

The Clinician's Guide to Autism

John W. Harrington, MD,*
Korrie Allen, PsyD[†]

Author Disclosure
Drs Harrington and Allen have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Educational Gaps

1. Because 1% to 2% of children will be diagnosed as having an autism spectrum disorder, pediatricians need adequate training in screening and diagnosis, particularly with the changes presented in the *Diagnostic Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). Initiating interventions for autism, both evidence-based and complementary, also requires the pediatrician to be familiar with available treatments.
2. Children with autism are likely to have a co-occurring mental health disorder that pediatricians should be able to recognize so that they can initiate treatment or provide timely referral.
3. Children with autism are less likely to have a medical home when compared with other children with special health care needs.

Objectives

 After completing this article, readers should be able to:

1. Describe the signs and symptoms of an autism spectrum disorder and therefore be aware of the changes recently made to the DSM-5.
2. Be aware of appropriate screening devices for autism and how to use them effectively.
3. Consider a differential diagnosis and initiate an evaluation, as well as provide evidenced-based advice to a patient with newly diagnosed autism.
4. Recognize and provide screening devices for co-occurring mental health disorders in children with autism.
5. Become familiar with common complementary and alternative medicines and therapies.
6. Provide a more comprehensive medical home for children and families with autism.

Introduction

Autism spectrum disorder (ASD) includes a continuum of neurodevelopmental disorders characterized by deficits in social communication and interactions, along with restrictive, repetitive patterns of behaviors, interests, and activities. (For this article, *ASD* and *autism* are used interchangeably.) Pediatric clinicians can significantly affect the outcome of children with ASD by making an early diagnosis and providing referral for evidenced-based behavioral treatment. By recognizing the early signs and symptoms of autism and addressing common comorbid concerns, such as sleep problems, gastrointestinal problems, seizures, and behavioral and psychiatric concerns, as well as being aware of complementary and alternative medicine (CAM) therapies, clinicians can provide a more comprehensive medical home for their patients and parents.

Abbreviations

| | |
|---------|--|
| AAP: | American Academy of Pediatrics |
| ABA: | applied behavioral analysis |
| ADHD: | attention-deficit/hyperactivity disorder |
| ASD: | autism spectrum disorder |
| CAM: | complementary and alternative medicine |
| DSM-IV: | <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> |
| DSM-5: | <i>Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition</i> |
| M-CHAT: | Modified Checklist for Autism in Toddlers |

Epidemiology

Recent data from the National Survey of Children's Health from 2011–2012, which estimates parent-reported ASD

*General Academic Pediatrics, Children's Hospital of The King's Daughters, Department of Pediatrics, Eastern Virginia Medical School, Norfolk, VA.

[†]Department of Pediatrics, Eastern Virginia Medical School, Norfolk, VA.

diagnoses for school-aged children, placed the current prevalence of autism at 2%. (1) However, the Centers for Disease Control and Prevention's Autism and Developmental Disabilities Monitoring Network, which requires more definitive diagnostic testing, estimates the prevalence of ASD in the United States at 1 in every 88 children. Because males outnumber females 4 to 1, this translates into an incidence of 1 in 54 males and 1 in 252 females. (2) This recent estimated prevalence rate represents an increase of 23% compared with the 2006 estimate of 1 in 110 children. With the steady increase during the past 2 decades, ASD has become an urgent public health concern. A recent study by Hallmayer et al (3) of the largest collection of fraternal and identical twins revealed that genetic and environmental factors likely have an equal effect on determining an autism diagnosis with sibling risk rates at or above 25%.

The increase in diagnosis of autism during the last 20 years has raised public concern and questions on possible causes. Reasons for the increase include diagnostic substitution, broadening of the definition of ASD, and better screening and ascertainment. Diagnostic substitution assumes that children previously were diagnosed only as being developmentally delayed and/or intellectually disabled and not appropriately diagnosed as having an ASD. Monitoring networks have allowed multiple records (clinicians and schools) to be reviewed, which has led to better ascertainment of children diagnosed as having an ASD. In addition, concerted efforts by multiple sources (American Academy of Pediatrics, Autism Speaks, and FirstSigns.org) to improve screening at a younger age have had an effect. Finally, the broader definition of autism, now referred to as ASD has allowed more cases of ASD to be diagnosed. The most recent report from the Centers for Disease Control and Prevention indicates that the biggest increase in cases is among the higher-functioning patients with less severe disease and in African American and Hispanic populations. (1)(2)

ASD Symptoms and Signs

Communication, Social Reciprocity, and Repetitive or Restrictive Behaviors

Commonly, the first sign that alerts a pediatric clinician to a child with possible autism is a deficit in communication, manifested by a delay in or abnormal use of language, at approximately ages 18 to 24 months. A child with autism may initially be mute, have a significant delay in language acquisition, or have a regression in language. If the child is speaking, he or she may only exhibit echolalia, repeating words and phrases previously heard. In some instances, children with autism may develop language normally and be

quite verbose, but they only speak tangentially about their specific interests without any concern about the listener's response. Children with autism may also have trouble modulating their vocal tone (ie, monotone), with little inflection in their voice. Because of these deficits in language and reciprocity, many children tend to have an inability to initiate or sustain a conversation with others.

