A hologram is a 3-dimensional photographic image. But it is much more. If you take a glass plate that stores any holographic image and break it into a thousand pieces, each fragment when illuminated with a laser will recreate the entire image. Autism is a hologram for chronic disease. In it is reflected all the causes and cures for chronic disease.

The discoveries that have led to the picture of autism as a reversible systemic disorder that is influenced by genetics and that affects the brain, rather than a genetically determined fixed brain-based disorder, emerged from a unique process in the history of medicine—the mining of the collective intelligence of scientists, clinicians, and parents of children with autism. What they have discovered is this: the broken brain of autism is caused by a broken body. Fix the body, and the brain can recover. Out of their experience emerged a road map that can be generalized to nearly all chronic illness because the roots of the biochemical disasters and metabolic dysfunction are the same—genetic predispositions (rather than determinants), a toxic environment, and a nutrient-deficient diet. In the case of autism, the effects of these insults are magnified by the overuse of medications such as antibiotics and vaccinations, which increase susceptibility to infections and promote allergy and autoimmunity.

What has emerged is the extraordinary insight that autism is a complex, multisystem disorder rooted in a series of toxic, infectious, and allergic insults. Inflammation, disruptions in normal energy metabolism and ATP production resulting in mitochondrial dysfunction, and impairment in critical regulation of oxidative stress and detoxification through a breakdown in the twin interconnected cycles of methylation (B<sub>6</sub>, folate- and B<sub>12</sub>-dependent transfer of methyl groups or CH<sub>3</sub>) and sulfation (which produces glutathione) produce a metabolic encephalopathy.

Remove the dates of birth from the laboratory results and remove the diagnostic labels from a patient with autism and a patient with Alzheimer’s, and you will discover the same biological forces at work—inflammation, oxidative stress, impaired methylation and detoxification, mitochondrial dysfunction, and even the genetic polymorphisms. What are we to make of this observation? Is it coincidence, or does it reflect deeper patterns hidden in biological systems?

IS RECOVERY POSSIBLE? PATTERNS AND SYSTEMS, NOT DIAGNOSES AND SYMPTOMS

A desperate mother came to see me because her 2½-year-old son, "Sam," had just been diagnosed with autism. He was born bright and happy, breast-fed, had the best medical care available (including all the vaccinations he could possibly have). He talked, walked, loved, and played normally—until his measles, mumps, and rubella vaccination at 22 months.

He was vaccinated for diphtheria, tetanus, whooping cough, measles, mumps, and rubella, chicken pox, hepatitis A and B, influenza, pneumonia, hemophilous, and meningitis—all before the age of 2 years.

After this string of vaccinations, he lost his language, became detached, withdrawn, less interactive, and was unable to relate in normal ways with his parents and other children—all signs of autism. He also developed foul-smelling, sticky stools, dark circles under his eyes, and itchy ears. How could a normal boy be transformed so quickly?

He was taken to the best doctors in New York and "pronounced" as having autism (as if it were his fate), and told that there was nothing to be done except arduous, painful, and minimally effective behavioral and occupational therapy. The doctor told his mother the progress would be slow and she should keep her expectations low.

Devastated, his mother sought other options and found her way to me. When I first saw this little boy, he was deep in the inner wordless world of autism—watching him was like watching someone on a psychedelic drug trip. We dug into his biochemistry and genetics and found many things to account for the problems he was having.

We looked carefully at the few biological systems that go awry, manifesting as the clinical features of autism: gut and immune dysfunction, mitochondrial dysfunction and oxidative stress, and genetic polymorphisms that set the stage for biochemical train wrecks. In autistic children, test results often reveal deviations that are far more significant than in other chronic illness, but nonetheless, the same patterns exist. By unraveling the tangled roots of his distress, we were able to address the systemic causes of his broken brain.

Let's examine each of these areas of dysfunction.

Genetic Polymorphisms (Predispositions)

Impaired Glutathione Metabolism

- Homozygous for 2 glutathione S-transferase P1 (GSTP1++) genes (I105V and A114V).<sup>12</sup> This reduces the ability to biotransform...
toxicants such as toxic metals, xenobiotics, solvents, pesticides, herbicides, and polycyclic aromatic hydrocarbons. Point mutations in the gene coding for glutathione-s-transferase enzymes have been associated with increased risk for autism.

