Review Article

Autism Spectrum Disorders in Infancy and Toddlerhood: A Review of the Evidence on Early Signs, Early Identification Tools, and Early Diagnosis

Josephine Barbaro, BBSc (Hons), Cheryl Dissanayake, PhD

ABSTRACT: To date, the biological basis of autism spectrum disorders (ASDs) remains unknown. Thus, identification and diagnosis are reliant on behavioral presentation and developmental history. There have been significant advances in our knowledge of the early signs of ASD through the use of retrospective videotape analysis, parental report, screening studies, and more recently, studies on high-risk infant siblings. Despite behavioral markers being identified within the first year of life, the current average age of diagnosis for ASD remains at approximately 3 years or older. Consequently, these children are not receiving intervention in their early years, which is increasingly recognized as an important time to begin intervention. There remains little research on the prospective identification of these children in a community-based sample before 18 months. It is recommended that future prospective studies monitor behavior repeatedly over time, thereby increasing the opportunity to identify early manifestations of ASD and facilitating the charting of subtle behavioral changes that occur in the development of infants and toddlers with ASD.

*(J Dev Behav Pediatr 30:*447–459, 2009) **Index terms:** autism spectrum disorder, autistic disorder, infancy, early identification, early diagnosis, screening tools.

The last decade has seen significant advances in our scientific knowledge about the early signs vastly precedes spectrum disorders (ASDs), beginning with the use of standard practice, with the average age of diagnosis still retrospective home videotapes for the purpose of exam- at approximately 3 years. Thus, the purpose of this ining behavioral features in infants who later received a article is to bring together recent advances in the field, diagnosis of an ASD (Unless otherwise stated, ASD will including recent research involving "high-risk" infants, be used throughout the review to refer to autistic to inform practitioners about the very early signs of disorder, Asperger's disorder, and pervasive develop- ASDs, as well as the instruments used to identify these mental disorder-not otherwise specified). This increas- signs, consequently informing their current practice. ing knowledge of the early ASD phenotype has led to Together, this body of work will be reviewed with the attempts to prospectively identify ASDs in infancy and ultimate aim of reducing the age at which ASDs are diag- toddlerhood. Importantly, prospective studies allow the nosed. Early identification and diagnosis provide the best researcher to elicit behaviors at a specific age, rather opportunity for early intervention, which can prevent than relying on spontaneous presentation on videotape ASDs from becoming fully manifest in the developing child, or retrospective parental report. More recently, prospec- thereby serving to maximize developmental outcomes.[1,2] tive studies of infant siblings of children with an ASD have also contributed to increased knowledge of the early phenotype.

Despite the unquestioned neurobiological basis of ASDs, limited knowledge regarding the underlying neuropathology for these related conditions has meant that diagnosis is reliant on behavioral presentation and developmental history. Although there is now increasing em- pirical information on the very early developmental his-

Age of Onset/Recognition of Symptoms

Although the DSM-IV-TR[3] and the International Clas- sification of Diseases-10[4] state that the onset of impair- ment

in autistic disorder must be before 36 months, a large proportion of children manifest developmental problems between 12 and 24 months,[5–7] with some showing abnormalities before 12 months.[8–15]
Neither the DSM-IV-TR[3] nor the International Classifi- cation of Diseases-10[4] specify an age of onset criterion
From the Olga Tennison Autism Research Centre, School of Psychological Sci-
for Asperger's disorder. However, onset in Asperger's ence, La Trobe University, Bundoora, Victoria, Australia.
disorder is usually reported to be later than in autistic Address for reprints: Cheryl Dissanayake, PhD, Olga Tennison Autism Research
disorder because these children develop language at an Centre, School of Psychological Science, La Trobe University, Bundoora, Victoria
3086, Australia; e-mail: c.dissanayake@latrobe.edu.au.

appropriate age and display less severe symptoms. As there are fewer symptoms to alert parents and profes- sionals that development is impaired, Asperger's disorder

not is typically not identified before children becoming part
the act of requesting attention. Clifford et al[25] also of a preschool or school setting (i.e., usually after 4
found a lack of protodeclarative showing in children years[16,17]). Nonetheless, it is possible to identify some
with autistic disorder compared with TD and develop- (albeit a very small percentage) children with Asperger's
mentally delayed infants. disorder before 36 months.[18,19] Thus, it is the recogni-
Although the use of retrospective home videotapes is tion of impairments in Asperger's disorder, and not on-
an effective means of charting the very early develop- set, which occurs later than 36 months.
ment of children with an ASD, there are limitations to Individuals with pervasive developmental disorder-
this methodology. First, the behaviors observed are con- not otherwise specified, by definition, do not need to
strained to selective and less naturalistic representations have an onset of impairment before 36 months.[3,4] How-
of the child's behavior because the videotapes are usu- ever, this is not typical of most individuals with perva-
ally of the child's birthday party or a family event and not sive developmental disorder-not otherwise specified.[20]
of undesirable or unpredictable situations. Furthermore, it

INFANT SIGNS OF AUTISM SPECTRUM DISORDERS: REVIEW OF THE RETROSPECTIVE LITERATURE

is not possible to elicit a desired behavior, such as response to a social smile, thus limiting observations to behaviors spontaneously demonstrated in the situation.[11]

Retrospective Videotape Analyses

Retrospective Parental Reports

Adrien et al[8–10] were the first researchers to use home
Retrospective parental reports have long been used as videotapes to assess the behaviors of children with and
a source of information about the development of ASDs without an autism spectrum disorder (ASD) before and
in infancy. Vostanis et al[26] requested the parents of after their first birthday. Using the Infant Behavioral
children with an ASD, learning disabilities, and language Summarized Evaluation Scale, the key behaviors that
disorders to complete a questionnaire about their child's differentiated the groups were in the areas of socializa-
development between 12 and 18 months. The children tion (ignores people, prefers aloneness, poor social in-
with an ASD were rated significantly lower on items teraction, and no eye contact) and communication (lack
involving social attention and communication, including of vocal communication, lack of appropriate facial ex-
imitation, pointing at objects, playing peek-a-boo, seek- pressions, no social smile, lack of gestures, no or poor
ing and enjoying cuddles, checking for their parents, imitation of others).
interest in other children, and waving bye-bye without In their study of first birthday videotapes, Osterling
being asked. and Dawson[12] found that 4 behaviors correctly differen-
Young et al[27] asked 153 parents of children with an tiated 90% of their sample of children later diagnosed
ASD to complete a questionnaire concerning their child's with an ASD from those without an ASD. These were a
very early development and the age of onset of problem- low frequency of looking at others (including eye con-

atic behaviors. Parents were primarily concerned about tact) and orienting to name call, an absence of showing their child's difficulties in social awareness and under- objects, and a lack of pointing. These findings were later standing, lack of shared enjoyment in interaction, and replicated.[13,21] A deficit in orientating to name call has poor eye contact. Little interest in other children and consistently been found to differentiate children with lack of social referencing (joint attention behaviors) and without an ASD as early as 8 months, in both retro- were also reported, with 95% of parents indicating that spective and prospective studies.[11,15,22] Interestingly, Os- these behaviors occurred before the age of 2 years. terling et al[115] found that while 12-month-old children The Early Development Interview was recently devel- with an ASD and associated intellectual disability oriented oped to chart the development of children with an ASD to their names and looked at others less frequently than from birth to 2 years.[23,28] The parents of young children infants with only an intellectual disability, both groups with an ASD, developmental delay, and TD children engaged in repetitive motor actions more frequently when were interviewed with the Early Development Interview compared with typically developing (TD) infants. Thus, regarding various behaviors including social attention repetitive and stereotyped behaviors may not be specific to and communication behaviors. The children with an ASDs, but associated with intellectual disability; the find- ASD were reported to have more social deficits than TD ings suggest that social attention and communication be- children from as early as 3 to 6 months, and more deficits haviors are better early indicators of ASDs.[23] than children with developmental delay at 13 to 15 Observations of home videotapes by Clifford and Dis- months. Consistent with the retrospective videotape sanayake[24] revealed that infants later diagnosed with an studies, these deficits included poor eye contact, failure ASD showed deficits in social smiling and eye contact as to orient to their name, deficits in the use of joint early as 6 months compared with infants without an attention, and little engagement in social interaction. ASD. In toddlerhood, affected children showed deficits Werner and Dawson[23] concluded that social behaviors in initiating and responding to joint attention behaviors. were the best indicators of diagnostic differences be- They found that requesting behaviors were less problem- tween children with an ASD and TD children, as well as atic, indicating that it is the sharing quality of joint between children with an ASD and developmental delay, attention behaviors that is deficient in these children and albeit at a later age.

the Baranek and coworkers[29,30,31] developed a parental literature is showing that signs of ASDs are present in questionnaire that focuses on the behavior of children at the first year of life, the mean ages for diagnosis are still risk for ASDs before 12 months, called the First Year very high, especially for ASDs other than AD. There are Inventory. To examine the construct validity of the First a number of reasons for the late diagnosis of ASDs de- Year Inventory, Watson et al[31] developed a retrospective spite their early behavioral manifestations. version and gave this to parents of preschoolers with an ASD, developmental disability, and TD children. The