Social reciprocity is the give and take of social interaction and requires the child to have the ability to recognize another person's perspective. Children with autism have difficulty with social reciprocity; thus, they have trouble establishing relationships with same-aged peers. This inability to socially share or reciprocate implies that a child with autism may not empathize well. These social deficits impair one's ability to maintain joint attention (ability to attend to an activity with another person), read body language, and respond to nonverbal cues. A red flag for these difficulties is an inability to point to a desired object at 18 months (protoimperative pointing), but even more important is whether the child uses pointing to draw something to the attention of another, referred to as protodeclarative pointing. Children with autism may pull their caregiver by the hand to a desired object by hand guiding. Direct eye contact may be difficult and avoided by children with autism. A study from Yale compared the eye gaze pattern of children with autism and neurotypical peers during a video simulation of play with an adult. Children with autism tended to spend more time looking at the adult's mouth rather than the eyes, whereas the neurotypical peers spent little time looking at the mouth and most of the time looking at the eyes of the speaker. (4)

The repetitive and restrictive behaviors noted in autism can be the most isolating symptoms of the disorder. Often children strongly desire a rigid routine and are extremely upset if there is deviation from the routine. This reliance on maintaining a nonfunctional routine to avoid conflict can make a family's life stressed. Repetitive motor movements, such as hand flapping or an intense preoccupation with parts of an object, like spinning wheels on a toy car, highlight these behaviors. Children with autism may also have difficulty with onset or maintenance of sleep, as well as restricted food preferences, and hypersensitivity or hyposensitivity to any of the 5 senses. Repetitive and restrictive behaviors along with these sensory issues have gained new prominence and hallmark some of the classification changes recently implemented in the *Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*.

Understanding the DSM-IV to DSM-5 Changes

There had been some debate about the upcoming changes to the *Diagnostic and Statistical Manual of*

Mental Disorders, Fourth Edition (DSM-IV). The newer DSM-5 was accepted and published in May 2013. The DSM-5 merges communication and social interaction behaviors into one symptom category and increases the importance of the repetitive and restrictive behavior into the requirements for a diagnosis of an ASD. The DSM-5 also allows the use of co-occurring diagnoses to exist with autism, whereas before a child under the DSM-IV could not have both autism and attention-deficit/hyperactivity disorder (ADHD). To obtain more specifics concerning the diagnostic features, differential diagnosis, and comorbidities, the reader is referred to the full publication of the DSM-5.

The DSM-5 criteria are listed below (reprinted with permission from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* [Copyright 2013], American Psychiatric Association).

To diagnose an ASD from the DSM-5, a child will need to meet the criteria in A, B, C, D, and E:

“A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following; currently or by history (examples are illustrative, not exhaustive):

1. Deficits in social-emotional reciprocity; ranging, for example, from abnormal social approach and failure of normal back and forth conversation; to reduced sharing of interests, emotions, or affect, to failure to respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction; ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expression and nonverbal communication.
3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

Specify current severity:

Severity is based on social communication impairments and restricted, repetitive patterns of behavior (see Table 1).

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping object, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of environment (e.g. apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

Specify current severity:

Severity is based on social communication impairments and restricted, repetitive patterns of behavior (see Table 1).

- C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Note: Individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger’s disorder, or pervasive developmental disorder not otherwise specified should be given the diagnosis of autism spectrum disorder. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.”

Once the diagnosis of ASD is made, the DSM-5 provides a severity level rating that can be used to help grade

Table 1. Severity Levels for Autism Spectrum Disorder

| Severity Level | Social Communication | Restricted, repetitive behaviors |
|---|--|--|
| Level 3: Requiring very substantial support | Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches. | Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action. |
| Level 2: Requiring substantial support | Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interests, and who has markedly odd nonverbal communication. | Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action. |
| Level 1: Requiring support | Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful responses to social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful. | Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence. |

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the level of functioning for the child. As stated in the criteria for diagnosis, the severity level rating is based on both social communication impairments and restricted, repetitive patterns of behavior but should be rated separately. This process is outlined in Table 1.

It may be tempting to use this severity grading of function to determine eligibility of services for children; however, severity may vary over time and in certain situations, and therefore providing services should be decided on an individual level. Table 2 summarizes specific changes to the DSM-IV in the DSM-5.

The changes in the DSM-5 may help to clarify the diagnostic process for autism, but some opponents to this change are worried that it will decrease the overall incidence by only recognizing the most severely affected,

thus overlooking children who may benefit from autism services. Proponents believe that this will not happen. However, in recent studies using the DSM-5 criteria vs the DSM-IV, up to 48% fewer toddlers would be diagnosed as having autism. (5) Reconciling the new changes to the DSM will be challenging in the next few years, when considering that the previous increase in the incidence of autism during the last 2 decades is still not completely understood.

