Chapter C.2

DEVELOPMENTAL DISORDERS

AUTISM SPECTRUM DISORDERS

Joaquín Fuentes, Muideen Bakare, Kerim Munir, Patricia Aguayo, Naoufel Gaddour, Özgür Öner & Marcos Mercadante*

This publication is intended for professionals training or practicing in mental health and not for the general public. The opinions expressed are those of the authors and do not necessarily represent the views of the Editor or IACAPAP. This publication seeks to describe the best treatments and practices based on the scientific evidence available at the time of writing as evaluated by the authors and may change as a result of new research. Readers need to apply this knowledge to patients in accordance with the guidelines and laws of their country of practice. Some medications may not be available in some countries and readers should consult the specific drug information since not all dosages and unwanted effects are mentioned. Organizations, publications and websites are cited or linked to illustrate issues or as a source of further information. This does not mean that authors, the Editor or IACAPAP endorse their content or recommendations, which should be critically assessed by the reader. Websites may also change or cease to exist.

©IACAPAP 2012. This is an open-access publication under the Creative Commons Attribution Non-commercial License. Use, distribution and reproduction in any medium are allowed without prior permission provided the original work is properly cited and the use is non-commercial. Send comments about this book or chapter to jmreyATbigpond.net.au


Clay art by Santiago, an 11 year old with autism spectrum disorder. Photo: Lynn Albrink
The term autism spectrum disorders (ASD) refers to a group of neurodevelopmental conditions defined by impairment in three areas: social interaction, communication or use of verbal and non-verbal language, and a stereotyped, restricted or repetitive pattern of behavior, interests and activities. Symptoms are generally obvious before the age of three years, but in most areas of the world these conditions are not diagnosed until a few years later. The increased identification of these disorders, the emotional impact they have in families and the challenging financial demands associated with their treatment and support currently make ASDs an important illness at the scientific, public health and human rights level. The treatments now available can achieve a far better quality of life for sufferers than was the case just a few years ago, but it must be recognized that ASDs cannot yet be cured and most people with ASD, particularly in developing countries – with a few fortunate exceptions – are not receiving specialized treatment or any treatment at all.

This chapter seeks to describe the current knowledge in the classification, epidemiology, etiology, clinical picture, assessment, prognosis and treatment of ASD. It is hoped this material will be useful for clinicians committed to changing global health practices involving these patients and their families.

**HISTORY**

Eugen Bleuler (1857–1939), a Swiss psychiatrist, coined the terms *schizophrenia* and *autism*. He derived the latter from the Greek word *autos* (meaning “self”), to describe the active withdrawal of patients with schizophrenia to their own fantasy life in an effort to cope with intolerable external perceptions or experiences (Kuhn, 2004). The use of the term *autism* in its current sense started 30 years later when the Austrian pediatrician Hans Asperger adopted Bleuler’s terminology of *autistic psychopaths* in a lecture he delivered at the Vienna University Hospital (Asperger, 1938). Asperger subsequently published his second PhD thesis in 1944 (first transcribed in 1943) (Asperger, 1944) where he described a group of children and adolescents with deficits in communication and social skills and also with a restricted, repetitive pattern of behaviors.

At the same time, in 1943 – separated by distance, the Second World War and apparently unaware of each other’s work – Leo Kanner, at Johns Hopkins University Hospital in the US, described 11 children with striking behavioral similarities to those depicted by Asperger in his classical paper "Autistic disturbances of affective contact" (Kanner, 1943). Most of the characteristics described by Kanner such as “autistic aloofness” and “insistence on sameness” are still part of the criteria to diagnose autism in current classifications. Children described by Asperger differed from those of Kanner in that they had no significant delays in cognitive or language development.

Asperger’s paper, published in German, remained largely unknown until Uta Frith translated it into English (Asperger, 1944), which made it widely available. These ideas were further disseminated by Lorna Wing (Wing, 1997) in the UK. As a result, there has been a gradual acknowledgement that autism constitutes a spectrum with a continuum from mild to severe symptoms and that Asperger’s disorder is part of that continuum.
It was a misfortune that the original meaning of Bleuler’s term and its theoretical relationship with schizophrenia, combined with the psychoanalytic theories dominant in the mid twentieth century, amalgamated ASDs with psychotic disorders, classifying them under the rubric of childhood schizophrenia. The apparent withdrawal of ASD patients was misinterpreted as the same mechanism as that seen in schizophrenia, a defensive retreat from an intolerable external situation, the result of a pathogenic family (as it was then widely conceptualized). Unfortunately, some of these discredited ideas are still held by some. The relative importance of ASDs in relation to other health conditions continues to be underestimated by governments and international agencies. In Africa, for example, clinical work on ASDs did not start until three decades after Kanner and Asperger had published their work (Lotter, 1978; Bakare & Munir, 2011).

**DEFINITION**

ICD-10 (World Health Organization, 1990) classifies autism under the pervasive developmental disorders, a group of conditions characterized by qualitative abnormalities in reciprocal social interaction, idiosyncratic patterns of communication and by a restricted, stereotyped, repetitive repertoire of interests and activities. These qualitative abnormalities are a feature of the sufferer's functioning in all situations. DSM IV (American Psychiatric Association, 2000) also uses the term pervasive developmental disorders, although its subdivision is different in the two classifications. Both taxonomies utilize a list of behaviors, require that a number of criteria be met to warrant a diagnosis and are periodically reviewed to incorporate new research data. In fact, both are currently undergoing a detailed review; DSM-5 is expected to be released in 2013 and ICD-11 in 2015. Important changes to DSM-5 are expected while up to this point, ICD-11 does not seem to be planning major modifications.

The changes proposed for DSM-5 have been polemical in scientific and lay circles. DSM-5 proposes to eliminate the division existent in DSM-IV between autism, Reut’s disorder, Asperger’s disorder, childhood disintegrative disorder, and pervasive developmental disorders not otherwise specified. According to the DSM-5 proposal, there will be a unique category of ASD, characterized by:

- Persistent deficits in social communication and social interaction across contexts not accounted for by general developmental delays
- Restricted, repetitive patterns of behavior, interests, or activities
- Presence from early childhood (but may not become fully manifest until social demands exceeds the child’s limited capacities), and
- Limitation and impairment in everyday functioning.