Current Diagnostic Criteria

items that were most useful in distinguishing between A significant limitation to an early diagnosis is the fact ASDs and developmental disability were orienting to that many of the characteristic behaviors currently used name call, following a point, social orienting, interest in in diagnosis of ASDs, based on the DSM-IV-TR[3] and the their age, social smiling, facial expression, playing peek- International Classification of Diseases-10[4] criteria, are a-boo, and demanding attention of the caregiver. Items not apparent before 36 months. These criteria are based on imitation, expressive communication, sensory pro- on symptoms that are rarely seen in infants and toddlers cessing, regulatory patterns, reactivity, and repetitive with ASDs but are common in older children and behaviors generally differentiated children with an ASD adults.[42,43] For example, difficulties socializing with peers and developmental disability from TD children but were and deficits in language skills are symptoms that develop not good at distinguishing the former groups. Thus, once later in childhood and are thus not easily observed in again, the items that best distinguish children with and infancy.[14] Some of the behaviors may also be secondary, without an ASD are located in the realm of social atten- developing to compensate for the primary "core" defi- tion and communication.

cits of ASDs, which are those that are seen early in the development of the disorder.[44,45]

In addition, the DSM-IV-TR[3] and International Classification of Diseases-10[4] require a presence of repetitive behaviors, interests, stereotypies, or rituals to diagnose an ASD. This is problematic when attempting to diagnose very young children because these behaviors are present in only a minority of children before 18 months and tend to develop, or become more apparent, at approximately 3 to 4 years.[42,45–47] Therefore, the absence of these behaviors in infants and toddlers with social communication impairments does not exclude the possibility of an ASD.[42] However, more recently, data suggest that repetitive and stereotyped movements can distinguish between children with an ASD and those with delayed or typical development late in the second year of life.[48] The focus on behaviors evident later in development means that the diagnosis of infants and toddlers is delayed. To promote early diagnosis, the criteria in current diagnostic manuals require modification to reflect those behaviors that are present in the infancy period.[49]

Late Onset/Regression

Although most children with an ASD show problems before 12 months, there is a cohort of children who appear to develop typically in the first 15 to 21 months of life. These infants reach appropriate language and social skill milestones, but then progressively "lose" these skills, with the majority losing skills between the ages of 13 and 18 months.[23,50–54] This "regression" occurs in approximately 20% of children with an ASD, although this figure has been reported to be as high as 49%.[51,55–58] The differing percentages may be an outcome of the diagnostic status of the child, with a recent report[54] charting the incidence of regression to be highest in those with a diagnosis of AD (as opposed to AspD and pervasive developmental disorder-not otherwise specified). The most frequently reported skill loss is language, followed by social skills.[50,55,58] However, it should be noted that most cases of regression do not involve completely normal development before regression,[23,59,60] with some children having lower language abilities than their typically developing peers before regression.[58,61] Nonetheless, the existence of regression in a subset of children with ASDs means that professionals must remain cognizant of this group of children. If this period of regression remains unrecognized, diagnoses may

AGE OF DIAGNOSIS

A limitation of parental report studies is that parents' responses are vulnerable to incorrect memory recall, recall biases, and distortion of events.[32] Furthermore, various factors, including parental alertness in recognizing behavior, socioeconomic status, personality, intelligence, and parental mental health can influence their responses, reducing reliability of the data.[33] However, it is worth noting that the findings from the parent report studies do largely concur with the findings from the videotape studies.[24]

In addition to the behavioral signs identified by retrospective studies, more recently, biological markers, namely enlarged head circumference, have been investigated as possible signs of ASDs. Although head circumference size is normal or near normal at birth, subsequent accelerated head growth during the first 2 years of life leads to approximately 20% of children with an ASD having a head circumference above the 97th percentile.[34–36] Used together with social attention and communication behaviors, head circumference data may be a useful accompaniment when determining the diagnostic status of a child. However, this information must be used with caution as no prospective data have yet been collected to show whether atypical head growth in very early infancy can predict a diagnosis of an ASD.[36]

IMPORTANCE OF EARLY DETECTION AND DIAGNOSIS

Despite the accumulating evidence that signs of autism spectrum disorders (ASDs) are present in early infancy, the interval between many parents' first concerns and a definitive diagnosis is approximately 3 to 4 years.[37] This interval increases to as high as 9 years for those diagnosed with Asperger's disorder (AspD).[27,38–41] Reductions in the early identification field have lowered the average age of diagnosis for the United States being 3.1 years for autistic disorder (AD), 3.9 years for pervasive developmental disorder-not otherwise specified, and 7.2 years for AspD.[37] However, given that some children having lower language abilities than their typically developing peers before regression.[58,61] Nonetheless, the existence of regression in a subset of children with ASDs means that professionals must remain cognizant of this group of children. If this period of regression remains unrecognized, diagnoses may

be un- necessarily delayed.

Early identification of the signs of autism spectrum disorders (ASDs) is the first step to facilitating early referral and diagnosis. Early diagnosis provides the best opportunity for early intervention, which serves to max- imize developmental outcomes for affected children and their families. It is widely recognized that the earlier intervention begins in child's development, the better

Language Development

It is usually the absence of typically developing lan- guage, which becomes evident at about 2 years, that leads to children being referred and diagnosed with an ASD.[62] Delay in language development is one of the first and most frequently expressed concerns of parents of children later diagnosed with an ASD.[5,27,40] It is thus not surprising that delays in referral are seen when a child is verbal and are exacerbated when the child does not have associated intellectual disability. These children usually receive a diagnosis of AspD, which, as previously men- tioned, is diagnosed much later than AD.[16,17] Indeed, Mandell et al[37] found that children with severe language deficits received a diagnosis of an ASD 1.2 years earlier than children with less severe language deficits.

the opportunities to move the young child toward a more typical developmental trajectory because of the plasticity of the young brain.[1,69] However, few studies have investigated the efficacy of intervention before 2 years, and there continues to be a need for more ran- domized controlled trial studies in this area.[1,70,71] De- spite this, the results from these few studies, including those that use case reports and single-subject designs, are promising.[1,71–78]

Importantly, the onset of secondary (compensatory) behaviors may be prevented, or at least minimized, with early intervention.[27,45] Furthermore, if a child is referred before a "drop off" in language and social skills, the impact of early intervention is even greater, as it may prevent some of these losses.[1] Mundy and Crowson[79] proposed a "cybernetic model" of ASDs, whereby an

Knowledge of Infant Symptoms

Most general practitioners and pediatricians do not have specialized skills or training regarding ASDs in in- fancy.[38] Consequently, they do not possess sufficient clinical expertise to identify the subtle symptoms of ASDs in infancy and often attribute any abnormalities to general developmental problems.[5] Too often, parents are reassured by their physician and told "not to worry," and that "they'll grow out of it." Howlin and Asgharian,[40] studying more than 770 families in the United Kingdom, found that over a quarter of parents of children with AD and a third of parents of children with AspD were reas- sured that their child was developing normally. The average age of the children with AD when parents first sought help was 2 years, and with AspD, 3.5 years; however, on average, a diagnosis was given at 5.5 years for the children with AD and 11 years of age for the children with AspD.

What is most concerning is the lack of familiarity among practitioners with the tools to identify ASDs. Wiggins et al[63] found that 70% of practitioners do not use a diagnostic instrument when assessing for an ASD. Fur- thermore, Dosreis et al[64] found that 82% of the pediatri- cians sampled screened for general developmental de-

initial pathological process (i.e., a decrease in attending to and processing social stimuli) feeds back on itself during the first 2 years of life, resulting in a secondary neurological disturbance (i.e., resulting in secondary def- icits of ASDs). They argue that without early interven- tion, the effects of secondary neurological disturbance push the child with an ASD further away from the path of typical development, as the initial pathological pro- cess and secondary neurological disturbance continue to feedback on the child's developing nervous system. Thus, early detection leading to early intervention re- duces the cumulative effects of secondary neurological disturbance, consequently keeping the child closer to the path of typical development, in comparison with those who do not receive such intervention (Fig. 1).

