



CONVERGENCE

News, Links, and Insights
by JEFFREY BLAND, PHD



May 2019

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In this issue: The Sotto Voice of the Oral Microbiome; Study the Exposome to Help Understand Autism; Synbiotic Aids GI, Behavioral, and Immune Measures in ASD; May Educational Events From inVIVO Planetary Health and Metagenics Institute; The Seventh Annual Thought Leaders Consortium

The Sotto Voce of the Oral Microbiome

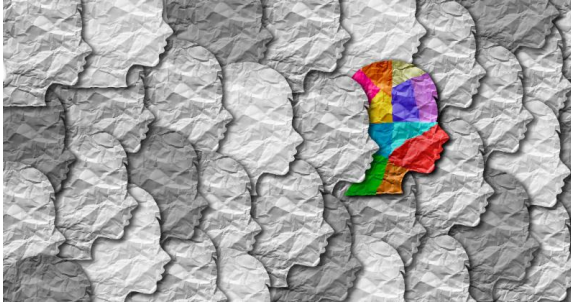


The mouth is a vocal part of the digestive tract, quietly eloquent about systemic health and the body's multiple microbiomes; even the composition of saliva and of the oral microbiome have something to say about immune regulation and propensity for inflammation and related chronic disease. According to dentist Dr. Gerry Curatola, around 85% of adults over the age of 35 have some degree of gum disease, and this has much to do with the way we treat our microbes and the biofilms they weave. He is concerned about the way soap-like toothpastes and mouthwashes reinforce the pathogenicity of opportunistic members of the oral microbial community, and states that "bacteria really run us, we don't run them."

Oral health, and especially periodontal inflammation, can relate to conditions as diverse as autoimmune disease, HDL cholesterol metabolism, health during pregnancy, dysbiosis, pancreatic cancer, diabetes, and kidney and liver disease, as Drs. Bland and Curatola discuss in [this FMU interview](#). Speaking at a conference about [oral contributions to systemic inflammation](#) and his new book *The Mouth-Body Connection*, Dr. Curatola describes how this relationship is bi-directional, and what it may mean when a common oral bacterium is the main microbe found in colorectal tumors. Dietary choices between refined and minimally-processed, prebiotic-rich foods influence both oral and gut microbiomes, and even episodic events like dental care may be able to shift immune expression. A recently-published clinical study found that, in rheumatoid arthritis patients with periodontal disease, a single instance of [deep dental cleaning significantly reduced RA disease activity](#) up to 8 weeks afterwards. Treated subjects also showed a marked drop in C-reactive protein (CRP) levels, a change not seen in controls. Increasing

awareness of oral-systemic connectivity is reflected in the movement towards microbiome-aware dentistry and away from the “kill, kill, kill” approach. In his recent book *The Dental Diet*, dentist Dr. Steven Lin takes a close look at how [diet and the oral microbiome interact with epigenetic factors](#) to influence whole-body health and describes the virtues of salt as a tooth powder base.

Study the Exposome to Help Understand Autism



The concept of the exposome, [introduced in 2005](#) to complement other -omics made possible by the sequencing of the human genome, encompasses the totality of internal and external exposures received in a lifetime by an organism.

Consideration of the exposome can aid deeper understanding of the etiology of disease, and it has gained traction as the incidence of neurodevelopmental

conditions like autism and attention deficit-hyperactivity disorder increase. Teasing out the cause of diseases such as these has proven challenging, with clues pointing to genetic, environmental, metabolic, and stress-related factors; a common chord among them is their effects on the development of the central nervous system, particularly in the earlier months and years of this extended process. Exposures occur mainly through oral and respiratory routes, infection, mother’s blood supply in utero, skin, through perception and interpretation of events, and also through physiological barriers (especially brain, gut, skin, and placental) that may be compromised. In terms of the exposome, physical activity may also be thought of as an exposure, as it constitutes a physiologic event that alters both short- and long-term responsivity.

