Autism Spectrum Disorder

A New Paradigm for Integrative Management

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We are in the midst of a unique public health crisis in this nation. Debates about etiologies aside, most medical authorities concur that there are more children diagnosed with neurodevelopmental disorders than ever before. The Centers for Disease Control and Prevention estimates that 1 in 166 children in the United States has been diagnosed with autism.[1]

When Kanner and Asperger first reported their experiences with children with autism in the 1940s, prevalence rates were thought to be approximately 2–4 per 10,000 children.[2–4] Epidemiologic studies until the late 1980s were remarkably consistent with respect to prevalence rates but, in the past 20 years, prevalence estimates have risen to the current level of 40–100 per 10,000, or nearly 1 percent.[5–8]

If one widens the net a bit further and includes children with related disorders (i.e., attention-deficit hyperactivity disorder and learning disabilities)—as some scientists suggest we should[9]—prevalence rates of children with neurodevelopmental disorders reach the order of 1 in 6 children.[10]

Autism spectrum disorder (ASD) includes classic autistic disorder, Asperger's syndrome, pervasive developmental disorder (PDD-NOS), childhood disintegrative disorder, and Rett's syndrome.[11] Although qualitatively different, these disorders are all hallmarked by significant impairments in communication, social interaction, and behavior. The perception of ASD as a primarily psychologic/psychiatric disorder has not changed appreciably over time, despite overwhelming evidence that autism is a complex, multisystemic medical disorder. Accepting this reality will allow us to collaborate more effectively with families to ensure the best quality of care for individuals with ASD.

Families often incorporate use of complementary and alternative medicine (CAM) therapies[12–14] because such families believe conventional medicine does not address both root causes and clinical symptoms particularly well. Physicians, particularly primary care providers, need to feel comfortable discussing CAM use with these families to deliver optimal care.

My intention is to introduce a new paradigm of integrative medical care for ASD that integrates conventional and complementary therapies safely, effectively, and ethically, and that best addresses the need for a holistic and comprehensive system of care.

Defining ASD as a Complex Multisystemic Disorder

Children with ASD present with a panoply of physiologic and clinical differences, in addition to these children's developmental issues. In a recent survey we published, based on primary care practices in two Northeastern U.S. suburbs, a significant number of parents of chidren with ASD reported gastrointestinal (GI; 67.6 percent), neurologic (66.2 percent), and allergy/immune-related (62.2 percent/45.9 percent, respectively) symptoms.[12] These numbers generally correlate with prior studies of medical symptom reports about children with ASD.[15–16]

Clearly, however, not all patients with ASD have all of these difficulties. One of the keys to understanding autism is realizing how unique each and every child's clinical presentation (phenome) and underlying metabolism is. There is a great need to develop methods of subtyping autism phenomes not only by developmental differences but also by medical individuality.

Clinical symptoms most often reported are GI in nature, including diarrhea, constipation, abdominal pain, vomiting, and gastroesophageal reflux.[15,17] These clinical presentations correlate with distinct physiologic and pathologic findings, indicative of a novel autistic panenteric inflammatory bowel disease.[18] Studies have confirmed GI inflammation in the esophagus, stomach, small and large bowel. [17,19,20] With regard to microscopic findings, researchers have described a unique cellular inflammation responsible for these changes, with both nutritional and viral antigens implicated in the disorder's etiology.[21–24] Other GI abnormalities reported include increased intestinal permeability, or "leaky gut,"[25] and microorganism overgrowth.[26]

Interestingly, autistic enterocolitis has been linked to specific immunologic changes.[27–30] Studies support the theory that certain individuals with ASD have an immune dysregulation disorder consistent with a shift toward Th2 dominance.[31–34]

Clinically, children with ASD present with more frequent ear and upper respiratory tract infections as well as high rates of allergic disorders, especially in the first 2 years of life.[35] These children tend to come from families with higher rates of atopic and autoimmune disorders.[16,36–40] Skewed immune responses extend to neurologic tissues, as evidenced by inflammation and autoantibodies in children with ASD.[41,42]

These studies support the hypothesis of a brain–gut–immune connection and the link between abnormal physiologic markers and physical symptoms. Abnormal brain growth patterns, electrical activity (seizures), and neurohormone production are some of the neurologic events noted in children with ASD. [43–47]

Martha Herbert, M.D., a noted pediatric neurologist from Harvard Medical School, Boston, questions whether or not the brain itself is responsible for associated physical changes in autism, suggesting that, instead, the brain is "downstream" and that the neuropsychiatric symptoms are the end result of biochemical and metabolic derangements. [43]

