Autism spectrum disorder (ASD) is one type of a set of chronic conditions (pervasive developmental disorders) that develop in early childhood. It is characterized by (1) impaired social interaction, (2) problems with verbal and nonverbal communication, and (3) unusual, repetitive, or severely limited activities and interests. Autism is a broad-spectrum disorder, with different degrees of severity, that was described almost simultaneously by Kanner (in 1943) and Asperger (in 1944). ASD occurs in 1 out of 150 individuals, and is four times more likely to occur in males than females. Among a group of children with mental retardation, Kanner observed individuals who appeared to be asocial, lacking in communicative skills and committed to repetitive ritualistic behaviors, but who retained certain intellectual capacities such as retentive memory, skilled sensory and motor aptitudes, etc. Asperger's observations included somewhat older children who were less completely disabled. Autism may be a single syndrome of varying severity and multiple etiologies, or may be more than one disease. While a minority of affected individuals may be able to live independently, most will require lifetime care. Evidence supports autism as a disorder of the association cortex, both its neurons and their projections. In particular, it is a disorder of connectivity, primarily involving disruption of connections within each hemisphere. Early brain overgrowth is a key factor in the pathobiology of autism.

Primary manifestations include impairment of communication skills and impaired ability to relate socially with other people, although other debilitating symptoms may also occur, including seizures in up to 30% of patients. Up to 60% of people with autism are also mentally retarded; a small fraction are gifted in some areas such as music, drawing or calculations (e.g. in Asperger’s syndrome.) Deficits in high-functioning individuals occur in processing that places high demands on integration of information and coordination of multiple neural systems. Intact or enhanced abilities share a dependence on low information-processing demands and local neural connections.

The first behavioral signs of autism may appear between 1 and 2 years of age, with diagnosis commonly made by 2-4 years of age. Regardless of the time of and rapidity of onset, the autistic child exhibits a striking disregard for other persons. No eye contact is made and the patient is no more interested in another person than in an article of furniture. Patients seem to have trouble inferring what other people think and feel. In any group of autistic children, there is a wide range of deficits in sociability, drive, affect, and language, from the averbal negativistic, completely isolated state to one showing considerable language skill and some capacity for attachment to certain people and scholastic achievement. In addition to core symptoms, children with autism frequently have serious behavioral disturbances, such as self-injurious behavior, aggression, and tantrums in response to routine environmental demands. These behavioral problems interfere with therapeutic efforts and pose large challenges to parents and educators.

The etiology of autism is complex, and in most cases the underlying pathologic mechanisms are unknown. On the basis of family and twin studies, there appears to be a genetic basis for a wide "autistic syndrome." About a quarter of cases of autism are associated with genetic disorders such as fragile X syndrome or with infectious diseases such as congenital rubella. Genetic studies have shown an association with markers of brain development. E.g., mutations in two different neuroligins, involved with postsynaptic differentiation, are associated with autism in males. Another associated gene involves the MET receptor tyrosine kinase gene that codes for a protein that relays signals turning on a cell's internal signaling cascades that can result in
increased proliferation, motility, differentiation, process outgrowth, or survival. Current estimates suggest that 10 to 20 different interacting genes are involved. In some cases, autism is associated with **insults early in gestation**. Autism may arise from abnormal central nervous system functioning, since most autistic patients have indications of brain dysfunction, and about half of them have abnormal electroencephalograms. There have been reports indicating frontal lobe dysfunction in autism, with deficits in executive function, spatial working memory, and the capacity for suppressing context-inappropriate responses. **Structural abnormalities and/or alterations in tissue volume** have been reported in several brain regions. Autistic children have **less oxytocin**, a neuropeptide that regulates social behavior in animals.

One major hypothesis involves early brain overgrowth at the beginning of life with slowing or arrest of growth during early childhood. This hypothesis involves an excess of neurons and their axonal and dendritic processes and synapses in key frontal and temporal cortical regions that mediate higher-order social communication, emotion, and language functions. By 1-2 years of age, head circumference in autistic children was abnormally increased. By the time children with autism reach 2-4 years of age, overall MRI brain volume (including both gray and white matter) is abnormally enlarged by about 10%. The frontal and temporal lobes, and amygdala, are sites of peak overgrowth. There appears to be premature myelination in frontal, but not posterior, white matter regions in very young autistic children. White matter connecting association cortex areas (i.e. not including internal capsule or corpus callosum) was prominently disturbed. The cellular and molecular bases of this overgrowth are unknown.

Autism is as common as many other childhood medical disorders such as diabetes and leukemia. However, children with autism and related disorders, pervasive developmental disorders (PDDs), are often not diagnosed until several years after initially presenting for medical or behavioral evaluation. This is due in part to the lack of uniform guidelines for surveillance, diagnostic evaluation, and follow-up of children with autism and related disorders. Early diagnosis, however, may be essential to successful intervention in children with autism or other developmental language delay. At this point, management depends largely upon the expert judgment of clinicians experienced in autism, language delay, and pediatric neurology and psychiatry, rather than data gathered from controlled clinical trials. The multiple developmental and behavioral problems associated with these conditions often require the care of multiple providers. Early, sustained intervention is indicated, as is the use of various treatment modalities (e.g., pharmacotherapy, special education, speech/communication therapy, and behavior modification).

**References:**
Adams, Victor & Ropper, Principles of Neurology
http://www.cureautismnow.org/
NINDS Autism Fact Sheet

**Good books related to autism:**
The Speed of Dark by Elizabeth Moon
The Curious Incident of the Dog in the Night-time by Mark Haddon
Animals in Translation by Temple Grandin and Catherine Johnson (Temple Grandin is autistic, and now has a Ph.D. and is a specialist in animal behavior)