While the exposome encompasses all of an organism’s experiential exposures, their quantity and timing partly determine the magnitude of their effects in autism, mediated through the individual’s adaptive responses. A simplified version of the related sequence of events is ingestion, metabolism and detoxification (affected by co-exposures, the microbiome, and genetic, epigenetic, mitochondrial, and environmental variables), responses (immune, antioxidant, hormonal, metabolic, etc.), epigenetic effects, and elimination. In autism, each of these steps may be influenced by the subject’s age and gender, parents’ ages, and the family’s lifestyle, occupations, nutritional status and diet, daily habits, genotypes, detoxification capacity, living situation, immune status, physical activity, co-morbidities, socioeconomic and educational status, climate, season, social support, and stress perceptions. The [genetic component of autism](#) is felt to be strong, with [contributions from spontaneous mutations](#) and 60% or more co-occurrence between identical twins. However, concordance between fraternal twins is higher than that for siblings, reflecting the importance of the shared uterine environment. While the period of fetal development is most sensitive to exposures, other susceptibilities include the presence of genetic variants affecting metabolism and detoxification and during times of illness, stress, and synaptic formation and remodeling.

Proving that exposure to a given substance increases risk for autism is difficult, but clinical and pre-clinical evidence have clarified the contributions of several. DeFelice et al report significant [neurodevelopmental toxicity](#) associated with heavy metals (especially lead and methylmercury), pesticides (like DDT), polychlorinated biphenyls (PCBs), dry-cleaning and [flame retardant chemicals](#), and many others are under active study. Research is complicated by the fact that a multitude of biochemical pathways affect development in different ways at different stages of development, and a given substance may affect only one such nexus at a particular dosage level, necessitating numerous studies to discover and confirm effects. The above DeFelice study and others describe association between autistic spectrum disorders (ASD) and living near a freeway, prenatal exposure to [organophosphate or pyrethroid](#) pesticides, [air pollution](#), medications used in [asthma, epilepsy, and depression](#), thalidomide, [maternal fever](#) during pregnancy, maternal rubella during the first trimester of pregnancy, or previous

maternal cytomegalovirus infection. Factors that may have additive effects with others include exposure to nicotine, alcohol, or cocaine, maternal anxiety during pregnancy, low birth weight, and premature birth.

To be able to adapt to a great variety of potential future needs, [the developing brain](#) is thought to create surplus synaptic connections that are subsequently winnowed down and become specialized according to living experience. While heightened prenatal brain plasticity increases susceptibility to negative impacts, it also allows for adaptivity and resilience when encouraged by healthful influences. [Maternal vitamin supplementation](#) is negatively associated with autism, adequate maternal [iron and polyunsaturated fat](#) intakes relate to lower risk for ASDs, and [better maternal folate status](#) may help protect against some of the early developmental toxicity of pesticides. And though pre-natal factors relate most strongly to autism risk, it is often noted that considerable brain growth and synaptic remodeling occur in concert with development of an infant's microbiome after birth, and a number of studies suggest that [alterations in the gut environment](#) can also contribute to the condition through impacts on immune balance, barrier function, and hypothalamic-pituitary-adrenal axis function. Autism is not infrequently accompanied by gastrointestinal and feeding difficulties, and a 2017 study in 18 autistic children found that an extended [fecal microbial transplantation](#) protocol improved their behavioral and gastrointestinal symptoms as well as augmenting populations of *Bifidobacterium* and *Prevotella* in subjects' microbiomes.

Brain and gut function are complementary in that both gather, interpret, and act on information—and they share “data” to coordinate a response to internal and external environments. The immune-related activities of the gut are particularly crucial in protecting and informing brain function, and preclinical research suggests that microbiome composition may even impact [neurotransmitter balance](#) and how microglia help direct synaptic remodeling. Therapies aimed at improving microbiome composition and restoring gastrointestinal function take advantage of these gut-brain network interactions and provide foundational opportunity to aid management of autism and related conditions.

Synbiotic Aids GI, Behavioral, and Immune Measures in ASD

It can be a touchy situation when treating those with autistic spectrum disorders (ASD): even effective treatments may upset some aspect of previously-achieved homeodynamic balance. Gastrointestinal dysfunction is particularly common and challenging in ASD, and encouraging change is often a long-term process of retraining body and mind.