The Iceberg Model

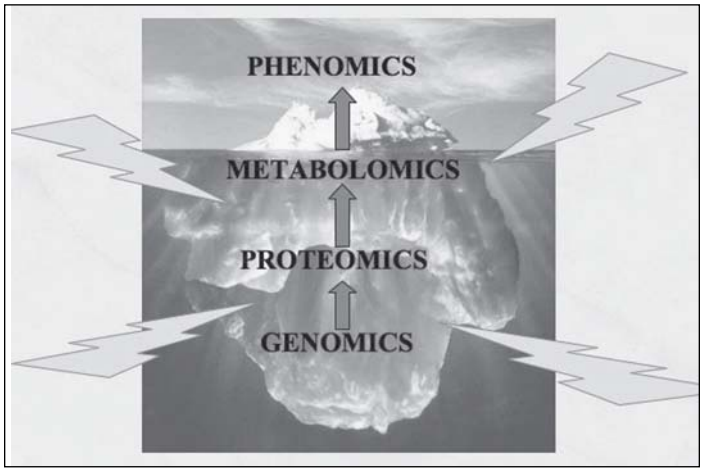
There is, therefore, a wide spectrum of phenomics in individuals with autism. Phenomics are, however, only the "tip of the iceberg." Under the surface are a host of genetic and biochemical differences unique to subsets of children with ASD. This functional medicine model provides a rationale for a new paradigm for ASD assessment and treatment.

If we can elucidate the genomic, proteomic, and metabolomic differences associated with subtypes of ASD, then we can develop therapies targeted at correcting these imbalances. The ultimate goal is not just treating visible symptoms but actually rebalancing biochemistry (and perhaps genetics?) to prevent autism from developing at all.

This paradigm assumes that we can intervene at these intervals and arrest or reverse processes that are programmed or already underway. It is likely that there are specific environmental stressors that trigger a cascade reaction when a genomic predisposition is present.[48–52] In fact, it is plausible that genes themselves can be altered (epigenetic phenomena) in the presence of certain environmental events (viruses, toxins), leading to changes in protein expression, metabolic function, and finally, clinical phenomena.[53]

Indeed, various metabolic differences have been described in children with ASD, most commonly involving amino-acid and fatty-acid pathways.[54–57] Mutations such as single nucleotide polymorphisms in the MTHFR gene have been associated with alterations in the methionine-homocysteine cycle, leading to increased oxidative stress, in turn leading to inflammation and impaired detoxification ability.[58–61] Several researchers have demonstrated, in vivo, an impaired ability to excrete toxins, especially mercury.[62,63]

We need to pay attention to these early warning signs. If we can intervene before "cracks in the ice" develop, perhaps we can prevent some of the clinically obvious sequelae from developing. The Iceberg Model thus provides a rationale for biochemically directed interventions.



The Iceberg Model for autistic spectrum disorder.

The Medical Home: A Model for Care

Given the limited ability of conventional treatment to address these underlying phenomena, many families of children with ASD turn to CAM. Rates of CAM use in children with ASD range from 30 percent in a population at a regional autism referral center[64] to 92 percent in a population seeking care in two Northeastern suburban primary care practices.[12] There are other reasons why families turn to CAM approaches, and why they do not often disclose this use to their physicians.[65] Parents often believe that environmental factors (e.g., nutrition, vaccines) play a large role in the etiology of their children's autism,[66] while their physicians generally do not believe this.

A recent survey showed that families of children with autism were generally dissatisfied with their primary care providers in several aspects of care, especially regarding the providers' knowledge about CAM. [67]

Pediatricians, it seems, agree. In a 2001 American Academy of Pediatrics (AAP) Periodic Survey of Fellows,[68] fewer than 5 percent of respondents stated they felt "very knowledgeable" about individual CAM therapies that their patients asked them about. More than 80 percent of these pediatricians desired additional information about CAM. This survey highlights the great need for more education and to develop more effective models of care.

The AAP has published several policy statements aimed at addressing these areas of concern, encouraging pediatricians to engage in an open-minded dialogue about CAM therapies with the parents of their patients, particularly with regard to children with special needs.[69,70] In 2005, the AAP granted provisional status to a new Section on Complementary, Holistic and Integrative Medicine,[71] which is charged, in part, with increasing awareness of evidence-based clinical models of care.

