Learning and Developmental Disorders

PART IV

Chapter 49

Neurodevelopmental and Executive Function and Dysfunction

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TERMINOLOGY AND EPIDEMIOLOGY

A **neurodevelopmental function** is a basic brain process needed for learning and productivity and involves the following core neurodevelopmental domains: sensory, motor, language, visual-spatial/visual-perceptual, intellectual, memory, social cognition, and executive function. **Executive function (EF)** is a broad term used to describe specific neurocognitive processes involved in the regulating, guiding, organizing, and monitoring of thoughts and actions to achieve a specific goal. Processes considered to be "executive" in nature include inhibition/impulse control, cognitive/mental flexibility, emotional control, initiation skills, planning, organization, working memory, and self-monitoring.

Neurodevelopmental variation refers to differences in neurodevelopmental functioning. Wide variations in these functions exist within and between individuals. These differences can change over time and need not represent pathology or abnormality.

Neurodevelopmental and/or executive dysfunctions reflect any disruptions or weaknesses in these processes, which may result from neuroanatomic disturbance or neuropsychologic malfunctioning.

Neurodevelopmental and/or executive dysfunction places a child at risk for developmental, cognitive, emotional, behavioral, psychosocial, and adaptive challenges. Preschool-age children with neurodevelopmental or executive dysfunction may manifest delays in developmental domains such as language, motor, self-help, or social-emotional development and self-regulation. For the school-age child, an area of particular focus is academic skill development. It is at this age that disorders of learning are often diagnosed. The *Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition* (DSM-5) classifies disorders of learning within the group of neurodevelopmental disorders as **specific learning disorder (SLD)**, with separate specifiers recognizing impairments in reading, written expression, and mathematics. In the *International Classification of Diseases, Tenth Edition* (ICD-10), neurodevelopmental disorders include **specific developmental disorders of scholastic skills** with specific reading disorder, mathematics disorder, and disorder of written expression. **Dyslexia** is a term used more frequently by neurologists and by some advocacy groups to describe reading disorders. **Disorders of EF** have traditionally been viewed as a component of **attention-deficit/hyperactivity disorder (ADHD)**, which is also classified in DSM-5 as a neurodevelopmental disorder. **Frontal lobe and executive function deficit** is a recognized diagnostic term used primarily by neuropsychologists.

There are no prevalence estimates specifically for neurodevelopmental dysfunction, but overall estimates for learning disorders range from 5% to 10% or more with a similar range reported for ADHD. These disorders frequently co-occur. The range in prevalence is related to differences in criteria used for classification and diagnosis, the overlap and interaction of neurodevelopmental variations, and differing methods of assessment.

ETIOLOGY AND PATHOGENESIS

Neurodevelopmental and executive dysfunction may result from a broad range of etiologic factors, including genetic, medical, psychologic, environmental, and sociocultural influences.

A high degree of **heritability** is reported in learning and attention disorders, with estimates ranging from 45% to 80%, but identification of specific gene associations is elusive. Neurodevelopmental dysfunctions generally fall along a continuum of traits with disorders becoming evident at extremes of dimensions or thresholds of dysfunction. The same genetic and early environmental risk factors that are associated with a disorder such as ADHD also predict trait levels in the general population. Specific genes have been identified as associated with reading disorders, including the *DYX2* locus on chromosome 6p22 and the *DYX3* locus on 2p12. Neuroimaging studies have confirmed links between gene variations and variations in cortical thickness in areas of the brain known to be associated with learning and academic performance, such as the temporal regions. Chromosomal abnormalities can lead to unique patterns of dysfunction, such as visual-spatial deficits in females diagnosed with Turner syndrome (see Chapter 99.4) or executive and language deficits in children with fragile X syndrome (see Chapter 99.6). Chromosome 22q11.2 deletion syndrome (see Chapter 99.3) has been associated with predictable patterns of neurodevelopmental and executive dysfunction that can be progressive, including a higher prevalence of intellectual disability and deficits in visual-spatial processing, attention, **working memory** (e.g., the ability to hold and manipulate information over short periods), verbal learning, arithmetic, and language.

Perinatal factors, including very low birthweight, severe intrauterine growth restriction, perinatal hypoxic-ischemic encephalopathy, and prenatal exposure to substances such as alcohol and drugs or infections, may independently disrupt neurodevelopment or exacerbate genetic vulnerabilities. Increased risk of neurodevelopmental and executive dysfunction has also been associated with environmental toxins, including lead (see Chapter 761); drugs such as cocaine; infections such as meningitis, HIV, and Zika; and brain injury associated with intraventricular hemorrhage, periventricular leukomalacia, or head trauma. The negative academic impact of concussion in children and adolescents, although usually temporary, has been well characterized, including impaired concentration and slowed processing speed. Repeated injuries have a much higher likelihood of long-term negative neurocognitive effects.

Early **psychologic trauma** may result in both structural and neurochemical changes in the developing brain, which may contribute to neurodevelopmental and executive dysfunction. Exposure to trauma, abuse, or other adverse experiences in early childhood in the absence of positive experiences—primarily safe, stable, and nurturing relationships—can lead to diminished regulatory influences mediated by key brain regions (hippocampus and prefrontal cortex) and may influence right hemisphere function with associated risk for problems with information processing, memory, focus, and self-regulation. Environmental and sociocultural deprivation can also lead to, or potentiate, neurodevelopmental and executive dysfunction, and numerous studies have indicated that parent/caregiver executive functioning affects the development of EFs in children.

Investigations of neuroanatomic substrates have yielded important information about the underlying **pathogenesis** in neurodevelopmental and executive dysfunction. Differences have been demonstrated in the left parietotemporal and left occipitotemporal brain regions of individuals with dyslexia compared to those without reading difficulties (see Chapter 51). Studies have also described the neural circuitry, primarily in the parietal cortex, underlying mathematical competencies such as the processing of numerical magnitude and mental arithmetic. The associations between executive dysfunction and the *prefrontal/frontal cortex* have been established, and injury to the frontal lobe regions often

result in dysfunction of executive abilities (e.g., poor inhibitory control). Although the prefrontal/frontal cortex may be the primary control region for EFs, there is considerable interconnectivity between the brain's frontal regions and other areas, such as *arousal* systems (reticular activating system), *motivational and emotional* systems (limbic system), *cortical association* systems (posterior/anterior; left/right hemispheres), and *input/output* systems (frontal motor/posterior sensory areas).

CORE NEURODEVELOPMENTAL FUNCTIONS

The neurodevelopmental processes that are critical to a child's successful functioning may best be understood as falling within **core neurodevelopmental domains** that are highly integrated.

Sensory and Motor Function

Sensory development begins well before birth in the primary visual, auditory, and somatosensory cortical regions along with the olfactory and gustatory cortices. This neurodevelopmental process is crucial in helping children experience, understand, and manipulate their environments. Sensory development progresses in association with environmental exposure and with the development of other cognitive processes, such as motor development. Through sensory experiences, children's brains mature as new neuronal pathways are created and existing pathways are strengthened.

There are three distinct, yet related, forms of **neuromotor** ability: fine motor, graphomotor, and gross motor coordination. **Fine motor function** reflects the ability to control the muscles that produce small, exact movements. Deficits in fine motor function can disrupt the ability to communicate in written form and to excel in artistic and crafts activities and can interfere with learning a musical instrument or mastering a computer keyboard.

Graphomotor function refers to the specific motor aspects of written output. Several subtypes of graphomotor dysfunction can significantly impede writing. Children who harbor weaknesses of visualization during writing have trouble picturing the configurations of letters and words as they write (orthographics), with poorly legible written output and inconsistent spacing between words. Others have weaknesses in orthographic memory and may labor over individual letters and prefer printing (manuscript) to cursive writing. Some exhibit signs of finger agnosia and have trouble localizing their fingers while they write, needing to keep their eyes very close to the page and applying excessive pressure to the pencil. Others struggle to produce the highly coordinated motor sequences needed for writing. It is important to emphasize that a child may show excellent fine motor dexterity (as revealed in mechanical or artistic domains) but very poor graphomotor fluency (with labored or poorly legible writing).

Gross motor function refers to control of large muscles. Children with gross motor incoordination often have problems in processing "outer spatial" information to guide gross motor actions. Affected children may be inept at catching or throwing a ball because they cannot form accurate judgments about trajectories in space. Others demonstrate diminished body position sense. They do not efficiently receive or interpret proprioceptive and kinesthetic feedback from peripheral joints and muscles. They are likely to evidence difficulties when activities demand balance and tracking of body position and movement. Others are unable to meet the motor planning demands of complex motor procedures such as those needed for dancing, gymnastics, or swimming.

The term **dyspraxia** relates to difficulty in developing an ideomotor plan and activating coordinated and integrated visual-motor actions to complete a task or solve a motor problem, such as assembling a model or learning a new movement.

Developmental coordination disorder is categorized in DSM-5 as a motor disorder where the learning and execution of coordinated motor skills is below age level given the child's opportunity for skill learning, and the motor difficulties significantly interfere with activities of daily living, academic productivity, and play.

Language

Language is one of the most critical and complex cognitive functions and can be broadly divided into **receptive** (auditory comprehension/understanding) and **expressive** (speech and language production and/or communication) functions (see Chapter 53). Children who primarily experience receptive language problems may have difficulty understanding verbal information, following instructions and explanations, and interpreting what they hear. Expressive language weaknesses can result from problems with speech production and/or problems with higher-level language development. **Speech production difficulties** include oromotor problems affecting articulation, verbal fluency, and naming. Some children have trouble with sound sequencing within words. Others find it difficult to regulate the rhythm or prosody of their verbal output. Their speech may be dysfluent, hesitant, and inappropriate in tone. Problems with **word retrieval** can result in difficulty finding exact words when needed (as in a class discussion) or substituting definitions for words (circumlocution).

The basic components of language include **phonology** (ability to process and integrate the individual sounds in words), **semantics** (understanding the meaning of words), **syntax** (mastery of word order and grammatical rules), **discourse** (processing and producing paragraphs and passages), **metalinguistics** (ability to think about and analyze how language works and draw inferences), and **pragmatics** (social understanding and application of language). Children who evidence higher-level expressive language impediments have trouble formulating sentences, using grammar appropriately, and organizing spoken (and possibly written) narratives.

To one degree or another, all academic skills are taught largely through language, and thus it is not surprising that children who experience language dysfunction often experience problems with academic performance. In fact, some studies suggest that up to 80% of children who present with a specific learning disorder also experience language-based weaknesses. Additionally, the role of language in executive functioning cannot be understated, because language serves to guide cognition and behavior.

Visual-Spatial/Visual-Perceptual Function

Important structures involved in the development and function of the visual system include the retina, the optic nerves, the brainstem (control of automatic responses, e.g., pupil dilation), the thalamus (e.g., lateral geniculate nucleus for form, motion, color), and the primary (visual space and orientation) and secondary (color perception) visual processing regions located in and around the occipital lobe. Other brain areas, although considered to be outside of the primary visual system, are also important to visual function, helping to process *what* is seen (temporal lobe) and *where* it is located in space (parietal lobe).

Critical aspects of visual processing development in the child include appreciation of **spatial** relations (ability to perceive objects accurately in space in relation to other objects), visual discrimination (ability to differentiate and identify objects based on their individual attributes, e.g., size, shape, color, form, position), and visual closure (ability to recognize or identify an object when the entire object cannot be seen). Visual-spatial processing dysfunctions are rarely the cause of reading disorders, but some investigations have established that deficits in orthographic coding (visual-spatial analysis of character-based systems) can contribute to reading disorders. Spelling and writing can emerge as a weakness because children with visual processing problems usually have trouble with the precise visual configurations of words. In mathematics, these children often have difficulty with visual-spatial orientation, with resultant difficulty aligning digits in columns when performing calculations and difficulty managing geometric material. In the social realm, intact visual processing allows a child to make use of visual or physical cues when communicating and interpreting the paralinguistic aspects of language. Secure visual functions are also necessary to process proprioceptive and kinesthetic feedback and to coordinate movements during physical activities.

Intellectual Function

A useful definition of **intellectual function** is the capacity to think in the abstract, reason, problem-solve, and comprehend. Intelligence is viewed as a global construct composed of more specific cognitive

functions (e.g., auditory and visual-perceptual processing, spatial abilities, processing speed, and working memory).

The expression of intellect is mediated by many factors, including language development, sensorimotor abilities, genetics, heredity, environment, and neurodevelopmental function. When an individual's measured intelligence is >2 standard deviations below the mean (a standard score of <70 on most IQ tests) and accompanied by significant weaknesses in adaptive skills, the diagnosis of **intellectual disability** may be warranted (see Chapter 56). Functionally, some common characteristics distinguish children with intellectual disability from those with average or above-average abilities. Typically, those at the lowest end of the spectrum (e.g., profound or severe intellectual disability) are incapable of independent function and require a highly structured environment with constant aid and supervision. At the other end of the spectrum are those with unusually well-developed intellect ("gifted"). Stronger intellect has been associated with better-developed concept formation, critical thinking, problem solving, understanding and formulation of rules, brainstorming and creativity, and *metacognition* (ability to "think about thinking"). Although high levels of intellectual functioning offer many opportunities, they can also be associated with functional challenges related to socialization, learning, and communication style.

Individuals whose intellect falls in the below-average range (sometimes referred to as the "borderline" or "slow learner" range) tend to experience greater difficulty processing and managing information that is abstract, making connections between concepts and ideas, and generalizing information (e.g., may be able to comprehend a concept in one setting but be unable to carry it over and apply it in different situations). In general, these individuals tend to do better when information is presented in more concrete and explicit terms (with repetition) and when working with rote information (e.g., memorizing specific material).

Memory

Memory is a term used to describe the complex, cognitive mechanism by which information is acquired, retained, and recalled. Major brain areas involved in memory processing include the hippocampus, fornix, temporal lobes, and cerebellum, with connections in and between most brain regions. Memory consists of multiple distinct and interconnected subsystems that are categorized based on the length of time information is stored (e.g., short-term memory, long-term memory), type of information stored (e.g., events, facts, procedures, emotional associations, conditioned reflexes), modality of the information (e.g., visual, auditory, olfactory), and whether memories are consciously recalled (**explicit memory**) or unconsciously recalled (**implicit memory**). Information processing models also include **working memory** as a distinct component.

Memory formation begins with sensory input (e.g., auditory, visual, tactile) that is identified, or **registered**, and subsequently **encoded**. Encoding is a mental process that transforms perceptual input into a representational code for the memory system. Information in **short-term memory** is transferred into **long-term memory** through the process of **consolidation** and **storage**. Information capacity in short-term memory is limited and brief, lasting for seconds to minutes, whereas information in long-term memory is potentially unlimited in terms of capacity and can be available for hours or as long as a life span.

Once information finds its way into long-term memory, it must be accessed. In general, information can be retrieved spontaneously (a process known as **free recall**) or with the aid of cues (**cued or recognition recall**). With deliberate, repeated practice, children can develop **automaticity**, the ability to instantaneously and effortlessly access information that has been learned in the past. Automaticity frees cognitive resources to process other information and promote learning. For example, automaticity in decoding words allows a child to focus on the meaning of the text.

Social Cognition

The development of effective social skills is heavily dependent on secure **social cognition**, which consists of mental processes that allow an individual to understand and interact with the social environment. Although some evidence shows that social cognition exists as a discrete area of neurodevelopmental function, multiple cognitive processes are involved with social cognition. These include the ability to recognize, interpret, and make sense of the thoughts, communications (verbal and nonverbal), and actions of others; the ability to understand that others' perceptions, perspectives, and intentions might differ from one's own (commonly referred to as "theory of mind"); the ability to use language to communicate with others socially (pragmatic language); and the ability to make inferences about others and the environment based on contextual information. It can also be argued that social cognition involves processes associated with memory and EFs, such as flexibility and shifting. Children with autism spectrum disorder harbor deficits in social cognition (see Chapter 58).

Executive Function

EF involves multiple skills (Table 49.1) that begin development early in life (early indications of inhibitory control and even working memory have been found in infancy), mature significantly during the preschool years, and continue to develop through adolescence and well into adulthood. Some studies suggest that secure EF may be more important than intellectual ability for academic success and have revealed that a child's ability to delay gratification early in life predicts competency, attention, self-regulation, frustration tolerance, aptitude, physical and mental health, and even risk for substance dependency in adolescence and adulthood. Conversely, deficits in other areas of neurodevelopment, such as language development, affect EF.

Attention is far from a unitary, independent, or specific brain function. This may be best illustrated through the phenotype associated with ADHD (see Chapter 50). Disordered attention can result from faulty mechanisms in and across subdomains of attention. These subdomains include *selective* attention (ability to focus attention on a particular stimulus and to discriminate relevant from irrelevant information), *divided* attention (ability to orient to more than one stimulus at a given time), *sustained* attention (ability to maintain one's focus), and *alternating* attention (capacity to shift focus between stimuli).

Attention problems in children can manifest at any point, from arousal through output. Children with diminished alertness and

Table 49.1 Symptom Expression of Executive Dysfunction

EXECUTIVE FUNCTION DEFICIT	SYMPTOM EXPRESSION
Inhibitory control	Impulsivity/poor behavioral regulation Interrupts "Blurts things out"
Shifting	Problems with transitioning from one task/activity to another Unable to adjust to unexpected change Repeats unsuccessful problem-solving approaches
Initiation	Difficulty independently beginning tasks/activities Lacks initiative Difficulty developing ideas or making decisions
Working memory	Challenges following multistep instruction (e.g., only completes one of three steps) Forgetfulness
Organization and planning	Fails to plan ahead Work is often disorganized Procrastinates and does not complete tasks "Messy" child
Self-monitoring	Fails to recognize errors and check work Does not appreciate impact of actions on others Poor self-awareness
Emotional control	Experiences behavioral and emotional outbursts (e.g., tantrums) Easily upset/frustrated Frequent mood changes

arousal can exhibit signs of mental fatigue in a classroom or when engaged in any activity requiring sustained focus. They are apt to have difficulty directing and sustaining their concentration, and their efforts may be erratic and unpredictable, with extreme performance inconsistency. Weaknesses in determining saliency often result in allocating cognitive resources to the wrong stimuli, at home, in school, and socially, and missing important information. **Distractibility** can take the form of listening to extraneous noises instead of a teacher, staring out the window, or constantly thinking about the future. Attention dysfunction can affect the output of work, behavior, and social activity. It is important to appreciate that most children with attentional dysfunction also have other forms of neurodevelopmental dysfunction that can be associated with academic disorders (with some estimates suggesting up to 60% comorbidity).

Inhibitory control (IC) can be described as one's ability to restrain, resist, and not act (cognitively or behaviorally/emotionally) on a thought. IC may also be seen as one's ability to stop thoughts or ongoing actions. Deficits in this behavioral/impulse regulation mechanism are a core feature of the **combined** or **hyperactive impulsive** presentation of ADHD and have a significant adverse impact on a child's overall functioning. In everyday settings, children with weak IC may exhibit difficulties with self-control and self-monitoring of their behavior and output (e.g., impulsivity), may not recognize their own errors or mistakes, and often act prematurely and without consideration of the potential consequences of their actions. In the social context, disinhibited children may interrupt others and demonstrate other impulsive behaviors that often interfere with interpersonal relationships. The indirect consequences of poor IC can include challenges with behavior, emotional regulation, and academic functioning and have adverse impacts on social interactions and safety.

Shifting is the ability to transition from one activity, topic, or aspect of a problem to another when needed. Effective shifting allows a child to flexibly move through their day, tolerating changes in schedule and routine. Additionally, shifting allows a child to change strategies when working a problem and adjust to changes in topics when conversing with others. Children with difficulties in shifting can become quickly upset in novel situations (e.g., when presented with a substitute teacher) and show marked resistance to change in routine. They can get stuck on one problem-solving strategy, which compromises their work efficiency. Socially, problems with shifting can result in one-sided conversations, negatively affecting a child's ability to build and maintain friendships.

Initiation refers to the ability to independently begin an activity, a task, or thought process (e.g., problem-solve). Children who present with initiation difficulties often have trouble "getting started." This can be exhibited behaviorally, such that the child struggles to start on physical activities like getting out of bed or beginning chores. Cognitively, weaknesses in initiation may manifest as difficulty coming up with ideas or generating plans. In school, children who have poor initiation abilities may be slow or unable to start homework assignments or tests. In social situations, initiation challenges may cause a child to have difficulty beginning conversations, calling on friends, or going out with friends.

Deficits in "primary" initiation are relatively rare and are often associated with significant neurologic conditions and treatments (e.g., traumatic brain injury, anoxia, effects of radiation treatment in childhood cancer). More often, initiation deficits are secondary to other executive problems (e.g., disorganization) or behavioral (e.g., oppositional/defiant behaviors), developmental (e.g., autism spectrum disorder), or emotional (e.g., depression, anxiety) disorders.

Working memory (WM) can be defined as the ability to hold, manipulate, and store information for short periods. In its simplest form, WM involves the interaction of short-term verbal and visual processes (e.g., memory, phonologic awareness, and spatial skills) with a centralized control mechanism that is responsible for coordinating all the cognitive processes involved (e.g., temporarily suspending information in memory while manipulating it). Ultimately, this function enables new information arriving in short-term memory to be linked to prior knowledge or procedures held in long-term memory. As such, working memory is critical to be able to complete multistep problems and more complex instructions and tasks. WM capacity can double or triple between the preschool years and adolescence. In the classroom, a child with a weakness in working memory might appear inattentive or careless when completing their work. When doing math, a child with WM dysfunction might have difficulty carrying a number and following the expected procedure. When reading a paragraph, a child might not recall key facts or be able to integrate information when reading, particularly long paragraphs. For writing tasks, a child might leave out ideas they intended to express while they are recalling grammar rules, such as placing a comma, and working on spelling a word correctly.

Planning refers to the ability to effectively generate, sequence, and put into motion the steps and procedures necessary to realize a specific goal. In real-world settings, children who struggle with planning are typically described by caregivers and teachers as being inept at independently gathering what is required to solve a problem or as unable to complete more weighty assignments. These children commonly exhibit poor time management skills.

Organization is an ability that represents a child's proficiency in arranging, ordering, classifying, and categorizing information. Planning and organizing depend on **discrimination** ability, which refers to the child's ability to determine what is and is not valuable when trying to problem-solve or organize. Common daily life challenges associated with organizational difficulties in childhood include problems with gathering and managing materials or items. When children struggle with organization, indirect consequences may include becoming overwhelmed with information and being unable to complete a task or activity. Effective organization is a vital component in learning (more specifically, in memory/retention); many studies, along with clinical experience, have shown that poor organization significantly affects how well a child recalls information.

Self-monitoring involves awareness and assessment of one's actions, whether it be a work product (e.g., writing an essay) or social interaction with another. This EF allows one to evaluate and make necessary corrections. Children with difficulty in self-monitoring fail to recognize errors in their work and struggle with editing. When interacting with others, they may not realize how their verbal and nonverbal behaviors are being perceived, ultimately missing opportunities to correct their behavior and resulting in poor social interactions.

Emotional control is the ability to regulate emotions in order to realize goals and direct one's behavior, thoughts, and actions. It has been well established that affective/emotional states have an impact on many aspects of functioning. Conversely, executive function or dysfunction often contributes to modulation of affect. Although emotional control is highly interrelated with different EFs (e.g., disinhibition, self-monitoring), separating it conceptually facilitates an appreciation for and recognition of the often-overlooked role that a child's emotional state plays in cognitive and behavioral functioning. Children with weak emotional control may exhibit explosive outbursts, poor temper/anger control, and oversensitivity. Understanding a child's emotional state is vital to understanding its impact not only on executive functioning but also on functioning as a whole (e.g., socially, mentally, behaviorally, academically).

Any discussion involving emotional control should also recognize **motivation**. *Motivation/effort* may be defined as the reason or reasons one acts or behaves in a certain way. Less motivated children are less likely to engage and utilize all their abilities. Such a disposition not only interferes with application of executive skills but also results in less-than-optimal performance and functioning. The less success a child feels, the less likely the child is to put forth effort and to persevere when things become more challenging. If a child's initial efforts are met with a negative reaction, the likelihood that the child will continue putting forth adequate effort diminishes. If left unchecked, a child's overall level of functioning will likely be compromised. More importantly, the child's sense of personal efficacy (e.g., self-esteem) and competence may suffer.

CLINICAL MANIFESTATIONS

The symptoms and clinical manifestations of neurodevelopmental and executive dysfunction differ with age. **Preschool-age children**

might present with delayed language development, including problems with articulation, vocabulary development, word finding, and rhyming. They often experience early challenges with learning colors, shapes, letters, numbers, the alphabet, and days of the week. Children with visual processing deficits may have difficulty learning to draw and write and have problems with art activities. These children might also have trouble discriminating between left and right. They might encounter problems recognizing letters and words. Difficulty following instructions, overactivity, and distractibility may be early symptoms of emerging executive dysfunction. Difficulties with fine motor development (e.g., grasping crayons/pencils, coloring, drawing) and social interaction may develop. These manifestations should be considered as potential "red flags" for future learning challenges (see "Assessment and Diagnosis").

School-age children with neurodevelopmental and executive dysfunctions can vary widely in clinical presentations. Their specific patterns of academic performance and behavior represent final common pathways of neurodevelopmental strengths and deficits interacting with environmental, social, or cultural factors; temperament; educational experience; and intrinsic resilience (Table 49.2). Children with language weaknesses might have problems integrating and associating letters and sounds, decoding words, deriving meaning, and being able to comprehend passages. Children with early signs of a mathematics weakness might have difficulty with concepts of quantity or with adding or subtracting without using concrete representation (e.g., their fingers when calculating). Difficulty learning time concepts and confusion with directions (right/left) might also be observed. Poor fine motor control and coordination and poor planning can lead to writing problems. Attention and behavioral regulation weaknesses observed earlier can continue, and together with other EF weaknesses (e.g., organization, initiation skills), further complicate the child's ability to acquire and generalize new knowledge. Children with weaknesses in WM may struggle to remember the steps necessary to complete an activity or problem-solve. In social settings, these children often have difficulty keeping up with more complex conversations.

Table 49.2 Neurodevelopmental Dysfunction Underlying Academic Disorders*

ACADEMIC DISORDER	POTENTIAL UNDERLYING NEURODEVELOPMENTAL DYSFUNCTION
Reading	Language • Phonologic processing • Verbal fluency • Syntactic and semantic skills Memory • Working memory Sequencing Visual-spatial Attention
Written expression, spelling	Language • Phonologic processing • Syntactic and semantic skills Graphomotor Visual-spatial Memory • Working memory Sequencing Attention
Mathematics	Visual-spatial Memory • Working memory Language Sequencing Graphomotor Attention

*Isolated neurodevelopmental dysfunction can lead to a specific academic disorder, but more often there is a combination of factors underlying weak academic performance. In addition to the dysfunction in neurodevelopmental domains as listed in the table, the clinician must also consider the possibility of limitations of intellectual and cognitive abilities or associated social and emotional problems.

In **middle school children** the substantial increase in cognitive, academic, and regulatory demands can cause further difficulties for those with existing neurodevelopmental and executive challenges. In reading and writing, middle school children might present with transposition and sequencing errors; might struggle with root words, prefixes, and suffixes; might have difficulty with written expression; and might avoid reading and writing altogether. Challenges completing word problems in math are common. Difficulty with recall of information might also be experienced. Although observable in both lower and more advanced grades, behavioral, emotional, and social difficulties tend to become more salient in middle school children who experience cognitive or academic problems.

High school students can present with deficient reading comprehension, written expression, and slower processing efficiency. Difficulty in answering open-ended questions, dealing with abstract information, and deploying executive control (e.g., self-monitoring, organization, planning, self-starting) is often reported.

Academic Problems

Reading disorders (see Chapter 51) can stem from a number of neurodevelopmental dysfunctions, as described earlier (see Table 49.2). Most often, language and auditory processing weaknesses are present, as evidenced by poor phonologic processing that results in deficiencies at the level of decoding individual words and, consequently, a delay in *automaticity* (e.g., acquiring a repertoire of words readers can identify instantly) that causes reading to be slow, laborious, and frustrating. Deficits in other core neurodevelopmental domains might also be present. Weak WM might make it difficult for a child to hold sounds and symbols in mind while breaking down words into their component sounds, or might cause reading comprehension problems. Some children experience temporal-ordering weaknesses and struggle with reblending phonemes into correct sequences. Memory dysfunction can cause problems with recall and summarization of what was read. Some children with higher-order cognitive deficiencies have trouble understanding what they read because they lack a strong grasp of the concepts in a text. Although rare as a cause of reading difficulty, problems with visual-spatial functions (e.g., visual perception) can cause children difficulty in recognizing letters. It is not unusual for children with reading problems to avoid reading practice, and a delay in reading proficiency becomes increasingly pronounced and difficult to remediate.

Spelling and writing impairments share many related underlying processing deficits with reading, so it is not surprising that the two disorders often occur simultaneously in school-age children (see Table 49.2). Core neurodevelopmental weaknesses that underlie *spelling difficulties* include phonologic and decoding difficulties, orthographic problems (coding letters and words into memory), and morphologic deficits (use of suffixes, prefixes, and root words). Problems in these areas can manifest as phonetically poor, yet visually comparable, approximations to the actual word (*faght* for *fight*), spelling that is phonetically correct but visually incorrect (*fite* for *fight*), and inadequate spelling patterns (*plade* for *played*). Children with memory disorders might misspell words because of coding weaknesses. Others misspell because of poor auditory WM that interferes with their ability to process letters. Sequencing weaknesses often result in transposition errors when spelling.

Writing difficulties have been classified as **disorder of written expression**, or **dysgraphia** (see Table 49.2). Although many of the same dysfunctions described for reading and spelling can contribute to problems with writing, written expression is the most complex of the language arts, requiring synthesis of many neurodevelopmental functions (e.g., auditory, visual-spatial, memory, executive; see Chapter 52.2). Weaknesses in these functions can result in written output that is difficult to comprehend, disjointed, and poorly organized. The child with WM challenges can lose track of what the child intended to write. Attention deficits can make it difficult for a child to mobilize and sustain the mental effort, pacing, and self-monitoring demands necessary for writing. In many cases, writing is laborious because of an underlying *graphomotor dysfunction* (e.g., fluency does not keep pace

with ideation and language production). Thoughts may also be forgotten or underdeveloped during writing because the mechanical effort is so taxing.

Weaknesses in mathematical ability, known as **mathematics disorder** or **dyscalculia**, involve the assimilation of both procedural knowledge (e.g., calculations) and higher-order cognitive processes (e.g., WM) (see Table 49.2). There are many reasons why children struggle with mathematics (see Chapter 52.1). It may be difficult for some to grasp and apply math concepts effectively and systematically; good mathematicians are able to use both verbal and perceptual conceptualization to understand such concepts as fractions, percentages, equations, and proportion. Children with language dysfunctions have difficulty in mathematics because they have trouble understanding their teachers' verbal explanations of quantitative concepts and operations and are likely to experience frustration in solving word problems and in processing the vast network of technical vocabulary in math. Mathematics also relies on visualization. Children who have difficulty forming and recalling visual imagery may be at a disadvantage. They might experience problems writing numbers correctly, placing value locations, and processing geometric shapes or fractions. Children with executive dysfunction may be unable to focus on fine detail (e.g., operational signs), might take an impulsive approach to problem solving, engage in little or no self-monitoring, forget components of the problem, or commit careless errors. When a child's memory system is weak, the child might have difficulty recalling appropriate procedures and automatizing mathematical facts (e.g., multiplication tables). Moreover, children with mathematical disabilities can have superimposed mathematics **phobias**; anxiety over mathematics can be especially debilitating.

Nonacademic Problems

The impulsivity and lack of effective self-monitoring of children with executive dysfunction can lead to unacceptable actions that were unintentional. Children struggling with neurodevelopmental dysfunction can experience excessive performance anxiety, sadness, or clinical depression; declining self-esteem; and chronic fatigue. Some children may lose motivation and feel no need to exert effort and develop future goals. These children may be easily led toward dysfunctional interpersonal relationships, detrimental behaviors (e.g., delinquency, substance abuse), and the development of mental health disorders, such as mood disorders (see Chapter 39) or conduct disorder (see Chapter 42).

ASSESSMENT AND DIAGNOSIS

Pediatricians have a critical role in identifying and treating the child with neurodevelopmental or executive dysfunction (Fig. 49.1). They have knowledge of the child's medical and family history and social-environmental circumstances and have the benefit of longitudinal contact over the course of routine health visits. Focused **surveillance and screening** will facilitate early identification of developmental-behavioral and preacademic difficulties and interventions to facilitate optimal outcomes.

