

It's not me
It's my
germs

Mindd
Health
Talks



Nancy O'Hara MD MPH


It's Not Me - It's My
Germs!

How the gut affects ASD, ADHD,
Learning Differences
and Mood Disorders

MINDD
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Nancy Hofreuter O'Hara, MD, MPH
www.ihealthnow.org


What lies behind us and what lies before us
are small matters compared to
what lies within us.



The GUT: A Complex Organ


60 -70% of immune cells

100 million neurons



Surface of approximately 300m²

100 trillion bacteria "Gut Microbiota"



**DANONE
NUTRICIA**
Early Life Nutrition

Historical Clues: Gut Dysfunction

- Difficulty breastfeeding
- Persistent colic
- Gastro-esophageal reflux
- Food sensitivities
- Insatiable appetite (germ overgrowth)
- Failure to thrive
- Frequent antibiotics (abnormal flora)
- Abnormal posturing
- Hands in pants/probing
- Self injurious behavior/aggression
- Poor sleep



Not a New Finding

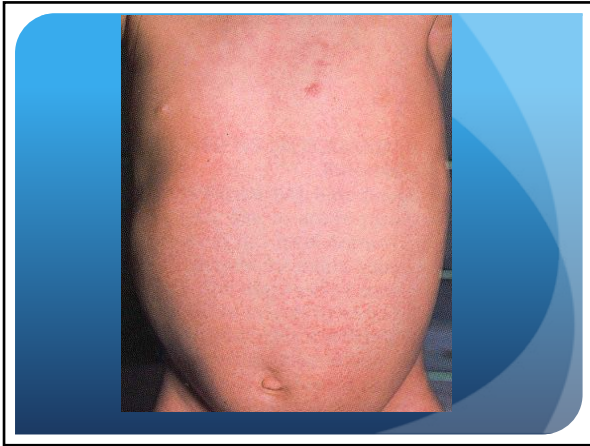
• Those who are mad on account of phlegm are quiet, but those on account of bile are vociferous, vicious, and do not keep quiet”

- Hippocrates

Physical Exam Clues: Gut Dysfunction

- Abnormal Stools
 - Grainy (insoluble bile salts)
 - Diarrhea/constipation/encopresis
- Wasted buttocks and failure to thrive
- Distended abdomen/bloating/doughy
- Esophagitis (inflammation)/GERD
- Gastritis
- Colitis (duodenitis/ileitis/proctitis)







Gut Dysfunction and Germs

Historical and Physical Exam Clues for Dysbiosis

- Parasites/Clostridia
 - Anal itching and probing
 - Picking, biting, licking, grinding, aggression
- Yeast
 - Rash/peeling feet/ridged, discolored nails
 - Inflamed cheeks/red anus
 - Ring worm/tinea corporis or capitis

Ridged, Discolored Nails



Psychophysiological Associations with Gastrointestinal Symptomatology in Autism Spectrum Disorder

We examined the relationship between gastrointestinal symptomatology, examining upper and lower gastrointestinal tract symptomatology separately, and **autonomic nervous system functioning**, as assessed by heart rate variability and skin conductance level, in a sample of 120 individuals with ASD. Relationships with co-occurring medical and psychiatric symptoms were also examined. While the number of participants with significant upper gastrointestinal tract problems was small in this sample, **42.5% of participants met criteria for functional constipation**, a disorder of the lower gastrointestinal tract. **Heart rate variability, a measure of parasympathetic modulation of cardiac activity, was found to be positively associated with lower gastrointestinal tract symptomatology at baseline.** This relationship was particularly strong for participants with co-occurring diagnoses of **anxiety disorder** and for those with a history of regressive ASD or loss of previously acquired skills. These findings suggest that autonomic function and gastrointestinal problems are intertwined in children with ASD; although it is not possible to assess causality in this data set. Clinicians should be aware that gastrointestinal problems, anxiety, and autonomic dysfunction may cluster in children with ASD and should be addressed in a multidisciplinary treatment plan.

