

Screening for Autism Spectrum Disorders in Young Children: A Review

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Introduction

Autism Spectrum Disorders (ASDs) are severe disorders of development affecting many children throughout the world; current prevalence estimates in the US range up to 1 in 150 (Fombonne et al., 2006)⁴⁰⁾. There is clear evidence that early detection and intervention can lead to substantially better prognosis (Filipek et al., 2000; Harris & Handleman, 2000; Howard et al., 2005; Lord & McGee, 2001; Myers, Johnson et al., 2007; Sallows and Graupner, 2005)^{37,50,54,73,84,100)}. Early educational intervention optimizes long-term prognosis, including successful inclusion in regular education classroom (Eaves & Ho, 2004; Lord, 1995; Prizant & Wetherby, 1988)^{32,70,91)}. Children with autism who develop early language have better prognoses, and children who receive early intervention are more likely to develop communication (Jocelyn et al., 1998; Siegel et al., 1988)^{56,104)}. Interventions for children with ASD may show diminishing returns as the child gets older (Mars et al., 1996)⁸¹⁾, reinforcing the importance of starting intervention early. Since interventions do not usually begin before diagnosis, early screening and diagnosis are crucial (Filipek et al., 1999)³⁶⁾. Repeated screening at pediatric visits lowers the age at which children are referred for intervention, and boosts intervention rates to be consistent with prevalence rates (Pinto-Martin et al., 2005; Earls & Hay, 2006)^{90,31)}. Recently published guidelines by the American Academy of Pediatrics, (Filipek et al., 1999; AAP, 2006; Glascoe, 2005; Johnson, Myers et al., 2007)^{36,110,42,57)}, conclude that the positive effect of early diagnosis far outweighs the negative effects, and families express the desire to be informed as early as possible.

The American Academy of Pediatrics (Johnson & Myers, 2007)⁵⁷⁾ has recently recommended that children *suspected* of ASD be sent for early intervention, without

waiting for a formal diagnosis. This is a laudable goal, since many children wait for long periods of time to get a diagnosis, and currently, early intervention agencies may provide minimal or no services without a diagnosis. However, it is not clear how the early intervention system in the US will meet the burden of providing intensive services for all of these children, since they are already stretched to provide adequate services to children who have been formally diagnosed. Johnson and Myers (2007)⁵⁷⁾, speaking for the AAP, recommend that if either 3 risk factors (older sibling with ASD, parent concern or other caregiver concern, physician concern) *or* a positive screen for ASD, are present, referral for expert autism evaluation, audiology, and early intervention (or school program) be made. This seems a prudent course, which will allow most children at risk for ASD to be detected and treated early. However, there is no widely accepted, fully validated screener for ASD, and the AAP recommendations would seem to depend at least in part on the accuracy of the formal screening process. In what follows, we will review some of the current candidates for autism screening instruments, and discuss some of the theoretical and practical issues surrounding their use. These issues include the best age for screening, the validity of early diagnosis and the utility of diagnostic instruments for very young children, the use of parent report vs. clinician observation, general developmental surveillance vs. standardized autism-specific screening, barriers to standardized screening, and cultural issues in screening.

What is the best age for autism screening?

Evidence of neurobiological abnormalities in the first year of life (Courchesne et al., 2004)²¹⁾ as well as retrospective evaluation of infant behavior (Baranek, 1999; Osterling & Dawson, 1994)^{4,86)}, suggests that symptoms of ASD may often be present by

12 months. The average age at which parents first report concerns is generally around 17-18 months (and recent data suggests some initial parental concerns at 14-15 mos, with some below 11 mos (Chawarska et al., 2007a)¹⁸⁾ – but in the US, most children are not diagnosed until age 4 or later; this is especially true for urban children of low socioeconomic status (Fombonne et al., 2001; Howlin and Asgharian, 1999; Mandell, et al., 2002; Pinto-Martin, et al., 2005; Wiggins, Baio, & Rice, 2006; Williams & Brayne, 2006a; Zwaigenbaum et al., 2007)^{39,55,78,90,126,128,133)}.

Researchers have identified some potential tools for the identification of ASD in younger children. Infants who go on to develop autism display less eye contact and diminished social responsiveness and are less likely to demonstrate vocal or motor imitation (Dawson, 2000; Volkmar, Chawarska & Klin, 2005)^{26,116)}. Retrospective studies of home videotapes also indicate that autism can sometimes be detected in children younger than 12 months. Werner, Dawson, Osterling, & Dinno (2000)¹¹⁹⁾ found that infants with autism are less likely to orient to their name and can be distinguished from typically developing infants at eight to ten months. Osterling and Dawson (1994)⁸⁶⁾ studied first birthday home videotapes and identified reliable differences between infants with autism and typically developing infants in showing behaviors, pointing, and orienting to speech. They report that the frequency with which the child looked at others served as the single best predictor of a later ASD diagnosis. Zwaigenbaum et al. (2005)¹³²⁾ found that abnormal ability to disengage and move one's focus of attention may occur in infants who go on to develop ASD. Despite work in these and other labs to identify signs of risk for autism in the first year of life, findings remain at the level of

group differences; there is, as yet, no group of biological or behavioral signs that are valid for identifying risk at the level of the individual child in the first year of life.

Currently, no reliable biological markers for ASDs have been identified (Volkmar, Lord, Bailey, Schultz, & Klin, 2004)¹¹⁵⁾ (although accelerated head growth in the first two years is a marker of elevated risk, see below); this means that autism screeners must focus on specific observable behaviors in order to identify children at risk for ASDs. Most of the evidence about the efficacy of early screening applies to children above the age of two, and since the clinical presentations of autism may differ by age, screening procedures that work for older children may not be valid in younger age groups (Pandey, Wilson, Verbalis & Fein, 2008)⁸⁹⁾. Research has shown that two-year-old children with autism present primarily with symptoms from the social and communication domains, particularly with negative symptoms such as delayed speech, decreased imitation and pointing, and a lack of eye contact and symbolic play. The positive symptoms (unusual sensory and motor behavior and resistance to change) may not yet be present, which can make early screening difficult (Filipek et al., 1999)³⁶⁾. Stone et al. (1999)¹⁰⁷⁾ found that impaired use of nonverbal behaviors, delayed speech, and deficits in social and emotional reciprocity were the most prevalent characteristics in young children with autism; behaviors from the domain of repetitive interests and activities were endorsed with less consistency for this age group, which suggests that these behaviors may have limited utility in identifying two year olds with ASDs.