DSM-5 will thus eliminate the diagnosis of Asperger’s disorder while formalizing the “spectrum” concept espoused by Lorna Wing, who favored considering Asperger’s disorder a sub-category of a unified ASD construct (Wing et al, 2011).

Clinicians will find the classical symptoms grouped in these two areas (deficits in social communication and restricted, repetitive patterns of behavior) with the addition of hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment. Also, there will be a complementary
classification of severity, categorized as “requiring support”, “requiring substantial support” and “requiring very substantial support”.

A recent study by Frazier et al (2012) supports the validity of the proposed criteria. They report increased specificity compared with DSM-IV and suggest that a relaxed algorithm should be considered to improve identification and decrease cost, thus maximizing intervention resources. William et al (2012) tested the construct validity and reported the DSM-5 model was superior to DSM-IV, and the model fit in their sample was good, stable across age and gender and in those with clinical and sub-threshold autistic presentations.

**EPIDEMIOLOGY**

Autism was once considered a relatively rare condition. Recent epidemiological data have radically altered this perception. Based on large surveys in the US, the Centers for Disease Control and Prevention (CDC), estimates the prevalence of ASD as 1 in 88 children, occurring in all racial, ethnic and socioeconomic groups, although it is five times more common among boys (1 in 54) that girls (1 in 252). The CDC website also offers data from numerous studies in Asia, Europe and North America showing an average prevalence of ASDs of about 1%. A recent survey in South Korea, which screened children in the schools, reported a prevalence of 2.6% (3.7% among boys and 1.5% among girls) (Kim et al, 2011). Another study in England estimated a prevalence of ASD at almost 1% in adults (Brugha et al, 2011).

However, epidemiological studies are difficult to compare. They vary in the composition of the population surveyed, recruitment mechanisms, sample size, design, awareness, participation rates, diagnostic criteria, instruments used as well as whether impairment criteria are included (Fombonne, 2009). Nevertheless, using the same methodology over a period of eight years, the CDC’s Autism and Developmental Disabilities Monitoring Network has found increasing rates of ASDs in the US.

<table>
<thead>
<tr>
<th>Survey year</th>
<th>Year of birth</th>
<th>Prevalence per 1,000 children (range)</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>1992</td>
<td>6.7 (4.5–9.9)</td>
<td>1/150</td>
</tr>
<tr>
<td>2002</td>
<td>1994</td>
<td>6.6 (3.3–10.6)</td>
<td>1/150</td>
</tr>
<tr>
<td>2004</td>
<td>1996</td>
<td>8.0 (4.6–9.8)</td>
<td>1/125</td>
</tr>
<tr>
<td>2006</td>
<td>1998</td>
<td>9.0 (4.2–12.1)</td>
<td>1/110</td>
</tr>
<tr>
<td>2008</td>
<td>2000</td>
<td>11.3 (4.8–21.2)</td>
<td>1/88</td>
</tr>
</tbody>
</table>

Source: CDC website
Although studies do not rule out temporal or external demographic factors (such as being born to older parents; survival of premature or high risk low birth weight babies; earlier diagnosis of young children with higher IQ who spontaneously make progress over time that would not have been diagnosed years ago; or only counting older children receiving special support), experts in the field explain this rising in prevalence by increased awareness and improvement in the recognition and detection of the disorder. This may explain why the prevalence of ASD is reported to be lower in China (6.4 in 10,000) (Li et al, 2011). While there is much research on ASD in Europe and North America, there is not a single epidemiological study of ASD in sub Saharan Africa (Bakare & Munir, 2011), but a significant increase of ASD among children of Ugandan mothers (Gillberg et al, 1995) and of Somali women living in Sweden (Barnevik-Olsson et al, 2008) has been reported.

**EARLY DETECTION**

It is acknowledged that early detection constitutes a major advancement in that it enables prompt intervention that may improve prognosis in a significant proportion of children with ASD, but also because it clarifies the doubts and anguish of parents and allows adequate public planning for future school placements and community support.

It was known that there was a higher incidence of ASD among siblings of already identified cases; this observation has led to a more detailed examination of newborn siblings and follow up during their first years of life. Trying to identify early developmental signs that precede a diagnosis of ASD in siblings that eventually develop the disorder has been a fruitful area of investigation. This change, from a retrospective view of abnormal development to a prospective follow-up of children at risk, constitutes a remarkable scientific advance. It has been shown in these high-risk infants that there were no notable findings during the first six months in those later classified as ASD; however, in the following six months, social interaction problems started to unfold (Zwaigenbaum et al, 2005). By two years of age, toddlers in the spectrum had clear problems in social communication, play, language and cognition, as well other sensory and motor difficulties (Zwaigenbaum et al, 2009). These findings confirm the notion that ASD can be identified earlier than usual in some cases and that for many children 24 months of age coincides with a peak in new symptoms that would facilitate recognition. The same authors reported (in an oral presentation at the 2011 IMFAR-San Diego) that 25% of the 277 siblings followed up in their study were diagnosed with ASD at 36 months of age, but cautioned that in 46% of those there had been no diagnosis assigned in their evaluation at 24 months of age. Therefore, at least in this probably non-representative sample, trajectories are quite different from what was considered retrospectively.

Relevant information to guide clinicians comes from the longitudinal research conducted by the First Words Project (Florida State University) that identified red flags for ASD, although they insist there is not a pathognomonic symptom that guarantees the presence of ASD. Not all children with ASD show all and every one of the symptoms all the time; and this should prevent clinicians from saying “this child does not have autism, because I saw him looking at the eyes of others” or similar. The First Words Project came up with nine red flags that helped
to distinguish children with ASD from children with developmental disabilities and typically developing children, and four red flags that distinguished children with ASD and developmental disabilities from children with typically developing children (Wetherby et al, 2004).

