NCC Pediatrics Continuity Clinic Curriculum:
Development II: Atypical Development

Pre-Meeting Preparation:

Please read or skim the following enclosures and click on the video links below:

- "Autism Spectrum Disorder" *(PIR, July 2021)*
- "Intellectual Disabilities" (PIR, June 2018)
- *Excerpts from* "A Rational Approach to the Medical Evaluation of a Child with Developmental Delay"*(Contemporary Pediatrics, 2004)*
- Key Points and Figures From "AAP: Hearing Assessment in Infants and Children: Recommendations Beyond Neonatal Screening *(Pediatrics, 2009)*
- **CDC Autism Case Study Video Library**

Conference Agenda

- *Review* Development II Quiz
- Complete Development II Cases
- Development II Board Review
- **"Autism Speaks" Reflections**:
  - Which videos were particularly impactful. What were the major differences between "typical" and "atypical" children?
  - Do these videos resonate with your clinical experiences? Think about patients you follow with "atypical development", not only including ASDs.

Extra-Credit:

- "Developmental Delay: When and How to Screen" *(AAFP, 2017)*
- "Current evidence-based recommendations on investigating children with global developmental delay" *(BJM, 2017)*
- "Evaluation of the child with global developmental delay and intellectual disability" *(CanPaedSoc, 2018)*
- "Language & Speech Disorders in Preschool Children" *(PIR—2005)*
- "Recognition of Autism Before Age 2 Years" *(PIR—2008)*
- "Identification & Evaluation of Children with ASDs" *(AAP Clinical Report- 2007)*
- "Sugar Coaters and Straight Talkers: Communicating About Developmental Delays in Primary Care" *(Pediatrics, 2009)*
- Parent Resource: **The Parents' Place of Maryland, Parent Education Advocacy Training Center** (VA), **Parent Education and Training Center** (DC)

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Autism Spectrum Disorder

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PRACTICE GAP

With autism spectrum disorder (ASD) prevalence rising and a shortage of specialists available for diagnosis and management, pediatricians will need to be increasingly comfortable 1) giving a provisional diagnosis of ASD to create access to critical early behavioral interventions, 2) managing the comorbidities that significantly affect quality of life, and 3) supporting families to navigate the increasingly complex web of ASD-related services.

OBJECTIVES *After completing this article, readers should be able to:*

1. Appreciate the evolution in prevalence data over time and recognize the disparities that exist in diagnosis based on race and sex.
2. Recognize the heterogeneity of autism spectrum disorder (ASD) clinical presentation depending on the child's age, sex, and developmental abilities.
3. Understand the diagnostic criteria for ASD.
4. Distinguish findings associated with ASD from those of isolated speech and language delay, intellectual disability, and profound hearing loss.
5. Determine age-appropriate screening for ASD and be prepared to discuss results and next steps with families.
6. Plan for appropriate management of core symptoms of ASD and identify the common medical and psychiatric comorbidities with ASD.
7. Recognize the complexity of care coordination required to support families of children with ASD and the importance of advocating for a pediatric medical home.

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ABBREVIATIONS

AAP	American Academy of Pediatrics
ABA	applied behavior analysis
ADHD	attention-deficit/hyperactivity disorder
ASD	autism spectrum disorder
CBD	cannabidiol
CDC	Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*
EEG	electroencephalogram
FDA	Food and Drug Administration
ID	intellectual disability
MCHAT-R/F	Modified Checklist for Autism in Toddlers, Revised, with Follow-up

EPIDEMIOLOGY

Autism spectrum disorder (ASD) is a neurodevelopmental disability characterized by differences in social and communication functioning and by restricted and repetitive behaviors and interests. The increasing prevalence of ASD has been the subject of intense attention in the medical literature and lay press. In the United States, the Centers for Disease Control and Prevention (CDC) Autism and Developmental Disabilities Monitoring Network, which measures confirmed diagnoses of ASD, has found an increased prevalence of ASD among 8-year-old US children from 1 in 150 in 2000 to 2002 to 1 in 54 during 2016. (1) Reasons for the observed increase in ASD prevalence likely include increased

screening and diagnosis due to public awareness, evolving clinical practice recommendations, broadening diagnostic criteria, improving service availability, diagnostic substitution (in which children are diagnosed as having ASD rather than another condition), and possibly increased incidence due to biological risk factors. (2)

ASD may be reliably diagnosed as early as age 14 to 16 months. (3) However, the average age at diagnosis of ASD has not changed substantially since 2000, remaining at approximately age 4 years, although "catch-up" diagnoses of older children might mask progress toward earlier diagnosis. (1)(4)(5) Available evidence suggests that children with intellectual disability (ID) are more likely to receive diagnostic evaluation at younger ages. (5)

Girls are diagnosed as having ASD less frequently than boys, although among children with comorbid ID this difference is less pronounced. (6) The male-to-female ratio is commonly reported to be 3:1 to 4:1 overall but has been reported to be 2:1 among individuals with ID and 8:1 among individuals in mainstream schools. (4)(7)(8)(9) Girls diagnosed as preschoolers have been found to be more likely to have comorbid ID and, therefore, are diagnosed as having ASD at an earlier age. (4) Conversely, girls without ID are often identified with ASD later than boys due to a range of factors likely to include biological factors, a different autistic phenotype and/or developmental trajectory, different rates of comorbidity, or a better ability to "camouflage" ASD traits. (7) For example, girls with ASD have been noted to be more likely to stay on the periphery of social groups rather than being entirely alone and to have socially acceptable restricted/repetitive behaviors and interests such as books and animals. (10)(11) In addition, diagnostic criteria and instruments are typically norm-reference tests derived from study populations consisting primarily of boys, (12) thereby raising concerns that girls with ASD are being underdiagnosed (13) and that diagnostic modifications such as sex-specific cutoff scores or instruments might be indicated. (14)

Minority children, those with low socioeconomic status, and those from non–English-speaking households have lower prevalence rates and often a later age at diagnosis of ASD, likely reflecting barriers to accessing diagnostic services and long-standing effects of structural racism. (1)(15)(16)(17)(18) Although the Autism and Developmental Disabilities Monitoring Network data for 2016 did not find a lower prevalence of ASD among black versus white children for the first time since its data collection began, black children were still less likely to have been evaluated by age 36 months. (1)(4)

ETIOLOGY

Given the complexity and heterogeneity of ASD, it is not surprising that a single cause of ASD has yet to be identified. Research suggests that likely an interplay between genetic and environmental risk factors leads to atypical brain development, specifically alterations in the balance of synaptic growth and pruning at the neuron level and atypical neuroconnectivity at the whole brain level. (19)(20) These neurologic changes likely begin early in fetal development, long before clinical symptoms are evident. (21) It is not yet clear how these molecular and structural changes mediate the behaviors seen in ASD. Ongoing basic and clinical research is seeking biomarkers with the potential to aid both diagnosis of and intervention for ASD.

There is very strong evidence for a genetic basis of ASD. Genetic studies of twins have consistently demonstrated a 98% concordance rate for monozygotic twins and a 53% to 67% rate for dizygotic twins. (2)(22) Recurrence rates of ASD in families who already have 1 child with ASD are approximately 10% and are more than 30% in families who have 2 or more children with ASD. (2) Siblings of individuals with ASD also have an approximately 25% risk of having a different neurodevelopmental or psychiatric disorder, (2) highlighting the overlapping nature of risk of genetic conditions.

There is no specific genetic mutation that is unique to ASD. More than 100 genes have been linked to ASD. (19)(23) It is thought that changes associated with protein-coding regions (or exons) likely have the largest effect on risk, specifically proteins involved in synapse structure and function and chromatin remodeling, among others. (19) All of these genetic variants are considered rare because no individual variant is responsible for more than 1% of ASD cases. (2) Although there are some well-known single-gene causes of ASD (eg, fragile X syndrome), it is thought that for most cases, several genetic variations interact with each other and with environmental risk factors to determine an individual's risk of ASD. (23)

Environmental factors likely play a smaller but nonetheless important role in conferring risk of ASD. There are several prenatal events that may increase risk of ASD, including the following: advanced parental age, short interpregnancy interval (<12 months), multiple gestation, maternal obesity, gestational diabetes, gestational bleeding, in utero exposure to medication (eg, valproate), fetal growth restriction, and maternal infection or immune activation while pregnant. (24)(25) Intrapartum and neonatal events such as preterm birth, low birthweight, intrapartum hypoxia, and neonatal encephalopathy are additional risk factors. (24)(25) These environmental factors may directly affect brain development or

may alter gene function in an individual who already has a genetic predisposition to develop ASD. (2)

The American Academy of Pediatrics (AAP) recommends genetic testing for all children with ASD. (2) Potential benefits to establishing a genetic diagnosis include enhancing the accuracy of counseling about prognosis and recurrence risk, allowing for adequate monitoring for potential comorbid conditions, empowering the family with enhanced etiologic knowledge, and in the more distant future, potentially facilitating access to personalized treatment. (2) If a pediatric geneticist is not available for consultation, the pediatrician may initiate a genetic evaluation. Recommendations are to start with a chromosomal microarray analysis and consider specific testing for fragile X syndrome for all children and for Rett syndrome for girls. If these studies do not reveal a genetic etiology, whole exome sequencing can be considered. (2) Insurance coverage is variable, and out-of-pocket expenses for this type of genetic testing can be high ($500–$5000 depending on insurance and coverage). (26) There are other associated genetic syndromes to consider screening for on a case-by-case basis, including neurofibromatosis, tuberous sclerosis, *PTEN* hamartoma tumor syndrome, Smith-Lemli-Opitz syndrome, and Timothy syndrome. (27) These conditions are important to identify because they may affect prognosis and monitoring for comorbidity (eg, for optic glioma in neurofibromatosis). It is important to communicate to families that genetic testing is not a diagnostic test for ASD. Negative genetic testing results do not change the fact that a child was clinically diagnosed as having ASD.

Importantly, there is no evidence that vaccines cause ASD or contribute to increased risk of ASD. This message should be clearly communicated to all families of children with ASD or suspected ASD. There have been concerns raised in the past that measles-mumps-rubella vaccine, thimerosal, aluminum, and/or the increased level of antigenic exposure from multiple vaccines are related to the rise in ASD prevalence. Fortunately, dozens of studies looking at millions of children have contributed to a robust body of scientific data disproving any relationship between vaccines and ASD. (2)(28) Most recently, the results of the largest single cohort study to date, including more than 600,000 children in Denmark, confirmed that measles-mumps-rubella vaccine does not increase risk of ASD or "trigger" ASD in siblings and does not cause clustering of new ASD diagnoses. (29)

CLINICAL PRESENTATION

Broadly speaking, the core social communication impairment and restrictive/repetitive behaviors of ASD are present early in childhood, persist through adulthood, and cause substantial impairment in functioning. (30) The clinical presentation of ASD can vary considerably depending on the child's age, developmental and/or intellectual ability, language skills, and ASD trait intensity. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* criteria for the diagnosis of ASD (Table 1) combines the 4 previously separate *DSM-IV* diagnoses of autistic disorder, pervasive developmental disorder not otherwise specified, Asperger disorder, and childhood disintegrative disorder. All children who were previously diagnosed as having an ASD using *DSM-IV* criteria are defined as meeting ASD diagnostic criteria under *DSM-5*.

To further demonstrate the heterogeneous clinical presentations of children with ASD, we present the following 3 cases:

Case 1: You are seeing a 21-month-old new patient in your primary care practice. There are no records available, but according to his mother he was previously identified as having expressive language delay at his 18-month health supervision visit and was referred for speech-language therapy. He has not made progress with his speech despite initiating therapy services. During the past few months his parents have noticed that he is no longer saying "bye" or "cat" spontaneously. He also has become a very selective eater, and he refuses everything except milk from a bottle and plain pasta. His parents have become increasingly concerned about hand movements that he makes when he is excited. His mother also notes that he "doesn't want to see me." She will sometimes hold his chin to turn his face toward her.

Case 2: You are seeing a 5-year-old boy for a health supervision visit. He has a history of developmental delay and behavior concerns, with multiple missed connections to early intervention services and developmental specialists. His family expresses several concerns at the start of the visit. He has frequent and prolonged tantrums at home and at school, especially when they are trying to get him out of the house for school in the morning or when his tablet is taken away. His teachers report that he has significant difficulty participating in academic tasks even when he is pulled out of the classroom for individual developmental therapy. He prefers to play by himself and is often aggressive toward his peers.

Case 3: You are seeing an 11-year-old girl whom you have known since birth. She met her motor and

Table 1. DSM-5 Criteria for Autism Spectrum Disorder

DOMAIN	CRITERIA: DEFICITS
A. Persistent deficits in social communication and social interaction across multiple contexts as manifested by all 3 of the following, currently or by history	1. Social-emotional reciprocity
	2. Nonverbal communicative behaviors used for social interaction
	3. Developing, maintaining, and understanding relationships
B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by ≥2 of the following, currently or by history	1. Stereotyped or repetitive motor movements, use of objects, or speech
	2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior
	3. Highly restricted, fixated interests that are abnormal in intensity or focus
	4. Hyperreactivity or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment
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 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 the criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.	
Specify whether with or without accompanying intellectual impairment; with or without accompanying language impairment; associated with another neurodevelopmental, mental, or behavioral disorder; with catatonia; or associated with a known medical or genetic condition or environmental factor.	

DSM=Diagnostic and Statistical Manual of Mental Disorders.

language milestones on time. In elementary school she was a quiet child with good grades who passionately loved cats. Since transitioning from elementary to middle school, she has had increasing anxiety and low mood. Her teachers report that she does not participate in class and eats by herself at lunch. When she gets home she has meltdowns when she is asked to do homework. She recently disclosed to her mother that she is being bullied at school because she is not interested in the same things as the other girls. She finds it very uncomfortable to wash her hair, and she wears only elastic clothes made of soft fabric.