Another difficulty with screening before age two is the possibility of a higher false positive rate for the youngest children (Charwarska et al., 2007a)¹⁸⁾. Although screening data on very young children is quite limited, the fact that some children show

early developmental concerns that later resolve suggests that false positive rates may be higher for this age group (Dietz, Swinkels, van Daalen, et al., 2006)²⁸⁾. Many clinicians are concerned that this high false positive rate will raise unnecessary concerns and that parents of children who are screened and incorrectly suspected of an ASD may suffer unnecessary distress (Williams & Brayne, 2006a)¹²⁸⁾. However, recent research suggests that the high false positive rate in the younger age group is unlikely to raise unnecessary concerns for caregivers because the majority of the children who falsely screen positive for ASD are not typically developing. Pandey et al. (2008)⁸⁹⁾ reported on a large sample of younger (16-23 months) and older (24-30 months) low-risk (unselected population screen) and high-risk (referred for early intervention but not yet diagnosed) children who were screened with an autism specific screener (the Modified Checklist for Autism in Toddlers (M-CHAT)). While positive predictive power (PPP) was good for the high-risk younger group, and for the high-risk and low-risk older groups, PPP was only .28 for the younger low-risk group. However, 72% of this group were diagnosed with a specific developmental disorder (ASD, language delay, or global developmental delay), and only 8% of the false positive children were judged to be typically developing. Therefore, unnecessary alarm is not likely to be a serious risk for the large majority of even the young low risk children.

One likely reason for the lower specificity and higher false positive rate in the youngest age groups is that a significant number of typical children may show mild, transient delays in language and joint attention, or that normal development includes significant variation in the age at which language and joint attention milestones are

achieved. These children may screen positive for possible ASD at age 12-15 months, but then catch up by 18 months.

Another risk associated with screening before age two is that the screening will miss children who regress after they are screened. A subset of young children, around 20-40%, who are later diagnosed with ASD, appear to develop typically and then show a regression and later emergence of autistic symptoms (Werner & Dawson et al., 2005; Volkmar, Chawarska & Klin, 2005)^{121,116}). However, most cases of regression occur before age two, with an average onset between 15 and 21 months., These children would likely be identified by screening at 24 months (Lord, Shulman, & DiLavore, 2004; Bryson et al, 2007; Landa & Garrett-Mayer, 2006; Baird et. al., 2000)^{74,13,67,3}). Screening at 24 months rather than 18 months may have improved sensitivity due to the fact that children who regress after 18 months will be identified at 24 months (Robins, Fein, Barton & Green, 2001)⁹⁴). Additionally, regression after the age of two is seldom missed by parents or professionals. Therefore, one screening at 24 months, or screening at both 18 and 24 months, is likely to identify the largest number of children without compromising specificity.

In the United States, well-child visits are advised at 18 and 24 months and the American Academy of Pediatrics recommends autism specific screening at these ages (AAP, 2006; Gupta et al, 2007; Johnson et al, 2007)^{110,48,57}). A recent study (Rydz et al., 2006)⁹⁸) confirmed the feasibility of an 18-month autism screening in a pediatric setting (90% of parents participated) but reported a sensitivity that was not satisfactory for a one-time screening of development. These findings suggest that two-point screening may be

more effective at identifying ASDs than a one-time screening. However, a two time point screening is more costly and may not be feasible for a general population model.

There are drawbacks and benefits to screening at different ages and the best age for autism screening may have to be identified by a series of longitudinal studies that screen and follow a cohort of children over many years (Charman et al., 2001)¹⁵⁾. At present, the data seem to support screening at both 18 and 24 months, as recommended by the AAP. If only one screening is done, 24 months will be more accurate than 18 months, while still allowing for intervention to begin quite early.

Validity of Early Diagnosis

One barrier to screening at age 18 or 24 months is the belief that a diagnosis of ASD made at that age, or shortly thereafter, will not be reliable or valid. However, a growing literature indicates that a diagnosis of autism is valid and stable when the diagnosis is made as young as age two (Baird et al., 2000; Baron-Cohen et al., 1996; Charman et al, 2005; Kleinman et al., 2007a; Lord, 2005; Robins, Fein, Barton & Green, 2001; Stone, Coonrod, & Ousley, 2000)^{3,6,16,61,75,94,108)}. In a follow up study of children referred for possible autism, Lord (1995)⁷⁰⁾ reported that 88% of a sample of 16 children who were diagnosed at age two with Autistic Disorder received an independent confirmatory diagnosis of at age three. Similarly, Stone et al. (1999)¹⁰⁷⁾ reported that 95% of a sample of 37 children diagnosed with ASD at age two retained the diagnosis at a one year follow up. However, the research suggests that while a diagnosis of Autistic Disorder is generally stable over time, a diagnosis of an autism spectrum disorder, such as pervasive developmental disorder not otherwise specified (PDD-NOS), is less stable. In a sample of 172 children, Lord (2006a)⁷⁶⁾ found that diagnostic stability at age nine

was very high for those with a diagnosis of autism at age two, but it was less high for those who had received a diagnosis of PDD-NOS. However, Chawarska et al. (2007b)¹⁹⁾ noted that children in their study had a high short-term stability of PDD-NOS.

Stone, Lee, Ashford et al (1999)¹⁰⁷⁾ and others found that several of the diagnostic criteria for ASD in the DSM-IV cannot readily be applied to children under 3 years old. In particular, stereotyped motor behaviors and resistance to change may not appear until later (if they do appear in 2-year-olds, they may be confirmatory of a diagnosis of ASD, but children with mental retardation or sensory impairments may also engage in such stereotyped behaviors). In addition, elaborate pretend play is not developmentally expected at this age, especially in the presence of general developmental delay, nor is good conversational ability, and language is often too sparse to judge whether repetitive language is present. Therefore, Stone et al suggest the following four criteria for a “provisional” diagnosis of ASD at that age: three of the four social criteria (nonverbal communication, joint attention, and emotional reciprocity, but not impaired peer relationships), and language delay. Although these criteria have not yet been adopted by the APA or incorporated into a new DSM, if all four criteria were met, the child would meet criteria for PDD-NOS, so the current practitioner can use them in this way.