Many questionnaires have been developed as possible screening tools for developmental assessment of children as well as for ASD screening. Information, sound practical advice and a description of the most useful ones can be found in the ASD website of the US Centers for Disease Control and Prevention. Common myths shared by many professionals and policy-makers about developmental screening are summarized in Table C.2.2. A variety of practice flowcharts are also available, largely produced by national societies, but the one produced by the American Academy of Pediatrics represents the current gold standard for screening ASD in developed countries (Johnson & Mayers, 2007).

**Screening instruments**

Among the many instruments available (click here for an exhaustive list), there are currently two that merit special mention since they are free, tackle different age groups (one younger children and the other older ones), have gone through cross-cultural adaptation and appropriate translation to many languages, and have been researched in various countries. These are the Modified Checklist for Autism in Toddlers (M-CHAT) (Robins et al, 2001) and the Childhood Autism Spectrum Disorders Test (CAST) (formerly known as Childhood Asperger Syndrome Test).

The M-CHAT can be complemented with the M-CHAT Follow-Up Interview, also available at the M-CHAT website. It is recommended that M-CHAT
### Table C.2.2  Myths about developmental screening

<table>
<thead>
<tr>
<th>Myth #</th>
<th>Myth Description</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>“There are no adequate screening tools for preschoolers”</td>
<td>Although this may have been true decades ago, today sound screening measures exist. Many screening measures have sensitivities and specificities greater than 70%</td>
</tr>
<tr>
<td>#2</td>
<td>“A great deal of training is needed to administer screening correctly”</td>
<td>Training requirements are not extensive for most screening tools. Many can be administered by paraprofessionals</td>
</tr>
<tr>
<td>#3</td>
<td>“Screening takes a lot of time”</td>
<td>Many screening instruments take less than 15 minutes to administer, and some require only about 2 minutes of professional time</td>
</tr>
<tr>
<td>#4</td>
<td>“Tools that incorporate information from the parents are not valid”</td>
<td>Parents’ concerns are generally valid and are predictive of developmental delays. Research has shown that parental concerns detect 70% to 80% of children with disabilities</td>
</tr>
</tbody>
</table>

Source: CDC / Autism website

---

Users also incorporate the M-CHAT Follow-up Interview into the screening, given recent findings demonstrating that use of the interview greatly reduces false positive cases, avoiding unnecessary referrals. The CAST is also available free for non-commercial purposes and in many languages at the website of the Autism Research Centre of the University of Cambridge.

The American Academy of Pediatrics recommends screening for ASD of 18 and 24 months old children using a staged procedure (Johnson & Meyers, 2007). However, there are practical and ethical difficulties to do so and it is questionable if this screening should be routinely implemented worldwide. First, the psychometric properties of these instruments are not perfect. Some, like M-CHAT, identify a proportion of false positive cases that indeed do not have ASD. Health authorities may not consider this a problem since it detects children that require support for other conditions (e.g., developmental delays, speech problems). There are also false negatives: children having the condition who are not identified by the screening – there is no screening instrument with perfect sensitivity and specificity. Al-Qabandi et al (2011) challenge the belief that screening should be done because there is an effective treatment (e.g., early behavioral intervention) – although promising, treatments are not equally effective in all children with ASD and we are just beginning to understand who will be best served with what treatment but many questions remain. It is widely recognized that screening for a condition without having the resources or treatments (as it happens for ASDs in most regions of the world) may be unethical. In the same line, it is not clear whether young children with ASD are more easily recognized using universal screening instruments administered by professionals than, for example, through a culturally sensitive, community campaign. Despite all these controversies it is accepted that increasing information, educating families, teachers and medical staff to recognize ASD is a step forward.

---

There are practical and ethical difficulties in screening for ASDs and it is questionable whether screening should be routinely implemented worldwide.
The mechanisms to detect ASD are likely to be different for each country and region, depending on culture and child rearing practices, but mainly depending on the availability of developmental surveillance (not isolated “checking” for a specific condition). Most children in the world do not have access to well-baby programs and to developmental surveillance. Access to health should include empowering communities and health systems to identify the most prevalent disabilities in a given community. In developed countries these include intellectual disability, cerebral palsy, deafness, blindness, and ASD. In other parts of the planet, the priorities for surveillance might be very different. In summary, we propose that context-friendly developmental surveillance should be conducted for all children with administration of screening instruments to those suspected of having ASDs.

ETIOLOGY AND RISK FACTORS

In the US, in the 1950s and early 1960s, autism was thought to be due to the defective upbringing of children by cold and rejecting parents, thereby leaving the child with no alternative but to seek comfort in solitude, as once claimed by Bruno Bettelheim. He compared autism to being a prisoner in a concentration camp (something he had experienced himself in Germany during WWII) (Finn, 1997) in his book “The Empty Fortress: Infantile Autism and the Birth of the Self”. In 1964, Bernard Rimland opened the way for the current understanding of autism by introducing the notion that it was a disorder of brain development with his seminal book “Infantile Autism: The Syndrome and Its Implications for a Neural Theory of Behavior” (Rimland, 1964).

Genetic factors

Evidence for the importance of genetic factors in the etiology of autism comes from many sources, including twin and family studies (Muhle et al, 2004). Autism is, for example, 50 to 200 times more prevalent in siblings of autistic probands than in the general population. Among probands' relatives who do not
have autism, there is also an increased prevalence of milder forms of developmental
difficulties related to communication and social skills. Concordance rates for
autism range from 36% to 96% in monozygotic twins but only 0% to 27% in
dizygotic twins (Shaddock & Shaddock, 2008).

Although the heritability of autism has been estimated to be as high as 90%
(Freitag, 2007), genetic factors are heterogeneous, complex and for the most part
poorly understood. The precise mechanisms are being explored through whole-
genome screening, cytogenetics, and evaluation of candidate genes (Muhle et al,
2004). In studies of candidate genes, there are replicated findings of increased
risk for autism associated with variants in single genes on chromosomes 2, 3, 4,
6, 7, 10, 15, 17 and 22 (Freitag et al, 2010). Cytogenetic studies have implicated
abnormalities at the 15q 11-q 13 locus in individuals with autism (Muhle et al,
2004; Smalley, 1991). Genome-wide association studies have found slight effects
on autism risk with genetic variants at the 5p14.1 and 5p15 loci (Ma et al, 2009;
Weiss et al, 2009). Also, replicated copy number variations, found in genome-wide
association studies to be more common in individuals with autism than in controls,
are located on chromosome regions 1q21, 2p16.3, 3p25-26, 7q36.2, 15q11-13,
16p11.2 and 22q11.2 (Freitag at al, 2010). Future directions for genetic research
in autism lie in identifying specific gene-environment interactions.