A **family history** of a parent who still struggles with reading or time management or an older sibling who has failed at school should spur an increased level of monitoring. **Risk factors** in the medical history, such as extreme prematurity or chronic medical conditions, should likewise be flagged. Children with low birthweight and those born prematurely who appear to have been spared more serious neurologic problems might only manifest academic problems later in their school career. **Nonspecific physical complaints** or unexpected **changes in behavior** might be presenting symptoms. Warning signs might be subtle or absent, and parents might have concerns about their child's learning progress but may be reluctant to share these with the pediatrician unless prompted, such as through completion of **standardized developmental screening questionnaires** or direct questioning regarding possible concerns. Concerns voiced to parents or caregivers by daycare, preschool, or early elementary teachers might be the first indicators of neurodevelopmental dysfunctions. There should be a low threshold for initiating further school performance screening and assessment if there are any concerns or "red flags" (see "Clinical Manifestations").

In elementary school, review of **school report cards** and teacher comments can provide very useful information. In addition to patterns of grades in the various academic skill areas, it is also important to review ratings of classroom behavior and work habits. Group-administered **standardized tests** provide further information, although interpretation is required because poor scores could result from a learning disorder, ADHD, emotional problems, lack of motivation, or some combination. Conversely, a discrepancy between above-average scores on standardized tests and unsatisfactory classroom performance could signal motivation, adjustment issues, or instructional mismatches. Challenges related to **homework**, such as excessive time to complete, can provide further insight regarding EFs, academic skill, and behavioral factors or factors related to the home environment.

Underlying or associated medical problems should be ruled out. Any suspicion of sensory difficulty should warrant referral for **vision or hearing testing**. The influence of chronic medical problems or potential side effects of medications should be considered. **Sleep deprivation** is increasingly being recognized as a contributor to academic problems, especially in middle and high school. **Substance use** must always be a consideration as well, especially in the adolescent previously achieving well who has shown a rapid decline in academic performance.

The physician should be alert for **dysmorphic physical features**, minor congenital anomalies, or constellations of physical findings (e.g., cardiac and palatal anomalies in 22q11.2 deletion syndrome) and should perform a detailed **neurologic examination**, including an assessment of fine and gross motor coordination and any involuntary movements or soft neurologic signs. Genetic testing is often recommended for children with intellectual disability or autism spectrum disorder; electroencephalogram and brain MRI are generally not indicated in the absence of specific medical findings or a family history.

Early signs of **executive dysfunction** can also be subtle and easily overlooked or misinterpreted. Informal inquiry might include questions about how children complete schoolwork or tasks, how organized or disorganized they are, how much guidance they need, whether they think through problems or respond and react too quickly, what circumstances or individuals affect their ability to employ EFs, how easily they begin tasks and activities, and how well they plan, manage belongings, and control their emotions.

Pediatricians who are interested in performing further assessment before referral, or who are practicing in areas where psychologic testing resources are limited, can use **standardized rating scales and inventories** or brief, individually administered tests to narrow potential diagnoses and guide next steps in diagnosis and treatment. Such instruments, completed by the parents, teachers, and the child (if old enough), can provide information about emotions and behavior, patterns of academic performance, and traits associated with specific neurodevelopmental dysfunctions (see Chapter 32). Screening instruments such as the *Pediatric Symptom Checklist* and behavioral questionnaires such as the *Child Behavior Checklist* (CBCL) and *Behavior Assessment System for Children, Third Edition* (BASC-3) can aid in evaluation.

EFs can be further assessed by instruments such as the *Behavior Rating Inventory of Executive Function, Second Edition* (BRIEF-2), which provides a comprehensive measure of real-world behaviors that are closely tied to executive functioning in children age 5-18 years. Tests that can be directly administered to gauge intellectual and language functioning include the *Kaufman Brief Intelligence Test, Second Edition* (KBIT-2) and *Peabody Picture Vocabulary Test, Fifth Edition* (PPVT 5; assessing receptive vocabulary). A relatively brief test of academic skills is the *Wide Range Achievement Test5* (WRAT5). It should be recognized that these are midlevel tests that can provide descriptive estimates of function but are not diagnostic.

Children who are struggling academically are entitled to evaluations in school. Such assessments are guaranteed in the United States under Public Law 101-476, the **Individuals with Disabilities Education Act (IDEA)**. One increasingly common type of evaluation model supported by IDEA is referred to as a **Response to Intervention (RtI)** model (see Chapter 52.1). In this model, students who are struggling with academic skills are initially provided research-based instruction. If a child does not respond to this instruction, an individualized

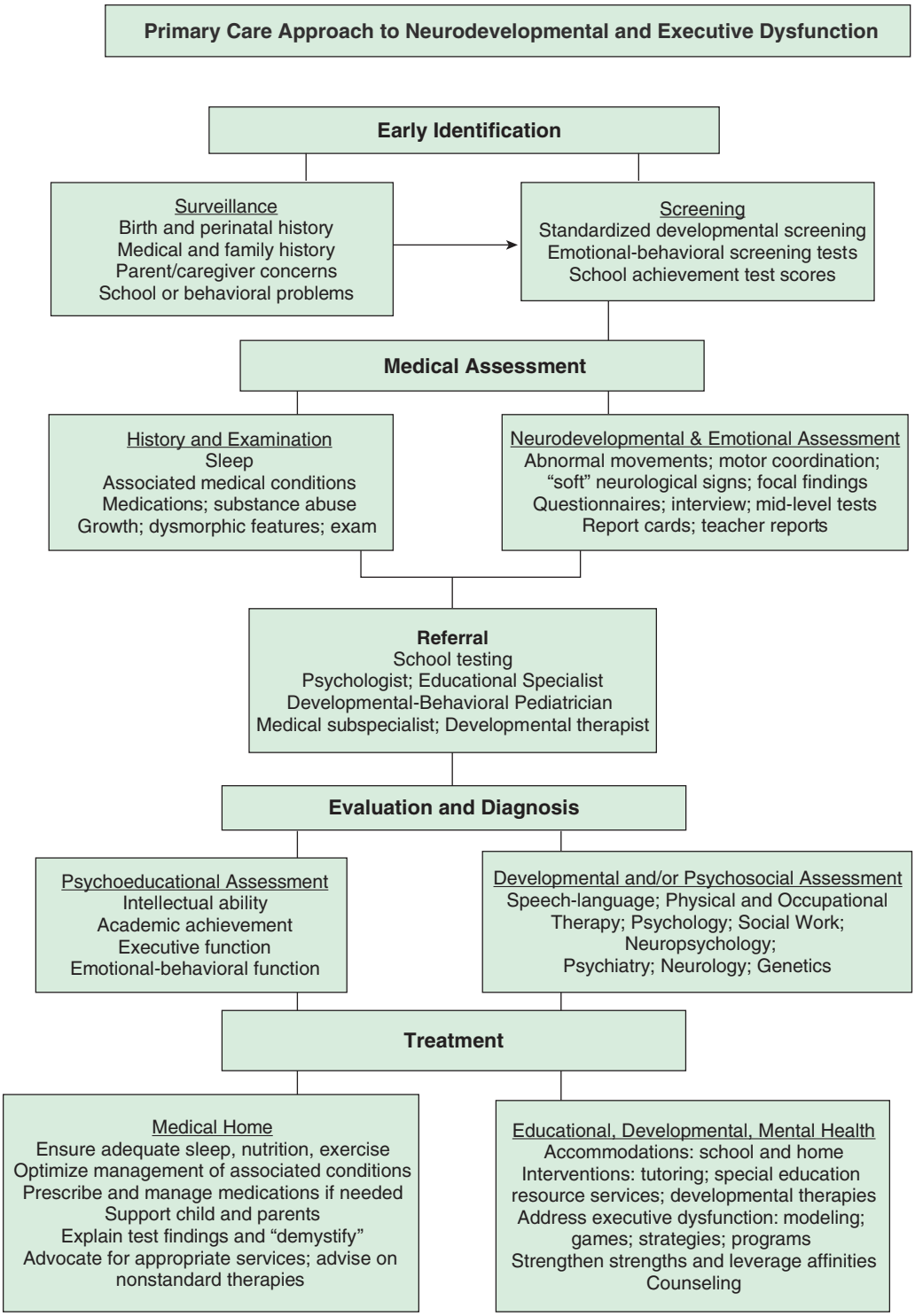

Fig. 49.1 Algorithm showing components of a primary care approach to identification, diagnosis, and comprehensive multidisciplinary management of neurodevelopmental and executive dysfunction.

evaluation by a multidisciplinary team is conducted. Children found to have attentional dysfunction and other disorders might qualify for educational accommodations in the regular classroom under Section 504 of the Rehabilitation Act of 1973 (**504 Plan**) or might qualify for an **individualized education program (IEP)**.

The pediatrician should advise and support parents regarding steps to request evaluations by the school. Multidisciplinary evaluations are focused primarily on determining whether a student meets the eligibility criteria for special education services and to assist in developing an IEP for those eligible for these services. **Independent evaluations** can provide second opinions outside the school setting. The multidisciplinary team should include a psychologist and preferably an educational diagnostician who can undertake a detailed analysis of academic skills and subskills to pinpoint where breakdowns are occurring in the processes of reading, spelling, writing, and mathematics. Other professionals should become involved, as needed, such as a speech-language pathologist, occupational therapist, and social worker. A mental health specialist can be valuable in identifying family-based issues or psychiatric disorders that may be complicating or aggravating neurodevelopmental dysfunctions.

In some cases, more in-depth examination of a child's **neurocognitive status** is warranted. This is particularly true for children who

present with developmental or cognitive difficulties in the presence of a medical condition (e.g., epilepsy, traumatic brain injury, childhood cancers/brain tumors, genetic conditions). A **neuropsychologic evaluation** involves comprehensive assessment to understand brain functions across domains. Neuropsychologic data are often analyzed together with other tests, such as MRI, to look for supporting evidence of any areas of difficulty (e.g., memory weaknesses associated with temporal lobe anomalies). Neuropsychologists can also provide more in-depth evaluation of EFs. Assessment of EFs is typically completed in an examination setting using tools specifically designed to identify any weaknesses in these functions. Although few tools are currently available to assess EF in preschool-age children, the assessment of school-age children is better established. Problems with EFs should be evaluated across measures and in different settings, particularly within the context of the child's daily demands.

TREATMENT

Treatment for neurodevelopmental and executive dysfunction involves a **multimodal, multidisciplinary "cross-sector" approach to foster optimal outcomes.** This process begins with **demystification**, which involves educating the child and family about the nature of the child's delay or dysfunction while also identifying a child's strengths. The explanation of the dysfunction should be provided in nontechnical language, communicating a sense of optimism for improvement with appropriate intervention. Children need to have their affinities, potentials, and talents identified clearly and emphasized as an integral component of the long-term treatment plan. It is as important to **augment strengths** as it is to attempt to **remedy deficiencies**. Athletic skills, artistic inclinations, creative talents, and mechanical abilities are among the potential assets of certain students who are underachieving academically. Parents and school personnel need to create opportunities for such students to build on these assets. These well-developed personal assets can ultimately have implications for the transition into young adulthood, including career or college selection.

In the clinic setting, the pediatrician plays an important role as a **consultant and advocate** in overseeing and monitoring the implementation of a comprehensive multidisciplinary management plan for children with neurodevelopmental dysfunctions. The primary care provider should **identify and treat any underlying or associated medical problems** that might contribute to neurodevelopmental and EF dysfunction, such as iron deficiency, elevated lead levels, and sleep problems, including inadequate sleep related to poor sleep hygiene or poor quality of sleep (e.g., obstructive sleep apnea). Additionally, the pediatrician will need to monitor for **conditions that often co-occur** with neurodevelopmental delays and executive dysfunction or that may develop over time, including anxiety, depression, and substance use disorder.

Bypass Strategies (Accommodations)

Numerous techniques can enable a child to circumvent neurodevelopmental dysfunctions. Such strategies are typically used in the regular classroom and can be incorporated into a 504 Plan or IEP. Accommodations change *how* the child learns, allowing them to access material and meet the same expectations as their peers. Examples of accommodations include using large print for those with visual impairment and using a frequency modulation (FM) system for students with hearing impairment. For children with learning disorders, accommodations may include using a calculator while solving mathematical problems, writing essays with a word processor and use of spellcheck, or presenting oral instead of written reports. Children with executive dysfunction might benefit from being seated near the teacher to minimize distractions and taking tests untimed. These bypass strategies do not cure neurodevelopmental dysfunctions, but they minimize their academic and nonacademic effects and can provide a scaffold for more successful academic achievement.

Curriculum Modifications

Many children with neurodevelopmental dysfunctions require alterations in the school curriculum to succeed, especially as they progress through secondary school. A modification changes *what* the child is taught or expected to learn. Modifications include a student learning different material (e.g., continuing to work on addition and subtraction facts while peers move on to fractions) and instructors assigning grades using a different standard. In high school and college, students with memory weaknesses might need to work with an advisor to select courses that avoid an inordinate cumulative memory load in any single semester. For adolescents with learning disorders, the timing of foreign language learning and the selection of mathematics and science courses are critical to their academic success.

Remediation/Targeted Intervention

Interventions can be implemented at home and in school to strengthen academic skills. **Early identification** is critical so that appropriate instructional interventions can be introduced to minimize the long-term effects of academic disorders. Any interventions should be empirically supported (e.g., phonologically based reading intervention has been shown to significantly improve reading skills in school-age children). **Remediation** may take place in a resource room or learning center at school and is usually limited to children who have met the educational criteria for special education services described earlier. Reading specialists, mathematics tutors, and other professionals can use diagnostic data to select techniques that use a student's neurodevelopmental strengths to improve decoding skills, writing ability, or mathematical computation skills. Remediation need not focus exclusively on specific academic areas. Many students need assistance in acquiring study skills, cognitive strategies, and productive organizational habits.

Speech-language pathologists offer intervention for children with various forms of language disability. **Occupational therapists** focus on sensorimotor skills, including the motor skills of students with writing problems, and **physical therapists** address gross motor incoordination.

Treatment of Executive Dysfunction

Interventions to strengthen EFs can be implemented throughout childhood but are most effective if started at a young age. Preschool-age children first learn EFs by way of the **modeling, boundaries, and rules** observed and put in place by their parents/caregivers, and this modeled behavior must gradually become "internalized" by the child. Early **play** has been shown to be effective in promoting executive skills in younger children with games such as peek-a-boo (WM); pat-a-cake (WM and IC); follow the leader, Simon Says, and "Ring Around the Rosie" (self-control); imitation activities (attention and impulse control); matching and sorting games (organization and attention); and imaginary play (attention, WM, IC, self-monitoring, cognitive flexibility).

In school-age children it is crucial to establish consistent **cognitive and behavioral routines** that foster and maximize independent, goal-oriented problem solving and performance through mechanisms that include modification of the child's environment, modeling and guidance with the child, and positive reinforcement strategies. Interventions should promote **generalization** (teaching executive routines in the context of a problem, not as a separate skill) and should move from the external to the internal (from "external support" with active and directive modeling to an "internal process"). An intervention could proceed from external modeling of multistep problem-solving routines and external guidance in developing and implementing everyday routines, to practicing application and use of routines in everyday situations, to a gradual fading of external support and cueing of internal generation and use of executive skills. Such approaches should make the child a part of intervention planning, should avoid labeling, reward effort not outcomes, make interventions positive, and hold the child responsible for his or her efforts. Studies have consistently shown that a **combination of medication and behavioral treatments** are most effective, although evidence for long-term efficacy is lacking. It is important that any treatment plans aimed at bolstering attention and EF also include interventions that address the specific deficits associated with any comorbid diagnoses.

In addition to behavioral approaches, **cognitive training**, both computerized and noncomputerized, has been shown to strengthen the cognitive skills on which one is trained. Some computerized training

programs show lasting improvements in WM skills in children, though benefits are narrow and limited only to the aspects of WM specifically trained. Recently, game-based digital therapy has been shown to improve attention in children with ADHD-inattentive type and combined type. Noncomputerized cognitive training has shown greater improvements in EF than any type of computerized cognitive training. This may be the result of instructor-trainee interaction. Also evidencing positive outcomes are curriculum-based **classroom programs**, such as the *Tools of the Mind* (Tools) and *Promoting Alternative Thinking Strategies* (PATHS), which have been shown to improve IC.

Emerging evidence suggests **physical activity** can improve EF. Children who are more physically active and have better aerobic fitness have been shown to have better EF than children who are sedentary. Although plain aerobic exercise (e.g., walking, running) has not been found to improve EF, encouraging findings have been noted when an activity involves aerobic exercise and is also cognitively demanding. Basketball and dance, for example, are high in physical exertion while also requiring cognitive engagement through motor coordination and planning. In contrast, resistance training has not been shown to improve EF.

Approaches that use **mindfulness techniques** are also gaining prominence. Mindfulness practices incorporating movement (e.g., tai chi) improve EF better than those performed in a seated position. **Martial arts** such as taekwondo, which stresses discipline and self-regulation, have demonstrated improvements that generalize in many aspects of EFs and attention (e.g., sustained focus).

COUNSELING AND PARENT TRAINING PROGRAMS

The pediatrician is often in a close, trusting relationship with families and is well-positioned to identify adverse home factors that may require additional supports, including counseling and parent training. When academic difficulties are complicated by family problems or identifiable psychiatric disorders, **psychotherapy** may be indicated. Mental health professionals may offer long-term or short-term therapy. Such intervention may involve the child alone or the entire family. **Cognitive-behavioral therapy** is especially effective for mood and anxiety disorders. It is essential that the therapist have a firm understanding of the nature of a child's neurodevelopmental dysfunctions. Formal **parenting interventions** have also demonstrated strong evidence for effectiveness. Four programs that have the most empirical support are the *Triple P, Parent-Child Interaction Therapy* (PCIT), *Incredible Years,* and *New Forest Parenting Programme*.

Table 49.3 outlines interventions to target the specific components of EF. Although interventions may target each component separately, success will be determined by how well treatments can be integrated across settings and generalized to other areas of function. Whenever possible, working with more than one EF simultaneously is encouraged as a means of scaffolding intervention and building on previously mastered skills.

Medication

Psychopharmacologic agents may be helpful in lessening the toll of some neurodevelopmental dysfunctions. Most often, **stimulants** are used in the treatment of children with attention deficits. Although most children with attention deficits have other associated dysfunctions, such as language disorders, memory problems, motor weaknesses, or social skill deficits, medications such as methylphenidate, dextroamphetamine, lisdexamfetamine, and mixed amphetamine salts, as well as nonstimulants such as α_2-**adrenergic agonists** and **atomoxetine**, can be important adjuncts to treatment by helping some children focus more selectively and control their impulsivity. When depression or excessive anxiety is a significant component of the clinical picture,

Table 49.3 Executive Function Categories: Presenting Symptoms, Suggested Dysfunction, and Potential Interventions

SYMPTOM/PRESENTING COMPLAINT	SUSPECTED AREA OF DYSFUNCTION	POSSIBLE "REAL-WORLD" INTERVENTIONS
Acts before thinking Interrupts Poor behavioral and/or emotional control	Inhibitory control	Increase structure in environment to set limits for inhibition problems. Make behavior and work expectations clear and explicit; review with child. Post rules in view; point to them when child breaks rule. Teach response-delay techniques (e.g., counting to 10 before acting).
Cannot follow multistep instructions Forgetful	Working memory	Repeat instructions as needed. Keep instructions clear and concise. Provide concrete references.
Struggles starting assignments/tasks Lacks initiative/motivation Has trouble developing ideas/strategies	Initiation	Increase structure of tasks. Establish and rely on routine. Break tasks into smaller, manageable steps. Place child with partner or group for modeling and cueing from peers.
Does not plan ahead Uses trial-and-error approach	Planning	Practice with tasks with only a few steps first. Teach simple flow charting as a planning tool. Practice with planning tasks (e.g., mazes). Ask child to verbalize plan before beginning work. Ask child to verbalize second plan if first does not work. Ask child to verbalize possible consequences of actions before beginning. Review incidents of poor planning/anticipation with child.
Work/belongings is/are "messy" Random/haphazard problem solving Procrastinates/does not complete tasks	Organization	Increase organization of classroom and activities to serve as model, and help child grasp structure of new information. Present framework of new information to be learned at the outset, and review again at the end of a lesson. Begin with tasks with only a few steps and increase gradually.
Gets "stuck" Trouble transitioning Does not adapt to change	Flexibility/shifting	Increase routine to the day. Make schedule clear and public. Forewarn of any changes in schedule. Give "2-minute warning" of time to change. Make changes from one task to the next or one topic to the next, clear and explicit. Shifting may be a problem of inhibiting, so apply strategies for inhibition problems.

antidepressants or **anxiolytics** may be helpful. Other medications may improve behavioral control (see Chapter 33). Children receiving medication need regular follow-up visits that include a history to check for side effects, a review of current behavioral checklists, a complete physical examination, and appropriate modifications of the medication dose. Periodic trials off medication are recommended to establish whether the medication is still necessary.

Nonstandard Therapies

Pediatricians should be aware of nonstandard therapies that purport to treat neurodevelopmental and executive dysfunction or components therein. A variety of treatment methods for neurodevelopmental dysfunctions have been proposed that currently have little to no known scientific evidence of efficacy. This list includes dietary interventions (vitamins, elimination of food additives or potential allergens), neuromotor programs or medications to address vestibular dysfunction, eye exercises, filters, tinted lenses, and various technologic devices. Parents should be cautioned against expending the excessive amounts of time and financial resources usually demanded by these remedies. In many cases, it is difficult to distinguish the nonspecific beneficial effects of increased support and attention paid to the child from the purported target effects of the interventions.

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Chapter 50

Attention-Deficit/ Hyperactivity Disorder

Elizabeth B. Harstad

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common and extensively studied neurobehavioral disorders of childhood and is among the most prevalent chronic health conditions affecting school-age children. ADHD is characterized by inattention, including increased distractibility and difficulty sustaining attention; poor impulse control and decreased self-inhibitory capacity; and motor overactivity and restlessness (Table 50.1, Fig. 50.1). Definitions vary in different countries. In the International Classification of Diseases (ICD) 2022 update from ICD-10 to ICD-11, hyperkinetic disorder was replaced with ADHD, which aligns with *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) terminology. Under ICD-11, the essential features of ADHD are described, but without giving age of onset, duration, or minimum number of symptoms needed for the diagnosis as specified in DSM-5 (Table 50.2). Children with ADHD may experience academic underachievement, problems with interpersonal relationships with family members and peers, and low self-esteem. ADHD often coexists with other emotional, behavioral, language, and learning disorders. Evidence also suggests that for many people, the disorder continues, with varying manifestations across the life cycle, leading to significant underemployment and unemployment, social dysfunction, and increased risk of antisocial behaviors (e.g., substance abuse), difficulty maintaining relationships, encounters with the law, and death from suicide or accidents (Figs. 50.2 and 50.3).

EPIDEMIOLOGY

Studies of the prevalence of ADHD worldwide have generally reported that 5–10% of school-age children are affected, although rates vary considerably by country, perhaps in part because of differing sampling and testing techniques and a varying symptom threshold for diagnosis. ADHD is more common in males than in females (male to female ratio 4:1 for the predominantly hyperactive-impulsive presentation and 2:1 for the predominantly inattentive presentation). Many children with ADHD will have coexisting diagnoses, including learning disabilities, mood disorders, and/or language disorders. Children with high intellectual quotient (IQ) are just as likely to have ADHD as those with average IQ, but children with below-average IQ have increased risk of having coexisting ADHD.

ETIOLOGY

There is no single etiology identified for ADHD; many factors play a role in its development. A genetic contribution to the etiology of ADHD is well established. Twin studies show 70–80% heritability, and there is a 5- to 10-fold increased risk for ADHD among first-degree relatives of those with ADHD. However, there are many ways in which genetic variants contribute to ADHD; it is thought that ADHD is a polygenic disorder in which multiple common genetic variants act together to increase the risk for ADHD.

Structural and functional abnormalities of the brain have been identified in children with ADHD. These include dysregulation of the frontal subcortical circuits; small cortical volumes in this region or more widespread throughout the brain; and abnormalities of the cerebellum, particularly midline/vermian elements. There is a median of a 3-year delay in attainment of peak cortical thickness in prefrontal regions of the brain in those with ADHD. Although neuroimaging studies have advanced knowledge related to ADHD, neuroimaging does not typically have a role in the clinical diagnosis or inform ongoing management.

Brain catecholamine metabolism, specifically for dopamine and norepinephrine, appears to play a role in the pathophysiology of ADHD. Animal studies suggest that an imbalance between these systems (specifically a decrease in inhibitory dopamine activity and increase in norepinephrine activity) contributes to ADHD. These findings are supported by human studies showing that individuals with ADHD have an increase in dopamine transporter density (which clears away dopamine too quickly) compared to non-ADHD controls. Additionally, studies showing that stimulant medications work to treat ADHD by increasing the amount of available dopamine and norepinephrine at the synapse support a role for catecholamine metabolism in the etiology of ADHD.

Some environmental factors also may contribute to the pathogenesis of ADHD. Prenatal exposure to tobacco smoke or alcohol is associated with increased risk for ADHD. Prematurity, including even late-preterm birth, is also associated with increased risk for ADHD. Maternal mental illness increases the risk for ADHD in offspring, and research indicates underlying maternal mental illness itself, rather than treatment of the mental illness, is the associated risk factor. Diet is not thought to play a role in the pathogenesis of ADHD for most children with the condition. A small subset of children with ADHD may be uniquely sensitive to certain foods, sugars, or additives, but this remains controversial, as studies reporting these findings are typically small and often not rigorously designed.

CLINICAL MANIFESTATIONS

Development of the DSM-5 criteria for ADHD has occurred mainly in field trials with children 5-12 years of age (see Table 50.1). The DSM-5 criteria state that the inattentive or hyperactive-impulsive behaviors must be developmentally inappropriate (substantially different from that of other children of the same age and developmental level), must begin before age 12 years, must be present for at least 6 months, must be present in two or more settings, and must not be secondary to another disorder. To meet criteria for ADHD, the symptoms must interfere with social, academic, or occupational functioning.

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Table 50.1 DSM-5 Diagnostic Criteria for ADHD

A. A persistent pattern of inattention and/or hyperactivity/impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms of inattention have persisted for ≥6 mo to a degree that is inconsistent with development level and that negatively affects directly on social and academic/occupational activities:
   a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
   b. Often has difficulty sustaining attention in tasks or play activities.
   c. Often does not seem to listen when spoken to directly.
   d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not the result of oppositional behavior or failure to understand instructions).
   e. Often has difficulty organizing tasks and activities.
   f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork, homework).
   g. Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, tools).
   h. Is often easily distracted by extraneous stimuli.
   i. Is often forgetful in daily activities.
2. **Hyperactivity/impulsivity:** Six (or more) of the following symptoms of inattention have persisted for ≥6 mo to a degree that is inconsistent with development level and that negatively affects directly on social and academic/occupational activities.
   a. Often fidgets with hands or feet or squirms in seat.
   b. Often leaves seat in classroom or in other situations in which remaining seated is expected.
   c. Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).
   d. Often has difficulty playing or engaging in leisure activities quietly.
   e. Is often "on the go" or often acts as if "driven by a motor."
   f. Often talks excessively. Impulsivity.
   g. Often blurts out answers before questions have been completed.
   h. Often has difficulty awaiting turn.
   i. Often interrupts or intrudes on others (e.g., butts into conversations or games).

B. Several inattentive or hyperactive/impulsive symptoms were present before 12 yr of age.

C. Several inattentive or hyperactive/impulsive symptoms are present in two or more settings (e.g., at school [or work] or at home) and are documented independently.

D. There is clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. Symptoms do not occur exclusively during the course of schizophrenia, or another psychotic disorder, and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

CODE BASED ON TYPE

314.01 Attention-deficit/hyperactivity disorder, combined presentation: if both Criteria A1 and A2 are met for the past 6 mo.

314.00 Attention-deficit/hyperactivity disorder, predominantly inattentive presentation: if Criterion A1 is met but Criterion A2 is not met for the past 6 mo.

314.01 Attention-deficit/hyperactivity disorder, predominantly hyperactive-impulsive presentation: if Criterion A2 is met but Criterion A1 is not met for the past 6 mo.

Specify if:

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and if the symptoms result in no more than minor impairments in social and occupational functioning.

Moderate: Symptoms or functional impairment between "mild" and "severe" are present.

Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

From American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, Text Revision, Washington, DC: American Psychiatric Association; 2000, and *Fifth Edition* (Copyright 2013 American Psychiatric Association.)

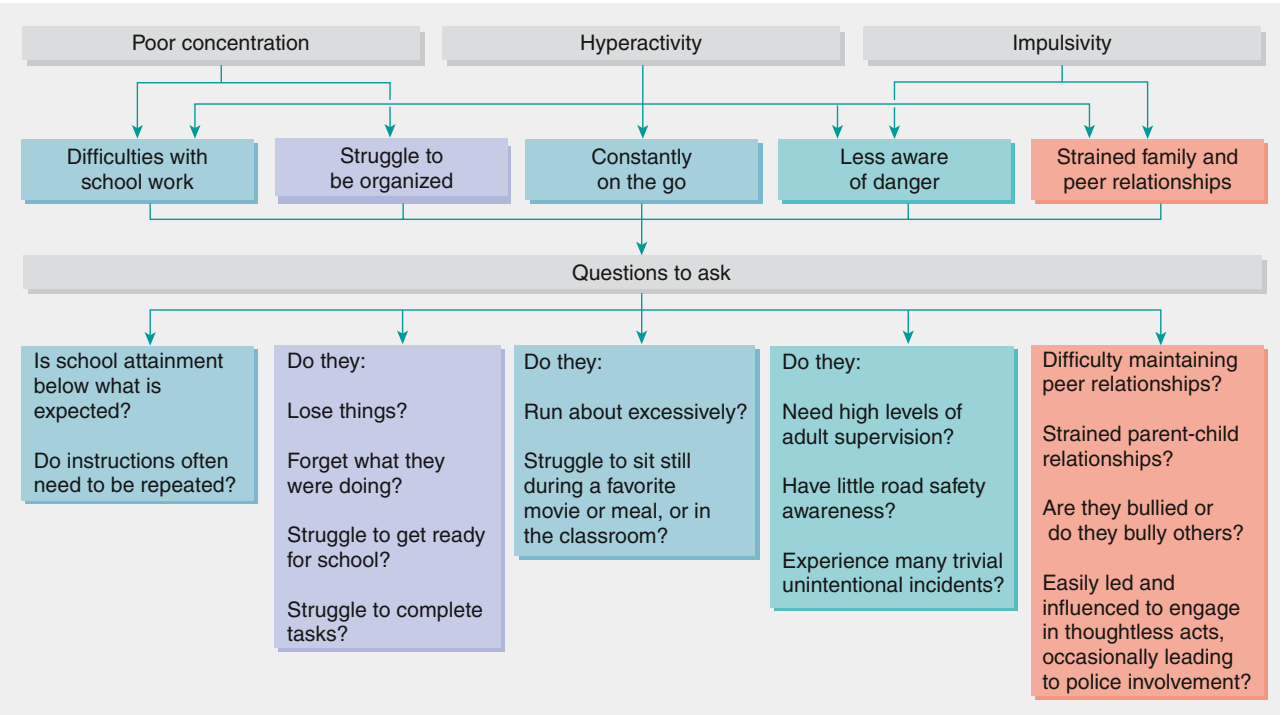

Fig. 50.1 How to assess children for attention-deficit/hyperactivity disorder. *(From Verkuijl N, Perkins M, Fazel M. Childhood attention-deficit/hyperactivity disorder. BMJ. 2015;350:h2168, Fig. 2, p. 146.)*

Table 50.2 Differences Between U.S. and European Criteria for ADHD or HKD

DSM-5 ADHD	ICD-10 HKD	ICD-11 ADHD*
SYMPTOMS		
Either or both of the following: • At least 6 of 9 inattentive symptoms • At least 6 of 9 hyperactive or impulsive symptoms	*All of the following:* • At least 6 of 8 inattentive symptoms • At least 3 of 5 hyperactive symptoms • At least 1 of 4 impulsive symptoms	*No minimum numbers of symptoms but must have:* • Persistent pattern (≥6 mo) of inattention and/or hyperactivity-impulsivity that has a direct negative impact on academic, occupational, or social functioning
PERVASIVENESS		
Some impairment from symptoms is present in one or more settings	Criteria are met for one or more settings	Symptoms must be evident across multiple situations or settings but are likely to vary according to the structure and demands of the setting

*ICD-11 went into effect on January 1, 2022.
ADHD, Attention-deficit/hyperactivity disorder; HKD, hyperkinetic disorder; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ICD-10, International Classification of Diseases, Tenth Edition.
Modified from Biederman J, Faraone S. Attention-deficit hyperactivity disorder. *Lancet*. 2005;366:237–248.

