

CHANGING THE COURSE *of* AUTISM



A SCIENTIFIC
APPROACH FOR
PARENTS AND
PHYSICIANS

BRYAN JEPSON, M.D. *with* JANE JOHNSON

chapter four

THE AUTISM EPIDEMIC

BEFORE 1980, AUTISM WAS RARE. PREVALENCE STUDIES DONE BEFORE then consistently estimated the rate to be 2-5 per 10,000 people.¹²³ Most general practitioners and pediatricians went through their entire careers without ever seeing a case. If mentioned at all in medical school, it was relegated to part of a lecture on “rare but interesting” psychiatric disorders. In 1958 Kanner wrote, “The fact that an average of not more than eight patients per year [over twenty years] could be diagnosed with reasonable assurance as autistic in a center serving as a sort of a diagnostic clearinghouse, speaks for the infrequency of the disease, especially if one considers that they recruit themselves from all over the North American continent.”⁴

Arn Van Krevelen, the first child psychiatrist in Europe to publish a case of infantile autism (and hence their one and only resident expert at the time), admitted that he’d begun to doubt the existence of autism because there was no mention of it in the European literature for nearly a decade following Kanner’s paper. When he finally did encounter an autistic child, he said she was “...as much like those described by Kanner as one raindrop is like another.” In the decade following the publication of his paper, Van Krevelen, the expert for an entire continent, saw only ten more cases.⁵

Clearly autism was once highly unusual. It wasn't brought into public awareness in the US until 1988, when Dustin Hoffman portrayed an autistic savant in the movie *Rainman*. Despite impressive abilities in memory and mathematical calculation, the character he played had very rote language, no social skills, and a disabling need for routine. For most people, the savant character in *Rainman* defined autism because they had no other model.

Concern in California

Starting in the mid-1980s, more and more children were being diagnosed. Through the 1990s, rates rose exponentially. The State of California has tracked the numbers of people with autism enrolled in their developmental services program since 1960. In 1969, the Lanterman Act established regional centers to care for people with developmental disabilities throughout the state; in 1973 autism was included in the list of disabilities for which the centers were required to provide services. It's estimated that 75-80% of developmentally disabled children in California are enrolled in this system.⁶

In March 1999, the California Department of Developmental Services (DDS) issued a report entitled "Changes in the Population of Persons with Autism and Pervasive Developmental Disorders in California's Developmental Services System: 1987 through 1998." They reported a 273% increase in DSM-IV full-criteria autism cases enrolled in their program during that decade. Other ASDs increased at an even higher rate—1,965%. Alarming, the explosion of cases was from the youngest age groups.

The following graph shows the number of enrolled cases in the California system per birth year between 1960 and 1991. You can see that the rates were fairly flat until the late 1970s when they began to rise:

In 1987, the number of cases was pretty evenly distributed across the age groups, at least between age five and age twenty-nine, after which it dropped off. There is a large percentage increase in 1998 in the five to nine year olds, and two-thirds of the cases were younger than fourteen (up from about 37% in 1987). The rate of general population growth in California between 1987 and 1998 was 20%.

Other disabilities included under the Lanterman Act were also increasing, but not at a rate anywhere close to the rate of autism:

Of all of the children in the California system with developmental disabilities, the percentage of those cases with autism nearly doubled from 4.85 to 9.37%.

What was happening? Why was this previously rare disorder suddenly overwhelming the system? Experts quickly dismissed the idea that these numbers represented a true rise in incidence.^{7 8} They reasoned that autism was, after all, a genetic illness, and since there is no such thing as a genetic epidemic, there had to be another explanation. They suggested that changes in the diagnostic criteria had skewed the numbers.^{9 10 11 12} Or, that what had been called "mental retardation" was now being called autism.^{13 14} Or, that doctors were now more aware of the condition and were better at diagnosing it. Or, that parents were now seeking services for their children with autism instead of keeping them at home, as parents must have done in the past. Or, people with autistic children were moving to California from all over the country to take advantage of better services. Or even that since California was

	1987	1998	Percent Change
Autism (All Combinations)	3,864	11,995	210.43%
Cerebral Palsy (All Combinations)	19,972	28,529	42.84%
Epilepsy (All Combinations)	22,683	29,645	30.69%
Mental Retardation (All Combinations)	72,987	108,563	48.74%
Whole Population	80,483	136,383	69.46%

Table 1: Percent increase in diagnostic populations from 1987 to 1998. Source: DDS Report to the Legislature 3/1/99.

chapter ten

WHY CAN'T THEY DETOXIFY?