All 3 of these patients were found to meet the *DSM-5* criteria for ASD, highlighting the challenges and difficulties for a pediatrician to learn and apply the diagnostic criteria to a developmentally diverse group of patients. It can be helpful to examine more closely the 2 broad categories of symptoms—social communication deficits and abnormal behavior patterns—and to explore how children of different ages and/or developmental abilities may manifest symptoms in these areas (Table 2).

Note that although social communication deficits are present in all children with ASD, receptive and expressive language delays are not included in the diagnostic criteria. Children with ASD may have varying levels of language ability ranging from mutism to precocious verbal abilities. Most children diagnosed in the toddler years, however, will have language delay. Up to 25% of children show regression of language skills, most often between ages 15 and 24 months, although the clinical distinction between a true loss of skills and the dramatic slowing of developmental progress can be difficult. (19)(31) Note that although regression in language skills in children diagnosed as having ASD may be common in this early toddler age group, regression is not normal in older children, and those children should be referred for further evaluation. (2)

The differential diagnosis of ASD is broad (Table 3). Note that several conditions from Table 3 can co-occur with ASD (most commonly, language disorder, ID, attention-deficit/hyperactivity disorder [ADHD], mood disorder, anxiety, and obsessive-compulsive disorder), underlining the importance of a comprehensive evaluation to help delineate whether a child has ASD, another disorder, or both.

SCREENING

The February 2016 Final Recommendation Statement from the US Preventive Services Task Force concluded that there was insufficient evidence to recommend routine ASD screening for children 18 to 30 months old in whom

Table 2. Examples of Autism Spectrum Disorder Behaviors by Age/Developmental Ability

	EXAMPLES BY AGE/DEVELOPMENTAL STAGE		
DIAGNOSTIC DOMAIN	**TODDLERS**	**OLDER CHILDREN**	**ADOLESCENTS**
Social-emotional reciprocity	• Not following gaze of others • Not responsive to name • Not engaging in social games where you take turns (eg, peek-a-boo) • Not showing or pointing out objects of interest to others • Not shifting gaze from object to person and back to object	• Does not initiate conversation • One-sided conversation (lacking typical back-and-forth), and typically narrow subject matter • Difficulty expressing own feelings and understanding others' feelings • Does not share–either objects or enjoyment of others	• Difficulty understanding the intent of others (eg, takes things literally, misunderstands metaphors or sarcasm) • Failure to initiate or respond to social interactions
Nonverbal communication	• Poor eye contact • Limited gestures (reaching, giving, pointing, shaking head 'no') • Using another person's hand as a tool (eg, taking parent's hand to an object they want)	• Difficulty understanding body language of others • Impaired use or understanding of body posture (eg, facing away during interactions) • Dysprosody/abnormal speech (eg, monotone or sing-song voice)	• Decreased eye contact • Abnormal use or understanding of affect • Difficulty integrating nonverbal and verbal communication
Relationships	• Odd social approach to other children (eg, aggressive) • Prefers to play alone (and persisting beyond age 2 years) • Indiscriminate affection	• Difficulty sharing imaginative play • Motivated to socialize but not able to sustain relationships—difficulty anticipating the interests of others • Difficulty picking up on social cues (eg, does not notice when another person is disinterested, laughing inappropriately)	• Difficulty with peer relationships • Easier time with younger children or adults • Unable to take another person's perspective • Difficulty adjusting behavior based on changing social context • Poor understanding of social conventions (eg, greetings, awareness of personal space) • Withdrawn, aloof
Stereotyped/repetitive movements	• Echolalia • Flapping hands, rocking body, spinning in circles • Manipulate parts of an object (eg, wheel of toy car) rather than using it functionally	• Repetitive speech, sometimes taken from movies or books	• Idiosyncratic phrases
Inflexible/ritualized behavior	• Frequent, prolonged tantrums • Extreme distress at small changes • Limited food preferences • Always lining up toys in a certain order rather than playing with them	• Difficulties with transitions • Strong preference for familiar routines (eg, insistence on taking same route to school each day) • Rigid expectation that other children follow the rules	
Fixated/restricted interests	• Attachment to unusual objects (eg, hard objects such as wooden spoons, spinning objects)	• Special interests of abnormal intensity or focus (eg, obsession with facts or extensive collections)	
Sensory behavior	• Overreactions or underreactions to certain sounds/textures/tastes • Excessive smelling or touching of objects • Fascination with flickering lights • Apparent indifference to pain		

Table 3. Differential Diagnosis of ASD

DIAGNOSIS	DISTINGUISHING FROM ASD
Intellectual disability	Children may present with some of the same language or cognitive deficits seen in ASD, but the core ASD traits of social communication/nonverbal difficulties and restricted/repetitive behaviors are typically absent. Note that children with both ASD and intellectual disability will typically have social communication deficits out of proportion to other delayed skills (eg, problem solving).
Language disorder	Children may present with communication difficulties and there may be social repercussions, but typically nonverbal communication (eg, gestures, pointing) is unaffected, and restricted/repetitive behaviors are absent.
Social pragmatic communication disorder	Children may present with social communication difficulties but not the restricted/repetitive behaviors found in ASD.
Tic disorders or other movement disorders	Children may present with atypical movements but will not have the social communication differences found in ASD.
Profound hearing loss	A formal audiology evaluation is a crucial component of any evaluation for ASD or language delay to assess for hearing loss or deafness as an etiology for the presenting concerns.
Rett syndrome	Children may initially present very similarly; however, regression and hand stereotypies are more prominent in Rett syndrome. They will also have deceleration of head growth velocity.
Psychiatric conditions	
ADHD	There can be significant overlap in symptoms, especially in the toddler years. Typically, nonverbal communication skills are intact and children lack the restricted/repetitive behaviors found in ASD. Note that up to 59% of children with ASD also have ADHD.
Mood and anxiety disorders	Early development is typically unremarkable. Children will not have social communication impairment or restricted/repetitive behaviors. Family history is often useful in diagnosis.
Posttraumatic stress disorder	Development will typically be normal until the onset of the trauma.
Obsessive-compulsive disorder	Repetitive behaviors may resemble ASD but are more likely to be a source of stress/anxiety to the child. Also, children with OCD are unlikely to have social communication deficits.
Schizophrenia	Early development is usually not markedly atypical. True hallucinations and delusions are uncommonly seen in ASD, but children with ASD may describe their experiences in a way that makes distinguishing from psychosis difficult.
Selective mutism	Early development is typically normal. Children will not have social communication impairment even in settings in which he or she is mute, or the restricted/repetitive behaviors.
Reactive attachment disorder	Children may have a known history of severe neglect/abuse. Symptoms will often improve in a new/appropriate caregiving environment.

ADHD=attention-deficit/hyperactivity disorder, ASD=autism spectrum disorder, OCD=obsessive-compulsive disorder.
Adapted from American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*. 5th ed. Washington, DC: American Psychiatric Association; 2013; Hyman SL, Levy SE, Myers SM, et al. Identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*. 2020;145(1):e20193447; Volkmar F, Siegel M, Woodbury-Smith M, et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. *J Am Acad Child Adolesc Psychiatry*. 2014;53(2):237–257; Salazar F, Baird G, Chandler S, et al. Co-occurring psychiatric disorders in preschool and elementary school-aged children with autism spectrum disorder. *J Autism Dev Disord*. 2015;45(8):2283–2294.

no concerns about ASD had been raised. (32) However, despite this, the AAP strongly recommends universal developmental surveillance and use of an ASD-specific screening tool at the 18- and 24-month health supervision visits, in addition to general developmental surveillance at the 9-, 18-, and 30-month health supervision visits, because structured screeners have been shown in subsequent research to increase the likelihood of early identification of both ASD and other developmental delays. (2)(33)(34) The dramatic increase in missed health supervision visits during the coronavirus disease 2019 (COVID-19) pandemic raises concerns that many children may miss these screening opportunities and have subsequent delay in the identification of developmental concerns.

Although multiple screening tools are available, the most commonly used and widely studied is the Modified Checklist for Autism in Toddlers, Revised, with Follow-up (MCHAT-R/F). (35)(36) The MCHAT-R/F is validated for use in children aged 16 to 30 months and is freely available online in multiple languages. Screening is widely implemented in the United States per AAP guidelines, with a recent study finding that the MCHAT-R/F was used at 80% to 90% of 18- and 24-month health supervision visits. (37) However, the accuracy of the MCHAT-R/F in real-world conditions has recently been the topic of much debate. A medical record review of 26,000 primary care visits found that the MCHAT-R/F sensitivity was 39% for ASD, and the positive predictive value was 15% for ASD and 72% for any developmental delay, including ASD. (34) Therefore, for a positive MCHAT-R/F screen, parents can be counseled that although there is a low chance of an eventual ASD diagnosis, additional evaluation is indicated because developmental intervention of some sort is likely warranted. Similarly, for a negative MCHAT-R/F screen,

parents can be counseled that this screen misses approximately 60% of children eventually diagnosed as having ASD, so additional evaluation is still indicated if there are clinical concerns.

A recent study found that only one-third of toddlers were referred for specialist evaluation by primary care providers after positive MCHAT-R/F scores. (37) Providers' clinical awareness of the limitations of the MCHAT-R/F and other screening tools is one possible explanation for the low rates of referral for specialist ASD evaluation after positive screen results, along with long waits for diagnostic evaluation due to a shortage of ASD specialists, parental stress, and parental inability or reluctance to access recommended evaluations. Primary care providers may respond to a positive screen with a referral to state-funded early intervention, schools, or private practice services. However, referral to these services alone is often not sufficient because diagnosing ASD is frequently outside their scope of practice. Without an ASD diagnosis, the child is unlikely to be eligible for often scarce evidence-based ASD interventions and ultimately to receive these services during the period of development in which they are most likely to be helpful. (37)(38) Therefore, children who screen positive on ASD-specific instruments should be referred for both school/early intervention evaluation and a specialist ASD diagnostic evaluation. (2)

Screening instruments for older children are considerably less well-characterized. (39) Three widely used tools are 1) the Social Communication Questionnaire, a proprietary 40-item parent report instrument for children 4 years and older (40); 2) the Social Responsiveness Scale, a proprietary 65-item parent/teacher report instrument for patients 2½ years and older (41); and 3) the Autism Spectrum Quotient, an open-access 50-item parent- or self-report instrument with child, adolescent, and adult versions. (42) Of note, the Autism Spectrum Quotient is freely available online in more than 15 languages, but it was designed for research use. (43)

EVALUATION

The gold standard for diagnosis of ASD is a multidisciplinary evaluation, including 1) a thorough developmental, medical, social, and family history, including specific questioning on the history of ASD traits; 2) direct observation of the individual for ASD traits; 3) evaluation of cognitive and developmental level; 4) evaluation of adaptive functioning; 5) evaluation for comorbid genetic and medical conditions; 6) speech-language evaluation; 7) audiology evaluation; and (8) referrals to other medical specialists (eg, neurology or gastroenterology) as clinically indicated. (44) Neuroimaging, electroencephalography (EEG), and laboratory studies are not routinely recommended unless indicated by the clinical presentation. All 8 elements of the gold standard evaluation do not need to occur simultaneously and are not all necessary for the initial diagnosis of ASD.

In research and clinical settings, the lengthy, semistructured Autism Diagnostic Interview–Revised is often used to characterize parent report of ASD traits. (45) The shorter Social Communication Questionnaire and Social Responsiveness Scale are often used to provide structured support of information gathered during the clinical interview. (2) The gold standard observational instrument for ASD diagnosis is the proprietary Autism Diagnostic Observation Schedule, Second Edition. (46) This schedule is a series of semistructured play tasks administered by a trained clinician with a kit of standardized play materials. Other structured instruments may be more feasible for supporting the clinician's diagnostic observations. For example, the proprietary Childhood Autism Rating Scale, Second Edition and the open source Autism Mental Status Examination do not require particular clinician training or specific play materials. (47)(48)(49)

The COVID-19 pandemic and resulting recommendations for mask wearing in health-care settings and physical distancing have introduced new challenges to the assessment process for children suspected of having ASD. There is accumulating evidence for the utility, feasibility, and accuracy of diagnostic tools that can be administered via telehealth, and this field is evolving rapidly. Although telehealth may in fact promote increased access to ASD diagnostic assessment for certain patient populations traditionally underserved in this area (eg, rural populations), it may impede access for other populations (eg, those without Internet access). (50)(51)(52)(53)(54)(55)

Given the extended wait for specialist ASD evaluation and the demonstrated benefit of early intervention to clinical outcomes in ASD, pediatricians may facilitate the initiation of services by providing an initial clinical diagnosis of ASD based on *DSM*-5 criteria after careful developmental history and longitudinal observation of the child. (2) Notably, no particular instrument is required for the diagnosis of ASD. (56) Separate referrals to school/early intervention and medical specialists can then lead to a timelier if piecemeal comprehensive characterization of the child's strengths and needs. The benefit of a provisional diagnosis in the primary care setting should be balanced with the potential risk of an inappropriate diagnosis persisting in the electronic medical record or educational records and the potential psychological burden of diagnostic uncertainty on the family and patient.