Ferguson, et al., 2016 Autism Res, in press

Sleep and gastrointestinal disturbances in autism spectrum disorder in children

Sleep disorders reported in ASD include, among others, increased bedtime resistance, insomnia, parasomnia, sleep disordered breathing, morning rise problems, and daytime sleepiness. Sleep-related problems have been shown to affect overall autism scores, social skills deficits, stereotypic behavior, and cognitive performance. Additionally, problematic sleep in children with ASD has been associated with higher levels of parental stress. Underlying causes specifically related to sleep disorders are not fully known. **Gastrointestinal (GI) disorders are commonly associated with sleep problems** in these patients. Children with ASD and GI symptoms have been found to have a higher prevalence of sleep disturbances compared with typically developing peers who do not have GI symptoms. Treatment approaches to children with sleep disorders are varied and range from lifestyle modifications and behavioral interventions to drug therapies and surgical interventions. Physicians should take into account GI disorders as possible underlying causes of sleep-related problems in children with ASD.

Klukowski, et al., 2015 Dev Period Med 19(2):157-161

Rigidity, OCD associated with GI symptoms

- Based on clinical experience, we hypothesized that rigid-compulsive behaviors are associated with **severe constipation** and co-occurring diarrhea or underwear staining in children with autism spectrum disorder. Using data from the Autism Treatment Network, we evaluated the association between these gastrointestinal symptoms and measures of rigid compulsive behavior in children ages 2-17. Following statistical correction, four of five primary measures were significantly associated with constipation and diarrhea or underwear staining, including parental report of repetitive behavior, parental report of compulsive behavior, clinician diagnosis of obsessive-compulsive disorder, and report of rituals observed on the autism diagnostic observation schedule. This association could point to a causal connection between these symptoms or to a common biological pathway that impacts both gut and brain.

- Peters, et al., 2014 J Autism Dev Disord 44(6):1425-1432



Anxiety, over-responsivity and GI symptoms

- The current study examined bivariate and multivariate relations among anxiety, sensory over-responsivity, and chronic GI problems in a sample of 2,973 children with ASD enrolled in the Autism Treatment Network (ages 2-17 years, 81.6 % male). Twenty-four percent of the sample experienced at least one type of chronic GI problem (**constipation, abdominal pain, bloating, diarrhea, and/or nausea lasting three or more months**). Children with each type of GI problem had significantly higher rates of both anxiety and sensory over-responsivity. Sensory over-responsivity and anxiety were highly associated, and each provided unique contributions to the prediction of chronic GI problems in logistic regression analyses. The results indicate that anxiety, sensory over-responsivity and GI problems are possibly interrelated phenomenon for children with ASD, and may have common underlying mechanisms.

- Mazurek, et al., 2013 J Abnorm Child Psychol 41(1):165-176

GER and Agression/SIB

- **Aims**
 - To evaluate autistic children with GI complaints and aggression or self-injurious behavior in order to determine if these behaviors may be symptoms of GER. Methods: Six consecutive autistic children (ages 8-19 years) undergoing endoscopy and scheduled for BRAVO (wireless) pH probe were evaluated for histology and pH meter results.
- **Findings**
 - GER was identified in 5 of 5 patients tested by BRAVO pH testing. Esophagitis was seen in 3 of 6 patients biopsied.
- **Conclusions**
 - Aggressive or self-injurious behavior may be a manifestation of pain from GER and should prompt consideration of further investigation.

• Buie, 2005 J Pediatr Gastroenterol Nutr 41(4):505



When you see Aggression & SIB, OCD, Mood Disorders...

- Think about
 - What's going on in his/her gut?
 - Gas, bloating, pain
 - Constipation
 - Reflux
 - Germ Overgrowth
 - What causes dysbiosis?

Factors Effecting Microbiota

- Colonization at birth
 - Vaginal delivery vs. C-section
- Diet
 - Breastfeeding vs. infant formula
 - Introduction of new foods - Types of foods
- Environment (e.g., rural or urban setting)
- Pet exposure
- Hospitalization and antibiotic exposure

C-Section vs Vaginal Delivery

- C-section
 - Infant gut colonization more closely resembles maternal skin colonization (e.g, *Staphylococcus* spp.)
- Vaginal delivery
 - Infant gut colonization represents the maternal vaginal and intestinal microbiota
 - Greater total numbers and diversity of microbiota
 - Predominant bacteria are *Bifidobacteria*

Dominguez-Bello MG, et al. Proc Natl Acad Sci USA. 2010; 107; 11971-11975. Biasucci G, et al. J Nutr. 2008; 138: 1796s-1800.; Huurre A, et al. Neonatology, 2008; 93; 236-40.