Recent [research on children with ASD](#) highlights the effects of a synbiotic composed of *Bifidobacterium longum* ssp. *infantis* and a prebiotic colostrum complex. This small and relatively brief (12 weeks) pilot study found this synbiotic well-tolerated by these children, and virtually all showed improvements in gastrointestinal function that reverted after discontinuation of treatment. Interestingly, significant behavioral changes were seen mainly during the colostrum-only study period, and included improvements in irritability, hyperactivity, and stereotypical behaviors; lethargy improved during the combination treatment period. Despite each treatment period lasting only 5 weeks, production of tumor necrosis factor- α decreased slightly but significantly during the colostrum-only period and production of interleukin-13 (a Th2 mediator generally associated with allergic response and asthma) decreased significantly during combination treatment.

Significant shifts in metabolomes or fecal microbiome composition were not seen during this relatively brief study, but these positive findings suggest that strategic—and individualized—administration of colostrum complex with or without *B. infantis* to children with ASD may be worth consideration.



Upcoming Events this Month! There's Still Time to Register

inVIVO Planetary Health Conference Detroit, MI May 15-17, 2019

Dr. Jeff Bland is scheduled to speak at the "Woodstock" of planetary health.

Find details here:

<https://www.invivoplanet.com/program.htm>
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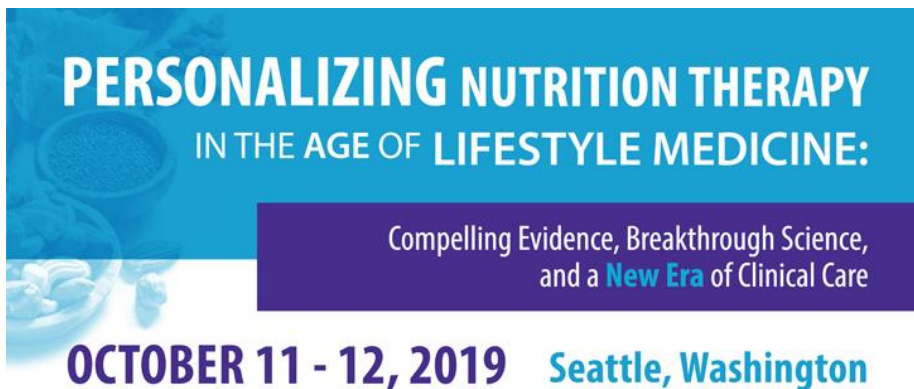
HALF-DAY SEMINAR
with **SARA GOTTFRIED, MD**

Brain Body: Personalized Lifestyle
Medicine for the Gut-Brain Axis
Seattle, WA
May 11, 2019
Grand Hyatt Seattle
721 Pine Street, Seattle, WA 98101
Register today!
800.692.9400

 Metagenics Institute

Brain Body: Personalized Lifestyle Medicine for the Gut-Brain Axis Seattle, WA May 11, 2019 Featuring Sara Gottfried, MD Sponsored by Metagenics Institute

Find details here: bit.do/bb-seattle

The poster for "Personalizing Nutrition Therapy in the Age of Lifestyle Medicine" features a blue background with images of a bowl of food and pills. The text reads: "PERSONALIZING NUTRITION THERAPY IN THE AGE OF LIFESTYLE MEDICINE: Compelling Evidence, Breakthrough Science, and a New Era of Clinical Care" and "OCTOBER 11 - 12, 2019 Seattle, Washington".

THE SEVENTH ANNUAL THOUGHT LEADERS CONSORTIUM

Registration is open and seats are filling quickly! Dr. Jeff Bland is the conference host and facilitator. Join more than 300 attendees from around the world in Seattle this fall.

Click [HERE](#) to view the current program schedule.

Click [HERE](#) for a conference overview.

NEW! Click [HERE](#) to visit our 2019 Speaker Gallery.

Click [HERE](#) to register for the 2019 Thought Leaders Consortium.

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