INTERVENTIONS: BEHAVIORAL THERAPY, DEVELOPMENTAL THERAPIES, AND THE EDUCATIONAL SYSTEM

The lifetime cost of supporting an individual with ASD is estimated to be $1.4 million to $2.4 million, (57) with services provided through a maze of overlapping programs and funding streams. Broadly speaking, children with ASD receive services through 3 main systems of care: health-care, education/early intervention, and federal/state services. Treatment planning should identify entry points and potential services in each system of care. Health-care services paid for by health insurance typically require a medical diagnosis of ASD and can include in-home behavioral therapy, mental health services, private speech/language therapy, and private occupational therapy. Education/early intervention services are provided in accordance with the federal Individuals with Disabilities Education Act and other legislation. Parents should be directed to contact their local Early Intervention Program for Infants and Toddlers with Disabilities (age <3 years) or Child Find/public school (age ≥3 years). Federal and state services vary widely by jurisdiction and include disability, social services, and juvenile justice services. The state Parent Training and Education Center can often provide initial assistance with navigation.

Treatment planning for ASD is highly individualized but generally includes targeting the core symptoms of ASD (social communication deficits and repetitive/restricted behaviors), enhancing functional independence, and reducing problem behaviors that may be interfering with the acquisition of adaptive skills. (2) The modality of behavior therapy with the strongest evidence base for improving outcomes in ASD is applied behavior analysis (ABA). (58)(59)(60) The guiding principles of ABA are to increase positive behaviors (eg, social communication) and decrease negative behaviors (eg, tantrums or self-injurious behaviors) by modifying the reinforcement derived from events just before (antecedents) or after (consequences) the target behavior. See Table 4 for examples. ABA direct services, which are individualized and highly structured, are typically provided by registered behavior technicians and overseen by board-certified behavior analysts. The intensity and duration of treatment with ABA depends on a child's deficits and specific behavior challenges and are best determined by the professional behavior analyst. Focused ABA treatment is generally delivered at 10 to 25 hours per week of direct service and targets a limited number of behaviors. It often addresses behaviors that put the child and/or others at risk for harm. Comprehensive ABA treatment is generally delivered at 30 to 40 hours of direct service per week and targets multiple affected developmental domains, including cognitive, communicative, social, emotional, and adaptive functioning. (61) Several studies have shown that high-intensity treatment leads to the largest gains, especially in the youngest children (ie, those who initiate treatment before age 3 years). (60) Unfortunately, insurance coverage of this type and intensity of therapy is variable and often requires a medical diagnosis of ASD, making the long wait lists for specialist ASD evaluation a barrier to time-sensitive, evidence-based treatment. Pediatricians who are equipped to make provisional ASD diagnoses can accelerate access to ABA services.

Many patients benefit from additional developmental therapies. Speech-language therapy is the most common type of treatment provided to children with ASD. (2) Increased communication leads to decreased frustration, which can lead, in turn, to improved behavior. Interventions are designed to improve core deficits in expressive, receptive, and pragmatic language. For patients with ASD who remain nonverbal or minimally verbal (approximately 30%), (62) referral to a speech therapist with expertise in ASD and use of augmentative and alternative communication devices may be considered. Social skills groups aim to improve social competence and friendship quality. They target impairments in use of nonverbal behaviors (eg, eye contact and facial expression), promote development of appropriate peer relationships, and help with social and emotional reciprocity. Occupational therapy may be used to address deficits in adaptive functioning and fine motor skills, including participation in play and help with self-care. Sensory-based therapy has a limited evidence base, although it is commonly requested by parents. (2)

As soon as there is developmental concern, and, at the latest, at the time ASD is medically diagnosed, children should be referred for evaluation for early intervention or special education services. A medical diagnosis of ASD does not automatically translate into eligibility for school-based services. The availability of these services varies by location, and families may need to supplement school-based services with private therapies such as ABA, speech-language therapy, and occupational therapy. Advocating for an educational setting with appropriate supports in place is an important job of the primary care provider and other treatment team members. Children with ASD should be receiving academic, language, adaptive, and social skills development, and educators should be preparing them for postsecondary education or employment. (2)(63) Some children may be best served in a

Table 4. Applied Behavior Analysis in Practice: Simple Examples of Targeting a Behavior by Modifying Events that Occur Just Before and After the Behavior

CONDITION	ANTECEDENT	BEHAVIOR	CONSEQUENCE
Before intervention	Cafeteria is loud	Child bangs head on table	Child is removed from cafeteria and eats alone
After intervention, modifying antecedent	Cafeteria is loud so child is given ear defenders to wear[a]	Child eats calmly at table	Child is able to remain in the mainstream environment with peers successfully
Before intervention	Child dislikes putting toys back in toybox	Child tantrums	Child avoids putting toys away and tantrum is rewarded
After intervention, modifying consequence	Child dislikes putting toys back in toybox but is aware that she will get a reward after she finishes	Child puts away toys	Child gets reward[a] and toys are put away

[a]Primary intervention.

traditional classroom in a traditional school setting; others may thrive in a specialized school with ASD-specific classrooms.

COMMON COMORBIDITIES

Comorbid Medical Conditions

Children with ASD are at increased risk for comorbid medical conditions, including seizure disorder, gastrointestinal and feeding problems, and sleeping difficulties. Although prevalence rates vary widely in the literature, it is estimated that up to 25% of children with ASD and concomitant ID also have epilepsy. (64) A routine screening EEG is not recommended for all children with ASD, but if the history is in any way concerning for seizures, the child should be referred to a neurologist for evaluation and consideration of an overnight EEG. (2)

Gastrointestinal symptoms (eg, constipation, diarrhea, abdominal pain) and feeding issues are reported in up to 75% of children with ASD. Although not specific, differences in stooling patterns and food selectivity may be evident as early as 6 months of age in children who later receive a diagnosis of ASD and may, therefore, be among the earliest signs. (65) It is not known whether there is a specific biological reason linked to ASD that places children with ASD at high risk for these symptoms. Certainly, behavioral aspects of the disorder, including resistance to change and sensory issues, may affect feeding behaviors, which can, in turn, affect stooling patterns. It is important to get a complete dietary and nutrition history at all preventive care visits and to consider evaluation for nutritional deficiencies as indicated. If food selectivity affects nutrition or is severely disruptive for the family, referral to a feeding specialist may be considered. Several members of a child's therapy team might be engaged in supporting improved feeding behaviors, from occupational therapy to speech-language therapy to ABA. Note that obesity is a real risk for children with ASD and may be linked to repetitive and selective eating habits, medication adverse effects (eg, antipsychotics), increased sedentary time, and fewer opportunities for regular exercise. (66) Families and therapists/teachers should be encouraged to consider a reward other than food to motivate behavior change, especially for children with elevated body mass index.

Some final medical considerations for children with ASD include referral to an ophthalmologist for careful and thorough visual assessment if the child does not make eye contact, has stereotypical behaviors that involve the eyes (eg, eye poking), or shows signs of visual inattentiveness. (2) Children with pica should have blood tests for elevated lead and iron deficiency, and families should be counseled about reducing risk of toxic or otherwise harmful ingestion. And last, families may need extra encouragement and support in accessing routine dental care.

Sleep Problems

Sleep problems are reported in up to 83% of children with ASD and can negatively impact behavior, mood, and cognitive functioning. (67) It is important to work through all of the potential causes of disrupted sleep, including common causes that are not unique to ASD, such as excessive screen time close to bedtime, lack of a consistent calming bedtime routine, medication adverse effects, and obstructive sleep apnea. Comorbid medical conditions such as seizure disorder and comorbid psychiatric conditions such as ADHD or mood disorder may also impact sleep. Behavioral approaches have been shown to be very effective in children with ASD and are recommended as first-line treatment. Multiple double-blind randomized controlled trials have demonstrated efficacy of melatonin in improving sleep onset latency and sleep duration as well as daytime behaviors. (68) It is generally believed to be safe and well-tolerated, at least in the short- to medium-term, whereas research into long-term safety is ongoing. (69)

Recommendations are to use high-purity pharmaceutical-grade melatonin and to start with a low dose (1–3 mg) given 30 to 60 minutes before bedtime and titrate to effect with a maximum dose of 10 mg per day. (67)

Comorbid Psychiatric Conditions

Individuals with ASD have a substantially increased risk of developing most psychiatric disorders, including ADHD, anxiety disorders, sleep-wake disorders, depressive disorders, obsessive-compulsive disorder, bipolar disorders, and schizophrenia spectrum disorders. (70)(71) Clinical practice pathways have been published for the treatment of comorbid conditions, including ADHD, (72)(73) anxiety disorders, (74) irritability and aggression, (75) and insomnia. (67)(76) Evidence for the psychopharmacologic management of psychiatric comorbidity in youth with ASD is limited, and youth with ASD are often more likely to experience adverse effects from medication. (77) Aripiprazole and risperidone have the most evidence for improving irritability and aggression in ASD and have Food and Drug Administration (FDA) indications for this purpose. (78) Although these drugs are commonly prescribed, their utility is limited by potentially severe adverse effects, including metabolic syndrome. (79)

Depression, self-injurious behavior, and suicidality should be screened for carefully in individuals with ASD. Adolescents and adults with ASD with and without ID are at increased risk for suicidal thoughts, self-harm with suicidal intent, and (in adults) dying by suicide, but there are not yet any validated tools for assessing suicidal ideation in youth or adults with ASD. (80)(81)(82)(83)(84)(85) However, the Ask Suicide-Screening Questions toolkit, a freely available 4-item instrument, is currently being investigated in youth 8 years and older with ASD. (86)(87)

Overall, before psychopharmacologic intervention is considered for a problem behavior, the following potential causes of the behavior should be carefully assessed and addressed: 1) medical problems (eg, constipation, dental pain, or ear pain), 2) difficulties with communication, 3) psychosocial stressors, 4) maladaptive reinforcement patterns, and (5) co-occurring psychiatric symptoms, including sensory issues. (75) Safety concerns, including suicidality and aggression, should be assessed and documented carefully. Telephonic Child Psychiatry Access Programs have been developed in some states to improve access to mental health consultations and referrals in complex cases, including for youth with ASD. (88)

FAMILY COUNSELING AND ANTICIPATORY GUIDANCE

Safety

Individuals with ASD are at substantially increased risk for accidental and nonaccidental injury. They are 3 times as likely to die of unintentional injury, with asphyxiation, suffocation, and drowning particularly prevalent among children with ASD younger than 16 years. (89) Youth with ASD have also been found to be at increased risk for emergency department visits due to poisoning and self-injurious behavior, although not more likely to visit the emergency department overall. (90) Youth with ASD are more likely to be referred to Child Protective Services (91) and to have experienced substantiated maltreatment. (92) Women with ASD have been found to be 3 times more likely to be coercively sexually victimized as children. (93) Children with ASD are bullied at 3 to 4 times the rate of neurotypical peers. (94) Families of children with ASD should, therefore, be routinely counseled about safety, supervision, child abuse, dating/relationship safety, and bullying risks.

Wandering is a particularly common and intense concern for many parents of children with ASD. One survey of parents found that one-quarter had children who wandered away from caretakers at least monthly, half had requested changes to the child's individualized education program due to wandering concerns, and three-quarters had wandering concerns impact their willingness to allow the youth to spend time with friends or family without the parent present. (95)(96) To reduce the risk of wandering, parents should be counseled to 1) secure their home (using locks, alarms, printed "STOP" signs on doors, etc); 2) consider a GPS locating device; 3) consider a medical identification bracelet; 4) teach their child to swim; 5) introduce their child to neighbors (in person or via a picture); and 6) alert first responders and work with them to create alert documents in advance. (97)

Integrative, Complementary, and Alternative Medicine

Given that there are no medications that target the core symptoms of ASD, many families seek complementary and alternative treatment options. It is always important to ask about these modalities because some are not evidence-based and have been shown to be harmful, such as chelation and hyperbaric oxygen therapy. (98) As with any treatment decision-making process, it is important to weigh how the available evidence of risks and benefits aligns with patient/family circumstances and preferences. The National Center for Complementary and Integrative Health has a special

Table 5. Familiarizing Yourself with Your Local ASD Resources

ENTITY	DESCRIPTION	WEBSITE
Family Voices	National family-led organization to support children and youth with special health-care needs and disabilities.	www.familyvoices.org Use the search tool to find your local Family-to-Family Health Information Center or Family Voices Affiliate Organization.
Autism Speaks	Large national ASD advocacy organization with local chapters.	www.autismspeaks.org Comprehensive resource guide with filters to narrow by state, age group, and level of support.
Center for Parent Information and Resources	Funded by the US Department of Education to support families of children with disabilities.	https://www.parentcenterhub.org/ Search for your local Parent Training and Information Center (>100 in the United States).
Autism Society	The first national autism organization, with local and state affiliates.	https://www.autism-society.org/ Use the search tool to find your local affiliate. If one does not exist, the national office will support.
The Arc	Supports community inclusion and participation of persons with intellectual and developmental disabilities.	https://thearc.org/ Use the search tool to find a chapter in your state/region.
Parent to Parent USA	Provides emotional and informational support to families of children with special needs.	https://www.p2pusa.org/ Use the interactive map to find a chapter in your state/region.

ASD=autism spectrum disorder.

online section devoted to ASD and can be a resource for providers and families. The gluten-free, casein-free diet is commonly used in ASD, despite inconclusive evidence that behavioral symptoms improve while on the diet. Potential harms include nutrient and/or vitamin deficiencies, lower weight and BMI, further social stigmatization, and increased financial burden for the family. (99)(100)

Although there is anecdotal evidence of the benefits of cannabidiol (CBD) oil for behavioral symptoms, including self-harm behaviors, there is currently inadequate data to support this, and potential adverse effects are important to consider. Pharmaceutical-grade CBD, FDA-indicated for refractory epilepsy, is associated with somnolence, loss of appetite, diarrhea, and transient transaminase elevation. (101) Preparations of CBD that contain tetrahydrocannabinol theoretically might further increase the risk of psychosis in youth with ASD. (102)(103)

Family Stress

Families of children with ASD report lower quality of life, with increased stress, anxiety, and depression, compared with families of children with other disabilities. (104)(105)(106) Beyond causing suffering and adverse physical health outcomes for parents, parent stress interferes with their ability to implement intervention strategies and coordinate services for their children. This, in turn, leads to worse outcomes for children with ASD and their siblings. (107) The integration of parent mindfulness strategies in early intervention for young children has recently been found to reduce parent stress. Parent support groups can also be helpful, particularly if they include families of children with similar disabilities, have flexible structure and content, and have qualified leaders. (108) Family navigators, when available, can also help reduce barriers to care and, in turn, reduce burdens on families. (109) See Table 5 for a list of websites for finding local resources to support families of children with ASD.