ASD Possible Causes and Vaccine Concerns

It is well known that certain genetic disorders (eg, fragile X syndrome, neurofibromatosis, and tuberous sclerosis) are more likely to be associated with autism and should

Table 2. Comparison of Changes in the DSM-IV and DSM-5 for ASD

| DSM-IV for ASD | DSM-V Changes for ASD |
|--|---|
| <ol style="list-style-type: none"> 1. Rett disorder 2. Pervasive developmental disorder not otherwise specified, Asperger disorder, and childhood disintegrative disorder 3. Unusual sensory behaviors not part of the criteria. 4. 3 symptom categories (impairment in social interaction, impairment in communication, and repetitive and restrictive behaviors) | <ol style="list-style-type: none"> 1. Rett disorder is eliminated because it is considered a genetic disease 2. These 3 disorders will now officially be called ASD 3. Unusual sensory behaviors will be added to the criteria 4. 2 symptom categories (deficits in social communication and social interaction combined, and repetitive and restrictive behaviors) but more criteria required per category |

ASD=autism spectrum disorder; DSM-IV=*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; DSM-5=*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.

be considered when making a diagnosis of ASD (Table 3). In addition, with refined genetic techniques, such as comparative genomic hybridization microarrays, whole genome linkage, and gene association studies, researchers have found "hot spots" on almost every chromosome that can coincide with either a specific single-nucleotide polymorphism or copy number variant. (6) Interestingly, it is not always the gene but the intervening sequences between genes (introns) and how they are methylated that play a critical role in how genes are turned on and off. However, even with an advanced ability to view up to 10,000 base pairs on the genome, approximately 75% of children diagnosed as having autism have no measurable genetic abnormality when rigorously tested. (7)

Without a consistent genetic association for autism, a search for a possible environmental cause has led some to consider implicating vaccines because these are given throughout early infancy and at the same time when children are diagnosed as having autism. Initially, the measles-mumps-rubella vaccine was linked as a cause of autism through a small, poorly conceived case series by a British gastroenterologist named Andrew Wakefield. This report was later retracted by *Lancet* when it was found to be tainted by inappropriate recruitment and bias. When the measles-mumps-rubella vaccine link was disproven, a recycled theory concerning mercury as a preservative (thimerosal) in multidose vial vaccines became popular as a cause of autism, which was also subsequently disproven. Furthermore, the manufacturers removed thimerosal from their vaccines. Unfortunately, some parents and antivaccine websites still try to manipulate temporal data into causality. It is therefore important for pediatric clinicians to be aware of this misguided information and to be able to counter this argument with the multitude of

studies that have disproven any causal association between vaccines and autism. (8) It is important to make parents aware of the risks of not vaccinating. If a parent is steadfastly against vaccinating their child for fear of causing autism, even after an exhaustive use of evidenced-based data to the contrary, then the American Academy of Pediatrics (AAP) recommends that they fill out a refusal to vaccinate form (<http://www2.aap.org/immunization/pediatricians/pdf/RefusaltoVaccinate.pdf>).

Historically, certain exposures and environmental factors were associated with an increased risk of autism: rubella infection, exposure to thalidomide or valproic acid in the first trimester, and untreated phenylketonuria. A search for additional environmental factors was launched in California in 2000, called the Childhood Autism Risk from Genetics and Environment. Some factors that have been established as incurring risk include prematurity, twins or multiple pregnancy, and advanced maternal or paternal age at conception. A recent study from Denmark also suggested a possible immune response based on prolonged fever in mothers during pregnancy. (9) Currently, no definitive environmental factors can predict diagnosis; therefore, the pediatric clinician's ability to screen children early for autism becomes extremely important.

Screening

The AAP in 2007 recommended to pediatric clinicians that all 18- and 24-month-old children be screened for an ASD. Providing an early diagnosis of autism allows parents to access intensive behavioral treatments (ie, applied behavioral analysis [ABA]) that can ultimately improve a child's overall outcome in language, adaptive behaviors, academic performance, and IQ. Research has confirmed that the diagnosis of an ASD can reliably be made in the

Table 3. Syndromes Associated With Autism^a

| Autism-Related Syndrome | Physical Examination and/or History Findings | Associated Gene(s) | Patients With Syndrome Who Have Autism, % | Patients With Autism Who Have Syndrome, % | Testing to Consider |
|-------------------------|--|-----------------------------|---|---|---|
| Tuberous sclerosis | Ash leaf spots, adenoma sebaceum, shagreen patches, tubers, seizures, and intellectual disability | <i>TSC1</i> and <i>TSC2</i> | 20-40 | 1 | MRI, ophthalmology, cardiac and renal evaluation |
| Neurofibromatosis | 2 criteria of the following: 6 café au lait spots, ≥2 neurofibromas or 1 plexiform, axillary or inguinal freckling, optic glioma, ≥2 Lisch nodules, sphenoid dysplasia or tibial pseudoarthrosis, first-degree relative with neurofibroma type 1 | <i>NF1</i> | 40-50 in some studies | 0.3 | Ophthalmology consultation, MRI, spinal examination for scoliosis, cardiac for murmurs, and blood pressure for hypertension |
| Angelman syndrome | Language and Intellectual deficits, seizures, hypermotoric and ataxic movements, paroxysms of laughter, and happy disposition | <i>UBE3A</i> | 50 | Rare | FISH or microarray testing for 15q11.2-q13, EEG, MRI |
| Fragile X syndrome | Inconsistent physical examination findings, microcephaly and macrocephaly, large jaw, large hands, macro-orchidism | <i>FMR1</i> | 25 (males) and 6 (females) | 1-2 | Fragile X testing looking for CGG repeats >200 |
| Rett syndrome | Regression in development, hand-wringing behavior, female, microcephaly | <i>MECP2</i> | All females, but with DSMV will be considered separate disorder | Rare | EEG, <i>MECP2</i> gene testing |

