Psychiatry. 2019;9(1):317. Published 2019 Nov 26. doi:10.1038/s41398-019-0653-9



Antibiotics & Risk for Anxiety

- Treatment with a single antibiotic course associated with higher risk for depression and anxiety with **all** antibiotic groups tested
 - Penicillins, quinolones, sulfonamides
- Increased risk with each recurrent antibiotic exposure
 - Lurie I et al. Antibiotic exposure and the risk for depression, anxiety, or psychosis: a nested case-control study. [J Clin Psychiatry](#). 2015 Nov;76(11):1522-8. doi: 10.4088/JCP.15m09961.

Antibiotics & the Gut Microbiome



Antibiotics are the single biggest
ACUTE disruptor to the gut microbiome

1. Use antibiotics judiciously and appropriately
2. Work with patients to restore gut microbiome resilience after antibiotics and other microbiome-disrupting meds



Microbiome-Disrupting Medications

- Antibiotics
- NSAIDs (like ibuprofen)
- Reflux/antacid medications
- Steroids
- Oral contraceptives
- SSRIs



How many children/teens have
been on **ALL** of these?



References for Microbiome-Disrupting Medications

- Q. Le Bastard, G. A. Al-Ghalith, M. Gregoire, et al., “Systematic Review: Human Gut Dysbiosis Induced by Non-Antibiotic Prescription Medications,” *Alimentary Pharmacology and Therapeutics* 47, no. 3 (February 2018): 332–45. <https://pubmed.ncbi.nlm.nih.gov/29205415/>
- Ceri Proffitt, Gholamreza Bidkhori, David Moyes, and Saeed Shoaie, “Disease, Drugs and Dysbiosis: Understanding Microbial Signatures in Metabolic Disease and Medical Interventions,” *Microorganisms* 8, no. 9 (September 2020): 1381. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7565856/#app1-microorganisms-08-01381>
- Rinse K. Weersma, Alexandra Zhernakova, and Jingyuan Fu, “Interaction Between Drugs and Gut Microbiome,” *Gut* 69, no. 8 (August 2020). <https://gut.bmj.com/content/69/8/1510>
- Lisa Maier, Mihaela Pruteanu, Michael Kuhn, et al., “Extensive Impact of Non-Antibiotic Drugs on Human Gut Bacteria,” *Nature* 555 (2018): 623–28. <https://www.nature.com/articles/nature25979>



Psychobiotics – Probiotics with Psychological Benefit

- 2 meta-analyses of 17 randomized controlled human trials show psychological benefit from probiotic supplementation
 - Pirbaglou M et al. Probiotic supplementation can positively affect anxiety and depressive symptoms: a systematic review of randomized controlled trials. [Nutr Res](#). 2016 Sep;36(9):889-898. doi: 10.1016/j.nutres.2016.06.009.
 - McKean J et al. Probiotics and Subclinical Psychological Symptoms in Healthy Participants: A Systematic Review and Meta-Analysis. [J Altern Complement Med](#). 2017 Apr;23(4):249-258. doi: 10.1089/acm.2016.0023.
- *Lactobacillus helveticus* NS8 works better than citalopram in reducing stress-induced anxiety, depression, and cognitive dysfunction; lowers cortisol and restores serotonin to normal.
 - Mital et al. 2016. Neurotransmitters: The critical modulators regulating the gut-brain-axis. [J Cell Physiol](#). Aug 11. doi: 10.1002/jcp.25518.
- *Lactobacillus plantarum* strain **PS128** increases dopamine and serotonin
 - Daily administration improves 2 core sx of autism
 - Persistent deficits in social communication and social interaction
 - Restricted, repetitive patterns of behavior or activities
- *Lactobacillus helveticus* Rosell-52 and *Bifidobacterium longum* Rosell-175 reduces anxiety, depression and psychological distress
 - Messasoudi et al. Assessment of psychotropic-like properties of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in rats and human subjects. [Br J Nutr](#). 2011 Mar;105(5):755-64. doi: 10.1017/S0007114510004319.

QUIZ

Why are fermented foods good for you?





Fermented Foods Can Reduce Social Anxiety

- Study of 710 young adults (445 females)
- Looked at association between eating fermented foods, neuroticism and social anxiety
- “Neurotic” patients who consumed fermented foods more frequently had less social anxiety.
- **CONCLUSION:** Fermented foods that contain probiotics may have a protective effect against social anxiety symptoms for those at higher genetic risk, as indexed by trait neuroticism.



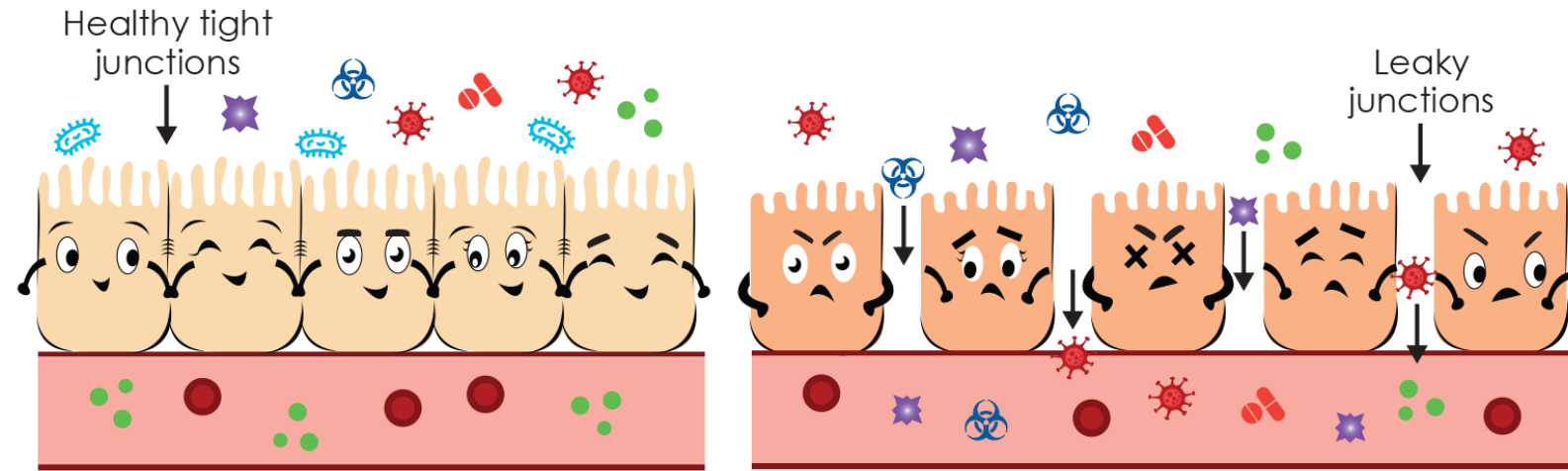
Consumption of fermented foods that
contain probiotics may serve as a low-risk
intervention for reducing social anxiety.

Hilmire MR et al. Fermented foods, neuroticism, and social anxiety: An interaction model. [Psychiatry Res.](#) 2015 Aug 15;228(2):203-8. doi: 10.1016/j.psychres.2015.04.023.



NOTE: Benefit of fermented foods may be due to POSTBIOTICS (neurotransmitters, butyrate, etc.)

When the Gut Microbiome is Disrupted



HEALTHY GUT

Good stuff gets in.
Bad stuff stays out.
Immune system stays calm.

VS.

LEAKY GUT

Bad stuff gets in.
Good stuff stays out.
Immune system is unhappy.



Nutrients



Probiotics



Blood
Cells



Pathogens/
Infections



Toxins

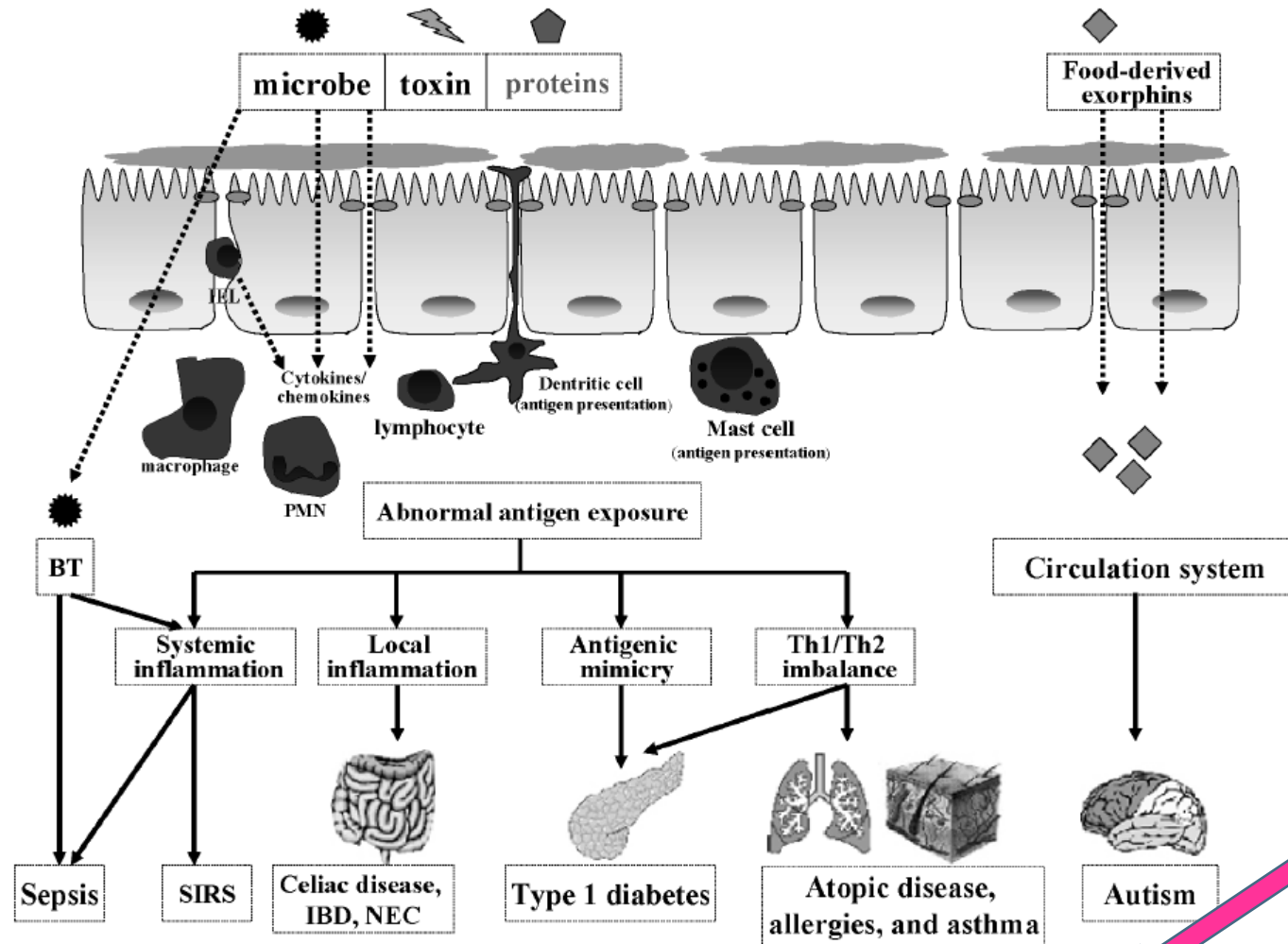


Drugs



Inflammatory
Food

Leaky Gut & Children's Health



QUIZ

What year was the first published connection between leaky gut and children's health?





Leaky Gut & Children's Health – How Long Have We Known the Connection?