**Neuroanatomic and neuroimaging findings**

Neuroanatomic and neuroimaging findings, though not diagnostic,
have consistently revealed increased cerebral volume that affects both gray and
white matter, as well as enlarged ventricles. Neuroimaging findings also include
abnormalities in brain chemistry, serotonin synthesis, and brain electrophysiology

The autism “spectrum” is now understood to be neurodevelopmental,
meaning that there are differences in the pattern of brain development. For
example, early brain overgrowth has been documented in the first two years of
life (Courchesne et al, 2001) and, in later development, there are clear differences
in the function and structure of the “empathy circuit” of the brain (amygdala,
ventromedial prefrontal cortex, temporo-parietal junction, orbitofrontal cortex,
anterior cingulate, and other related brain regions) (Lombardo et al, 2011). There
are also differences in connectivity between frontal and parietal lobe functions that
are thought to relate to cognitive style, in particular an over-reliance on processing
details and a relative under-reliance on processing gist or holistic information
(Belmonte et al, 2004).

**Environmental factors**

A number of environmental factors have been claimed, particularly in the
Internet, as playing a role in etiology of ASDs, including mercury, cadmium, nickel,
trichloroethylene, vinyl chloride (Kinney et al, 2010). It is important to note
that the previously suggested link between MMR vaccines and autism spectrum
disorders (Wakefield et al, 1998) had been debunked by international agencies
that included Centers for Disease Control and Prevention, Institute of Medicine
of the US National Academy of Sciences, the UK National Health Service and
suggested the association between the MMR vaccine and autism has since been
declared fraudulent and officially withdrawn (Goodlee et al, 2011).
Associations between different environmental factors contributing to vitamin D deficiency and increased risk of autism has also been proposed (Grant & Soles, 2009). This requires further studies.

**Epigenetic factors**

There are indications that, in addition to genetic and environmental factors, epigenetic factors also play some role through the fact that several genetic syndromes that are co-morbid with ASD show dysregulation of epigenetic marks that help regulate gene expression (Grafodatskaya et al, 2010). The epigenetic line of research also holds promise in offering an explanatory model to understand the putative increased incidence of autism suggested by epidemiological findings.

**Risk factors**

The NICE (2011) guideline “Autism: Recognition, Referral and Diagnosis of Children and Young People on the Autism Spectrum”, while stressing the low quality of evidence found, lists the risk factors for ASDs that are clinically and statistically important as:

- A sibling with autism
- A sibling with another ASD
- Parental history of schizophrenia-like psychosis
- Parental history of affective disorder
- Parental history of another mental or behavioral disorder
- Maternal age older than 40 years
- Paternal age between 40 and 49 (ASD)
- Paternal age older than 40 years (autism)
- Birth weight less than 2500 g
- Prematurity (under 35 weeks)
• Admission to a neonatal intensive care unit
• Presence of birth defects
• Male gender
• Threatened abortion at least 20 weeks
• Residing in a capital city
• Residing in suburb of a capital city.

In relation to medical conditions associated with ASD, with the same proviso of low quality of the evidence, the NICE guideline lists the prevalence of ASDs in several medical conditions (prevalence of ASDs between parentheses):

• Intellectual disability (8%-27.9%)
• Fragile X syndrome (24%-60%)
• Tuberous sclerosis (36%-79%)
• Neonatal encephalopathy/epileptic encephalopathy/infantile spasms (4%-14%)
• Cerebral palsy (15%)
• Down syndrome (6%-15%)
• Muscular dystrophy (3%-37%)
• Neurofibromatosis (4%-8%).

Neonatal physical illnesses such as post-encephalitic infections and sepsis had been documented to precede the onset of symptoms of ASDs, especially in sub-Saharan Africa. Autoimmune factors have also been claimed as a possible etiological factor in ASDs. This would result, if finally demonstrated, from reactions between maternal antibodies and the fetus (Bakare & Munir, 2011).

In summary, although heritability of autism has been estimated as extremely high, the challenges faced in understanding the etiology of autism lie in the observation that genetic factors are heterogeneous, complex, and the interaction between genes and environment are poorly understood. There are on-going and ambitious individual and familial longitudinal studies that promise to give us useful data in this regard.

Future directions for genetic research in autism lie in identifying specific gene-environment interactions. Research must overcome the challenges of elucidating the roles of genetic heterogeneity, epigenetic mechanisms and environmental modifiers. It is hoped that technological advances, combined with longitudinal projects, will help us understand in the near future the etiological complexities of these disorders and will advance specific ways to treat and to prevent them.

**CLINICAL ASPECTS**

**Qualitative impairments in social interaction**

Of the three core symptom domains that define autistic disorder, impairment in social interaction is central. This includes impairments in nonverbal behaviors used to regulate social interactions, failure to develop peer relationships appropriate to the child’s developmental level, and lack of spontaneous seeking to share enjoyment, interests or achievements with others (e.g., by a lack of showing, bringing or pointing objects of interest to the attention of others). Children with impairments in these areas lack social or emotional reciprocity.
Responding to joint attention and initiating joint attention is very important in social learning and is associated with language and cognitive development. Impairment in joint attention is a very important early symptom that can be seen even in very young children with autism.

Research on the theory of mind has shown that children’s ability to imitate others lies at the origin of understanding the perspective of others. Theory of mind enables one to have an idea of the mental state of others and, to some extent, predict their actions. This is also related to the ability to understand deception and other people’s emotions (empathy). Theory of mind impairments negatively affect pretend play, empathy, sharing, social and emotional reciprocity and peer
relationships. Theory of mind impairments can be seen in all individuals with ASD regardless of age and intelligence when mental-age-appropriate tests are used (Baron-Cohen, 2009). However, theory of mind deficits are not exclusive to ASD and can be seen in schizophrenia and in some personality disorders.