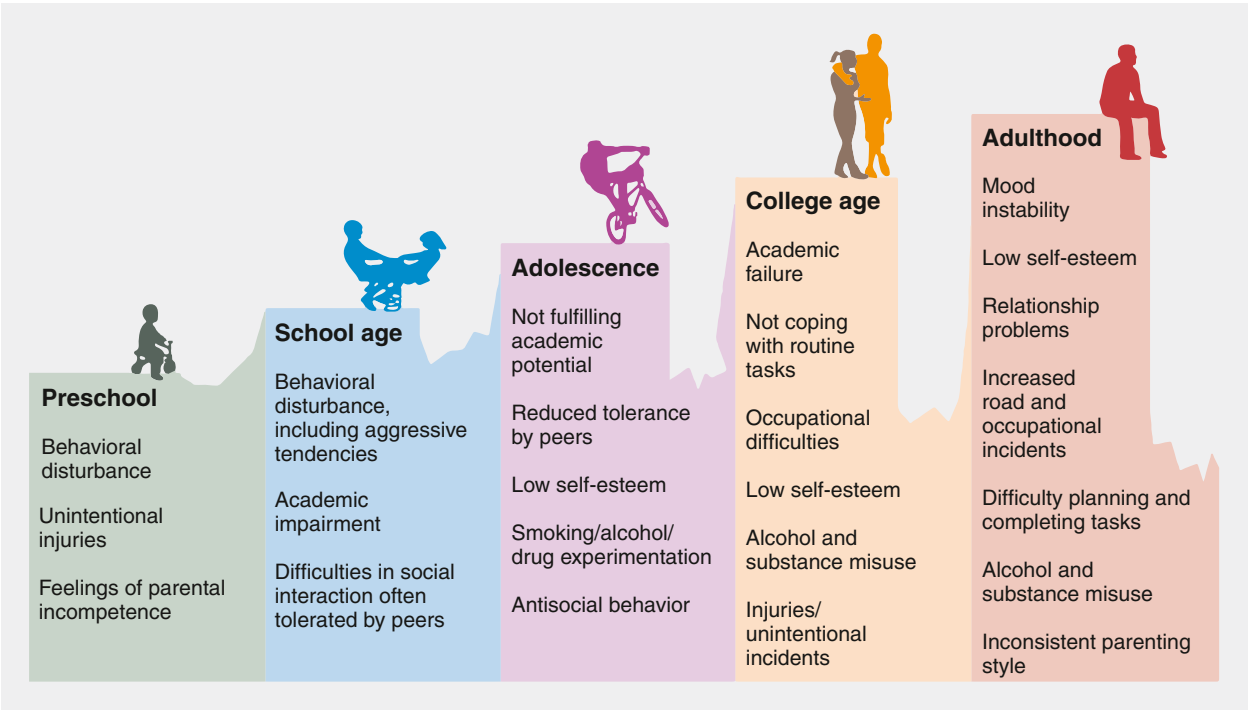

Fig. 50.2 Possible developmental impacts of attention-deficit/hyperactivity disorder. *(From Verkuijl N, Perkins M, Fazel M. Childhood attention-deficit/hyperactivity disorder. BMJ. 2015;350:h2168, Fig. 1, p. 145.)*

DSM-5 identifies three presentations of ADHD: the inattentive presentation, hyperactive-impulsive presentation, and combined presentation. Clinical manifestations of ADHD may change with age; thus the specific ADHD presentation for an individual may not be stable over time but describes current symptomatology (see Fig. 50.2). The symptoms may vary from motor restlessness and aggressive and disruptive behavior, which are common in preschool children, to disorganized, distractible, and inattentive symptoms, which are more typical in older adolescents and adults. Although hyperactivity generally decreases in late childhood and adolescence, symptoms of impulsivity and inattention often persist. Females with ADHD are relatively more likely than males to be diagnosed with the inattentive presentation, and this presentation is more commonly associated with internalizing symptoms (anxiety and low mood).

DIAGNOSIS

An evaluation for ADHD should be initiated in any child ≥4 years of age with symptoms of inattention, hyperactivity, and/or impulsivity (Fig. 50.4). This evaluation includes a careful history and clinical interview to rule in ADHD or to identify other causes or contributing factors, completion of behavior rating scales by different observers from at least two settings (e.g., teacher and parent), and a physical examination. It is important to systematically gather and evaluate information from a variety of sources, including the child, parents, teachers, and, when appropriate, other caretakers or professionals involved in the child's care.

The evaluation for ADHD may require several office visits. A thorough assessment should be conducted at the time of initial diagnosis, and reevaluation should occur if there are worsening or new symptoms, given the common occurrence of coexisting conditions.

Clinical Interview and History

The clinical interview allows a comprehensive understanding of whether the symptoms meet the diagnostic criteria for ADHD and to assess for coexisting conditions. The interview should collect information about the history and duration of presenting problems, the child's attainment of developmental milestones, school performance, social skills, mood, sleep, medical illnesses, sensory impairments, or

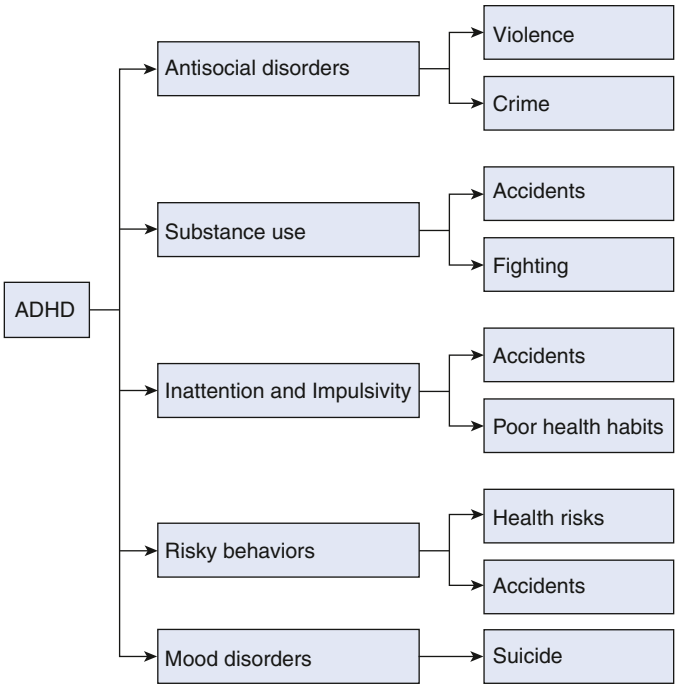

Fig. 50.3 Pathways to premature death in persons with attention-deficit/hyperactivity disorder (ADHD). *(From Faraone SV. Attention deficit hyperactivity disorder and premature death. Lancet. 2015;385:2132–2133.)*

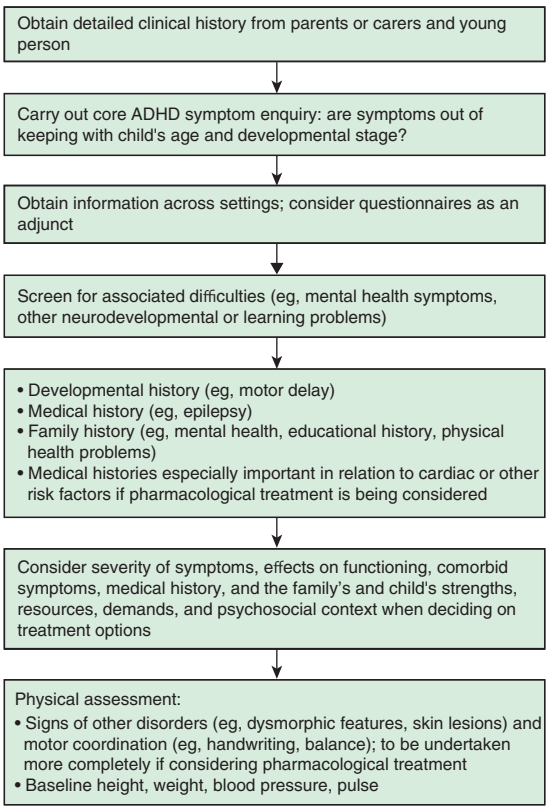

Fig. 50.4 Summary of the clinical assessment process for ADHD. ADHD, Attention-deficit/hyperactivity disorder. *(From Thapar A, Cooper M. Attention deficit hyperactivity disorder. Lancet. 2016;387[10024]:1240–1250, Fig. 2.)*

medication use that might affect the child's functioning. Disruptive social factors, such as family discord, situational stress, and abuse or neglect, can result in hyperactive or anxious behaviors. A family history of first-degree relatives with ADHD, mood or anxiety disorders, learning disability, antisocial disorder, or alcohol or substance abuse might indicate an increased risk of ADHD and coexisting conditions.

Behavior Rating Scales

Behavior rating scales can help to elicit information about ADHD symptoms across contexts (i.e., home and school). The *Vanderbilt ADHD Rating Scale* (which has parent and teacher versions) is a commonly used screening measure for ADHD in primary care. It has specific questions about inattention and hyperactivity/impulsivity that correspond directly with the DSM-5 ADHD diagnostic criteria and questions about overall performance to assess for functional impairment, as well as subscales for some common coexisting conditions (anxiety/depression and oppositional behaviors/conduct disorder). Additional ADHD-specific rating scales include the *Conners 3 ADHD Index* and *ADHD Rating Scale 5*, among others that can be used. Broadband rating scales (such as *Achenbach Child Behavior Checklist* [CBCL] or *Behavioral Assessment Scale for Children* [BASC] or *Conners 3 Full Length Forms*) can be useful in assessing for coexisting conditions. Electronic capture of rating scale information is increasingly available and may facilitate completion and scoring. Rating scales provide information about the type, frequency, and severity of ADHD or other behavioral/mood symptoms, but interpretation requires clinical judgement. Contextual factors (such as triggers for a certain behavior, responses to a behavior that may inadvertently reinforce it) should be considered when interpreting rating scales. When there are discrepancies between results of rating scales for parents and teachers, the context and level of support provided in each setting should be assessed. ADHD rating scales can help with both the initial diagnostic assessment and with monitoring treatment response over time. Although there is no universal standard to use as a criterion for a positive response to treatment in terms of rating scale results, a decrease in ADHD symptom scores by 25% or more is generally considered significant improvement. However, improvement in functional outcomes may be more important to consider than changes in symptom scores. For children on medication, it is important to consider if the medication was "active" when the child was observed (i.e., stimulant medication may work to reduce ADHD symptoms during the school day, but the symptoms may return as the medication wears off in the afternoon/evening when the child is home).

Physical Examination, Laboratory, and Other Assessments

Most children with ADHD will have a normal physical exam, but one should be conducted as part of the diagnostic evaluation. Particular attention should be paid to cardiac and neurologic evaluations, thyroid, hearing and vision, and assessment for dysmorphic features that may signify an underlying condition, such as fetal alcohol syndrome. A child's behavior in the clinic visit may not represent the child's usual behaviors, as some children may be able to remain focused or calm for brief periods and others may exhibit more impulsivity or high activity level when nervous in the context of a clinic visit. Laboratory tests and brain imaging are not routinely recommended as part of an ADHD assessment. The presence of hypertension, ataxia, or asymmetric neurologic examination or symptoms of a sleep, seizure, or thyroid disorder may prompt further diagnostic tests. Lead levels could be considered if there are other factors associated with risk for lead toxicity. The clinician should identify possible vision or hearing problems. Computerized attentional tasks and quantitative electroencephalographic assessments are not needed to make the diagnosis. They are subject to high rates of false-positive and false-negative results and thus are of limited utility in the diagnostic assessment.

Educational testing should be considered if there are concerns about academic progress, as specific learning disabilities in reading,

mathematics, or written expression often coexist with ADHD (see Chapters 51 and 52). If there has been slow attainment of developmental milestones, intelligence or developmental testing should be conducted. If there are concerns about a child's social communication skills combined with restricted, repetitive behaviors or interests, a clinical assessment for autism spectrum disorder may be indicated (see Chapter 58).

Differential Diagnosis and Coexisting Conditions

Given that the symptoms of ADHD can overlap with other conditions, a broad differential diagnosis should be considered. For ease of presentation, the differential diagnosis for ADHD can be grouped into specific categories of developmental, psychiatric, medical, and psychosocial (Table 50.3). Children at either end of the developmental/cognitive level (i.e., with significant cognitive delays or with superior intelligence) can appear inattentive and/or distracted and sometimes also disruptive if the material in school or expectations at home are not appropriate for their developmental level. In differentiating impulsivity and challenging behaviors associated with ADHD versus an externalizing disorder (oppositional defiant disorder [ODD] or conduct disorder), consider whether the child "acts without thinking" and/or is more reactive (easily upset over demands for sustained attention or other small triggers), which would be more consistent with ADHD, versus proactively looks to aggress, fight, and challenge authority, which may be indicative of an externalizing disorder. Tic disorders can both present with some symptoms similar to ADHD (e.g., fidgeting, squirming, making sounds that seem impulsive) and also commonly coexist with ADHD. For cases in which ADHD symptoms are reported in one setting but not another, psychosocial causes should be considered, such as unrealistic classroom expectations, distress at home, or untoward parenting strategies. However, clinicians should be aware that inappropriate parenting strategies may be the result of the child's ADHD, as parents try anything (often unsuccessfully) to help their child. These parents are in need of parenting and behavioral supports, without feeling blamed for their child's symptoms.

Sleep disorders, including those secondary to chronic upper airway obstruction from enlarged tonsils and adenoids, often result in behavioral and emotional symptoms that can resemble or exacerbate ADHD (see Chapter 31). Periodic leg movements of sleep/restless legs syndrome have been associated with symptoms of inattention, and inquiry regarding this should be made during the history. Behavioral and emotional disorders can cause disrupted sleep patterns as well.

Mental health disorders: Depression and anxiety disorders can cause many of the same symptoms as ADHD (inattention, restlessness, inability to focus and concentrate on work, poor organization, forgetfulness) but can also coexist with ADHD (see Chapters 38 and 39). Obsessive-compulsive disorder can mimic ADHD, particularly when recurrent and persistent thoughts, impulses, or images are intrusive, interfering with normal daily activities. Adjustment disorders secondary to major life stresses (death of a close family member, parents' divorce, family violence, parents' substance abuse, or a move) or parent–child relationship disorders involving conflicts over discipline, overt child abuse and/or neglect, or overprotection can result in symptoms similar to those of ADHD.

When considering a new diagnosis in an adolescent patient, there should be an opportunity to interview the adolescent privately, and the adolescent should be specifically asked about mood symptoms and psychosocial stressors; frequent digital media use; and screened for use of alcohol, marijuana, and illicit substances.

Table 50.3 Differential Diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD)

GENERAL CATEGORY	SPECIFIC CONDITIONS, CAUSES
Developmental	Low developmental level/cognitive abilities Very high cognitive abilities Specific learning disabilities in reading, mathematics, or written expression Communication or language disorder Autism spectrum disorder Fetal alcohol syndrome
Psychiatric	Anxiety/depression Oppositional defiant disorder/conduct disorder Bipolar disorder/disruptive mood dysregulation disorder Substance use disorder Posttraumatic stress disorder/adjustment disorder
Medical	Sleep disorder, obstructive sleep apnea Hearing or vision impairment Specific medications, such as some antiepileptics or high-dose steroids Thyroid disorders Tic disorders Posttraumatic head injury or encephalitis Genetic conditions, such as fragile X, Klinefelter syndrome, Turner syndrome, tuberous sclerosis, and neurofibromatosis
Psychosocial	Response to abuse, neglect Response to distress in home, inappropriate expectations or parenting practices Response to inappropriate classroom setting

TREATMENT

Overall Treatment Approach

ADHD is considered a chronic condition and should be managed as such, with education about ADHD at the time of diagnosis and regular follow-up visits to monitor and treat symptoms. Parent support groups with appropriate professional consultation to such groups can be very helpful. Treatment of ADHD should be multimodal and involve behavioral therapy, school-based supports, and/or medications. The treatment plan should be developed in collaboration with the child (if developmentally appropriate) and family. The recommended initial treatments for ADHD vary by age.

Preschool-age children: For children up until 6 years of age, the recommended first-line treatment is evidence-based parent- and/or teacher-administered behavior therapy. If behavior interventions do not provide significant improvements and there is moderate to severe impairment in the child's functioning as a result of ADHD symptoms, medication should be considered. If behavioral interventions are not available, the risks of medication should be compared with risks of not treating ADHD symptoms.

School-age children and adolescents: For children ages 6 years old and older, ADHD medications should be considered first-line treatment, along with behavior and educational interventions. Organizational skills training, coaching, or cognitive-behavioral therapy may be helpful for adolescents and adults.

Behaviorally Oriented Treatments

Behavioral interventions should be an integral part of the treatment plan for all children with ADHD. Behavioral interventions involve modifying the environment and empowering caregivers with strategies to promote positive behaviors and minimize negative behaviors. Behavioral strategies typically focus on promoting a limited number of well-defined appropriate behaviors, using positive reinforcement with increased adult attention, tangible rewards, or access to privileges. A token economy in which a child earns (or loses) tokens that can be exchanged for rewards may be used. Any rules should be clearly defined and consistently enforced. Behavioral parent training, also known as *parent training in behavioral management,* is a well-established combination of behavioral interventions shown to reduce problematic behaviors and improve adaptive skills for children with ADHD. It involves teaching parents how to use behavior modification strategies to address specific behaviors, with a strong emphasis on positive reinforcement (described earlier) while ignoring or, if necessary, systematically implementing appropriate consequences for maladaptive behaviors. Treatments geared toward behavioral management for ADHD often occur in the time frame of 8-12 sessions but may sometimes require more sessions.

Although there is much less research published on psychosocial treatments for adolescents with ADHD, behavioral parent training can be modified to focus on improving communication between parents and adolescents with ADHD, developing a behavioral contract, and problem-solving around challenging situations. For children and adolescents with ADHD and coexisting anxiety disorders and/or depression, cognitive-behavioral therapy may help address anxiety or low mood.

At least 60 minutes of moderate to vigorous exercise is recommended for the general health of all children ≥6 years old, and some studies indicate exercise may reduce ADHD symptoms in children; thus encouraging regular exercise is reasonable. Interventions including cognitive training, electroencephalogram (EEG) biofeedback, and diet modification do not have the level of evidence needed to recommend them for most children.

Educational Supports and Accommodations

Behavioral classroom management strategies can be used by teachers to implement strategies within the whole classroom that will help children with ADHD. These include clear expectations and consistency in follow-through, positive reinforcement for work completion and on-task behaviors, and appropriate consequences when rules are not followed. Additionally, children with ADHD may benefit from individualized educational supports and accommodations, such as preferential seating near the source of instruction and away from distractions, motor breaks as needed, frequent teacher check-ins, being able to take tests in a less distracting environment, and an individualized positive behavior plan. A daily report card or communication log can be used to facilitate regular communication between the parents and teachers. A daily report card is individually designed for each child to include target problem behaviors in academic and/or social domains in the classroom (e.g., following directions, turning in work, getting along with others). The teacher provides a rating for each behavior on the report card, which is sent home daily, and the child is given home-based rewards for meeting goals set for the ratings from school.

Children with ADHD often need explicit instruction in organization and executive functioning skills and may not develop these skills at the same pace as non-ADHD peers. The use of an agenda book to record assignments, color coding for different classes, and teacher check-ins regularly to help with organization may be helpful for some children, and others may require a higher level of more individualized instruction in the executive functioning domains of staying organized, planning, initiating tasks, shifting gears, and self-monitoring.

Children with ADHD and coexisting learning disorders, communication or developmental delays, significant mental health or oppositional challenges, or autism spectrum disorder often need more specialized educational supports than those that can be provided through accommodations in a general classroom. In the United States, these children would qualify to have an individualized educational plan (IEP) developed through the public school system.

Medications

Before medication initiation, a history and physical examination and an assessment for baseline sleep, eating, and mood should be conducted because these need to be monitored for a child on medication. Children with ADHD and their families should be educated on the benefits, risks, and side effects of medication, with a discussion about goals and expectations for medication treatment. It is common for a child to need to try several trials of different medications or doses to find the optimal ADHD pharmacologic treatment that both reduces core ADHD symptoms and is well tolerated. ADHD rating scales can be used to assess for medication effectiveness and side effects, both at initiation and during medication maintenance, and should be collected from parents and teachers when possible.

The types of medications used to treat ADHD fall into one of the following three categories: stimulants, norepinephrine reuptake inhibitors, and α_2-adrenergic agonists. Stimulants are the most commonly used medications to treat ADHD and have been used to treat this condition since the 1930s. Stimulant medications have a slightly larger treatment effect size (standardized mean difference) than nonstimulants (approximately 1.0 for stimulants versus approximately 0.7 for both norepinephrine reuptake inhibitors and α_2-adrenergic agonists). Although stimulants are generally recommended as the first-line ADHD medication, nonstimulant medications may be considered in the context of active substance use disorder for an adolescent with ADHD or household family member or if there is a strong family desire for a nonstimulant medication. Stimulants have been found to have relatively high rates of adverse effects (particularly moodiness and irritability) in preschool-age children and in children with intellectual disability or autism spectrum disorder, leading some physicians to choose nonstimulant medication in these situations, as described later.

When starting a stimulant, the clinician can select either a methylphenidate-based or an amphetamine-based medication. The decision about which stimulant medication to use for a specific child or adolescent with ADHD is often based on factors such as duration of action (short, intermediate, long acting), preparation (pills, capsules that can be swallowed whole or whose contents can be "sprinkled" into food, chewable tablets, and liquids), and clinician preference or insurance company formularies. Stimulant medications have a rapid onset of action (ranging from about 20 minutes to up to an hour, depending on the formulation), and most leave the system within 3-12 hours, depending on if they are short, intermediate, or long acting. A child who responds poorly to one stimulant medication may do well with a different medication in that class or the other class (methylphenidate versus amphetamine). Stimulant medications should be initiated at the lowest available dose and titrated upward, assessing for both effectiveness and side effects, until reaching a dose that reduces ADHD symptoms and has minimal to no side effects. Common side effects of stimulant medication include decreased appetite, headaches, stomachaches, and difficulty falling asleep. If mood lability occurs, it should be noted whether this is while the stimulant medication is active (which may indicate that a different medication should be tried instead) or as the medication is wearing off (also called *rebound* and may indicate that a short-acting preparation should be replaced by a longer-acting preparation or a low dose of a short-acting preparation should be added about 30 minutes before the onset of the rebound symptoms).

Height, weight, pulse, and blood pressure should be periodically monitored. Stimulants may be associated with a slight reduction in linear growth, although studies of the impact of stimulants on adult height range from findings of a slight impact to no significant difference. Children with decreased appetite from stimulants and difficulty with weight gain can be counseled to increase caloric intake later in the day when the appetite returns. Significant reductions (i.e., crossing two lines on the growth curve) in either height or weight for a child on stimulant medication may prompt changing to a different ADHD medication.

Before starting stimulants, children should be screened for symptoms or signs suggestive of a cardiomyopathy, coronary artery disease, cardiac arrhythmias, or a family history of cardiac arrhythmias or sudden death under 50 years of age, and if these symptoms are present, an electrocardiogram and/or evaluation by a cardiologist to determine if it is safe to start these medications is recommended. Most children with tics can be treated with stimulant medication, but occasionally these medications may exacerbate tics. In these cases, the risks and benefits of continuing versus changing or stopping the medication should be considered.

Treatment of ADHD with stimulant medication is associated with reduced substance use risks. However, stimulant medications themselves are controlled substances with potential for misuse, diversion, and abuse. Therefore clinicians should regularly counsel adolescent patients about this risk, the importance of taking the medication only as prescribed, and about safe medication storage practices (e.g., keeping medication in a secure location).

Two types of selective norepinephrine reuptake inhibitors are approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD in children and adolescents: atomoxetine and viloxazine. These medications take up to 4 weeks to achieve effectiveness and should be taken consistently to be effective. Both atomoxetine and viloxazine have common side effects of fatigue, decreased appetite, nausea, vomiting, and irritability and a rare potential for suicidal thinking and behaviors for which the child must be monitored.

α_2-Adrenergic agonist medications include guanfacine and clonidine. Long-acting preparations of both have U.S. FDA approval for the treatment of ADHD in children ≥6 years old either as monotherapy or an adjunctive therapy with stimulant medication. Short-acting preparations are sometimes used off-label to treat young (<6-year-old) children with ADHD (especially those with coexisting autism spectrum disorder or sleep disorders). α_2-Adrenergic agonists may take up to 2 weeks to achieve an initial response. These medications can also treat motor and vocal tics and so may be a reasonable choice in a child with a coexisting tic disorder. Common side effects of α_2-adrenergic agonists can include sedation, headaches, and hypotension, and they should be stopped gradually because abrupt discontinuation could result in rapid increase in blood pressure.

Medication alone may not be sufficient to treat ADHD in children, particularly when children have additional psychiatric disorders, developmental disabilities, or significant psychosocial challenges. When children do not respond to medication, it may be appropriate to refer them to a mental health specialist. Consultation with a child psychiatrist, developmental-behavioral pediatrician, or psychologist can be beneficial to determine the next steps for treatment, including adding other components and supports to the overall treatment program. Evidence suggests that children who receive careful medication management, accompanied by frequent treatment follow-up, all within the context of an educational, supportive relationship with the primary care provider, are likely to experience behavioral gains.

PROGNOSIS

More than half of individuals with a childhood diagnosis of ADHD will manifest a mental health condition (e.g., anxiety, depression, substance use disorders) in adulthood. Approximately one third to two thirds of those diagnosed with ADHD in childhood will continue to manifest significant symptoms of ADHD in adulthood. In children with ADHD, a reduction in hyperactive behavior often occurs with age. Other symptoms associated with ADHD can become more prominent with age, such as inattention, impulsivity, and disorganization, and these exact a heavy toll on adolescent and young adult functioning. Adolescents and young adults with ADHD have an increased likelihood of risk-taking behaviors (early sexual activity, delinquent behaviors, motor vehicle accidents, substance use), seizures, psychosis, educational underachievement or employment difficulties, and relationship difficulties. With proper treatment, the risks associated with ADHD, including injuries, can be significantly reduced. Consistent treatment with medication and adjuvant therapies appears to lower the risk of adverse outcomes, such as substance abuse.

SECONDARY PREVENTION

Parent training can lead to significant improvements in ADHD symptoms and oppositional behaviors in preschool and school-age children with ADHD. To the extent that parents, teachers, physicians, and policymakers support efforts for earlier detection, diagnosis, and treatment, prevention of long-term adverse effects of ADHD on affected children's functioning can be considered within the lens of secondary prevention of the long-term effects of untreated or ineffectively treated ADHD on children and youth.

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Chapter 51

Dyslexia

Sally E. Shaywitz and Bennett A. Shaywitz

DEFINITION

Dyslexia has always been defined as an unexpected difficulty in reading, which has been codified in U.S. Federal law (First Step Act of 2018, PL: 115–391) as the most up-to-date, evidence-based definition of dyslexia: "The term *dyslexia* means an unexpected difficulty in reading for an individual who has the intelligence to be a much better reader, most commonly caused by a difficulty in the phonological processing (the appreciation of the individual sounds of spoken language), which affects the ability of an individual to speak, read, and spell." In typical readers, development of reading and intelligence quotient (IQ) are dynamically linked over time. In dyslexic readers, however, a developmental uncoupling occurs between reading and IQ (Fig. 51.1), such that reading achievement is significantly below what would be expected given the individual's IQ.

The uncoupling between reading achievement and IQ provides the long-sought empirical evidence for the seeming paradox between cognition and reading in individuals with developmental dyslexia, and this discrepancy is recognized in the federal definition as unexpected difficulty in reading. However, clinicians may see other approaches to diagnosis. The *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5) describes specific learning disorder with impairment in reading for children with reading skills significantly below those expected for the child's age where the deficits are not explained by intellectual disability, sensory deficits, neurologic disorders, or psychosocial adversity. This definition can be problematic in failing to differentiate primary problems with reading comprehension from the reading problems experienced by children with dyslexia despite strong evidence that the two are distinct. Further, excluding children with psychosocial adversity is concerning because children who struggle with reading due to psychosocial adversity suffer similar adverse long-term consequences and have been shown to benefit from interventions designed to help children with dyslexia.

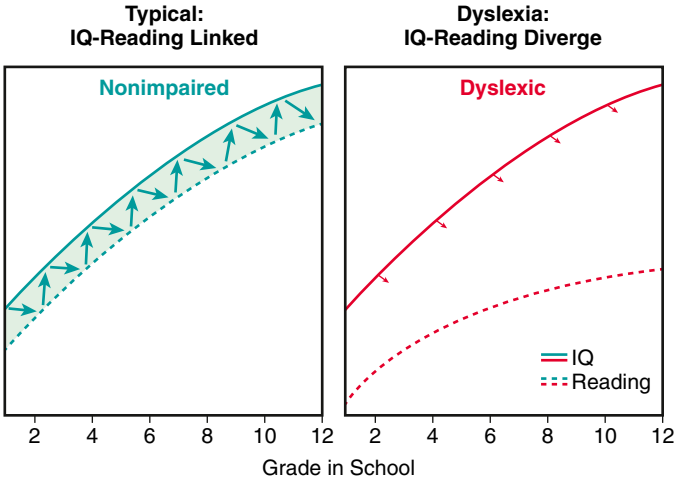

Fig. 51.1 Uncoupling of reading and IQ over time: empirical evidence for a definition of dyslexia. *Left,* In typical readers, reading and IQ development are dynamically linked over time. *Right,* In contrast, reading and IQ development are dissociated in dyslexic readers, and one does not influence the other. *(Copyright Sally Shaywitz, MD. Adapted from Shaywitz S, Shaywitz J. Overcoming Dyslexia, 2nd ed. New York: Vintage Books;2020: 103.)*

EPIDEMIOLOGY

Dyslexia is the most common of the learning disabilities, affecting 80–90% of children identified as having a learning disability. Dyslexia may be the most common neurobehavioral disorder affecting children, with prevalence rates ranging from 20% in unselected population-based samples to much lower rates in school-identified samples. The low prevalence rate in school-identified samples may reflect the reluctance of schools to screen, assess, and identify dyslexia. Dyslexia occurs with equal frequency in males and females in survey samples in which *all* children are assessed. Despite such well-documented findings, schools continue to identify more males than females, probably reflecting the more rambunctious behavior of males who come to the teacher's attention because of misbehavior, whereas females with reading difficulty, who are less likely to be misbehaving, are also less likely to be noticed and identified by the schools. Dyslexia fits a dimensional model in which reading ability and disability occur along a *continuum*.

PATHOGENESIS

Evidence from a number of lines of investigation indicates that dyslexia reflects deficits within the language system, and more specifically, within the **phonologic component** of the language system engaged in processing the sounds of speech. Individuals with dyslexia have difficulty developing an awareness that spoken words can be segmented into smaller elemental units of sound (phonemes), an essential ability given that reading requires that the reader map or link printed symbols to their sounds. Increasing evidence indicates that disruption of attentional mechanisms may also play an important role in reading difficulties.

Functional brain imaging in both children and adults with dyslexia demonstrates an inefficient functioning of left hemisphere posterior brain systems, a pattern referred to as the *neural signature of dyslexia* (Fig. 51.2). These differences can be observed before the start of formal reading instruction, suggesting they represent a biologic predisposition to reading difficulties as opposed to a result of inadequate instruction. Although functional magnetic resonance imaging (fMRI) consistently demonstrates differences between *groups* of dyslexic compared to typical readers, brain imaging is not able to reliably differentiate an *individual* case of a dyslexic reader from a typical reader and thus is not useful in diagnosing dyslexia.

CLINICAL MANIFESTATIONS

Reflecting the underlying phonologic weakness, children and adults with dyslexia manifest problems in both spoken and written language. Spoken language difficulties are typically manifest by mispronunciations, lack of glibness, speech that lacks fluency with many pauses or hesitations and "ums," word-finding difficulties with the need for time to summon an oral response, and the inability to come up with a verbal response quickly when questioned; these reflect *sound-based,* not semantic or knowledge-based, difficulties.

Struggles in decoding and word recognition can vary according to age and developmental level. The cardinal signs of dyslexia observed in school-age children and adults are a labored, effortful approach to reading involving decoding, word recognition, and text reading. Listening comprehension is typically robust. Older children improve reading accuracy over time, but without commensurate gains in reading fluency; they remain slow readers. Difficulties in spelling typically reflect the phonologically based difficulties observed in oral reading. Handwriting is often affected as well.