Lab Options for Gut Issues

- History and Physical Exam
- Urine Organic Acids Test (OAT, MAP)
- Stool Microbiology
- Stool Mycology and Parasitology
- Stool Inflammatory markers (calprotectin, lysozyme)
- Fecal Fat
- Breath Test for Fructose Malabsorption
- Breath test for SIBO
- Inflammatory Markers (CBC, ESR, CRP, ANA, cytokines)
- Ammonia - blood
- IgG/IgE Food Panel, total IgE
- Celiac Panel (TTG, IgA, HLA)
- IBD Serology (prometheus testing)
- Endoscopy, Colonoscopy if necessary

WHAT DO WE DO?

- Exercise/Activity
- Basic Nutritional Changes
 - Fresh, unprocessed, unrefined, organic, whole foods - anti-inflammatory
 - Varied and rotational
 - Non allergenic (children crave that which most sensitive to)
 - Protein (every 4-5 hours)
 - Avoid excitotoxins (caffeine, MSG, dyes); phenolics (grapes, strawberries)
 - Juicing; raw foods; fermented foods (kefir); good fats
 - Organic (especially chicken, rice, pears, apples, peppers, celery, strawberries, cherries, grapes, spinach, lettuce, potatoes)

Disruptive Behavior and Dietary Approaches

- The effect of particular foods on levels of hyperactivity, uncontrolled laughter, and disruptive behaviors was studied in an 8-year-old autistic boy. The floor of the child's room was taped off into 6 equal-sized rectangles to measure general activity level. Frequency data were recorded on **screaming, biting, scratching, and object throwing**. During an initial 4-day period the child was fed a normal American diet. A 6-day fasting period followed, during which time only spring water was allowed. The third phase lasted 18 days and involved the presentation of individual foods. During the final phase the child was given only foods that had not provoked a reaction in the third phase. Results showed that foods such as **wheat, corn, tomatoes, sugar, mushrooms, and dairy products** were instrumental in producing behavioral disorders with this child.

• O'Banion, et al., 1978 J Autism Child Schizophr 8(3):325-337

Excellence is the result of caring more than others think is wise, risking more than others think is safe, dreaming more than others think is practical and expecting more than others think is possible



What To Do - Gut Problems

● Probiotics

- Discourage pathogens
- Support digestion
- Produce SCFAs, reduce pH, synthesize vitamins
- Control inflammation and promote oral tolerance
- Encourage peristalsis
- Minimum of 10 billion CFU/day (50 billion to 450 billion and more)
- Diet - Fermented foods

What To Do - Gut Problems

■ Saccharomyces boulardii

- Discourages pathogens, including Candida
- Stimulates IgA production & mucosal repair
- Natural yeast, skin of lycee fruit
- Destroyed by antifungals, not antibiotics
- Dose: 5 billion cells (250 mg)/day and much more

What To Do - Gut Problems Treatment of Constipation

- Fiber
- Fluids
- Exercise, especially swimming
- Vitamin C: 1000-2000 mg/day, sometimes up to 6000 mg/day
- Magnesium Citrate (100-500 mg/day); Epsom salts
- Aloe Vera: 1oz (children) to 2 oz (teens) (www.miracleofaloe.com)
- Senna (Smooth Move Tea)
- Oils
- Enemas if impacted

What To Do - Gut Problems - Natural Treatments for GER

- Baking Soda (not baking powder) 5 to 15 cc in 4 ounces of water prn
- Apple Cider Vinegar - 5 to 15cc in small amount of water before meals
- Aloe Vera Juice - 1 to 2 ounces before meals
- DGL (licorice) - chewable tabs or powder before meals
- Digestive enzymes before meals
- Probiotics
- Slippery elm and marshmallow root - Lozenges/capsules

What To Do: Bacterial Overgrowth

- Bacteria (history of + behavioral response to antibiotics, OCD, tics, anxiety, agitation)
 - Gram Negative bacteria (Klebsiella, Enterobacter)
 - Clostridia (smearing, probing, diarrhea after abx, OCD, temper)
 - Strep (PANDAS - Pediatric Autoimmune Neuropsychiatric Disorder Associated with Strep)
 - Lyme and co-infections
 - Other - Mycoplasma, Viruses (PANS - Pediatric Acute-Onset Neuropsychiatric Syndrome)

PANS/PANDAS - Acute Onset of...