Early detection and diagnosis also means that the delays and the resulting distress that families often face when trying to obtain a diagnosis for their child are avoided or minimized.[58] Indeed, the main factor associated with pa- rental satisfaction in the diagnostic process is early diagno- sis.[41] Thus, it is no surprise that parents want to be told at the earliest possible opportunity if there is any concern about their child's development or well-being.[80]

SCREENING STUDIES

lays but only 8% screened for ASDs. The main reason

The increasing knowledge of the early signs of autism cited was lack of familiarity with specific tools for ASDs

spectrum disorders (ASDs) coupled with the benefits of (62% of respondents).
early intervention has led researchers to develop screen- Even in toddlerhood, many physicians are not rec-
ing tools to identify ASDs in infancy and toddlerhood. ognizing the signs of ASDs and are unnecessarily de-
Although the majority of these studies are based on Level laying diagnosis. As a consequence, children with an
2 screening (i.e., screening for ASDs in populations with ASD are not receiving intervention in their critical
developmental anomalies), some studies have attempted early years.[1,39,65–68]
to identify children with an ASD who have not previously

Figure 1. Path of typical development. Mundy and Crowson's cybernetic model of ASDs.

been identified with developmental problems. Prospec- tive scree
studies conducted in the general pop- ulation are known as Lev
screening studies.[81,82] Prospective studies have also been conducted
sib- lings of children with an ASD (ASD-sibs), as they are at incre
(genetic) risk of developing an ASD.[83–85]

Delayed Population (Level 2) Screening Studies

Level 2 screens focus specifically on differenti
children at risk for an ASD from other developmental difficulties,
as general developmental or language delays, and are more detailed
Level 1 (or general population based) screens. They are usually adm
tered in specialized settings, take more time to adminis- ter,[81,82] and
thus provided substantial information about ASDs in infancy
toddlerhood.

The Screening Tool for Autism in Two-Years-Olds (S
(Stone WL, Ousley OY, unpublished manuscript, 1997) was design
differentiate 2-year-old children at risk of autistic disorder (AD)
those at risk of other developmental disabilities. It is an interaction-b
mea- sure of 12 items assessing play, motor imitation, commu- nica
oint attention skills. To develop a scoring algorithm that would
mize identification of AD, and also to examine the validity of the
, Stone et al[86] used this tool with 19 children with AD and 54
en with non-AD developmental disorders. The development
ses resulted in a sensitivity of 1.00, and a specificity of 0.91, and
alidity analyses resulted in a sensitivity of 0.83 and a specificity of

To develop cutoff scores for the STAT, Stone et al[87] used
l detection procedures with developmentally matched groups of 26
en with AD and 26 children
non-ASD disorders. The specificity, sensitivity, and positive (PPV)
negative predictive values (NPV) were all very high, and the
-rater agreements and test-retest reliability were also high. However,
ite the excellent psychometric properties of the STAT, it is designed
use with children aged 2 to 3 years and is only aimed at
rentiating AD (rather than all ASDs) from other developmental
rders.[88]

To determine the utility of the STAT with children younger
24 months, and its ability to distinguish between the milder forms of
s and other develop- mental problems, Stone et al[89] administered it
71 high-risk children (59 ASD-sibs and 12 referred due to

developmental concerns) aged 12 to 23 months. Using an incr
cutoff score to reflect less developed social and communication sk
younger children, the screening properties for identifying children
an ASD at 14 months and older were good (sensitivity: 0.93; speci
0.83; PPV: 0.68; NPV: 0.97) but inadequate for 12- to 13-mont
children. As the sample size of the children who went on to rec
diagnosis of an ASD was small (n 19), these results should be
preted with caution until they are replicated in larger samples.

A new tool, the Autism Detection in Early Chil

months,
the presence of 7 risk markers prospectively identified 6 of the 7 children diagnosed with an ASD at 24 months, compared with 2 of the 58 non-ASD siblings, and none of the 23 low-risk controls. Thus, the sensitivity and specificity of the Autism Observation Scale for Infants were 0.84 and 0.98, respectively.
The individual markers on the Autism Observation Scale for Infants that predicted a diagnosis of an ASD at 24 months were abnormal eye contact, visual tracking, disengagement of visual attention, orienting to name, imitation, social smiling, reactivity, social interest, and sensory-orienting behaviors (all p .003, adjusting for multiple comparisons). These preliminary data need to be replicated in the full sample. Unfortunately, as there was no non-ASD developmentally delayed comparison group, we cannot be sure whether these behavioral markers are specific to ASDs or whether they share these markers with other developmentally disabled groups of infants.[32]
Bryson et al[91] prospectively followed 9 of the ASD-sibs from the Zwaigenbaum et al study[32] who received an ASD diagnosis (at 24 months) at 6 monthly intervals until 24 months, and then again at 36 months. All of these children showed, in varying degrees, a combination of impaired social-communicative development. Furthermore, there was evidence for the emergence of 2 subgroups, with the first subgroup defined by a drop in cognitive development from 12 to 24 months; the second subgroup maintained their cognitive profiles of average or near-average intelligence. The cognitive profiles of these 2 groups were indistinguishable at 12 months (8 of the 9 infants had average or close to average intelligence quotients) however, 6 of these children had severe cognitive impairments by 24 and/or 36 months.

cians as well as professionals, and can be used with children as young as 12 months. The behaviors targeted are early social and communication behaviors. The psychometric properties of the ADEC were assessed in a sample of 149 children with AD, 60 typically developing (TD) children, and 60 children with language or other developmental disorders (Young R, Brewer N, Williamson P, unpublished data, 2007). It was shown to have good internal consistency (Cronbach's α 0.85), good test-retest reliability (r .82), and very high inter-rater reliability (r .97). The specificity of the ADEC was 0.80, and the sensitivity was 0.70, with these figures increasing to 0.90 and 0.88, respectively, when only children younger than 30 months were considered. These preliminary data need to be replicated in the full sample. Unfortunately, However, despite the promising psychometric properties of the ADEC, these data are preliminary and are yet to be published in a peer-reviewed journal. Furthermore, these data are based on children with AD, many of whom were older than the targeted age. Thus, the properties of the ADEC for use with young children with all forms of ASD are yet to be established. Moreover, the study needs to be replicated with a younger, community-based sample.

Prospective Studies

Prospective studies of ASDs, conducted in community-based samples, are highly desirable for a number of reasons. First, the researcher can attempt to elicit the behaviors of interest at a particular age and under standardized conditions, allowing comparison between different groups and at different time points in the child's life. Furthermore, behaviors can be studied longitudinally, so that the relationship between early deficits and later behavioral manifestations can be examined. In addition, prospective studies have the added benefit of not

months. only informing us of the signs of ASDs in infancy (as do
Landa and Garrett-Mayer[92] compared a group of ASD- Level 2 screens) but also of being able to identify previ-
sibs (n 60) and TD infants (n 27) at 6, 14, and 24 ously unrecognized cases of ASDs. Prospective studies
months, on their performance on each of the subscales have been conducted on both high-risk populations
of the Mullen Scales of Early Learning[93] (fine and gross (ASD-sibs) and in the general population.
motor, visual reception, and receptive and expressive **Sibling Studies**
language). As with Zwaigenbaum et al[32] and Bryson Twin studies indicate that there is 60 to 92% concor-
et al,[91] there were no statistical differences in the behav- dance rate for ASDs in monozygotic twins and 0 to 10%
ioral presentations of ASD and non-ASD groups at age 6 concordance rate in dizygotic twins and siblings of af-
months, and there was "developmental worsening" be- fected individuals.[83–85] Consequently, studies of ASD-
tween 14 and 24 months for the ASD group. This period sibs have been an invaluable source of information on
of slowed development between 14 and 24 months the very early development of ASDs. The Autism Obser-
emphasizes the importance of early intervention, as this vation Scale for Infants[90] was developed to investigate
increase in developmental delay may be minimized if the behavioral manifestations of ASDs between 6 and 18
intervention begins before this stage. months in a sample of ASD-sibs. It includes 18-specific
Sullivan et al[94] conducted a prospective study on risk markers for ASDs, and uses a standardized procedure
response to joint attention (RJA) with 51 ASD-sibs at 14 for detecting each of these markers through a semistruc-
and 24 months and again at 30 to 36 months. Three tured, play-based assessment. Using the Autism Observa-
groups were established: ASD (n 16), "broader autism tion Scale for Infants, Zwaigenbaum et al[32] conducted a
phenotype" (BAP; n 8), which comprised children longitudinal study of 150 ASD-sibs ("high-risk" for ASDs)
who displayed language and/or social delays but were and 75 "low-risk" infants matched on sex, birth order,
not given a classification of an ASD at 3 years, and and age. Observations at 6 months did not predict clas-
non-BAP (n 27), which included children who did not sification of an ASD at 24 months. However, by 12
meet classification of BAP or an ASD at 3 years. Deficits

designed in RJA were present by 14 months in the children later
to compare groups based on risk status and not diagnosed with an ASD and BAP. However, although
on eventual diagnosis. If the ultimate aim in these pro- there were large improvements in RJA for the BAP and
spective studies is to improve knowledge of the early non-BAP groups at 24 months, there was minimal im-
signs of ASDs in infancy, and to use these signs to provement for the ASD group. Moreover, as perfor-
prospectively identify young children, then eventual di- mance on RJA at 14 months predicted later language and
agnostic status of these ASD-sibs becomes critical.[99] Sec- ASD outcome, Sullivan et al concluded that RJA is an
ond, high-risk samples are unique and are not represen- important behavior for the early screening of ASDs and
tative of a "true" prospective sample. Children who have subsequent intervention.
grown up in an environment already affected by an ASD Another prospective study investigating the BAP was
may have different symptomatology in comparison with conducted by Cassel et al.[95] In comparison with non-
those children with an ASD who were not reared in that ASD siblings (n 19), ASD-sibs (n 12) were found to
environment. Moreover, it has been found that children engage in lower rates of higher level behavioral requests
with an ASD from multiplex families are higher function- (i.e., pointing at, or giving the examiner a desired toy,
ing in adaptive skills and cognitive development than with or without eye contact) at 12 months, lower rates
those from singleton families.[100] of initiating JA (i.e., pointing at an object or event out of
Thus, numerous factors need to be considered as interest, with or without eye contact; holding up a toy to
possible influences contributing to differences in devel- show it to the examiner) at 15 months, and lower rates
opment, including alteration in parent– child interaction, of RJA (i.e., following the examiner's gaze or point) at 18
early recognition of symptoms and subsequent interven- months. Although the diagnostic status of these infants
tion, affected parenting styles because of exposure to has not yet been determined, the results demonstrate the
early intervention techniques, and parental stress.[99] In BAP in both ASD-sibs who do not go on to receive a
addition, genetic expression of ASDs may differ in mul- diagnosis of an ASD and those who do.

tiplex compared with singleton families, although there is little research to date investigating this possibility.