History often reveals early subtle language difficulties in dyslexic children. During the preschool and kindergarten years, at-risk children display difficulties playing rhyming games and learning the names for letters and numbers. Kindergarten assessments of these language skills can help identify children at risk for dyslexia. Although a dyslexic child enjoys and benefits from being read to, the child might avoid reading aloud to the parent or reading independently.

Dyslexia may coexist with attention-deficit/hyperactivity disorder (see Chapter 50); this comorbidity has been documented in both referred samples (40% comorbidity) and nonreferred samples (15% comorbidity).

DIAGNOSIS

A large achievement gap between typical and dyslexic readers is evident as early as first grade and persists (Fig. 51.3). These findings provide strong evidence and impetus for early screening and identification of and early intervention for young children at risk for dyslexia. One source of potentially powerful and highly accessible screening information is their teacher's judgment about the child's reading and reading-related skills. Evidence-based screening can be carried out as early as kindergarten, and also in grades 1-3, by the child's teacher. Their teachers' responses to a small set of questions (10-12 questions) predict a pool of children who are at risk for dyslexia with a high degree of accuracy. This evidence-based screening takes less than 10 minutes, is completed on a tablet, and is extremely efficient and economical. Children

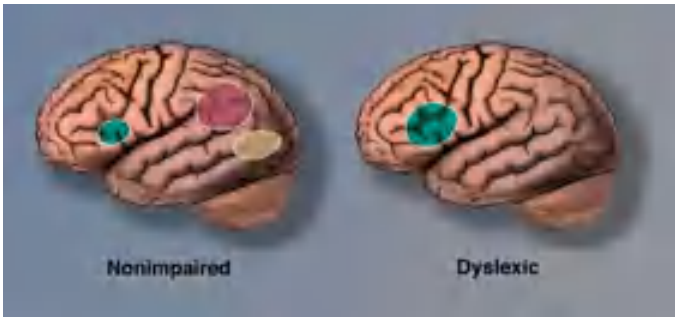

Fig. 51.2 A neural signature for dyslexia. Image on left shows left hemisphere brain systems in typical (nonimpaired) readers. The three systems for reading are an anterior system in the region of the inferior frontal gyrus (Broca's area), serving articulation and word analysis, and two posterior systems: one in the occipitotemporal region serving word analysis and a second in the occipitotemporal region (the word-form area) serving the rapid, automatic, fluent identification of words. In dyslexic readers (*right* image), the two posterior systems are functioning inefficiently and appear underactivated. This pattern of underactivation in left posterior reading systems is referred to as the neural signature for dyslexia. *(Copyright Sally Shaywitz, MD. Adapted from Shaywitz S. Shaywitz J. Overcoming Dyslexia, 2nd ed. New York: Vintage Books;2020: 78.)*

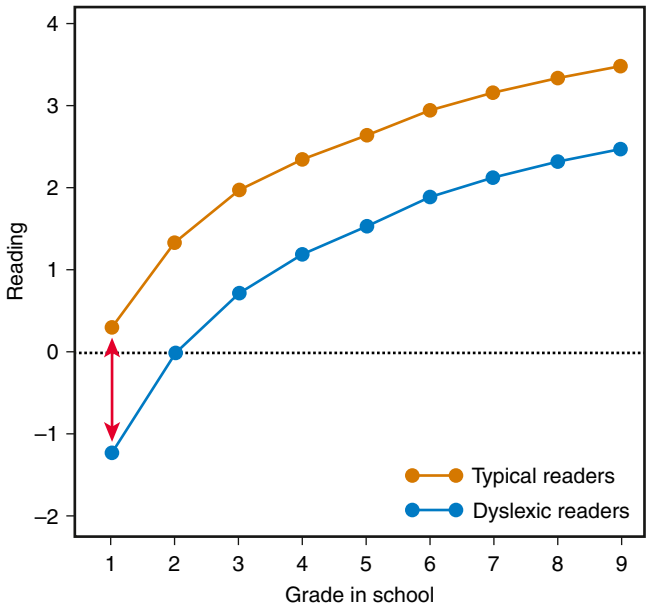

Fig. 51.3 Reading from grades 1 through 9 in typical and dyslexic readers. The achievement gap between typical and dyslexic readers is evident as early as first grade and persists through adolescence. *(Copyright Sally Shaywitz, MD. Adapted from Shaywitz S. Shaywitz J. Overcoming Dyslexia, 2nd ed. New York: Vintage Books;2020: 56.)*

found to be at risk will then have further assessment and, if diagnosed as dyslexic, should receive evidence-based intervention.

Dyslexia is a clinical diagnosis, and history is especially critical. The clinician seeks to determine through history, observation, and psychometric assessment if there are unexpected difficulties in reading (based on the person's intelligence, chronologic/grade, level of education, or professional status) and associated linguistic problems at the level of phonologic processing. No single test score is pathognomonic of dyslexia. The diagnosis of dyslexia should reflect a thoughtful synthesis of all clinical data available.

Dyslexia is distinguished from other disorders that can prominently feature reading difficulties by the unique, circumscribed nature of the *phonologic deficit,* one that does not intrude into other linguistic or cognitive domains. A core assessment for the diagnosis of dyslexia in children includes tests of language, particularly phonology; reading, including real and pseudowords; reading fluency; spelling; and tests of intellectual ability. Additional tests of memory, general language skills, and mathematics may be administered as part of a more comprehensive evaluation of cognitive, linguistic, and academic function.

For informal screening, in addition to a careful history, the primary care physician in an office setting can listen to the child read aloud from the child's own grade-level reader. Keeping a set of graded readers available in the office serves the same purpose and eliminates the need for the child to bring in schoolbooks. **Oral reading** is a sensitive measure of reading accuracy and fluency. The most consistent and telling sign of a reading disability in an accomplished young adult is slow and laborious reading and writing. In attempting to read aloud, most children and adults with dyslexia display an effortful approach to decoding and recognizing single words, an approach in children characterized by hesitations, mispronunciations, and repeated attempts to sound out unfamiliar words. In contrast to the difficulties they experience in decoding single words, persons with dyslexia typically possess the vocabulary, syntax, and other higher-level abilities involved in comprehension.

Fluency forms the bridge between decoding, that is, reading a word accurately, and comprehension, understanding what is read. Fluent reading is reading accurately and rapidly, with good intonation (prosody) indicating an understanding of the text. The failure either to recognize or to measure the lack of fluency in reading is perhaps the most common error in the diagnosis of dyslexia, especially in older children and accomplished young adults. Simple word identification tasks will not detect dyslexia in a person who is accomplished enough to be in honors high school classes or to graduate from college or obtain a graduate degree. Tests relying on the accuracy of word identification alone are inappropriate to use to diagnose dyslexia because they show little to nothing of the *struggle* to read. Because they assess reading accuracy but not automaticity or prosody, the types of reading tests used for school-age children might provide misleading data on bright adolescents and young adults. Among the most critical tests are those that are *timed;* they are the most sensitive in detecting dyslexia in a bright adult. Few standardized tests for young adult readers are administered under timed and untimed conditions; the *Nelson-Denny Reading Test* is an exception. The helpful *Test of Word Reading Efficiency* (TOWRE) examines simple word reading under timed conditions, and the Achievement Improvement Monitoring System (AIMSweb) and Dynamic Indicators of Basic Early Literacy Skills (DIBELS) measure reading connected text under timed conditions. Any scores obtained on testing must be considered relative to peers with the same degree of education or professional training.

IS FAMILY HISTORY HELPFUL IN DIAGNOSING DYSLEXIA?

Although dyslexia is familial, family history is not effective as a screening measure for dyslexia and does not improve the classification accuracy provided by an evidence-based early screening measure.

Genome-wide association studies (GWASs) in children with dyslexia have demonstrated that a large number of genes are involved, each producing a small effect. Complex traits such as reading are the work of thousands of genetic variants working in concert (see Chapter 103). Thus pediatricians should be wary of recommending any genetic test to their patients that purports to diagnose dyslexia in infancy or before language and reading have even emerged. It is unlikely that a single gene or even a few genes will reliably identify people with dyslexia. Rather, dyslexia is best explained by multiple genes, each contributing a small amount toward the expression of dyslexia.

MANAGEMENT

The management of dyslexia demands a life-span perspective. Early in life the focus is on **remediation** of the reading problem. Applying knowledge of the importance of early language, including phonologic skills and vocabulary, leads to significant improvements in children's reading accuracy, even in predisposed children. As a child matures and enters the more time-demanding setting of middle and then high school, the emphasis shifts to the important role of providing accommodations. Based on the work of the National Reading Panel, evidence-based reading intervention methods and programs are identified. Effective intervention programs provide systematic instruction in five key areas: phonemic awareness, phonics, fluency, vocabulary, and comprehension strategies. These programs also provide ample opportunities for writing, reading, and discussing literature.

Taking each component of the reading process in turn, effective interventions improve phonemic awareness: the ability to focus on and manipulate phonemes (speech sounds) in spoken syllables and words. The elements found to be most effective in enhancing **phonemic awareness**, reading, and spelling skills include teaching children to manipulate phonemes with letters, focusing the instruction on one or two types of phoneme manipulations rather than multiple types, and teaching children in small groups. Providing instruction in phonemic awareness is necessary, but not sufficient, to teach children to read. Effective intervention programs include teaching **phonics**, or making sure that the beginning reader understands how letters are linked to sounds (phonemes) to form letter-sound correspondences and spelling patterns. The instruction should be explicit and systematic; phonics instruction enhances children's success in learning to read, and systematic phonics instruction is more effective than instruction that teaches little or no phonics or that teaches phonics casually or haphazardly. Important but often overlooked is starting children on reading connected text early on, optimally at or near the beginning of reading instruction. Reading connected text is critical in building vocabulary and increasing background knowledge—both important in improving reading comprehension.

Fluency is of critical importance because it allows the automatic, rapid recognition of words. Although it is generally recognized that fluency is an important component of skilled reading, it is often overlooked in teaching. One approach is to have a child practice oral reading with a teacher or parent providing positive and helpful feedback. Here practice is critical. Interventions for vocabulary development and reading comprehension are not as well established. The most effective methods to teach reading comprehension involve teaching vocabulary and strategies that encourage active interaction between the reader and the text. Emerging science indicates that it is not only teacher content knowledge but the teacher's skill in engaging the student and focusing the student's attention on the reading task at hand that is required for effective instruction.

The interventions described here can be provided in multiple settings, but specialized schools for children with dyslexia that provide intensive intervention over 4 years or more have been very effective. Typically, these schools are costly, although increasingly offering scholarships. Some school districts are considering developing public schools specializing in educating children with dyslexia.

For those in high school, college, and graduate school, provision of **accommodations** most often represents a highly effective approach to dyslexia. Imaging studies now provide neurobiologic evidence of the need for extra time for dyslexic students; accordingly, college students with a childhood history of dyslexia require extra time in reading and writing assignments and in examinations. Many adolescent and adult students have been able to improve their reading accuracy, but without commensurate gains in reading speed. The accommodation of extra time reconciles the individual's often high cognitive ability and slow reading, so that the exam is a measure of that person's ability rather than disability. Another important accommodation is helping the student access text-to-speech programs. Excellent text-to-speech programs and apps are available for Apple and Android systems and the PC and include Voice Dream Reader, Immersive Reader (available for free in all Microsoft Office programs, including Word, OneNote, and PowerPoint), Kurzweil Firefly, Read & Write Gold, Read: OutLoud, and Natural Reader. Voice-to-text programs are also helpful, often part of the suite of programs, as well as the popular Dragon Dictate. Voice-to-text is found on many smartphones. Other helpful accommodations include the use of laptop computers with spelling checkers, access to lecture notes, tutorial services, and a separate quiet room for taking tests.

In addition, the impact of the primary phonologic weakness in dyslexia mandates special consideration during oral examinations so that students are not graded on their lack of glibness or speech hesitancies, but on their content knowledge. Unfortunately, speech hesitancies or difficulties in word retrieval often are wrongly confused with insecure content knowledge. The major difficulty in dyslexia—reflecting problems accessing the sound system of spoken language—causes great difficulty learning a second language. As a result, an often-necessary accommodation is a waiver or partial waiver of the foreign language requirement; the dyslexic student may enroll in a course taught in English on the history or culture of a non–English-speaking country.

PROGNOSIS

Application of evidence-based methods to young children, when provided with sufficient intensity and duration, can result in improvements in reading accuracy and, to a much lesser extent, fluency. Improvements in fluency can be effected with frequent practice in reading aloud with the helpful input of a teacher or parent. As noted earlier, accommodations are critical in allowing the dyslexic child to demonstrate his or her knowledge.

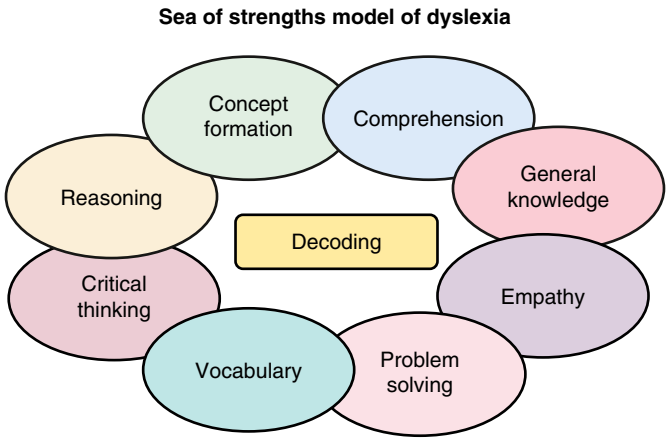

Fig. 51.4 Sea of strengths model of dyslexia. In dyslexia, a circumscribed, encapsulated weakness in decoding is surrounded by a sea of strengths in higher-level thinking and reasoning. The weakness in decoding masks what are often excellent thinking and comprehension skills. *(Copyright Sally Shaywitz, MD. Adapted from Shaywitz S. Shaywitz J. Overcoming Dyslexia, 2nd ed. New York: Vintage Books;2020: 141.)*

A person who is dyslexic experiences through life aligns with our Sea of Strengths model of dyslexia (Fig. 51.4). This model indicates that in dyslexia there is a weakness in decoding reflecting the difficulties connecting letters to sounds, a weakness that is very visible early on when learning to read. At the same, this weakness is surrounded by a sea of strengths in higher-level cognitive, big-picture thinking, including reasoning, problem solving, vocabulary, empathy, concept formation, and critical thinking. It is this sea of strengths that comes to the fore and supports a positive future as a person with dyslexia matures. The sea of strengths was very "visible" in a recent report examining the academic and social experiences in college and outcomes in the workplace 5 or more years after graduation in Yale graduates with dyslexia compared with a matched group of Yale graduates who were typical readers. Dyslexic college graduates did not differ from typical graduates either in college or in the workplace. Parents of dyslexic children often ask about their child's future. These findings should reassure those pediatricians and parents that dyslexic students can succeed all along the developmental pathway throughout school, and now through college and the workplace. With proper support, dyslexic children can succeed in a range of future occupations that might seem out of their reach, including medicine, law, journalism, and writing.

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Chapter 52
Math and Writing Disabilities

52.1 Math Disabilities

Kenneth L. Grizzle and Brittany J. Bice-Urbach

Data from the U.S. National Center for Educational Statistics for 2009 showed that 69% of U.S. high school graduates had taken algebra 1, 88% geometry, 76% algebra 2/trigonometry, and 35% precalculus. These percentages are considerably higher than those from 20 years earlier. However, concerns remain about the limited mathematics literacy level for children, adolescents, and those entering the workforce; poor math skills predict numerous social, employment, and emotional challenges. The need for number and math literacy extends beyond the workplace and into daily lives, and weaknesses can negatively affect daily functioning. Research into the etiology and treatment of **math disabilities** falls behind the study of reading disabilities (see Chapter 51), and yet the database needed to effectively identify, treat, and minimize the impact of math challenges on daily functioning and education is growing.

MATH LEARNING DISABILITY DEFINED

Understanding learning challenges associated with mathematics requires a basic appreciation of domain-specific terminology and operations. The *Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition* (DSM-5) has published diagnostic criteria for learning disorders. Specific types of learning challenges are subsumed under the broad term of **specific learning disorder (SLD)**. The DSM-5 identifies

the following features of a SLD with an **impairment in math**: difficulties mastering number sense, number facts, or fluent calculation and difficulties with math reasoning. Symptoms must be present for a minimum of 6 months and persist despite interventions to address the learning challenges. **Number sense** refers to a basic understanding of quantity, number, and operations and is represented as nonverbal and symbolic. Examples of number sense include an understanding that each number is 1 more or 1 less than the previous or following number, knowledge of number words and symbols, and the ability to compare the relative magnitude of numbers and perform simple arithmetic calculations.

The DSM-5 definition can be contrasted with an **education-defined learning disability in mathematics**. Two math-related areas are identified as part of the **Individuals with Disabilities Education Act (IDEA)**: mathematics calculation and mathematics problem solving. Operationally, this is reflected in age-level competency in arithmetic and math calculation, word problems, interpreting graphs, understanding money and time concepts, and applying math concepts to solve quantitative problems. The federal government allows states to choose the way a *learning disability* (LD) is identified if the procedure is "research based." Referred to specifically in the IDEA as methods for identifying an LD are a **discrepancy model** and "use of a process based on the child's response to scientific, research-based intervention." The former refers to identifying an LD based on a pronounced discrepancy between intellectual functioning and academic achievement. The latter, referred to as a **response to intervention (RtI)** model, requires school systems to screen for a disability, intervene using evidence-based treatments for the identified disability, closely monitor progress, and make necessary adjustments to the intervention as needed. If a child is not responding adequately, a multidisciplinary team is created, and an evaluation is then completed to determine whether the child qualifies for special education programming. Not responding to the interventions alone does not result in automatic qualification for services outside of regular education. Rather, it is a three-step process: lack of adequate progress to the interventions, an evaluation of the area(s) of concern, and then determination by the team if an **individualized educational plan (IEP)** is needed. The IEP team typically consists of teachers, special education teacher, school psychologist, school district representative, parents, and, depending on their age, the student.

It is important that primary care providers understand the RtI process because many states require or encourage this approach to identifying LDs. Confusion can be avoided by helping concerned parents understand that a school may review their child's records, screen the skills of concern, and provide intervention with close progress monitoring before initiating the process for an IEP. Traditional psychoeducation testing (IQ and achievement) may only be completed if a child has not responded well to specific interventions. The RtI approach is a valuable, empirically supported way to approach and identify a potential LD but is very different from a medical approach to diagnosis and treatment. First and foremost, this allows for early intervention, which has been shown repeatedly to decrease the likelihood of a later identified LD. Intervening early also allows educators to avoid the "wait to fail" model that all too often waited for children to enter third or fourth grade before receiving needed services.

Terminology

The term **dyscalculia**, often used in medicine and research but seldom used by educators, is reserved for children with a SLD in math when there is a pattern of deficits in learning arithmetic facts and accurate, fluent calculations. The term **math learning disability (MLD)** is used generically here, with dyscalculia used when limiting the discussion to children with deficient math calculation skills. A distinction is also made between children with a MLD and those who are **low achieving (LA) in math**; both groups have received considerable research focus. Although not included in either definition provided earlier, research into math deficits often require that individuals identified with MLD have math achievement scores below the 10th percentile across multiple grade levels. These children start out poorly in math and continue poor performance across grades, despite interventions. LA math students consistently score below the 25th percentile on math achievement tests across grades, often showing the same weak math-related characteristics as those with MLD but with less severity. Complicating the identification of MLD and its differentiation from LA math students is the variability in relative complexity of math concepts that may result in short-lived math difficulties.

EPIDEMIOLOGY

Prevalence

Depending on how MLD is defined and assessed, the prevalence varies. Based on findings from multiple studies, approximately 7% of children will show a MLD profile before high school graduation. An additional 10% of students will be identified as LA. Because research in the area typically requires that individuals show deficits for consecutive years, the respective prevalence estimates are lower than the 10th percentile cutoff for being identified as having an MLD or the 25th percentile cutoff for being identified as LA. It is not unusual for children to score below the criterion one year and then above the criterion in subsequent years. Males are at greater risk to experience MLD.

Risk Factors

Genetics

The heritability of math skills is estimated to be approximately 0.50. The heritability or genetic influence on math skills is consistent across the continuum from high to low math skills. This research emphasizes that although math skills are learned across time, the stability of math performance is the result of genetic influences. Math heritability appears to be the product of multiple genetic markers, each having a small effect.

Medical/Genetic Conditions

Numerous genetic syndromes are associated with math problems. Although most children with **fragile X syndrome** have an *intellectual disability* (ID), approximately 50% of females with the condition do not. Of those without an ID, ≥75% have a math disability by the end of third grade and are already scoring below average in mathematics in kindergarten and first grade. For females with fragile X MLD, weak working memory seems to play an important role. The frequency of MLD in **Turner syndrome (TS)** is the same as that found in females with fragile X syndrome. A consistent finding is females with TS complete math calculations at significantly slower speed than typically developing students. Although females with TS have weak calculation skills, their ability to complete math problems not requiring explicit calculation is similar to that of their peers. The percentage of children with **22q11.2 deletion syndrome** (22q11.2ds) with MLD is not clear. Younger children with this genetic condition (6-10 years old) showed similar number sense and calculation skills as typically developing children but weaker math problem solving. Older children with 22q11.2ds showed slower speed in their general number sense and calculations, but accuracy was maintained. Weak counting skills and magnitude comparison have been found in this group of children, suggesting weak visual-spatial processing. Children with **myelomeningocele** are at greater risk for math difficulties than their unaffected peers. Almost 30% of these children have MLD without an additional diagnosed learning disorder, and >50% have both math and reading learning disorders. Although broad, deficits are most pronounced in speed of math calculation and written computation.

Comorbidities

It is estimated that 30–70% of those with MLD will also have a reading disability. This is especially important because children with MLD are less likely to be referred for additional educational assistance and intervention than students with reading problems. Unfortunately, children identified with both learning challenges perform poorer across psychosocial and academic measures than children with MLD alone. Having a MLD places a child at greater risk for not only other learning challenges but also psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder, conduct disorder, generalized anxiety disorder, and major depressive disorder.

Individuals with MLD have been found to have increased social isolation and difficulties developing social relationships in general.

CAUSES OF MATH LEARNING DISABILITY

There is a consensus that individuals with MLD are a heterogeneous group, with multiple potential broad and specific deficits contributing to their learning difficulties. Research into the causes of MLD has focused on math-specific processes and broad cognitive deficits, with an appreciation that these two factors are not always independent.

Broad Cognitive Processes

Intelligence

Intelligence affects learning, but if intellectual functioning were the primary driver of poor math performance, the math skills of low-IQ children would be similar or worse than individuals with MLD. On the contrary, children with MLD have significantly poorer math achievement than children with low IQ. Children with MLD have severe deficits in math not accounted for by their cognitive functioning. Individuals with lower cognition may have difficulty learning mathematics, but their math skills are likely to be commensurate with their intelligence.

Memory

Working memory (WM) refers to the ability to keep information in mind while using the information in other mental processes. WM is composed of three core systems: the central executive, the language-related phonologic loop, and the visual-based sketch pad. The central executive coordinates the functioning of the other two systems. All three play a role in various aspects of learning and in the development and application of math skills in particular; children with MLD have shown deficits in each area.

Committing math facts to and/or retrieving facts from memory has consistently been found to be problematic for children with MLD. This is not necessarily limited to inaccurate retrieval of facts but also speed of retrieval, independent of broader speed of processing deficits. Unfortunately, unlike some typically developing peers who may be slower but accurate in their fact retrieval, students with MLD are often slow and inaccurate. Weak fact encoding or retrieval alone do not determine an MLD diagnosis. Many math curricula in the United States do not include development of math facts as a part of the instructional process, resulting in children not knowing basic facts.

Processing Speed

Individuals with MLD are often slower to complete math problems than their typically developing peers, a result in part of their poor fact retrieval rather than broader speed of processing deficits. However, young children later identified with a MLD when beginning school have numerical-processing speed that is considerably slower than same-age same-grade peers. This is reflected in the time required to recognize numbers, correctly order fractions, and complete word problems.

Problem Solving

Not only do children with MLD struggle to quickly and accurately engage in numerical-related activities, in part because of these difficulties, they commonly rely on less efficient and laborious problem-solving practices. This is seen in children relying on finger counting beyond second grade, use of repeated adding for multiplication facts, pronounced difficulty moving beyond reliance on manipulatives, and drawing objects to help with calculation. Difficulties with math processes across multiple levels can result in math being a time-intensive and time-consuming process for kids with MLD.

Executive Skills

Difficulties with executive functioning (EF) can lead to challenges in multiple areas of a child's life, academic and nonacademic (see Chapter 49). Performance in math is but one example. EF refers to skills including but not limited to sustained attention, managing impulses, cognitive and behavioral flexibility, and WM. Anyone who has worked with children diagnosed with ADHD, a group of kids notorious for having EF challenges, can appreciate the impact these behaviors could potentially have on math. Deficits in WM, auditory and visual, can negatively affect a child's development of math skills. A child approaching a word problem exemplifies the impact of various executive skills on math. The child must keep in memory the content read and integrate it with what they know about the topic and possible operation to apply, all the while not responding to the irrelevant information contained within the passage. Creating a mental representation of the problem requires use of the visual sketch pad (visual WM).

Math-Specific Processes

Number Sense

The term *number sense* has been defined in different ways, though the general agreement is that the concept refers to an intuitive preverbal ability to identify an approximation of items within a set that precedes formal math instruction. This is seen in the ability to recognize and manipulate nonsymbolic properties without having to apply a name to the process—for example, recognizing that a box of three dots is fewer than a box containing five dots. Unlike their peers, children with MLD are more likely to count the number of items within the comparison rather than recognizing the apparent difference.

Math is a symbolic process and cannot be efficiently learned and mastered without understanding this numerical skill. There is considerable evidence that young children who struggle to develop symbolic numerical representation, in contrast to number sense, are at considerable risk to have difficulty developing higher-level math skills. Examples of symbolic representations range from recognizing that the numeral 4 and word *four* reflect a quantity and quickly recognizing the larger (or smaller) of two numbers, all the way to understanding fractions and more complex notations.

Procedural Errors

The type of errors made by children with a, MLD are typical for any child, the difference being that children with a LD show a 2- to 3-year lag in understanding the concept. An example of a common error a first-grade child with a, MLD might make when "counting on" is to undercount: "6 + 2= ?"; "6, 7" rather than starting at 6 and counting an additional two numbers. As children with math deficits get older, it is common to subtract a larger number from a smaller number. For example, in the problem "63 − 29 = 46," the child makes the mistake of subtracting 3 from 9. Another common error is not decreasing the number in the 10s column when borrowing: "64 − 39 = 35." For both adding and subtracting, there is a lack of understanding of the commutative property of numbers and a tendency to use repeated addition rather than fact retrieval. It is not that children with an MLD do not develop these skills, it is that they develop them much later than their peers, thereby making the transition to complicated math concepts much more challenging.

Unlike dyslexia, in which deficits have been isolated and identified as causal (see Chapter 51), factors involved in the development of a MLD are much more heterogeneous. Alone, none of the processes previously outlined fully account for MLD, although all have been implicated as problematic for those struggling with math.

TREATMENT AND INTERVENTIONS

The most effective interventions for MLD are those that include explicit instruction on solving specific types of problems and that take place over several weeks to several months. Skill-based instruction is a critical component; general math problem solving will not carry over across various math skills unless the skill is part of a more complex math concept. Clear, comprehensive guidelines for effective interventions for students struggling with math have been provided by the U.S. Department of Education in the form of a *Practice Guide* released through the What Works Clearinghouse. This document gives excellent direction in the identification and treatment of children with math difficulties in the educational system. Although not intended for medical personnel or parents, the guide is available free of charge and can be helpful for parents when talking to teachers about their child's learning. Table 52.1 lists additional resources for parents concerned about their young child's development of math facts.

Table 52.1 Parent Resources for the Child with Math Learning Disability

Let's Talk About Math. Available from http://www.zerotothree.org/parenting-resources/early-math-video-series. Accessed September 19, 2021.

Mixing in Math. Available from https://www.terc.edu/mixinginmath/. Accessed September 19, 2021.

PBS Parents. Math resources available to parents through the Public Broadcasting Service website. Accessed September 19, 2021.
http://www.pbs.org/parents/earlymath/index.html
http://www.pbs.org/parents/education/math/

Understood: Math. Available from https://www.understood.org/topics/en/math.

U.S. Department of Education. *Helping your child learn mathematics*. Available from https://www2.ed.gov/parents/academic/help/math/index.html. Accessed September 19, 2021.

Table 52.2 Risk Factors for a Specific Learning Disability Involving Mathematics

The child is at or below the 20th percentile in any math area, as reflected by standardized testing or ongoing measures of progress monitoring.

The teacher expresses concerns about the child's ability to "take the next step" in math.

There is a positive family history for math learning disability (this alone will not initiate an intervention).

Parents think they have to "reteach" math concepts to their child.

Awareness that most public school systems have implemented some form of an RtI model to identify LDs allows the primary care physician to encourage parents to return to the school seeking an intervention to address their child's concern. Receiving special education services in the form of an IEP may be necessary for some children. However, the current approach to identifying children with an LD allows school systems to intervene earlier, when problems arise, and potentially avoid the need for an IEP. Pediatricians with patients whose parents have received feedback from school with any of the risk factors outlined in Table 52.2 should encourage the parents to discuss an intervention plan with the child's teacher.

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52.2 Writing Disabilities

Kenneth L. Grizzle and Brittany J. Bice-Urbach

Oral language is a complex process that typically develops in the absence of formal instruction. In contrast, *written language* requires instruction in acquisition (word reading), understanding (reading comprehension), and expression (spelling and composition). Unfortunately, despite reasonable pedagogy, a subset of children struggle with development in one or several of these areas. The disordered output of written language is currently referred to within the *Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition* (DSM-5) as a **specific learning disorder with impairment in written expression** (Table 52.3).

Various terminology has been used when referring to individuals with writing deficits; this subchapter uses the term **impairment in written expression (IWE)** rather than "writing disorder" or "disorder of written expression." **Dysgraphia** is often used when referring to children with writing problems, sometimes synonymously with IWE, though the two are related but distinct conditions. Dysgraphia is primarily a deficit in motor output (paper/pencil skills), and IWE is a conceptual weakness in developing, organizing, and elaborating on ideas in writing.

The diagnoses of IWE and dysgraphia are made largely based on phenotypical presentation; spelling, punctuation, grammar, clarity, and organization are factors to consider with IWE concerns. Aside from these potentially weak writing characteristics, however, no other guidelines are offered. Based on clinical experience and research into the features of writing samples of children with disordered writing skills, one would expect to see limited output, poor organization, repetition of content, and weak sentence structure and spelling despite the child taking considerable time to produce a small amount of content. For those with comorbid dysgraphia, the legibility of their writing product will also be poor, sometimes illegible.

Table 52.3 DSM-5 Diagnostic Criteria for Specific Learning Disability with Impairment in Written Expression

A. Difficulties learning and using academic skills that have persisted for at least 6 months, despite the provision of interventions that target those difficulties.
Difficulties with written expression (e.g., makes multiple grammatical or punctuation errors within sentences; employs poor paragraph organization; written expression of ideas lacks clarity).

B. The affected academic skills are substantially and quantifiably below those expected for the individual's chronologic age and cause significant interference with academic or occupational performance or with activities of daily living, as confirmed by individually administered standardized achievement measures and comprehensive clinical assessment. For individuals age 17 years and older, a documented history of impairing learning difficulties may be substituted for the standardized assessment.

C. The learning difficulties begin during school-age years but may not become fully manifest until the demands for those affected academic skills exceed the individual's limited capacities (e.g., as in timed tests, reading or writing lengthy complex reports for a tight deadline, excessively heavy academic loads).

D. The learning difficulties are not better accounted for by intellectual disabilities, uncorrected visual or auditory acuity, other mental or neurologic disorders, psychosocial adversity, lack of proficiency in the language of academic instruction, or inadequate educational instruction.

315.2 (F81.81) With impairment in written expression:
Spelling accuracy
Grammar and punctuation accuracy
Clarity or organization of written expression
Specify current severity:

Mild: Some difficulties learning skills in one or two academic domains, but of mild enough severity that the individual may be able to compensate or function well when provided with appropriate accommodations or support services, especially during the school years.