- 1981 Eczema
- 1982 Crohn's and Celiac disease
- 1985 Food allergies
- 1986 Pollen allergies
- 1989 Migraines
- 1990 Irritable Bowel Syndrome
- 2000 Juvenile arthritis
- 2003 Autism
- 2005 Type 1 diabetes
- 2018 ADHD
- 2020 Hashimoto's thyroiditis
- 2020 Childhood obesity
- 2021 Multisystem Inflammatory Syndrome in Children (MIS-C)



References for Leaky Gut & Kids

- P. G. Jackson, M. H. Lessof, R. W. Baker, et al., “Intestinal Permeability in Patients with Eczema and Food Allergy,” *Lancet* 317, no. 8233 (June 1981): P1285–86. <https://pubmed.ncbi.nlm.nih.gov/6112605/>
- A. D. Pearson, E. J. Eastham, M. F. Laker, et al., “Intestinal Permeability in Children with Crohn’s Disease and Coeliac Disease,” *British Medical Journal* 285 (July 1982): 20–21. <https://pubmed.ncbi.nlm.nih.gov/6805795/>
- “Gastrointestinal Permeability in Food-Allergic Children,” *Nutrition Reviews* 43, no. 8 (August 1985): 233–35. <https://pubmed.ncbi.nlm.nih.gov/3931008/>
- C. Moller, K. E. Magnusson, T. Sundqvist, et al., “Intestinal Permeability as Assessed with Polyethyleneglycols in Birch Pollen Allergic Children Undergoing Oral Immunotherapy,” *Allergy* 41, no. 4 (May 1986): 280–85. <https://pubmed.ncbi.nlm.nih.gov/3752418/>
- W. K. Amery and P. P. Forget, “The Role of the Gut in Migraine: The Oral 51-Cr EDTA Test in Recurrent Abdominal Pain,” *Cephalalgia* 9, no. 3 (September 1989): 227–29. <https://pubmed.ncbi.nlm.nih.gov/2507165/>
- Z. Liu, N. Li, and J. Neu, “Tight Junctions, Leaky Intestines, and Pediatric Diseases,” *Acta Paediatrica* 94, no. 4 (April 2005): 386–93. <https://pubmed.ncbi.nlm.nih.gov/16092447/>
- Tiffany Hensley-McBain and Jennifer A. Manuzak, “Zonulin as a Biomarker and Potential Therapeutic Target in Multisystem Inflammatory Syndrome in Children,” *Journal of Clinical Investigation* 131, no. 14 (July 2021): e151467. <https://pubmed.ncbi.nlm.nih.gov/34160366/>
- Lael M. Yonker, Tal Gilboa, Alana F. Ogata, et al., “Multisystem Inflammatory Syndrome in Children Is Driven by Zonulin-Dependent Loss of Gut Mucosal Barrier,” *Journal of Clinical Investigation* 131, no. 14 (July 2021): e149633. <https://pubmed.ncbi.nlm.nih.gov/34032635/>



QUIZ

Zonulin is secreted by enterocytes
AND what other organ systems?





Leaky Gut & ADHD

- Higher Zonulin and Occludin found in children with ADHD
 - Zonulin = marker of leaky gut (?and leaky brain, heart, lungs, liver, kidneys, skin, immune cells, adipose tissue)
- The higher the zonulin, the more the hyperactivity and social impairment
 - Lee SY, Li SC, Yang CY, Kuo HC, Chou WJ, Wang LJ. Gut Leakage Markers and Cognitive Functions in Patients with Attention-Deficit/Hyperactivity Disorder. Children (Basel). 2023;10(3):513. Published 2023 Mar 5. doi:10.3390/children10030513
 - Aydoğan Avşar P, Işık Ü, Aktepe E, Kılıç F, Doğuç DK, Büyükbayram Hİ. Serum zonulin and claudin-5 levels in children with attention-deficit/hyperactivity disorder. Int J Psychiatry Clin Pract. 2021;25(1):49-55. doi:10.1080/13651501.2020.1801754
 - Özyurt G, Öztürk Y, Appak YÇ, et al. Increased zonulin is associated with hyperactivity and social dysfunctions in children with attention deficit hyperactivity disorder. Compr Psychiatry. 2018;87:138-142. doi:10.1016/j.comppsy.2018.10.006



Leaky Gut & OCD

- Higher serum Claudin-5 found in children with OCD
 - Transmembrane tight junction protein
- Serum zonulin levels not significantly different
 - Asbjornsdottir B, Snorradottir H, Andresdottir E, et al. Zonulin-Dependent Intestinal Permeability in Children Diagnosed with Mental Disorders: A Systematic Review and Meta-Analysis. *Nutrients*. 2020;12(7):1982. Published 2020 Jul 3. doi:10.3390/nu12071982

Leaky Gut & MIS-C

- Increased Zonulin found in children with MIS-C
 - Larazotide, an experimental medicine for Leaky Gut resulted in:
 - Decreased plasma SARS-CoV-2 spike antigen levels
 - Decreased inflammatory markers
 - IMPROVED clinical outcomes
-
- Kılıç AO, Akın F, Yazar A, Metin Akcan Ö, Topcu C, Aydın O. Zonulin and claudin-5 levels in multisystem inflammatory syndrome and SARS-CoV-2 infection in children [published correction appears in J Paediatr Child Health. 2023 Aug;59(8):1010]. J Paediatr Child Health. 2022;58(9):1561-1565. doi:10.1111/jpc.16033
 - Hensley-McBain T, Manuzak JA. Zonulin as a biomarker and potential therapeutic target in multisystem inflammatory syndrome in children. J Clin Invest. 2021;131(14):e151467. doi:10.1172/JCI151467
 - Yonker LM, Gilboa T, Ogata AF, et al. Multisystem inflammatory syndrome in children is driven by zonulin-dependent loss of gut mucosal barrier. J Clin Invest. 2021;131(14):e149633. doi:10.1172/JCI149633



The Perfect Storm:

Gut Dysbiosis + Leaky Gut → Metabolic Endotoxemia

- LPS-induced metabolic endotoxemia
 - LPS is an endotoxin derived from the outer membrane of gram-negative bacteria.
 - Circulating LPS binds to LBP and LPS-LBP complexes → activate NKFb and increase inflammatory cytokines **wherever they end up** – brain, gut, joints, etc.
 - Metabolic endotoxemia occurs when serum endotoxins (LPS) are absorbed through a **Leaky Gut** lining
 - Metabolic endotoxemia associated with increased risk for anxiety, depression, autoimmunity, diabetes, obesity and cardiovascular disease, even COVID-19
- Endotoxin-producing Gram-negative Bacteria
 - Escherichia coli, Salmonella, Shigella, Pseudomonas, Klebsiella, Citrobacter, Enterobacter, Proteus, Serratia
- Microorganisms that produce endotoxin-like compounds
 - Streptococcus, Candida

Metabolic Endotoxemia in Pediatric Neuropsychiatric Conditions

- Children with PANS/PANDAS
 - Loffredo L, Spalice A, Salvatori F, et al. Oxidative stress and gut-derived lipopolysaccharides in children affected by paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. BMC Pediatr. 2020;20(1):127. Published 2020 Mar 18. doi:10.1186/s12887-020-02026-8
- Children with autism and ADHD
 - Bundgaard-Nielsen C, Lauritsen MB, Knudsen JK, et al. Children and adolescents with attention deficit hyperactivity disorder and autism spectrum disorder share distinct microbiota compositions. Gut Microbes. 2023;15(1):2211923. doi:10.1080/19490976.2023.2211923
- Children with mental disorders
 - Asbjornsdottir B, Snorraddottir H, Andresdottir E, et al. Zonulin-Dependent Intestinal Permeability in Children Diagnosed with Mental Disorders: A Systematic Review and Meta-Analysis. Nutrients. 2020;12(7):1982. Published 2020 Jul 3. doi:10.3390/nu12071982



Endotoxemia, Probiotics & Anxiety During Puberty

- Study: A single exposure to LPS during puberty → enduring depression in females and anxiety in males into adulthood (in mice)
- Probiotics given to mice during puberty after exposure to LPS :
 - Reduced LPS-induced sickness behavior
 - Prevented LPS-induced increases in pro-inflammatory cytokines
 - Prevented LPS-induced changes to gut microbiota
 - Reduced cytokine production in the BRAIN
 - Hypothalamus, hippocampus, and PFC)
 - Prevented enduring LPS-induced anxiety and depression into adulthood

CONCLUSION: Probiotics during puberty mitigates inflammation and decreases stress-induced vulnerabilities to emotional behaviours later in life

- Murray E et al. Probiotic consumption during puberty mitigates LPS-induced immune responses and protects against stress-induced depression- and anxiety-like behaviors in adulthood in a sex-specific manner. [Brain Behav Immun](#). 2019 Jun 15. pii: S0889-1591(19)30338-1. doi: 10.1016/j.bbi.2019.06.016.

Reducing Endotoxemia: Serum-derived Immunoglobulin (SBI)

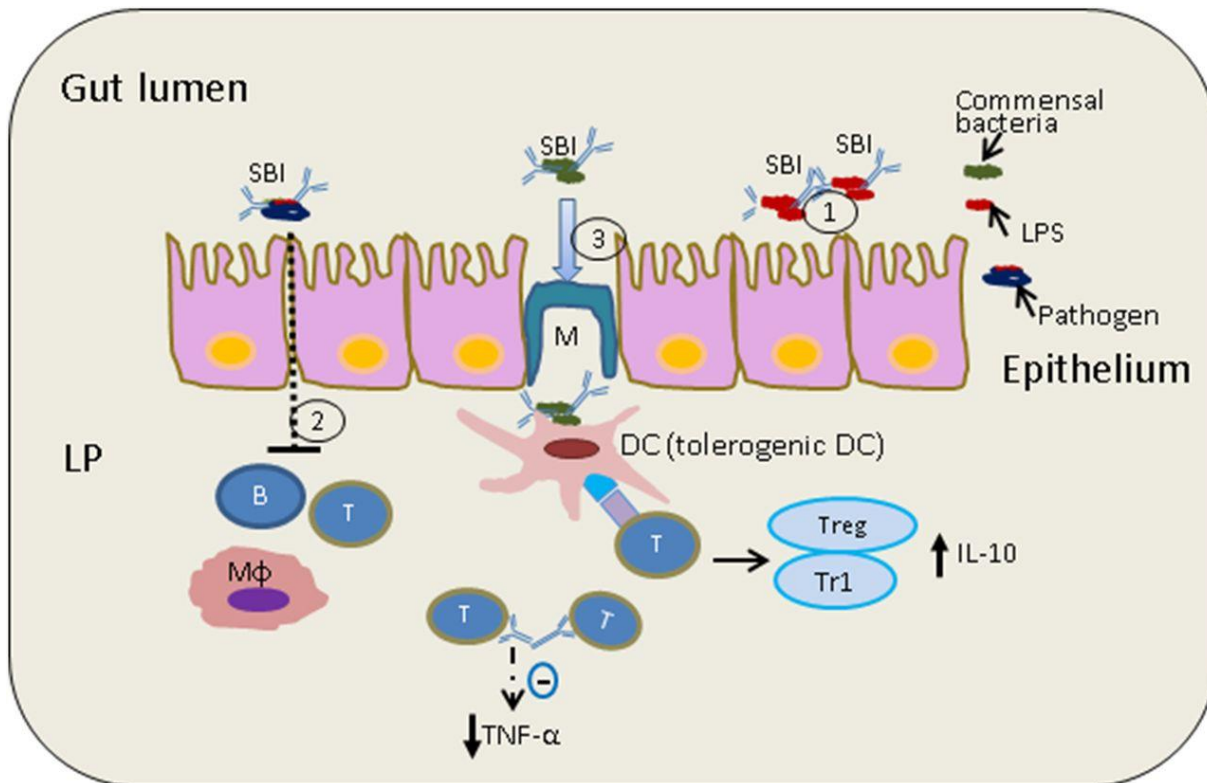


FIGURE 1 Proposed mechanisms of action of oral Ig SBI....