Promoting Healthy Outcomes

Some children with ASD move along a more favorable life trajectory and achieve better-than-expected outcomes. (110) Intervening early and intensively can dramatically improve core symptoms and outcomes for some individuals. Indeed, approximately 9% of children diagnosed early (ie, age 2–3 years) with ASD may no longer meet diagnostic criteria by age 19 years. (111) In neurotypical children, parent, environmental, and individual factors all have been found to contribute to resilience to psychopathology after adversity. (112) The study of resilience to childhood psychopathology is only beginning to be extended to ASD, but it is possible that the goodness of fit between the individual with ASD and the environment is an important contributor to outcome. (113) Consideration of the impact of the parent-child relationship, family dynamics, school, and community on the development of the child with ASD can sometimes lead to additional strategies for

intervention. In addition, introducing the child to role models with ASD, through meeting or reading about contemporary and historical figures, can help build self-esteem and sense of potential. The work of the ASD self-advocacy movement has helped many families, clinicians, researchers, and others understand the diverse opinions and experiences of people with ASD and, in turn, guide parenting and treatment strategies.

Adults with ASD, even those without ID or severe language disorder, are at high risk for being unemployed or underemployed, socially isolated, and dependent on others. (114) In addition to the intensity of ASD traits, ID, language level, and challenging behaviors, other factors that have been found to contribute to adult functioning include family resources and participation, access to special education services in high school, perceived stress, and physical and mental health. (19)(114)(115) Early planning for the transition to adulthood, including accessing special education, vocational training, financial supports, living assistance, and community participation resources, can help improve long-term outcomes. (19) Identifying adult medical providers equipped to support adults with ASD often requires additional effort and resources.

Pediatric Medical Home

Navigating systems of care for children with ASD can be challenging for even the most experienced pediatrician, let alone for a family with a child with suspected or newly diagnosed ASD. Not surprisingly, children with ASD have high rates of health-care utilization given the complexity of the care required to support their condition, high rates of comorbidities, and often substantial behavioral/mental health needs. Unfortunately, compared with children with other chronic special health-care needs, they are half as likely to receive care from a medical home. (116) Research has shown that families of children with ASD who do access care from a medical home are 4 times as likely to report that they are receiving all of the services that they need. (117) Key components to creating an ASD medical home for children include 1) incorporating shared decision making with families regarding treatment planning; 2) creating systems for communicating with important members of the care team, including behavioral therapists, school professionals, and other medical specialists; 3) familiarizing yourself with community resources and support; and 4) seeing them frequently for care coordination and to monitor for comorbid medical and psychiatric conditions. (118) For children with more significant behavioral challenges, communicating in advance with the family about what to expect at a particular visit may be beneficial. Families or office staff may use a picture schedule, a narrative with photos, or other visual prompts to prepare for the visit. It can also be helpful to limit excessive visual and auditory stimuli by scheduling patients at the beginning or end of the day, and minimizing time spent in a busy waiting room.

CONCLUSIONS

ASD is a complex and heterogeneous disorder. There is strong evidence that early and intensive behavioral intervention is critical for long-term outcomes. With rising prevalence rates and a shortage of services in many geographic areas, pediatricians are increasingly being called on to take a more active role in the identification and management of ASD. Pediatricians' roles are expanding to include finding creative ways to support families in navigating the complex web of diagnostic and treatment services for patients with ASD, identifying and managing comorbid conditions, and sometimes diagnosing ASD. Given the racial and socioeconomic status disparities in timely diagnosis, service access, and service quality, addressing barriers with a health equity lens is crucial. Compounding these existing barriers will be the long-lasting effects of the COVID-19 pandemic, which we anticipate may be associated with decreased screening rates, longer wait times for specialty assessment, and decreased rates of connection to therapeutic services.

Summary

- Based on strong research evidence (Level A), the prevalence of autism spectrum disorder (ASD) in the United States has increased in recent years. (1)
- Based on strong research evidence (Level A), girls, minority children, and children from non–English-speaking households are more likely to have missed or delayed ASD diagnoses; particular attention should be given to screening in these populations. (1)(13)(15)(16)(17)
- Based on some research evidence as well as consensus (Level B), the American Academy of Pediatrics recommends use of an ASD-specific screening tool at the 18- and 24-month health supervision visits because structured screeners have been shown to increase the likelihood of early identification of both ASD and other developmental delays. Due to concerns about low sensitivity, clinicians should refer for specialist

ASD evaluation based on clinician and parent concerns and not solely based on screening results. (2)(33)(34)

- Based primarily on consensus due to lack of relevant clinical studies (Level C), children who screen positive on ASD-specific instruments should be referred for both school/early intervention evaluation and a specialist ASD diagnostic evaluation.
- Based on some research evidence as well as consensus (Level B), the gold standard for diagnosis of ASD is a multidisciplinary evaluation, but not all elements are necessary for the initial diagnosis and initiation of early intervention services. Pediatricians may want to consider provisional in-office diagnoses to help children access specialized services earlier in development, when the potential therapeutic benefits may be greater. (44)
- Based on some research evidence as well as consensus (Level B), the behavioral intervention with the strongest evidence base is applied behavior analysis therapy, with several studies showing high-intensity treatment leading to the largest gains especially for children younger than 3 years. (58)(59)(60)
- Based on some research evidence as well as consensus (Level B), youth with ASD are at increased risk for certain medical comorbidities, most psychiatric diagnoses, and intentional/unintentional injury. Pediatricians should routinely screen for and counsel families about these conditions. (89)(90)(91)(92)(93)(94)(95)(96)(97)

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Intellectual Disabilities

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Education Gaps

1. Pediatricians must have knowledge of the diagnostic criteria and levels of severity of intellectual disability (ID).
2. Pediatricians should be informed about current developments in the evaluation of a child with ID.
3. Pediatricians must be familiar with treatment and resources for children with ID.

Objectives

After completing this article, readers should be able to:

1. Formulate a plan for the evaluation of children with intellectual disability (ID) both in terms of coming to a diagnosis (evaluation of cognitive and adaptive skills) and performing a diagnostic evaluation.
2. Formulate treatment options and referral for services for children with ID.

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ABBREVIATIONS

AAIDD	American Association of Intellectual and Developmental Disabilities
AAP	American Academy of Pediatrics
CDC	Centers for Disease Control and Prevention
CT	computed tomographic
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
GDD	global developmental delay
ID	intellectual disability
IEP	Individualized Education Program
MRI	magnetic resonance imaging
WISC-V	Wechsler Intelligence Scale in Children-V
WPPSI-IV	Wechsler Preschool and Primary Scale of Intelligence-IV

Intellectual disability (ID) is a neurodevelopmental disorder that is characterized by deficits in both intellectual functioning and adaptive functioning, whose onset is in the developmental period. (1) It affects approximately 1% to 3% of the population. (2) *Intellectual disability* has replaced the former term, *mental retardation,* through a federal statute (Rosa's Law, Public Law 111-256). *Global developmental delay (GDD)* is the term used to describe children aged 0 to 5 years with significant delays in 2 or more areas of development. (1) Although these delays may be transient, it is estimated that approximately two-thirds of children diagnosed as having GDD would eventually carry the diagnosis of ID after 5 years of age. (3)

As part of routine health-care visits, the American Academy of Pediatrics (AAP) recommends developmental surveillance at every well-child visit and formal developmental screening at ages 9, 18, and 24 or 30 months. (4) Screening instruments such as the Ages and Stages Questionnaire, the Pediatric Evaluation of Developmental Skills, and the Denver Developmental Screening Test-II help to identify children who will require more formal developmental assessments, where a child's developmental skills are more thoroughly evaluated and that will likely include testing of cognitive abilities.

PRESENTATION

Intellectual disability may present in various ways and at different ages in the pediatric patient. The more severe the impairment, the more likely ID is to present and be diagnosed earlier. Correspondingly, the milder the impairment, the more likely it is to manifest at an older age. It is possible that milder forms of ID may go unrecognized until the school-age years. A child with ID may present initially with receptive and expressive language delays, adaptive skills delays (eg, toileting, dressing), fine motor deficits, difficulties in problem-solving skills, social immaturity, and behavioral difficulties. It is important to consider that intelligence/developmental tests during the first 3 years of life involve many sensorimotor tasks that may affect the accurate measurement of the cognitive level of a child with a motor problem (eg, cerebral palsy, hypotonia) or sensory impairment (visual and auditory). Among the different areas of development monitored in early childhood (language, problem-solving, gross/fine motor, personal-social skills), gross motor skills are the least correlated with ID.

ASSESSMENT

Assessment of Intellectual Functioning

Intellectual functioning is measured by standardized instruments such as the Wechsler Intelligence Scale in Children-V (WISC-V), the Wechsler Preschool and Primary Scale of Intelligence-IV (WPPSI-IV), and the Stanford-Binet Intelligence Scales-V. These are generally performed by a certified psychologist or special educator. These instruments are designed to measure a child's general intellectual ability and include verbal and nonverbal subtests. Persons with ID exhibit deficits in both verbal and nonverbal domains, although not necessarily to the same degree. An overall full-scale IQ score is derived from the combination of verbal and nonverbal IQ scores.

The WISC-V and WPPSI-IV include the following indices: verbal comprehension index, visuospatial index, fluid reasoning, working memory, and processing speed. The Stanford-Binet subtests include knowledge, quantitative reasoning, visuospatial reasoning, working memory, and fluid reasoning. These instruments can be administered in children as early as approximately age 2 years (Stanford Binet-V) to 2½ years (WPPSI-IV), although it is important to note that intelligence scores become more stable after 5 years of age. (5)(6)(7) People with intelligence scores more than 2 SD below the mean are considered to fall in the ID range. Using the normal curve to delineate levels of intelligence with a mean IQ score of 100 and a standard deviation of 15, it is estimated that approximately 2.5% of the population would fall in the ID range with IQ scores less than 70 (2 SD below the mean). Those with IQ scores of 70 to 84 are considered to have borderline intelligence. In school, children with borderline intelligence may be considered "slow learners" but not to the same degree as children with ID. Making a diagnosis of ID is not always straightforward; it may require a few visits to fully assess a child, and ongoing follow-up may be necessary.

Assessment of Adaptive Functioning

Adaptive functioning is measured through questionnaires such as the Vineland Adaptive Behavior Scales and the Adaptive Behavior Assessment System, (5) which are administered by certified clinicians such as psychologists or social workers with information obtained from the patient's primary caregivers. In the *Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition,* adaptive functioning is operationalized in terms of 3 domains: the conceptual domain (eg, competence in memory, language, academics, judgment), the social domain (eg, social awareness, interpersonal communication skills, friendships), and the practical domain (eg, learning and self-management). Impairment in at least 1 of these domains, wherein ongoing support is needed, should be present to meet the definition of ID. (1)

The American Association of Intellectual and Developmental Disabilities (AAIDD), the oldest interdisciplinary professional organization that has been instrumental in the definition and recognition of ID and its earlier iterations, uses a similar definition of ID as the *DSM-V*. The AAIDD defines ID as a disability characterized by "significant limitations in both intellectual functioning and adaptive behavior" with the onset of deficits before 18 years of age. (8)

LEVELS OF SEVERITY

The *DSM-V* and the AAIDD characterize the severity of ID based on a person's adaptive functioning and the amount of support a person needs. These are described and summarized in the following subsections (Table 1). (1)(6)

Mild ID

A person with mild ID may manifest difficulties in late preschool or the early school-age years. They may have difficulties in the academic setting (early reading, writing, arithmetic, time, and money) and seem more socially immature compared with other children their age. Communication and thinking may be more concrete and less mature than that of their peers. Although they may function

TABLE 1. **Levels of Severity of Intellectual Disability (ID)**

LEVEL OF ID (% CHILDREN WITH ID)	LEVEL OF SUPPORT (IN CONCEPTUAL, SOCIAL, PRACTICAL DOMAINS)	ASSOCIATED ESTIMATED IQ SCORE	PROJECTED ULTIMATE ACADEMIC ACHIEVEMENT
Mild (85%)	Intermittent	55–70	Up to sixth-grade level
Moderate (10%)	Limited	40–55	Up to second-grade level
Severe (3%–4%)	Extensive	25–40	Preschool level
Profound (1%–2%)	Pervasive	<25	–

Note: The level of severity is based on the level of adaptive functioning and support. (1)(6)

appropriately in matters of personal care and many even eventually live independently, they may need support intermittently, particularly in complex daily living situations. Some may be able to reach a sixth-grade level in academic functioning.

Moderate ID

A person with moderate ID generally presents earlier than those with mild ID, manifesting with learning and language difficulties in the preschool years and deficits in social and communication behavior, which require limited although possibly substantial support. Those affected may ultimately be able to perform basic tasks for personal care (eg, dress, toilet, and eat independently), but significant amounts of support time and teaching may be needed. During adulthood, they may be employed in jobs that require minimal communication and cognitive skills and may be able to participate in all household tasks but with ongoing support and teaching. Some may be able to reach a second-grade level in academic functioning.