Several authors have attempted to discern which of the commonly used diagnostic tools are most valid for use with young children. Measures such as the Autism Diagnostic Observation Schedule (ADOS), Childhood Autism Rating Scale (CARS) and clinical judgment, which permit a diagnosis of PDD-NOS, appear to be more valid for use with young children than measures such as the ADI-R which include only classification as Autistic Disorder vs. non-autistic (Klin, et al, 2000, Lord et al, 2000a, Ventola, et al

2006)^{64,71,113}). This limited validity with the youngest children appears to be due primarily to the fact that ADI-R autism requires the presence of repetitive behaviors or restricted interests. Several authors have reported that a significant number of young children who later receive a diagnosis of an autism spectrum disorder, do not exhibit restricted or repetitive behaviors at age 2 (Cox et al, 1999; Lord, 1995; Lord & Richler, 2006b; Stone et al 1999)²³⁹⁷⁰⁾⁷⁷⁾¹⁰⁷⁾. When repetitive behaviors and/or restricted interests are evident in young children, they may be associated with more negative long-term outcomes (Lord et al, 2006a)⁷⁶⁾. Conversely, when those behaviors are not evident at two, there is no guarantee that they will not develop later.

Cox et al (1999)²³⁾ report on a study of children aged 20-21 months, in which they assessed agreement between the ADI-R and clinical judgment based on DSM-IV criteria. They found that the social and communication domains of the ADI-R agreed with clinical judgment, but the repetitive behavior domain did not. Cox and colleagues further reported that when they reduced the criteria for the repetitive behavior domain, sensitivity of the ADI-R improved but specificity was reduced. Saemundson and colleagues (2003)⁹⁹⁾ reported similar results using the ADI-R and the CARS in a sample of slightly older children. Ventola et al (2006)¹¹³⁾ reported on a study of 45 toddlers with a mean age of 22 months (range =16-31 months). They calculated agreement between the ADOS-G, the CARS, the ADI (either Revised version or Toddler form) and clinical judgment based on DSM IV. Ventola reports significant agreement for the diagnosis of autistic disorder between the ADOS and the CARS, between the ADOS and clinical judgment and between the CARS and clinical judgment. There was not significant agreement between the ADI-R and any of the other measures. In a second series of analyses, Ventola

calculated sensitivity estimates for the ADOS, the CARS and the ADI-R as compared to clinical judgment. Both the ADOS and the CARS had high sensitivity rates (.97 and .89 respectively) while the ADI-R had relatively poor sensitivity (.53). Chawarska, Klin et al, (2007b)¹⁹⁾ reported similar findings.

In addition to concerns with the utility of repetitive behaviors as a criterion for diagnosis, several caveats in the use of any diagnostic tool with young children seem warranted. First, diagnostic accuracy is improved when information is gathered from multiple sources and through the use of multiple tools. Second, all currently available tools, with the exception of those designed for use with infants, require that children have a mental age of 15 months or greater. Using tools such as the ADI-R or the ADOS in children younger than 15 months may result in misdiagnosis of children who have significant developmental delays but who do not have autism (Bishop, Luyster, Richler & Lord, 2008)¹¹⁾.

Specific Screening Instruments for Autism

Increased awareness of the importance of early detection of ASD has led to the development of several screening tools. Most of these have strong evidence of inter-rater and test-retest reliability, and consistently distinguish children with ASD from children with typical development; many of the measures distinguish children with ASD from children with other developmental delays as well. One shortcoming in the development of most of these measures is that they have been used to identify children with ASD from a sample of children with known or suspected disabilities. Few of the measures have been evaluated as population screens that could identify children from an unselected group. Even fewer have been evaluated longitudinally in order to identify false negative or false

positive results. While more research is needed on all of the existing measures, considerable progress has been made in this area in recent years. The following discussion is not an exhaustive list of such screeners; additional ones are appearing in the literature on a regular basis.

The first screening tool designed to identify symptoms of autism in toddlers in the general population was the *Checklist for Autism in Toddlers (CHAT)*, developed for use by home health visitors in the United Kingdom (Baron-Cohen et al, 1992)⁵⁾. The CHAT included nine parent report items, and five items observed by health visitors. Initial reports based on a population study of 16,000 children suggested that most of the children identified by the measure as being at high risk for autism (n=10) received a diagnosis of autism; the remainder of children identified by the CHAT received a diagnosis of developmental delay (n=2). Follow-up of the population sample, however, revealed poor sensitivity, such that approximately 62-80% of children who later received a diagnosis of autism were missed by the CHAT (Baird et al, 2000; Baron-Cohen et al, 2000)^{3,7)}. Charman and Baron-Cohen (2006)¹⁷⁾ note that the original CHAT asked parents if their children had *ever* engaged in behaviors of interest. They suggest that potential reasons for the low sensitivity of the CHAT may include the fact that parents of children with ASD positively endorsed typical behaviors even if those behaviors occurred very rarely, and that typical behaviors may be observed in children with ASD but with diminished frequency. Baron Cohen et al (2002)⁸⁾ addressed these concerns in a revision of the CHAT called the Quantitative Checklist for Autism in Toddlers. The Q-CHAT contains 25 items including several reflective of behaviors from all three domains specified in the diagnostic criteria for ASD, and it offers a five point response format,

ranging from 1 (no symptoms) to 5 (maximal symptoms). Initial pilot data suggest that children with ASD score higher on the Q-CHAT than unselected controls, and autism symptoms as indexed by the Q-CHAT appear to be normally distributed in an unselected population. The authors are currently conducting a large scale epidemiological study to study the utility of the Q-CHAT as a population screening tool for ASD (Allison, et al, 2008)²⁾.