© 2016 American Society for Nutrition

- (1) SBI binds luminal bacteria and their endotoxins (LPS) to prevent circulating LPS
- (2) Reduced transepithelial antigen absorption across the small and/or large intestine has been linked to reduced immune activation
- (3) SBI may interact with healthy commensals to induce tolerogenic DCs.

Oral SBI found to decrease **systemic** inflammation and leaky gut in people with HIV → significantly decreased IL-6 and Zonulin

- Utay NS, Somasunderam A, Hinkle JE, et al. Serum Bovine Immunoglobulins Improve Inflammation and Gut Barrier Function in Persons with HIV and Enteropathy on Suppressive ART. *Pathog Immun.* 2019;4(1):124-146. Published 2019 May 3. doi:10.20411/pai.v4i1.276



How Do Kids' Gut Microbiomes Become Dysregulated?

Microbiome Mischief Makers



QUIZ

What are the most common
microbiome disruptors our
kids/teens face today?





Microbiome Mischief Makers

- Microbiome-disrupting antibiotics/medications
 - Antibiotics
 - NSAIDs (like ibuprofen)
 - Reflux/antacid medications
 - Steroids
 - Oral contraceptives
 - SSRIs
- Our ultra-processed SAD diet
 - Reduce food additives
 - Reduce added sugars and artificial sweeteners
 - Reduce/remove gluten and casein
 - Reduce glyphosate exposure
- Psychological stress



QUIZ

Children/teens consume at least
XXX of their calories as
ultraprocessed foods.





Ultraprocessed Foods & the Gut Microbiome



Ultraprocessed foods are insidious & ubiquitous microbiome disruptors

Children/teens consume at least 2/3 of their calories as
ultraprocessed foods.

Wang L, Martínez Steele E, Du M, et al. Trends in Consumption of Ultraprocessed Foods Among US Youths Aged 2-19 Years, 1999-2018. *JAMA*. 2021;326(6):519-530. doi:10.1001/jama.2021.10238



Ultraprocessed Foods & Kids' Brains

- **Ultra-processed foods** changes brain morphology in children with smaller cerebral white matter volume at age 10
 - Higher quality diet associated with higher IQ, greater brain gyrification and larger cerebral gray matter volume at age 8
 - Mou Y, Blok E, Barroso M, Jansen PW, White T, Voortman T. Dietary patterns, brain morphology and cognitive performance in children: Results from a prospective population-based study. *Eur J Epidemiol.* 2023;38(6):669-687. doi:10.1007/s10654-023-01012-5
- **Ultra-processed foods** associated with ADHD, anxiety, depression, cognitive decline
 - Prescott SL, D'Adamo CR, Holton KF, Ortiz S, Overby N, Logan AC. Beyond Plants: The Ultra-Processing of Global Diets Is Harming the Health of People, Places, and Planet. *Int J Environ Res Public Health.* 2023;20(15):6461. Published 2023 Jul 27. doi:10.3390/ijerph20156461
- **Ultra-processed foods** during pregnancy increases risk for ADHD in offspring
 - Zupo R, Castellana F, Boero G, et al. Processed foods and diet quality in pregnancy may affect child neurodevelopment disorders: a narrative review. *Nutr Neurosci.* Published online April 11, 2023. doi:10.1080/1028415X.2023.2197709
- It takes only 2 months of a steady diet of processed foods
 - → to LOWER brain chemicals responsible for learning and memory
 - Molteni R, Barnard RJ, Ying Z, Roberts CK, Gómez-Pinilla F. A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning. *Neuroscience.* 2002;112(4):803-814. doi:10.1016/s0306-4522(02)00123-9
- 4.5 year-olds who ate a junk food diet
 - → much more likely to have behavioral problems when they turned 7
 - Wiles NJ, Northstone K, Emmett P, Lewis G. 'Junk food' diet and childhood behavioural problems: results from the ALSPAC cohort. *Eur J Clin Nutr.* 2009;63(4):491-498. doi:10.1038/sj.ejcn.1602967



The Standard American Diet & the Gut Microbiome (it's so SAD 😞)



I'll have fries with that...



And don't forget the Diet Coke!



FDA-Approved Food Additives, Colors, and the Gut Microbiome

- Cause direct harm to gut microbiome and cause gut dysbiosis and leaky gut
- Artificial food dyes are poison to kids' gut-brain connections
- Food additives (esp emulsifiers) directly correlated with increased risk of autoimmune disease
 - **Emulsifiers (surfactants)** disrupt tight junctions and directly cause leaky gut and gut inflammation
 - Look for mono- and diglycerides, carrageenan, polysorbate 80, carboxymethylcellulose, *potassium sorbate*
 - Harmful effects of sucrose fatty acid esters found at 50 mg/L
 - FDA allows infant formula to have levels up to 120 mg/L!



- Gultekin F, Oner ME, Savas HB, Dogan B. Food additives and microbiota. North Clin Istanbul. 2019;7(2):192-200. Published 2019 Jul 17. doi:10.14744/nci.2019.92499
- Chassaing B, Compher C, Bonhomme B, et al. Randomized Controlled-Feeding Study of Dietary Emulsifier Carboxymethylcellulose Reveals Detrimental Impacts on the Gut Microbiota and Metabolome. Gastroenterology. 2022;162(3):743-756. doi:10.1053/j.gastro.2021.11.006
- Lerner A, Matthias T. Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease. Autoimmun Rev. 2015;14(6):479-489. doi:10.1016/j.autrev.2015.01.009
- Csáki KF. Synthetic surfactant food additives can cause intestinal barrier dysfunction. Med Hypotheses. 2011;76(5):676-681. doi:10.1016/j.mehy.2011.01.030

Added Sugar & the Gut Microbiome

- High-sugar, high-fat Western diets induces intestinal Paneth cell dysfunction leading to **gut dysbiosis and gut inflammation**
 - Liu TC, Kern JT, Jain U, et al. Western diet induces Paneth cell defects through microbiome alterations and farnesoid X receptor and type I interferon activation. Cell Host Microbe. 2021;29(6):988-1001.e6. doi:10.1016/j.chom.2021.04.004
- Sugar and yeast dysbiosis
- Sugar compromises cognitive abilities (learning and memory) → ADHD
- Sugar linked with depression & schizophrenia
- Sugar worsens anxiety and body's ability to cope with stress
- Sugar and glucose/insulin dysregulation
- Sugar is as **ADDICTIVE**, or more, than cocaine
- Added sugar is found EVERYWHERE





QUIZ

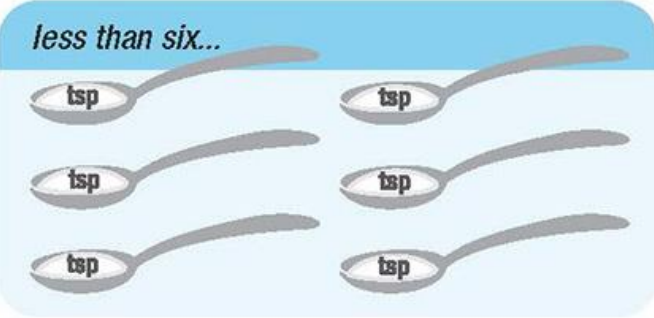

Children should have NO MORE than **XXX** grams of added sugar daily.




How much added sugar is “too” much?

HEALTHY KIDS ARE SWEET ENOUGH

Kids age 2-18 should have **LESS THAN 25 GRAMS** or **SIX TEASPOONS** of **ADDED SUGARS DAILY** for a healthy heart.



Source: American Heart Association statement:
Added Sugars and Cardiovascular Disease Risk in Children

 **American Heart Association.**
life is why™

1 tsp = 4.2 grams sugar

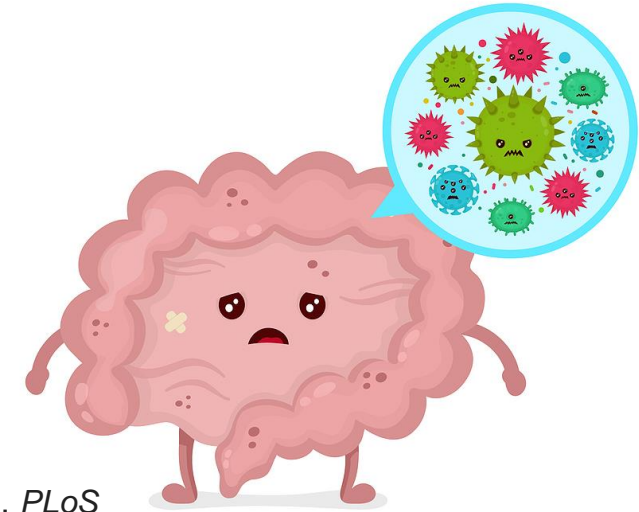
QUIZ

Cocaine-addicted rats chose which artificial sweetener over cocaine?



“Sugar-Free” Isn’t Better

- FDA-approved artificial “high-intensity sweeteners”
 - Just as addictive as refined sugar and cocaine
 - Rats already addicted to cocaine **chose saccharin** over cocaine
 - Lenoir M, Serre F, Cantin L, Ahmed SH. Intense sweetness surpasses cocaine reward. *PLoS One*. 2007;2(8):e698. Published 2007 Aug 1. doi:10.1371/journal.pone.0000698
 - **Can disrupt the gut microbiome** (esp saccharin and sucralose)
 - Del Pozo S, Gómez-Martínez S, Díaz LE, Nova E, Urrialde R, Marcos A. Potential Effects of Sucralose and Saccharin on Gut Microbiota: A Review. *Nutrients*. 2022;14(8):1682. Published 2022 Apr 18. doi:10.3390/nu14081682
 - Acesulfame potassium affects brain in mice and decreases memory and cognitive function
 - Ibi D, Suzuki F, Hiramatsu M. Effect of AceK (acesulfame potassium) on brain function under dietary restriction in mice. *Physiol Behav*. 2018;188:291-297. doi:10.1016/j.physbeh.2018.02.024



“Fake sugar” to avoid

- Saccharin
- Aspartame (NutraSweet, Equal)
- Acesulfame potassium (Ace-K)
- Sucralose (Splenda)
- Neotame
- Advantame

QUIZ

Glyphosate was initially patented as
a **XXX**.





Glyphosate & the Gut Microbiome

- Glyphosate initially patented by Monsanto in 2010 as an **antibiotic**
 - Broad activity against a variety of bacteria and fungi
- Implicated in increasing problem of antibiotic resistance and multi-drug resistant bacteria
- **Directly causes gut dysbiosis**
 - Kills beneficial Lactobacillus and Bifidobacter species
 - Preserves pathogenic Clostridia and Salmonella species
 - Directly injures tight junctions, triggers zonulin release, and causes leaky gut
 - Tight junctions also present in linings of upper respiratory tract, kidneys and blood-brain barrier
 - Glyphosate may cause similar damage to BBB



Glyphosate References

- Raoult D, Hadjadj L, Baron SA, Rolain JM. Role of glyphosate in the emergence of antimicrobial resistance in bacteria?. J Antimicrob Chemother. 2021;76(7):1655-1657. doi:10.1093/jac/dkab102
- Mao Q, Manservigi F, Panzacchi S, et al. The Ramazzini Institute 13-week pilot study on glyphosate and Roundup administered at human-equivalent dose to Sprague Dawley rats: effects on the microbiome. Environ Health. 2018;17(1):50. Published 2018 May 29. doi:10.1186/s12940-018-0394-x
- Argou-Cardozo I, Zeidán-Chuliá F. Clostridium Bacteria and Autism Spectrum Conditions: A Systematic Review and Hypothetical Contribution of Environmental Glyphosate Levels. Med Sci (Basel). 2018;6(2):29. Published 2018 Apr 4. doi:10.3390/medsci6020029
- Gildea JJ, Roberts DA, Bush Z. Protective Effects of Lignite Extract Supplement on Intestinal Barrier Function in Glyphosate-Mediated Tight Junction Injury. J Clin Nutr Diet. 2017, 3:1. doi: 10.4172/2472-1921.100035
- Martinez A, Al-Ahmad AJ. Effects of glyphosate and aminomethylphosphonic acid on an isogeneic model of the human blood-brain barrier. Toxicol Lett. 2019;304:39-49. doi:10.1016/j.toxlet.2018.12.013

QUIZ

How quickly can psychological stress increase zonulin levels?