- Sleep disorders (80%)
- Separation anxiety (98%)
- Inability to concentrate (90%)
- Hyperactivity (70%)
- Urinary frequency/urgency, enuresis (90%)
- Handwriting deterioration (90%)
- Hyperalert (80%)
- Aggressive (60%)
- LD (60%)
- Eating disorder (20%)
- Tics (70%)
 - Swedo et al, *Am J Psych*

What To Do - Parasites

- Parasites (bizarre behavior, insatiable appetite, aggression, worse at full moon, picking/biting/itching/grinding/smearing)
- Probiotics and Prebiotics
- Antiparasitics (Metronidazole, Paromomycin, Mebendazole, Alinia)
- Natural remedies (artemesia, pumpkin seeds, coconut)

What To Do - Yeast Overgrowth The Antifungal Parade

(mood swings, inappropriate laughter, thickened nails, sugar cravings, urinary frequency, spaciness)

- Non-absorbable
 - S.boulardii: 3 months (at least 3-9/day)
 - Nystatin: 1,000,000 units 4X day
 - Amphotericin B: 250mg 4X day x 10 days, then 500mg 4X day x 10 days
- Systemic
 - Sporanox (Itraconazole): 100mg 2X day x 10 days, then 200mg x 10 days
 - Diflucan (Fluconazole): 5 mg/kg/day up to 200mg day x 10 days, then 400mg day x 10 days
 - Lamisil (Terbinafine): 250mg day x 10 days, then 500mg day x 10 days
 - Nizoral (Ketoconazole): 200mg day x 10 days, then 400mg day x 10 days

Follow liver and kidney function at least every 2 months

What To Do - Rotation of Herbals

- Natural Antimicrobials and Antifungals
 - Oil of Oregano (0.2 ml 2x/day)
 - Grapefruit Seed Extract (1/3 adult dose)
 - Caprylic acid (500-1000 mg with meals)
 - Biocidin
 - Berberine (Goldenseal)
 - Plant Tannins
 - Garlic (1-2 fresh cloves or pills/day)

Biofilm Protocol - What is Biofilm?

For suspected ongoing abnormal germ overgrowth

- Step 1 (lysis, breaking up the biofilm layer) - enzyme (InterFase, streptokinase, lumbrokinase)
- Step 2 (antimicrobial/germ-killing phase) - 15 to 30 minutes after step 1 - rotation of herbs
- Step 3 ("mop-up" phase; at least 1 ½ hrs after step 2, but using fiber for this step you can really do this anytime after steps 1 and 2) - ALOE, MG-CITRATE, PECTIN OR PSYLLIUM HUSK POWDER
- Step 4 (nourishing phase) - this really happens throughout the day and involves his diet, antioxidant, anti-inflammatory, and

Biofilm Protocol

- ** NOTE - Keep all good minerals as far away from steps 1 and 2 as possible (this includes the CALCIUM—MAGNESIUM and ZINC) - the good minerals help to hold the biofilm matrix together and thus can perpetuate the problem. If doing biofilm in the earlier part of the morning and the afternoon, then you would give any minerals (like calcium, zinc, etc - this includes any multivitamins) anytime from the evening to bedtime.
- ** NOTE -possible temporary die-off (often at 21 days) as adjust antimicrobial and biofilm therapy. Consider using activated charcoal as needed for die-off when not constipated.

Biofilm Specifics

- Step 1 - Lysis/Detachment
 - Polysaccharidases, disaccharidases to break down mucous (ENZYMES)
 - May use pineapple/papaya enzyme rich foods in sensitive children
 - Others - Disodium EDTA (orally), Apple Cider Vinegar
 - Natural chelators - Green tea, curcumin

Biofilm Specifics

- Step 2 - Antimicrobials
 - Vary agents depending on microbiology, mycology and parasitology
 - Often see die-off at 21 days
 - Start low, go slow and rotate
 - Most important to change gastrointestinal environment; DIET IS KEY!

Biofilm Specifics

- Step 3 Clean up/Binding
 - Fiber/Prebiotics
 - Pectin, ground flaxseeds, psyllium husks
 - Activated charcoal if needed for die-off
 - Alginates, Clay
 - Slippery Elm, Yucca
 - Burbur

Biofilm Specifics

- Step 4 - Rebuilding/Nourishing
 - Probiotic rich foods
 - Good fats - ghee
 - Soothing foods and spices - aloe, ginger, turmeric, okra
 - Fermented foods - kefir, kombucha, cabbage
 - Supportive supplements - comfrey, chamomile, colostrum
 - Bone broths
 - Green juicing