EEG=electroencephalography; FISH=fluorescent in situ hybridization; MRI=magnetic resonance imaging.

^aOther disorders associated with autism are as follows: 15 q duplication, 16p11 deletion, 22q deletion, cortical dysplasia-focal epilepsy syndrome, Joubert syndrome, Potocki-Lupski syndrome, *PTEN* hamartoma tumor syndrome, Smith-Lemli-Opitz syndrome, trisomy 21, and Timothy syndrome. (5)

second year of life, but the overall predictive reliability and stability of a diagnosis at this age are lower. Children suspected of having an ASD through screening must be further evaluated as soon as possible. The AAP developed Caring for Children with Autism Spectrum Disorders: A Resource Toolkit for Clinicians or more simply the

Autism Toolkit (www.aap.org) as a helpful guide for pediatric clinicians to screen, identify, and treat children with ASDs. The toolkit presents different practical items (clinician fact sheets and parent handouts) that help a primary care physician maintain a medical home for children with autism, discusses autism screening and identification, and

provides the following 3 screening tools (also available separately online) used at different ages (Table 4):

1. Children younger than 18 months can be screened with the Communication and Symbolic Behavior Scales and Developmental Profile.
2. Children age 18 to 30 months can be screened using the Modified Checklist for Autism in Toddlers (M-CHAT).
3. For Preschool and Elementary school children the screen suggested is the Childhood Autism Screening Test.

The Infant Toddler Checklist, also known as the Communication and Symbolic Behavior Scales and Developmental Profile, uses 24 total questions grouped into developmental milestones and social communication. There is also a final free-text question that asks, "Do you have any concerns about your child's development?" (<http://firstwords.fsu.edu/pdf/checklist.pdf>). The checklist has been studied as a broad-based screener for developmental problems and identified problems in 56 of 60 children ultimately diagnosed as having autism from a large population sample. (10) However, it could not easily distinguish between children with autism from children with other communication delays.

The M-CHAT was developed from the previous British version called the CHAT. The M-CHAT uses 23 yes/no questions that expand on the previous CHAT. The difficult aspect of the M-CHAT is that it requires the practitioner to do an M-CHAT follow-up interview questionnaire orally (http://www2.gsu.edu/~psydlr/Diana_L._Robins_Ph.D.html) for screens with positive results, which can happen in 1 of 10 screens. This second-level screen for a positive M-CHAT result was studied by using follow-up telephone calls, which can eliminate 5 of 6 as not requiring referral. (11) This 2-step screening process has

been combined and integrated into an online screening at www.m-chat.org. Unfortunately, the M-CHAT is unreliable in children older than 3 years. Therefore, a validated screening tool for autism at older than 3 years and especially in school-aged children is needed.

Children who meet DSM criteria for ASD are often diagnosed by age 2 to 3 years. However, identifying subtler cases of ASD may take longer. Most subtle cases occur in children with minimal intellectual dysfunction and better language skills. Difficulties with functioning may not be noticeable until school-age, when social demands become greater. Recognizing older children with ASD can be challenging for the practicing clinician, educator, and parent. The use of the Childhood Autism Screening Test may prove helpful. This test provides yes/no questions with 1 point scored for each ASD-relevant response to questions related to social abilities and interest in being around other people. There are 37 total questions with a maximum score of 31. The cutoff for a positive screen is 15 or greater. This is only a screening test, but it can be helpful when responding to concerns by teachers and parents or, if the result is positive, to consider a second-level diagnostic test, such as the Autism Diagnostic Observation Schedule. Some children, who may have not been diagnosed as having ASD by the time they reach elementary school, may have been labeled with behavioral concerns or co-occurring problems, such as hyperactivity, inattention, aggressiveness, mood disturbances, or learning disorders. Alternatively, a child may have been diagnosed as having ASD when in fact another disorder may explain the reason for their symptoms. In addition, some children with an initial ASD diagnosis may no longer fit ASD criteria over time naturally or as a result of therapy. Sometimes the diagnostic process may not be straightforward, and consideration of a differential diagnosis, along with targeted diagnostic testing, may be indicated.