Psychological Stress & the Gut Microbiome



Psychological stress is the single biggest **CHRONIC** disruptor to the gut microbiome

(Psychological stress increases zonulin within 1 hour)

Linninge C, Jönsson P, Bolinsson H, et al. Effects of acute stress provocation on cortisol levels, zonulin and inflammatory markers in low- and high-stressed men. *Biol Psychol.* 2018;138:48-55. doi:10.1016/j.biopsycho.2018.08.013



How to Heal the Gut-Brain Connection

to restore microbiome resilience
(the Gut ReSET)





Heal the Gut-Brain Connection

- **Step 1:** Evidence-based symptom relief

- **Step 2:** The Gut ReSET



- **Return to the “5 Things” for Microbiome Magic**

- **S**eal and heal the leaky gut
- **E**liminate dysbiotic gut microbiomes (if present)



- **T**ransform the gut microbiome

- **Step 3:** Address additional clinical imbalances

- Mitochondrial dysfunction, detoxification, chronic infections, mycotoxins, etc.



A solid foundation is essential for healing & lasting remission



Evidence-Based Symptom Relief: ADHD

- Saffron 20-30mg/day
 - Blasco-Fontecilla H, Moyano-Ramírez E, Méndez-González O, Rodrigo-Yanguas M, Martin-Moratinos M, Bella-Fernández M. Effectivity of Saffron Extract (Saffr'Activ) on Treatment for Children and Adolescents with Attention Deficit/Hyperactivity Disorder (ADHD): A Clinical Effectivity Study. *Nutrients*. 2022;14(19):4046. Published 2022 Sep 28. doi:10.3390/nu14194046
 - Bazar S, Aqamolaei A, Khadem E, et al. Crocus sativus L. Versus Methylphenidate in Treatment of Children with Attention-Deficit/Hyperactivity Disorder: A Randomized, Double-Blind Pilot Study. *J Child Adolesc Psychopharmacol*. 2019;29(3):205-212. doi:10.1089/cap.2018.0146
- Pycnogenol 1mg/kg/day
 - Blasco-Fontecilla H, Moyano-Ramírez E, Méndez-González O, Rodrigo-Yanguas M, Martin-Moratinos M, Bella-Fernández M. Effectivity of Saffron Extract (Saffr'Activ) on Treatment for Children and Adolescents with Attention Deficit/Hyperactivity Disorder (ADHD): A Clinical Effectivity Study. *Nutrients*. 2022;14(19):4046. Published 2022 Sep 28. doi:10.3390/nu14194046
- PS 300mg, 120mg EPA+DHA), Vitamin B6 (0.6mg/kg/d), Magnesium (6mg/kg/d), Zinc 55mg
 - Ahn J, Ahn HS, Cheong JH, Dela Peña I. Natural Product-Derived Treatments for Attention-Deficit/Hyperactivity Disorder: Safety, Efficacy, and Therapeutic Potential of Combination Therapy. *Neural Plast*. 2016;2016:1320423. doi:10.1155/2016/1320423
- L-theanine 400mg/day
 - Lyon MR, Kapoor MP, Juneja LR. The effects of L-theanine (Suntheanine®) on objective sleep quality in boys with attention deficit hyperactivity disorder (ADHD): a randomized, double-blind, placebo-controlled clinical trial. *Altern Med Rev*. 2011;16(4):348-354.



Evidence-Based Symptom Relief: OCD

- N-acetylcysteine (NAC) 900mg TID
 - Li F, Welling MC, Johnson JA, et al. N-Acetylcysteine for Pediatric Obsessive-Compulsive Disorder: A Small Pilot Study. *J Child Adolesc Psychopharmacol*. 2020;30(1):32-37. doi:10.1089/cap.2019.0041
- Zinc 440mg/day in adults receiving fluoxetine
 - Sayyah M, Olapour A, Saeedabad Ys, Yazdan Parast R, Malayeri A. Evaluation of oral zinc sulfate effect on obsessive-compulsive disorder: a randomized placebo-controlled clinical trial. *Nutrition*. 2012;28(9):892-895. doi:10.1016/j.nut.2011.11.027
- Inositol 18 grams/day in adults
 - Fux M, Levine J, Aviv A, Belmaker RH. Inositol treatment of obsessive-compulsive disorder. *Am J Psychiatry*. 1996;153(9):1219-1221. doi:10.1176/ajp.153.9.1219
- Milk Thistle 600mg/day in adults
 - Sayyah M, Boostani H, Pakseresht S, Malayeri A. Comparison of Silybum marianum (L.) Gaertn. with fluoxetine in the treatment of Obsessive-Compulsive Disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010;34(2):362-365. doi:10.1016/j.pnpbp.2009.12.016
- Valerian 765mg/day in adults
 - Pakseresht S, Boostani H, Sayyah M. Extract of valerian root (*Valeriana officinalis* L.) vs. placebo in treatment of obsessive-compulsive disorder: a randomized double-blind study. *J Complement Integr Med*. 2011;8:/j/jcim.2011.8.issue-1/1553-3840.1465/1553-3840.1465.xml. Published 2011 Oct 11. doi:10.2202/1553-3840.1465



Evidence-Based Symptom Relief: Anxiety

- Clinical evidence: Omega-3 fatty acids, Vitamin D3, Magnesium
- Omega-3 FAs (975mg EPA + 675mg DHA) + Inositol 2000mg (≥ 25 mg) or 80mg/kg (< 25 kg)
 - Wozniak J, Farrell A, DiSalvo M, et al. A Randomized, Double-Blind, Controlled Clinical Trial of Omega-3 Fatty Acids and Inositol as Monotherapies and in Combination for the Treatment of Pediatric Bipolar Spectrum Disorder in Children Age 5-12. *Psychopharmacol Bull.* 2022;52(4):31-51.
- L-Theanine 200mg + Vitamin B6 2.8mg
 - Rizzo R, Prato A, Scerbo M, Saia F, Barone R, Curatolo P. Use of Nutritional Supplements Based on L-Theanine and Vitamin B6 in Children with Tourette Syndrome, with Anxiety Disorders: A Pilot Study. *Nutrients.* 2022;14(4):852. Published 2022 Feb 18. doi:10.3390/nu14040852
- Ashwagandha 250mg-1000mg ÷ BID in adults
 - Speers AB, Cabey KA, Soumyanath A, Wright KM. Effects of *Withania somnifera* (Ashwagandha) on Stress and the Stress- Related Neuropsychiatric Disorders Anxiety, Depression, and Insomnia. *Curr Neuropsychopharmacol.* 2021;19(9):1468-1495. doi:10.2174/1570159X19666210712151556
- Walking in nature
 - Grassini S. A Systematic Review and Meta-Analysis of Nature Walk as an Intervention for Anxiety and Depression. *J Clin Med.* 2022;11(6):1731. Published 2022 Mar 21. doi:10.3390/jcm11061731

The Gut ReSET

- **S**eal and heal the leaky gut
 - Give your gut a break – eliminate food sensitivities and toxins
 - Gut Repair Nutrients – glutamine, zinc, fish oil, quercetin
- **E**liminate dysbiotic gut microbiomes (if present)
 - Do an ***age-appropriate*** comprehensive stool analysis
 - Antimicrobial agents
 - Consider Binders and Serum-derived Bovine Immunoglobulin (SBI)
- **T**ransform the gut microbiome
 - Pre-, Pro-, Postbiotic supplementation
 - Use broad spectrum probiotics, with psychobiotic potential, including:
 - Lactobacillus helveticus Rosell-52, Bifidobacterium longum Rosell-175, PS128
 - Increased Vagus Nerve support (**more to come**)
 - Acupuncture
 - Neurofeedback devices
 - Vagus Nerve stimulators



The Gut ReSET:

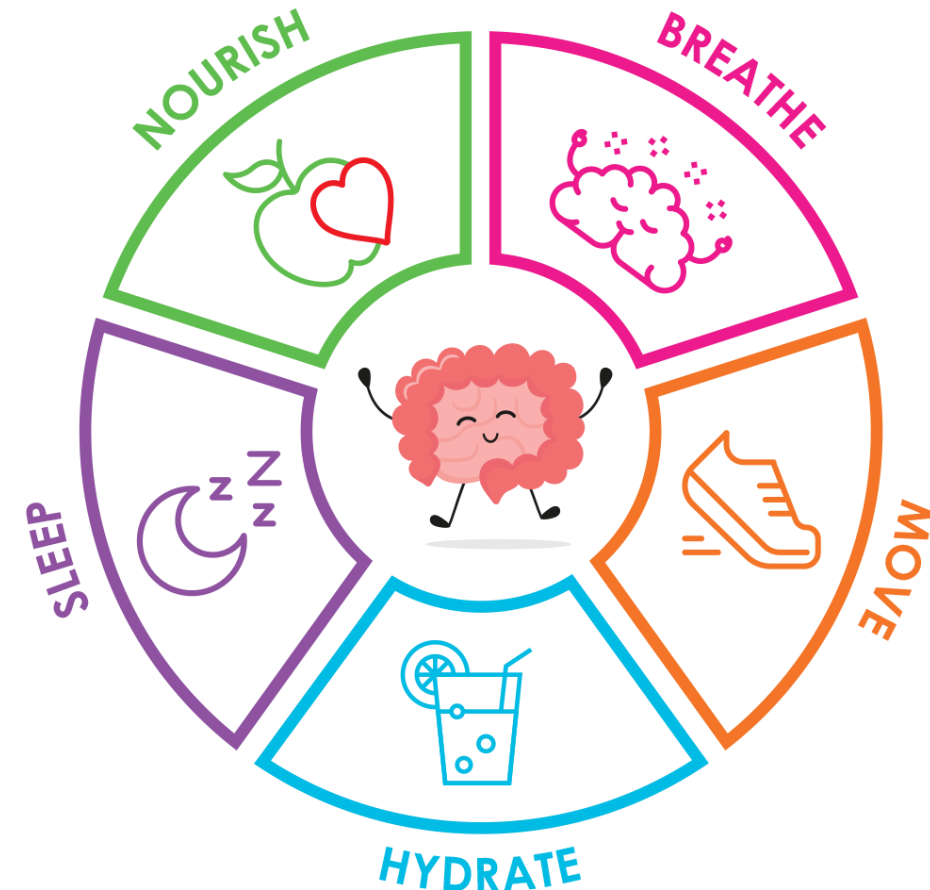
Return to the 5 Things for Microbiome Magic

- **Nourish:** Nurture your microbiome
 - Part 1: Get your Microbiome Champions in
 - Part 2: Keep your Microbiome Mischief Makers out
- **Breathe:** The Vagus Nerve to optimize the gut-brain connection
- **Move:** Daily movement
- **Hydrate:** Healing hydration
- **Sleep:** Restorative sleep for the gut and brain

“5 Things” for Microbiome Magic

- **Nourish:** Nurture your microbiome
- **Breathe:** The Vagus Nerve to optimize the gut-brain connection
- **Move:** Daily movement
- **Hydrate:** Healing hydration
- **Sleep:** Restorative sleep for the gut and brain