The CHAT was adapted for use in the United States by Robins et al (2001)⁹⁴⁾. This group retained the original 9 parent report items, eliminated the home visitor observation, and added fourteen parent report items, mostly related to early social-communication and joint attention. The *Modified Checklist for Autism in Toddlers (M-CHAT)* is a 23 item (yes/no) parent report checklist designed to identify signs of ASD in children aged 16-30 months. In an initial study of 1122 unselected children and 171 children referred for early intervention services, the M-CHAT successfully identified children with autism at age two. The authors selected six items which loaded most highly on discriminant function analyses as critical items. Failure on any three items from the entire screen or any two critical items resulted in a positive screen. Although final estimates await follow-up data, discriminant function analysis found high classification accuracy, but PPP was estimated at .36, which is quite low. A follow-up interview was added to the screening protocol to provide additional clarification for children who failed the initial screen. That procedure resulted in a decreased false positive rate and yielded an estimate of .68 for PPP. Most of the children diagnosed with autism in this study came from the high-risk group, so the authors could not fully address the utility of the measure in an unselected population.

A second study by the same group (Kleinman, et al 2007b)⁶²⁾ attempted to address that question and reported M-CHAT data from 3793 new children, most of whom (3,309) were screened by pediatricians during well-child visits. The remainder of the sample (484) were screened during intake with an early intervention service provider. The authors replicated reliability estimates from the earlier study and reported internal consistency estimates of .85 for the entire M-CHAT and .85 for the six critical items. Three hundred eighty five children screened positive on the M-CHAT, and 137 of those received a diagnosis of autism, resulting in a PPP of .36. When the follow-up interview was added to the screening process, 185 children screened positive on both the M-CHAT and the follow-up interview. Of those children, 137 were diagnosed with ASD, which resulted in a PPP of .74. Estimates of PPP for children from the high risk and low risk samples were compared. When the follow-up interview was included as part of the screening, PPP for children from the high-risk sample was .76; PPP for children from the low risk sample was .65. Without the follow-up interview, PPP for the high-risk group was .60. PPV for the low risk group was unacceptably low at .11, suggesting that the follow-up interview was especially important for the unselected sample. Kleinman et al (2007b)⁶²⁾ compared children from the high and low risk samples and noted that while the non-ASD high and low risk children differed on multiple variables, the ASD high and low risk children showed no significant differences, suggesting that the M-CHAT is detecting very similar children from the high and low risk populations.

Kleinman, et al (2007b)⁶²⁾ also reported on a follow-up of 1416 children from the original sample described in Robins et al, (2001)⁹⁴⁾. Of the 2,469 children old enough for re-screening, data were collected from 1,416 (57%). Of the 161 children who were

evaluated at Time 1, 120 (75%) were re-evaluated at age four. In addition 11 children were evaluated at time two because they had failed a screener at time 2 or were suspected of having autism in the interim by their healthcare professional. Of the new sample of 131 children, 80 received an ASD diagnosis, 39 received another diagnosis, and 12 received no diagnosis. Based upon the screening results at Time 1 and the evaluation results at Time 2, PPP was .38 for the M-CHAT alone. When the follow-up interview was included as part of the screening, PPP improved to .59 from Time 1 screening to Time 2 evaluation. As noted above, children who passed the M-CHAT at time 1 were re-screened by mail at Time 2 and additional efforts were made to identify missed children. Fifteen possible misses were identified, all of whom were evaluated, and 7 received a diagnosis of an ASD. Thus of the 80 children diagnosed with ASD at Time 2, 7 had been missed at Time 1. While it was not possible to evaluate all of the children who screened negative on the M-CHAT at Time 1 to identify all potential misses, the authors suggest that the value of 91% of children detected might be considered an upper limit of sensitivity.

Recently several additional investigators have reported on the psychometric properties of the M-CHAT in the United States and in other countries. Fine, Weissman, Gerdes and colleagues (2005)³⁸⁾ used the M-CHAT successfully to screen children with 22q11.2p deletions for autism. Eaves, Wingert and Ho (2006a)³³⁾ examined the M-CHAT in a group of 84 children aged 24-48 months referred to a specialty clinic for possible autism. They report that 64% of the children who failed the M-CHAT were diagnosed with autism, and the majority of the remainder had more than one diagnosis including developmental delay and language disorder. They report that the sensitivity of the M-

CHAT was .92 for the total score, but specificity was low at .27. Follow-up questions were not used to reduce false positives.

The M-CHAT and the CHAT have also been translated into Chinese and used with a sample of 212 children with mental ages of 18-24 months, about half of whom were diagnosed with an autistic spectrum disorder (Wong, et al 2004)¹³¹⁾. These authors compared the 23-item parent report scale and their 4-item observation measure. They report that failure on any three M-CHAT items resulted in sensitivity of .839 and specificity of .848, while failure on any two of the four observation items yielded sensitivity of .736 and specificity of .912. They also used discriminant function analyses to select items which best identified children with autistic spectrum disorders. The authors identified seven items which overlapped to a considerable extent with the six critical items identified by Robins et al. Like Baron-Cohen et al (2002)⁸⁾, Wong et al initially converted the parent response items to a dimensional scoring system, but they later collapsed the dimensions into a pass/fail format. Wong et al recommend using the M-CHAT as an initial screen to be followed by observation of those children who fail the screen. Children who fail two of the four observation items should be referred for comprehensive evaluation.

Kamio and Inada (2006)⁵⁹⁾ constructed a Japanese version of the M-CHAT and assessed it with a sample of 659 children coming for a health screening at 18 months of age, in Japan. They used the screener in a two-stage procedure, as do the American authors, with an initial parent form, and a follow-up interview to probe the failed items. Fifteen children screened positive and were given diagnostic evaluations; of these 15 children, 11 were diagnosed with an ASD, resulting in a PPV of 73.3. Items found to be

most discriminating of ASD related to social interest, imitation, joint attention, pretend play, and language. Thus, as with the Chinese study, the most critical items were similar to, although not identical to, the critical items found by Robins et al (2001)⁹⁴⁾ and tapped the same domains, primarily social.

Most recently, the M-CHAT has been used in a study of 228 children, about half of whom screened positive for ASD, in nine Arabic speaking countries (Seif, et al, 2008)¹⁰⁸⁾. The authors report sensitivity of .86, specificity of .80 and positive predictive value of .88, but their study did not include a population sample.