Another important concept is stimulus overselectivity: children with ASD exhibit overly selective attention. This is also not unique to ASD and can be seen in children with intellectual disabilities.

Stimulus overselectivity can be due to restricted attention or bias towards non global, local information. The latter has been described as the “weak central coherence theory” (Happe & Frith, 2006). The bias explanation allows individuals with ASD to have superior local information processing ability. Enhanced perceptual functioning theory (Mottron et al, 2006) posits that individuals with ASD have biased perception, which is more locally oriented; detail perception is enhanced and movement perception is reduced. Baron-Cohen and associates (2009) argue that sensory hypersensitivity leads to excellent attention to details and “hyper-systemizing” leads to law-based pattern recognition, which can produce talent.

Children with ASD use nonverbal behaviors such as eye contact, gestures, body postures and facial expressions less often than typically developing children. One of the most important findings in recent years has been the observation that two-year-olds with autism fail to orient towards biological motion – human bodies in motion (Klin et al, 2009) – and they do not preferentially look to the eyes of approaching adults (Jones et al, 2008).

Children with ASD show several atypical behaviors, probably due to sensory hypersensitivity, that can be observed in visual, auditory and tactile modalities and can be specific to certain stimuli (Baron-Cohen et al, 2009). Visual hypersensitivity may lead to lateral vision – staring at objects with pupils at the corner of the eyes (Mottron et al, 2006). Lateral vision has been interpreted as an attempt to limit excessive information or to focus on optimal information. Auditory and tactile hypersensitivities can be very stressful. On the other hand, sensory hypersensitivity may also lead to exceptional attention to detail.

Even high-functioning individuals with ASD may have problems in peer relations. While some of the subjects do not have any interest at all in relating to peers, others may have impairments in playing in different sides of a game (both seeking and hiding). Some children with ASD may want to have peer relations but they may have problems in interpreting other’s actions and responding accordingly. Many subjects with ASD do not have insight into the nature of social relations, particularly in their part and role in relationships. Many individuals with ASD may fail to develop empathy. All of these difficulties lead to impairments in social relations.

Qualitative impairments in communication

This core symptom domain includes delay in, or total lack of development of spoken language, which is not accompanied by compensatory attempts; marked impairment in the ability to initiate or sustain conversations; stereotyped, repetitive or idiosyncratic language; and lack of varied, spontaneous imitative or make-believe play. Language delays, lack of language, and peculiarities in spoken language are common in ASDs and they are often the parents’ initial concern.
The important distinction lies in the compensation attempts; children with other developmental and sensory disabilities usually use non-verbal means – such as gestures – for communication. In children with speech, functionality and social directedness of the speech is very important. Repetition of another person’s words, echolalia is frequent in ASDs. The rate, volume and intonation of speech can be abnormally high, low, fast, slow, jerky, monotonous, etc. Individuals with ASDs may invent their own words or phrases and language can be repetitive, may repeat the same phrases even when they are inappropriate to the context. Even high-
A typical child of 15 months uses speech-like sounds or babbling in a meaningful, interactive way. The same typical child at 22 months uses clear words to name animals while pointing to pictures in the book.

A child with ASD at 22 months has desire and shows effort to communicate with a lot of gestures and minimal vocalization, but he does not have words yet. The same child at 28 months is trying to imitate the words “more” and “open” verbally.

A child with ASD at 28 months produces unusual sounds for language. A child with ASD at 36 months has unusual sounds for language. It seems more like self-talk since she never looks at others.

Click on the picture to access the Autism Speaks website. This is an excellent resource documenting all the symptoms and signs. The facility is free; information cannot be downloaded but can be used online by professionals who want to show these symptoms (video clips) to families or in training sessions. The video clips contrast the behavior seen in children with ASDs with that of typically developing children. The Video Glossary was created by Amy M. Wetherby, PhD, director of the Florida State University Autism Institute and Nancy D. Wiseman, founder and president of First Signs®.
functioning individuals with ASD can have problems initiating and sustaining a conversation. This includes lack of small-talk, not providing enough information, not asking for information and not building on other people’s comments. When combined with restricted interests, conversation with persons with ASD can be very difficult to sustain.

Play can be functional or imaginative. Functional play is when toys are used as intended, for example using a toy fork as a fork or pressing the buttons of a cause-and-effect toy. Problems in make-believe and imitative play are apparent in many children with ASD. Typically developing children play with several materials in a flexible and creative way. For example, in typical make-believe play children can use a puppet as a general and a wooden block as the car of the enemy soldier (imaginative play). Everything can be used in an imaginative way.

**Repetitive, restricted, stereotyped patterns of behavior, activities and interests**

According to DSM-IV, this third core symptom domain includes preoccupation with stereotyped and restricted patterns, inflexible adherence to routines, stereotyped and repetitive motor mannerisms, and persistent preoccupation with parts of objects. It has been suggested that this domain is very broad and contains at least two subtypes of behaviors: (a) repetitive sensory motor behaviors (lower-order) and insistence on sameness – and possibly circumscribed interests – (higher-order). Repetitive sensory motor behaviors are more frequently seen in young children and are associated with lower non-verbal intelligence.

Many individuals show strong interests in some topics; they read extensively about them, collect items related to them, can talk on that subject for hours, and may proceed as young adults to join interest groups or societies dedicated to their interest. The difference between these normal behaviors and those of individuals with ASD can be explained in terms of narrowness of the focus, inflexibility, perseveration and lack of social quality. Individuals with ASD can focus on a very specific part of the object of their interest; for example, only the number of teeth in dinosaurs. They can have problems in switching to other topics even when other people are clearly not interested in what they are talking about. They keep focusing on the topic when they are supposed to do other tasks and may become distressed or even agitated when they are interrupted. They may show less interest in sharing their hobby in social ways, like joining a club.

Inflexible adherence to specific, non-functional routines or rituals is also a typical symptom of ASDs. Difficulties with minor changes in personal routine and resistance to even small changes in the environment can cause significant problems in their and their families’ daily lives.