Severe ID

A person with severe ID has limited capacity to understand written language and the concepts of numbers and time and would need extensive support from caretakers throughout life. Spoken language is also very limited, and they may have limited understanding of speech/language and gestural communication. Children with severe ID would require extensive support and supervision for all activities of daily living. Some may reach the pre-K level in academic functioning.

Profound ID

A person with profound ID has conceptual skills that do not go beyond the concrete, and ability mainly involves manipulation of objects, at best. They have very limited understanding of symbolic language, although they may be able to understand basic instructions. A person with profound ID requires pervasive support and is dependent in all aspects of personal care and daily living.

In the *DSM-IV* and *DSM-IV-TR*, the previous editions of the *DSM*, (9) levels of ID were extrapolated by increasing standard deviations from the mean IQ; thus, mild ID was defined as IQ scores between 2 and 3 SD below the mean of 100 (IQ scores from 50–55 to approximately 70); moderate ID corresponded to IQ scores between 3 and 4 SD below 100 (IQ scores from 35–40 to 50–55); severe ID was defined as IQ scores between 20 to 25 and 35 to 40; and profound ID corresponded to IQ scores less than 20 to 25. Although this classification may still be useful, using IQ scores solely does not accurately and completely reflect how well an individual is able to function, hence the shift in the classification of the levels of ID based on the individual's level of adaptive function.

ETIOLOGY

There are many different etiologies for ID: genetic disorders (eg, chromosomal disorders, including X chromosome disorders, contiguous gene deletions, and single-gene disorders), environmental causes (eg, alcohol and other teratogens, prenatal infections), traumatic brain injury, neurologic/brain disorders, nutritional deficiencies, and inborn errors of metabolism. A significant number of people with ID have no identifiable cause (Table 2). It is more likely to identify a biological cause in more significant forms of ID (such as moderate, severe, and profound ID) than in mild ID, which may be influenced by cultural, linguistic, and societal difficulties. (5)

Genetic Causes of ID

Online Mendelian Inheritance in Man (10) lists approximately 800 genetic syndromes associated with ID. These syndromes may have X-linked, autosomal dominant, or

TABLE 2. **Causes of Intellectual Disability**

Genetic syndromes
Chromosomal disorders, eg, Down syndrome
Contiguous gene deletions, eg, Williams syndrome, Angelman syndrome
Single-gene deletions, eg, fragile X syndrome, Rett syndrome
Environmental causes
Alcohol and other teratogens
Prenatal infections
Early childhood central nervous system infections
Traumatic brain injury
Central nervous system disorders/malformations
Inborn errors of metabolism
Nutritional (eg, severe malnutrition, chronic iron deficiency)
Not known

autosomal recessive inheritance. Medical evaluation for those with syndromic forms of ID will be based on known clinical manifestations of the genetic syndrome. (10)(11)(12) Table 3 summarizes some of the more common genetic syndromes associated with ID.

Down syndrome is the most common genetic cause of ID, with prevalence of 1 in 800, with 95% of cases due to trisomy 21, 4% to 5% due to an unbalanced translocation between chromosome 21 and another chromosome (usually chromosome 14), and 1% attributed to mosaicism. The clinical phenotype is very well-known and includes a distinct facies, congenital heart disease, hypothyroidism, gastrointestinal disorders, and hypotonia. Intelligence is usually in the mild-moderate range of ID, with verbal skills weaker than nonverbal skills. It is also associated with early Alzheimer disease and depression. The AAP has published health maintenance guidelines for children with Down syndrome. (13)

Fragile X syndrome is a trinucleotide repeat disorder (CGG) and is the most common inherited cause of ID, affecting 1 in 4,000 individuals. Although it is much more common in males, fragile X syndrome may be diagnosed in girls as well. Fully affected males (with triplet repeats >200) manifest with significant ID as well as clinical features that may include relative macrocephaly, an elongated face, prominent ears, hyperextensible joints, and large testes in postpubertal individuals. Females with fragile X syndrome may present with milder forms of cognitive impairment. Fragile X syndrome also has a well-recognized association with autism spectrum disorders. (2)

Rett syndrome is due to a mutation of the *MECP2* gene found in the X chromosome. It is primarily seen in girls (although it has also been identified in boys), where the clinical presentation includes a deceleration in the rate of head growth during the second year of life, hand-wringing and handwashing movements, language deficits/regression, and ID. It is more likely that males with *MECP2* mutations present with neonatal encephalopathy than with GDD/ID. (2)

Certain contiguous gene disorders are also associated with ID. (10)(11)(12) Williams syndrome is caused by a deletion in chromosome 7q11 and presents with elfinlike facial features, mild to moderate ID (with nonverbal function being a significant weakness), and cardiac and renal manifestations. Angelman and Prader-Willi syndromes are a result of genetic imprinting, where clinical manifestations depend on which parent contributes to the deletion in chromosome 15q11.2-q13. Less commonly, these syndromes can also be attributed to uniparental disomy (2 copies of a chromosome from the same parent). Angelman syndrome is due to a maternally derived deletion (or paternal disomy) and is associated with severe-profound ID, microcephaly, prognathism, and abnormal hand movements, whereas Prader-Willi syndrome is caused by a deletion in the paternally derived chromosome (or maternal disomy). The clinical course of patients with Prader-Willi syndrome is unique and consists of hypotonia and feeding difficulties in the neonatal period and obesity, atypical facial features, some degree of ID (low average to moderate ID), and psychiatric conditions (eg, obsessive compulsive disorder, skin picking) starting in toddlerhood or the preschool years. Smith-Magenis syndrome is caused by a deletion in the short arm of chromosome 17 (17p11.2) and is characterized by facial features such as midface hypoplasia and a broad nasal bridge, short stature, medical conditions such as visual problems, peripheral neuropathy, mild-moderate ID, sleep disturbances, and stereotypic and self-injurious behaviors. Miller-Dieker syndrome is due to a deletion in chromosome 17 and is associated with significant ID, microcephaly, and lissencephaly, where the brain is small and smooth due to a paucity of gyri and sulci.

Single-gene deletions associated with ID, aside from fragile X syndrome and Rett syndrome, include Rubinstein-Taybi syndrome (ID, short stature, microcephaly, abnormalities of the thumbs and toes) and tuberous sclerosis (skin manifestations, ID, autism, seizures, particularly infantile spasms). (10)(11)(12)

Environmental Causes of ID

Environmental causes of ID may also present with a set of symptoms that compose a syndrome. Fetal alcohol spectrum disorder results from prenatal exposure to alcohol and

TABLE 3. **Common Genetic Syndromes Associated with Intellectual Disability (ID)**

SYNDROME	GENETIC ABNORMALITY	DEVELOPMENTAL PROFILE	COMMON PHYSICAL FINDINGS
Down	Trisomy 21 (95%) Translocation (4%) Mosaicism (1%)	Mild to moderate ID (Verbal - low) Hypotonia Early Alzheimer disease	Down facies Congenital heart disease Hypothyroidism Gastrointestinal abnormalities
Fragile X	CGG trinucleotide repeat (>200)	ID (typically moderate) Learning disorders Autism spectrum disorder	Elongated face Macrocephaly Prominent ears Hyperextensible joints Enlarged testes (postpuberty)
Rett	*MECP2* deletion	ID Stereotypic hand mannerisms Language regression	Deceleration in head growth Gait abnormalities
Williams	7q11 deletion	Mild to moderate ID (nonverbal - low)	Elfinlike facial features Cardiac (eg, supravalvular aortic stenosis) Renal abnormalities Hypertension
Angelman	Maternally derived deletion 15q (or paternal disomy)	Severe to profound ID Atypical hand mannerisms	Microcephaly Prognathism
Prader-Willi	Paternally derived deletion 15q (or maternal disomy)	ID (variable levels) Psychiatric conditions	Neonate: hypotonia/feeding difficulties Toddler: obesity, excessive appetite

is characterized by alcohol-related birth defects, microcephaly and growth retardation, facial features such as short palpebral fissures, thin upper lip, smooth philtrum, neurocognitive problems such as ID and ADHD, and behavioral difficulties. (14) Intrauterine infections (TORCH) may present with developmental disabilities, growth defects, retinopathy, intracranial calcifications, and abnormalities in head size such as microcephaly (eg, cytomegalovirus) or macrocephaly (eg, toxoplasmosis associated with hydrocephalus). Most recently, congenital Zika infection has been implicated in causing significant microcephaly and other brain abnormalities in infants, which may likely lead to ID. (15)

Significant hypoxic-ischemic injury in the neonate may present early on with significant GDDs, motor impairment such as muscle hypertonicity/spasticity, microcephaly or poor head growth, and seizures. Many children with severe hypoxic-ischemic encephalopathy will eventually be diagnosed as having ID as well as cerebral palsy. Prematurity, especially for children with younger gestational age and more complicated courses, also places a child at risk for intellectual impairment and developmental disorders. (16)

In the United States, there has been a significant decrease in the levels of environmental lead due to successful public health efforts implemented during the past few decades. Consequently, there has been a dramatic decrease in blood lead levels in children. Mildly elevated lead levels are still detected, and these have been shown to be associated with mild cognitive delays. Lead toxicity has been associated with a decline of 1 to 2 IQ points (measured at 5 years or older) for every 10-point increase in lead level (17)(18) and a decrease of more than 7 IQ points for the first 10 μg/dL. (19) The AAP recommends further research to look more closely into these associations, through studies where confounders such as socioeconomic factors are better controlled for. (17)

Through newborn screening, conditions that may have led to ID if left untreated are being identified. These conditions include phenylketonuria and congenital hypothyroidism. In 2006, the American College of Medical Genetics Newborn Screening Expert Group recommended that 29 treatable conditions be universally screened in the newborn. (20) There are variations in each state as to the complete set of disorders that are being tested for. Pediatricians should be familiar with the conditions that are tested for in their state and ensure that each newborn undergoes the state's newborn screening. The AAP has provided recommendations for pediatricians and medical homes as newborn screening has expanded. (21)

APPROACH TO EVALUATION

The approach to the evaluation for the etiology of the ID includes a thorough history, focused physical and neurologic

examinations, and appropriate laboratory testing as warranted. (2)(7) History and physical examination together can identify the etiology in approximately 17% to 34% of cases of developmental delay. (7) Based on the history and physical examination findings, initial evaluation, including laboratory testing, genetic testing, and imaging, is determined.

History

The medical history includes a child's current developmental functioning and a chronology of attainment of developmental milestones, a history of educational interventions, and a detailed prenatal/perinatal/neonatal history, which should include any history of maternal medical conditions and outcomes of previous pregnancies, maternal infections, medication intake and substance use/abuse, and a review of the newborn metabolic and hearing screens. A 3-generation family history of developmental problems; ID; learning deficits; neurologic, metabolic, or genetic conditions; and consanguinity should be explored. The child's medical history should include any previous head injuries, central nervous system infections (such as meningitis or encephalitis), seizures and other neurologic conditions, and regression in skills.

Physical and Neurologic Examination

The physical examination focuses on growth parameters (especially head circumference), a thorough skin examination looking for lesions that may signify a neurocutaneous syndrome, a full neurologic examination, and evaluation for dysmorphic features that may suggest a genetic syndrome.

Evaluation of Head Size. Microcephaly, or a head circumference less than the third percentile for age, is highly associated with ID and is a manifestation of many disorders. Macrocephaly or a head circumference greater than the 97th percentile for age is associated with ID in the setting of certain genetic syndromes, such as fragile X syndrome and Sotos syndrome, as well as in patients with hydrocephalus. Autism spectrum disorder has also been associated with an enlarged head, especially in the first 5 years of life, (22) and in some of these cases, ID may be present.

Examination of the Skin. Neurocutaneous syndromes may also be associated with ID. (10)(11) Tuberous sclerosis is associated with skin findings such as ash leaf spots (hypopigmented macules), shagreen patches ("peau d' orange"–textured skin lesions), and facial angiofibromas. Neurofibromatosis, which is associated with attention-deficit/hyperactivity disorder, learning disorders, and, less commonly, ID, is characterized by café au lait spots, inguinal and axillary freckling, Lisch nodules on eye examinations, and neurofibromas in the body.

Dysmorphic Features. The clinician should take note of dysmorphic features and atypical features that may be manifestations of certain genetic syndromes as described previously.

LABORATORY EVALUATION

Evaluation of Syndromic Forms of ID

If the clinician suspects a specific syndrome as an etiology for the ID/GDD, laboratory tests to confirm or rule out this syndrome should be performed. This may include chromosome analysis for Down syndrome and fluorescence in situ hybridization testing when specific genetic disorders are suspected, such as Prader-Willi/Angelman syndrome, Smith-Magenis syndrome, Williams syndrome, 22q11 deletion, Miller-Dieker syndrome, cri du chat syndrome, and Wolf-Hirschhorn syndrome.

For patients with suspected TORCH and Zika infections, serologic testing, neuroimaging, eye examination, and hearing tests are recommended. (23) A referral to a genetics specialist may be considered for further evaluation of dysmorphic features.