Table 4. Screening Tools for Autism Spectrum Disorder

| Measure | Acronym | Age Range | Description |
|---|-------------|-----------|---|
| Infant and Toddler Checklist also called Communication and Symbolic Behavior Scales and Developmental Profile | ITC CSBS-DP | 9-24 mo | Designed to screen for communication delays but recently has tested well for early autism screening (http://firstwords.fsu.edu/pdf/checklist.pdf) |
| Modified Checklist for Autism in Toddlers | M-CHAT | 16-30 mo | 23-Item yes/no questionnaire (www.firstsigns.org and www.m-chat.org) (online free versions with scoring) |
| Childhood Autism Screening Test | CAST | 4-11 y | Has some research toward use as a universal screening device (http://www.autismresearchcentre.com/project_9_cast) (public domain) |

Initial Workup and Differential Diagnosis

All children being assessed should undergo a complete physical examination, specifically noting any neurologic abnormalities (macrocephaly and hypotonia) or oddities, such as toe-walking, dysmorphic features suggestive of any syndromes, and neurocutaneous skin findings consistent with neurofibromatosis or tuberous sclerosis, such as café au lait or ash leaf spots (Table 3). In addition, the practitioner should review the medical and family histories, focusing on developmental and behavioral issues. Children younger than 3 years with developmental delays should be immediately referred to an early intervention program whether or not the clinician is certain about a diagnosis of autism. If the child is older than 3 years, referral to the special education department at the local school should occur. Generally, the assessment teams for these services will have a speech-language pathologist, physical therapist, and an occupational therapist. Having multiple therapists and evaluations helps clarify the diagnosis and treatment planning.

Children with communication problems and/or language delay should undergo audiology testing. This can be difficult and may ultimately require a sedated auditory brainstem response or a brainstem auditory evoked response test. Deciding on laboratory or diagnostic testing will be guided by a physical examination and medical history. For children diagnosed as having autism, testing for lead exposure, fragile X syndrome, and a comparative genomic hybridization array should be standard; moreover, the use of neuroimaging, electroencephalography, or metabolic testing should be reserved if indicated from physical examination or historical findings.

Diagnostic dilemmas can occur when certain disorders are paired together and can simulate a diagnosis of autism, such as having a language disorder with ADHD or having an intellectual disability and visual impairment. In addition, when considering the differential diagnosis of a child with significant developmental delays, it is important to remember that harsh psychosocial conditions can elicit a response that may briefly mimic autism and other developmental delays. These disorders can include posttraumatic stress disorder, reactive attachment disorder, and child abuse. Generally, these disorders can be diagnosed over time after repeated evaluations, counseling, and therapy. This may require several months, and a diagnosis of autism may be withheld until the child's environment is evaluated for safety and stability. Mandated reporting of child abuse or neglect should be immediate when suspected, and follow-up communication with authorities is important.

After confirming the diagnosis of autism, it is important to help the family identify a treatment strategy to provide the most effective therapy for their child. Intensive psychological and educational interventions are currently the primary treatments for addressing the core deficits in children with autism.

The assessment and diagnostic process is often stressful for the family and the child; treatment and clinical care can be stressful too. Engagement of parents after the diagnostic process should be geared toward providing education, obtaining resources, and accessing supports. Autism Speaks is one of the largest advocacy and science organizations dedicated to the needs of individuals and families struggling with autism. They provide 2 useful parent toolkits: one that addresses children with lower functioning autism (http://www.autismspeaks.org/docs/family_services_docs/100_day_kit.pdf) and another for children with minimal intellectual disability and higher functioning (http://www.autismspeaks.org/docs/family_services_docs/AS-HFA_Tool_Kit.pdf).

As mentioned earlier, the AAP provides helpful handouts from the Autism Toolkit, including the educational booklet *Understanding Autism Spectrum Disorders*, which helps parents navigate the consequences of an initial diagnosis of autism.

Another helpful learning tool for residents and practitioners is Autism Case Training: A Developmental-Behavioral Pediatrics Curriculum (<http://www.cdc.gov/nbddd/actearly/act/class.html>).

Evidence-Based Treatments

Because of the rapid increase in the prevalence rate of ASD, many treatment services are not readily available, and treatment burden falls on clinicians. Families often look initially to the pediatric clinician for guidance to make treatment and educational decisions. Children with an ASD have high service use rates because of the complexity and early onset of the disorder, lifelong prevalence, and associated impairments. Many children also have co-occurring disruptive behaviors (eg, aggression, tantrums, and self-injury), which are common reasons for referral to medical and mental health services.

There are several established behavioral and educational therapies and treatments available to treat the core symptoms of autism. Previously known as behavior modification, ABA is a behavioral treatment approach designed to increase socially appropriate behavior and decrease the severity and/or emergence of challenging behaviors. Widely recognized as an effective treatment for autism, ABA has been endorsed by a number of state and federal agencies, including the US Surgeon General. (12) ABA

focuses on identifying the function of problem behavior and building skills to improve such behaviors. To facilitate appropriate behavior, ABA focuses on teaching specific behaviors in a systematic manner in the context of repeated trials. The therapy is tailored to meet the needs of the individual and requires support of the family.

Research has demonstrated that ABA results in improvements in communication, social relatedness, and decreasing repetitive behaviors; however, these skills require additional training to generalize to environments and situations. ABA is extremely labor intensive and expensive and may be needed for several years.