Moderate: Marked difficulties learning skills in one or more academic domains, so that the individual is unlikely to become proficient without some intervals of intensive and specialized teaching during the school years. Some accommodations or supportive services at least part of the day at school, in the workplace, or at home may be needed to complete activities accurately and efficiently.

Severe: Severe difficulties learning skills, affecting several academic domains, so that the individual is unlikely to learn those skills without ongoing intensive individualized and specialized teaching for most of the school years. Even with an array of appropriate accommodations or services at home, at school, or in the workplace, the individual may not be able to complete all activities efficiently.

From the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Washington, DC: American Psychiatric Association; 2013:66–67.

EPIDEMIOLOGY

The incidence of IWE is estimated at 6.9–14.7%, with the relative risk for IWE ~2.5 times higher for males than for females. The risk for writing problems is much greater among select populations; >50% of children with oral language disorders reportedly have IWE. The relationship between attention-deficit/hyperactivity disorder (ADHD) and learning disorders in general is well established, including IWE estimates in the 60% range for the combined and inattentive presentations of ADHD. Because of the importance of working memory (WM) and other executive functions in the writing process, any child with weakness in these areas will likely find the writing process difficult (see Chapter 49).

SKILL DEFICITS ASSOCIATED WITH IMPAIRED WRITING

Written language, much like reading, occurs along a developmental trajectory that can be seamless as children master skills critical to the next step in the process. Mastery of motor control that allows a child to produce letters and letter sequences frees up cognitive energy to devote to spelling words and eventually stringing words into sentences, paragraphs, and complex composition. Early in the development of each individual skill, considerable cognitive effort is required, although ideally the lower-level skills of motor production, spelling, punctuation, and capitalization (referred to as **writing mechanics** or **writing conventions**) will gradually become automatic and require progressively less mental effort. This effort can then be devoted to higher-level skills, such as planning, organization, application of knowledge, and use of varied vocabulary. For children with writing deficits, breakdowns can occur at one, some, or every stage.

Transcription

Among preschool and primary grade children, there is a wide range of what is considered "developmentally typical" as it relates to letter production and spelling. However, evidence indicates that poor writers in later grades are slow to produce letters and write their name in preschool and kindergarten. Weak early spelling and reading skills (letter identification and phonologic awareness; see Chapter 51) and weak oral language have also been found to predict weak writing skills in later elementary grades. Children struggling to master early **transcription** skills tend to write slowly, or when writing at reasonable speed, the legibility of their writing degrades. Output in quantity and variety is limited, and vocabulary use in poor spellers is often restricted to words they can spell.

As children progress into upper elementary school and beyond, a new set of challenges arises. They are now expected to have mastered lower-level transcription skills, and the focus turns to the application of these skills to more complex text generation. In addition to transcription, this next step requires the integration of additional cognitive skills that have yet to be tapped by young learners.

Oral Language

Language, though not speech, has been found to be related to writing skills. Writing difficulties are associated with deficits in both expression and comprehension of oral language. Writing characteristics of children with **specific language impairment (SLI)** can differ from their unimpaired peers early in the school experience and persist through high school (see Chapter 53). In preschool and kindergarten, as a group, children with language disorders show poorer letter production and ability to print their name. Poor spelling and weak vocabulary also contribute to the poor writing skills. Beyond primary grades, the written narratives of SLI children tend to be evaluated as "lower quality with poor organization" and weaker use of varied vocabulary.

Pragmatic language and higher-level language deficits also negatively affect writing skills. **Pragmatic language** refers to the social use of language, including though not limited to greeting and making requests, adjustments to language used to meet the need of the situation or listener, and following conversation rules verbally and nonverbally. Higher-level language goes beyond basic vocabulary, word form, and grammatical skills and includes making inferences, understanding and appropriately using figurative language, and making cause-and-effect judgments. Weaknesses in these areas, with or without intact foundational language, can present challenges for students in all academic areas that require writing. For example, whether producing an analytic or narrative piece, the writer must understand the extent of the reader's background knowledge and in turn what information to include and omit, make an argument for a cause-and-effect relationship, and use content-specific vocabulary or vocabulary rich in imagery and nonliteral interpretation.

Executive Functions

Writing is a complicated process and, when done well, requires the effective integration of multiple processes. Executive functions (EFs) are a set of skills that include planning, problem solving, monitoring, and adjusting as needed (see Chapter 49). Three recursive processes have consistently been reported as involved in the writing process: *translation* of thought into written output, *planning,* and *reviewing.* Coming up with ideas, although challenging for many, is simply the first step when writing a narrative (story). Once an idea has emerged, the concept must be developed to include a plot, characters, and storyline and then coordinated into a coherent whole that is well organized and flows from beginning to end. Even if one develops ideas and begins to write them down, *persistence* is required to complete the task, which requires *self-regulation.* Effective writers rely heavily on EFs, and children with IWE struggle with this set of skills. Poor writers seldom engage in the necessary planning and struggle to self-monitor and revise effectively.

Working Memory

WM refers to the ability to hold, manipulate, and store information for short periods. The more space available, the more memory can be devoted to problem solving and thinking tasks. Nevertheless, there is limited space in which information can be held, and the more effort devoted to one task, the less space is available to devote to other tasks. WM has consistently been shown to play an important role in the writing process, because weak WM limits the

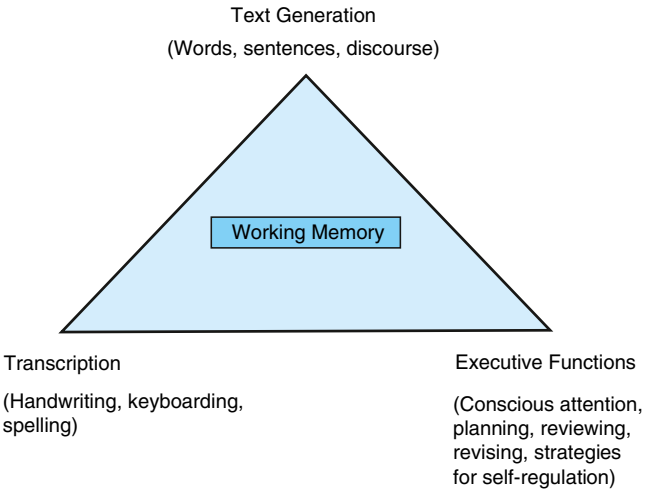

Fig. 52.1 Simple view of writing. *(From Berninger VW. Preventing written expression disabilities through early and continuing assessment and intervention for handwriting and/or spelling problems: Research into practice. In: Swanson HL, Harris KR, Graham S [eds]. Handbook of Learning Disabilities. New York: The Guilford Press;2003.)*

space available. Further, when writing skills that are expected to be *automatic* continue to require effort, precious memory is required, taking away what would otherwise be available for higher-level language.

The **Simple View of Writing** is an approach that integrates each of the four ideas just outlined to describe the writing process (Fig. 52.1). At the base of the triangle are transcription and EFs, which support, within WM, the ability to produce text. Breakdowns in any of these areas can lead to poor writing, and identifying where the deficit(s) are occurring is essential when deciding to treat the writing problem. For example, children with weak **graphomotor** skills (e.g., dysgraphia) must devote considerable effort to the accurate production of written language, thereby increasing WM use devoted to lower-level transcription and limiting memory that can be used for developing discourse. The result might be painfully slow production of a legible story or a passage that is largely illegible. If, on the other hand, a child's penmanship and spelling have developed well but their ability to persist with challenging tasks or to organize their thoughts and develop a coordinated plan for their paper is limited, one might see very little information written on the paper despite considerable time devoted to the task. Lastly, even when skills residing at the base of this triangle are in place, students with a language disorder will likely produce text that is more consistent with their language functioning than their chronologic grade or age.

TREATMENT

Poor writing skills can improve with effective treatment. Weak graphomotor skills may not necessarily require intervention from an **occupational therapist (OT)**, although *Handwriting Without Tears* is a curriculum frequently used by OTs when working with children with poor penmanship. An empirically supported writing program has been developed by Berninger, but it is not widely used inside or outside school systems *(PAL Research-Based Reading and Writing Lessons)*. Her research suggests that for children with dysgraphia, lower-level transcription skills should be emphasized to the point of becoming automatic. The connection between transcription skills and composition should be included in the instructional process; that is, children need to see how their work at letter production is related to broader components of writing. Further, because of WM constraints that frequently affect the instructional process for students with learning disorders, all components of writing should be taught within the same lesson. Building upon Berninger's sequencing of skills, Otaiba, Gillespie-Rouse, and Baker summarized features of effective handwriting instruction for kids who struggle: direct instruction on letter formation that is modeled and followed using verbal and visual instruction; retrieving letters from memory using such strategies as a child viewing the letter, covering, and reproducing the letter; children identifying their own errors; newly learned letters are integrated into word and sentence context and then into a child's own writing product; integration of multisensory strategies; and handwriting interventions included practice, occurred regularly, and were relatively brief but meaningful (children learned that writing had a purpose beyond accurately producing letters).

Explicit instruction of writing composition strategies combined with implementation and coaching in self-regulation will likely produce the greatest gains for students with writing deficits beyond transcription. Emphasis will vary depending on the deficit specific to the child. A well-researched and well-supported intervention for poor writers is **self-regulated strategy development (SRSD)**. The six stages in this model include developing and activating a child's background knowledge, introducing and discussing the strategy that is being taught, modeling the strategy for the student, assisting the child in memorization of the strategy, supporting the child's use of the strategy during implementation, and independent use of the strategy. SRSD can be applied across various writing situations and is supported until the student has developed mastery. The model can emphasize the areas most needed by the child.

An additional excellent resource is entitled *Teaching Elementary School Students to Be Effective Writers* and is found within the What Works Clearinghouse maintained by the U.S. Department of Education's Institute of Education Science.

Educational Resources

Children with identified learning disorders can potentially qualify for formal education programming through special education or a Section 504 plan. **Special education** is guided on a federal level by the **Individual with Disabilities Education Act (IDEA)** and includes development of an **individual education plan** (IEP) (see Chapter 49). The processes involved in pursuing an IEP are somewhat complex and outlined in the chapter on math learning disability (MLD). A **504 plan** provides accommodations to help children succeed in the regular classroom. Accommodations that might be provided to a child with IWE, through an IEP or a 504 plan, include dictation to a scribe when confronted with lengthy writing tasks; additional time to complete exams that require writing; and use of technology such as keyboarding, speech-to-text software, and writing devices that record teacher instruction.

Speech-to-text capability is available on most smartphones, which can be helpful for students from a functional standpoint. Educational resources that can be accessed inside and outside the classroom are often readily available for all children but may need to be included as an accommodation for a child with dysgraphia. Examples of easily available software include Voice Dictation in Google Docs and Dictation in Microsoft Word, both available at no cost. More sophisticated apps that can be purchased include Co:Writer for Chrome, Read & Write, and Kurzweil 3000. Kurzweil 3000 is a comprehensive assistive technology device that, in addition to speech-to-text and text-to-speech, offers multiple valuable resources for students with any type of literacy-based learning disability. Editing is a critical component of the writing process and, for children struggling with written expression, can present quite a challenge. Microsoft Word has built-in spelling and grammar correction suggestions, as do other word processing programs such as Pages and Google Docs. Apps for use when using the internet are also available to help with spelling, grammar, and writing mechanics. One example—though there are others—is Grammarly. When recommending that parents pursue assistive technology for their child as a potential accommodation, the physician should emphasize the importance of instruction to mastery of the device being used. Learning to use technology effectively requires considerable time and is initially likely to require additional effort, which can result in frustration and avoidance.

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Chapter 53

Language Development and Communication Disorders

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There are over 6,000 languages in the world, each with a distinct set of symbols, defined as words or signs that signify objects, actions, ideas, or relationships. By combining symbols in novel ways, humans can create an infinite number of meanings. Human communication (Table 53.1) encompasses language, speech, nonverbal gestures, and written language. Typically developing children learn language skills seemingly without effort or explicit education early in the course of development. However, there is wide variation in how and when children learn and use language, speech, and communication. Globally, families differ in the specific languages and number of languages they speak and in the ways in which they communicate to convey their beliefs, values, and circumstances. Children vary in their rates of learning language and the highest level of skills they attain. Milestones within each domain (language, speech, communication) signify the unfolding steps by which new structures and skills come into children's language abilities (Table 53.2 and Fig. 53.1). Some children require explicit education or clinical support to learn language or to make their speech easily interpretable.

TYPICAL DEVELOPMENT

Development of Phonology

Every language is made up of an inventory of **speech sounds** or **phonemes** (see Table 53.1), and the number of speech sounds varies across languages (e.g., Hawaiian = 13, Cantonese = more than 36, English = 46). **Speech perception** depends on the physical structures of the ear and the auditory processing system. Fetuses detect sound as early as 28 weeks' gestation, and within 5 days after birth, infants can demonstrate the ability to discriminate vowel sounds (i.e., English vs Swedish) and show preferences for their own prenatal monolingual or bilingual language environments (i.e., English vs Tagalog-English). Infants develop their speech sound perception, built on the ability to track the statistical probabilities of sound combinations (e.g., *b* + *a* is more prevalent in language than *b* + *d*), segment sounds and words from a stream of speech, and become attuned to the speech sounds in their respective language or languages. Older children or adults learning a new language need to learn a new speech sound inventory.

Speech production involves activating the physical structures of the respiratory tract and oral cavity, such as the lips, tongue, and vocal cords, all of which work in concert. Infants begin producing nonspeech **cooing** sounds at 4-6 weeks. By 6-8 months, many infants engage in canonical **babbling** (e.g., *bababa*) followed by variegated babbling (e.g., *badadeda*). Infants who are exposed to **sign language** from birth demonstrate manual babbles at around the same time as hearing infants begin vocal babbles. These skills lay the stage for infants' first words and subsequent word combinations. Speech production continues to develop throughout early childhood, with easier consonant sounds maturing early, around age 3 (e.g., in English *p, b, m, h, w*) and difficult sounds (e.g., in English *l, s, r, v, ch, th*) maturing late, typically by around age 7.

Development of the Lexicon, Morphology, and Syntax

It is difficult to pinpoint when in development children typically understand their first word, but many children may say their first words by around 1 year; English-speaking families in the United States report first words appearing as young as 7 and as late as 15 months. Children's first words mark their expressive skills in their **lexicon** (see Table 53.1), and first words may come from a variety of categories (e.g., people, objects, and greetings). Many children recognize their own name between 7 and 15 months old. Initial word learning is typically very slow, but the rate of acquisition of new words gradually accelerates. Expressive lexical errors are common at this age and can include overextensions (e.g., all edible objects are "*apples*") or underextensions (e.g., only one specific spoon is labeled "*spoon*"). Between 1 and 2 years, children build a lexicon of over 50 words. The **vocabulary spurt** is rapid acceleration in word learning, usually after children reach 50 words in expressive language and coincident with the beginning of two-word phrases.

By approximately 2 years, children begin to demonstrate their developing understanding of **morphology** and **syntax** (see Table 53.1). Morphology and syntax rules differ by language. Children's receptive syntax skills are evident when they can follow simple directions or answer *wh-* questions. Notable expressive morphologic milestones in English include the use of the present progressive tense (e.g., "*go-ing*") and the plural -s (e.g., *dog-s*). Expressive syntax skills are evident via children's early creative word combinations, starting with two-word combinations, which are likely to vary from adult models (e.g., in English "*me down!*" or "*ick eggs!*"). By 3 years, children begin to produce sentences as long as five words and with increasingly complex grammar, such as negation (e.g., in English "*I no want to*") and questions (e.g., "*What he do?*"). As in these examples, lexical, morphologic, and/or syntax errors in understanding and production are common during this early phase of syntactic development. Morphologic or syntax errors in production may consist of overgeneralizations (e.g., in English, generalizing the "*-ed*" ending to all verbs such as "*runned*" rather than "*ran*"; in Spanish, Italian, or French, using the masculine articles with feminine nouns). By 4-5 years, children are able to use sentences with adult-like grammar (e.g., in English "*I fell because I was running too fast.*"), although they may still make mistakes (e.g., in English "*I gots 1 game and he got 3 games.*"). Children also engage in longer, coherent, connected discourse, such as telling or retelling stories and recounting the steps of a familiar activity, such as taking a bath.

Development of Pragmatics

Pragmatic skills begin in infancy. The ability to attend to and follow another's **eye gaze** develops as early as 3-4 months old. As young as 3 months old, children can engage in **protoconversations**, turn-taking patterns with caregivers that resemble early conversations. Responsive, contingent interactions between caregivers and children provide infants the opportunity to experience, imitate, and practice the timing, rhythm, and rate of nonverbal pragmatic skills, such as facial expressions, body language, and intonation. By 6 months, many infants can passively follow the adult's line of visual regard, resulting in a joint reference to the same objects and events in the environment. The ability to share the same experience is critical to the development of further language, social, and cognitive skills as infants "map" specific meanings onto their experiences. By 10-13 months, many infants can actively show, give, and point to objects. Children vary widely in when these skills first appear; English-speaking families have reported pointing skills as early as 6 months and as late as 16 months.

An important facet of typical communication development and a building block of conversational turn-taking skills includes establishing a **joint focus of attention**, a sharing of the topic of conversation with a communicative partner, both in comprehension (e.g., infants turn their heads to the object an adult is pointing at) and in production (e.g., a child saying "look at that dog over there," then looking back at their caregiver and expressing a desire for a dog). Conversation skills are important for forming relationships and especially strong social bonds and friendships. As children reach school age and adolescence, they develop **nonliteral** or **figurative language skills** (see Table 53.1), including hints, idioms, metaphors, hyperbole, humor, and sarcasm. In lexical development, understanding often occurs before production; in children's humor development, children's production may precede full understanding of their meaning. Another notable milestone of

Table 53.1 Definitions of Basic Terms in Communication, Language, and Speech

TERM	DEFINITION	EXAMPLES
Communication	• Broad umbrella term that encompasses understanding and producing language, speech, nonverbal communicative gestures, and written language	• Humans share ideas using verbal or signed speech and language • Nonverbal communicative gestures include nodding one's head up and down to convey "yes" in some cultures
Language	• Verbal, signed, written, or other systems that use arbitrary but conventional, rule-governed symbols to communicate about objects, events, and ideas in the past, present, and future	• Verbal symbols include words (e.g., *apple* in English or *manzana* in Spanish, both of which represent a red, tasty fruit) • Signed symbols include the word *apple* in American Sign Language, produced by the twist of the knuckle of the index finger on the cheek
Speech	• Perception of the meaningful units of sounds that comprise verbal language and production of these sounds by coordinating the mouth, tongue, airflow, and vibration of the vocal folds	• Speech sounds or phonemes make a difference in meaning (e.g., *b, p, a, i,* and *t* affect the meaning of *bat, bit, pat,* and *pit*) • Speech does not include all vocal sounds, such as coughs or throat clearing • Phonemes in sign language are based on spatial, temporal features, such as hand shape
Receptive language	• Hearing and understanding verbal or sign language	• Recognizing own name • Following two-step directions
Expressive language	• Speaking using verbal or sign language	• Speaking first words or signs in a sign language • Telling stories
Phonology	• The system of relationships among speech sounds or phonemes that constitute a fundamental component of language	• Understanding *seetheredball* can be segmented into *see the red ball* • Babbling, consonant-vowel combinations that use phonemes
Lexicon	• All of the words or vocabulary of a person or a language	• The lexicon of the mathematician may vary from the lexicon of the lawyer
Morphology	• Units of meaning that can be combined to form vocabulary	• In English *dogs* is made of two morphemes, *dog* and the plural *-s; untie* is made of *un-* and *tie*
Syntax	• Grammar and word order to make sentences	• In English word order, *the dog chases the cat,* while in Hindi word order, *the cat the dog chases*
Pragmatics	• Verbal and nonverbal communication skills that govern how language and communication are used in context • Includes intonation, facial expression, and body language	• Use of eye contact and gestures to make a point forcefully • The timing and responsiveness between communication partners (e.g., engaging, responding, and maintaining reciprocal exchanges)
Nonliteral or figurative language skill	• Meaning of a word or phrase that is not literal but understood in context	• Hints (e.g., a teacher saying, "*I think I hear children talking*") • Idioms (e.g., "*Give me a hand*") • Metaphor (e.g., "*You are my sunshine*") • Hyperbole (e.g., "*That's the biggest thing I've ever seen!*")
Advanced language skills	• Ability to listen, speak, read, write, and reason using language	• Academic language • Ability to debate and deliver speeches
Literacy skills	• Skills required for reading and writing	• Reading an alphabetic language requires awareness of the sounds of language, print, and the relationship between letters and sounds • Spelling is a literacy skill
Bilingualism and multilingualism	• Ability to speak and/or sign two or more languages	• Ability to communicate verbally in Chinese and English • Ability to communicate verbally in English and to use American Sign Language • Ability to use Chinese, English, and American Sign Language
Biliteracy and multiliteracy	• Ability to read and write in two or more languages	• Ability to read and write Chinese, Spanish, and English
Phonologic processes	• Errors in speech production that affect more than a single sound and are based on violations of predictable, rule-based features	• Fronting, when a sound that should be made in the back of the mouth (cat) is made in the front of the mouth (tat) • Cluster reduction, when a consonant cluster (as in stop) is reduced to a single consonant (top)

Table 53.2 Speech, Language, and Communication Milestones from Birth to 5 Years, Based on Typically Developing Children Acquiring a Single Verbal Language

HEARING AND UNDERSTANDING	SPEAKING
BIRTH TO 3 MO	
• Startles at loud sounds • Recognizes voices and quiets if crying • Turns head toward sounds • Watches faces • Quiets or smiles when spoken to	• Makes pleasure sounds (cooing, gooing) • Cries differently for different needs
4-6 MO	
• Moves eyes in direction of sounds • Responds to changes in tone of voice • Notices music and sounds • Recognizes familiar people and things at a distance	• Vocalizes differently to show excitement, being tired, or in pain • Makes sounds when alone and when playing • Makes babbling sounds that are speechlike and uses consonant sounds, such as *p, b,* and *m* • Reaches for toys or objects • Engages in turn-taking and protoconversations
7-12 MO	
• Listens when spoken to • Turns and looks in direction of sounds • Enjoys social games, such as peek-a-boo and pat-a-cake • Responds to own name • Recognizes words for common items, such as *cup, shoe,* and *juice* • Begins to respond to simple requests *(Come here; Want more?)* or *No* • Looks when an adult points at something	• Uses speech sounds or gestures to get and keep attention and to respond to others • Imitates different speech sounds and gestures • Babbles with long and short groups of sounds, such as *bababa upup bibi,* and mixes different syllables, such as *badadeda* • Says one or two words *(bye-bye, dada, mama)* • Points to or shows things to spontaneously share interest with familiar people • Uses gestures such as waving for *hi* and *bye* or shaking head for *no*
1-2 YR	
• Listens to simple stories, songs, and rhymes • Follows simple commands and understands simple questions *(Roll the ball; Kiss the baby; Where's your shoe?)* • Points to things when asked or when named such as body parts and objects	• Learns to say more words every month • Uses some one- and two-word questions *(Where kitty? Go bye-bye? What's that?)* • Combines two words in their own ways *(more cookie, no juice, mommy book)* • Uses consonant sounds such as *p, b, m, h,* and *w* in English
2-3 YR	
• Understands differences in meaning (e.g., go–stop, in–on, big–little, up–down) • Follows two-step requests *(Get the book and put it on the table.)*	• Often asks for or directs attention to objects by naming them • Has a word for almost everything • Uses prepositions like *in, on,* and *under* • Often uses two- to three-word "sentences" • Speech is mostly understood by familiar listeners • Uses consonant sounds such as *k, g, f, t, d,* and *n* in English
3-4 YR	
• Understands simple *who, what, where,* and *why* questions • Understands words for colors like *red, blue,* or *green* and shapes like *circle* or *square* • Responds when you call from another room	• Uses pronouns like *I, you, me, we,* and *they* • Uses sentences that have four or more words with more complex grammar such as negative *(I no want to)* and questions • Talks about activities outside the home • Usually understood by people outside the family
4-5 YR	
• Hears and understands most of what is said at home and in school • Pays attention to a short story and answers simple questions about it • Understands words for time like *yesterday, today,* and *tomorrow* • Understands words for order like *first, next,* and *last* • Follows longer directions such as *(Find an animal you like, draw a circle around it, and bring the paper to me)*	• Uses sentences that include details (I like to read my books) and different action words like jump or play; may still make some grammar mistakes (I gots one game and he got three games) • Tells simple stories using mostly full sentences • Communicates easily with other children and adults • Says most sounds correctly except a few that are harder to say, such as *l, s, r, v, z, ch, sh,* and *th* in English

Milestones may not apply to bilingual children, children exposed to sign languages, children learning a second language, and children with language and learning disorders
For Spanish translations and more information, including activities for families:
• American Speech-Language-Hearing Association: http://www.asha.org/public/speech/development/chart.htm
• The American Academy of Pediatrics: https://healthychildren.org/English/Pages/default.aspx
• Centers for Disease Control and Prevention Milestones checklist: https://www.cdc.gov/ncbddd/actearly/milestones/index.html
Adapted from the American Speech-Language-Hearing Association (2021), the American Academy of Pediatrics (2009), and the Centers for Disease Control and Prevention Milestones checklist (2021).

pragmatic skills is the ability to adapt how to narrate events or stories for different audiences (e.g., friends vs teachers).

Advanced Language Skills

Once children enter school, they continue to develop new vocabulary and use increasingly complex sentence constructions to communicate about abstract, hypothetical, and imaginary topics. By adolescence, many students in Westernized school systems are required to deliver expository speeches or to debate. Formal schooling also affords new situations to communicate with a broader network of individuals, including teachers, coaches, and supervisors. The diversity of the situations requires nuanced attention to social rules and conventions and increases exposure to diverse forms of nonliteral language use, though proficiency in the use of nonliteral language varies by the language and culture of the speaker and addressee. Finally, the introduction of formal schooling presents children with the demands of acquiring

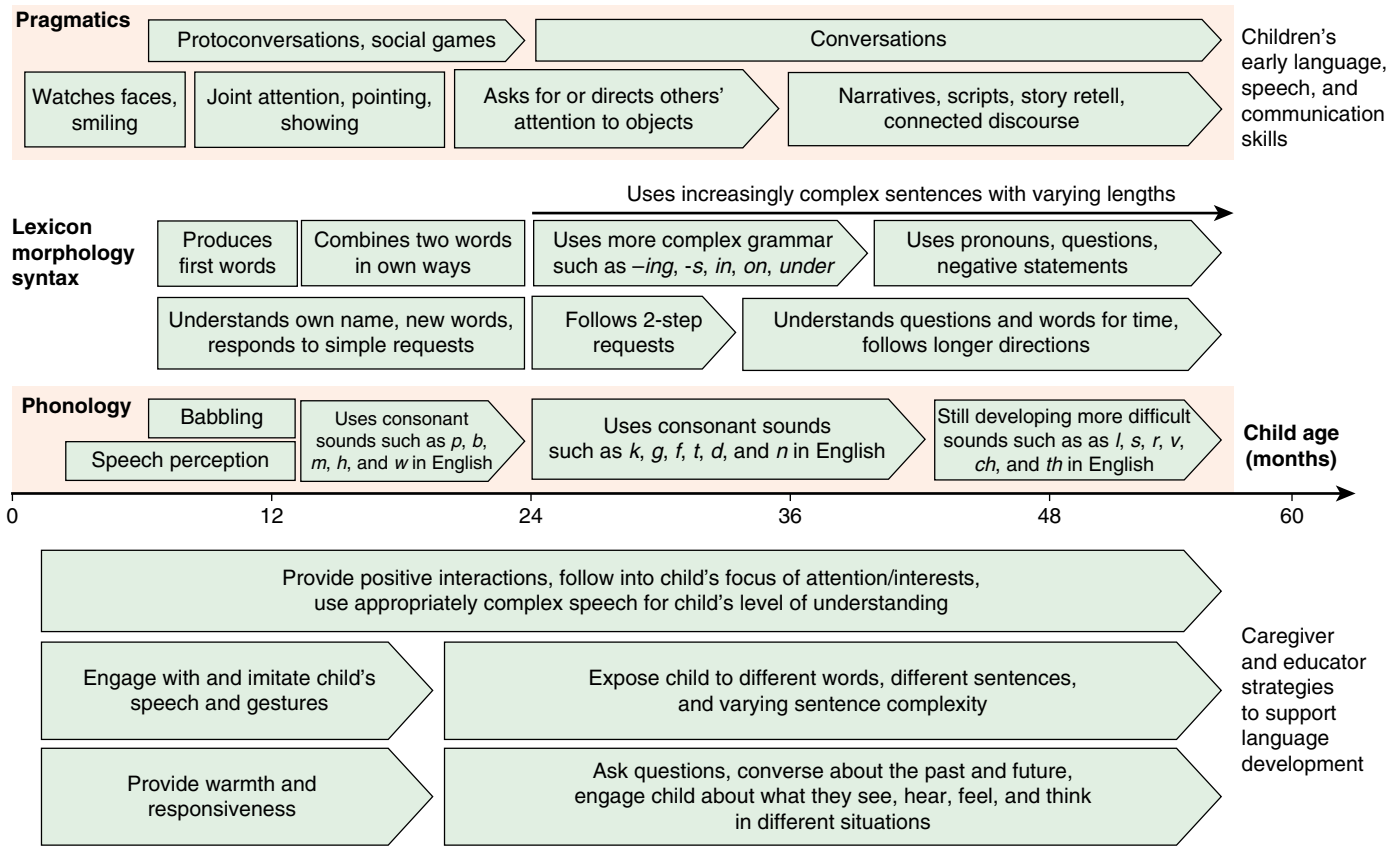

Fig. 53.1 Timeline of children's early language, speech, and communication skills and caregivers' and educators' strategies to support that development. The timing and width of boxes for the child skills are adapted from milestones from the American Speech-Language-Hearing Association, The American Academy of Pediatrics, and the Centers for Disease Control and Prevention. More information on milestones can also be seen in Table 53.1. Caregivers and educators should be encouraged to engage with the child using the language with which they are most comfortable because children, even children with delays, are capable of becoming bilingual. Specific child skills and caregiver/educator strategies may vary according to language and cultural practices.

literacy skills (see Table 53.1), those skills required for reading and writing. Early oral language skills are a robust predictor of children's early reading skills, and early oral language and reading skills are in turn predictors of children's writing skills (see Chapters 51 and 52.2). Language skills become critical to support high-level school- and work-related literacy skills.

BILINGUALISM AND MULTILINGUALISM

Worldwide, learning more than one language is more common than learning just one; many regions and countries in the world are home to individuals who routinely speak two or more languages. The timing of exposure, balance between languages, and level of skill in each language in dual-language or multilanguage learners varies across situations. **Simultaneous bilinguals** refers to those regularly exposed to both languages prenatally or from birth. **Sequential bilinguals** refers to those exposed to the second language after the first language, often when they enter school, though the timing of when the second language is introduced varies. Once children learn two languages, the balance in skill level between them may vary. For example, a child who was born in Nigeria, exposed to Igbo, and then immigrated to Greece at age 5 years will initially be more proficient in Igbo than in Greek. As the child attends school in Greece, Greek proficiency will improve (likely also supported through the introduction of reading and writing in a Greek monolingual school environment), and thus the balance will shift and the child may become more proficient in Greek over Igbo. A high level of skill across all domains of phonology, lexicon, syntax, and pragmatics is considered an ideal picture of bilingualism, but this ideal is not always the case or necessary for many bilingual learners. Bilingual learners often demonstrate **code-switching**, that is, alternating between languages, or **code-mixing**, mixing their languages together, especially when speaking with other bilingual speakers. A distinction between **conversational** and **academic** language skills may be made in reference to bilinguals. Bilingual speakers may master conversational language, the language used to communicate casually with family or friends, but remain less skilled in academic language, the complex, technical, and specialized vocabulary and syntax required in academic or work settings, particularly when school is presented in a language different from the language of the home. Some bilingual learners may experience **language attrition**, a reduction in the proficiency in one language over time. Factors within the child, family (e.g., one caregiver/one language, caregivers speaking both languages), community (e.g., availability of bilingual schooling, minority vs majority language of the community, perceived prestige of a language), and policy (e.g., national acknowledgement of multiple languages or requirements of accessibility of documents in school or business sectors) contribute to proficiency in both languages.