Evaluation of Nonsyndromic ID of Unknown Etiology

The American Academy of Neurology has released reports with recommendations for the evaluation of nonsyndromic GDD/ID of unknown etiology. (7)(24) It is widely regarded among clinical geneticists that chromosomal microarray analysis, with a yield of approximately 15% to 20%, (25) should be the first-line cytogenetic test for these cases. There has been less universal consensus for fragile X testing, but many experts recommend fragile X testing in boys and girls with ID who have clinical features of fragile X syndrome (macrocephaly, prominent ears, hyperextensible joints, perseverative speech, enlarged testes in pubertal boys), as well as unexplained GDD/ID (in both sexes) if there is a family history of ID. Many geneticists also recommend fragile X testing for unexplained ID if the microarray result is normal. Karyotyping is recommended if there is a suspicion of aneuploidy (presence of an abnormal number of chromosomes in a cell) such as Down syndrome, a history of many miscarriages, or a family history of chromosomal abnormalities. Some clinicians recommend all 3—chromosomal microarray analysis, fragile X testing, and karyotyping—as the first-line evaluation for both boys and girls with nonsyndromic ID of unknown etiology considering the yield of approximately 2% for fragile X testing and 4% for karyotyping for these cases. (24) Microarray analysis does not detect balanced translocations (which a karyotype is able to), point mutations, or low level of mosaicism. (25) If microarray

analysis reveals an abnormality, further genetic testing of the parents may be recommended. For females with severe to profound ID, testing for Rett syndrome (*MECP2* gene) is recommended. (24)(25)

Consultation and collaboration with a clinical geneticist may be very useful in the evaluation of children with ID, especially those with unexplained ID, syndromic ID, or more severe levels of ID. Clinical geneticists and genetic counselors may also be helpful in the interpretation of the results of genetic testing. (25) A newer form of genetic testing, whole exome sequencing, may be able to identify a genetic cause in up to 40% of patients with unexplained ID; however, it is not widely available at this time, and the implications of using whole exome sequencing in the routine evaluation of all children with ID, wherein other genetic abnormalities not related to ID may be unearthed, is still not fully understood and must be explored further. (2)(25)

Inborn errors of metabolism account for a small percentage (approximately 0%–5%) of children with unexplained ID. (2)(7)(26) Testing for these conditions has been recommended for cases that are clinically suggestive of a metabolic disorder. Most of these conditions are associated with neurologic symptoms (ie, hypotonia, ataxia, dementia, epilepsy, spasticity), sensory deficits (visual and hearing impairment), and nonneurologic features, such as gastrointestinal symptoms, dermatologic findings, atypical odor, and problems in growth. Specific metabolic testing includes acylcarnitine profile, amino acids and urine organic acids, glycosaminoglycans, oligosaccharides, serum total homocysteine, purines, pyrimidines, and GAA/creating metabolites. (2) Recent reports have identified 89 inborn errors of metabolism associated with ID that are amenable to treatment. In line with this, a 2-tiered algorithm in testing for treatable forms of inborn errors of metabolism in a person with ID has been proposed. (26) Further studies are needed to fully comprehend the efficacy and implications of this approach in the evaluation of a child with unexplained ID. (7)(27)

Magnetic resonance imaging (MRI) may be helpful in the evaluation of children with nonsyndromic ID/GDD in the setting of abnormal neurologic findings such as microcephaly, macrocephaly, or focal neurologic signs, (28) with the likelihood of finding a structural abnormality increasing to 28% from a rate of 7.5% if the GDD/ID was isolated and not associated with abnormalities in head size or focal neurologic findings. The risk in the use of sedation or anesthesia in MRI studies, although low, should also be weighed in the evaluation of these children. An MRI is preferred over computed tomographic (CT) scan in identifying abnormal brain architecture and myelination and in the evaluation of deeper brain centers. A CT scan is useful to visualize calcifications, which may be present in prenatal infections such as toxoplasmosis and cytomegalovirus.

DIFFERENTIAL DIAGNOSES

In the evaluation of persons suspected of having ID, it is important to differentiate ID from neurodegenerative disorders, specific learning disorders, receptive/expressive language disorders, autism spectrum disorders, and sensory deficits (visual impairment and hearing impairment).

Neurodegenerative disorders present with significant regression in different aspects of functioning due to a progressive neurologic condition. This is in contrast to ID, whose etiology is nonprogressive (eg, genetic abnormality or a nonprogressive brain lesion). Specific learning disorders are neurodevelopmental disorders characterized by persistent difficulties in learning (eg, reading, mathematics, and/or written expression) that are not explained by and are not commensurate with one's cognitive potential. Children with specific learning disorders can be differentiated from those with ID in that they may have impairment in specific areas of learning (eg, reading/phonological skills) but have age-appropriate adaptive skills and cognitive skills, whereas children with ID will have global impairment in cognitive and adaptive skills. Language deficits may also be present in ID, but in ID there are also significant nonverbal deficits, leading to a more global impairment in function. Autism spectrum disorder is frequently associated with ID but is a separate disorder characterized by persistent social-communication and social interaction deficits, restricted/repetitive patterns of behavior, and atypical sensory reactivities. (1) The cognitive level of children with autism may range from significant ID to normal intelligence. Last, in the evaluation of a child with suspected ID, it is important to rule out any significant visual and hearing impairment that may contribute to the child's deficits in functioning.

MANAGEMENT

Special Education and Early Intervention

The mainstay of treatment and management of children with ID/GDD is the utilization of special education and early intervention programs. (6)(29) The Individuals with Disabilities Education Act provides individuals with ID/GDD the right to receive free and appropriate public education with goals and services as specified in their Individualized Education Program (IEP) or Individualized Family Service Plan (for children <3 years old). Studies have shown that early childhood education programs have long-term beneficial effects on cognition, language, academics (reading and

math), and youth behavior. (30)(31) There has been research as well showing that participation of children with ID (eg, Down syndrome) in early childhood educational programs may, at the very least, minimize the decline of intellectual functioning that occurs in these children. (32)(33)

During well-child visits, the pediatrician may detect developmental differences and delays through developmental surveillance or screening. Children who are suspected of having ID/GDD or other neurodevelopmental disorders should be referred to the state early intervention program (for children 0–3 years old) or to the Board of Education's Committee on Preschool Special Education (for children 3–5 years old) or Committee on Special Education (for children 5–21 years old) for evaluation and services.

The Individuals with Disabilities Education Act stipulates that children with disabilities receive their educational services in the least restrictive environment that is possible and appropriate to address their educational needs. Because of this, there has been a thrust toward mainstreaming wherein children with disabilities, even those with ID, may participate in more typical school environments for most or part of the school day. An inclusion or collaborative team teaching classroom is such a setting where children with special needs participate in the same classroom as typically developing children under the tutelage of 1 main teacher and 1 or more special education teachers. Children with disabilities may also receive related services such as speech/language therapy, occupational therapy, physical therapy, and counseling. In addition, classroom modifications and accommodations may be given to children with learning or intellectual disabilities through Section 504 of the Rehabilitation Act, (6) a federal law that protects individuals with disabilities from discrimination in various settings, including the public school system. Enhancing a person with ID's ability to communicate, not only through speech/language therapy but also through the use of a picture exchange communication system or augmentative communication devices, may be an important aspect of a child with ID's educational plan. Compared with typically developing children, children with ID learn at a much slower pace and may require more frequent repetitions before mastering a skill. Furthermore, the gap between these 2 groups will be increasingly wider as the years go by—an important tenet when counseling parents.

For children with more severe impairment, such as those with moderate to profound ID, a self-contained classroom may be needed wherein there is a small student to teacher ratio and the provision of individual or group paraprofessionals as needed. The child's IEP should reflect appropriate goals, which may be educational, vocational, or adaptive, while taking into consideration one's strengths and weaknesses. As the child reaches 16 years of age, the development of an Individualized Transition Plan would ensure continued support, beyond the educational realm, in areas such as employment, adult living skills, and recreation. (29)

Throughout this educational process, pediatricians play a key role, starting with the timely referral and identification of individuals with ID/GDD to being important advocates for their patients to receive services and interventions until they transition into adulthood. The Center for Parent Information and Resources (funded by the US Department of Education) offers helpful online information for pediatricians and parents about ID and the educational process, including the IEP and Individualized Transition Plan (http://www.parentcenterhub.org/intellectual/#school and http://www.parentcenterhub.org/transitionadult/).

Medical Home

The AAP and the US Department of Health and Human Services through its Healthy People 2010 have recommended that children, especially those with special health-care needs, which includes ID, receive "regular, ongoing, comprehensive care within a medical home." (34) In the medical home model of care, the pediatrician in collaboration with other medical subspecialists and professionals such as social workers and community health workers work as a team in the care of children with special needs, who, in addition to their primary disability, may have significant comorbid medical and psychiatric conditions and family challenges. The involvement of the family and addressing its needs are important components of the medical home.

Management of Comorbid Medical Conditions. Individuals with ID, especially those with moderate to profound ID, may have comorbid medical conditions such as seizure disorders, cerebral palsy, gastrointestinal disorders, and respiratory problems, which may have a significant effect on their daily functioning, progress, and need for additional support. (1)(5) Other important medical issues to explore in the care of people with ID are matters of sexuality and abuse, obesity and nutrition, physical activity and fitness, dental issues, and pain management. In addition to referring to appropriate subspecialists, the pediatrician has a role in providing information and resources to families about the child's disability, recommending healthy lifestyle options for diet and recreation, assuming the role of a conduit between the family and medical subspecialists, and being advocates for services that may address a patient's and family's needs. Online resources from the Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/intellectualdisability.pdf and https://www.cdc.gov/ncbddd/disabilityandhealth/healthyliving.html) and Parent Center

Hub (http://www.parentcenterhub.org/find-your-center/) are examples of resources that may aid the pediatrician in this role.

Management of Comorbid Mental Health Conditions. Thirty percent of individuals with ID may have comorbid mental health conditions. (35) This rate is significantly higher than the rate observed in the general population. These mental health conditions include attention-deficit/hyperactivity disorder, depression, mood disorders, aggressive behaviors, and self-injurious behaviors. Behavioral interventions should be implemented in those with major behavioral difficulties, such as hyperactivity, aggressive behaviors, and self-injury. These interventions may be implemented in the home or school setting, with carryover to other settings to provide maximal benefit. Treatment with appropriate psychopharmacologic medications, based on target symptoms (eg, hyperactivity, aggressive behavior, self-injury), should be considered in those not fully controlled by behavioral measures, and referral to a child psychiatrist for medication management may be necessary.

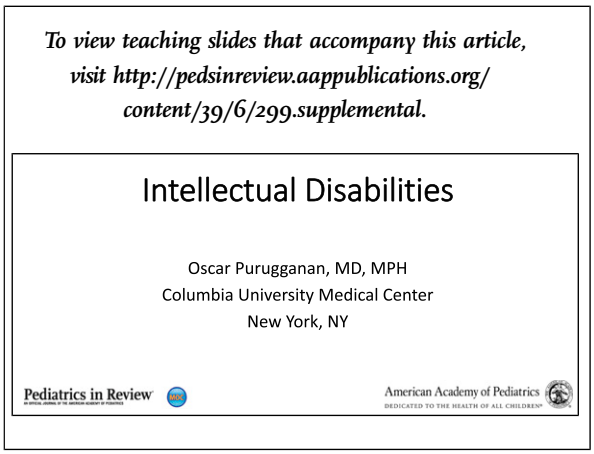
Referral to State/Community Programs and Family Supports. It is important for the pediatrician to be aware of the state and community programs that are available for persons with ID and other developmental disabilities in their community. A social worker, who may be consulted within the practice (if available) or in community agencies, may be an invaluable resource in providing support for families and in directing them to the appropriate community programs. In New York State, children with significant ID and other developmental disabilities, such as autism, are directed to the New York State Office for People with Developmental Disabilities (https://opwdd.ny.gov/). After undergoing an eligibility evaluation, each child with a disability is assigned a service coordinator who assists the family in obtaining access to community programs, respite services, home care support and after-school programs, behavior-management training, transportation services, crisis intervention, etc. (36)(37) The pediatrician or social worker may also refer the child to entitlement programs such as Social Security and Medicaid, which may provide invaluable supports for families.

As a child with ID reaches adulthood, issues such as legal guardianship, transitioning to an adult health-care provider, and employment come to the forefront and must be addressed. There is growing research that shows that given appropriate support and guidance, persons with ID may strive for competitive or supportive employment. (29) With these educational, medical, and community interventions, the ultimate goal is for persons with ID to reach their maximum potential as individuals and as members of the community.

Summary

- According to the definition, intellectual disability (ID) is a neurodevelopmental disorder that is characterized by deficits in both intellectual functioning and adaptive functioning (>2 SD below the mean as measured by standardized tests and questionnaires), with onset in the developmental period or younger than 18 years of age. The severity of ID is based on a person's adaptive functioning and level of supports. (1)
- Based on some research evidence as well as consensus, the initial approach to the evaluation for the etiology of the ID includes a thorough history, a detailed physical examination, and a focused evaluation based on the history and physical examination findings, which may include laboratory testing, genetic testing, and imaging. (7)
- Based on some research evidence as well as consensus, the recommendation for the evaluation of nonsyndromic ID of unknown etiology includes genetic testing with chromosomal microarray analysis, fragile X testing, and karyotyping. For females with severe-profound ID, testing for Rett syndrome is also recommended. (24)
- Based on some research evidence as well as consensus, the mainstay of treatment and management of ID/global developmental delay is the utilization of special education and early intervention programs through the Individuals with Disabilities Education Act. Individuals with ID, especially those with moderate to profound ID, should also be evaluated for comorbid medical and mental health conditions, which are more prevalent in this population than in the healthy population. Finally, children with ID, as with other children with special health-care needs, are best followed in a medical home–type setting where there is collaboration between the pediatrician, other health professionals, community workers, and the child's family. (6)(29)(30)

To view teaching slides that accompany this article, visit http://pedsinreview.aappublications.org/content/39/6/299.supplemental.



References for this article are at http://pedsinreview.aappublications.org/content/39/6/299.