THE WHEEL OF Whole Gut Wellness

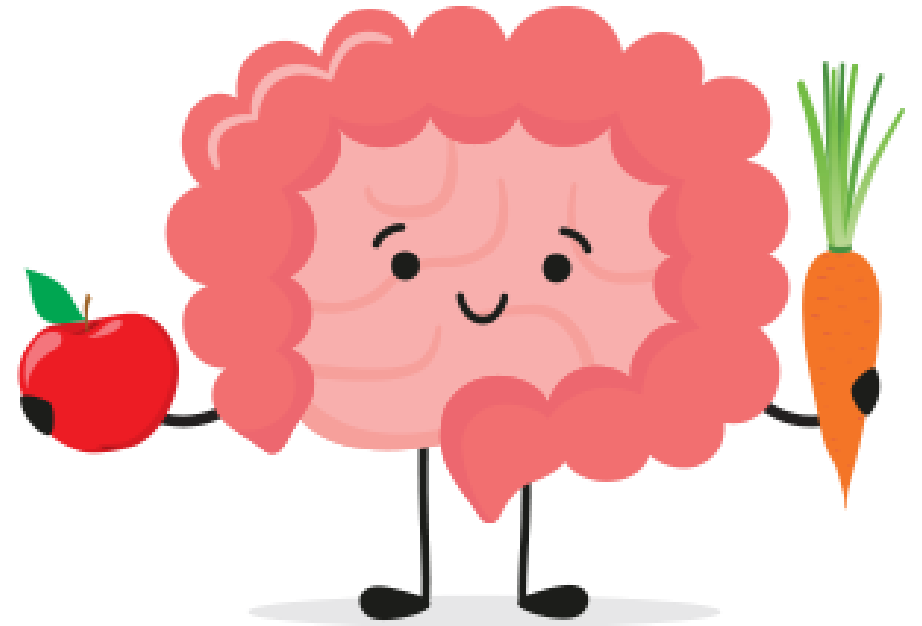




Nourish Part 1:

Get your Microbiome Champions In

- Get in the Whole Gut Rainbow (the 3 F's)
 - Fiber/prebiotics
 - Phytonutrients (color)
 - Fermented foods



QUIZ

1 in **XXX** kids don't eat any
vegetables on any given day.



QUIZ

1 in **XXX** kids don't eat any fruit on any given day.



The 3 F's: Fiber

• The “Fiber Gap”

- Most US adults and kids get < half the recommended daily fiber intake
- Only ~5% meet recommended intake
- 1 in 2 kids don't eat **any** vegetables in any given day
- 1 in 3 kids don't eat **any** fruit in any given day
 - Hamner HC, Dooyema CA, Blanck HM, et al. Fruit, Vegetable, and Sugar-Sweetened Beverage Intake Among Young Children, by State - United States, 2021. MMWR Morb Mortal Wkly Rep. 2023;72(7):165-170. Published 2023 Feb 17. doi:10.15585/mmwr.mm7207a1Tanzania's Hadza people
- Average 100-150 grams of daily fiber
- NO processed foods
- Some of the richest gut microbial diversity in the world
- The lower the fiber and higher the refined sugar/processed foods → the lower the gut microbial diversity

Age/Gender	Recommended daily fiber intake
Adult males > 50 years	30 grams
Adult females > 50 years	21 grams
Adult males <50 years	38 grams
Adult females <50 years	25 grams
Teen males 14-18 years	38 grams
Teen females 14-18 years	26 grams
Boys 9-13 years	31 grams
Girls 9-13 years	26 grams
Children 4-8 years	25 grams
Children 1-3 years	19 grams

- <https://www.healthline.com/health/food-nutrition/too-much-fiber#daily-fiber-intake>
- Smits SA, Leach J, Sonnenburg ED, et al. Seasonal cycling in the gut microbiome of the Hadza hunter-gatherers of Tanzania. Science. 2017;357(6353):802-806. doi:10.1126/science.aan4834

The Colors of Fiber

Red	guava, raspberries, strawberries, apples (with skin on), beets, red bell pepper
Orange/Yellow	sweet potatoes, pumpkin, carrots, apricots, persimmon, grapefruit, orange, nectarine
Green	artichoke, avocado, broccoli, kale, collard beans, spinach, cabbage, brussels sprouts, squash (crookneck, summer, zucchini, acorn), okra, green beans, peas, asparagus, kiwifruit
Blue/Purple	blackberries, blueberries, prunes, raisins, passionfruit
Tan/Brown	seeds (pumpkin, chia, sunflower, flax), nuts (coconut, almonds, chestnuts, pinenuts, pistachios, hazelnuts), legumes (lentil, navy, lima, adzuki, pinto, black, garbanzo, kidney), whole grains (whole wheat, barley, bran, quinoa, oat, popcorn, brown rice, bulgur, spelt, teff), potato (with skin), mushrooms
White	parsnips, jicama, cauliflower, kohlrabi, Asian pear, bananas, pears

Tan/Brown
packs the
biggest fiber
punch per
bite!



Fiber in Foods – Make It Concrete

- 1 cup of raspberries – 9 grams
- 1 cup of blueberries – 3.5 grams
- 1 medium apple w/skin – 4-5 grams
- 1 cup of broccoli – 5 grams
- ½ medium avocado – 5 grams
- 1 cup cooked carrots – 5 grams
- 1 cup raw carrots – 3.5 grams
- ½ cup of brown rice – 2 grams
- ½ cup of white rice – 0.5 grams
- 1 tablespoon of chia seeds – 5 grams
- 2 tablespoons of peanut butter – 2 grams
- 1 cup of lentils – 16 grams
- 1 cup of edamame – 8 grams

- Betty W. Li, Karen W. Andrews, and Pamela R. Pehrsson, “Individual Sugars, Soluble, and Insoluble Dietary Fiber Contents of 70 High Consumption Foods,” *Journal of Food Composition and Analysis* 15 (2002): 715–23.
- https://www.ars.usda.gov/arsuserfiles/80400525/articles/jfca15_715-723.pdf
- Food Sources of Dietary Fiber, 2020–2025 Dietary Guidelines and Online Materials, Dietary Guidelines for Americans. <https://www.dietaryguidelines.gov/resources/2020-2025-dietary-guidelines-online-materials/food-sources-select-nutrients/food-0>.

The 3 F's: Phytonutrients

- Get in a variety of **COLOR** – each color has different Phytonutrient Power
 - Promote growth of beneficial microbiota; inhibit pathogenic microbiota
 - Influence production of metabolites (postbiotics) by beneficial microbiota
 - Kan J, Wu F, Wang F, et al. Phytonutrients: Sources, bioavailability, interaction with gut microbiota, and their impacts on human health. Front Nutr. 2022;9:960309. Published 2022 Aug 16. doi:10.3389/fnut.2022.960309
- **The Phytonutrient Gap**
 - 8 in 10 Americans has a phytonutrient gap – in EVERY color
 - 83% don't get enough White
 - 80% don't get enough Orange/Yellow
 - 76% don't get enough Blue/Purple
 - 74% don't get enough Red
 - 69% don't get enough Green
 - <https://boletin.inmegen.gob.mx/boletin2/images/AmericaPhytonutrientReport.pdf>

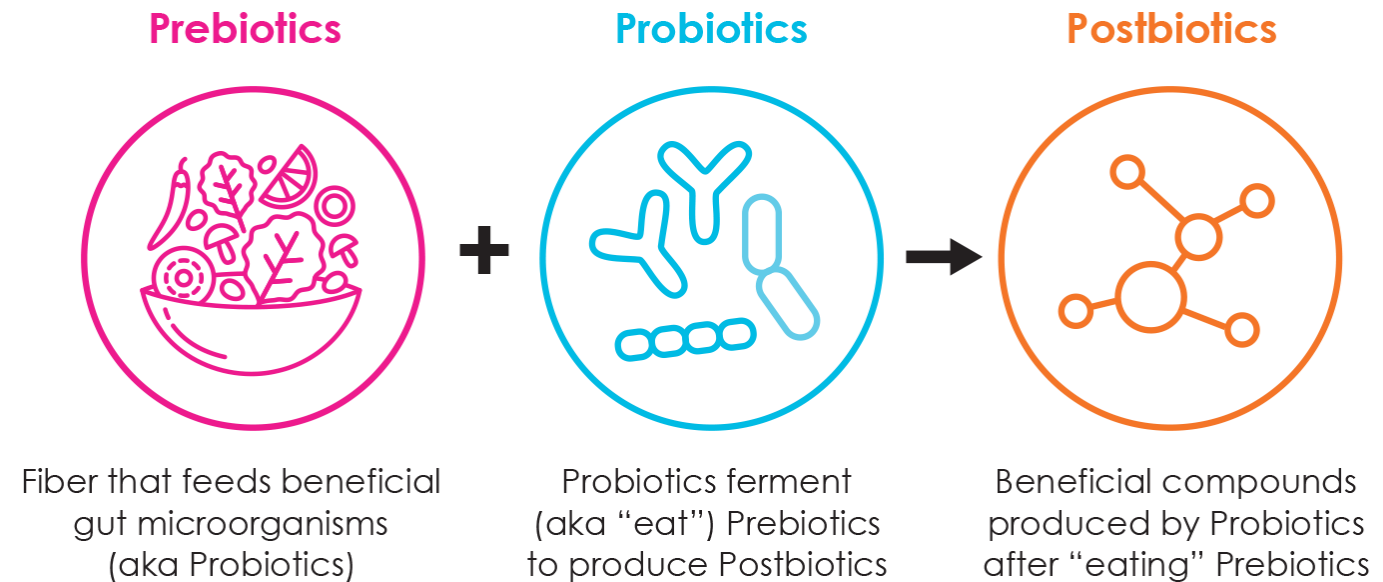


The 3 F's: Fermented Foods

- **Fermented Foods: Probiotics with a Postbiotic Punch!**

- Yogurt (caveat: avoid dairy if “phlegmy”)
 - Options – almond, coconut, cashew
- Kefir (dairy, coconut, water)
- Kombucha
- Kvass
- Sauerkraut
- Real pickles & pickled vegetables
- Raw unfiltered apple cider vinegar
- Miso
- Natto
- Tempeh
- Kimchi

Prebiotic vs. Probiotic vs. Postbiotic





QUIZ

Which is better for your gut
microbiome?