Bilingualism or multilingualism is typical language development for many children and not an adequate explanation for language delays as long as the child's skills in both languages are assessed. Even children with language and developmental disorders, such as intellectual disability and autism spectrum disorder, may be successful bilingual or multilanguage learners. It is difficult to predict developmental trajectories in bilingual development because of the wide variety of factors associated with the level of skill in different domains. *Children in homes with two or more languages who show delays in language development (considering the accumulated accomplishments in all languages) should be promptly referred for evaluation.*

DRIVERS OF VARIATION IN TYPICAL LANGUAGE DEVELOPMENT

Genetic

Similarities in language abilities across members of the same family suggest that genetic factors contribute to individual differences in language abilities. Genetic factors have been studied more often in the context of disorders of language learning than in the context of normal variation (see below).

Environment

Interactions between young children and their caregivers that are positive, responsive, and warm allow children to practice their early word learning (e.g., social games, routines). Living in stable home environments is better for language development than living in an unstable condition. The Bucharest Early Intervention Project conducted a randomized controlled trial to examine the role of being raised in a home (foster care) versus in institutionalized care in Romanian orphanages that were providing infants with low levels of responsive interactions. Children taken from the orphanages and placed in foster care by age 15 months had language skills that were similar to typically developing peers at 30 and 42 months in the same Romanian community living with their biologic families; children placed in foster care after 24 months had persistent expressive language delays.

The role of caregivers specifically is one of the few levers available to influence language outcomes in clinical practice and public programs. Positive links have been found between variability in socioeconomic backgrounds and children's later language skills; caregivers have been shown to mediate this link. Caregivers' **child-directed speech** refers to changes to caregivers' prosody (intonation patterns), phonology, grammar, and lexicon when engaging with young children. This child-directed speech has been measured across a wide variety of features, which can be broadly categorized into measures of quantity (e.g., total number of words spoken), quality (e.g., number of different words spoken), and interaction (e.g., warmth and responsiveness). Taken together, these factors constitute **language nutrition**, which, like dietary nutrition, is associated with rates of growth. However, the causal links between caregivers' child-directed speech and children's language outcomes are still unclear in children with typical development or language delays or disorders. Meta-analyses of interventions targeting improved language nutrition to date have generally reported either null effects or small to moderate positive effects on children's language skills. The specific role of book-sharing interventions to support children's language development is also mixed among different meta-analyses. Wide heterogeneity across intervention studies, including the method of delivery (e.g., one-on-one coaching vs caregiver groups), intensity (e.g., 1 hour per week for 12 weeks vs two 45-minute visits), measures of caregiver-child interaction, and child language outcomes, may contribute to differences in results. Caregivers' mental health has been found to be an important mediator of child outcomes; higher caregiver depression has been linked to poorer children's language outcomes.

Greater amounts of screen time and early age of screen time are negatively related to children's early language skills. However, high-quality screen-time practices (e.g., co-viewing, educational programs) are positively related to children's language skills; effect sizes are small to moderate.

Misattributions of Language Delay

Several common conditions have been erroneously implicated as an adequate explanation for language delays and disorders. Typically developing twins learn to talk at the same age as typically developing single-born children. Birth-order effects on language development have not been consistently found. **Ankyloglossia** (tongue-tie), an extremely tight lingual frenulum, does not prevent the acquisition of speech, but ankyloglossia may be the result of abnormalities associated with disorders of speech, such as neural injury and cerebral palsy. Frequent ear infections and serous otitis media in early childhood *do not* result in persisting language disorder. Prompt placement of tympanostomy tubes for chronic serous otitis media *does not* lead to better skills than watchful waiting. Biologic sex differences have been found in many studies of language development. Though males are generally slower to develop than females, the differences do not usually rise to the level of being clinically apparent. However, males are more likely to develop language disorders than females. Based on these findings, *children with moderate to severe delays in the development of language and speech deserve a prompt evaluation, even if they are males, non–first born children, twins, tongue-tied toddlers, and/or children with chronic otitis media.*

LANGUAGE, SPEECH, AND COMMUNICATION DISORDERS

Impairment in language, speech, and communication may occur in isolation or may be associated with other conditions.

Isolated Language Disorders with or Without Accompanying Speech Disorders

Clinical Presentation

Primary disorders of speech and language development are significant difficulties found in the absence of major cognitive, sensory, or motor dysfunction. The literature uses the term **specific language impairment** (SLI) or **language impairment**, the term we use here, also called *developmental language disorder* or *developmental dysphasia.* Children with language impairment typically perform >1.25-1.5 standard deviations below the mean on standardized language assessments. The *Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition* (DSM-5) criteria for a language disorder are provided in Table 53.3. Many children with language impairment eventually become competent language users, though they may show persistent and subtle difficulties with skills related to phonology, lexicon, and/or syntax. As adolescents and adults, compared to peers, they are generally less proficient at producing stories, descriptions, and scripts of everyday events, collectively known as **oral narratives**. Their narratives tend to be shorter, including fewer prepositions, main story ideas, and devices fostering cohesion. Children with language impairment may have significant difficulty in higher-level language skills (see Table 53.1), reasoning skills (e.g., drawing correct inferences and conclusions), the ability to take another person's perspective, and the ability to paraphrase and rephrase. Some children with language impairment show difficulties with social interaction because social interactions are often mediated by verbal language. Young children with language impairment may interact more successfully with older children or adults, who can adapt their communication to match the child's level of function, than with peers.

Epidemiology

Over 15% of 2-year-olds may not produce a vocabulary of 50 words or two-word utterances; estimates may vary for children exposed to two or more languages. Almost half of preschool-age children, age 3-5 years old, who qualify for special education meet eligibility based only on speech-language impairment. By age 5, approximately 6% of children are identified as having a speech impairment alone, 5% as having both speech and language impairment, and 8% as having language impairment alone. Males are nearly twice as likely to have an identified speech or language impairment as females.

Etiology

Genetic factors appear to play a major role in influencing how children learn to talk. A family history may identify current or past speech or language problems in up to 30% of first-degree relatives of proband children. Concordance rate for low language test scores and/or a history of speech therapy within twin pairs is about 50% in dizygotic pairs and 90% in monozygotic pairs. Consistent pathogenic genetic variations have not been identified. Instead, multiple genetic regions and epigenetic changes may result in heterogeneous genetic pathways causing language disorders. Several single-nucleotide polymorphisms (SNPs) involving noncoding regulatory genes, including *CNTNAP2* (contactin-associated-protein-like-2) and *KIAA0319,* are strongly associated with early language acquisition and are also thought to

affect early neuronal structural development. Several chromosomal **copy number variants** (see Chapter 96) have also been associated with abnormalities of language and speech; these variants may be associated with distinctive physical features (e.g., tall stature in Klinefelter syndrome) or neurobehavioral conditions (e.g., autistic features). Environmental, hormonal, and nutritional factors may exert **epigenetic** influences by dysregulating gene expression. These forces result in aberrant sequencing of the onset, growth, and timing of language development.

All of the family, community, and sociopolitical factors that appear to contribute to variation in typical language learning may contribute to the rate of learning in children with disorders. Improving the quality of the verbal environment, and in particular the quantity and quality of child-directed speech (see above), may moderate the impact of genetic and epigenetic factors.

Pathogenesis

Language functioning is widely distributed across the brain through interconnected neural networks. Frank neurologic injury is typically absent in children with language impairment. Language disorders have been attributed to a fundamental difficulty in the brain's capacity to process complex information rapidly. Limitations in the amount of information that can be stored in verbal working memory (see Chapter 49) may also limit the rate at which language information is processed. Electrophysiologic studies show abnormal latency in the early phase of auditory processing in children with language impairment. Neuroimaging studies identify an array of anatomic abnormalities, implicated in language processing. MRI scans in children with language impairment may reveal white matter lesions and volume loss, ventricular enlargement, focal gray matter heterotopia within the right and left parietotemporal white matter, abnormal morphology of the inferior frontal gyrus, atypical patterns of asymmetry of language cortex, or increased thickness of the corpus callosum in a minority of affected children. Postmortem studies of children with language disorders found evidence of atypical symmetry in the plana temporale and cortical dysplasia in the region of the sylvian fissure. A high rate of atypical perisylvian asymmetries has been documented in the parents of children with language impairment.

Language Disorders Associated with Cognitive Impairment and Intellectual Disability

Speech and language impairment may be the first indication of a global neurodevelopmental disorder. **Global developmental delay** or **early developmental impairment** is defined as delays in two or more domains. Children with substantial delays in adaptive function and scores 2 or more standard deviations below the mean on intelligence testing may meet criteria for **intellectual disability** (see Chapter 56). Most children with a mild intellectual disability learn to communicate adequately, though they are likely to encounter difficulties with higher-level language skills (see Table 53.1). Children with an IQ as low as 25 may eventually acquire a small lexicon and ability to combine words. Specific genetic syndromes have distinctive language profiles: in Down syndrome, verbal skills are more impaired than nonverbal skills; in William syndrome, language skills may be relatively preserved compared to nonverbal skills; in fragile X syndrome, unusual word or sound repetition may be present.

Autism Spectrum Disorder

A disordered pattern of language, speech, and communication development characterizes autism spectrum disorder (ASD) (see Chapter 58). The core characteristics of ASD are persistent difficulties in social communication and social interaction relative to age expectations and restricted, repetitive patterns of behavior, interests, or activities. Children with ASD show a wide range of language and communication abilities. At the severe end, language and speech may be extremely limited (nonverbal). Approximately 30–50% of children with ASD also meet criteria for intellectual disability, which contributes to the challenges of developing communication skills. Parents report regression in language and social skills (**autistic regression**) in approximately 20–25% of children with ASD, usually between 12 and 36 months of age. The cause of the regression is not known; it is associated with an increased risk for intellectual disability and severe ASD. Individuals with ASD who are high functioning may have large vocabularies and use grammatically correct sentences but have unusual or impaired social-pragmatic features, such as odd intonation patterns, off-topic comments, and atypical conversational skills. For example, they may engage in long monologues about a topic of special interest, without considering the interest of their conversational partner. Some individuals with ASD have highly specialized, isolated, "savant" skills, such as calendar calculations or **hyperlexia** (the precocious ability to recognize written words beyond expectation based on general intellectual ability).

DSM-5 identified **social (pragmatic) communication disorder (SPCD)** as a category of communication disorder distinct from ASD (see Table 53.3). Symptoms of SPCD include extreme literalness and inappropriate verbal and social interactions. Socially appropriate use and understanding of figurative language (see Table 53.1) depends on correct interpretation of the meaning and the context of language and the ability to draw proper inferences, skills limited in SPCD. SPCD has been recognized as a symptom of a wide range of disorders, including right-hemisphere brain injury and nonverbal learning disabilities.

Hearing Impairment

Hearing loss may be caused by a sensorineural loss, a conductive loss, or a mixed picture in one or both ears. Although it is not possible to accurately predict the impact of hearing loss on a child's verbal language development, the type, degree, and laterality of hearing loss; the age of onset; and the duration of the auditory impairment before amplification play important roles (see Chapter 55). Newborn screening programs are designed to identify congenital hearing loss but fail to identify children with progressive or acquired hearing loss or deafness after birth. *Any child who shows a speech or language problem should have a hearing assessment by an audiologist, even if they passed their newborn hearing screen.*

Conductive hearing loss occurs when sounds cannot get through the outer and middle ear to stimulate the auditory nerve. In children, the most common cause of conductive hearing loss is **acute** or **chronic serous otitis media**. Otitis media is typically transient and may increase the sound threshold at which children can detect tones or understand language. Persistent fluid in the middle ear may be treated with **tympanostomy or ventilation tubes**. However, treatment of chronic serous otitis media with tympanostomy tubes does not improve outcomes in the domains of speech and language, cognition, academic skills, or psychosocial functioning from preschool years through middle childhood.

Neurologic Conditions

Epilepsy Syndromes

Children with Landau-Kleffner syndrome or verbal auditory agnosia have a history of typical language development until they experience a regression in their ability to comprehend spoken language—verbal auditory agnosia—along with the development of seizures, usually between 3 and 7 years of age. Expressive language skills also typically deteriorate. An electroencephalogram (EEG) may show a distinct pattern of status epilepticus in sleep (continuous spike wave in slow-wave sleep), and up to 80% of children with Landau-Kleffner syndrome eventually exhibit clinical seizures. Use of antiepileptic medication, corticosteroids, and intravenous gamma globulin has led to varying results. The prognosis for return of typical language ability is uncertain, even if seizures resolve.

Epileptic interictal discharges are more frequently found on EEGs of children with language impairments than EEGs of otherwise typically developing children. The discharges are likely a manifestation of an underlying disorder of brain, distinct from the language impairment. Only when seizure symptoms or regression in language ability is present is a routine EEG recommended in the evaluation for a child with speech and/or language impairment.

Table 53.3 DSM-5 Diagnostic Criteria for Communication Disorders

LANGUAGE DISORDER

A. Persistent difficulties in the acquisition and use of language across modalities (i.e., spoken, written, sign language, or other) due to deficits in comprehension or production that include the following:
   1. Reduced vocabulary (word knowledge and use).
   2. Limited sentence structure (ability to put words and word endings together to form sentences based on the rules of grammar and morphology).
   3. Impairments in discourse (ability to use vocabulary and connect sentences to explain or describe a topic or series of events or have a conversation).
B. Language abilities are substantially and quantifiably below those expected for age, resulting in functional limitations in effective communication, social participation, academic achievement, or occupational performance, individually or in any combination.
C. Onset of symptoms is in the early developmental period.
D. The difficulties are not attributable to hearing or other sensory impairment, motor dysfunction, or another medical or neurologic condition and are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay.

SPEECH SOUND DISORDER

A. Persistent difficulty with speech sound production that interferes with speech intelligibility or prevents verbal communication of messages.
B. The disturbance causes limitations in effective communication that interfere with social participation, academic achievement, or occupational performance, individually or in any combination.
C. Onset of symptoms is in the early developmental period.
D. The difficulties are not attributable to congenital or acquired conditions, such as cerebral palsy, cleft palate, deafness or hearing loss, traumatic brain injury, or other medical or neurologic conditions.

SOCIAL (PRAGMATIC) COMMUNICATION DISORDER

A. Persistent difficulties in the social use of verbal and nonverbal communication as manifested by all of the following:
   1. Deficits in using communication for social purposes, such as greeting and sharing information, in a manner that is appropriate for the social context.
   2. Impairment of the ability to change communication to match context or the needs of the listener, such as speaking differently in a classroom than on a playground, talking differently to a child than to an adult, and avoiding use of overly formal language.
   3. Difficulties following rules for conversation and storytelling, such as taking turns in conversation, rephrasing when misunderstood, and knowing how to use verbal and nonverbal signals to regulate interaction.
   4. Difficulties understanding what is not explicitly stated (e.g., making inferences) and nonliteral or ambiguous meanings of language (e.g., idioms, humor, metaphors, multiple meanings that depend on the context for interpretation).
B. The deficits result in functional limitations in effective communication, social participation, social relationships, academic achievement, or occupational performance, individually or in combination.
C. The onset of the symptoms is in the early developmental period (but deficits may not become fully manifest until social communication demands exceed limited capacities).
D. The symptoms are not attributable to another medical or neurologic condition or to low abilities in the domains of word structure and grammar and are not better explained by autism spectrum disorder, intellectual disability (intellectual developmental disorder), global developmental delay, or another mental disorder.

From the *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.* Washington, DC: American Psychiatric Association; 2013:42, 44, 47–48.

Cerebellar Mutism Syndrome

In the aftermath of operations for tumors in the posterior fossa, such as **medulloblastoma**, many children lose the ability to speak. Fortunately, though the presentation is initially profound, most children recover the ability to use language. **Cerebellar mutism syndrome** demonstrates that the cerebellum probably plays a fundamental role in language and communication. The syndrome is thought to result from damage to the superior cerebellar peduncle that connects the cerebellum to language centers in the frontal lobes.

Stroke

Strokes in childhood can occur prenatally, in the perinatal period, or at any time in childhood. As in adults, a brain territory frequently affected is supplied by the middle cerebral artery resulting in damage to the **left frontal and temporal lobes** that are associated with language function in adults. However, young children with stroke show greater plasticity of language function than do adults with similar brain injuries. Many children with left hemisphere stroke go on to demonstrate typical or near-typical language functions. Functional imaging studies document that these children activate uninjured regions of the left hemisphere around the stroke or homologous regions in the right hemisphere. This demonstrates that though under usual circumstances the left hemisphere serves language, alternative networks can substitute in the case of early injury. The quality of the home language environment is strongly associated with the language skills of children with strokes.

Metabolic and Neurodegenerative Disorders (see Part IX and Chapter 639)

Regression of language development may accompany loss of neuromotor function at the outset of a number of metabolic diseases, including lysosomal storage disorders (metachromatic leukodystrophy), peroxisomal disorders (adrenal leukodystrophy), ceroid lipofuscinosis (Batten disease), and mucopolysaccharidosis (Hunter disease, Hurler disease). A creatine transporter deficiency was identified as an X-linked disorder that manifests with language delay in males and with mild learning disability in female carriers.

Hydrocephalus (see Chapter 631.11)

Children with hydrocephalus may be described as having cocktail-party syndrome. In this syndrome, children may use sophisticated words, but their comprehension of abstract concepts is limited, pragmatic conversational skills are weak, their analyses are superficial, and/or they appear to be carrying on a monologue.

Language in the Context of Psychologic or Mental Health Conditions

Selective Mutism

In **selective mutism**, children do not speak in specific social situations, such as school or other settings outside the home, though they speak normally in certain settings, such as within their home or when they are alone with their parents. Other symptoms include excessive shyness, withdrawal, dependency on parents, and oppositional behavior. Most cases of selective mutism are the manifestation of a chronic pattern of **anxiety**. Children with selective mutism often report that they want to speak in social settings but are too afraid, worried, or distressed to do so. The family history is often positive for anxiety symptoms. Children with selective mutism may also have a language or speech impairment, contributing to their sense of distress in speaking. Treatment of selective mutism generally uses evidence-based approaches to reducing general anxiety, including cognitive-behavioral therapy and/or selective serotonin reuptake inhibitors in conjunction with speech-language therapy.

Schizophrenia

A characteristic of schizophrenia is abnormal communication, including highly disorganized language that is difficult to follow and frequent changes in topic (see Chapter 47.1). This communication challenge accompanies the thought disturbance that is the hallmark of schizophrenia. Schizophrenia usually presents in individuals in adolescence or young adulthood. The communication disorder is linked to other features of schizophrenia, including slower processing speed, poorer cognitive control, and weaker working memory relative to typically developing peers.

Adverse Psychosocial Conditions

Orphanages

An estimated 8 million children worldwide are living in residential care or orphanages, despite recognition of the severe adverse impacts of institutionalization on children's health and development. Children in orphanages have poor receptive and expressive language skills, most likely the result of limited language exposure and lack of consistent warm relationships with caring adults. Children from orphanages may be adopted. In an international adoption, the children typically face a new challenge: learning a different language (see Chapter 9). Outcomes for internationally adopted children are mixed; meta-analyses suggest trends for stronger language outcomes when children are adopted before the age of 1 year than after 1 year. However, findings were not statistically significant, likely because of the wide variety of challenges that the children face and difficulty identifying appropriate comparison groups.

Foster Care

Approximately 30–75% of the children 6 years of age or younger in foster care are delayed, and therefore **assessing language skills for them is imperative** (see Chapter 10). An important contribution to the language delay in many children in foster care, like that of children in orphanages, is the lack of consistently warm, responsive parenting that is fundamental to language nutrition. Encouraging foster parents to increase language nutrition may positively affect the language skills of children in foster care.

High-Stress, Low-Verbal Environments

Children from homes where they may experience stressors, such as food insecurity, housing insecurity, poor childcare facilities, and high levels of community violence, are at risk for slower language development relative to peers in stable environments. All of these factors may contribute to initial delays in physical and cognitive development, with language development being one of the most noticeable to track developmental progress. If language delays persist, the chances that the children will catch up with others from more resourced environments, even if their circumstance change, are limited. Thus, what begins as a delay may end up as a disorder. Referral of children from stressed, low-verbal environments to public and community-based prevention programs designed to provide stability and to enhance language input may improve the children's outcomes.

SPEECH DISORDERS

Structural Anomalies of the Organs of Speech

Cleft Lip and Palate

Cleft lip is a split in the formation of the lip. **Cleft palate** is a split in the hard and/or soft palate (see Chapter 356). These conditions often occur together but may occur separately. Cleft lip or palate is the most common structural abnormality at birth in the United States. The cleft is often easy to see but may be subtle if isolated to the soft palate. A child with isolated cleft lip may have minimal speech problems. A child with cleft palate is likely to have speech difficulties, including **hypernasal speech** in which air escapes through the nose, making it difficult to produce consonants that need pressure to build in the mouth for proper execution (e.g., *b, k,* and *s*). In addition, children with cleft palate may have severe and persistent serous otitis media, leading to moderate to severe conductive hearing loss beyond the frequency and complications of children with an intact palate. Therefore most children with cleft palate need long-term therapy with a speech-language pathologist (SLP). Cleft palate may occur in isolation, called **nonsyndromic cleft palate**, or in conjunction with other malformations, called **syndromic cleft palate**. **Velocardiofacial syndrome (VCFS)** is an autosomal dominant condition that results from a deletion on the long arm of chromosome 22 (deletion22q11) and may include cleft palate. Many different phenotypes are associated with this deletion, demonstrating the complex relationship of genes, anatomic structure, and function. The prognosis for speech and language in such cases is dependent on the specific syndrome associated with the cleft palate.

Velopharyngeal Insufficiency

Velopharyngeal insufficiency (**VPI**) is an abnormality of the soft palate, such that the soft palate cannot regulate the flow of air between the mouth and nose in speech. It may occur as part of cleft palate or may be an isolated finding. VPI may not be apparent in early development when the adenoids are large and bolster the soft palate. As the adenoids regress, it may become clear that the soft palate is not closing off the passage to the nose, creating hypernasal speech. Evaluation of the intactness of the soft palate is important before adenoidectomy because removal of the adenoids can bring on VPI suddenly. Surgery or use of prosthetic devices may be required for individuals who cannot be helped by speech therapy.

Speech Sound Disorders

Speech sound disorders is an umbrella term that refers to difficulties with perception, motor production, or phonologic representation of speech sounds and/or speech segments (see Table 53.3). Speech sound disorders may be organic in origin, including neurologic conditions, structural conditions, or sensory conditions. Speech sound disorders are considered **functional** when no known cause can be identified. Speech sound disorders may be accompanied by subtle difficulties in speech perception.

Phonologic Disorders

Phonologic disorders are functional speech sound disorders that affect linguistic aspects of speech. **Phonologic processes** (see Table 53.1) are errors in speech production based on violations of predictable, rule-based features of speech. These phonologic processes are typical at young ages and resolve at specific ages. Phonologic processes become disorders when they persist to older ages and impair intelligibility.

Articulation Disorders

Articulation disorders focus on errors (such as distortions and substitutions) in production of individual speech sounds regardless of where in a word or phrase the sound occurs. Articulation errors are not the result of neuromotor impairment, but rather seem to reflect an inability to correctly process the words they hear. As a result, they lack understanding of how to fit sounds together properly to create words. Children with articulation or other speech sound disorders are at risk for later reading and learning disability.

Childhood Apraxia of Speech

In childhood apraxia of speech (CAS), difficulty in planning and coordinating movements for speech sound production results in inconsistent distortions or errors of speech sounds, even vowel sounds. The same word may be pronounced differently each time, making intelligibility poor. Intelligibility also tends to decline as the length and complexity of the child's speech increase. Consonants may be deleted and sounds transposed. As they try to talk spontaneously or imitate others' speech, children with CAS may display oral groping or struggling. Children with CAS frequently have a history of early feeding difficulty, limited sound production as infants, and/or delayed onset of spoken words. They may point, grunt, or develop an elaborate gestural communication system in an attempt to overcome their verbal difficulty. Apraxia may be limited to verbal motor skills, may extend to oral-motor function, or may be a more generalized problem affecting fine and/or gross motor coordination. Childhood apraxia of speech may co-occur with disorders of language and learning.

Dysarthria

This motor speech disorder often originates from neuromotor disorders, such as cerebral palsy, muscular dystrophy, myopathy, and facial palsy. Dysarthria is characterized by lack of strength and muscular control and manifests as slurring of words and distorting vowels. Speech patterns are often slow and labored. Feeding difficulty, drooling, open-mouth posture, and protruding tongue may accompany the dysarthric speech.

Disorders of Fluency, Voice, and Resonance

Stuttering

Under normal circumstances, most people do not speak smoothly all the time, but rather repeat words or sounds, hesitate to find a word, pause, add "uh" or "you know" to the flow of speech, or repeat a sound or word more than once. These disruptions are called **dysfluencies** and are discussed further in Chapter 53.1. **Stuttering** in children over age 4 that lasts longer than 6 months, includes repetition of individual sounds, and/or creates emotional distress should be evaluated by a speech and language pathologist.

Voice

A **voice disorder** is an abnormality in voice quality, pitch, and loudness that is unexpected or inappropriate for an individual's age, gender, cultural background, or geographic location. Voice disorders can be subdivided into organic and functional. **Organic voice disorders** are physiologic in nature and result from alterations in respiratory, laryngeal, or vocal tract mechanisms. **Aerodigestive disorders** cover congenital or acquired conditions of the aerodigestive tract; they include abnormalities of the **airway** (pharynx and larynx), **pulmonary tract** (trachea, bronchi, and lungs), and **upper digestive tract** (esophagus). These structural problems may affect respiratory and swallowing functions and speech, especially voice. **Functional voice** disorders result from improper or inefficient use of the vocal mechanism in the context of normal physical structure. Psychologic stress can also lead to habitual and maladaptive voice quality, known as **psychogenic voice disorders**. These categories may overlap. Vocal nodules result from behavioral voice misuse that leads to repeated trauma to the vocal folds and structural changes to the vocal fold tissue.

ASSESSMENT OF LANGUAGE AND SPEECH DISORDERS

Screening

Developmental surveillance at each well-child visit should include specific questions about typical language developmental milestones and observations of the child's behavior. Clinical judgment, defined as eliciting and responding to parents' concerns, can detect many children with speech and language challenges. The American Academy of Pediatricians (AAP) recommends clinicians employ standardized developmental screening questionnaires and observation checklists at select well-child visits (see Chapter 28). However, the U.S. Preventive Services Task Force reviewed screening for language impairment in young children in primary care settings and found inadequate evidence to support screening in the absence of parental or clinician concern about children's speech, language, hearing, or development. At present, when parents, other caregivers, or physicians are concerned about speech or language development, the child should be referred for a diagnostic evaluation and intervention.

Diagnostic Evaluation

A developmental delay indicates abnormally slow timing relative to same-age peers in the development of the skill. A language delay becomes a language disorder when it persists to school age; is functionally impactful in terms of communication, social skills, or learning and cognition; or is qualitatively different from normal patterns or sequences of development. Language and communication skills should be interpreted within the context of that child's overall cognitive, social, and physical abilities. A multidisciplinary evaluation of a child with language delay or disorder is often warranted. At a minimum, the diagnostic evaluation should include psychologic or neurodevelopmental evaluation, including an assessment of social skills, a speech-language evaluation, an audiologic assessment, and a pediatric examination.

Psychologic or Neurodevelopmental Evaluation

The two main goals for the psychologic evaluation of a young child with a communication disorder are to assess nonverbal cognitive ability and social skills. A broad-based cognitive assessment is important to determine the breadth and severity of developmental difficulties. At a minimum, the child should have an assessment of both verbal and nonverbal skills. As children reach school age, they may be assessed with an intelligence test and an assessment of adaptive function to determine if they meet criteria for intellectual disability (see Chapter 56). If the child has findings of global developmental delay or intellectually disability, their language and speech skills should be evaluated within that context. Language and speech disorders may coexist with other conditions, so that the psychologic evaluation at all ages should consider mental health conditions, such as anxiety, mood disorder, and attention-deficit/hyperactivity disorder (ADHD) and, at older ages, learning challenges.

A child's social behaviors must be assessed to determine whether the child meets diagnostic criteria for ASD (see Chapter 58). Children with language impairment may display an interest in social interaction, even if they may have difficulty socializing because of limitations in communication skills, such as difficulties initiating conversation or taking turns. Children with ASD do not display social interest in typical ways. However, the distinction may be challenging in the context of a clinical evaluation when the child needs to interact only with professional adults and not with peers. Observational tests include specific maneuvers, such as calling the child's name, making exaggerated gestures, and attempting to engage the child in a reciprocal interaction around blowing bubbles, to make this distinction.

Speech and Language Evaluation

A certified SLP should perform a speech and language evaluation on a child with delays or difficulties in language and speech. A typical evaluation includes assessment of language, speech, and the physical mechanisms associated with speech production. Both expressive and receptive language (see Table 53.1) are assessed, using a combination of standardized measures, informal interactions, and pertinent observations. All components of language are assessed, including phonology, lexicon, morphology, syntax, and pragmatics (see Table 53.1). Speech assessment similarly uses a combination of standardized measures and informal observations and includes assessment of speech sounds, fluency, voice, and resonance. Assessment of physical structures includes oral structures and function, respiratory function, and vocal quality.

Audiologic Assessment (see Chapter 677)

In many settings, an SLP works in conjunction with an audiologist, who can do an appropriate hearing evaluation of the child. If an audiologist is not available in that setting, a separate referral should be made. No child is too young for a hearing evaluation. Passive methods can be used in children who are young or unable to cooperate with testing. Repeat assessment with an active assessment can be accomplished at older ages. A referral for full hearing evaluation is appropriate whenever there is suspicion of language or speech impairment.

Pediatric Evaluation

History and physical examination should focus on the identification of potential contributors to the child's language and communication difficulties. A family history of delay in talking, need for speech and language therapy, or academic difficulty can suggest a genetic predisposition to language disorders. Pregnancy history might reveal risk factors for prenatal developmental anomalies, such as polyhydramnios or decreased fetal movement patterns. Small size for gestational age at birth, symptoms of neonatal encephalopathy, or early and persistent oral-motor feeding difficulty may presage speech and language difficulty. Developmental history should focus on the age when various language skills were mastered and the sequences and patterns of milestone acquisition. *Regression or loss of acquired skills should raise immediate concern.*

Physical examination should include measurement of height (length), weight, and head circumference, even in children over age 2 years. The skin should be examined for lesions consistent with phakomatosis (see Chapter 636). Anomalies of the head and neck, such as white forelock and hypertelorism (Waardenburg syndrome), ear malformations (Goldenhar syndrome), facial and cardiac anomalies (Williams syndrome, VCFS), retrognathism of the chin (Pierre Robin anomaly), or cleft lip/palate, are associated with hearing and speech abnormalities. Neurologic examination might reveal muscular hypertonia or hypotonia, both of which can affect neuromuscular control of speech. Generalized muscular hypotonia, with increased range of motion of the joints, is frequently seen in children with language impairment. The reason for this association is not clear, but it might account for the fine and gross motor clumsiness often seen in these children. However, mild hypotonia is not a sufficient explanation for the impairment of receptive and expressive language. Language impairment may be a component of a syndrome or other recognizable condition. The physical examination gathers information to make other diagnoses.

No routine diagnostic studies are indicated for isolated language disorders with the exception of the hearing assessment. When language delay is a part of a generalized cognitive or physical disorder, referral for further genetic evaluation, genetic testing (e.g., fragile X testing, microarray, whole exome or whole genome sequencing), neuroimaging studies, and EEG should be considered.

Treatment of Language and Speech Disorders

Disorders of language and speech are often treated by SLPs working alone or as part of a multidisciplinary team with others, such as early intervention specialists or occupational therapists. SLPs may work in hospital in-patient and out-patient settings. More commonly, they work in schools and early intervention programs. The nature and intensity of treatment are predicated on the nature and cause of the language or speech disorder and the explicit objectives of treatment. **Childhood apraxia of speech** typically requires that the child participate in four or five short sessions per week to achieve intelligible speech, whereas language impairment disorder may require once- or twice-weekly therapy in a peer-group setting to increase communicative attempts. Speech-language therapy for young children is typically play-based. Even drills are couched in naturally occurring, enjoyable, or fun activities. Group therapy with other young children is often well suited to children with language and communication disorders because children practice their emerging skills with peers in naturalistic settings. A strong family component to therapy is important to leverage the limited time that therapists can spend with children. Caregivers can be taught to use effective techniques designed to meet the objectives of the treatment program. For children who do not develop useful verbal language, the SLP may consider the use of assistive and augmentative communication (AAC; see Chapter 54), which may use high-technology devices, such as voice-generating computer programs, or low-technology solutions, such as sign language or picture exchanges. The use of AAC allows the nonverbal child to communicate within the human community. Several systematic reviews and meta-analyses provide compelling data that speech-language therapy is effective for improving many aspects of language and speech. Therefore a timely referral for treatment with an SLP is recommended over watchful waiting for many children with delays and disorders of language and speech.

