

Speaking of Autism Part I: Causes of Autism

For many pediatricians, autism spectrum disorders (ASD) have joined politics and religion as topics to avoid in casual conversation. For parents autism is a deeply emotional topic, threatening the reciprocal expression of love at the core of the parent-child relationship. The rapidly emerging science of autism is full of competing theories and intriguing studies. A few of these paths have led to solid evidence; many more will wind up blind alleys. The gap between our deepest fears and the slow, messy process of scientific discovery provides fertile ground for conjecture, debate, even conspiracy theories.

I'm fascinated by the leading edge of science, but in thirteen years of practice I have seen many initially promising ideas wither in the face of more rigorous testing. So today I'll try to outline what the best data so far tell us about the causes of autism. Next month we'll review ASD diagnosis, and in February we'll discuss therapies for ASD.

What's the difference between autism and autism spectrum disorders (ASD)?

The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* defines three separate but related diagnoses under the umbrella of ASD. Autistic Disorder (AD), Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), and Asperger's Syndrome (AS) are thought to represent a range of developmental disorders affecting a child's ability to relate to others. The mildest forms of ASD present as social awkwardness born of an impaired ability to interpret social and emotional cues. The most severe forms affect all areas of development, profoundly impairing the patient's ability to carry on activities of daily living.

How common is autism?

By current definitions ASD affects 6-7 children per 1000 in North America and Europe (one in 143 to one in 167). Boys are much more commonly diagnosed, with ratios estimated as high as 6.5 boys for every girl.

Is autism growing more common?

Fierce debate continues over whether rates of ASD have risen over the last few decades. Widening definitions of ASD and exploding awareness of the disorder among parents, educators, and clinicians make this question almost impossible to answer. Autism as a diagnosis was "born" in 1980 with the publication of the *DSM-III-R*. In 1994 the *DSM-IV* expanded the definition by including Asperger's Syndrome. The passage of the Individuals with Disabilities in Education Act (IDEA) and the Americans With Disabilities Act (ADA) in 1990 drove many to re-define some children previously labeled as mentally retarded in order to qualify them for newly available services. Whether there is an epidemic of autism or an epidemic of autism diagnosis is a question likely to fuel debate for years to come.

Is autism a genetic disease?

It's clear that ASD have a genetic basis: siblings of an autistic child have a 2% to 8% rate of also having autism. About 10% of cases are associated with an identifiable genetic disorder or medical condition, most commonly Fragile X in boys and Rett Syndrome in

girls. Older parents, both mothers and fathers, are more likely to have autistic children. As genetic science advances, many different genetic abnormalities are being associated with ASD, some more convincingly than others.

What about vaccines and mercury?

This may be the most emotional and contentious question of all. Early popular theories about the role of vaccines and mercury (particularly thimerosal) in the development of autism have been extensively studied and, to the extent that science can “disprove” anything, disproved. The most intriguing new studies involve children who seem to develop normally then regress rapidly, exactly the ones in whom vaccines seem to “cause” their symptoms. Home videos of these children often demonstrate subtle signs of autism appearing months before these children receive the suspect vaccines. Unvaccinated and vaccinated children have identical rates of autism, and assays of mercury, both direct and historical have failed to show differences in affected versus unaffected children.

Is autism caused by the immune system?

Some small retrospective studies have implicated autoimmune diseases in the development of autism. The most intriguing of these found children with autism seemed to have increased levels of antibodies against brain antigens. Larger prospective studies failed to confirm these results. While this is an area of much ongoing research, the data so far do not show any convincing relationship between immune diseases and ASD.

What’s different about the brains of children with autism?

The more we’re able to study the brains of children with ASD, the more differences we seem to find. These differences become evident very early in brain development, starting long before birth. Children with autism start with head sizes somewhat below average. A period of rapid brain growth follows, leading to head sizes above average in the first year of life. By adulthood brain size seems to be no larger than average, suggesting the growth slows down at some point. The nerve cells in autistic brains appear to have fewer connections to other cells in some places and may differ in number and density in some regions of the brain compared to matched controls. There are also differences in the ratios of “white matter” and “gray matter” that correspond to how nerve cells in the brain are insulated.

Functional neuro-imaging studies (MRI) show that patients with ASD process information in different brain regions that seem to correlate to the symptoms of autism. The areas of the brain that recognize faces and facial expressions seem to be most affected. New research is examining the role of the “mirror neuron system,” the parts of our brain that allow us to guess what other people must be feeling. These studies have provided fascinating insights into the neurologic basis of ASD, but there is still no “brain scan” to diagnose autism. For this reason routine brain imaging is not recommended in diagnosing ASD.

Where do we go from here?

As medical science advances we often discover that diseases that appear singular have many different underlying causes. The common cold, for example, is really a set of symptoms caused by thousands of different viruses. It's already clear that the symptoms we label ASD arise from a multitude of genetic defects and environmental factors, and as we learn more we will move farther from finding *the* cause of autism and closer to finding the causes of autism.

Next Month: Diagnosing ASD