The Early Screener for Autistic Traits (ESAT) (Deitz, Swinkels, van Daalen, van Engeland & Buitelaar, 2006)²⁸⁾ is a level one screener designed for use with 14-15 month old children, which has been studied in a population sample. The ESAT consists of fourteen parent report items, which include a variety of play skills, as well as items reflective of early social communication. Dietz et al screened 31,724 Dutch children in a two-part process. Initially children were screened at well baby visits using a four-item questionnaire administered by physicians. A psychologist using the 14-item ESAT then evaluated children who screened positive in their homes. Children who failed three or more items were invited for a comprehensive psychiatric evaluation. Eighteen children with ASD were detected and an additional 55 children were identified as having developmental concerns. This yields a PPP of .25, although none of the children identified by the ESAT were typically developing. Children who received an ASD diagnosis were re-evaluated at age 42 months, and stability of diagnosis was observed in 14 of 16 children. Two children no longer met criteria for an autism diagnosis; in addition, two children met criteria for a diagnosis at age 42 months, but not at the earlier

assessment. The authors report that the tool is a promising screener, but they note concerns with the false positive rate, and with the fact that many parents declined further evaluation at each stage of the process (31% declined following prescreening and 27% following screening with the ESAT). Comparison of the number of cases detected by the ESAT with prevalence figures cited by the author suggests that the sensitivity of the test may be low. In addition, the requirement that a mental health professional administer the measure reduces its utility as a screening tool.

The *Social Communication Questionnaire (SCQ)*, is a 40 item parent report measure, originally designed for use with children aged four and older (Berument, et al, 1999)¹⁰. It is based on the Autism Diagnostic Interview – Revised, and was originally titled The Autism Screening Questionnaire. Despite early evidence of strong psychometric properties with older children, data regarding the use of the SCQ with younger children has been less compelling. Eaves et al (2006a)³³ report sensitivity of .74 and specificity of .54 using the SCQ with a sample of 94 children aged 39 to 75 months. In a second study Eaves, et al. (2006b)³⁴, described the use of the SCQ in 151 children aged 36-82 months, about a third of whom had ASD diagnoses. They report sensitivity and specificity estimates of .71 and .79 respectively, with lower estimates for children with high verbal IQs. Allen et al (2007)¹ present data from a sample of 81 children aged 26-84 months, referred for assessment. They report that sensitivity and specificity estimates for the entire sample were .93 and .58 respectively, but estimates for the subgroup of children aged 2-3 years were .89 and .29 respectively. Wiggins, Bakeman, Adamson & Robins (2007)¹²⁷ examined screening validity of the SCQ in a sample of very young children referred for early intervention. They report that the recommended

cut-off score of 15 yielded sensitivity of .47 and specificity of .89. When they adopted a lower cut-off score of 11, sensitivity and specificity improved to .89 and .89 respectively. They suggest that researchers who use the SCQ with young children should consider a lower cut-off score.

The *Developmental Behavior Checklist – Early Screen* is a 17-item parent report measure, which consists of items empirically selected to differentiate children with autism and developmental delay from children without autism (Gray and Tonge, 2005)⁴⁵. Items were selected originally from the Developmental Behavior Checklist, a broad measure of emotional and behavioral problems in children with intellectual delays. Gray et al (2008)⁴⁶ report on a study of 207 children aged 20-51 months, who were referred for assessment due to suspected developmental concerns. About two thirds of the sample subsequently received a diagnosis of an ASD. Children were regarded as screening positive if they attained a score greater than 11 on the DBC-ES. The measure yielded strong internal consistency estimates of reliability and good agreement between parents. Comparison of DBC scores with diagnosis based upon clinical judgment yielded a sensitivity estimate of .83 and a specificity estimate of .48. The study is limited by the fact that the data were collected from a sample of children suspected of having significant delays, and not a community sample, and no data regarding long-term follow-up are yet available.

The *Communication and Symbolic Behavior Scale – Developmental Profile* (CSBS-DP) is a three part system designed to identify communication delays in children between the ages of 6 months and two years (Wetherby & Prizant, 2002)¹²². It includes a 24-item parent questionnaire, the Infant-Toddler Checklist, which serves as a level one

screen, although this tool is not specific to ASD. Children who screen positive on this measure are administered a more detailed Caregiver Questionnaire and an observational assessment of social communicative behaviors and interactive and symbolic play. The latter assessment is videotaped and coded for 29 items, known as the Systematic Observation of Red Flags (SORF). Wetherby et al (2004)¹²³⁾ evaluated the SORF in a sample of 3,021 children between the ages of 12 and 24 months, who were not previously identified with developmental delays, and an additional five children with known developmental delay. She identified a sample of 18 children with ASD, 18 children with developmental delay and 18 typically developing children, and coded SORF items from videotapes of the CSBS-DP behavioral sample. Inter-rater reliability was excellent for trained raters (mean Cohen's Kappa = 0.94) and significant differences between the groups were found on 13 of the 29 items. Discriminant function analysis using those 13 items resulted in correct classification of all children with ASD and typical development, and 15 of 18 children with Developmental Delay. While these data suggest that the SORF may be sensitive to ASD in children between the ages of 2 and 3, replication with an independent sample as well as further study with a community sample are warranted. In addition, the SORF is labor intensive and serves as a level two screen.

The *Pervasive Developmental Disorders Screening Test II* (PDDST-II) is a multi-stage screening tool developed by Siegel and colleagues (Siegel, 2004)¹⁰⁵⁾. Stage 1 of the measure includes 22 items descriptive of typical behavior in 12-24 month old children and is designed for use as a level 1 screen in primary care settings. Siegel evaluated the measure in 681 preschool children referred for suspected autism and 256 preterm infants

and reports sensitivity of .92. The PDDST-II Stage 2 is a 14-item screen designed for use in developmental clinics to distinguish children with ASD from those with other developmental delays. Siegel (2004)¹⁰⁵ reports sensitivity of .73 and specificity of .49 based on 490 children with confirmed ASD and 194 children with suspected ASD not confirmed. Stage 3 is a 12-item screen designed to be administered in autism clinics to distinguish children with autism from those with other autism spectrum disorders. Reported sensitivity and specificity are .58 and .60 respectively (Siegel, 2004)¹⁰⁵ .