Stereotyped and repetitive motor mannerisms and persistent preoccupation with parts of objects may be more evident in younger children and individuals with intellectual disability. These include hand and finger flicking, mannerisms, rocking, toe walking, sniffing and licking non-food objects, spinning, and unusual visual gaze, among others. Persistent preoccupation with parts of objects can be seen, for example spinning wheels, flickering the eyes of dolls, among others.

Stereotyped behaviors can be observed in several other conditions including Tourette’s Disorder, Fragile X syndrome, Rett’s disorder, obsessive compulsive disorder, deafness, blindness, schizophrenia and a variety of intellectual disabilities.
A typical child at 20 months engages in make-believe play by offering “coffee” to everyone and scooping food for Big Bird and himself. A child with ASD at 20 months does not engage in make-believe play but instead explores objects by turning them over and rolling them.

A typical child at 15 months engages in make-believe play by hugging and feeding Big Bird with the bottle, and stirring, pouring, and blowing on food. He shifts his focus from one toy to another and from the toy to people. A child with ASD at 16 months does not engage in make-believe play but instead is very focused on wobbling the bowl and cup.

A child with ASD at 5 years zeroes in on (and gets stuck on) a ball that looks like a globe. He has been intensely interested in planets for a few years, so he was particularly drawn to the ball, to the exclusion of all the other toys. Same child with ASD at 5 years gets stuck on the camera. He has shown an interest in the camera and other mechanical or electronic things for a few years.

Click on the picture to access Autism Europe’s “Persons with Autism Spectrum Disorders: Identification, Understanding, Intervention”
without ASD. It seems that the frequency but not the pattern – which is related to
the developmental level – of the behavior is what is distinctive for ASDs (Bodfish
et al, 2000).

**DIAGNOSIS**

There is a wide agreement that, once the presence of ASD is suspected, the
child should be referred for a multi-disciplinary assessment in which all members
of the team should have some ASD training and at least one member should be
trained in the assessment and diagnosis of ASD using standardized instruments.
Also, it is recommended that the child should be ideally observed in several
different settings, both structured and unstructured. It needs to be recognized,
however, that the vast majority of child and adolescent mental health services
worldwide do not have the state-of-the-art instruments used in specialized clinics in
wealthy countries such as the Autism Diagnosis Observation Schedule, the Autism
Diagnostic Interview, the Diagnostic Interview for Social and Communication
Disorder or the Developmental, Dimensional and Diagnostic Interview. This
highlights the need for dissemination, training and development of multi-cultural,
multi-language, cheap, reality-oriented, user-friendly, instruments.

The NICE guideline is freely available and considers all the aspects of
the ASD-specific diagnostic assessment, provides recommendations about its
core elements, autism-specific diagnostic tools and how best to communicate to
parents a diagnosis of autism for their child. In summary, the NICE guideline
reiterates what has been established in other guidelines including a detailed
enquiry into the specific concerns raised by family and teachers; medical history;
home life, education and social care; and history and observation focusing on the
developmental and behavioral features specified ICD-10 and DSM-IV. This core
information is usually sufficient to establish a diagnosis of autism when diagnosis
is straightforward. Beyond the diagnosis of ASD, a diagnostic assessment should
also include a profile of strengths, needs, skills and impairments. The instruments
needed for this will depend on the age of the patient and the developmental level,
but should be instrumental in helping to identify:

- Intellectual ability and learning style
- Academic skills
- Speech language and communication skills
- Fine and gross motor skills
- Adaptive (including self-help) skills
- Socialization skills
- Mental and emotional health including self-esteem, physical health
  and nutrition
- Sensory hyper- and hypo-sensitivities
- Behavior likely to affect participation in life experiences, future support
  and management.

**Physical examination**

A comprehensive physical examination should also be undertaken. Findings
from the physical examination may be useful to detect coexisting conditions or
symptoms of disorders that may have a causative role or increase the suspicion
of an ASD. Particular attention should be given to identifying skin stigmata of
neurofibromatosis and tuberous sclerosis, as well as congenital abnormalities and dysmorphic features including micro and macrocephaly. The examination should also look for signs of physical injury, such as self-harm or maltreatment.

**Differential diagnosis**

Autistic disorder, when presenting in its full typical form, is not difficult to recognize by a professional with experience. However, clinicians should rule out medical, genetic, neurological or sensory dysfunctions or disorders. The situation is different for clinical pictures that do not fit the traditional descriptions of the disorder, which are becoming more frequent due to the widening of the construct into the autistic spectrum and this can lead to diagnostic disagreements.

**Infants and toddlers**

Differential diagnosis at this age should rule out disorders that interfere with normal development of language and social skills:

- *Hearing loss* can be suspected if the child has lost his babbling, shows poor vocalizations or indifference to auditory stimuli. Routine exam in very young children who cannot be expected to cooperate include otoacoustic emissions and impedance audiometry. If they are normal, there is no need for further testing. If they are abnormal, the external ear should be examined and both tests should be repeated in two-three months. If the results are again abnormal, auditory evoked potentials should be studied.

- *Severe psycho-social deprivation*. It is well known that severe emotional deprivation in childhood leads to serious psychological impairments including pseudo-autistic clinical pictures (Rutter et al., 1999). The autistic-like symptoms in these cases usually consist of a relative indifference to the environment, communications delay, restricted interests and repetitive behaviors. Unlike in autism, social reciprocity is not completely abnormal – although bonding may be affected – and deficits can be reversed quickly in the majority of cases if environment improves.

- *Intellectual disability* (formerly known as mental retardation). It is often a difficult diagnosis to exclude in the early years of life because evaluation of cognitive functioning is more difficult (see Chapter C.1). Some symptoms (e.g., facial dysmorphia, microcephaly) may suggest the existence of genetic or neurological problems known to cause intellectual disability may be suspected. It is also documented that severity of intellectual disability is positively correlated with social interaction deficits (Wing & Gould, 1979). Therefore, attributing communication and socialization defects, self-injurious or stereotypic behaviors to autism or severe intellectual disability can be challenging. This can be provisionally solved if there is evidence of an abnormal development in social, communication and imaginative skills discordant with the general level of intelligence (very difficult to clarify when mental age is below 18 months). It is important here to highlight that the association of AUDs and intellectual disability is very common and that many known causes of intellectual disability, such as...
chromosomal abnormalities often present with autistic symptoms (e.g., Fragile X syndrome, Prader-Willi syndrome) (see Chapter C.1).