General Population (Level 1) Screening Studies

Level 1 ASD screens are used to identify children for general developmental disability, with specific emphasis on the signs of ASDs. These screens are used in the general population and are usually applied in community health services, such as in infant and child health centers or in general medical practice settings.[81,82] There are currently very few screening studies for ASDs that have been conducted in community-based settings, and many of these have used tools that screen for ASDs at only one specific age.

Baron-Cohen et al conducted the first prospective study of ASDs. They developed the Checklist for Autism in Toddlers (CHAT),[38] designed to be administered in a primary health care setting to identify 18-month-old children at risk for an ASD. This brief observational tool was initially administered to 41 ASD-sibs and 50 TD children, all aged 18 months. Three key items (protodeclarative pointing, gaze monitoring, and pretend play) were successful in identifying children who later received an ASD diagnosis at 36 months. Baron-Cohen et al[101] subsequently used the CHAT on 16,235 18-month-old children during their routine developmental checkup. Twelve children were identified as "at risk," with 10 of these receiving a diagnosis of an ASD and 2 receiving a diagnosis of developmental delay; these diagnoses remained stable at 3.5 years, giving a false-positive rate of 16.6%. In a long-term follow-up study of this same population, Baird et al[102] found that although the CHAT had excellent specificity (0.98), it lacked sensitivity (0.38), as 50 additional children were identified at the age of 7 years as having an ASD, none of whom had been identified as at risk at 18 months. The low sensitivity of the CHAT reduces its use as a screening instrument, as a large percentage of children with an ASD (approximately 60%) will not be identified by the CHAT at 18 months.

A modified version of the CHAT was developed in an attempt to increase the sensitivity of the tool. The M-CHAT,[103] a quantitative version of the CHAT, relies entirely on parental report and is demarks a major revision of the instrument. Like the M-CHAT, it relies solely on parental report and contains 25-items rated on a 5-point Likert scale. Its test properties and clinical validity have not yet been established, although preliminary data on a sample of 779 children (unselected group: mean age 21 months; ASD group:

tiplex compared with singleton families, although there Mitchell et al,[96] in their prospective study of 97 ASD-
is little research to date investigating this possibility. sibs and 49 low-risk controls, found that the children
General Population (Level 1) Screening Studies who received a diagnosis of an ASD at 24 months (n
Level 1 ASD screens are used to identify children for 18) showed deficits in language and communication as
general developmental disability, with specific emphasis early as 12 months. These infants understood fewer
on the signs of ASDs. These screens are used in the phrases and produced fewer gestures by 12 months
general population and are usually applied in community (e.g., giving, pointing, showing, shaking and nodding
health services, such as in infant and child health centers head, holding arms up to be lifted, and knowledge of
or in general medical practice settings.[81,82] There are appropriate use of real and toy objects); at 18 months,
currently very few screening studies for ASDs that have they showed delays in their understanding of phrases
been conducted in community-based settings, and many and single words, use of gestures, and production of
of these have used tools that screen for ASDs at only one single words. As production and comprehension of
specific age. words did not differ significantly between children with
Baron-Cohen et al conducted the first prospective and without an ASD until 18 months, the authors argue
study of ASDs. They developed the Checklist for Autism that use of gestures may be more important in prospec-
in Toddlers (CHAT),[38] designed to be administered in a tively identifying ASDs in children younger than 18
primary health care setting to identify 18-month-old chil- months.
dren at risk for an ASD. This brief observational tool was In addition to the social and communication impair-
initially administered to 41 ASD-sibs and 50 TD children, ments that are consistently reported in infants with
all aged 18 months. Three key items (protodeclarative ASDs, behavioral reactivity, difficulties with transitions,
pointing, gaze monitoring, and pretend play) were suc- and impaired motor control have also been found to
cessful in identifying children who later received an ASD account for unique variance in ASD risk in a sample of
diagnosis at 36 months. Baron-Cohen et al[101] subse- 115 18-month-old ASD-sibs.[97] Furthermore, Ozonoff et al[98]
quently used the CHAT on 16,235 18-month-old children found that 12-month-old ASD-sibs engaged in signifi-
during their routine developmental checkup. Twelve cantly more spinning, rotating, and unusual visual explo-
children were identified as "at risk," with 10 of these ration of objects than the non–ASD-sibs. Thus, although
children receiving a diagnosis of an ASD and 2 receiving social and communication impairments have been found
a diagnosis of developmental delay; these diagnoses to be the best predictors of ASDs in infancy, future
remained stable at 3.5 years, giving a false-positive rate research should focus on the subtle and very early be-
of 16.6%. In a long-term follow-up study of this same havioral manifestations alongside social and communica-
population, Baird et al[102] found that although the CHAT tion impairments.
had excellent specificity (0.98), it lacked sensitivity (0.38), Despite the recent surge of research with ASD-sibs
as 50 additional children were identified at the age of 7 and the invaluable insights gained into their early devel-
years as having an ASD, none of whom had been identified opment, some caution needs to be exercised when in-
as at risk at 18 months. The low sensitivity of the CHAT terpreting the results from these studies. First, many are
reduces its use as a screening instrument, as a large per-

The centage of children with an ASD (approximately 60%) will
M-CHAT may be useful in identifying children in not be identified by the CHAT at 18 months.
need of further assessments but should not be used as a A modified version of the CHAT was developed in an
screen to exclude the possibility of an ASD.[108] attempt to increase the sensitivity of the tool. The M-
The Q-CHAT,[109] a quantitative version of the CHAT, CHAT[103] relies entirely on parental report and is de-
marks a major revision of the instrument. Like the M- signed for use with 24-month-old children; unlike the
CHAT, it relies solely on parental report and contains CHAT, it has a lower threshold for identifying ASDs. A
25-items rated on a 5-point Likert scale. Its test proper- nonselected population of 1,122 18- to 25-month-old
ties and clinical validity have not yet been established, children and a high-risk sample (referred from early
although preliminary data on a sample of 779 children intervention services) of 171 18- to 30-month-old chil-
(unselected group: mean age 21 months; ASD group: dren were screened using the M-CHAT. Six items in the