What To Do - Mood & Gut Problems

- Mucosal health - Promoting Immunity
 - Remove stressors (e.g., allergenic foods, gluten, yeast, bacteria, parasites, clostridia)
 - Supply nutrients (e.g., diet (GF/CF/SF/YF/SCD/BED/GAPS), antioxidants (Vitamins A,C,D), zinc, magnesium)
 - Anti-inflammatories (Ibuprofen, EFAs (1000 mg), Aloe, Quercetin, Resveratrol, Curcumin, Marshmallow root, Slippery Elm, bioflavonoids)
 - Supply probiotics (up to 450 bil CFU or more; discourage pathogens, control inflammation, encourage peristalsis) and prebiotics (S Boulardii)
 - Encourage digestion (e.g., disscahridases, peptidases)

RESTORING THE BIOME: HELMINTHS For A HEALTHY IMMUNE SYSTEM

You are 10% YOU

The adult human body has about 10 trillion cells (with your own DNA)

The adult human body has about 100 trillion other organisms...with their own DNA
YOU ARE AN ECOSYSTEM



So what happens if you change even one element in an ecosystem?

Reintroduction of wolves to Yellowstone National Park

Wolves reduced the elk population

The elk had been eating the willows

With more willows -> more beavers

Beavers built dams -> changed stream hydrology

Changes in the water and ecosystem!

Now let's look at the YOU

In the last 100 or so years, we completely changed our evolutionary-history lifestyles:

- Started to use toilets
- Started wearing shoes everywhere, all the time
- Started eating highly processed foods
- Started drinking processed water
- Stopped regularly breastfeeding
- Started to use antibiotics
- Started doing c-sections more and more
- Started wearing sunscreen and working indoors more often
- Etc. etc. etc.

ENTER HDC



Why HDC is Our Organism of Choice

- > The low cost of cultivation facilitates its use for normalization of the immune system by the population as a whole. (\$)
- > No transmission from human-to-human is possible
- > The distribution of the HDCs in the human body is strictly limited to the lumen (inside) of the gut, unlike nematodes currently in use (hookworms and whipworms) which breach the barrier of the gut. Minimal risk of infestation.
- > HDCs are raised in grain beetles (*Tenebrio molitor*), which are normally found in the human food supply as a harmless contaminant in a wide variety of grains.
- > HDC is a mutualist! NOT A PARASITE!
- > HDCs evoke an immune system response which we NEED as it is a normal part of our immune conditioning.
- > Do NOT use if constipated, slow motility, immunosuppressive medications, nonverbal; stop if any abdominal pain
- > www.biomerestoration.com



Oxidative Stress, Antioxidants & Mood

- Multiple studies showing relationship between OCD and oxidative stress (Behl et al, Neuroschobiology, 2010)
- OCD, oxidative stress and altered glutathione metabolism (Chakraborty et al, Progress in Neuropsychopharm and Bio Psychiatry, 2009)
- Lower levels of vitamin E, C and A vs controls
- Higher levels of oxidative stress (as measured by MDA - Malondialdehyde; by product of lipid peroxidation)

Treatment options - N-Acetyl Cysteine

- Precursor of GLUTATHIONE - Powerful antioxidant
- Excellent treatment option for
 - Trichotillomania (Grant et al, Arch Gen Psych, 2009)
 - Compulsive gambling (Grant et al, Biol Psychiatry, 2007)
 - Nail biting and skin picking (Berk et al, CNS Spectr, 2009)
- Multiple studies of NAC in OCD
 - Systematic Review - Oliver et al, Clin Psychopharm Neurosci, 2015; Afshar et al, J Clin Psychopharm, 2012
- Form
 - Easily oxidized when exposed to air
 - Effervescent tablets - even distribution, buffered, individually packed

Herbal Adaptogens for Mood Disorders

- Role in adrenal support, helping the body to more effectively deal with stress and promote better mood and energy regulation.
- Can be given as needed
- Ashwagandha (*Withania somnifera*)
 - Comparable efficacy in mice models to fluoxetine
 - Asian Pac J Trop Med, 2012
- Rhodiola (Arctic root)
 - Benefits in anxiety and depression
 - Bystritsky et al, J Alternative and Complimentary Med, 2008
 - Darbinyan et al, Nordic J of Psychiatry, 2007