**Impaired Methylation**
- Methyleneetrahydrofolate reductase (MTHFR 677C>T and 1298<A>C) heterozygous polymorphism. MTHFR is the enzyme involved in the final methylation step of folic acid, producing 5-methyltetrahydrofolate from 5,10 methylenetetrahydrofolate. Impairment of this enzyme usually results in an elevated homocysteine, as 5-methyltetrahydrofolate is required to recycle homocysteine back to methionine. However, in autistic children, increased oxidative stress results in shunting of homocysteine to provide cysteine for glutathione production, resulting in the low levels of homocysteine. James demonstrated in 2004 that treating ASD children with methyl donors including B12, p-aminobenzoic acid and trimethylglycine normalized glutathione and homocysteine levels. This patient had a series of genetic predispositions and insults that led to accumulation of toxins and increased oxidative stress, triggering the vicious cycle of impaired methylation and glutathione production. This was manifested by his low homocysteine of 3 mmol/L (nl 6-8 mmol/L).
- Catechol-O-methyltransferase (COMT 472G>A) was heterozygous, which tends to slow the detoxification of the neurotransmitters needed for attention, focus, and cognitive skills, such as dopamine, epinephrine, and norepinephrine. COMT polymorphisms have been noted to occur with increased incidence in autistic children.

**Allergy and Autoimmunity**
- Elevated IgG anti-gliadin antibodies of 91 units (nl<20), indicating an autoimmune response to gluten.
- Elevated total IgG antibodies to not only wheat but to 28 foods, including dairy, eggs, yeast, and soy, indicating disrupted intestinal permeability.

**Digestive Function**
- Stool analysis cultured 3 species of yeast and a deficiency of beneficial flora, including Lactobacillus and Bifidobacteria.
- Elevated stool markers in intestinal inflammation consistent with allergy, infection, or inflammatory bowel disease (cosinophil protein X 18.2 mg/g (nl<7 mg/g) and calprotectin 46 mg/g (nl<40 mg/g).
- The urinary organic acids revealed very high levels of D-lactate—an indicator of overgrowth of bacteria in the small intestine resulting in intestinal fermentation of carbohydrates.
- Urinary peptide analysis revealed very elevated IAG (indolylacryloylglycine 161 mg/mg creatinine (nl<9.5), a toxic phenylalanine metabolite derived from dysbiotic bacterial metabolism and deltorphins and enkephalins. These are neuroactive peptides, which disrupt cognitive function and have been associated with autism spectrum disorder.¹⁸

**Nutritional Deficiencies**
- Low amino acids reflect inadequate protein intake (unlikely) or malnutrition, malabsorption, or overutilization in phase 2 detoxification pathways because of toxicity. For example, methionine and threonine are metabolized to cysteine and glycine respectively, which when combined with glutamate form the glutathione tripeptide.
- Mineral deficiencies: zinc (important for immune function, activation of digestive enzymes, as a cofactor for metallothionein, necessary for intracellular detoxification of heavy metals and 200+ other enzymes), magnesium (a natural N-D-methyl aspartate or NMDA receptor antagonist that reduces brain excitotoxicity and is a cofactor for 300+ enzymes), and manganese (a cofactor for super oxide dismutase, a critical mitochondrial antioxidant enzyme).
- Impaired methylation: elevated urinary methylmalonic acid, indicating B12 deficiency, and low homocysteine.
- Vitamin A and vitamin D deficiencies.
- Essential fatty acid deficiencies: eicosapentaneoic acid (EPA) deficiency and elevated AA/EPA ratio (an excess of inflammatory to anti-inflammatory fatty acids) are associated with autism spectrum disorder.²⁵

**Mitochondrial Dysfunction and Oxidative Stress**
- Organic acid analysis revealed widespread impairment in fatty acid, carbohydrate, and citric acid metabolism (elevated lactate, citrate, isocitrate, succinate, malate), indicating mitochondrial dysfunction resulting in energy deficits linked to cognitive dysfunction and demonstrated in 70% of autistic children.¹⁶
- Elevated suberate indicated impaired fatty acid transport into the mitochondria from carnitine deficiency.
- Very elevated lactate (L-Lactate) 101 mg/mg creatinine (nl<22), indicating cellular acidosis and coenzyme Q10 deficiency.
- Increased oxidative stress indicated by elevated DNA adducts or an 8-Hydroxy-2'- deoxyguanosine of 11.5 mg/mg creatinine (nl<5).