mean age 44 months) have resulted in a range of scores areas of social relatedness and communication were
that approximate a normal distribution. Thus, the Q-CHAT found to best discriminate between children diagnosed
may be a useful instrument to measure trait differences in with and without an ASD (protodeclarative pointing,
the general population and not just in the ASD population. response to name, interest in peers, bringing things to
However, its revision into a parental report only measure show parents, following a point, and imitation). Using
lends itself to the problems associated with these types of various cutoff scores on the checklist, sensitivity ranged
measures, as discussed previously. from 0.87 to 0.97, specificity ranged from 0.95 to 0.99,
An ongoing longitudinal, prospective study, called the and PPV ranged from 0.36 to 0.80, depending on which
FIRST WORDS® project, uses the Communication and cutoff scores were used, and whether the M-CHAT was
Symbolic Behaviors Scales[110] as a screen with children in followed-up with a scripted telephone interview. These
the general population, recruited from health and child preliminary data suggest that the M-CHAT is able to discrim-
care clinics.[111] The Communication and Symbolic Behav- inate between ASDs and other DDs by 24 months and has
iors Scales comprises an Infant-Toddler Checklist that a higher sensitivity for detecting ASDs than the CHAT.
parents complete when their child is younger than 24 In a study by Ventola et al,[104] 195 children (mean age:
months, and a behavior sample, which is a direct evalu- 24 months) who failed the M-CHAT were grouped into
ation of the child after 18 months by a clinician, which developmental delay (n 15), developmental and lan-
is videotaped for later analysis. Wetherby et al.[112] exam- guage disorder (n 30), and ASD (n 150) to investi-
ined the social and communication behaviors of 123 gate differences in symptom presentation. Once overall
children (50 with an ASD, 23 with developmental delay, language level was controlled for, only 4 items signifi-
and 50 TD children) aged 18 to 26 months using the cantly differed between the DD/developmental and lan-
Communication and Symbolic Behaviors Scales who were guage disorder and ASD groups. These were all joint
recruited from the FIRST WORDS® project. Compared attention and social responsiveness items (response to
with children with developmental delay, who were name, pointing for interest and to request, ability to
matched on age and developmental level, the children with follow a point) reinforcing past literature that social
an ASD were found to display 5 core social and communi- responsiveness and joint attention behaviors are core,
cation deficits. These included deficits in gaze shifts, fol- and particularly unique, deficits in ASDs.
lowing of gaze/points, rate of communicating, acts for joint To address the usefulness of the M-CHAT as a screen
attention, and inventory of conventional gestures. for ASDs in a community-based sample, as well as to
To determine the efficacy of the Infant-Toddler Check- establish absolute sensitivity and specificity, Kleinman
list as a general population screening tool, 5385 children et al[105] screened 3309 low-risk children (new cases) as part
from the general population were administered this of their well-child care visits, and a further 484 high-risk
checklist between 6 and 24 months.[113] Of the 60 chil- children referred for early intervention. All children
dren who went on to receive an ASD diagnosis, 56 (93%) were screened at 16 to 30 months (Time 1) and fol-
screened positive between 9 and 24 months. However, lowed-up at 42 to 54 months (Time 2). For the total
although the sensitivity of the Infant-Toddler Checklist sample, PPV at Time 1 was close to that of the original
between 9 and 24 months is excellent, it is unable to study (0.36–0.74), again depending on whether a fol-
distinguish between children with an ASD and those low-up phone interview was used; PPV for the total
with communication delays, as 813 children were iden- sample at Time 2 was similar (.59 –.74). However, for the
tified on the Infant-Toddler Checklist as needing further low-risk sample, PPV at Time 1 was extremely low
developmental surveillance. (0.11 0.05) when the M-CHAT was used alone. When
Only one other community-based ASD screening used in conjunction with a follow-up phone interview, it
study has been conducted to date. Swinkels et al[114] increased to 0.65 0.17. Thus, the PPV increases to an
developed an instrument known as the Early Screening acceptable level, but only in conjunction with a fol-
of Autistic Traits Questionnaire. A population of 31,724 low-up phone interview, which is consistent with the
children aged 14 to 15 months were first prescreened at findings of both Pandey et al[106] and Robins.[107] These
well-baby clinics using a 4-item screening instrument, data suggest that the use of the M-CHAT alone as a screen
and screen-positive infants were then evaluated using for ASDs in a community-based sample is problematic.
the 14-item Early Screening of Autistic Traits Question-

development, naire. Eighteen children were found to have an ASD,
the authors propose that the scores on the indicating that it is possible to identify unrecognized
new algorithms should be used to indicate ranges of con- cases of ASDs as early as 14 months. The items that were
cern (i.e., little, moderate, and significant concern), rather most predictive of ASDs were once again social-commu-
than using traditional "cut-off" scores. The data await rep- nicative in nature. "Stereotypical movements" was least
lication with a larger sample, and data on the stability of predictive, reinforcing the earlier suggestion that social-
diagnosis using the toddler version are not yet available. communicative behaviors are the strongest predictors of
Given that there are some problems associated with ASDs, and repetitive behaviors (or stereotypies) are, per-
the ADOS in correctly differentiating the ASDs, and with haps, more indicative of general intellectual disability.[23,115]
the ADI-R in correctly diagnosing AD in children with men- The use of the Early Screening of Autistic Traits Ques-
tal ages younger than 18 months,[125–127] it has been sug- tionnaire as a general population screen in its current
gested that the 2 instruments be used together.[121] Le form would be problematic, as it was found to have a
Couteur et al[128] found good agreement between the large number of false positives (42 in total); however,
instruments in a preschool sample aged 24 to 49 months, none of these were TD children. Although the authors
especially for those with "classic autism" (AD). How- could not determine overall sensitivity, they indicated
ever, Ventola et al[129] found poor agreement with the that it would have been low as their number of identified
ADOS and ADI-R in young children as they did not cases of ASDs was low in comparison with current prev-
display enough repetitive behaviors and stereotyped in- alence rates.[116]
terests to meet the cutoff for AD on the ADI-R. There-

DIAGNOSING AUTISM SPECTRUM DISORDERS IN TODDLERS: INSTRUMENTS AND STABILITY OF DIAGNOSIS

fore, Wiggins and Robins[130] excluded the behavior do- main on the ADI-R when assessing toddlers at risk for an ASD and found a significant improvement in agreement between the ADI-R and other measures (including the The findings from the screening studies reviewed
ADOS). These findings indicate that it is advisable to use earlier indicate that it is possible to identify autism spec-
the ADI-R together with the ADOS, in conjunction with trum disorders (ASDs) in infancy and toddlerhood. It has
clinical judgment, when diagnosing very young children. also been shown that it is possible to accurately diagnose
ASDs as early as 2 years with instruments such as the

Reliability of Diagnosis at Age 2 Years Autism Diagnostic Interview-Revised (ADI-R),[117] a stan-
Diagnoses of ASDs at approximately 2 years have dardized, semistructured parental interview, and the
been found to be accurate and stable over time.[131] Autism Diagnostic Observation Schedule (ADOS),[118,119]
Lord,[49] using clinical judgment, found that 27 of 30 an observational instrument consisting of 4 modules
children retained their diagnostic classification of an devised for individuals with varying language abilities.
ASD from 2 to 3 years. Eaves and Ho[132] found that 79% However, it has been found that the ADOS sometimes
of children given a diagnosis of an ASD at age 2½ years has lower specificity and sensitivity for classification
retained their diagnosis at age 4½ years. However, the between autistic disorder (AD) and other ASDs.[120–122]
stability of diagnoses for ASDs other than AD was not as Recently, Gotham et al[122] attempted to improve the
stable across time. Turner et al[133] examined the devel- sensitivity and specificity of the ADOS in differentiating
opmental outcomes of 2-year-old children 7 years after the various ASDs, by altering the current algorithm. A 12
they received a diagnosis of an ASD. It was found that to 31% increase in specificity in differentiating between
88% of the children who received an ASD diagnosis at the ASDs was achieved with nonverbal children. Further-
age 2 years received the same diagnosis at 9 years. In more, a replication study by Gotham et al[123] found that
their study of 77 children aged 16 to 35 months, the sensitivity and specificity of these revised algorithms
Kleinman et al[134] reported that 80% remained in the approximated or exceeded those of the original algo-

same diagnostic category at 42 to 82 months. As with previous studies, a diagnosis of AD was more stable than that of a pervasive developmental disorder-not otherwise specified diagnosis (85% vs. 47%). Charman et al,[135] also investigating the outcome of children aged 7 years after their initial diagnosis at 2 years, found that 22 of the 26 children diagnosed with ASD at 2 years (based on clinical judgment) continued to meet this diagnosis at 9 years. However, their findings on the stability of diagnosis based on psychometric and standardized tests, as opposed to clinical judgment, were not as clear, with children crossing diagnostic boundaries as they aged. Charman et al concluded that the assessment of early social-communication behaviors (using, e.g., the ADOS) gives a better indication of the diagnostic profile of young, nonverbal children than

ing standard psychometric tests measuring intelligence tool at a single given age. In contrast to this approach, the repeated monitoring of infant development will serve to increase the chances of identifying early manifestations of ASDs, consequently increasing the sensitivity of the screening tool used. In addition, repeated sampling will help to track the subtle changes that occur in infants with an ASD overtime[137] and aid investigation into what seems to be a critical period between 12 and 24 months, where a subset of children with an ASD progressively lose cognitive skills, whereas another maintains cognitive abilities.[91,92] Furthermore, the phenomenon of regression is well known to occur during this time period. Thus, future prospective studies should focus on systematically investigating not only the behavioral changes that occur during this important developmental period but also the milestones that children with an ASD reach in relation to those reached by their typically developing peers. In addition to aiding early identification, such a focus on the early development of the ASD phenotype will ultimately contribute to understanding the underlying neuropathology leading to the cognitive and behavioral deficits in ASDs.

SUMMARY AND FUTURE DIRECTIONS

The prevalent finding from studies on autism spectrum disorders (ASDs) in infancy and toddlerhood is that abnormalities in social attention and communication behaviors are evident from the first year of life and are the most predictive early signs of an ASD diagnosis. In the area of social attention, these markers include a lack of eye contact, social interaction, social smiling, imitation, orienting to name call, appropriate facial expressions, and interest and pleasure in others. In the area of communication, joint attention skills (protodeclarative pointing, following a point, gaze monitoring, and referencing objects/events), showing and requesting behaviors, and gestures. Impairments in imagination skills, such as the use of pretend play, have also been found to be important markers in late infancy/toddlerhood. Although sensory/motor behaviors and stereotypies are seen in some infants with an ASD, these behaviors may be more indic-

ACKNOWLEDGMENTS

The first author was supported by a Sir Robert Menzies Memorial Foundation Allied Health Scholarship during the writing of this article. We thank Izabela Fedyszyn and Pat Monteleone for providing feedback on earlier drafts of this article.