THE EXPLOSION OF CASES OF AUTISM STARTING IN THE MID-1980S implicates a strong environmental role in this disorder, but a definite cause is still unknown. Is there some new toxin introduced in the last thirty years that makes babies develop autism? Or has the general toxic load increased in the environment to the point that children with limited detoxification capacities are neurologically affected? We should be able to find the answers to these questions by examining both the toxic exposures we now live with and the detox capacities of autistic children.

Detoxification 101

We're constantly exposed to substances that can cause damage to our tissues. Toxins are in the air we breathe, the water we drink, and the food we eat. To prevent injury from these substances, we have a multi-layered and complex system for detoxification.

The liver is the main organ of detoxification; it's the first stop for harmful substances absorbed from the gut into the bloodstream. It pro-

cesses most toxins before they can reach and damage the other organs—this is called *first-pass metabolism*. The liver uses different metabolic pathways to safely excrete harmful substances via the urine or the stool. The main detoxification pathways are called glucuronidation and trans-sulfuration. Depending on their structure, toxins are usually metabolized more effectively by one or the other.

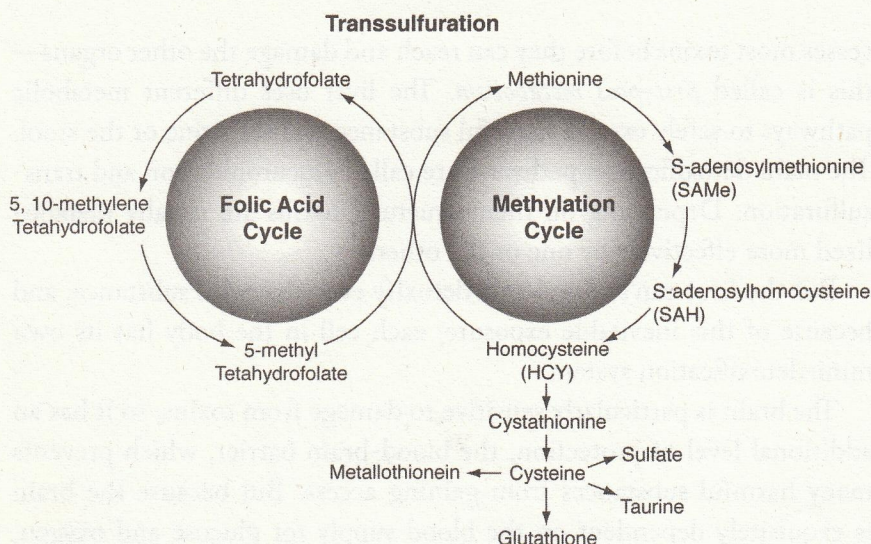
But the liver can't completely detoxify every harmful substance, and because of this inevitable exposure, each cell in the body has its own mini-detoxification system.

The brain is particularly sensitive to damage from toxins, so it has an additional level of protection, the blood-brain barrier, which prevents many harmful substances from gaining access. But because the brain is exquisitely dependent on the blood supply for glucose and oxygen, certain small toxic molecules are able to slip through.

Many substances that are initially innocuous become toxic during normal metabolism. Some of these metabolic by-products are known as free radicals, and are produced by a process called oxidation. A counter-process, reduction, converts free radicals back into a harmless form. Imbalance between oxidation and reduction (redox) creates oxidative stress, which can result in tissue injury; anti-oxidants, including sulfate, cysteine, glutathione (GSH), and several vitamins and minerals (particularly vitamin C, vitamin E, vitamin B6, zinc, and selenium) combat this problem.