- **Rett’s disorder.** DSM-IV includes this condition among the pervasive developmental disorders. However, DSM-5 proposes not to include Rett’s disorder because although patients often have autistic symptoms they are apparent only for a brief period during early childhood, so inclusion in the autism spectrum is not appropriate for most individuals. Rett’s disorder is an X-linked neurodevelopmental disorder that affects girls almost exclusively. Typically, there is normal development until 6–18 months of age, then development stops and a regression appears (loss of speech and of purposeful hand use) with specific hand stereotypies and social withdrawal, which mimic an autistic picture. Besides, there is a deceleration in head growth leading to acquired microcephaly and seizures may appear. Research has led to identification of a gene (MECP2) on the X chromosome (explaining the higher frequency in girls, but some male cases have been reported) (Amir et al, 1999).

- **Receptive-expressive language disorders.** Expressive language disorder is very common in children and usually consists in a simple delay in mastering phonology, lexicon and syntax that looks very selective in the context of a typical development of social skills, non verbal communication, cognitive skills and imagination. The situation is more challenging in a minority of non-autistic children of normal non-verbal intelligence who have severe receptive-expressive language impairment. This situation has been described as “semantic-pragmatic disorder” with problems in the social communication aspects of conversational interchange, including echolalia. However, unusual preoccupations and rituals are much less common than in autism. It is of note that this disorder is not included in DSM-IV or ICD-10,

- **Landau–Kleffner syndrome.** Acquired aphasia with epilepsy or Landau–Kleffner syndrome is characterized by a normal development until age three to four followed by a massive regression of receptive and later expressive language, typically in conjunction with the development of seizures or sleep electroencephalogram abnormalities. The regression may be associated with transient social withdrawal but a complete autistic picture is not observed. There is a sub-type of pervasive developmental disorder, childhood disintegrative disorder, where regression is evident, but the regression occurs earlier (18 to 24 months of age).

- **Selective mutism and separation anxiety.** Withdrawal, anxiety and communication problems are common. However, it can be easily distinguished from autism because of the existence of normal communication and social skills at home or in other familiar environments.

**Older children**

Differential diagnosis in typical autistic presentations is easier in older children, but it can be difficult in cases within the broader phenotype: cases in the “periphery” of the spectrum, especially in high functioning children or cases with
a partial disorder. An accurate medical history, establishing the onset of symptoms before or after the age of three years, is often an important indicator.

Clinicians should consider childhood schizophrenia (see Chapter H.5). The potential confusion between this rare condition and ASD may arise from poor expression of emotions and negativism. However, hallucinations and delusions are specific to schizophrenia. Furthermore, most children with early onset schizophrenia do not show the language delay or abnormalities and the social deficits that are typical of ASDs.

Other psychiatric conditions to be excluded are attention deficit hyperactivity disorder especially as both can coexist, and obsessive compulsive disorder because of the rituals and selected interests, but the differential diagnosis can easily be made on the bases of the history and the global clinical presentation. It is of interest to highlight that some authors refer to a disorder not included in the current classifications: multiple complex developmental disorder (Towbin et al, 1993), which consists of impaired regulation of affective state, with primitive anxieties, impaired social reciprocity and thought disorders, but failing to meet criteria for ASDs.

**PROGNOSIS AND ADULT OUTCOMES**

ASDs are disorders that start in infancy; therefore, significant changes occur with development that will impact adult outcome. These changes should not be overlooked and require on-going monitoring and individualized adaptation to optimize support programs. Baghdadli et al (2007) have stressed the high variability in short-term outcomes of preschoolers, emphasizing the importance of considering individual characteristics and adaptive strategies. They suggest that these differences may be due to certain initial characteristics like speaking skills and severity of autistic symptoms.

The more severe the comorbid intellectual disability the poorer is the outcome. It is generally accepted that speech before the age of six and a higher IQ are associated with a better outcomes (Billstedt et al, 2011). However, there is limited research data about the whole spectrum across the life cycle. Therefore,
Clinicians must be cautious when predicting the distant future of their patients. ASDs are lifetime disorders and cannot be cured. Nevertheless, disability depends not only on the characteristics of the individual but also on the environment that is offered to that person, adapted or not, to minimize the disabilities.

In this regard, uncertainty comes from three sources. First, little research has been done about the role played by the supports provided. Second, there is a younger and less severely affected group of individuals now diagnosed with ASDs in industrialized countries; their prognosis and response to treatment may be better than traditionally expected. Finally, there is limited epidemiological data on adults, particularly those with Asperger’s disorder. Marriage and Wolverton (2009) showed that despite adequate academic achievement, work, living and mental health status can be poor in this population. Lehnardt et al (2011) estimate that the lifetime rate of psychiatric consultations for this group can be as high as 78%.

Overall, it can be said that the vast majority of children with ASD will continue to show deviance and difficulties in social interactions throughout their lives. It should be assumed that they will need support and help in many areas. However, their quality of life can be improved when adequate programs are available in their communities. Community based programs should be adapted to each individual, taking into consideration areas of difficulty and strengths, as well as the resources that the community has to offer. People with autism will need structure, clarity and predictability throughout their lives.

Behavior and adaptive skills tend to improve with age. Nordin and Gillberg (1998) found that measures of flexibility and cognitive shifting abilities tend to be predictors of good social outcome. Unfortunately, more research is needed on the adult population, so programs may be adequately tailored to meet their needs as well as supporting transition into adulthood.

Prognosis should be discussed with the family to avoid unrealistic expectations and focus all efforts on early intervention and fostering family involvement and knowledge, as well as community participation. It is important to underline that current efforts in treatments and creation of services (nonexistent in most countries), will shape the future functioning of the children diagnosed and treated now, as they grow and become adults.