REFERENCES ative of general intellectual disability,[23,115] and these behaviors may not become apparent until at least 3 years in some children.[42,45] Currently, they may not serve as

1. Dawson G. Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. *Dev Psychopathol.* 2008;20:775–803. important predictors of ASDs in infancy. Level 1 screening instruments, using social attention and communication behaviors as key items, have been able to prospectively identify previously unidentified cases of ASDs in community-based samples. A highly

2. Helt M, Kelley E, Kinsbourne M, et al. Can children with autism recover? If so, how? *Neuropsychol Rev.* 2008;18:339–366. 3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR)*. 4th ed. Washington, DC: American Psychiatric Association; 2000. predictive, but brief, observational tool containing a

4. World Health Organization. Mental Disorders: A Glossary and Guide to Their Classification in Accordance with the 10th Revision of the International Classification of Diseases: Research Diagnostic Criteria (ICD-10). Geneva: WHO; 1993. 5. De Giacomo AD, Fombonne E. Parental recognition of developmental abnormalities in autism. *Eur Child Adolesc Psychiatry.* 1998;7:131–136. checklist of the behaviors that are absent in infants with an ASD would prove invaluable for the detection of these infants, as children who would previously go un- recognized could be identified through routine develop- mental monitoring and reliably diagnosed at 2 years. This is important because only 50% of parents of children with an ASD suspect a problem before 12 months.[13] However, it is apparent from the studies reviewed here that, as acknowledged by Charman,[136 (p. 1)] there are

6. Rogers SJ, Di Lalla D. Age of symptom onset in young children with pervasive developmental disorders. *J Am Acad Child Adolesc Psychiatry.* 1990;29:863–972. 7. Short A, Schopler E. Factors relating to age of onset in autism. *J Autism Dev Disord.* 1988;18:207–216. currently no instruments available with adequate sensitiv-

8. Adrien JL, Fauer M, Perrot A, et al. Autism and family home movies: Preliminary findings. *J Autism Dev Disord.* 1991;21:43–49. 9. Adrien JL, Barthelemy C, Perrot A, et al. Validity and reliability of the Infant Behavioral Summarized Evaluation (IBSE): a rating scale for the assessment of young children with autism and developmental disorders. *J Autism Dev Disord.* 1992;22:375–394. ity and specificity to recommend universal screening. Therefore, there remains a need for more prospective stud- ies of infants conducted in community-based settings, as the few conducted, to date, have reported poor sensitivity on the measures used or have high false-positive rates.

10. Adrien JL, Lenoir P, Matineau J, et al. Blind ratings of early symptoms of autism based upon family home movies. *J Am Acad Child Adolesc Psychiatry.* 1993;32:617–626. 11. Baranek GT. Autism during infancy: a retrospective video analysis of sensory motor and social behaviours at 9–12 months of age. *J Autism Dev Disord.* 1999;29:213–224. The routine and repeated monitoring of behaviors throughout the infancy period, rather than a single screening at a given age, may prove more useful in detecting ASDs in infancy. The 2 large-scale prospective community-based studies reviewed here used a screen-

12. Osterling J, Dawson G. Early recognition of children with autism: a study of first birthday home videotapes. *J Autism Dev Disord.* 1994;24:247–257. 13. Osterling J, Dawson G. Early recognition of infants with autism versus mental retardation. Poster presented at: Meeting of the Society for Research in Child Development; April 15–18, 1999; Albuquerque, NM. 14. Stone W, Hoffman E Lewis SE, Ousley DY. Early recognition of autism. *Arch Pediatr Adolesc Med.* 1994;148:174–179. 15. Werner E, Dawson G, Osterling J, Dinno N. Brief report: recognition of autism spectrum disorder before one year of age: a retrospective study based on home videotapes. *J Autism Dev Disord.* 2000;30:157–162. 16. Brereton A, Tonge B. Asperger's disorder (i). In: Holt G, Bouras N, eds. *Autism and Related Disorders: The Basic Handbook for Mental Health, Primary Care, and Other Professionals.* Great Britain: World Psychiatric Association Henry Ling Limited; 2002:25–31. 17. Fitzgerald M, Corvin A. Diagnosis and differential diagnosis of Asperger syndrome. *Adv Psychiatric Treatment.* 2001;7:310–318. 18

nachie H, Le Couteur A, Honey E. Can a diagnosis of ger syndrome be made in very young children with suspected autism spectrum der? *J Autism Dev Disord.* 2005;35:167–176. 19. Scott F. Can Asperger Eome be diagnosed at 24 months Paper presented at: Autism2005 AWARES.org conference centre. Available at: /www.awares.org/conferences. Accessed November 11, 2005. 20. Buitelaar JK, Van aag R, Klin A, Volkmar F. Exploring the boundaries of pervasive developmental ler not otherwise specified: analyses of data from the DSM-IV autistic disorder trial. *J Autism Dev Disord.* 1999;29:33–43. 21. Mars AE, Mauk JE, Dowrick PW. toms of pervasive evelopmental disorders as observed in pre-diagnostic home videos of infants and llers. *J Pediatrics.* 1998;132:500–504. 22. Nadig AS, Ozonoff S, Young GS, Rozga A, Sigman M, Rogers SJ. rospective study of response to name in infants at risk for Autism. *Archf Paediatr*

Adolesc Med. 2007;161:378–383. 23. Werner E, Dawson G. Validation of the phenomenon of autistic
disorder regression using home videotapes. *Archi Gen Psychiatry.* 2005;62:889–895. 24. Clifford SM, Dissanayake C. The early development of joint attention in infants with autistic disorder using home video observations and parental interview. *J Autism Dev Disord.* 2008;38:791–805. 25. Clifford S, Young R, Williamson P. Assessing the early
characteristics of autistic disorder using video analysis. *J Autism Dev Disord.* 2007;12:301–313. 26. Vostanis P, Smith B, Corbett J, et al. Parental concerns of early development in children with autism and related disorders. *Autism.* 1998;2:229–242. Young R, Brewer N, Pattison C. Parental identification of early
behavioural abnormalities in children with autistic disorder. *Autism.* 2003;7:125–143. 28. Werner E, Dawson G. *Early Development Interview*. Seattle:
University of Washington Autism Center; 2006. 29. Baranek GT, Watson LR, Crais ER, Reznick JS. *First Year*
Inventory (FYI) (Version 2.0). Chapel Hill, NC: The University of North Carolina at Chapel Hill; 2003. 30. Reznick S, Baranek GT, Reavis S, Watson LR, Crais ER. A parent-report instrument for identifying one-year-olds at risk for an eventual diagnos autism: the First Year Inventory. *J Autism Dev Disord.* 2007;37:1691–1710. 31. Wats LR, Baranek GT, Crais ER, Reznick JS, Dykstra J,
Perryman T. The First Year Inventory: retrospective parent responses to a questionn designed to identify one-year-olds at risk for autism. *J Autism Dev Disord.* 2007;37:49–61. 32. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J,
Szatmari P. Behavioral manifestations of autism in the first year of life. *Int J De Neurosci.* 2005;23:143–152.
33. Gillberg C. Early symptoms in autism. In: Gillberg C, ed.
Diagnosis and Treatment of Autism. New York: Plenum Press; 1989:23–32. 34. Dissanayake C, Bui QM, Huggins R, Loesch DZ. Growth in
stature and head circumference in high-functioning autism and Asperger disorder d the first 3 years of life. *Dev Psychopathol.* 2006;18:381–393. 35. Fukumoto A, Hashimoto T, Ito H, et al. Growth of head
circumference in autistic infants during the first year of life. *J Autism Dev Disord.* 2008;38:411–418. 36. Zwaigenbaum L, Stone WL, Dobkins K, et al. Prospective
evaluation of head growth in infants at increased risk of autism. Paper presented a Annual International Meeting for Autism Research; May 15–17, 2008; London, En 37. Mandell DS, Novak MM, Zubritsky CD. Factors associated with
age of diagnosis among children with autism spectrum disorders. *Pediatrics.* 2005;116:1480–1486. 38. Baron-Cohen S, Allen J, Gillberg C. Can autism be detec 3-months? The needle, the haystack, and the CHAT. *Br J Psychiatry.* 2;161:839–843. 39. Chung MC, Smith B, Vostanis P. Detection of children with
autism. *Edu Child Psychol.* 1995;12:31–36. 40. Howlin P, Asgharian A. diagnosis of autism and Asperger
lrome: findings from a survey of 770 families. *Dev Med Child Neurol.* ;41:834–839. 41. Howlin P, Moore A. Diagnosis in autism: a survey of over 1200
patients in the UK. *Autism.* 1997;1:135–162. 42. Gray KM, Tonge BJ. there early features of autism in infants
and preschool children? *J Pediatr Child Health.* 2001;37:221–226. 43. e WL, Lee EB, Ashford L, et al. Can autism be diagnosed
rately in children under 3 years? *J Child Psychol Psychiatry.* ;40:219–226. 44. Rogers SJ, Pennington BF. A theoretical approach to the
deficits in infantile autism. *Dev Psychopathol.* 1991;3:137–162. 45. ng R, Brewer N. Conceptual issues in the classification and assessment of autistic rder. In: Gidden LM, ed. *International Review of Research in Mental Retardation.* 23. San Diego, CA: Academic Press; 2002. 46. Mooney EL, Gray KM, Tonge BJ. y features of autism:
titive behaviours in young children. *Eur Child Adolesc Psychiatry.* ;15:12–18. 47. Turner M. Repetitive behavior in autism: a review of
hological research. *J Child Psychol Psychiatry.* 1999;40: 839–849. 48. Morgan L, nerby AM, Barber A. Repetitive and stereotyped movements in children with autism trum disorders late in the second year of life. *J Child Psychol Psychiatry.* 2008;49: -837. 49. Lord C. Follow-up of two-year-olds referred for possible autism.
J Child Psychol Psychiatry. 1995;36:1365–1382. 50. Goldberg WA, n K, Filipek PA, et al. Language and other
ession: assessment and timing. *J Autism Dev Disord.* 2003; 33:607–616. 51. Kurita H. ntile autism with speech loss before the age of 30
months. *J Autism Dev Disord.* 1985;24:191–196. 52. Volkmar F, Stier D, en D. Age of recognition of pervasive developmental disorder. *Am J Psychol.* ;142:1450–1452. 53. Volkmar F, Cohen D, Hoshino Y, Rende R, Paul R.
nomenology and classification of the childhood psychoses. *Psychol Med.* ;18:191–201. 54. Interactive Autism Network. IAN Research Report 6,
ression. Available at: http://www.iancommunity.org. Accessed August 17, . 55. Davidovitch M, Glick L, Holtzman G, Tirosh E, Safir MP.
elopmental regression in autism: maternal perception. *J Autism Dev Disord.* ;30:113–119. 56. Filipek PA, Accardo PJ, Baranek GT, et al. The screening and
diagnosis of autistic spectrum disorders. *J Autism Dev Disord.* 1999;29:439–484.