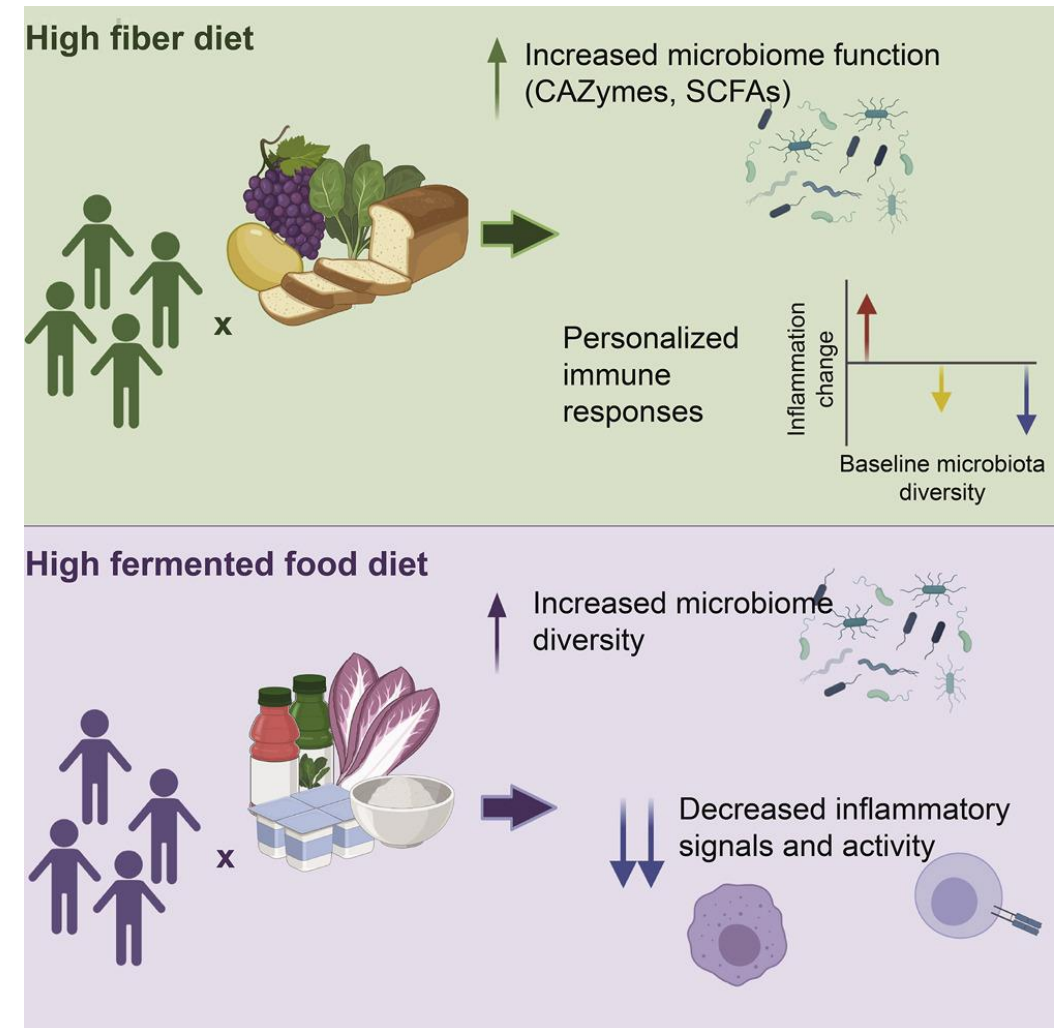
Fiber or Fermented foods



Fermented Foods vs. Fiber

- **Fermented foods may win over fiber**
- 17-week randomized prospective study of plant-based fiber vs. fermented foods
- High-fiber diet increased microbiome-function despite stable microbial community diversity
- High-fermented-food diet steadily increased microbiota diversity and decreased inflammatory markers
- **CONCLUSION:** “Fermented foods may be valuable in countering the decreased microbiome diversity and increased inflammation pervasive in industrialized society.”

- Wastyk HC, Fragiadakis GK, Perelman D, et al. Gut-microbiota-targeted diets modulate human immune status. *Cell*. 2021;184(16):4137-4153.e14. doi:10.1016/j.cell.2021.06.019



NOURISH Part 2:

Keep Microbiome Mischief Makers Out

- Move from an ultra-processed SAD diet to a Gut Hero one!
 - Reduce food additives
 - Reduce added sugars and artificial sweeteners
 - Reduce/remove gluten and casein
 - Reduce glyphosate exposure



Eat REAL food with REAL ingredients

Become a Gut Hero Food Label Detective!



Skout Organic Strawberry Jam
Kids Snack Bar



Kellogg's Nutri-Grain Soft Baked
Strawberry Breakfast Bar

Nutrition Facts

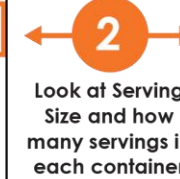
1 serving per container
Serving size 1 bar (24g)

Amount per serving
Calories 90

	% Daily Value*
Total Fat 2g	3%
Saturated Fat 1.5g	8%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 10mg	0%
Total Carbohydrate 16g	6%
Dietary Fiber 2g	7%
Total Sugars 10g	
Includes 0g Added Sugars	0%
Protein 2g	4%
Vitamin D 0mcg	0%
Calcium 20mg	2%
Iron 0.7mg	4%
Potassium 150mg	4%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

Ingredients: Organic Dates, Organic Strawberries, Organic Coconut Milk Powder, Organic Sunflower Seed Protein Powder, Organic Cocoa Butter, Organic Strawberry Essence, Organic Lemon Juice Concentrate. Contains: Coconut.



Nutrition Facts

1 servings per container
Serving size 1 bar (37g)

Amount per serving
Calories 130

	% Daily Value*
Total Fat 3.5g	4%
Saturated Fat 0.5g	3%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 140mg	6%
Total Carbohydrate 25g	9%
Dietary Fiber 1g	5%
Total Sugars 12g	
Includes 12g Added Sugars	24%
Protein 2g	
Vitamin D 0%	Calcium 130mg 10%
Iron 1.8mg 10%	Potassium 80mg 0%
Vitamin A 10%	Thiamin 10%
Riboflavin 10%	Niacin 10%
Vitamin B6 10%	Zinc 10%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

Ingredients: Crust: Whole Grain Oats, Enriched Flour (Wheat Flour, Niacin, Reduced Iron, Vitamin B1 [Thiamin Mononitrate], Vitamin B2 [Riboflavin], Folic Acid), Soybean Oil, Whole Wheat Flour, Sugar, Dextrose, Fructose, Calcium Carbonate, Vegetable Glycerin, Invert Sugar, Salt, Whey, Soluble Corn Fiber, Wheat Bran, Cellulose, Natural Flavors, Potassium Bicarbonate, Mono-And Diglycerides, Soy Lecithin, Wheat Gluten, Niacinamide, Vitamin A Palmitate, Carrageenan, Zinc Oxide, Reduced Iron, Guar Gum, Vitamin B6 (Pyridoxine Hydrochloride), Vitamin B1 (Thiamin Hydrochloride), Vitamin B2 (Riboflavin), Filling: Invert Sugar, Corn Syrup, Strawberry Puree Concentrate, Vegetable Glycerin, Sugar, Modified Food Starch, Vegetable Juice For Color, Sodium Citrate, Sodium Alginate, Citric Acid, Natural Flavors, Dicalcium Phosphate, Methylcellulose, Malic Acid. Contains wheat, milk and soy ingredients.





Nutrition Facts Servings: 1, **Serv. size: 1 cup (150g),**
Amount per serving: **Calories 170, Total Fat 5g** (6% DV),
Sat. Fat 3.5g (18% DV), Trans Fat 0g, **Cholest.** 20mg
(7% DV), **Sodium** 45mg (2% DV), **Total Carb.** 20g (7% DV),
Fiber 0g (0% DV), Total Sugars 18g (Incl. 15g Added Sugars,
30% DV), **Protein** 11g (22% DV), Vit. D (2% DV), Calcium
(10% DV), Iron (0% DV), Potas. (4% DV).



22 Whole Grains & Seeds

27
OZ

2 slices = 8g of added
sugar

Nutrition Facts		
16 Servings Per Container		
Serving size 1 slice (48g)		
Amount per serving		
Calories 140		
% Daily Value*		
Total Fat 3g		4%
Saturated Fat 0g		0%
Trans Fat 0g		
Polyunsaturated Fat 1.5g		
Monounsaturated Fat 1g		
Cholesterol 0mg		0%
Sodium 220mg		10%
Total Carbohydrate 22g		8%
Dietary Fiber 4g		14%
Total Sugars 4g		
Includes 4g Added Sugars		8%
Protein 6g		4%
Vitamin D 0mcg	0% • Calcium 45mg	4%
Iron 1.2mg	6% • Potassium 130mg	2%
Vitamin A 0mcg	0% • Vitamin C 0mg	0%
Vitamin E 0.3mg	2% • Vitamin K 0mg	0%
Thiamin 0.1 mg	8% • Riboflavin 0.03mg	2%
Niacin 1.2mg	8% • Vitamin B6 0mg	0%
Folate 10mcg DFE	2% • Pantothenic Acid 0.13mg	2%
(0mcg Folic Acid)		
Phosphorus 70mg	6% • Magnesium 25mg	6%
Zinc 0.5mg	4% • Selenium 0mcg	0%
Copper 0.1mg	10% • Manganese 0.43mg	20%
*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.		

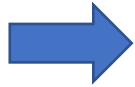


By lunchtime, your child could
have had
29 grams of added sugar or ~ 7
teaspoons of sugar

The sugar adds up

MAKE GUT HERO SWAPS

YUCK!



A little better



Better



Best



INGREDIENTS: CORN MASA FLOUR (PROCESSED WITH LIME), SOYBEAN AND/OR PALM AND/OR CANOLA OIL, IODIZED SALT, SUGAR, NATURAL AND ARTIFICIAL FLAVOR, CITRIC ACID, SOY PROTEIN, YEAST, MONOSODIUM GLUTAMATE, MALTODEXTRIN, SODIUM DIACETATE, PARTIALLY HYDROGENATED SOYBEAN OIL, ARTIFICIAL COLORS (RED No. 40 LAKE, YELLOW No. 6 LAKE), ONION POWDER, HOT CHILI PEPPER (CHILE), SODIUM BICARBONATE, SODIUM GUANYLATE, SODIUM INOSINATE, SILICON DIOXIDE (ANTICAKING), ANTIOXIDANT (BHT, TBHQ, PROPYLENE GLYCOL, BHA).

MAY CONTAIN MILK, WHEAT AND EGG.

INGREDIENTS: STONE GROUND YELLOW CORN, VEGETABLE OIL (HIGH-OLEIC SUNFLOWER OIL, HIGH-OLEIC SAFFLOWER OIL AND/OR OLEIC CANOLA OIL), HOT CHILI & LIME FLAVORED SEASONING (SALT, YEAST, CORNSTARCH, CANE SUGAR, CITRIC ACID [ACIDULANT], YEAST EXTRACT, CORN MALTODEXTRIN, GUM ARABIC, MALIC ACID, LIME JUICE CONCENTRATE, ONION POWDER, VEGETABLE JUICE [COLOR], PAPRIKA EXTRACT [COLOR], TURMERIC EXTRACT [COLOR], NATURAL FLAVOR, BETA CAROTENE [COLOR], TOCOPHEROL [TO PRESERVE], OLEORESIN CAPSICUM), TRACE OF LIME.

DIST. & SOLD EXCLUSIVELY BY:
TRADER JOE'S, MONROVIA, CA 91016

SKU# 61420

GLUTEN FREE

INGREDIENTS: Ground Corn, Expeller-Pressed Canola and/or Sunflower Oil, Vinegar Powder (Maltodextrin, White Distilled Vinegar), Sea Salt, Rice Flour, Paprika, Paprika Extract, Yeast Extract, Onion Powder, Cane Sugar, Citric Acid (for flavor), Chile Pepper, Garlic Powder, Chile Pepper Extract, Lime Juice Powder, Lactic Acid (for flavor)

Fuego Tortilla Chips: cassava flour, avocado oil, coconut flour, ground chia seed, sea salt, coconut milk powder, red beet powder, nutritional yeast, ground red chile powder, citric acid, lactic acid, tomato powder, jalapeño powder, onion powder, garlic powder, habanero powder.

QUIZ

Mindfulness/Meditation can
improve your gut microbiome
independent of diet.

Yes / No





The 5 Things: Breathe

(The Vagus Nerve & Gut Microbiome)



- HRV is a measure of Vagus Nerve function
 - HRV ~ Respiratory Sinus Arrhythmia
 - HRV > 15 bpm is NORMAL
 - ALL kids should have this or more...
 - <10 bpm in patients < 40 years or <5 bpm at any age is ABNORMAL
- Happiness/positive emotions and high Heart Rate Variability (HRV) associated with higher gut microbiome diversity in children
- High stress and low HRV associated with lower microbiome diversity in children
- Independent of diet
 - Michels N, Van de Wiele T, Fouhy F, O'Mahony S, Clarke G, Keane J. Gut microbiome patterns depending on children's psychosocial stress: Reports versus biomarkers. *Brain Behav Immun.* 2019;80:751-762. doi:10.1016/j.bbi.2019.05.024
- Optimal HRV lowers cortisol AND increases WBC ability to fight infections
 - Segerstrom SC, Taylor SE, Kemeny ME, Fahey JL. Optimism is associated with mood, coping, and immune change in response to stress. *J Pers Soc Psychol.* 1998;74(6):1646-1655. doi:10.1037//0022-3514.74.6.1646



QUIZ

What are some (free) ways to improve Heart Rate Variability?