"The Medical Home" is one such model proposed to serve children with special health care needs better, including children with autism. The medical home, according to the AAP, is "not a building, house, or hospital, but rather an approach to

providing comprehensive primary care. A medical home is defined as primary care that is accessible, continuous, comprehensive, family centered, coordinated, compassionate, and culturally effective."[72,73]

A recent report suggested that a significantly smaller percentage of children with autism (25.6 percent) are reported to have a medical home than children without autism (46.3 percent) or children with other special health care needs (44.7 percent).[74]

There are, of course, financial and practical realities that need to be considered when addressing the comprehensive care of children and youths with special health care needs (CYSHCN). It is estimated that CYSHCN account for 80 percent of pediatric health care expenditures and that this burden falls unevenly on the shoulders of families.[75] Indeed, health care costs for children with disabilities far exceed such costs for other children—with hospitalizations and emergency room visits accounting for much of the increased utilization and cost.[76]

A recent report based on the National Survey of Children's Health, including more than 100,000 parents, detailed the increased use of health services specifically for children with autism.[77] Insurers must recognize that the medical home model is likely to reduce expensive, hospital-based care of CYSHCN via careful primary care oversight; data suggest that it does.[78] Both total cost of health care for CYSCHN and cost to families should be reduced by more comprehensive and continuous community-based care, assuming insurers reimburse appropriately for increased complexity of care in the ambulatory setting.

Integrative pediatricians take into account the effect of the environment on health, and the impact of human living on the environment.

Integrative Pediatrics: A Solution

Pediatric integrative medicine is ideally suited as a model of care to support the medical home concept. Integrative pediatricians emphasize family centered and culturally effective care, focusing on the whole child with the idea that children are not "islands" unto themselves but exist within the context of family and community.

We value wellness and believe optimal health is not simply the absence of disease, but a presence of healthy mind, body, and spirit. We advocate individualizing therapies, knowing that a "one-size-fits-all" approach does not address adequately the diversity of clinical and biochemical issues noted in children with ASD.

Integrative pediatricians take into account the effect of the environment on health, and the impact of human living on the environment. Both the environment and social interactions are seen as potential allies for healing. In fact, the relationship between primary care provider and family is seen as part of the healing process, which addresses the concerns raised by Liptak et al.[67] Respectful collaboration is the model for the doctor–patient relationship, and for that matter, for the relationships among all health care providers.

This model allows families to work comfortably with CAM providers while their primary care providers assist in coordinating care—this is the medical home concept in a nutshell. Children with ASD would work with several therapists (behavioral, speech and language, occupational, physical, psychologic), educators, nutritionists, and other health care providers (i.e., homeopaths, naturopaths, chiropractors, energy healers). In addition, families would often blend CAM therapies and conventional medicine (i.e. psychiatry, neurology, developmental pediatrics, allergy/immunology), and integrative primary care pediatricians would seek to work actively as holistic "quarterbacks" to facilitate communication and to coordinate care.

The Ethical Dimension

How does one integrate CAM therapies with conventional treatments ethically? Fortunately, Cohen and Kemper have addressed this issue specifically.[79] Their general guidelines provide a structure for supporting CAM therapies based on safety and efficacy evidence.[80] If a treatment is deemed to be safe and effective, one is advised to recommend its use.

An example would be the use of probiotics for diarrhea. If a treatment is safe but of questionable efficacy, one should tolerate its use while monitoring the treatment. Another example is the gluten-free, casein-free diet.[81–83] If, however, a treatment is effective but of questionable safety—perhaps the trickiest ethical scenario—these two authors advise us to consider tolerating use of the therapy while monitoring safety very closely. For example, this might involve the use of a chelation agent, such as dimercaptosuccinic acid (DMSA), to remediate lead toxicity. Of course, if a treatment is both unsafe and ineffective, one should advise against its use. This might include long-term, high-dose vitamin A supplementation.[84]

This framework provides guidance for deciding how to evaluate specific CAM therapies for ASD and other chronic medical conditions.

Conclusions

While it is outside the scope of this article to delve into the details of specific CAM therapies for ASD, there is much research that supports many common CAM interventions. Nutritional and metabolic therapies have been the most widely examined but creative and sensory therapies are often overlooked. Music therapy, sensory integration therapy, Therapeutic Touch, massage therapy, and creative movement therapy have all produced clinical symptom relief in children with autism.[85–89]

Primary care providers must educate themselves about these and other widely used CAM therapies, and take an active role in evaluating behavioral and educational plans, in order to serve individuals with ASD best.

As demonstrated by the Iceberg Model, autism is a complex, multisystemic medical disorder marked by underlying genetic and metabolic differences. It requires comprehensive, compassionate attention to family centered, culturally competent care.

Those of us who work with families of children with ASD must consider adopting the principles of both the medical home and integrative medicine models of care. Only by embracing this new paradigm of assessment and treatment for autism can we begin the hard work of caring holistically for children affected by autism and other increasingly prevalent neurodevelopmental disorders. □

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