57. Hoshino Y, Kaneko M, Yashima Y, Kumashiro H, Volkmar FR,
Cohen DJ. Clinical features of autistic children with setback course in their infan *Jpn J Psychiatry Neurol.* 1987;41:237–245. 58. Siperstein R, Volkmar F. Brief repo parental reporting
regression in children with pervasive developmental disorders. *J Autism Dev Disord.* 2004;34:731–734. 59. Lord C, Shulman C, DiLavore P. Regression and word loss in
autism spectrum disorder. *J Child Psychol Psychiatry.* 2004;45:1–21 Richler J, Luyster R, Risi S, et al. Is there a 'regressive
phenotype' of autism spectrum disorder associated with the measles-mumps-rubella vaccine? A CPEA study. *J Autism Dev Disord.* 2006;36:299–316. 61. Brown J, Prelon PA. Brief report: the impact of regression on
language development in autism. *J Autism Dev Disord.* 1995; 25:305–309. 62. Rice ML, Warren SF, Betz SK. Language symptoms of
elopmental language disorders: an overview of autism, Down syndrome, fragile X, specific language impairment, and Williams syndrome. *Appl Psycholinguist.* 005;26:7–27. 63. Wiggins LD, Baio J, Rice C. Examination of the time between t evaluation and first spectrum diagnosis in a population- based sample. *J Dev v Pediatr.* 2006;27:S79–S87. 64. Dosreis S, Weiner CL, Johnson L, Newschaffer
CJ. Autism
spectrum disorder screening and management practices among general pediatric iders. *J Dev Behav Pediatr.* 2006;27:S88–S94. 65. Prizant B, Wetherby A. Providing
services to children with
n (ages 0 to 2 years) and their families. *Focus on Autistic Behavior.* 1988;4:1–16. inted from *Topics in Language Disorders.* 1988;9:1–23. 66. Rogers SJ. Brief
t: early intervention in autism. *J Autism*
Dev Disord. 1996;26:243–246. 67. Rogers SJ. Diagnosis of autism

before the age of 3. In: Glidden LM, ed. *International Review of Research in Mental Retardation: Autism.* Vol 23. San Diego, CA: Academic Press; 2001:1–31. 68. Rutter M. Cognitive deficits in the pathogenesis of autism. *J Child Psychol Psychiatry.* 1983;24:513–531. 69. Shonkoff JP, Phillips DA. From Neurons to Neighborhoods: The Science of Early Childhood Development. Committee on Integrating the Science of Early Childhood Development, Board on Children, Youth, and Families, Commission on Behavioral and Social Sciences and Education, National Research Council and Institute of Medicine. Washington, DC: National Academy Press; 2000. 70. McConachie H, Diggle T. Parent-mediated early intervention for young children with autism spectrum disorder: a systematic review. *J Eval Clin Pract.* 2007;13:120–129. 71. Rogers SJ, Vismara LA. Evidence-based comprehensive treatments for early autism. *J Clin Child Adolesc Psychol.* 2008;37:8–38. 72. Vismara LA, Rogers SJ. The Early Start Denver Model: a case study of an innovative practice. *J Early Intervention.* 2008;31: 91–108. 73. Vismara LA, Rogers SJ, Colombi C. Can one hour per week of therapy lead to lasting changes in young children with autism? *Autism.* 2009;13:93–102. 74. Harris SL, Handelman JS. Age and IQ at intake as predictors of placement for young children with autism: a four to six year follow-up. *J Autism Dev Disord.* 2000;30:137–142. 75. Green G, Brennan LC, Fein D. Intensive behavioral treatment for a toddler at high risk for autism. *Behav Modif.* 2002;26:69–103. 76. Mahoney G, Perales F. The impact of relationship focused intervention on young children with autism spectrum disorders: a comparative study. *J Dev Behav Pediatr.* 2005;26:77–85. 77. Mahoney G, Boyce G, Fewell P, Spiker D, Wheeden CA. The relationship of parent-child interaction to the effectiveness of early intervention services for at-risk children and children with disabilities. *Topics Early Childhood Spec Educ.* 1998;18:5–17. 78. McGee GG, Morrier MJ, Daly T. An incidental teaching approach to early intervention for toddlers with autism. *J Assoc Pers Sev Handicaps.* 1999;24:133–146. 79. Mundy P, Crowson M. Joint Attention and early social communication: implications for research on intervention with autism. *J Autism Dev Disord.* 1997;27:653–676. 80. Quine L, Pahl J. First diagnosis of severe handicap: a study of parental reactions. *Dev Med Child Neurol.* 1987;29:232–242. 81. Pinto-Martin JA, Levy SE. Early diagnosis of autism spectrum disorders. *Curr Treat Options Neurol.* 2004;6:391–400. 82. Volkmar F, Chawarska K, Klin A. Autism in infancy and early childhood. *Annu Rev Psychol.* 2005;56:315–336. 83. Szatmari P, Jones MB, Zwaigbaum L, MacClean JE. Genetics and autism: overview and new directions. *J Autism Dev Disord.* 1998;28:351–368. 84. Bailey A, Le Couteur A, Gottesman I, et al. Autism as a strongly genetic disorder: evidence from a British twin study. *Psychol Med.* 1995;25:63–77. Grice DE, Buxbaum JD. The genetics of autism spectrum disorders. *Neuromolecular Med.* 2006;8:451–460. 86. Stone WL, Coonrod EE, Ousley OY. Brief report: screening tool for autism in two-year-olds (STAT): development and preliminary data. *J Autism Dev Disord.* 2000;30:607–612. 87. Stone WL, Coonrod EE, Turner LM, Pozdol SL. Psychometric properties of the STAT for early autism screening. *J Autism Dev Disord.* 2004;34:691–701. 88. Coonrod EE, Stone WL. Screening for autism in young children. Volkmar FR, Paul R, Klin A, Cohen DJ, eds. *Handbook of Autism and Pervasive Developmental Disorders: Diagnosis, Development, Neurology & Behavior.* Vol 2. 3rd New York: Wiley; 2005:707–729. 89. Stone WL, McMahon CR, Henderson LM. Use of the screening tool for autism in two-year-olds (STAT) for children under 24 months: an exploratory study. *Autism.* 2008;12:557–573. 90. Bryson SE, Zwaigenbaum L, McDermott C, Rombough V, Brian J. The Autism Observation Scale for Infants: scale development and reliability data. *J Autism Dev Disord.* 2008;38:731–738. 91. Bryson SE, Zwaigenbaum L, Brian J, et al. A prospective case series of high-risk infants who developed autism. *J Autism Dev Disord.* 2007;37:12–24. Landa R, Garrett-Mayer E. Development in infants with autism spectrum disorder: a prospective study. *J Child Psychol Psychiatry.* 2006;47:629–638. Mullen EM. *Mullen Scales of Early Learning (MSEL*). Circle Pines, MN: AGS; 1995. 94. Sullivan M, Finelli J, Marvin A, Garrett-Mayer E, Bauman M, Landa R. Response to joint attention in toddler at risk for autism spectrum disorder: a prospective study. *J Autism Dev Disord.* 2007;37:37–48. 95. Cassel TD, Messinger DS, Ibanez LV, Haltigan JD, Acosta SI, Buchman AC. Early social and emotional communication in the infant siblings of children with autism spectrum disorder: an examination of the broad phenotype. *J Autism Dev Disord.* 2007;37:122–132. 96. Mitchell S, Brian J, Zwaigenbaum L, et al. Early language and communication development of infants later diagnosed with Autism Spectrum Disorder. *J Dev Behav Pediatr.* 2006;27:S69–S78. 97. Brian J, Bryson SE, Garon N, et al. Clinical assessment of autism in high-risk 18-month-olds. *Autism.* 2008;12:433–456. 98. Ozonoff S, Macari S, Young GS, Goldring S, Thompson M, Rogers SJ. Atypical object exploration at 12 months of age is associated with autism in a prospective sample. *Autism.* 2008;12:457–472. 99. Zwaigenbaum L, Thurm A, Stone W, et al. Studying the emergence of autism spectrum disorders in high-risk infants: methodological and clinical issues. *J Autism Dev Disord.* 2007;37:466–480. 100. Pandey J. The modified checklist for autism in toddlers (M-CHAT) sibling study: are younger siblings representative of the general ASD population? Dissertation Abstracts International: Section B: The Sciences and Engineering. 2008;68(8-B):5586.