The *Screening Tool for Autism in Two Year Olds (STAT)* (Stone et al, 2000; Stone et al, 2004)¹⁰⁸⁾¹⁰⁹ was designed as a level 2 screen to distinguish children with ASD from children with other developmental concerns. It includes twelve behaviors to be rated from observation of children in a structured play-based interaction and permits classification of children into high risk and low risk categories. A recent evaluation of the measure (Stone et al, 2004)¹⁰⁹ included several samples of children with Autistic Disorder, Pervasive Developmental Disorder and Developmental Delay or Language Impairment. The results suggest that the STAT has very strong test-retest and inter-rater reliability for the high and low risk classification. The study also demonstrated strong agreement between the STAT and the ADOS when the sample included children with autism and those with developmental delay or language impairment. Children with a diagnosis of PDD-NOS were equally likely to be classified as high and low risk on the STAT, suggesting reduced sensitivity for children with PDD-NOS. Sensitivity and specificity were estimated at .83 and .86 respectively. The authors note that additional data regarding the use of the STAT with larger sample sizes and with children matched for mental age are needed, but the measure appears to be highly promising as a level 2 screen.

The *Autism Observation Scale for Infants (AOSI)* is an 18 item observational measure designed to detect early signs of autism in children aged 6-18 months. It includes a set of semi-structured play activities designed to elicit specific behaviors including eye contact, visual tracking, social smiling and social interest. Each item is rated on a 0-3 scale with higher ratings indicating greater deviation from typical behavior. An initial report revealed that the AOSI has good inter-rater reliability and test-retest reliability at 12 months (Bryson, et al, 2007)¹³⁾. A subsequent study of siblings of children with ASD's demonstrated that the AOSI could be used to distinguish siblings with autism from siblings without the disorder as early as 12 months of age. Sensitivity and specificity in this sample are 84% and 98% respectively (Zwaigenbaum et al, 2005)¹³²⁾. Further attempts at replication with nonsibling samples or community samples have not been reported as yet.

A second tool designed to detect autism in 12 month olds has been described by Reznick et al (2007)⁹²⁾. The *First Year Inventory (FYI)* is a 63-item parent report measure designed to assess behaviors that might indicate risk for autism. The FYI was administered retrospectively to parents of three groups of children: those with a diagnosis of an ASD, those with developmental delays but no autism, and typically developing children. The authors report that the children with ASD were rated as being at greater risk than the children with developmental delays, and the latter group was viewed as being at greater risk than the typically developing children (Watson, et al, 2007)¹¹⁸⁾. While these data are encouraging, they await more information regarding sensitivity and specificity, as well as replication with a larger sample.

In addition to the Japanese version of the M-CHAT (see above), the Japanese have also added screening for ASD to their health monitoring system. Honda and Simizu (2002)⁵³⁾ reported on the Young Autism and other developmental disorders Checkup Tool (YACHT) which is administered to children at age 18 months and 36 months as part of a larger health screen. The authors report that sensitivity estimates for the YACHT were as high as 74 percent, although they provide little information regarding the calculation of those figures.

Parent report vs. Clinician Observation

The reader will have noticed that the screening instruments described above use either clinician observation, or parent report, or a combination of both. While it is well established that parent report and clinician observation are essential components for the actual diagnosis of ASD, the relative roles of parents and clinicians in screening are less defined. Parental concern should play a large role in any developmental screening because as Filipek et al. (1999)³⁶⁾ note, if there are parental concerns, there is almost always some type of problem with development. However, parents may not be accurate regarding the nature of the atypical development, and a lack of parental concern does not imply normative development. It is clear that skilled clinical opinion can enhance detection of children with ASDs; Glascoe (1999)⁴¹⁾ cites evidence indicating that using a screening instrument along with asking parents to describe the nature of their concerns improves the efficiency of the screener. However, removing clinician observation from the screening process has significant cost implications for a population based screener and may make screening more feasible for a wider range of children.

When comparing the original CHAT, which required direct assessment by a health practitioner, to a version of the CHAT that consisted only of a parent questionnaire, Baird et al. (2000)³⁾ found that at the high risk cutoff, the sensitivity at the first screen did not differ for the two versions. However, the authors note that parents in their sample did produce some false negatives; some parents reported that their children could point to show interest or exhibit pretend play although these behaviors were not observed by the clinician during administration of the CHAT Stage B screen.

Similarly, when comparing parental report to clinical observation in the diagnosis of autism, Chawarska et al. (2007a)¹⁸⁾ found differences in the severity rating of social behaviors in children diagnosed with autism. Parents rated nonverbal behaviors used to regulate social interactions, such as eye contact, social smiles, and facial expressions, as more typical in their children with autism than did clinicians. Parents also reported better pointing and fewer unusual preoccupations. While these findings related to diagnosis rather than screening, these findings indicate that there may also be important differences between parental report and clinician observation in screening for autism. It is easy to imagine that parents in some cases will rate development as more advanced and symptoms as milder than will a clinician; this might be because of the wider experience of the clinician as well as the possibility that the child shows more consistent or advanced communication skills in the home environment.

Cultural Issues in Early Screening

As the reader will be aware, it is not possible to merely translate psychological tests without regard for differences in language and culture and obtain a valid test. This issue has been addressed by many authors; see, for example, Hambleton, Merenda, &

Spielberger (2005)⁴⁹⁾ for a comprehensive treatment of this issue, as well as the websites of the International Test Committee (http://www.intestcom.org/test_adaptation.htm) and the American Psychological Association. Even when the new application is with a population with the same language but different culture, caution must be used in interpreting test results, and validation must be carried out with the new population.

Very little cross-cultural work has been done on early screening for developmental disorders. Heo et al (2008)⁵¹⁾ reported on a Korean translation and initial test of the Ages and Stages Questionnaire. They translated the instrument into Korean, changing items to accommodate differences in Korean culture, and consulted with developmental experts and parents, as well as the original English authors, to try to retain the efficacy of the screener while accounting for cultural differences. Although there were many similarities in the reliability and validity of the Korean and US versions, there were also significant differences, especially in communication, adaptive skills, and fine motor skills. The authors speculate on some cultural differences, such as Asian parents feeding their children until they are old enough to handle utensils, while American parents allow or encourage self-feeding with the hands, to account for some specific differences in how items were answered and their predictive value.