Optimize Vagus Nerve Function – An **ESSENTIAL** Prescription

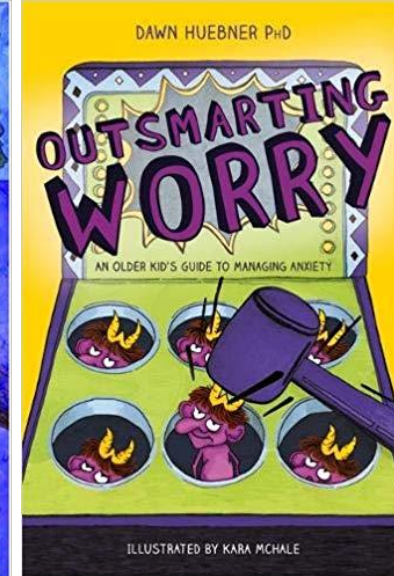
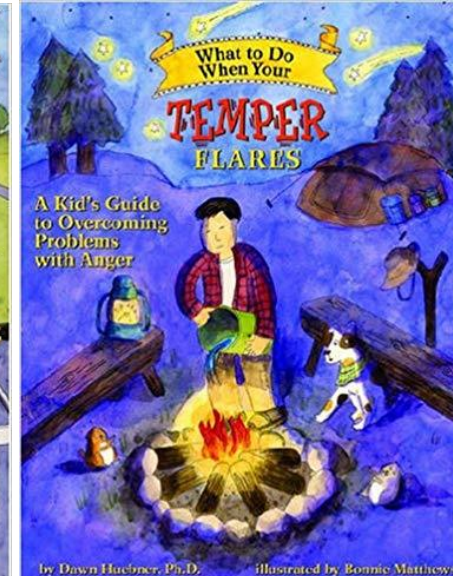
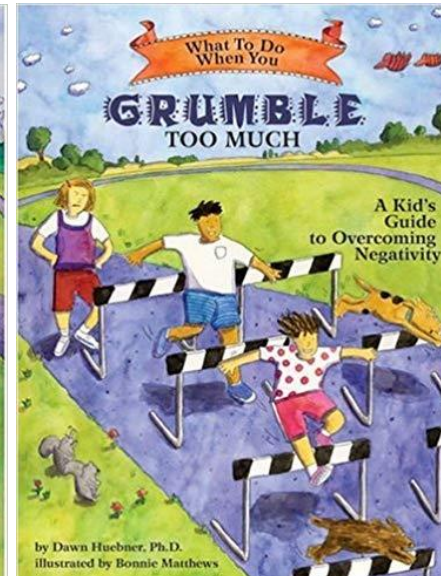
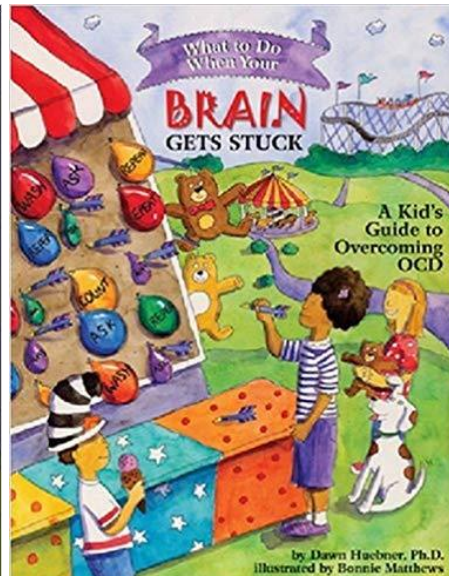
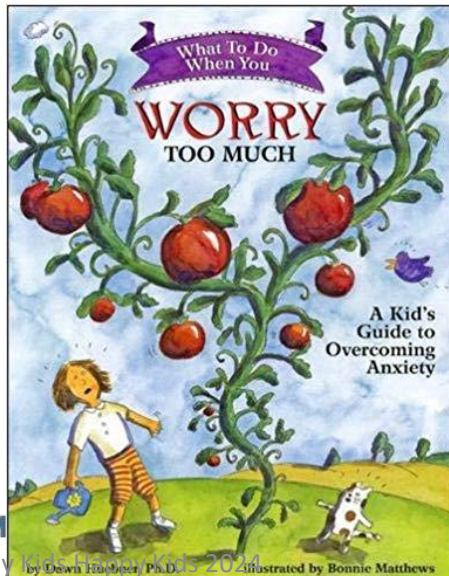
- Optimal HRV = Vagus Nerve Function = Optimal Gut Microbiome
- How to optimize HRV
 - Cognitive Behavioral Therapy
 - Mindfulness/Meditation
 - Heartmath
 - Diaphragmatic breathing
 - Gratitude/Loving Kindness
 - Laughter
 - EFT Tapping
 - Acupuncture
 - Vagus Nerve Stimulation



Mindfulness/Meditation can be practiced anywhere, anytime...

Optimize HRV – Cognitive Behavioral Therapy

- CBT is a cornerstone of treatment in PANS/PANDAS
- CBT can increase HRV
 - 43 young women with IBS → 8-week CBT intervention
 - Improvement in GI sx and HRV sustained at 24 weeks
 - Jang A, Hwang SK, Padhye NS, Meininger JC. Effects of Cognitive Behavior Therapy on Heart Rate Variability in Young Females with Constipation-predominant Irritable Bowel Syndrome: A Parallel-group Trial. *J Neurogastroenterol Motil.* 2017;23(3):435-445. doi:10.5056/jnm17017
- Individual or group CBT
- Dawn Huebner, PhD's kids' "self-help books"



Optimize HRV– Mindfulness/Meditation

- Inner Balance Heartmath app



- Mindfulness/meditation apps

- Insight Timer
- Headspace app
- Calm app
- Oak app

MEGAN WINKLER

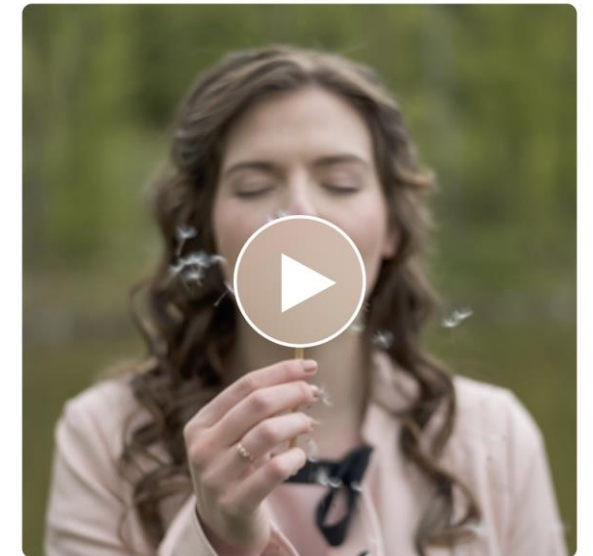
5-Minute Breathing Meditation

★★★★★

5 min

4.3k plays

Guided



This 5-minute meditation focuses on the breath. Soft prompts guide you through this quick, mindful break and a final prompt ...

Optimize HRV– Connection/Gratitude

- “Loving kindness” meditation x 6 weeks
 - Increased HRV, greater sense of connectedness to others, increased positive emotions (joy, interest, amusement, serenity, hope)
 - Kok BE, Coffey KA, Cohn MA, et al. How positive emotions build physical health: perceived positive social connections account for the upward spiral between positive emotions and vagal tone [published correction appears in Psychol Sci. 2016 Jun;27(6):931]. Psychol Sci. 2013;24(7):1123-1132. doi:10.1177/0956797612470827

May you feel safe
May you feel happy
May you feel healthy
May you live with ease



Optimize HRV– Breathe

- Diaphragmatic “belly breathing” to activate of the vagus nerve
 - Get out of fight-flight-freeze
 - Get into rest-digest-heal...
- Diaphragmatic breathing benefits:
 - Lower cortisol
 - Increased HRV
 - Increased energy, alertness, relaxation, mood
 - Decreased anxiety, depression, anger, confusion



Zaccar A et al. How Breath-Control Can Change Your Life: A Systematic Review on Psycho-Physiological Correlates of Slow Breathing. [Front Hum Neurosci](#). 2018 Sep 7;12:353. doi: 10.3389/fnhum.2018.00353



Teach Your Child to “Belly Breathe”

- Sit or lie comfortably
- Place one hand on chest
- Place the other hand on belly
- Pretend there’s a balloon in their belly that they need to inflate every time you take a deep inhale, and deflate fully with every exhale
- Breathe in through their nose and fill that balloon, noticing the hand on their belly rise, and the hand on their chest staying still
- Breathe out through their mouth, feeling the hand on their belly sink all the way down, while the hand on their chest remains still

Sesame Street: Common and Colbie Caillat – “Belly Breathe” with Elmo

<https://www.youtube.com/watch?v=mZbzDOpyIA>

Optimize HRV– Hum, Sing, Chant

- Not just any old song...
 - Coherent RSA highest in Mantra singing > Choir/hymn singing > Humming

A ♩ = 93

Härlig är Jorden

B.S Ingemann 1850, C Bååth-Holmberg 1884
Music: Trad. Silesian Folk Song 1842



B ♩ = 48

Just Relax

Björn Vickhoff / Rickard Åström



(A) The hymn *Fairest Lord Jesus* (Swedish *Härlig Är Jorden*). The tempo 93 bpm means that two bars take 5.156 s, which invites singers to a 0.194 Hz respiration rate. Four bars take 10.312 (0.097 respiration rate). **(B)** The mantra. Singers are asked to breathe solely between the phrases, which corresponds to a respiration rate of 0.1 Hz.

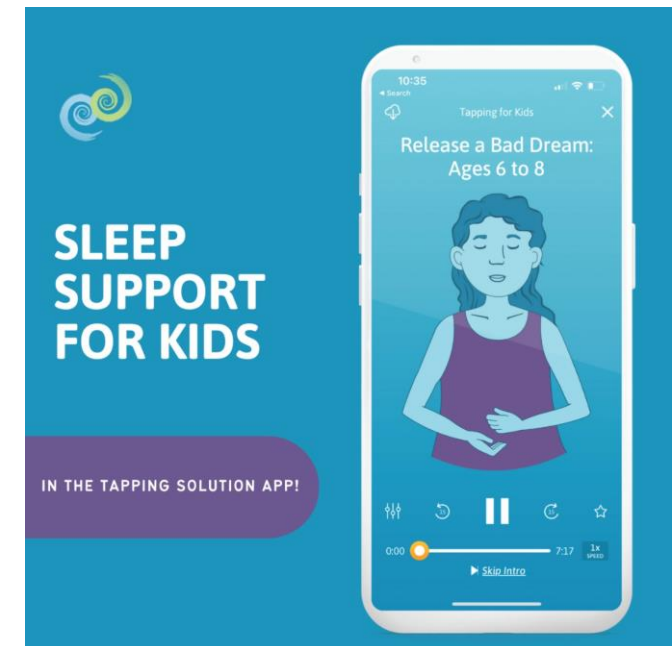
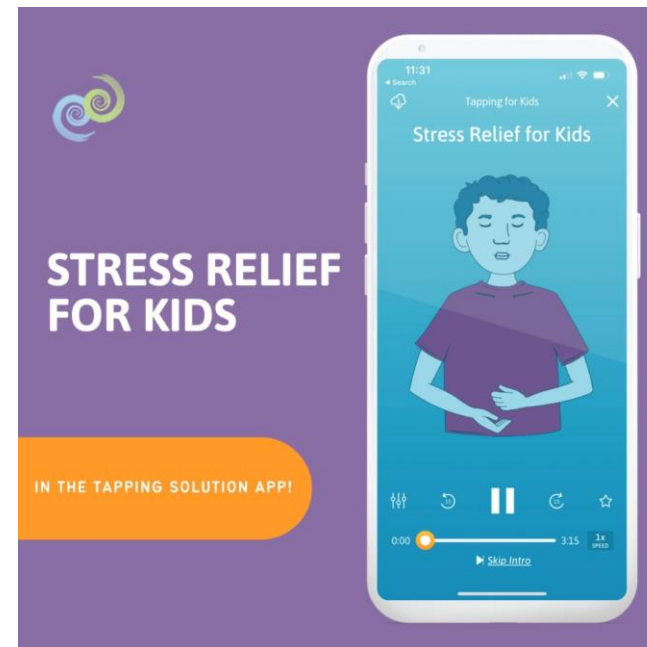
Optimize HRV— Laughter

- Laughter yoga improves HRV and mood
 - Dolgoff-Kaspar R, Baldwin A, Johnson MS, Edling N, Sethi GK. Effect of laughter yoga on mood and heart rate variability in patients awaiting organ transplantation: a pilot study [published correction appears in Altern Ther Health Med. 2012 Nov-Dec;18(6):79]. Altern Ther Health Med. 2012;18(5):61-66.
- Laughter really is good medicine!