Medical Evaluation of a Child with Developmental Delay

TABLE 1

Risk factors for developmental delay that can be identified on the developmental assessment

Area	Age	Findings
Motor	4½ mo	Does not pull up to sit
	5 mo	Does not roll over
	7–8 mo	Does not sit without support
	9–10 mo	Does not stand while holding on
	15 mo	Not walking
	2 yr	Not climbing up or down stairs
	2½ yr	Not jumping with both feet
	3 yr	Unable to stand on one foot momentarily
	4 yr	Not hopping
	5 yr	Unable to walk a straight line back and forth or balance on one foot for 5 to 10 sec
Fine motor	3½ mo	Persistence of grasp reflex
	4–5 mo	Unable to hold rattle
	7 mo	Unable to hold an object in each hand
	10–11 mo	Absence of pincer grasp
	15 mo	Unable to put in or take out
	20 mo	Unable to remove socks or gloves by self
	2 yr	Unable to stack 5 blocks or not scribbling
	2½ yr	Not turning a single page of a book
	3 yr	Unable to stack 8 blocks or draw a straight line
	4 yr	Unable to stack 10 blocks or copy a circle
	4½ yr	Unable to copy a square
	5 yr	Unable to build a staircase of blocks or copy a cross
Language	5–6 mo	Not babbling
	8–9 mo	Not saying "da" or "ba"
	10–11 mo	Not saying "dada" or "baba"
	18 mo	Has <3 words with meaning
	2 yr	No 2-word phrases or repetition of phrases
	2½ yr	Not using at least 1 personal pronoun
	3½ yr	Speech only half-understandable
	4 yr	Does not understand prepositions
	5 yr	Not using proper syntax in short sentences
Cognitive	2–3 mo	Not alert to mother, with special interest
	6–7 mo	Not searching for dropped object
	8–9 mo	No interest in peek-a-boo
	12 mo	Does not search for hidden object
	15–18 mo	No interest in cause-and-effect games
	2 yr	Does not categorize similarities (e.g., animals vs. vehicles)
	3 yr	Does not know own full name
	4 yr	Cannot pick shorter or longer of two lines
	4½ yr	Cannot count sequentially
	5 yr	Does not know colors or any letters
	5½ yr	Does not know own birthday or address
Psychosocial	3 mo	Not smiling socially
	6–8 mo	Not laughing in playful situations
	1 yr	Hard to console, stiffens when approached
	2 yr	Kicks, bites, and screams easily and without provocation
		Rocks back and forth in crib
		No eye contact or engagement with other children or adults
	3–5 yr	In constant motion
		Resists discipline
		Does not play with other children

Source: First LR, Palfrey JS: The infant or young child with developmental delay. *N Engl J Med* 1994;330:478–483.

Algorithm from:
"Evaluation of the child with global developmental delay and intellectual disability"
Stacey A. Bélanger, Joannie Caron
Paediatrics & Child Health, 2018, 403–410 doi: 10.1093/pch/pxy093
Position Statement

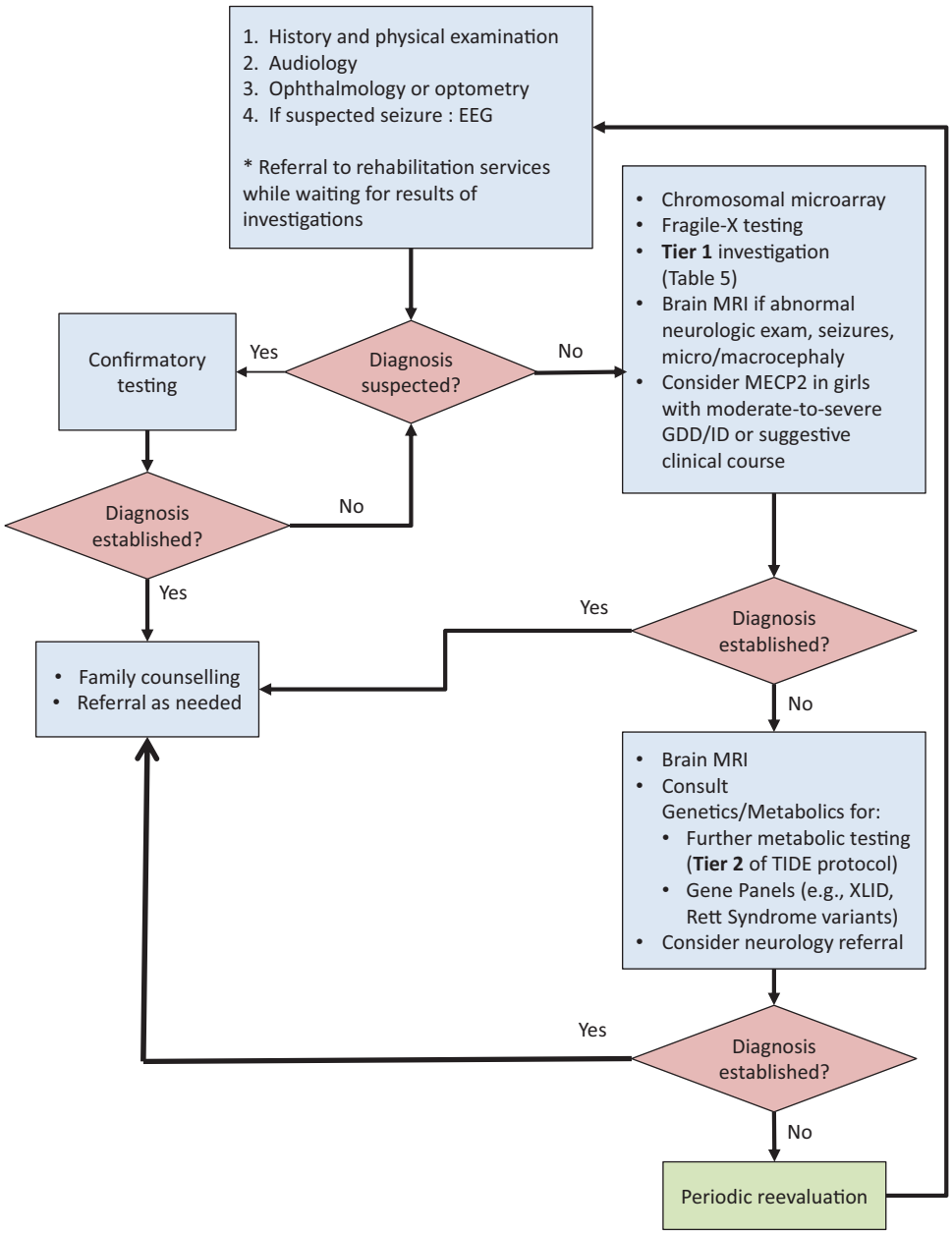


Figure 1. Algorithm for investigating global developmental delay or intellectual disability. Figure available in colour online.
EEG Electroencephalogram; GDD Global developmental delay; ID Intellectual disability; MRI magnetic resonance imaging; XLID X-linked intellectual disability

Table 5. Tier-1 laboratory investigations for unexplained GDD/ID

Blood*	Urine*
• Complete blood count	• Organic acids
• Glucose	• Creatine metabolites
• Blood gas	• Purines, pyrimidines
• Urea, creatinine	• Glycosaminoglycans
• Electrolytes (to calculate anion gap)	
• AST, ALT	
• TSH	
• Creatine kinase	
• Ammonia	
• Lactate	
• Amino acids	
• Acylcarnitine profile, carnitine (free and total)	
• Homocysteine	
• Copper, ceruloplasmin**	
• Biotinidase***	
• Ferritin, vitamin B12 when dietary restriction or pica are present	
• Lead level when risk factors for exposure are present	

ALT Alanine aminotransferase; AST Aspartate aminotransferase; GDD Global developmental delay; ID Intellectual disability; TSH Thyroid-stimulating hormone.

*Perform testing after 4 h to 8 h of fasting. **Recommended tier-1 test in the TIDE protocol, but not by AAP, AAN. Consider as a first-line investigation when hepatomegaly, dystonia, abnormal liver function findings are present. ***Clinical expert recommendation only. Consider biotinidase testing when severe hypotonia, seizures are present.

Hearing Assessment in Infants and Children: Recommendations Beyond Neonatal Screening

Allen D. Buz Harlor, Jr, Charles Bower

KEY POINTS

1. Every child with 1 or more risk factors on the hearing risk assessment should have ongoing developmentally appropriate hearing screening and at least 1 diagnostic audiology assessment by 24 to 30 months of age.
2. Periodic objective hearing screening of all children should be performed according to the recommendations for preventive periodic health care.
3. Any parental concern about hearing loss should be taken seriously and requires objective hearing screening of the patient.
4. All providers of pediatric health care should be proficient with pneumatic otoscopy and tympanometry. However, it is important to remember that these methods do not assess hearing.
5. Developmental abnormalities, level of functioning, and behavioral problems (ie, autism/developmental delay) may preclude accurate results on routine audiometric screening and testing. In this situation, referral to an otorhinolaryngologist and a pediatric audiologist who has the necessary equipment and expertise to test infants and young children should be made.
6. The results of abnormal screening should be explained carefully to parents, and the child's medical record should be flagged to facilitate tracking and follow-up.
7. Any abnormal objective screening result requires audiology referral and definitive testing.
8. A failed infant hearing screening or a failed screening in an older child should always be confirmed by further testing.
9. Abnormal hearing test results require intervention and clinically appropriate referral, including otolaryngology, audiology, speech language pathology, genetics, and early intervention.

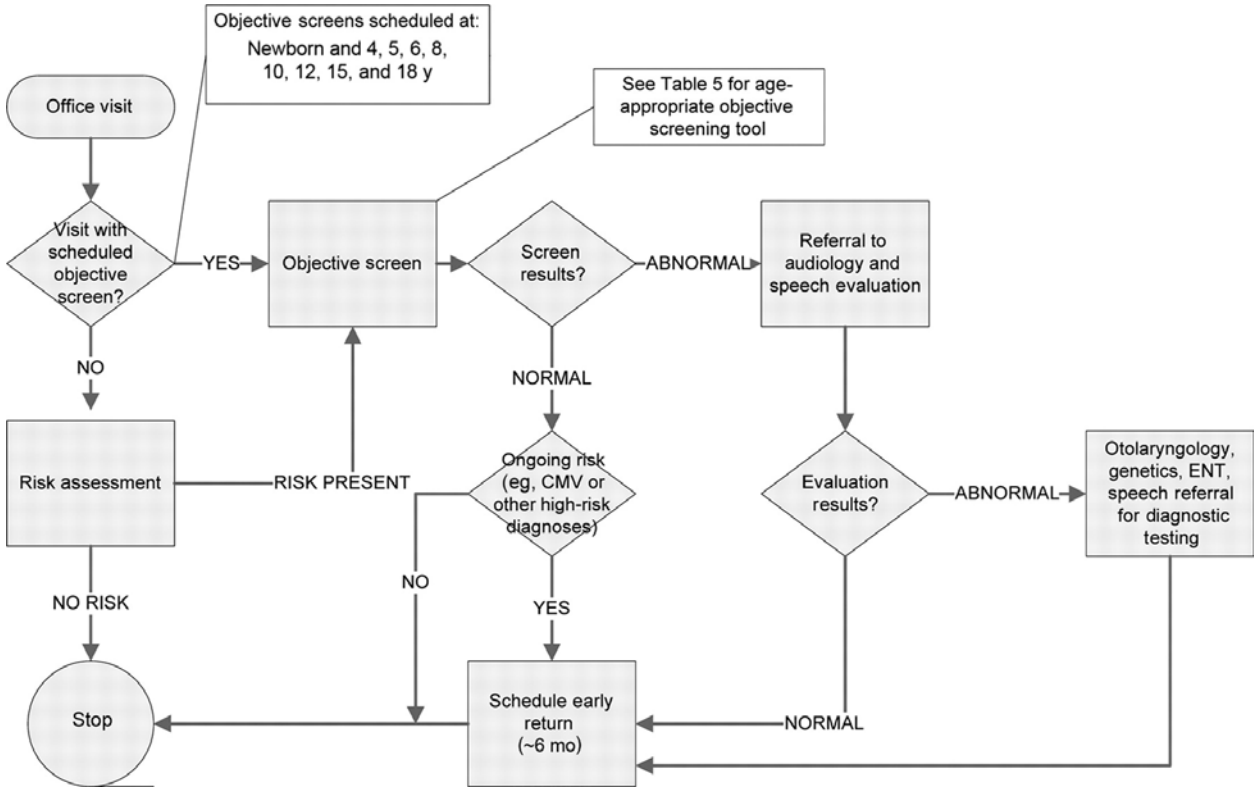


TABLE 3 American Academy of Pediatrics Joint Committee on Infant Hearing Year 2007 Position Statement[5]: Risk Indicators Associated With Permanent Congenital, Delayed-Onset, and/or Progressive Hearing Loss in Childhood

1	Caregiver concern[a] regarding hearing, speech, language, or developmental delay.
2	Family history[a] of permanent childhood hearing loss.
3	Neonatal intensive care of more than 5 days or any of the following regardless of length of stay: ECMO[a], assisted ventilation, exposure to ototoxic medications (gentamicin and tobramycin) or loop diuretics (furosemide/Lasix), and hyperbilirubinemia[19] that requires exchange transfusion.
4	In utero infections such as CMV[a], herpes, rubella, syphilis, and toxoplasmosis.
5	Craniofacial anomalies, including those that involve the pinna, ear canal, ear tags, ear pits, and temporal bone anomalies.
6	Physical findings, such as white forelock, that are associated with a syndrome known to include a sensorineural or permanent conductive hearing loss.
7	Syndromes associated with hearing loss or progressive or late-onset hearing loss[a], such as neurofibromatosis, osteopetrosis, and Usher syndrome; other frequently identified syndromes include Waardenburg, Alport, Pendred, and Jervell and Lange-Nielson.
8	Neurodegenerative disorders[a], such as Hunter syndrome, or sensory motor neuropathies, such as Friedreich ataxia and Charcot-Marie-Tooth syndrome.
9	Culture-positive postnatal infections associated with sensorineural hearing loss[a], including confirmed bacterial and viral (especially herpes viruses and varicella) meningitis.
10	Head trauma, especially basal skull/temporal bone fracture[a] that requires hospitalization.
11	Chemotherapy[a].
12	Recurrent or persistent otitis media for at least 3 months.