observation 101. Baron-Cohen S, Cox A, Baird G, et al. Psychological markers in schedule-generic: a standard measure of social and the detection of autism in infancy in a large population. *Br J* communication deficits associated with the spectrum of *Psychiatry.* 1996;168:158–163. autism. *J Autism Dev Disord.* 2000;30:205–223. 102. Baird G, Charman T, Cox A, et al. Screening and surveillance 120. Bishop DV, Norbury CF. Exploring the borderlands of autistic for autism and pervasive developmental disorders. *Arch Dis* disorder and specific language impairment: a study using *Child.* 2001;84:468–475. standardized diagnostic instruments. *J Child Psychol* 103. Robins DL, Fein D, Barton ML, Green JA. The modified *Psychiatry.* 2002;43:917–929. checklist for autism in toddlers: an initial study investigating 121. de Bildt A, Sytema S, Ketelaars C, et al. Interrelationship the early detection of autism and pervasive developmental

between autism diagnostic schedule-revised (ADI-R), and the disorders. *J Autism Dev Disord.* 2001;31:131–144.
diagnostic and statistical manual of mental disorders (DSM-IV- 104. Ventola P, Kleinman J, Pandey J, et al. Differentiating between
TR) classification in children and adolescents with mental autism spectrum disorders and other developmental disabilities
retardation. *J Autism Dev Disord.* 2004;34:129–137. in children who failed a screening instrument for ASD.
122. Gotham K, Risi S, Pickles A, Lord C. The autism diagnostic *J Autism Dev Disord.* 2007;37:425–436.
observation schedule: revised algorithms for improved 105. Kleinman JM, Robins DL, Ventola PE, et al. The modified
diagnostic validity. *J Autism Dev Disord.* 2007;37:613–627. checklist for autism in toddlers: a follow-up study investigating
123. Gotham K, Risi S, Dawson G, et al. A replication of the autism the early detection of autism spectrum disorders. *J Autism Dev*
diagnostic observation schedule (ADOS) revised algorithms. *Disord.* 2008;38:827–839.
J Am Acad Child Adolesc Psychiatry. 2008;47:642–651. 106. Pandey J, Verbalis A, Robins DL, et al. Screening for autism in
124. Luyster R, Guthrie W, Gotham K, Risi S, DiLavore P, Lord C. older and younger toddlers with the modified checklist for
The Autism Diagnostic Observation Schedule—Toddler module: autism in Toddlers. *Autism.* 2008;12:513–535.
preliminary findings using a modified version of the ADOS. 7th 107. Robins DL. Screening for autism spectrum disorders in primary
Annual International Meeting for Autism Research: Oral care settings. *Autism.* 2008;12:537–556.
Presentation 112.111, Invited Educational Symposium 140.5. 108. Eaves LC, Wingert H, Ho HH. Screening for autism: agreement
May 15–17, 2008. with diagnosis. *Autism.* 2006;10:229–242.
125. Lord C, Storoschuk S, Rutter M, Pickles A. Using the ADI-R to 109. Allison C, Baron-Cohen S, Wheelwright S, et al. The Q-CHAT
diagnose autism in preschool children. *Infant Mental Health J.* (Quantitative checklist for autism in toddlers): a normally
1993;14:234–252. distributed quantitative measure of autistic traits at 18–24 months of
126. Lord C, Pickles A, McLennan J, et al. Diagnosing autism: age: preliminary report. *J Autism Dev Disord.* 2008;38:1414–1425.
Analysis of data from the Autism Diagnostic Interview. 110. Wetherby A, Prizant B. *Communication and Symbolic*
J Autism Dev Disord. 1997;27:501–517. *Behavior Scales-Developmental Profile.* First Normed ed.
127. Pilowsky T, Yirmiya N, Shulman C, Dover R. The Autism Baltimore, MD: Paul H. Brookes Publishing; 2002.
Diagnostic Interview-Revised and the Childhood Autism Rating 111. Wetherby A, Woods J, Allen L, Cleary J, Dickinson H, Lord C.
Scale: differences between diagnostic systems and comparisons Early indicators of autism spectrum disorder in the second year
between genders. *J Autism Dev Disord.* 1998;28:143–151. of life. *J Autism Dev Disord.* 2004;34:285–299.
128. Le Couteur A, Haden G, Hammal D, McConachie H. Diagnosing 112. Wetherby AM, Watt N, Morgan L, Shumway S. Social
autism spectrum disorder in pre-school children using two communication profiles of children with autism spectrum
standardised assessment instruments: the ADI-R and the ADOS. disorder late in the second year of life. *J Autism Dev Disord.*
J Autism Dev Disord. 2008;38:362–372. 2007;37:960–975.
129. Ventola PE, Kleinman JM, Pandey J, et al. Agreement among 113. Wetherby AM, Brosnan-Maddox S, Peace V, Newton L.
four diagnostic instruments for autism spectrum disorders in Validation of the infant-toddler checklist as a broadband
toddlers. *J Autism Dev Disord.* 2006;36:839–847. screener for autism spectrum disorders from 9 to 24 months of
130. Wiggins LD, Robins DL. Brief report: excluding the ADI-R age. *Autism.* 2008;12:487–511.
behavioural domain improves diagnostic agreement in toddlers. 114. Swinkels SH, Dietz C, van Daalen E, Kerkhof IH, van Engeland
J Autism Dev Disord. 2008;38:972–976. H, Buitelaar JK. Screening for autistic spectrum in children
131. Chawarska K, Klin A, Paul R, Volkmar F. Autism spectrum aged 14 to 15 months. I: The development of the Early
disorder in the second year: stability and change in syndrome Screening Of Autistic Traits Questionnaire (ESAT). *J Autism*
expression. *J Child Psychol Psychiatry.* 2007;48:128–138. *Dev Disord.* 2006;36:723–732.
132. Eaves LC, Ho HH. The very early identification of autism: outcome 115. Osterling J, Dawson G, Munson J. Early recognition of one-year-
to age 4 1/2–5. *J Autism Dev Disord.* 2004;34:367–378. old infants with autism spectrum disorder versus mental
133. Turner LM, Stone WL, Pozdol SL, Coonrod EE. Follow-up of retardation: a study of first birthday party home videotapes.
children with autism spectrum disorders from age 2 to age 9. *Dev Psychopathol.* 2002;14:239–251.
Autism. 2006;10:243–265. 116. Dietz C, Swinkels S, van Daalen E, van Engeland H, Buitelaar
134. Kleinman JM, Robins DL, Ventola PE, et al. Diagnostic stability JK. Screening for autistic spectrum disorder in children aged
in very young children with autism. *J Autism Dev Disord.* 14 to 15 months: population screening with the Early
2008;38:606–615. Screening of Autistic Traits Questionnaire (ESAT). design and
135. Charman T, Taylor E, Drew A, Cockerill H, Brown J-A, Baird G. general findings. *J Autism Dev Disord.* 2006;36:713–722.
Outcome at 7 years of children diagnosed with autism at age 2: 117. Lord C, Rutter M, Le Couteur A. Autism diagnostic interview
predictive validity of assessments conducted at 2 and 3 years of revised: a revised version of a diagnostic interview for
age and pattern of symptom change over time. *J Child Psychol* caregivers of individuals with possible pervasive developmental
Psychiatry. 2005;46:500–513. disorders. *J Autism Dev Disord.* 1994;24:659–685.
136. Charman T. Screening and surveillance for autism spectrum 118. Lord C, Rutter M, DiLavore P, Risi S. *Autism Diagnostic*
disorder in research and practice. *Early Child Dev Care.* 2003; *Observation Schedule-WPS Edition.* Los Angeles: Western
173:363–374. Psychological Services; 1999.
137. Yirimya N, Ozonoff S. The very early autism phenotype. 119. Lord C, Risi S, Lambrecht L, et al. The autism diagnostic
J Autism Dev Disord. 2007;37:1–11.