**Toxicity and Impaired Detoxification**
- Elevated red blood cell aluminum and lead.
- Elevated hair antimony and arsenic, but low levels of mercury because of impaired ability to excrete mercury.
- Elevated post 2,3-dimercaptopropane sulfonate (DMPS) provocation urinary mercury 14 mg/gram creatinine (nl<3).
- Markers of impaired sulfur (low sulfite) and glutathione status (elevated pyrogallurate) on urinary organic acids. Pyrogallurate elevation is indicative of glutathione wasting via a number of possible mechanisms, including cysteine and glycine insufficiency, and a low urinary sulfate is a functional marker for total body sulfur stores.
- Elevated urinary porphyrins indicate enzymatic disruption of normal porphyrin metabolism from heavy metals, which has been documented in autism.

**TREATING THE WHOLE SYSTEM**
Is it possible to point to any one gene, biomarker, or biological dysfunction, and say "Aha! This is the cause of autism, and this is
what we should treat?" The answer is an unequivocal no. None of these is the cause of autism. All of them exist in varying degrees and patterns in each individual. The key to unraveling the tangle of molecules and metabolic disruption is seeing patterns and working systematically with those patterns in the right order.

Sam's treatment started with repairing his gut and immune system. We then added nutrients needed for optimal function and removed heavy metals after we had optimized his nutritional status, methylation, and transsulfuration, the highways of detoxification and the quenchers of oxidative stress.

### Step 1: Correct Digestive Imbalances and Remove Food Allergens and Sensitivities
1. Eliminate gluten and IgE food sensitivities.
2. Treat small bowel bacterial overgrowth with nonabsorbed antibiotic (rifaximin).
3. Treat intestinal yeast with antifungals (fluconazole, itraconazole).
4. Re-inoculate with beneficial bacteria (broad-spectrum probiotic) and Saccharomyces boulardii.
5. Correct malabsorption with plant-based enzymes, including diperptidyl peptidase IV (DPP-IV).

### Step 2: Correct Nutritional Deficiencies and Optimize Nutritional Status
1. Multivitamin, topical zinc, magnesium, methyl folate, methionylcobalamin, pyridoxine (B6)
2. Cod liver oil for EPA/DHA and vitamins A and D
3. Coenzyme Q10 to correct mitochondrial dysfunction (elevated L-Lactate)

### Step 3: Enhance Detoxification and Treat Oxidative Stress
1. High dose intramuscular methionylcobalamin B12 necessary to enhance methylation and overcome toxic injury to methionine synthase (part of the methylation cycle) and activate dopamine receptors
2. Topical glutathione to support detoxification
3. A chelating medication dimercaptosuccinic acid (DMSA) to remove mercury and lead

### Treatment Results
After 3 weeks on a gluten-free diet, Sam showed dramatic and remarkable improvements. He began to talk again and showed much more connection and relatedness to people.

After 4 months, he was more focused, used more words, and was able to enter a more mainstream school.

Ten months into treatment, he was retested. The gut inflammation resolved (normal eosinophil protein X and calprotectin), the small bowel bacterial overgrowth resolved (normal D-lactate), but a mild yeast overgrowth (elevated arabinitol) persisted. Urinary peptide markers (IAG, enkephalins) dramatically improved. His methylmalonic acid was still elevated but improved.

The glutathione deficiency markers improved (pyroglutamate and sulfur), and urinary porphyrins were improved but still elevated. Urinary organic acid testing revealed normalization of his mitochondrial function and a 50% reduction in L-lactate. The oxidative stress marker (8OHdG) was normal.

Most importantly, he went from nonverbal to verbally fluent and no longer qualified for a special school or special services because he "lost" his diagnosis of autism. And his bowel movements normalized.

Sam now has a wonderful sense of humor (typically completely absent in autistic children) and engages in spontaneous play and hugs with friends and family.

This is the result of the clinical application of systems biology, without which the puzzle of chronic disease cannot be solved.

### THE GUT-IMMUNE SYSTEM AND THE BRAIN

Many medical discoveries are made by accident. An open inquiry of observed phenomena sometimes reveals unexpected clues. Many doctors and scientists have ignored the fact that up to 95% of autistic children have intestinal problems, such as altered bowel function and abdominal distention. How can their intestinal problems affect their brains, interrupt their language, and lock them in their own private world?

Dr Wakefield asked how. He happened to notice inflammation (or lymphoid nodular hyperplasia) in the bowels of some children with autism. Could this observation be brushed off as coincidence? In a study of 148 children with autism compared to 30 normal controls (children without autism), 90% of autistic children showed inflamed bowels on biopsy compared to only 30% of controls (although 30% is a lot! This makes me wonder if many nonautistic children have bowel inflammation from poor diet and allergies as well). He also noticed the inflammation was much more severe in autistic children. Food allergens, bacteria, viruses, and toxins (such as mercury) could all be the cause.