As ABA has evolved, several treatment approaches have been developed that use the ABA framework to improve behaviors associated with autism. In addition, many children with ASD require additional therapy to address issues such as speech and language delays and sensory problems (Table 5).

Co-occurring Diagnoses

Up to half of children with an ASD have an intellectual disability as measured by standard testing. However,

many of these children may have strengths in visual spatial skills that are difficult to test. Many children with autism are first recognized by their language delay. In addition, impaired pragmatic and semantic language skills create learning difficulties for children with ASD. Children with an ASD are either in special education classrooms or the regular classroom with an individual education plan or 504 plan.

Children with autism may have common medical problems, such as sleep disorders, constipation, and irritability, that a clinician may feel comfortable treating. However, addressing the common comorbid mental health issues, such as anxiety, ADHD, and disruptive behaviors, may be more challenging. Because of the complexity of ASD, it is important to take into account all possible diagnoses to be able to address the needs of the child and family. As the child gets older, these co-occurring mental health disorders could become the problematic aspect or the defining diagnosis in some cases. A helpful website to review and download tests for co-occurring diagnoses can be found at http://www2.massgeneral.org/schoolpsychiatry/screeningtools_table.asp. However,

Table 5. Additional Interventional Therapies for Autism

| Treatments | Description |
|---|--|
| Pivotal Response Training | This method is a data-driven approach designed to improve language and social, behavioral, and play deficits common among children with ASD. |
| Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) | This method focuses on comprehensive services across the lifespan that are specific to the individual and their personal environment, skills deficits, and unique family situations. Parents play an integral role in the treatment process. Education strategies are established individually to assess the potential for acquisitions of learning abilities, rather than deficits. An assessment called the Psycho Education Profile is used to identify areas where skills are deemed passing, not developed yet, or where the skill is emerging. |
| Developmental, individual-difference, relationship-based model (DIR)/Floortime | The DIR model is an intensive program that requires parents to work with their children across multiple settings and sessions throughout the day, often for 20 minutes or longer at each session. At the core of the DIR model is Floortime, where the caregiver literally gets down on the floor to interact with the child, one-on-one, for ≥ 20 minutes in child-directed play or interactions. |
| Speech and language therapy | The purpose of speech and language therapy is to improve verbal and nonverbal communication through didactic and naturalistic behavior methods. This also may include sign language and augmentative communication techniques, such as the Picture Exchange and Communication System. |
| Occupational therapy | Occupational therapy is designed to improve fine motor deficits and improve academic and self-care skills. In addition, the therapy will address issues with the integration of sensory of information. |

these screening tools are not specific to screening children with ASD.

ANXIETY AND PHOBIAS. Anxieties and phobias can be found in up to half of all children diagnosed as having an ASD. Many children may have more than one phobia and/or anxiety related to objects or situations. Screening with the Spence Children's Anxiety Scale can help discern whether a child has separation and generalized anxiety, along with social phobia and panic disorders (<http://www.scaswebsite.com/>). The Self-report for Childhood Anxiety Related Disorders screens for 5 factors: general anxiety, separation anxiety, social phobia, school phobia, and physical symptoms of anxiety (<http://psychiatry.pitt.edu/research/tools-research/assessment-instruments>). Medication is rarely required in clinical practice unless the anxiety is debilitating. However, being able to recognize a mild anxiety disorder is helpful for parents when explaining how to modify these maladaptive behaviors.

OBSESSIVE-COMPULSIVE DISORDER. Obsessive-compulsive disorder is considered the second most common co-occurring condition with ASD and many times defines some early behaviors in children based on their unwillingness to change routines. More than one-third of children with an ASD continue with some type of obsession or compulsion that will limit their ability to interact socially. These behaviors are fairly easy to ask parents about and may not require any specific screening. Treatments with low doses of selective serotonin reuptake inhibitors have been administered in small trials with mixed success. Interestingly, a recent Cochrane review of selective serotonin reuptake inhibitor use in children with autism found no evidence of effect for either anxiety or obsessive-compulsive disorder. (13)

ADHD. ADHD is another common co-occurring condition in children with ASD. Use of the inclusive definition of all types of ADHD (inattentive, hyperactive, and combined) can encompass approximately two-third of all children with ASD. Children may be diagnosed as having and treated for ADHD with stimulants such as methylphenidates and amphetamines before a diagnosis of ASD is ever made. Some studies have suggested that ADHD may actually be considered somewhere along the continuum of the autism spectrum. (14) Screening and follow-up for ADHD can be accomplished with the Vanderbilt forms (http://www.pampapeditrics.com/client_images/File/vanderbilt-forms.pdf). The important caveat for children with autism who have ADHD is that they may be more sensitive to the

medications and can have adverse effects and irritability at lower doses than children without ASD. Therefore, the mantra is to "start low and go slow" with medications. A therapeutic model for assessment and treatment of ADHD in a child with autism is provided (Figure). (15)

DEPRESSION. Generally, depression can be seen in children with ASD as they get older and perhaps become more aware of their diagnosis. In middle school the pressure to conform is strong, and there is a low tolerance for being different. Children with ASD are likely to get teased and taunted or bullied and find it difficult to fit in. This may increase their social withdrawal and cause sadness, crying spells, and depression that may require medical treatment and counseling. The Pediatric Symptom Checklist is sometimes useful as a global screen when there may be more than one co-occurring disorder. The Pediatric Symptom Checklist has a short form (Pediatric Symptom Checklist 17) or longer form (Pediatric Symptom Checklist 35) (http://www.brightfutures.org/mentalhealth/pdf/professionals/ped_symptom_chkst.pdf).