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53.1 Childhood-Onset Fluency Disorder

Kenneth L. Grizzle and Karolyn Mirasola

Dysfluent speech describes speech, language, and voice behaviors that interrupt the production and fluency of sounds, words, and thoughts. All speakers produce dysfluent speech, but not all dysfluent speech is stuttering. The words *stuttering, stammering,* and *dysfluency* are often used interchangeably. *Stutter* is used informally, particularly in the United States, to describe when an individual is struggling to express themself and may speak in a halting manner. *Stammering* is used in the United Kingdom in place of stuttering (Table 53.4). It is important for clinicians to have a general understanding about what stuttering is and when to counsel and refer families to speech-language pathologists (SLPs). It is important to distinguish between stuttered and nonstuttered dysfluencies and other fluency disorders and to identify concomitant symptoms.

DIAGNOSIS

In the *Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition* (DSM-5), the term *stuttering* has been removed from the diagnostic classification, and the disorder is referred to as **childhood-onset fluency disorder** (Table 53.5). Note that impact on functional behavior is a component of the psychiatric diagnosis. In contrast, communication disorder specialists would consider anxiety and avoidance of various activities as concomitant symptoms, but not necessarily a requirement for the diagnosis of stuttering.

Child-onset stuttering (formerly known as developmental stuttering) is a speech disorder that often begins in the preschool period

Table 53.4 Terminology Related to Childhood-Onset Fluency Disorder

TERM	DEFINITION
Stuttering	A speech disorder manifested through abnormal speech patterns referred to as *dysfluencies*
Childhood-onset fluency disorder	Term used in DSM-5 that is synonymous with *stuttering*
Stammering	The clinical term used in the United Kingdom rather than stuttering; stammering also used informally to describe halting speech
Cluttering	A speech disorder characterized by an excessively rapid and irregular rate of speech
Dysfluency	Speech disruptions that can occur in normal or disordered speech

Table 53.5 DSM-5 Diagnostic Criteria for Childhood-Onset Fluency Disorder

A. Disturbances in the normal fluency and time patterning of speech that are inappropriate for the individual's age and language skills, persist over time, and are characterized by frequent and marked occurrences of one (or more) of the following:
   1. Sound and syllable repetitions.
   2. Sound prolongations of consonants and vowels.
   3. Broken words (e.g., pauses within a word).
   4. Audible or silent blocking (filled or unfilled pauses in speech).
   5. Circumlocutions (word substitutions to avoid problematic words).
   6. Words produced with an excess of physical tension.
   7. Monosyllabic whole-word repetitions (e.g., "I-I-I-I see him").

B. The disturbance causes anxiety about speaking or limitations in effective communication, social participation, or academic or occupational performance, individually or in any combination.

C. The onset of symptoms is in the early developmental period.
Note: Later-onset cases are diagnosed as 307.0 [F98.5] adult-onset fluency disorder.

D. The disturbance is not attributable to a speech-motor or sensory deficit, dysfluency associated with neurologic insult (e.g., stroke, tumor, trauma), or another medical condition and is not better explained by another mental disorder.

From the *Diagnostic and Statistical Manual of Mental Disorders. 5th ed.* Washington, DC: American Psychiatric Association; 2013:45–46.

and is not associated with stroke, traumatic brain injury, or other possible medical conditions. Stuttering behaviors can occur in typically developing children who do not have a speech disorder and in this situation are more accurately referred to as *developmental dysfluencies*. During the toddler and preschool years, children often produce repetition of sounds, syllables, or words, particularly at the beginning of sentences (normal dysfluencies). These developmental dysfluencies occur between the ages of 2.5 and 4 years old when the language, motor, and emotional systems are developing. These dysfluencies may occur as the child struggles to try to express more complex ideas in a rapid and precise manner.

Child-onset stuttering disorder also typically begins between 2 and 4 years of age. Onset of symptoms varies from pronounced stuttering within a few days to gradual worsening of symptoms across months. Symptoms may ebb and flow, including disappearing for weeks before returning, especially among young children. From 40% to 75% of young children who stutter will stop spontaneously, typically within months of starting. Although predicting which child will stop stuttering is difficult, risk factors for persisting include stuttering for >1 year, continued stuttering after age 6 years, and experiencing other speech or language problems. Additionally, certain types of dysfluencies are typically seen only in child-onset stuttering disorder.

Types of Dysfluencies

Dysfluencies interrupt the normal flow of speech through repeated or prolonged sounds, syllables, or words. Types of dysfluency that are *not* exclusive to children who stutter include *interjections* ("well, uhh, umm"), hesitations (pause), *revisions* ("I thought . . . I mean"), and *phrase repetitions* ("Did you say—Did you say"). In addition, the perspective of the speaker and cause of the dysfluency differ between true stuttering disorders and other types of dysfluency. The dysfluencies might sound the same but occur for different reasons. For example, a typically developing child with dysfluency may talk around a word or use a completely different word because of issues with word retrieval, complex thought formulation, or distractibility. But for children who stutter, they may talk around a word or retrieve a completely different word because even though they know exactly what they want to say, they are unable to produce or "get" the sounds out. This highlights the notion that stuttering is about more than what the listener observes. The "moment of stuttering" is different because something occurs that only the person who stutters can perceive.

Dysfluencies that occur in child-onset stuttering vary in type, frequency, and longevity. Specifically, children who stutter show greater part-word repetition ("b-b-b-b-but"), single-syllable word repetition ("My, my, my"), sound prolongation ("MMMMMM-an"), and in more severe cases, blocking. Blocking is a dysfluent behavior that is identified by a fleeting or sometimes lengthy blockage of the flow of air at the level of the vocal folds or articulators (tongue, teeth, and lips). Typically, the child has initiated an articulatory posture (tongue is in the position to produce "k"), but she is unable to release any air and/or phonation (i.e., voice). Often in response to this inability to produce sounds or words, the child will develop secondary behaviors that recruit movement from other parts of the body that the child feels they have more "control" over.

These types of behaviors and movements exist only within child-onset stuttering disorder. They are referred to as *secondary characteristics,* or physical concomitants that often occur as a response to stuttering. Common secondary characteristics include movements of the head (head turning or jerking), face (eye blinking/squinting, grimacing, opening or tightly closing the jaw), neck (tightening), and limbs (stomping feet, slapping hand); an increase in body tension; and irregular patterns of inhalations and exhalations.

Emotional Symptoms and Stuttering

Fear and anxiety are **emotional symptoms** associated with stuttering. Many people experience some level of fear and anxiety related to speaking in front of a group, but children who stutter often experience high levels of fear and anxiety related to all speaking situations, especially ones that occur with newer or unfamiliar people (e.g., ordering at a restaurant, calling a store to ask about store hours, introducing oneself). Along with their own feelings interfering with speech production, the reactions of those around them may also increase the anxiety of children who stutter. Negative interactions or comments may inhibit a child's future attempts to interact verbally with another person or in a group setting. Consider also the potential **social challenges** associated with entering a classroom for the first time, transitioning to middle/high school/college, beginning a job, dating, and so on. Not surprisingly, just as avoiding production of a perceived sound or word is common, *avoidance* of situations and people is a common way of coping with the anxiety created by the fear of stuttering. These avoidance behaviors indicate a need for intervention.

Differential Diagnosis

Although many dysfluencies are often referred to as stuttering, it is important to recognize that there are different types of fluency disorders. Cluttering is a fluency disorder that may occur with or separate from stuttering but is different in form and cause. Stuttering and cluttering have been identified to exist on a continuum. Unlike stuttering, for which distinct episodes can be identified and even counted, **cluttering** affects the entire speech output and is often diagnosed around age 7 years or later. In addition to elevated repetitions of partial words (as in stuttering), whole words, and phrases, those who clutter show speech bursts that are often choppy, and articulation can be slurred and imprecise. In addition, there is often an increase in disorganization of their language, unusual prosody, and listener perception of a fast rate of talking. The level of awareness of how their speech affects those listening, unlike children who stutter, is minimal for those who clutter. In fact, children with a cluttering disorder often experience a decrease in their dysfluent behaviors when they are speaking in front of a group because of an increased focus on their speech, whereas the impact for children who stutter is exactly the opposite.

In addition to cluttering, neurogenic (result of a stroke, head trauma, or other neurologic damage) and psychogenic (associated with psychologic trauma) stuttering also exist, though they rarely occur in childhood. Stuttering can also be confused with dysfluent speech that occurs for other neurologic reasons (e.g., Tourette syndrome, cerebral palsy, spasmodic dysphonia).

Epidemiology

Approximately 5% of children experience stuttering, with the highest rates among young children. Seldom does a child begin stuttering before 2 years of age or after 12 years; in fact, the mean age of onset is 2-4 years, and most children stop stuttering within 4 years of onset. Symptoms will disappear within 4 weeks for a minority of children. Stuttering is more common in males than in females, and the magnitude of the difference increases as children get older. The ratio among children <5 years is approximately 2:1 and jumps to 4:1 among adolescents and young adults.

Genetics

There is convergent evidence of a genetic link for childhood-onset fluency disorder. Concordance rates among monozygotic twins range from 20% to 83%, and for dizygotic twins, 4–19%. Family aggregation studies suggest increased incidence of approximately 15% among first-degree relatives of those affected, three times higher than the 5% rate for the general population. The variance in risk for stuttering attributed to genetic effects is high, ranging from 70% to 85%. Although evidence is limited, stuttering appears to be a polygenic condition, and several genes increase susceptibility.

Brain Structure and Function

Brain structure and function abnormalities found among individuals who stutter include deficits in white matter in the left hemisphere, overactivity in the right cortical region, and underactivity in the auditory cortex. Abnormal basal ganglia activation has also been identified.

EVALUATION

Comorbidities

Despite the widely held belief in a high degree of comorbidity between childhood-onset fluency disorder and other communication disorders, research to date does not necessarily support this association. SLPs consistently report high rates of comorbidity, although this would be expected in clinical samples. Speech sound (phonologic) disorders are the most commonly reported comorbidities, occurring in 30–40% of children seen by SLPs. However, studies have not found greater incidence of phonologic disorders among those who stutter compared to a control group. Similarly, SLPs report a much higher percentage of children with language disorders among their patients who stutter than the approximately 7% expected in the population at large, yet studies find the language functioning among individuals who stutter is no different than in the general population. The same pattern holds for learning disorders (LDs).

Children who stutter seem to experience more anxiety than their nonstuttering peers, although research is limited. The frequency of reported anxiety increases with age. Social anxiety and generalized anxiety disorder are common among adolescents who stutter. Although one should not assume that an individual who stutters will have an increased risk for any specific psychiatric disorder, assessing for anxiety is important, as children who stutter frequently avoid situations that demand speaking, as discussed earlier in the chapter.

Children who stutter have consistently been found to be bullied more than peers. In one study, these children were almost four times more likely to be bullied than their nonstuttering counterparts. About 45% of children who stuttered reported having been the victim of bullying.

Referral to Speech and Language Pathology

In deciding who to refer to an SLP, it is important to distinguish developmental dysfluencies from stuttering. In addition to the risks noted in Table 52.5, indications for referral include three or more dysfluencies per 100 syllables (b-b-but; th-th-the; you, you, you), secondary characteristics denoting escape or avoidance behaviors (pauses, head nod, blinking), discomfort or anxiety while speaking, family history of stuttering or other speech-language disorders, and suspicion of an associated neurologic or psychotic disorder. Most children with persistent stuttering after age 4 years should be evaluated by an SLP.

As a part of the evaluation, the SLPs will be able to address the many pressing concerns and worries of a parent whose child is stuttering. The outcome of a speech-language evaluation for stuttering should accomplish the following:

1. Obtain a strong family history related to the existence of speech and language disorders in general and more specifically related to stuttering and dysfluencies.
2. Interview the parent or child about the child's stress when speaking in various situations.
3. Record a speech sample to analyze the type, frequency, and complexity of the dysfluent behaviors and secondary characteristics that the child is producing.
4. Differentiate between developmental dysfluency behaviors, other causes of dysfluent behaviors, and a child-onset dysfluency disorder (aka stuttering).
5. Develop a plan with the family that involves a combination of direct and indirect speech and language therapy, parent education, and home programming.

TREATMENT

A true stuttering disorder is a lifelong condition. To date, no evidence supports the use of a pharmacologic agent to treat stuttering in children and adolescents, and there is no cure for stuttering. However, treatment in preschool-age children has been shown to improve stuttering. In fact, speech-language therapy is most effective when initiated during the preschool period. The broad focus of therapy allows for minimizing the adverse effects of the condition.

Based on the child's age, types and frequency of stuttered behaviors, severity of secondary characteristics, and impact on the child's qualify of life, the SLP will decide if a less direct or more direct therapeutic intervention is recommended.

Less direct therapy focuses on manipulating the situation and environment while allowing the child to experience increased fluency. Most preschool children respond to interventions taught by SLPs that are accompanied by behavioral feedback strategies implemented by parents and teachers. It is important to recognize that parental pressure or speaking pressure does not cause stuttering. A less direct therapy approach involves working with the caregiver to accomplish the following:

1. Limit situations and expectations that cause increased dysfluencies and stress
2. Demonstrate and model how to adjust speaking rate and complexity of language rather than reprimanding children for their speech errors or asking them to slow down
3. Increase opportunities for the child to experience fluent communication

More direct therapy is recommended and implemented when less direct therapy did not have an impact on the stuttering behaviors, the child has increasing worries related to stuttering, the child has a high risk of continuing to stutter, or the child is older and has been stuttering for some time. One of the overarching goals of the therapy implemented by an SLP is to help the child experience increased fluency and strategies to learn how to "stutter" better.

Therapy that is more direct adds the following elements:

1. Awareness and education: Recognizing and accepting that their speech is different, identifying and naming types of speech, nonjudgmentally noting episodes of stuttering using selected words and phrases (which are often accompanied by pictures) that were developed with and practiced by the child ("That was a bit bumpy"), appreciating others' reaction to the child when stuttering, managing secondary behaviors, admitting they are a person who stutters, and addressing avoidance behaviors as a result of the stress and anxiety they are experiencing.
2. Fluency-shaping behaviors: Regulating rate of speech and breathing and helping the child gradually progress from the fluent production of syllables to more complex sentences. The child should be involved in opportunities to identify speech disfluencies, implement self-correction, and respond to requests ("Can you say that again?").

Because stuttering rarely disappears, the thrust of therapy is often to "improve" the type of stuttering, decrease the occurrences of stuttering, and develop strategies for coping with the fear and anxiety that will continue to occur in various speaking opportunities.

Appreciating that dysfluency is a broad term and stuttering can be one of the causes for this behavior allows pediatricians to have a more accurate understanding of the symptoms, causes, and treatments associated with dysfluencies. Being armed with this information allows the provider to include in their referral to an SLP an accurate description of symptomology, which will be beneficial in the planning and execution of their initial evaluation.

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Chapter 54

Augmentative and Alternative Communication

Michelle M. Macias

Children must develop communicative competence to interact with others, to influence their environment, and to participate fully in society. If children are not able to effectively communicate, they will have minimal means to express what they need, exchange information with others, and develop social skills and relationships. Some children are unable to communicate effectively through natural means, including speech, gestures, or writing (see Chapter 53). These children with **complex communication needs (CCNs)** have more independent function through **augmentative and alternative communication (AAC)** methods to meet their communication needs and to avoid significant restrictions on their participation in all aspects of life.

AAC interventions have been helpful for individuals with no speech, limited speech, and those at risk for speech-language disorders; this includes individuals who rely on speech but need augmentation to enhance speech, those recovering from a traumatic brain injury, and those who may have temporary conditions affecting communication. AAC has changed from an emphasis on providing the means to express needs and wants to the recognition that communication must also foster exchange of information, development of social relationships, and participation in social routines. In addition, there is recognition that communication needs extend beyond face-to-face interactions and also include written communication in the school setting and even social media in peer communities.

DEFINITIONS

According to the American Speech-Language-Hearing Association (ASHA), AAC is "an area of clinical practice that addresses the needs of individuals with significant and complex communication disorders characterized by impairments in speech-language production and/or comprehension, including spoken and written modes of communication." AAC encompasses the communication methods used to supplement or replace speech or writing for those with impairments in the production or comprehension of spoken or written language. In pediatrics, AAC is used by youth with a wide range of speech and language impairments, including cerebral palsy (CP), traumatic brain injury, intellectual disabilities, autism spectrum disorder (ASD), and apraxia of speech. In addition, children and adolescents hospitalized in intensive care units can benefit from AAC.

AAC is **augmentative** when used to supplement existing speech and **alternative** when used in place of speech that is absent or not functional. AAC uses a wide variety of electronic and nonelectronic techniques from low technology to high technology, including manual signs, gestures, tangible objects, line drawings, picture communication boards and letter boards, and speech-generating devices. The term **assistive technology (AT)** is a more general term describing systems and devices that alleviate the effects of a disability and improve function, for example, bracing for a child with a neuromotor impairment as well as AAC.

Prevalence

Across countries, the overall prevalence of AAC use ranges from approximately 1.2% to 1.5% of the population; worldwide up to 0.6% of the school-age population has a severe speech impairment. A national survey of U.S. special educators reported that approximately 18% of students served in special education use a form of AAC for communication, with 7% using gestural modes, 6.5% using pictorial supports, and 4.8% using a speech-generating device (SGD). However, not all U.S. children with developmental disabilities or children with special healthcare needs have their communication needs met. The more severe a child's communication deficit, the more likely the child would benefit from AAC support.

Across particular pediatric populations, it has been estimated that 25–50% of children with ASD have limited speech and would benefit from AAC. Up to 45% of children with CP use AAC either exclusively or to supplement speech. Several studies have found that in intensive care units ~30% of patients had communication breakdowns and met AAC candidacy criteria, although alternative communication modes were rarely used.

Goals of Communicative Interactions and AAC Interventions

The ultimate goal of AAC is to enable individuals to effectively engage in interactions and participate in activities of their choosing. Broadly speaking, the goals of AAC interventions are to assist individuals with meeting their current communication needs and prepare them to meet their future communication needs. Communicative interactions can be said to fulfill four purposes: (1) communicate needs/wants, (2) transfer information, (3) social closeness, and (4) social etiquette. It is important to remember that adequacy of communication depends on the personal goals of the person using AAC, and the definition of success may vary by the professionals involved.

Most children with complex communication needs demonstrate some ability to communicate using speech, although some are entirely nonverbal. The effectiveness of natural speech for communication can be divided into 10 levels (Meaningful Use of Speech Scale; Robbins & Osberger):

1. Makes vocal sounds in communicative exchanges
2. Gets another person's attention using speech
3. Uses various vocal sounds depending on the intention and content of messages

Uses speech for communication about:

1. Known topics with familiar people
2. Known topics with unfamiliar people
3. New topics with familiar people
4. New topics with unfamiliar people
5. Messages that are understood by familiar people
6. Messages that are understood by unfamiliar people
7. Clarification messages as needed when communication breakdown occurs

AAC Systems

An "**AAC system**" refers to the integrated group of components used to support and enhance communication. These components include the specific forms of AAC, selection techniques, and strategies for use.

Individuals with complex communication needs must have access to a wide range of means to enhance their communication and participate fully within social and educational contexts. This may include **unaided AAC**, which does not require an external tool and requires some degree of motor control (e.g., gestures, sign language, finger spelling, speech approximations), or **aided AAC**, which requires either an electronic or a nonelectronic tool. Nonelectronic aided forms are referred to as **low-tech aided AAC** and include options such as communication boards/books, picture-exchange communication systems (PE or PECS, pictures, photographs), or visual schedules. Electronic forms are referred to as **mid-tech or high-tech AAC** systems and include traditional speech-generating devices (SGDs) or voice output communication aids (VOCAs), recordable devices, and computer/tablet options and applications ("apps"). SGDs/VOCAs include multiple options. **Single-level devices** have pictures/words on a single-level display, whereas **multilevel devices** can have vocabulary programmed on more than one level. **Static display devices** keep the same display, and the user can sequence symbols or words to generate a message. **Dynamic display devices** are usually those with a touch screen for the display in which pages can change using navigation keys and link buttons. **Text-to-speech devices** enable the user to spell messages that convert to synthesized speech. Some dynamic display devices include text-to-speech

Table 54.1 Types of Augmentative and Alternative Communication

	LOW TECH	MID-HIGH TECH
Unaided	• Sign language • Gestures	—
Aided	• Communication boards/books • Picture exchange systems • Visual schedules • Eye-gaze picture board • Simple single-message speech output devices	• Voice output communication aids (VOCAs)/speech-generating devices (SGDs) with prestored recordings of natural speech or computer-generated speech • Specialized software on electronic tablet, smartphone • Spelling and/or symbol systems to represent language

Unaided systems: Do not require special materials or equipment; rely on user's body to covey messages.
Aided systems: Require the use of tools or equipment; can require power or no power.

and use symbols as well as text. Table 54.1 provides examples of the range of AAC systems.

Mobile technology (e.g., iPad) and greater use of social media tools have increased acceptance of AAC and reduced attitudinal barriers to AAC use. However, the increased diversity of communication tools also means increased operational demands, given that each tool is designed with different representations, organizations, and layouts of information as well as different access techniques (e.g., swiping, tapping). Each design may reflect different motor, cognitive, perceptual, and linguistic learning demands. A combination of gestures/signs, low-technology systems, mobile technology devices, and SGDs can provide AAC users with the most effective communication options to suit their needs.

AAC Teams

AAC teams serving individuals with CCNs are the groups of people that guide the AAC intervention decision-making process and implement communication supports. Team members include the children and adolescents with CCN themselves, parents/caregivers, and professionals playing a variety of roles.

Children with CCN. The most important member of the team is the individual relying on AAC techniques. The role may change in response to the individual's maturation and capability, but to the extent possible, the child or adolescent should participate in the decision-making process regarding goals, social relationships, and support options related to the AAC system and interventions.

AAC facilitators. The term *facilitator* refers to parents/family members, friends, professionals, and frequent communication partners who assume some responsibility for keeping the AAC system operational and/or supporting the person with CCN to use it effectively. They support communication interactions by coaching, serving as interpreters, and/or helping resolve communication breakdowns. Importantly, the role of facilitator is to support independent communication by the individual with CCN, not to communicate *for* the individual.

AAC specialists. AAC specialists provide direct AAC intervention services by instructing and educating about AAC and designing and implementing AAC interventions. AAC specialists work with clinicians and educators, such as speech-language pathologists, occupational therapists, teachers, and pediatric healthcare providers who provide clinical and educational services to youth with CCN.

AAC Assessment

AAC assessment involves gathering information so that informed decisions can be made about the adequacy of current communication, the communication needs, the AAC techniques that are most appropriate, how to provide instruction in AAC techniques, and how to evaluate outcomes. Proper evaluation and support for the use of AAC devices are of paramount importance.

Studies comparing acquisition of communication skills reveal few differences in terms of how quickly many children can learn to use some of the available AAC options. For example, PEC and sign language comparison studies vary—some show PECs were acquired more easily than signing, and others suggest both PECs and signing were acquired at an equal pace. Studies comparing PECs with SGDs similarly vary in terms of effectiveness of device use.

Physicians, therapists, and other professionals who prescribe AAC must make sure the child (and family) receives training and monitoring for using the device and that the device is accessible across settings in which the child functions (e.g., home, school, community activities). A substantial number of AAC devices are abandoned shortly after implementation without support for their use. AAC assessment and intervention is a dynamic process, and usually ongoing, as often the children and adolescents requiring the AAC system are unable to speak or write because of physical, cognitive, language, and/or sensory impairments. Assessment generally consists of four phases as outlined here:

Phase 1: Referral. The "finder" role is an important role for pediatric healthcare providers. They may be the impetus for recognizing that a child has a CCN and that an AAC intervention may be helpful. They then assist the patient and their family by initiating a referral to an appropriate resource. The pediatric provider can support the AAC funding application by certifying a medical diagnosis and signing a prescription for the recommended service. Although the role is episodic, it is nonetheless a key role in the AAC assessment and treatment process.

Phase 2: Initial Assessment. The goal of this phase is to gather information to design an AAC intervention to match the child's existing needs and capabilities. The AAC specialist(s) assesses the child's current communication interaction needs and his or her physical, cognitive, language, and sensory abilities. This typically focuses on enabling communicative interactions between the child and familiar AAC facilitators. The intervention is refined as the child learns about the operational requirements of the AAC system and the AAC team gathers information on how well the system works for the child. Demonstrations and simulators are available to help with training before the actual equipment is ordered.

Phase 3: Assessment for Other Settings. The goal is to develop a solid communication system that supports the child with CCN in a variety of environments, including home, school, and recreational environments. A child must have access to a system that allows educational and social participation.

Phase 4: Follow-Up Assessment. This involves maintaining a comprehensive AAC system that accommodates the child's changing capabilities. The communication equipment must be examined regularly to assess the needs of new communication partners, detect replacement/repair needs, and reassess the child's capabilities as they change.

Specific Assessment Details

Assess Current Communication. The initial step is to assess the effectiveness of the child's current communication system. The assessment of communication access focuses on the operational and social aspects of communicative competence. A child with spastic quadriplegia, for example, may be unable to use eye gaze consistently and therefore operationally unable to use an eye-gaze AAC system. On the other hand, a minimally verbal adolescent with ASD may be able to operate an electronic AAC device but never use it to initiate a social interaction.

Some questions to ask regarding current communication behaviors in children with CCN include the following:

- What are the various methods your child uses to communicate? Examples: words/speech, vocalizations, gestures, signing, communication board, eye gaze, typing, and so on.
- What body part is used for each technique (e.g., left/right hand, eyes)?
- On a scale of 1 to 5, how accurately and efficiently is your child able to use this technique?
- On a scale of 1 to 5, how well is your child able to use this technique in an interactive, socially appropriate manner?

Screening Tools. Various screening instruments exist that help document communication behaviors. These include the Communication Matrix; the Inventory of Potential Communicative Acts (IPCA); and the Social Communication, Emotional Regulation, Transactional Support (SCERTS) Model Assessment, among others. The Communication Matrix focuses on individuals using any form of communication (presymbolic or AAC), and the IPCA focuses primarily on presymbolic communicators with physical and/or developmental disabilities. The SCERTS Model Assessment focuses on communication and social regulation behaviors in verbal and nonverbal children with ASD.

Assess Potential to Use or Increase Speech. A key issue in AAC assessment for children with CCN is whether AAC is needed to augment insufficient speech or serve as a replacement for speech. Parents are often concerned that using an AAC device will negatively affect speech development, as the child will have access to an "easier" alternative. The use of AAC techniques does not inhibit natural speech; conversely, AAC may enhance spoken language by supporting the development of communicative competence and language skills.

Assess Potential for Environmental Adaptations. Modifications of physical spaces or structures may be relatively straightforward or more complex, depending on the specific situation. For example, at home, furniture rearrangement or renovations to adapt the home to accommodate AAC devices may be necessary. In the school, desks/tables may need to be raised/lowered or a vertical workspace may need to be created with a slanted board.

Specific Issues Regarding AAC for Children with Disabilities

Cerebral Palsy

Communication impairments are commonly seen in children with CP, both related to impaired (motor) speech intelligibility and language disorders (see Chapter 638.1). The incidence of dysarthria varies depending on the type of CP and degree of motor impairment. Language impairments are associated with intellectual functioning and hearing loss, if present.

More than any other disability, communication interventions for children with CP require a multidisciplinary team approach. The wide variety of motor impairments entails the involvement of occupational and physical therapists, orthotics specialists, rehabilitation engineers, and speech-language pathologists. Positioning and seating adaptations may need to be developed for optimum stability and to allow efficient movement to access the AAC system. The team must consider the wide range of options available and what is necessary to optimally match the child with the system being used. Although up to half of children with CP may be able to access the AAC device through use of a finger, others will need alternative access techniques, including chin pointers, joysticks, optical indicators, or switches.

Emphasis on AAC needs to be balanced with other developmental interventions, including speech-language therapy, motor development training, and academic instruction. Some will require extensive motor training to be able to use alternative access methods such as eye tracker, head mouse, or a switch for scanning. Although speech, gestures, and facial expressions may be affected as a result of motor impairment, patients should still be encouraged in using these natural modes for communication. A balanced approach supports the use of multimodal systems, which can vary according to the situation. A child with CP may be able to communicate effectively with family members using natural speech and gestures but may need to rely on AAC techniques with unfamiliar partners.

Long-term planning for adulthood is essential, given the need to rely on AAC devices and techniques that can accommodate the range of demands that are communicative in nature, including interpersonal, academic, and employment demands. Without advance planning, AAC systems are unlikely to meet all these demands, or the individual will not have all the skills required to use the systems.

Intellectual Disability

As defined by the American Association on Intellectual and Developmental Disabilities (AAIDD), intellectual disability (ID; see Chapter 57) is characterized by "significant limitations both in intellectual functioning and adaptive behavior as expressed in conceptual, social, and practical skills." Appropriate supports, including AAC supports, can have a significant impact on the ability of individuals with ID to live and learn successfully in inclusive environments typical of their same-age peers. At least 30% of school-age individuals requiring AAC supports have an ID. One of the main barriers that exists for children with ID is simply recognizing that the use of AAC can be beneficial and that AAC use should be generalized across settings and not just used in highly structured settings such as school.

Although most youth with ID do not engage in socially inappropriate behaviors, problem behaviors occur more frequently in this population compared to those without ID. Many individuals with ID do not use speech as their primary mode of communication, and problem behaviors can be exacerbated by difficulty communicating. Many of the strategies used to support individuals with ID involve AAC strategies such as visual schedules or those used to teach choice making and functional communication training.

The nature of interventions directed at both natural speech development and AAC varies considerably given the diversity of syndromes and conditions that result in ID. Many individuals with ID may have multiple diagnoses that affect the nature of their intervention needs.

Autism Spectrum Disorder

ASD (see Chapter 58) is a highly variable disorder; individuals with ASD experience a wide range of complex issues related to language and communication, which presents challenges regarding speech-based and AAC interventions. Individuals with ASD *and* ID may require more extensive educational, behavioral, and community supports compared with those without ID, but those without ID still require supports in the core area of social communication. **Language forms** are the language structures and vocabulary (e.g., grammar, syntax). **Language function** refers to what individuals do with language as they engage and interact with others. Because ASD affects the nature of communication as a social mediator, it is important that AAC interventions emphasize the function, or pragmatic aspects of communication, as well as the communication aspects related to the form of language.

Interventions must start at the individual's level of social, communicative, and cognitive development and build skills in a natural developmental progression. The development of dynamic, interactive communication is critical, and the child with ASD needs to learn to use communication skills related to functional activities in daily life. The developmental profiles of youth with ASD are often characterized by an uneven distribution of skills. Children with ASD often perform much better with object permanence and tool use (causality) than those areas requiring interpersonal interaction, such as gestural or vocal imitation, symbolic understanding, or language comprehension. Therefore AAC interventions must be geared to the child's social and linguistic abilities rather than the child's object abilities (e.g., fine motor skills or object manipulation skills). Manual sign or pictorial systems (PECS) are often recommended for nonverbal children with ASD. This often presumes that the problem is only one of output and that communicative intent is intact; however, the child may not have the language or the social base on which communication must be built. Therefore interventions should initially build imitation, joint attention, and natural gestural communication skills before initiating formal language-based AAC or speech approaches.

SGDs and other speech-output technologies can be used effectively in children with ASD to teach both communication and literacy skills. SGDs can act as a "social bridge" to familiar and unfamiliar communicative partners. They can be programmed with whole messages (e.g., "do you want to play") in addition to single words and phrases and thereby increase communicative efficiency and decrease potential communication breakdowns. These output devices are available via touch-screen tablet and mobile devices.

Childhood Apraxia of Speech

ASHA defines childhood apraxia of speech (CAS) as a neurologic speech-sound disorder "in which the precision and consistency of movements underlying speech are impaired in the absence of neuromuscular deficits." Given consensus on diagnostic criteria is lacking, ASHA recommends that the term "suspected CAS" be used. There is consensus on motor speech behaviors in three areas: (1) inconsistent errors on consonants and vowels in repeated syllables or words; (2) lengthened, disrupted transitions between sounds and syllables; and (3) inappropriate prosody of speech (see Chapter 53).

Given CAS is primarily a motor speech disorder, AAC is usually a secondary intervention, with the primary intervention focused on improving natural speech production. Because children with CAS often evidence significant language delays related to the inability to practice language, it is important to provide them with AAC modalities early on. The use of AAC will not inhibit speech development and production, and generally use of AAC supports result in increased mean length of utterances for the child.