The Methylation Cycle

A number of researchers independently began looking at detox dysfunction in children with autism. They found abnormalities in the methylation cycle, a critical metabolic pathway that among other things produces precursor molecules for detoxification and anti-oxidation. Although this is complicated biochemistry, I am going to go through it in detail because it plays such an important part in so many of the pathways that appear to be disrupted in autism.



The diagram above gives an overview of the cycle, along with its interaction with two other metabolic pathways, the folic acid cycle and the transsulfuration pathway.

If we think of the methylation cycle as a central bank, the currency would be an organic molecule called a methyl group ($-\text{CH}_3$). When a larger biochemical is “methylated,” its structure and function change.

For example, a methyl group released from a chemical reaction with SAME can attach to specific DNA sequences in our genetic code. If methylated, gene expression of that particular DNA strand is turned off. If the methyl group is removed, the gene is turned on. Methylation therefore controls which genes are active and which are repressed. The methylation patterns are established during embryogenesis (early development of the embryo) and are inherited in a tissue-specific manner. This allows cells to differentiate or specialize, accomplishing different tasks in different tissues, and it helps stabilize the chromosome structure, resulting in fewer mutations. It allows the body to inactivate genes (like the extra X chromosome in females) and to activate the inherited genes that give us the characteristics of our family tree. It’s also used to suppress the expression of DNA sequences inserted by foreign invaders like viruses.¹

chapter 13

AUTISM AND THE BRAIN

WHILE AUTISM HAS BEEN VIEWED AS A BRAIN DISEASE FOR MANY decades, surprisingly little is actually understood about the brains of autistic patients. Various studies have looked at the structural and physiological differences in the autistic brain, but the results are inconsistent. This probably reflects the differences among subgroups of children with autism, all labeled with a common behavioral symptom complex but possibly stemming from different etiologies.

Neuroanatomy (Brain Structure)

With computerized tomography (CT) and magnetic resonance imaging (MRI) scans, we're now better able to study the anatomy of autistic brains (researchers used to have to work from scarce autopsy specimens). Functional PET (positron emission tomography) scans and Functional MRIs provide information not only about the structure but also the function of different brain regions. As expected, these technological innovations have revealed many abnormalities in the brains of autistic children. Some features are consistent, but there's wide individual variation of pathology.

A frequent finding is that autistic children have larger-than-normal head circumferences, correlating with larger-than-normal brains.

During the first year of life there appears to be a period of rapid brain growth in autism, followed by a plateau, and then a period of slower-than-normal growth extending into adolescence.¹ The rate of brain growth is different in different regions of the brain, with the cerebellum and cerebral cortex most consistently involved. Growth of white matter has been found to be more extensive than gray matter.² In the cerebral cortex, there is also a front-to-back distribution of growth rate with the frontal cortex growing much more rapidly than the occipital lobe.³

Other studies found growth abnormalities that didn't fit these patterns: one study detected abnormal enlargement in the cerebral cortex but not in the cerebellum;⁴ another study isolated cortical enlargement to the temporal, parietal, and occipital lobes, but not the frontal lobe;⁵ others have found abnormalities in the limbic system, the brain stem, the basal ganglia, and the corpus collosum.⁶ In some studies there was evidence of both enlargement and reduction of certain brain regions in different participants. For example, studies of the cerebellum show that while the majority of cases have a smaller than normal cerebellar vermis, a minority are larger than average (16%).⁷ Up to 50% of autistic patients in other studies had normal cerebellar size.⁸

On the microscopic level, there appears to be a disruption of the normal cellular structure and organization in particular regions of the brain. A consistent abnormality is the loss of Purkinje cells and granular cells in the cerebellum.^{9 10 11 12} The cerebellum is thought to be responsible for affect, motivation, social interaction, learning, and the processing of motor and sensory information.¹³ It is also responsible for tasks that require rapid shifts in attention—difficulty shifting attention could contribute to autistic behaviors.¹⁴

The majority of studies find abnormalities in the limbic system of the autistic brain, including increased cell-packing density and smaller neuronal size, consistent with an arrest in normal maturational development.¹⁵ The limbic system (the hippocampus, the amygdala, the cingulate gyrus, and the septal nuclei) takes part in the integration of memory and emotional behavior and accompanying changes in physiology, including heart rate, respiratory rate, and blood pressure.