DISRUPTIVE BEHAVIOR. Disruptive behavior may escalate to aggression, causing suspension from school and injury to siblings or parent. Behavioral therapy that targets these emotional outbursts can sometimes suffice, but many times the decision to start use of antipsychotic medications, such as risperidone or aripiprazole, may be necessary. It is important to perform a comprehensive evaluation to identify and assess target behaviors before launching into pharmacologic management. A comprehensive table, provided in the article by Myers et al, (16) that reviews the clinical approach before initiating pharmacologic management should be reviewed (Table 6).

BIPOLAR DISORDER. Occasionally, children with ASD may cycle rapidly through periods of depression and a decreased need for sleep with maniclike activity. If concerned about a bipolar diagnosis, it is best to refer to a psychiatrist for assessment and support. Anticonvulsant mood stabilizers, such as carbamazepine or valproic acid, or an atypical antipsychotic agent, such as risperidone or aripiprazole, are sometimes used.

Use of psychotropic medications as a treatment of acute symptoms of irritability or disruptive behaviors tends to occur as children get older and if the children have increased intellectual disability when placed in a more restrictive educational environment. It is therefore important to use combined therapies of parent training programs with medication in treating children with ASD and challenging behaviors. (17)

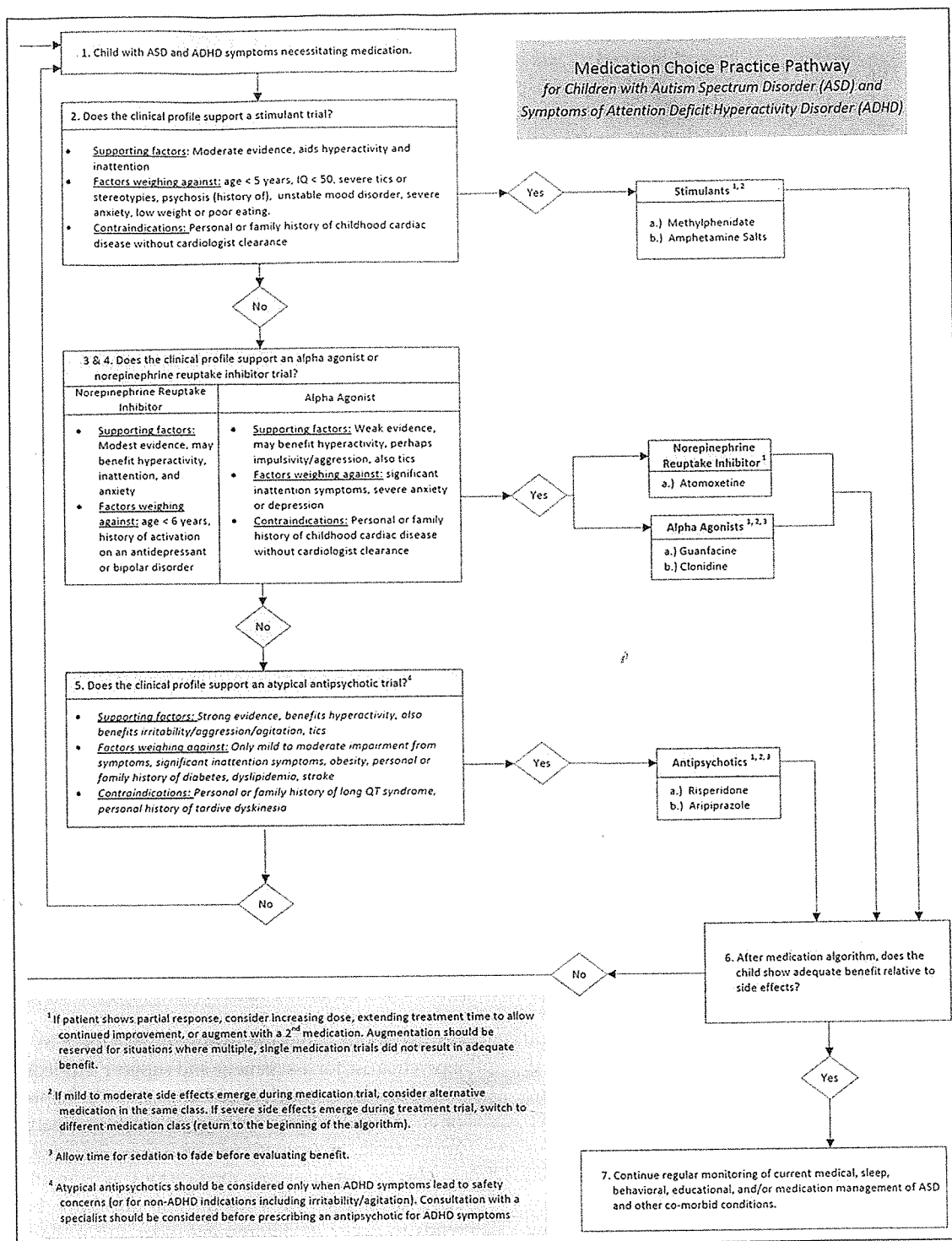


Figure. A therapeutic model for assessment and treatment of attention-deficit/hyperactivity disorder in a child with autism. (15) Reprinted with permission from Mahajan R, Bernal MP, Panzer R, et al. Clinical practice pathways for evaluation and medication choice for attention-deficit/hyperactivity disorder symptoms in autism spectrum disorders. *Pediatrics*. 2012;130(suppl 2):S125-S138.

CAM Therapies for Autism

There is a high use of CAM among children with ASD. Parents often use CAM therapies along with conventional treatments for their child with autism, a combination of treatments often referred to as integrative medicine. (18) Parents appear to be more likely to use CAM therapies if their child has a coexisting gastrointestinal issue, seizure, or behavioral disorder. It is important to be familiar with and provide an open and nonjudgmental approach when discussing CAM therapies with parents. Unfortunately, some CAM therapies receive media attention (eg, secretin and hyperbaric oxygen) and become fads that are used by parents that may or may not have disposable income. Regrettably, many of these therapies have not been rigorously studied, and vulnerable parents develop false hopes that each new treatment may provide a cure for their child with autism.

The following guidelines may be useful for parents who are interested in trying biomedical and/or CAM therapy:

1. Research the medication or therapy as much as possible. Seek information from the clinician and share perspectives on the efficacy and safety of the treatment.
2. Know the behavior to be improved. Is treatment directed to improving disruptive behaviors or increasing speech production?
3. Start only one new treatment at a time. Do not introduce 2 or 3 interventions at once; this will make it difficult to know which treatment is or is not working.