TREATMENTS

Treatment of ASDs depends on factors that make description of “the treatment” inadequate. Differences in age, degree of impairment, comorbid disorders, family and social situation, level of resources and community development, provision of education (or lack of it), health and welfare assistance, opportunities for sheltered employment and availability for inclusive living in the community in adult life will make a huge difference. If there are two words that would underline what should be done for ASDs, those two concepts would be “to personalize” and “to contextualize”.

Despite accepting these commonsense ideas, there is a tendency to search for a “cure” for ASD, as if there was a single cause, a unique mechanism and a single condition underlying the syndrome that, if identified, would lead to cure for all the ASDs. The Internet allows families and professionals to hear about many “treatments” — some based on current knowledge but others based on sheer
superstition or false beliefs – that most people feel confused about what to do. The worst aspect is that families (and professionals) feel that there is something else they should be doing and by not doing it, they are not providing the best treatment for the person with ASD. In the same line, very often there is a disregard for local limitations and possibilities. Thus, programs developed over the years in wealthy countries are copied or applied in completely different areas of the world without regard for the local circumstances, opportunities and feasibility of future maintenance.

While there is no cure for ASDs, there is strong evidence that appropriate, lifelong educational approaches, support for families and professionals, and provision of high quality community services can dramatically improve the lives of persons with ASD and their families. There are up to date practice guidelines in many countries such as Spain and the UK, which have reviewed the available evidence for a great variety of treatments advocated for ASD. The UK departments for Education and Skills and for Health have also produced guidance for the education of students with ASDs. Much has been learned about the practices

### Table C.2.3  Treatments for autism spectrum disorders, evidence supporting their effectiveness and recommendation about their use

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Intervention</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| Not supported by evidence            | • Doman-Delacato therapy  
• Irlen lenses                  
• Facilitated communication      
• Psychodynamic psychotherapy     
• Secretine                          
• Antimycotic therapy           
• Chelation                           
• Immunotherapy                     
• Craniosacral therapy            
• Animal assisted therapies    | Not recommended                                                                 |
| Weakly supported by evidence         | • Auditory integration            
• Sensory integration             
• Expressive psychotherapies (art and music) 
• Vitamins and dietetic supplements 
• Gluten and/or casein free diets | Recommended only in controlled research studies |
| Supported by evidence                | • Behavioral interventions      
• Risperidone (for comorbid severe irritability or challenging behaviors) | Recommended                                                                 |

that are supported by evidence and those that are not, and about which programs make a real difference to the lives of individuals with ASD. Unfortunately, this knowledge has not yet been incorporated into clinical practice around the world, even in more affluent societies. Thus, there remains a gap between knowledge and opportunity; it is evident that very few people with ASDs receive state-of-the-art support.

Recent reviews of the evidence conclude that relatively few treatments meet the necessary criteria when assessing the value of interventions. Nevertheless, evidence is improving, with growing numbers of well-conducted studies. Randomized control trials are also increasing in number. However, even when outcome is positive, most research still focuses on very short-term goals and on a limited number of outcome measures. There is little attempt to address questions such as whether treatment succeeds in maximizing the long-term potential of the individuals involved or if it truly improves their quality of life. Such issues may require very different research strategies such as audits and reviews, systematic analysis of problems, and measures of satisfaction. It is also crucial to collect the views of individuals with ASD themselves.

To date, programs involving behaviorally based interventions, those designed to improve parent-child interaction, and those with an emphasis on developing social and communication skills appear to have the strongest supporting evidence, at least in the short term. As Autism Europe states, there are many other elements that are essential to improve longer-term outcome:

- **Education**, as early as possible, with special attention to social, communication, academic and behavioral development, provided in the least restrictive environment by staff who have knowledge and understanding of both autism and the individual student.
- **Accessible community support** in terms of appropriate, well-informed, multi-agency services that will help each individual to realize their potential and life-time goals (either chosen by the individuals themselves, or those who know, love and legally represent them).
- **Access to the full range of psychological and medical treatments** (adapted as necessary to meet the needs of individuals with ASD) that are available to the general population.

According to Autism Europe, interventions that are best supported by evidence as examples of good practice include four principles:

- **Individualization**. There is not a single treatment that is equally effective for all persons with ASD. Diversity in the manifestations of this spectrum as well as individual skills, interests, life vision and circumstances mandate personalization.
- **Structure**. That is, adapting the environment to maximize each individual's participation by offering varying degrees of predictability and stability, more effective means of communication, establishing clear short and long-term goals, defining the ways in which these goals can be met and monitoring outcomes.
- **Intensity and generalization**. The interventions used should not be sporadic or short term, but applied in a systematic manner on a daily basis, across different settings, and by all those living and working...
with the person with autism. This will ensure that the skills acquired in more structured settings can be maintained in real life situations as well. Those responsible for carrying out the intervention should also have access to appropriate support and guidance from professionals with expertise in ASDs.

- **Family participation.** Throughout childhood and beyond, parents must be recognized and valued as the key elements of any intervention. Information, training and support, always within the context of family values and culture, should be the common denominator of any professional intervention. Other important sources of support, such as babysitting, respite care, short breaks, or tax benefits should be available to avoid the discrimination that many of these families still face. Adequate support for social, medical and educational services is necessary to ensure that these families are able to enjoy the same quality of life as everyone else.

Globally, given that the vast majority of people with ASDs are not receiving specialized treatment – more often than not, they are not receiving what could be considered adequate generic treatment – child mental health professionals should be devoting their efforts to the development of resources in the community where they practice and to support these children’s families. Regardless of their age, most people with ASDs around the world live with their families. It is of these families that one needs to ask how they want to be supported, what are their priorities, what are their dreams, what life project they would like for their child. The person with ASD should participate in this dialogue, directly or helped through interpersonal support and augmentative communication means; in the minority (at least 25%) that cannot express themselves at all, by delegation from people who know them well. Families are the essential support networks that cannot be replaced by governments. Their role should be gratefully recognized, our task being to maximize their potential in their own terms. We are talking not only about a health goal but also about fighting ignorance and discrimination.

Clay art by Santiago, an 11 year old with autism spectrum disorder. Photo: Lynn Albrink
REFERENCES


Autism spectrum disorders