Optimize HRV – Emotional Freedom Technique (“EFT” or “Tapping”)

- Tapping can increase Salivary IgA levels by 113%!
- Improves HRV and happiness
- Reduces cortisol, anxiety, depression, pain, cravings
 - Bach D, Groesbeck G, Stapleton P, Sims R, Blickheuser K, Church D. Clinical EFT (Emotional Freedom Techniques) Improves Multiple Physiological Markers of Health. J Evid Based Integr Med. 2019;24:2515690X18823691. doi:10.1177/2515690X18823691





QUIZ

What essential oils can improve
Heart Rate Variability?



Essential Oils & HRV

- Essential oils that improve HRV
 - Lavender
 - Sandalwood
- Essential oils with anxiolytic effects
 - Lavandula angustifolia
 - Citrus aurantium (bitter orange)
 - Citrus sinensis (sweet orange)
 - Bergamot
 - Achillea wilhelmsii (Iran)
 - Alpinia zerumbet (shell ginger)
 - Spiranthera odoratissima (Persia)



- Wu CY, Lee HF, Chang CW, Chiang HC, Tsai YH, Liu HE. The Immediate Effects of Lavender Aromatherapy Massage versus Massage in Work Stress, Burnout, and HRV Parameters: A Randomized Controlled Trial. *Evid Based Complement Alternat Med*. 2020;2020:8830083. Published 2020 Nov 23. doi:10.1155/2020/8830083
- Lin PH, Lin YP, Chen KL, Yang SY, Shih YH, Wang PY. Effect of aromatherapy on autonomic nervous system regulation with treadmill exercise-induced stress among adolescents. *PLoS One*. 2021;16(4):e0249795. Published 2021 Apr 13. doi:10.1371/journal.pone.0249795
- De souse DP et al. A Systematic Review of the Anxiolytic-Like Effects of Essential Oils in Animal Models. [Molecules](#). 2015 Oct 14;20(10):18620-60. doi: 10.3390/molecules201018620.
- Malcom BJ and K Tallian. Essential oil of lavender in anxiety disorders: Ready for prime time? [Ment Health Clin](#). 2018 Mar 26;7(4):147-155. doi: 10.9740/mhc.2017.07.147.
- Zhang N and L Yao. **Anxiolytic Effect of Essential Oils and Their Constituents: A Review.** [J Agric Food Chem](#). 2019 Jun 13. doi: 10.1021/acs.jafc.9b00433.



Optimize HRV– Acupuncture

- Acupuncture works similarly to vagus nerve stimulation (VNS)
 - Vagus nerve plays a critical role in maintaining homeostasis of the innate immune response
- Acupuncture at ST36 , DU26, GB34 found to decrease LPS-induced pro-inflammatory cytokines TNF- α , IL-1 β and IL-6 via the Cholinergic Anti-inflammatory Pathway (CAP) in animal studies
 - Torres-Rosas et al. Dopamine mediates vagal modulation of the immune system by electroacupuncture. Nat Med, 20(3), 291-295.
 - Song J et al. Electroacupuncture at ST26 attenuates pro-inflammatory cytokine release. African Journal of Traditional, Complement and Alt Med, 2014.11(2), 469.
 - Zhang L et al. Inhibiting effect of electroacupuncture at zusanli on early inflammatory factor levels formed by postoperative abdominal adhesions. Evid Based Complement Alt Med, 2014, 950326.

Optimize HRV– Acupuncture

- Auricular acupuncture at Shenmen and Point Zero increases HRV during the post-op period in patients undergoing hemicolectomy for colon cancer
 - Young-Chang PA et al. Auricular Acupuncture at the “Shenmen” and “Point Zero” Points Induced Parasympathetic Activation. [Evid Based Complement Alternat Med](#). 2013; 2013: 945063. Published online 2013 Jun 4. doi: [10.1155/2013/945063](https://doi.org/10.1155/2013/945063)



www.robinraygreen.com
Ear Image Courtesy of www.earseeds.com



Optimize HRV– Vagus Nerve Stimulators

- Transcutaneous Vagus nerve stimulators
 - One device authorized by Health Canada to treat Long COVID
 - FDA-cleared VNS devices for pediatric migraines and IBS
- Wearable vibroacoustic frequency device improves HRV
 - Reduces ADHD and anxiety symptoms in children
 - Improves sleep quality, cognitive performance, athletic recovery
 - Hallihan C, Siegle GJ. Effect of vibroacoustic stimulation on athletes recovering from exercise. Eur J Appl Physiol. 2022;122(11):2427-2435. doi:10.1007/s00421-022-05026-x
 - Rabin D, Siegle G. Toward Emotion Prosthetics: Emotion Regulation Through Wearable Vibroacoustic Stimulation. Bio Psych. 2018; 83(9): S380-S381. doi: <https://doi.org/10.1016/j.biopsych.2018.02.978>



QUIZ

Exercise can change your gut
microbiome independent of diet.

Yes / No



The 5 Things: Move

- Exercise has beneficial effects on gut microbiome diversity and function
 - Elevated fecal SCFAs, esp butyrate
 - Results more profound in lean vs. obese sedentary participants, and increases as lean mass increases
 - **INDEPENDENT** of diet
- Positive effects reversed with return to sedentary lifestyle
 - You've got to move it move it!
- Early life exercise has even better benefits for longterm microbiome composition and lean body mass
- NOTE: intense exercise can increase intestinal permeability (aka leaky gut)



- Allen JM, Mailing LJ, Niemi GM, et al. Exercise Alters Gut Microbiota Composition and Function in Lean and Obese Humans. *Med Sci Sports Exerc.* 2018;50(4):747-757. doi:10.1249/MSS.0000000000001495
- Clauss M, Gérard P, Mosca A, Leclerc M. Interplay Between Exercise and Gut Microbiome in the Context of Human Health and Performance. *Front Nutr.* 2021;8:637010. Published 2021 Jun 10. doi:10.3389/fnut.2021.637010
- Monda V, Villano I, Messina A, et al. Exercise Modifies the Gut Microbiota with Positive Health Effects. *Oxid Med Cell Longev.* 2017;2017:3831972. doi:10.1155/2017/3831972

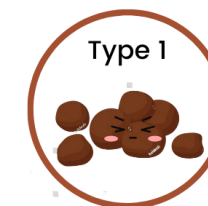
The 5 Things: Hydrate

- More than 50% of children don't drink enough water
- Low water drinkers are usually low fruit and vegetable eaters
- **Higher water drinkers have different gut microbiomes than low water drinkers**
 - Lower levels of harmful bacteria
 - Vanhaecke T, Bretin O, Poirel M, Tap J. Drinking Water Source and Intake Are Associated with Distinct Gut Microbiota Signatures in US and UK Populations. *J Nutr.* 2022;152(1):171-182. doi:10.1093/jn/nxab312

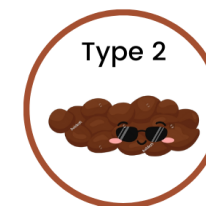


The BRISTOL STOOL CHART

CONSTIPATION

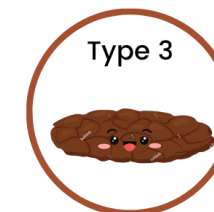


Separate hard lumps,
like pebbles

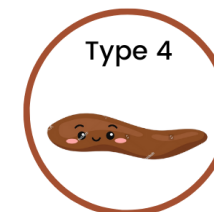


Hard lumps held together,
like a bunch of grapes

THE "PERFECT" POOP

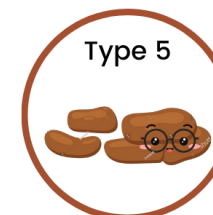


Like corn on the cob or
a sausage with cracks,

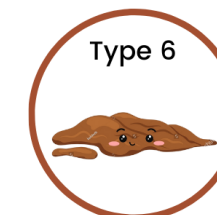


Like a smooth brown
banana or sausage

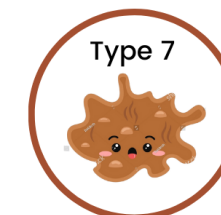
DIARRHEA



Soft brown blobs,
like blobs of cookie dough



Mushy blobs with ragged edges,
like watery oatmeal



Water with no solid pieces,
like gravy

QUIZ

How long does it take for sleep deprivation to alter your gut microbiome?



QUIZ

How long does it take to reverse the harmful effects of sleep deprivation on your gut microbiome?





The 5 Things: Sleep



- Sleep deprivation changes gut microbial composition and metabolites after **48 hours** → **GUT DYSBIOSIS**
 - Fecal butyrate significantly decreased after sleep deprivation
 - LPS (endotoxemia) increased after sleep deprivation with increased peripheral markers of inflammation
- Sleep deprivation decreases energy metabolism and oxidative phosphorylation in gut microbiota → **MITOCHONDRIAL DYSFUNCTION**
- Sleep deprivation alters tryptophan metabolism by gut microbiota and decreases fecal serotonin → **BRAIN DYSFUNCTION**
- Chronic sleep loss alters gut microbiota and induces **systemic inflammation**
- **Changes are reversible after 1 week of sleep recovery**

- Wang Z, Yuan K, Ji YB, Li SX, Shi L, Wang Z, Zhou XY, Bao YP, Xie W, Han Y, Shi J, Lu L, Yan W, Chen WH. Alterations of the Gut Microbiota in Response to Total Sleep Deprivation and Recovery Sleep in Rats. Nat Sci Sleep. 2022;14:121-133 <https://doi.org/10.2147/NSS.S334985>

Everyone can be a gut hero!





The Future is with Functional Medicine – and YOU!

- Teach the power of “Food as Medicine”
- Educate patients and peers with evidence-based, rational, calm dialogue
 - And most importantly, with KINDNESS and LOVE
- Vote with your dollars and your votes
- Work with schools to change nutrition, lifestyle and mindfulness education
- Work to change policy at the local, state and federal levels
- Give what you can – donate time, money, supplements
- Love, respect, and be kind to yourself ...



Nutrition Equity IS Health Equity

- The children are our future... ?
- **Nutrition Equity is the only way to end childhood chronic disease**
- I believe we CAN help kids THRIVE with a grassroots GLOBAL movement to:
 - Protect and optimize maternal prenatal nutrition, health and well-being
 - Prioritize nutrition and financial security for all families
 - Create global policies for a healthier food supply & sustainable/regenerative farming practices
 - Prioritize life and the pursuit of mindfulness...

And prioritize our kids!!!

Thanks for joining me today!

www.healthykidshappykids.com

IG: @healthykids_happykids





Saturday 12:30pm – 1:30pm

**Leaky Gut, Leaky Brain: An Integrative,
Evidence-Based Approach to Pediatric
Neuropsychiatric Disorders**

Please scan this QR code on you mobile
or tablet device to access the session feedback survey



Leaky Gut Leaky Brain: An Integrative Ev
idence-Based Approach to Pediatric Neurops
ychiatric Disorders