In addition to all the potential digestive problems that autistic children face, it also seems they are more susceptible to allergy and gut inflammation triggered by certain foods, such as gluten and casein. The extreme inflammation in the guts of autistic children contributes to their inflamed brains.

### Making Sense of the Measles Vaccine Controversy

Other studies have linked the live measles virus from vaccinations to the inflamed gut. Living measles viruses have been identified in some people with inflamed guts. Vaccines, even an "inactivated" live virus, stimulate the body's humoral immune system to produce protective antibodies. But sometimes, as in the case of autistic children, a weakened immune system can't manage this "inactivated" live virus. Then the live attenuated virus persists, producing low-grade inflammation—in both the gut and the brain.

A study of children with developmental delay found that 75 of 91 patients with autism and inflamed bowels had live measles virus detected in samples of their intestinal tissues. Only 7 of the 70 control patients were found to have the measles virus in their gut.

In another study, DNA analysis was performed on the measles strains found in autistic children and compared to that of strains found in nonautistic children with inflamed bowels. The DNA of the measles virus in autistic children came from vaccine strains of mea-
Atitism: Is it All in the Head?

Not wild types. A more recent study did not find persistent measles virus in children with autism, but even this does not rule out the possibility that the virus did its harm in a "hit and run" fashion. This doesn't mean that ALL children who are vaccinated have problems, but for some reason autistic children are unable to handle the live measles viruses used in immunizations, triggering an inflammatory response in the gut and the brain, and then the normally benign live measles virus in the vaccine takes root in the body and sends these kids into an even deeper spiral of brain dysfunction.

MIND AND METALS: A DANGEROUS COMBINATION

Through their organization Defeat Autism Now!, a group of dedicated parents, scientists, and doctors led by Sidney Baker, MD, John Pangborn, PhD, and the late Bernard Rimland has made clear that many children on the autism spectrum, and those with ADHD and even learning difficulties, are toxic. Autistic children have low levels of glutathione, the major detoxification compound in the body, so they cannot excrete metals. Their hair shows low levels of mercury because genetically they can't excrete it, but they have higher levels in their baby teeth. Chelation challenge tests using DMSA or DMPS show that autistic kids have more mercury and other metals than normal children.

Thimerosal and Autism

Until recently, mercury, in the form of thimerosal, was the most common disinfectant placed in vaccines (most flu vaccines still contain it) and contact lens fluid. A recent study "proved" that thimerosal has no link to autism or ADHD. The study, which appeared in The New England Journal of Medicine, apparently was designed to show no link. Here is how the vaccine industry–funded scientists designed the study, which could not accurately answer the question of the effect of thimerosal in autism:

1. They excluded all children with ADHD and autism. These are the children with the genetic susceptibilities to problems. These are the children who cannot detoxify. This is like doing a study to see if peanuts cause allergies but excluding all kids with an allergy to peanuts from the study.
2. They did not measure mercury in hair, urine, or blood or the total body burden of metals in the children—just their exposure. Children who were good detoxifiers would be able to excrete mercury. They should have measured the total body load of mercury in these children and then noted how that correlates to any neurologic or other effects. They also should have measured the genes involved in detoxification of mercury, such as apo E4, GSTM1, and MTHFR.
3. Manufacturers who put mercury in vaccines in the first place employed or funded the authors of the study and its accompanying editorial. That's like putting tobacco companies in charge of studies on the risks of smoking.
4. They didn't explain how it could be safe for babies to receive 187.5 μg of mercury by the time they were 6 months old when the safe level is 0.5 μg/kg of mercury at any one time, according to the EPA.

If thimerosal is as safe as studies like this attempt to suggest, why was it removed from use after 50 years from all childhood and adult vaccines in 2001 (except, of course, the ones we export to the third world)?

THE FUTURE OF MEDICINE AND HEALTHCARE

Autism is a hologram. Through it a 3-dimensional picture of the failure of our current medical paradigm and the promise of a new one has formed. The lessons learned from the dissection of the functional causes and mechanisms of autism can illuminate the path for whole systems medicine and clinical research and the potential for it to address the global crisis of chronic disease. All we have to do is shine the light through the fragments of the hologram scattered at our feet. Then we have to pay attention and act collaboratively socially, politically, environmentally, and personally.

REFERENCES