There are also few studies on the cross-cultural detection of autism specifically. Wong et al (2004)¹³¹⁾ translated the M-CHAT and the original CHAT into Chinese (see above), constructing the “CHAT-23”, and assessed its validity in screening for autism in China. Seven items were found to be the most effective discriminators of ASD: imitation, pretend play, pointing for joint attention, social referencing, bringing to show, following a point, interest in other children. Failing any two of these critical items resulted in a

sensitivity of .931 and a specificity of .768 (of this pre-diagnosed sample). Failing any six of the total 23 items resulted in a sensitivity of .839 and a specificity of .848. Thus, while not identical to the 6 critical items identified by Robins et al (2001)⁹⁴⁾, the critical item set was quite similar, and the instrument had good psychometric properties with this new population. Kamio and Inada (2006)⁵⁹⁾ (see above), also found a highly similar set of most discriminating items, most of which related to joint attention, and the remainder to language and play.

Three preliminary studies have been done in the US on the utility of the M-CHAT with cultural minority families. We investigated whether the M-CHAT seems to be operating differently among minority vs. non-minority American children (Dancel et al., 2008)²⁵⁾. In this sample of 279 children (18% minority), 73% of screen-positive non-minority children received a diagnosis of ASD, compared to 66% of minority children (ns). Total and critical item M-CHAT scores did not differ between groups; only 2 specific items differed on the initial screener, but disappeared when the phone interview follow-up was done. Results are consistent with the possibility that cultural and linguistic factors influence the ways in which underrepresented groups interpret and respond to the M-CHAT items, or that there are variations in the signs/symptoms between ethnic and cultural groups. Despite these possible differences, PPP did not differ between the minority and non-minority children, and providing specific examples on the follow-up interview seemed to eliminate any population differences. Another study (Troyb et al., 2008)¹¹¹⁾ examined age at screening, age at telephone follow-up, and age at diagnosis for minority and non-minority children. Despite the children coming from the same pediatric practices, there were small but significant, and accumulating, discrepancies: the minority

children were screened an average of 47 days older, followed up an average of 62 days later, and evaluated/diagnosed an average of 95 days later. Therefore, disparities exist between Caucasian and non-Caucasian American children in the child's age when screened for ASD, at follow-up and at diagnosis. These differences were not influenced by the socio-economic status (SES) of the families, as measured by family income, but may be the result of cultural dissimilarities in their outlooks on symptoms of first concern or attitudes toward help-seeking, or differences in pediatrician practice with families of different ethnicity; it is possible that practices serving more minority children, which in our study were primarily large inner-city clinics, might be more pressed for time and less consistent with their screening practice. A final study (Wilson et al, 2006)¹³⁰ examined parental satisfaction with the screening and diagnostic process (using the Post-Evaluation Satisfaction Questionnaire, designed for this study). Results indicate that in general satisfaction was high and no dissatisfaction with the screening process was expressed. Caregivers were 'mostly' to 'extremely' satisfied with the screening, diagnostic, and evaluation process (M = 3.42 on a 1-4 Likert scale). Furthermore, satisfaction was higher among lower SES families. No significant relationships were found between child diagnosis and satisfaction. Therefore, parents seem satisfied with the screening process, and overall satisfaction expressed was higher among families of lower SES.

Overall, therefore, very little data exists as yet on how screening for autism is different in different countries, or with different populations, although screening with translated versions of the M-CHAT is ongoing in at least 15 different countries. The little data that are available suggest that specific items may function somewhat differently, and that each application requires investigation of the utility and validity of specific items, but

that overall there seems to be a high degree of cross-cultural applicability to the basic early signs of autism.

General Developmental Screening

Autism screening must be viewed in the context of general developmental screening and surveillance for multiple types of developmental delays and disorders. Brief, repeated surveillance of overall development, coupled with age-targeted formal instrument-based screening has been recommended by pediatric experts on screening (Dworkin, 2007)³⁰⁾. The American Academy of Pediatrics currently recommends general developmental screening at ages 9, 12, 18 and 24 or 30 months, and autism-specific screening at 18 and 24 months (AAP, 2007; AAP, 2006; Johnson and Myers, 2007)^{110,57)}. Of course, ages for screening must depend on when children are seen for well-child visits or developmental check-ups, within each country or region. Recommended tools are described by the AAP (2006)⁵⁷⁾. As with autism screeners, general developmental screeners can rely on physician observation, or on parent report, and within those that rely on parent report, they can rely on expressions of parent concern (e.g. the PEDS; Glascoe, 2006)⁴³⁾ or on parent report of specific milestones (e.g. Ages and Stages; Bricker et al., 1995; the PEDS-Developmental Milestones (Glascoe, 2006)⁴³⁾)

A key empirical question that has not been answered is whether good general developmental surveillance, comprised of physician observation together with eliciting parent concern, can identify developing cases of autism without the use of a screener specific for autism. The previous recommendation of the AAP (2006)⁵⁷⁾ was to use an autism screen *if and when* the child elicited general developmental concern, while the new recommendation is that all children be screened for autism, regardless of pre-

existing developmental concerns. Several US researchers are collecting data that will help determine whether the general screens, such as the PEDS, detect most cases of autism; to date, we do not know the answer to this. One point that seems clear is that use of informal observation alone, with no structured screening leads to an unacceptably low sensitivity of only 20% to 30% for detecting autism (Earls & Hay, 2006; Sand et al., 2005; Sices et al., 2003)³¹⁾¹⁰¹⁾¹⁰⁶⁾. However, use of structured screeners for broad developmental issues, such as PEDS, PEDS-DM, or Ages and Stages might be sufficient to detect most cases of ASD.

Several investigators and clinicians have published guidelines or advice for specific questions to ask parents, or behaviors to observe, in the pediatric visit, in order to detect cases of possible autism. When tracking language development, Johnson (2008)⁵⁸⁾ suggests that pediatricians always ask about language *regression*, since parents may attribute it to an environmental event and not feel it important to mention. Although language regression may be present in other disorders, such as Rett's Disorder and Landau-Kleffner, it often signals autism, and always requires follow-up evaluation.