Other Interventions

- CBD (Hemp Oil) - Cannabidiol
 - Reverses mCPP (meta-chloro-phenyl-piperazine) induced marble burying in mice; Anti-compulsive effects
 - Nardo et al, Fundam Clin Pharm, 2014; Deiana et al, Psychopharm, 2012
- 5-HTP
 - Tryptophan removed after outbreak of eosinophilia-myalgia syndrome traced to contamination
 - Do not take with SSRI; 5-HTP Safety assured (Toxicol Lett, 2004)
 - Significantly lowered cholecystokinin-4-induced panic vs placebo in females; decreased somatic symptoms only in males
 - (Maron et al, J Psychopharm, 2004)
- INOSITOL (- 18 gm/day - (Palatnik et al, J Clin Psychopharm, 2001)
 - B vitamin affecting serotonin to reduce OCD symptoms, panic
- LITHIUM OROTATE
 - Crosses blood brain barrier more easily so lower doses more effective without dulled personality, memory loss, weight gain (O'Donnell et al, Eur Neuropsychopharm, 2003)

Other Interventions Continued

- Treat Dysbiosis - Probiotics, S Boulardii, Antimicrobials
- CBT (Cognitive Behavioral Therapy) and DBT
 - Exposure Response Prevention
 - Decrease Caudate glucose metabolic rates
 - Schwartz et al, Arch Gen Psych, 1996
- Mindfulness (Hansteded et al, J Nerv Ment Dis, 2008)
- Exercise (Otto et al, Oxford Univ Press, 2011)
- Sleep (Goldstein et al, j Neurosci, 2013)
 - Sleep loss amplifies preemptive responding in amygdala
 - Sleep loss significantly effected those susceptible to anxiety
 - Sleep resotoration may ameliorate anticipatory response and anxiety
- Diet (Lakhan et al, Nutr J, 2008)

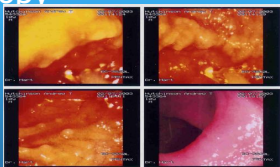
Drew: 12 year old male

- Normal pregnancy, born healthy, developed colic
- Fever, swelling at injection site with vaccines and hives one week after each immunization
- Delayed speech, hyperactivity, tantrums
- Delayed toileting, chronic constipation, megacolon
- Severe regression after pre-kindergarten shots
 - "Never the same again" : 6 days of fever, malaise, glassy eyed, aggressive, agitated
 - ADHD, adjustment disorder with mixed disturbance of emotions and conduct, Aspergers, fine motor delays
 - Suffering for 6 years

Drew - Further history

- Poor sleep since infancy
- He choked intermittently and sometimes seemed to have trouble swallowing.
- Parents wondered if food got stuck since he would bang on his sternum.
- PMH was significant for allergic rhinitis and eczema
- Is his agitation, aggression, SIB and tantrums just bad behavior?
- Or something else...

Endoscopy

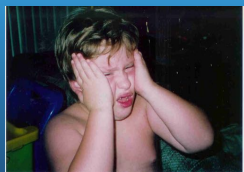


- Esophagitis with friability and cobblestoning of the mucosa and blunting of vascular markings
- Lymphoid nodular hyperplasia of ileum
- Submucosal hemorrhages of the colon

What To Do for Drew Natural Treatments for GER

- Apple Cider Vinegar - 5 cc in small amount of water before meals
- Aloe Vera Juice - 1 to 2 ounces before meals
- DGL (licorice) - capsule or powder before meals
- Digestive enzymes before meals
- Probiotics - high dose (450 billion CFU)

Before and After Treatment



IQ "60"



IQ 150

Two roads diverged...And I took the one less traveled by, and that has made all the difference. - Robert Frost



Basic biomedical interventions

- HEAL THE GUT
 - Treat dysbiosis
 - Treat constipation
 - Decrease inflammation
- Avoid what harms
 - Gluten? Casein?
 - Additives? Toxins?
- Give what heals
 - Nutrients
 - Probiotics
 - Omega 3 EFAs
- FIX METABOLIC PROBLEMS
 - Exercise/Physical activity
 - Sleep - Melatonin, 5-HTP
 - Folic acid
 - Magnesium
 - Glutathione, NAC
 - Anti-inflammatories
 - Detoxification
 - Sweat
 - Stool

How to develop treatment plans?

- Begin with considering the individual history of your child
- Test hypotheses about underlying problems by looking for physical exam clues and laboratory data
- Figure out if they are getting something they should not or if they are not getting what they need
- See treatments as clinical trials with an N of one





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