4. Understand that a child with autism over time will move forward in development, although the forward rate may be slow.
5. Keep in mind that a child with autism may naturally have good weeks and bad weeks.
6. Be observant of other factors that may affect treatment outcome (eg, life transitions, parental separation, and birth of a new sibling).
7. Assess poor sleep habits by removing electronic devices from the bedroom and maintain a consistent bedtime routine. Consider obstructive sleep apnea if a child diagnosed as having autism snores loudly, appears to stop breathing while sleeping, or has daytime sleepiness. Remember, insufficient sleep can negatively affect mood and cause disruptive behaviors, inattentiveness and hyperactivity, and ritualistic behaviors.

The types of CAM therapies marketed to parents include nutrition, immunomodulation, biochemical and metabolic therapies, detoxification, manipulative and

body-based practices, sensory integration therapy, music and other expressive therapies, and additional therapies, such as dolphin swim therapy, hippotherapy (horseback riding), and hyperbaric oxygen.

NUTRITION. Gluten-free and casein-free diets are common, as is the use of vitamins B₆ and magnesium, vitamin C, carnosine, ω 3 fatty acids, and combined hypervitamin therapies.

IMMUNOMODULATION. Antifungals and antibiotics, along with the use of prebiotics and probiotics, are popular based on the unproven hypothesis that children with autism may have underlying immunodeficiencies.

BIOCHEMICAL AND METABOLIC THERAPIES. Abnormalities have been proposed in metabolic pathways, and use of precursors and coenzyme factors are thought to be helpful (eg, dimethyl glycine, trimethyl glycine, and vitamin B₁₂ shots).

DETOXIFICATION. Parents may have nonstandardized hair analysis or serologic testing performed. The results of these unregulated tests may lead parents to believe that their child has heavy metal poisoning that requires chelation. Some clinicians offer chelation therapy, and parents should be advised that deaths have occurred from improper use of chelation protocols for children with autism. (19)

MANIPULATIVE AND BODY-BASED PRACTICES. These practices include chiropractic manipulation, craniosacral massage, massage therapy, and therapeutic touch.

SENSORY INTEGRATION THERAPY. This is sometimes grouped with occupational therapy but really refers to practices such as auditory integrative therapy, which purports to retrain the child's auditory reflexes.

MUSIC AND OTHER EXPRESSIVE THERAPIES. Generally, music and other expressive therapies involve listening or moving to music, along with using art, drama, and other theatrical activities.

For the clinician, a general ethical principal, developed by Cohen et al, (20) provides guidance using a simple 2 × 2 table philosophy that asks a yes/no question of safety and efficacy of CAM therapies. The 4 outcomes of these questions can look like this:

1. If a CAM therapy is safe and effective then *recommend*.
2. If a CAM therapy is safe but effectiveness is unknown then *tolerate*.
3. If a CAM therapy has a concern for safety but is effective then *monitor closely*.
4. If a CAM therapy is unsafe and not effective then *advise against*.