Greenspan et al (2008)⁴⁷⁾ point out that specific behavioral signs that may be taken as risk factors for autism must be interpreted in context, and that specific behaviors such as reduced eye contact and failure to respond to name might reflect shyness, sensory factors, or family dynamics rather than autism. Therefore, clinical judgment must be applied to judge the *quality* of the abnormal sign (e.g. does the avoidance of eye contact seem secondary to an overall anxious or behaviorally inhibited child, with good eye contact with mother, or does the child seem more oblivious to other people?) and the overall clinical picture.

In following the growth parameters of the child, it should be remembered that the single most replicated *physical sign* of autism is accelerated head circumference in the first two years, with head size generally normal or a bit small at birth (Courchesne, 2003; Dalbec-Mraz, 2007; Johnson, 2008)^{21,24,58}). There is, however, far from a one-to-one correspondence between accelerated head growth and autism; some normal children will show some increase in head circumference, some autistic children do not show this tendency, and some families where the parents have large heads will have normally developing children with large heads. Nonetheless, such acceleration shows striking group differences between typically developing and autistic children, and is present in many autistic children. Head increase which is not so striking as to trigger a neurological exam or MRI may still increase the index of suspicion for autism.

Younger siblings of children with ASD constitute a special case; they require increased vigilance on the part of the pediatrician or other health care professional. The prevalence of ASD in younger siblings of children already diagnosed with an ASD has been cited at about 10%, which is significantly higher than the general population risk. However, in our lab and others currently investigating this question, the risk of ASD in younger siblings is appearing to be even higher (closer to 20%). These have not been epidemiological studies, so it is possible that ascertainment or other biases have resulted in high estimates. It is also the case that younger siblings are at risk for other developmental problems, such as language delays. They may also be at risk for the mildest form of autistic behavior, the “broader autism phenotype”, which in many cases, resolves into normal functioning within a couple of years. It is therefore important for the practitioner to take special care with younger siblings, watching for signs of autistic

behavior, but also milder social delays or oddities, motor delays, and language delays that may benefit from early intervention.

One reason general developmental surveillance is so important is that the significance of autism-specific signs will depend on the mental age of the child. If joint attention behaviors (initiating pointing for joint attention, gaze shifting back and forth to the adult and the object of interest) are not fully developed until 14-16 months in typical development (Johnson, 2008), then a globally delayed child with a chronological age of 18 months but a mental age of 12 months may screen positive on this item (fail to show the behavior) but it will not necessarily signal autism. In order to indicate a true risk for autism on most autism screeners, such as the M-CHAT, the child should have a mental age of about 14-16 months. In many cases of global developmental delay, a child who screens positive on the M-CHAT will go on to merit a diagnosis of ASD, even if the mental age is below 16 months, but the results of such screening should be treated with more caution. In such cases, the social behavior of the child should be interpreted in light of their overall development; if their social behavior seems consistent with their overall developmental level, and much positive affect and emotional connectedness is present, ASD is less likely.

The American Academy of Neurology and Child Neurology Society Practice Parameters on Screening and Diagnosis of Autism (Filipek et al., 2000)³⁷⁾ suggests that the following "red flags" are absolute indications for immediate evaluation: no babbling or pointing or other gesture by 12 months; no single words by 16 months; no 2-word spontaneous (not echolalic) phrases by 24 months; and loss of language or social skills at any age. Johnson and Myers (2007)⁵⁷⁾ suggest, similarly, that general developmental

surveillance should occur at every health maintenance visit throughout childhood and include the following: eliciting and attending to parental concerns; maintaining a developmental history; observing the child; identifying risk and protective factors; and documenting the process and findings. They suggest, further, that the most useful very early signs of autism include: extremes of temperament and behavior (including irritability and passivity); poor eye contact; poor response to other's voices, especially to one's name being called; poor interactive play; more interest in objects than people; delayed pointing to request or share; decreased to-and-fro babbling; and lack of warm, joyful, reciprocating expressions. Johnson and Myers (2007)⁵⁷⁾ conclude that general developmental screening tools are important and appropriate for primary care populations and are likely to detect ASDs in many young children because of associated language and cognitive delays, but they are not specific for ASD and their sensitivity for ASD is unknown.

Barriers to screening

Several barriers to general developmental screening and autism-specific screening have been identified in surveys with physicians. These include: lack of familiarity with available tools, reluctance to rely on parent questionnaires, choosing to refer children to specialists, inadequate time during the visit, and inadequate reimbursement for screening (dosReis et al., 2006; Sices et al., 2003)^{29,106)}. Although pediatrician training on screening can lower the age of diagnosis, Holzer et al. (2006)⁵²⁾ found that this improvement only lasted as long as the awareness program existed. However, in this program, pediatricians were provided with the CHAT, which has a sensitivity of only 20-36% and requires staff observation; providing physicians with a more sensitive parent-report instrument may be

more conducive to ongoing screening. It is apparent that physicians need additional education about the importance and availability of autism specific screeners, and, in countries that rely on insurance payments, such as the US, that reimbursement for screening is essential. Organizations such as the American Academy of Pediatrics, the Centers for Disease Control, and Autism Speaks, are accelerating their awareness and information campaigns and hopefully, these will have a significant effect on screening practices in the US and other countries in the near future.

Conclusions and recommendations

Many questions concerning early autism screening remain unanswered. Among them are: (1) what screening age gives the best balance of accuracy against opportunities for early intervention; (2) can general developmental surveillance detect most cases of autism or are autism-specific screeners necessary; (3) are different questions needed to detect autism in young children in families from different cultures or language communities; (4) what is the most effective balance of clinician observation and parent report.

However, the development of autism screening has advanced to the point where it should be routinely used in pediatric surveillance of development. The advantages so clearly outweigh the disadvantages that universal screening should be a recommended and an achievable goal. The current recommendation of the AAP, that is, ongoing general developmental surveillance from birth into school age, and autism specific screening at 18 and 24 months, is not yet supported by empirical data, but constitutes a cautious and reasonable approach that is likely to detect most cases of ASD and provide early referral for intervention. The availability of effective early intervention, of course, is a separate

matter. Here, too, as with screening, we need a combination of carefully done research and the political will to fund effective intervention, so that the highest possible number of children can reach their full potential.

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