Risk indicators that are marked with [a] are of greater concern for delayed onset hearing loss. ECMO indicates extracorporeal membrane oxygenation; CMV, cytomegalovirus.

TABLE 5 Audiologic Tests for Infants and Children

Developmental Age of Child	Auditory Test/ Average Time	Type of Measurement	Test Procedures	Advantages	Limitations
All ages	Evoked OAEs/10-min test	Physiologic test specifically measuring cochlear (outer hair cell) response to presentation of a stimulus; stimuli may be clicks (transient evoked OAEs) or tone pairs (distortion product OAEs)	Small probe containing a sensitive microphone is placed in the ear canal for stimulus delivery and response detection	Ear-specific results; not dependent on whether patient is asleep or awake; quick test time; screening test	Infant or child must be relatively inactive during the test; not a comprehensive test of hearing, because it does not assess cortical processing of sound; OAEs are very sensitive to middle-ear effusions and cerumen or vernix in the ear canal
Birth to 9 mo	Automated ABR/15-min test	Electrophysiologic measurement of activity in auditory nerve and brainstem pathways	Placement of electrodes on child's head detects neurologic response to auditory stimuli presented through earphones or ear inserts 1 ear at a time	Ear-specific results; responses not dependent on patient cooperation; screening test	Infant or child must remain quiet during the test (sedation is often required); not a comprehensive test of hearing, because it does not assess cortical processing of sound
9 mo to 2.5 y	VRA/15- to 30-min test	Behavioral tests measuring responses of the child to speech and frequency-specific stimuli presented through speakers or insert earphones	Technique conditions the child to associate speech or frequency-specific stimuli with a reinforcer, such as a lighted toy or video clips; VRA requires a calibrated, sound-treated room	Assesses auditory perception of child; diagnostic test.	When performed with speakers, only assesses hearing of the better ear; not ear specific; if VRA is performed with insert, earphones can rule out a unilateral hearing loss
2.5 to 4 y	Play audiometry/ 15–30 min	Behavioral test of auditory thresholds in response to speech and frequency-specific stimuli presented through earphones and/ or bone vibrator	Child is conditioned to respond when stimulus tone is heard, such as to put a peg in a pegboard or drop a block in a box	Ear-specific results; assesses auditory perception of child; screening or diagnostic test.	Attention span of child may limit the amount of information obtained
4 y to adolescence	Conventional audiometry/ 15- to 30-min test	Behavioral test measuring auditory thresholds in response to speech and frequency-specific stimuli presented through earphones and/ or bone vibrator	Patient is instructed to raise his or her hand when stimulus is heard	Ear-specific results; assesses auditory perception of patient; screening or diagnostic test	Depends on the level of understanding and cooperation of the child
All ages	Diagnostic ABR	Electrophysiologic measurement of activity in auditory nerve and brainstem pathways	Placement of electrodes on child's head detects auditory stimuli presented through insert earphones 1 ear at a time	Ear-specific results; multiple frequencies are tested, creating a map of hearing loss similar to an audiogram; responses not dependent on patient cooperation; diagnostic test	Infant or child must remain quiet during the test (sedation is often required); not a true test of hearing, because it does not assess cortical processing of sound
All ages	Tympanometry	Relative change in middle-ear compliance as air pressure is varied in the external auditory canal	Small probe placed in the ear canal and pressure varied in the ear canal	Tests for possible middle-ear pathology and pressure-equalization tube function	Not a test of hearing; depends on ear canal seal; high-frequency tone probe needed for infants younger than 6 mo

Adapted with permission from: Bachmann KR, Arvedson JC. *Pediatr Rev.* 1998;19(5):155–165.

Development II Quiz:

1. Intellectual Disability (IQ<, or = to 2 SD below the mean IQ) is found in _____% of the population. Autism Spectrum Disorder is found in _____% of the population.

2. Complete the following table, related to Intellectual Disability:

TABLE 1. **Levels of Severity of Intellectual Disability (ID)**

LEVEL OF ID (% CHILDREN WITH ID)	LEVEL OF SUPPORT (IN CONCEPTUAL, SOCIAL, PRACTICAL DOMAINS)	ASSOCIATED ESTIMATED IQ SCORE	PROJECTED ULTIMATE ACADEMIC ACHIEVEMENT
Mild _____%	Intermittent	_____	Up to _____grade level
Moderate _____%	Limited	_____	Up to _____grade level
Severe _____%	Extensive	_____	_____ level
Profound _____%	Pervasive	_____	–

Note: The level of severity is based on the level of adaptive functioning and support. (1)(6)

True or False?

3. A good history and physical exam can identify the etiology of up to a third of cases of developmental delay.

4. Most children with ASD also have ID.

5. Whole exome sequencing has approximately twice the diagnostic yield as chromosomal microarray in evaluating unexplained intellectual disability.

6. Instruments for identifying intellectual disability (e.g. Stanford-Binet-V and WPPSI-IV) can not be administered until 5 years of age.

7. Restrictive, repetitive, or "just right" behaviors, interests, or activities in 2 to 6 year olds are usually associated with autism spectrum disorder.

8. According to the “Medical Evaluation” flow chart, what is the minimum medical work-up for a child with global developmental delay and normal physical exam?

***** In Oct 2010, President Obama signed into law “Rosa’s Law” which changed references in federal law from *mental retardation* to *intellectual disability*, and references to *a mentally retarded individual* to *an individual with an intellectual disability*. Read about the campaign to “Spread the Word to End the Word”, which started in MD.

Development II Cases:

Case 1:

Joshua, a 2 year old male, presents to your clinic for his well baby check. His family is new to the military and has never been seen in this clinic before. He lives in a household with his parents and grandparents; his parents speak English and Taiwanese, and his grandparents speak purely Taiwanese. Joshua seems like a "bright" toddler to his mother because he is so social – he enjoys being the center of attention. He seems to understand the language of others and can follow 2-step commands without gesture. He points to body parts when asked. However, he only has about a 25-word expressive vocabulary in English, and says approx 25 words in Taiwanese. Mother relates that he does try to imitate his older cousin's speech in both English and Taiwanese. She also relates that she's 'not concerned about his talking because a lot of boys on my husband's side of the family had trouble with talking.'

Does his language and social development concern you? Why or why not?

If his language concerns you, how would you classify his 'atypical pattern of development'?

Is his paternal family hx relevant? Does that decrease your concern for language disorder?

Does Joshua require a hearing screen?

Would you refer this patient? If so, to whom?

After presenting your A/P to Joshua's mother, she adds that she has been using Baby Signs since Josh was 9-months to help him "overcome or compensate" for his language delay. **Applying what you know about language development, do you think signing helped or hindered him?**

Case 2:

Katelynn is a 2 year old healthy female presenting for a well child visit. She comes into your office, immediately sits in a small chair on the opposite side of the room from her mother, and begins playing with the toy train on the table. As you conduct the interview, you note that her play with the train does not change; she runs the train in a circle again and again. In asking mom about this behavior, she relates that Katelynn also arranges her dolls in a specific order on her bed, and she gets very upset when the order has been altered. You also uncover that the child is rather 'quiet and shy' and only says ten words (although she seems to understand nearly everything she hears).

What language milestones would you expect of a 2 year old?

What other questions would you elicit in the developmental history?

You administer the M-CHAT shown on the next page. Score it and answer the next questions: **Are you concerned? If so, will you refer the patient? Would you do any further work-up?**

Once she has heard the likely diagnosis, mother reveals to you that she is 12 weeks pregnant and wonders if the unborn child has a higher risk of autism. **She wonders if there is a 'genetic test' that via amniocentesis to diagnose the unborn child. What is your response?**

Katelynn's mother seems understandably overwhelmed at the end of your appointment. You give her your card and offer to add Katelynn to your continuity panel. The next day, you see the following T-con in AHLTA: *"question about immunizations, per mom".* You call mother back, and she reports that she has done some internet research.

Did any of the immunizations Katelynn received lead to her symptoms? Do any immunizations contain thimerosal? (Flashback: Immunizations)

Modified Checklist for Autism in Toddlers (M-CHAT)

Please fill out the following about how your child **usually** is. Please try to answer every question. If the behavior is rare (e.g., you've seen it once or twice), please answer as if the child does not do it.

1.	Does your child enjoy being swung, bounced on your knee, etc.?	Yes	No
2.	Does your child take an interest in other children?	Yes	No
3.	Does your child like climbing on things, such as up stairs?	Yes	No
4.	Does your child enjoy playing peek-a-boo/hide-and-seek?	Yes	No
5.	Does your child ever pretend, for example, to talk on the phone or take care of dolls, or pretend other things?	Yes	No
6.	Does your child ever use his/her index finger to point, to ask for something?	Yes	No
7.	Does your child ever use his/her index finger to point, to indicate interest in something?	Yes	No
8.	Can your child play properly with small toys (e.g. cars or bricks) without just mouthing, fiddling, or dropping them?	Yes	No
9.	Does your child ever bring objects over to you (parent) to show you something?	Yes	No
10.	Does your child look you in the eye for more than a second or two?	Yes	No
11.	Does your child ever seem oversensitive to noise? (e.g., plugging ears)	Yes	No
12.	Does your child smile in response to your face or your smile?	Yes	No
13.	Does your child imitate you? (e.g., you make a face-will your child imitate it?)	Yes	No
14.	Does your child respond to his/her name when you call?	Yes	No
15.	If you point at a toy across the room, does your child look at it?	Yes	No
16.	Does your child walk?	Yes	No
17.	Does your child look at things you are looking at?	Yes	No
18.	Does your child make unusual finger movements near his/her face?	Yes	No
19.	Does your child try to attract your attention to his/her own activity?	Yes	No
20.	Have you ever wondered if your child is deaf?	Yes	No
21.	Does your child understand what people say?	Yes	No
21.	Does your child sometimes stare at nothing or wander with no purpose?	Yes	No
23.	Does your child look at your face to check your reaction when faced with something unfamiliar?	Yes	No

Development II Board Review:

1. An infant born at 34 weeks' gestation comes in for her 1-month-old evaluation. Her neonatal course was uncomplicated. Her parents ask if she will have delayed development due to her prematurity.

Of the following, the MOST appropriate response is that healthy preterm infants
A. have age-appropriate language skills by the time they are 12 months of age
B. have an increased risk of mild motor impairment
C. born at 32 to 36 weeks' gestation have a fourfold increase in intellectual disabilities
D. should have their developmental age corrected for the degree of prematurity until 4 years
E. show hand preference at an earlier age than term infants

2. You care for a 7-year-old boy who has moderate intellectual disability and autistic behavior. Molecular genetic testing has confirmed that he has findings consistent with classic fragile X syndrome. His pregnant mother has undergone prenatal testing, which revealed that she is carrying a female fetus that also has fragile X syndrome.

Of the following, the MOST accurate statement regarding fragile X syndrome in females is that
A. their affected sons have more severe intellectual disability than their affected brothers
B. they can have normal intelligence
C. they do not exhibit autistic behaviors
D. they typically are affected as severely as males who have fragile X syndrome
E. they usually are infertile

3. During the health supervision visit for an 18-month-old boy, his parents express concern that he is vocalizing but not saying any real words. He is holding a small piece of string that he moves back and forth repeatedly. When you call his name, he does not respond. You point to the light in the room and say "look," but he continues to look at the string with a sideways glance. You try to get him to look at you, but he avoids eye contact.

Of the following, the MOST likely diagnosis for this boy is
A. Asperger disorder
B. autistic disorder
C. expressive/receptive language disorder
D. obsessive-compulsive disorder
E. Rett syndrome

4. A 5-year-old girl recently was diagnosed with an autistic disorder and mental retardation. Her parents are upset by her lack of progress in her special education program and seek your guidance in treating her autism. At a parent support group, they were told about the use of complementary and alternative medical approaches to therapy. They ask whether they should pursue these interventions.

Of the following, your BEST response is to
A. explain to the parents that alternative treatments have been demonstrated to be ineffective
B. explain to the parents that they must consider the benefits, risks, and evidence regarding efficacy for each treatment
C. refer the parents for psychological counseling to deal with their guilt feelings
D. suggest the parents discuss the alternative treatments with the special education teachers
E. tell the parents that they should not expect much progress because their daughter has both mental retardation and autism

5. During the health supervision visit for a 4-year-old girl, her father reports that she has developed a stutter over the past 9 months. He explains that she is a little frustrated by the difficulty in expressing herself but otherwise seems happy and well-adjusted. In talking with the father, you also note that he has a mild stutter. He speaks to the child slowly and deliberately and encourages her to take her time when speaking to you.

Of the following, the risk factor that MOST strongly suggests the need for speech therapy for this girl is the
A. age of onset
B. child's reaction to stuttering
C. child's sex
D. father's stutter
E. time since onset

6. A 2-month-old infant has lost the vision in both of his eyes due to bilateral retinoblastoma. His distressed parents ask how the infant's blindness will affect his behavior and development.

Of the following, the child MOST likely will
A. begin saying single words at 16 to 20 months
B. begin walking between 18 and 22 months
C. display behaviors of an autism spectrum disorder
D. have a language-based learning disorder
E. have significant cognitive impairments