Children with suspected CAS who benefit from traditional AAC are those who primarily speak in single words, have largely unintelligible speech, and are not able to effectively communicate with family members, peers, and teachers. The children benefit from a wide range of AAC, from unaided techniques including gestures and signs and aided techniques such as PECS communication books and/or SGD. It is important that the AAC device facilitates both language development and social competence. The AAC system should be designed so that the child learns to create longer and more complex messages that are grammatically accurate.

Children with suspected CAS who can produce single-word utterances but struggle with multiword speech often benefit from AAC speech supplementation. This supplementation may be in the form of key symbol supplementation, in which they point to key symbols in conjunction with speech. This can help with topic setting—when the child introduces a new topic of conversation, they point to a symbol, which helps narrow the range of possibilities for the communication partner. Often children with suspected CAS prefer to use natural speech and unaided approaches, using aided AAC techniques only when communication breakdown occurs.

Special Considerations

Reimbursement and Funding. The AAC specialist (usually a speech-language pathologist) should be familiar with public and private funding options. Funding can come from schools, third-party payers (private or public insurance companies), or philanthropic sources. Low-tech AAC systems are usually developed by a speech-language pathologist and do not usually require additional funding. SGDs are considered durable medical equipment (DME), and funding can vary immensely. Coverage will need to be verified based on the patient's specific needs and insurance. Pediatric care providers are often asked to sign prescriptions and/or write letters of medical necessity for an AAC device. This should be done only after conferring with the AAC team members, especially the speech-language pathologist. The letter should include that the pediatric provider received the evaluation reports, reviewed the recommendations, and agrees that the recommended AAC devices are medically necessary for treatment of the child's CCN associated with the specific diagnosis. SGD vendors are often able to assist with funding questions.

The Assistive Technology Act. The Assistive Technology Act of 2004 provides all U.S. states and territories with federal funding to increase access to AT devices and services. This information can be found at the National Assistive Technology Act Technical Assistance and training (AT3) Center (https://www.at3center.net/stateprogram).

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Chapter 55

Outcomes Among Infants and Children Who Are Deaf/Hard of Hearing

Susan E. Wiley and Rachel D. St. John

See also Chapter 677.

Approximately 3 in every 1,000 infants in the United States are *born* deaf or hard of hearing (D/HH). Additionally, for infants who pass the newborn hearing screening, there are a number of risk factors for developing *delayed-onset* hearing loss at any time during infancy and childhood. Given that the large majority of deaf infants are born to hearing parents, there is the potential for a developmental crisis when an infant or child does not have an accessible shared language in common with their parents.

Acquisition of one's first language is a phenomenon of early development (see Chapter 53). The first months and years of a child's life are critical to developing an intact native language. When the process of language acquisition is delayed or fragmented, as can happen with an infant who is D/HH, it can have a significant and permanent effect on overall lifetime cognitive development. Timely identification and support of infants and children who are D/HH, including the provision of early access to language, is critical to the lifetime trajectory of outcomes, including language, pragmatics, academic success, executive functioning, and psychosocial well-being.

DEAF CULTURE

It is important to recognize that we as authors do not speak for Deaf individuals or parents of D/HH children but seek to bring awareness of some fundamental norms as a starting point for increasing familiarity and collaboration with these groups. Readers are encouraged to explore the resources cited in this chapter, as well as information provided by Deaf individuals and parents of D/HH children themselves.

Among individuals in America who are D/HH, there is a subset who self-designate as culturally Deaf (intentionally spelled with an uppercase D) who share American Sign Language (ASL) as their primary means of communication and a set of beliefs and traditions that are transmitted across generations. In the United States, the National Association of the Deaf is the organizational body that supports and represents this cultural Deaf community, with a mission "to preserve, protect and promote the civil, human and linguistic rights of deaf and hard of hearing people in the United States of America."

There is a potential conflict between the "hearing" medical community and the culturally Deaf community, with the medical community traditionally operating from a pathology model (identify and fix the problem) and the Deaf community operating from a sociocultural one (there is no problem in need of fixing). Hearing parents and professionals whose societal existence is grounded in listening and spoken language often view being D/HH as a limitation to interpersonal connection, education, and vocation. Deaf individuals, who achieve virtually all the same milestones as hearing individuals do by using a visual language medium, do not view being D/HH as a loss. Among culturally Deaf individuals, the terms "hearing loss" and "hearing impaired" are often viewed as inaccurate and potentially offensive. For those who were born deaf, the experience of hearing is something they never had and therefore have never missed. It is not something that holds them back, but instead is a source of maintaining a positive self-identity and pride in one's culture and community.

Hearing clinicians caring for deaf infants and children or members of the Deaf community must practice with the cultural humility necessary to appreciate the perspectives of the Deaf community (see Chapter 2).

Table 55.1 Common False Assumption About Deaf or Hard of Hearing (D/HH) Infants and Children

FALSE ASSUMPTION	ALTERNATIVE APPROACH
Being D/HH causes language delay.	Often, the parent and deaf infant do not share a common language, creating a language barrier leading to delays. Early identification (by 1-3 mo of age) and intervention by 6 mo of age are critical for language development.
Passing newborn hearing screening tests means one does not need to be concerned about hearing.	Many factors can cause delayed-onset hearing loss. A full audiologic evaluation is indicated for any caregiver concern about hearing or for delays in language development—a "wait and see" approach is never indicated.
All behavioral symptoms or developmental delays are caused by the hearing loss.	Young neurotypical deaf children with adequate access to language through amplification and spoken language, sign language, or both should not be expected to have challenges in development, behavior, or social engagement. Referral for evaluation is essential if these symptoms are present.
Sign language is a last resort for communication for D/HH infants or children.	American Sign Language (ASL) is a full and complex language with a clear syntax and grammar structure. Learning sign language can promote language development when children cannot access spoken language during a period when this input is critical for cortical brain development.

Including access to Deaf individuals as part of healthcare teams involved in the care of D/HH infants and children is an important first step in including this cultural perspective in health service delivery and decision-making.

It is also important to recognize the concept of **intersectionality** (the interconnected nature of social categorizations such as race, ethnicity, class, and gender), which plays a role in the Deaf community. Being Deaf and Black is not just the sum of the experiences of Deaf individuals and Black individuals—the two constructs existing simultaneously in the same person makes for a unique life experience. Intersectionality is recognized within the context of the **Deaf Plus** community because those individuals do not simply experience life as a Deaf person who also happens to have an additional condition. The interplay of these aspects of individuals is a critical part of identity formation, self-esteem, cultural engagement, potential experiences of disadvantage/discrimination, and personhood in general.

EARLY DETECTION AND LANGUAGE DEVELOPMENT

Deaf children who are born to deaf/signing parents are natively exposed to sign language from the first day of life and subsequently can be expected to acquire sign language milestones in a predictable manner similar to typically developing hearing children acquiring spoken language milestones. Deaf children of signing parents achieve their first signs, vocabulary expansion, combining of two discrete sign concepts, progression to more complex phrases and sentences, and other language-related milestones at expected ages if assessed in sign language. However, more than 90% of deaf infants are born to hearing parents who most often do not sign fluently. This creates an immediate and significant loss of a shared intact language. Families will turn to professionals for advice on making decisions regarding language, education, amplification technology, and social engagement. Sometimes these clinicians make false assumptions that delay detection or intervention for children who are D/HH (Table 55.1).

Clinicians should be aware that although language delay may be a presenting symptom in a D/HH child, being deaf in and of itself does not inherently cause delayed language development. Rather, the inability for a parent and an infant to share a common accessible language creates a barrier to the development of language. This is why early identification and support are critical for D/HH infants to support language access, whether to spoken language through amplification and therapy or access to sign language (or both). Even children who have passed their newborn hearing screening who have language delays must have a full audiologic evaluation, as a substantial number of factors can contribute to delayed-onset hearing loss (DOHL) at any time during early, middle, or late childhood. Parental concern about language delay or responsiveness of their child is a sensitive, but not specific, indicator of possible hearing loss. It is important to respond to parental concerns of hearing or language with referrals for hearing assessment, language evaluation, and age-appropriate therapeutic support systems.

Clinicians should also consider the possibility of hearing loss in young children with other behavioral changes. An older child may report a sudden dramatic hearing loss. However, younger children may not have the linguistic capacity or awareness to describe loss of hearing and may present instead with changes in behavior (being upset, aggressive, withdrawn). Some children with a progressive or sudden change in hearing status may appear to have a behavioral condition such as attention-deficit/hyperactivity disorder (ADHD) or may be described as defiant. Children with unidentified hearing changes and children with ADHD can share behaviors—they are perceived as not paying attention, they often are not aware of what is happening in the moment, they may not respond as expected when being addressed, and they may not focus on the things that are being discussed.

Another problematic issue known as **diagnostic overshadowing** can occur when all developmental or behavioral challenges are attributed to one cause (in this case, hearing status) when the symptoms should suggest the possibility of another disorder. For example young neurotypical D/HH children who have adequate access to language (through amplification technology and spoken language, sign language, or a combination of both) should not automatically be expected to have substantial challenges with language development, behavior, and social engagement. If clinicians reflexively attribute delays in social and language development to the fact that the child is D/HH, they may miss the diagnosis of a developmental disorder when they would not have missed the diagnosis in a hearing child.

Sign language has many benefits for D/HH infants and children and should not be regarded as an inferior last resort only to be used if spoken language efforts are not successful. ASL is a full and complex language. Much of the grammatical structure and concept complexity in ASL is conveyed through spatial placement of signs and body movements. Body movements can include body lean and eyebrow shift to indicate a question, furrowing of the brow and pursing of lips to convey negation, and shifting of body position in space to define multiple individuals involved in conversation, to name a few.

The active discouragement of using visual language with any D/HH child is a developmental disservice, particularly so with the profoundly deaf infant whose hearing level is too low to benefit from traditional hearing aids. For these infants, a cochlear implant is likely the only potential route for accessing spoken language input, and the earliest that the Food and Drug Administration (FDA) currently approves cochlear implantation is 9 months of age. There remains a number of children who are not achieving such early ages of cochlear implantation. Lack of access to sign language can mean up to a year or more of complete lack of accessible linguistic input during a period of cortical development when language input is critical; that lack of language input can in turn affect infant bonding with parents. Even after cochlear implantation, it takes a substantial amount of therapy (auditory-verbal/listening and speech-language therapy) to build spoken language skills.

INTERVENTIONS

Supporting children who are D/HH requires a combination of a proactive approach to care, ongoing monitoring for delays in all developmental domains, and timely recognition and intervention of gaps that can occur because of the impact of hearing status on language and overall development.

There is a tendency, especially for those who are not familiar with D/HH children, to assume that a child who does not hear will have reduced developmental outcomes compared to their hearing peers. There is robust evidence supporting the importance of early identification and intervention for long-term outcomes in children who are D/HH. A child's developmental and learning potential should not be defined by their hearing; clinicians should encourage and support families' high expectations for a child's development regardless of hearing status.

The medical home can fill a critical role in supporting a family's journey, though often primary care providers have relatively few children who are D/HH in their practice and may not be well-versed in how to monitor the medical and psychosocial needs of a D/HH child. This prompts the need to seek out information from a variety of sources and link families with reputable information. Because D/HH is a low-incidence condition, it is challenging for one setting (early intervention–based, school-based, clinical-based) to include a variety of children and match appropriate communication approaches. Interventions can be categorized in a variety of ways. A framework for various communication approaches is commonly used for understanding how to support language development in children who are D/HH (Table 55.2), including technology and environmental modifications.

Communication Approaches

Often different approaches to communication are presented as a choice to make during the early years of critical language growth. Many communication approaches have passionate national organizations advocating for a specific approach (Table 55.3). The educational philosophy known as total communication is often misunderstood to mean using both signing and spoken language; however, it refers to incorporating an array of communication modalities (formal signs and fingerspelling, gestures, body language, lip reading, speaking, listening), with the goal of optimizing language development that is tailored to be most effective for the individual child.

We have chosen to refer to the national organizations and the Centers for Disease Control and Prevention (CDC) to guide definitions of communication approaches (see Table 55.2). Each approach has specific components needed for successful implementation and language outcomes. The overall goal to support communication development can be an unfolding journey. Choices and strategies that worked well for a child in early childhood may not be as effective as the child matures, particularly as social engagement and academic demands evolve with age and advancement in school. Thus it is important for families to recognize that communication needs can change over time, prompting a shift from a prior decision to an alternative approach.

Technology

Hearing Aids

Hearing aid technology is very refined. Hearing aids are essentially minicomputers that take sound from the environment and are programmed to adjust how this sound is processed and delivered to the ear. Hearing aids have a number of different features that can augment the quality of sound a child will hear. Hearing aids can analyze the sounds coming into the device and preferentially reduce background noise. They can compress sound waves to preferentially make soft sounds louder and try to avoid distortion of loud sounds (wide dynamic range compression). Hearing aids can have microphones that can receive sound from many directions or focus primarily on sounds coming from in front of a child. A hearing aid can also carry a variety of programs for different listening settings. This allows a child to have a different program for a quiet environment compared to a noisy environment. Technology can also include Bluetooth to link to other devices. There are a number of apps to help monitor battery life and adjust the program for the setting through the app. Follow-up care with audiology is important to ensure continued supports for any amplification used and to monitor for changes in hearing. For children with conductive hearing changes, **bone conduction aids** may be indicated. These devices bypass the outer and middle ear, conducting sound through the skull directly to the cochlea and auditory nerve. When children are 5 years or older, they can be considered for a surgically implanted bone conduction aid called a *bone-anchored hearing aid* (BAHA). These devices also have the capacity to link to a frequency modulation (FM) system.

It is helpful to remember that even with advancements in technology, what children hear with hearing aids is not the same as what people hear with a typically functioning auditory system. It is equally important to consider environmental supports to optimize

Table 55.2 Communication Approaches for Children Who Are Deaf and Hard of Hearing (D/HH)

COMMUNICATION MODALITY	DESCRIPTION	CITATION/ORGANIZATION
American Sign Language (ASL)	ASL is the recognized sign language of the deaf community in the United States. ASL conforms to linguistic principles and is distinct from English.	National Association of the Deaf (https://www.nad.org/about-us/position-statements/position-statement-on-american-sign-language)
Conceptually Accurate Signed English (CASE)	Using conventional ASL signs in an English word order.	https://www.cdc.gov/ncbddd/hearingloss/parentsguide/building/case.html
Manually coded English	Signing Exact English is an example of a manually coded English. It is a sign system that matches signs with the English language and includes manual representation of all components of the English language.	www.signingexactenglish.com
Fingerspelling/Rochester method	The Rochester method was intended to support English literacy and uses fingerspelling for all words.	
Cued Speech	Cued Speech is a visual communication system that uses eight handshapes in four different placements near the face in combination with the mouth movements of speech to make the sounds of spoken language look different from each other.	National Cued Speech Association (https://www.mdaap.org/pdf/CuedSpeech.pdf)
Spoken language and listening	Children learn to listen and talk with the support of hearing technology such as hearing aids, assistive listening devices (such as an FM system), or cochlear implants. Auditory-oral approaches include gestures, listening, speech/lip reading, and spoken speech. Auditory-verbal relies on listening and spoken speech.	Communication Options (https://www.agbell.org/Families/Communication-Options) Centers for Disease Control and Prevention: How People with Hearing Loss Learn Language (https://www.cdc.gov/ncbddd/hearingloss/language.html)

Table 55.3 Resources for Families and Professionals

NATIONAL ORGANIZATIONS: FAMILY SUPPORT	
Hand and Voices (www.handsandvoices.org)	Supports families and children without a platform providing a specific mode of communication.
National Association for the Deaf	Advocates for use of American Sign Language and represents the culturally Deaf community.
Alexander Graham Bell Association for the Deaf and Hard of Hearing (www.agbell.org)	Advocates for people who are D/HH to hear and use spoken language.
Beginnings (www.ncbegin.org)	Promotes language accessibility through cued speech (see Table 55.2).
American Society for Deaf Children (www.deafchildren.org)	
DEAF HISTORY AND CULTURE	
The National Association of the Deaf	https://www.nad.org/about-us/
Deaf Heritage: A Narrative History of Deaf America	This 1981 book by Jack Gannon, a Deaf author and historian, is often referred to as a canon of Deaf culture in the United States. The book covers a number of events throughout history, including the establishment of schools for the deaf and the inception of the National Association of the Deaf and explores topics such as American Sign Language, Deaf artists, Deaf sports, and seminal Deaf publications.
Through Deaf Eyes	A 2007 documentary covering close to 200 years of being Deaf in the United States in a 2-hour run time through a diversity of interviews, movie shorts, and stories that capture the events that have affected Deaf lives throughout American history (https://www.youtube.com/watch?v=PL5d8kyZUQk).
DEAF MENTORS	
The National Center for Hearing Assessment and Management	Houses a directory of D/HH adult involvement programs by state (https://www.infanthearing.org/dhhadultinvolvement/states/index.html)
SKI HI Deaf Mentor Program	Curriculum for infants and young children who are D/HH (http://www.deaf-mentor.skihi.org)
Hand and Voices Deaf and HH Mentor/Guide/Role Model Programs	https://handsandvoices.org/fl3/topics/dhh-involvement/programs.html
American Society for Deaf Children: Deaf ASL Ambassadors Program	https://deafchildren.org/knowledge-center/asl-resources/sign-on/
PRACTICE GUIDELINES	
American Academy of Pediatrics Early Hearing Detection and Intervention Program	https://www.aap.org/en/patient-care-pages-in-progress/early-hearing-detection-and-intervention/
EHDI National Technical Resource Center	https://www.infanthearing.org
The Joint Committee on Infant Hearing	www.jcih.org

listening environments. Contralateral routing of signal aids (CROS) can be helpful for children with unilateral profound deafness. This amplification system uses a transmitter at the ear that does not hear and routes it to a receiver on the typically hearing ear. Assisted listening devices such as FM systems are used to help address problems hearing in background noise and when speakers are farther away. This system has a small transmitter with a microphone. The speaker wears the transmitter, and this then links directly into headphones or a personal amplification system (hearing aid or cochlear implant). FM systems are traditionally used in the classroom setting, although they may be employed in other settings that tend to have competing background noise such as restaurants or when the focus on a particular individual speaking is important. The teacher may also use a transmitter with microphone that links to a number of speakers around the room (**soundfield system**). In this way, the accommodation is available to all students in the classroom, may benefit children easily distracted by background noise as well as the D/HH student, and does not single out the D/HH child alone.

Cochlear Implants

Cochlear implants are surgically implanted devices that bring direct electrical stimulation to the cochlea. These devices are FDA-approved for children 9 months and older with profound sensorineural hearing loss and in lesser degrees of hearing changes (70 dB or more) when children are not receiving adequate benefit from traditional amplification. A period of hearing aid trial is recommended before implantation. In children with hearing loss caused by meningitis, it is important to monitor for bony changes in the cochlea via imaging. Early signs of ossification would prompt earlier cochlear implantation to ensure the electrodes are in an optimal position to stimulate the auditory nerve. Even for children who are bilaterally profoundly deaf, there can be reasons that a cochlear implant is not appropriate. For example, absence of an auditory nerve would preclude pursuing an implant.

Often pediatric cochlear implant centers use a multidisciplinary approach to determining cochlear implant candidacy and to ensure strong follow-up support. In the past, children with developmental disabilities were deemed not appropriate for cochlear implantation, as results were thought to be limited. Although outcomes can vary in this group of children, a developmental disability alone does not preclude receiving benefit from the device. Ensuring global developmental supports, addressing potential expectations and outcomes, and linking children and families to resources can help children gain benefit from access to sound.

Coordination of care and follow-up is essential in all children with cochlear implants. They initially will see audiologists at frequent intervals to program the implant, and speech therapy is a critical and ongoing component of fostering success with an implant. At the age of 2 years, they should receive the 23-valent pneumococcal vaccine to ameliorate the increased risk of meningitis. The

medical home can play an important role in managing this additional immunization, as well as in monitoring medical issues and developmental progress.

Early implantation has been associated with better hearing, speech perception, and spoken language outcomes, as it ensures early stimulation of the auditory cortex necessary for the development of spoken language. Although FDA approval is for children 9 months and older, there are situations where earlier implantation is indicated, and many in the field of pediatric audiology and pediatric otology are advocating for earlier implantation. Unilateral deafness is another emerging indication for cochlear implantation in children.

Other Supports and Factors Influencing Amplification Decisions

The cost of amplification devices can be quite high. Many insurance plans do not cover hearing aids, though more cover costs associated with BAHAs and cochlear implants. Services and coverages vary by state and insurance plan. Families often need to obtain insurance or additional coverage to cover replacement costs associated with damage or loss of the device. Technology updates can also add further expenses.

There are also many day-to-day factors that affect a child's acceptance of amplification. In early childhood there is rapid growth of the skull and ear canal. With hearing aids, children often need to return to audiology frequently to resize the ear molds to ensure a good fit. Children also can become very adept at removing their hearing aids. Young children in daycare are particularly vulnerable to potentially losing their amplification when rolling, crawling, or playing or when naturally curious peers and playmates attempt to take them. Parents, caregivers, and teachers routinely checking on hearing aids/cochlear implants is a critical support to using amplification technology successfully in young children.

A number of environmental supports can be helpful. For families seeking a spoken language approach, it is helpful to decrease background sounds. Turning off TVs and devices can help children be able to listen and hear what is said. Children often struggle hearing speakers from a distance. This affects incidental learning, as they have fewer opportunities to "overhear" peripheral conversations. Families are often coached in ways to optimize their child's listening environment and ways to highlight spoken language and concepts.

Technologic support can include captioning on the television, video-relay with sign language interpreters, texting, speech-to-text, visual fire alarms, and vibrating alarms. These types of technologies are often not covered through insurance, although some state agencies have programs to help defray costs. Other accommodations for communication access can include sign language interpreters, cued speech interpreters, and open captioning. The Americans with Disabilities Act ensures children, adolescents, and adults have the legal right to communication access. This is particularly important in medical settings. Family members should not be asked to serve as interpreters for the child, as this limits the ability for the parent to listen and be part of the conversation or may limit the child's access to the conversation at hand.

LANGUAGE LEARNING

Language is a critical component of the human condition and allows connection with others. The United Nations has recognized communication as a human right. Communication happens in many ways that can include behavior, nonverbal communication, tone, facial expressions, words, and sentences. These aspects of communication are universal irrespective of mode of communication.

Promoting language development needs to focus on far more than the ear and hearing. As in typical children, the quality and quantity of communication are important (see Chapter 53). Additionally, children who are D/HH are at high risk of missing learning via "the unwritten curriculum": social and cultural learning that occurs incidentally and passively. Hearing children repeatedly overhear conversations that do not directly include them but are related to them, such as when their parents talk to the pediatrician about their care or how the parents interface with office staff when they schedule the next appointment. D/HH children are vulnerable to missing years, if not decades, of incidental learning regarding everyday interactions. Direct teaching of incidental information, or making the implicit explicit, is a tenet of supporting the language development of children and youth who are D/HH. In the medical setting, this can be addressed for the signing D/HH child by having a sign language interpreter present to ensure the child can build an understanding of their own health history and expand health literacy, even if they may be too young to engage in the conversation directly. Although it may feel more comfortable and efficient to get information directly from parents, it is critical for the provider to engage the child directly as much as possible to maximize their involvement in their own plan of care. Addressing incidental learning for children who are D/HH should occur regardless of mode of communication.

As families hold an important role in their child's language development, building and empowering families in the development of skills and strategies is an important component of early intervention. Within the field of early intervention, coaching parents on how to engage and interact with their child to promote optimal development has been noted to be effective for a number of populations of children. Communication is interactional, and coaching puts the family in the position of providing the intervention and thus builds skills to support their child.

When a Child Is Not Progressing

If a child's language development is not progressing, it is necessary to reevaluate factors that could contribute to language development. Factors to consider include problems with devices that have not been fully optimized, aspects of access to language, and coexisting medical, developmental, or behavioral conditions impacting learning.

In evaluating a child's access to language, consider how the child is learning, the language environment, and whether a child is getting a quality language model for learning. If a communication modality is pursued that cannot be supported across the environments the child is in (e.g., school, home, community-based organizations), the D/HH child can lag behind their peers. Overt problematic scenarios include a deaf child without good acoustic access attempting to learn spoken language or a child learning sign language but with limited sign language proficiency in their home, community, and school environments. Regression of language should prompt reevaluation of hearing and consideration of brain-centered as opposed to hearing-centered problems with learning.

A child's response to a communication approach may be affected by broader developmental issues. A child may have a unique learning profile and benefit from alternative approaches to language-based learning. Whereas children who are D/HH often have strong visual problem-solving skills, some children who are D/HH are stronger in the auditory domain. Although it should not be automatically assumed that a D/HH child will have developmental delay, up to 40% also have a developmental disability or condition that can affect progress. Early recognition of a child's broader needs can help ensure children receive effective interventions for all of their needs.

ACADEMIC CONSIDERATIONS

The Individuals with Disabilities Education Act (IDEA) ensures a free, appropriate public education for all students with disabilities, including those who are D/HH. This law recognizes the right to be educated within the least restrictive environment (LRE), or to the maximum extent that is appropriate, education with their peers who do not have disabilities. This must be balanced with the individual student's communication, linguistic, academic, social, emotional, and cultural needs. Because of the varied settings and range of communication support needs, as well as the diversity of individual student strengths, endorsing one specific educational setting is not possible or appropriate.

Reading and literacy skills are associated with language fluency levels and tend to be improved by early age of identification and intervention. Standardized achievement testing from the early

2000s demonstrated that only half of D/HH high school graduates were reading above a fourth-grade level. However, these data are old and do not control for varying factors across students such as coexisting medical or developmental conditions, delays in identification and early language access, and varying teaching methodologies. Academic outcomes are likely to be optimized with early identification and support of language in infants who are D/HH and with the prompt recognition of, and support for, other developmental or behavioral challenges that may interfere with learning.

PSYCHOSOCIAL WELL-BEING

An important consideration for any individual is psychosocial well-being. Because the population of D/HH individuals is heterogenous, it is difficult to make overarching statements regarding mental health and wellness. Hearing loss in the elderly has been associated with depression. This is due—at least in part—to the loss of connection and communication with others. Similar effects can be seen across the life span for deaf individuals who did not develop enough formal language to communicate effectively. Studies have linked a lack of language proficiency with in-patient psychiatric care in adults and psychosocial difficulties in children. A large-scale study in Taiwan spanning over a decade estimated an 11.1% lifetime prevalence of clinically diagnosed unspecified anxiety disorder in the D/HH group, which was twice the incidence in the hearing control group.

A phenomenon described by some D/HH individuals, **deaf anxiety**, is related to interpersonal challenges a D/HH individual can experience when interfacing with a largely hearing society. Although advances in technology with hearing aids and cochlear implants continue to improve access to audiologic input, it is important to consider that these are tools with inherent limitations—they are not an equivalent "replacement" for natural hearing. D/HH adults have described fears such as missing/misunderstanding information, concern with appearing not to be interested in or not paying attention to someone speaking, disproportionately increased difficulty when dealing with noisy environments, and worry about missing significant information in nonaccessible environments such as being unaware that a fire alarm has gone off if there is no visual indicator in addition to the sound alarm.

The experiences of a deaf person in a predominantly hearing world contribute to the critical journey of identity formation for D/HH children as they become young adults. Deaf children, regardless of their success with technology, are still deaf. When a child takes off their hearing aids or cochlear implants to take a bath, swim, or rest, they are deaf. The technology does not change who they are fundamentally. Supporting families in their efforts to understand, accept, and value their child as a deaf individual can provide resilience for identity formation in adolescence. There also needs to be recognition that families are necessarily thrust into a position of making decisions for their young D/HH child with the knowledge they have at the time and may have concerns about how their child as an emerging adult may feel later on about those decisions. Families can benefit tremendously from access to programs that can connect them with other deaf children, deaf adults, and community resources that support a variety of ways to exist as a successful deaf individual.

DEAF PLUS

It is helpful to recognize that some of the risks associated with being D/HH are also risks for other conditions that impact functioning in children who are D/HH (Table 55.4). It is important to look beyond hearing status as the reason for delays so as not to miss other factors contributing to a child's slow rate of progress. Delayed recognition of these factors causes delays in accessing effective intervention strategies. Conversely, the presence of specific coexisting conditions should not be assumed to predict functioning or decisions about communication. A child who is deaf and also has cerebral palsy should not be assumed to be unable to use sign language because of impact on hand/arm movements, as these children may use sign language receptively for language understanding quite well. The need for individually tailored care and education plans is particularly critical in children who are Deaf Plus.

Table 55.4 Rates and Types of Disabilities Among Children Who Are D/HH and Within the General Population

TYPE OF DISABILITY	D/HH (%)	GENERAL POPULATION (%)
No developmental disability	60	83
Cognitive/intellectual disability	8.3	1
Cerebral palsy	8	0.3
Blindness and vision impairment	5.5	0.3
Attention-deficit/hyperactivity disorder	5.4	9
Specific learning disability	8	7
Autism spectrum disorders	7	1.7

Children who are D/HH have vision changes at nearly twice the rates compared to the general population. Vision differences are important to detect, as children who are D/HH often rely on their vision for accessing information. Even among children who receive effective amplification and good acoustic access to information, some reliance on lip reading and visual attention to the speaker can enhance a child's ability to process information. There are no specific standards regarding the timing and frequency of ophthalmologic evaluations and monitoring intervals, but it is important for all children who are D/HH to have regular monitoring of vision and eye health with a pediatric eye care specialist.

For children who have both hearing and vision changes (**DeafBlind**), intervention strategies can be increasingly complex. IDEA specifically defines DeafBlindness as "concomitant hearing and visual impairments, the combination of which causes such severe communication and other developmental and educational needs that they cannot be accommodated in special education programs solely for children with deafness or children with blindness." When the two conditions are present simultaneously, there are additional challenges to be considered regarding language access and acquisition. Each state has a federally funded DeafBlind project that provides resources and technical assistance to support children identified as DeafBlind. For children who are DeafBlind, many are advocating for interveners. Interveners are more than interpreters: they facilitate communication and inclusion and address social and emotional needs within educational settings.

FAMILY JOURNEY

Each family has a unique narrative to their overall family experience, as well as a specific pathway to supporting the growth and development of their D/HH child. Some families experience profound grief around the loss of an expected parenting story. Many families speak of being overwhelmed initially by an immense amount of information and pressured to make crucial decisions in a timely manner. Others move into an advocacy model and have their own unique take on the parenting journey. One

Table 55.5 Approaches in the Medical Home to Support the Family Journey

FAMILY JOURNEY THEMES	CONSIDERATIONS AND STRATEGIES
Family-centered decision-making: Ensure families are central in decision-making	Before the visit: • Physician reflection on their own knowledge, expertise, and biases At the visit: • Listen to family concerns actively and address concerns, referring to others when outside provider expertise is necessary
Families' need for **informed** choice	Before the visit: • Recognize that each family and child are unique and decisions may vary across families • Recognize that decisions may change over the life span of the child • Recognize the passion across communication modalities, which drive potential biases in information and guidance At the visit: • Listen actively to understand the family's values and intended goals and outcomes • Collaboratively seek information from a variety of reputable sources and discuss potential biases across various "experts" in the field (see resource list) • Incorporate the family's values in an action plan together • Refer to experts as appropriate
Family-to-family support: Because having a child who is D/HH can feel isolating and professionals do not carry the same day-to-day experiences, family-to-family connection is an important component of support	Before the visit: • Recognize the importance of family-to-family support • Identify resources to link families with other families (see resources) During the visit: • Discuss the possible isolation families face • Determine interest and readiness for family networking • Share resources that they can rely on when ready to reach out
Access to D/HH adults: To support the family's recognition of what success can be and to provide children with a conceptual framework for D/HH individuals as adults	Before the visit: • Recognize families may be experiencing grief over the loss of their child's expected future and that experiences with other individuals who are D/HH may be limited or nonexistent • Identify resources to link families with Deaf adults and Deaf mentoring programs (see Table 55.3) During the visit: • Discuss family's hopes and fears • Highlight the importance of high expectations for their child • Discuss ways to promote identity, connection, and independence for their child
Child interactions and supports	Before the visit: • Recognize the variability and uniqueness of children who are D/HH in terms of capabilities, skills, and opportunities At the visit: • Engage D/HH children directly rather than rely solely on family members for interpreting communication; for children who use sign language, access to an interpreter is a right under the Americans with Disabilities Act • Recognize children's strengths and resilience • Ensure children have access to their own health information (at their developmental level) and have the opportunity for inclusion in decisions as appropriate • Advocate with children and families to have high expectations for skills, recognizing that often medical and educational settings use a deficit model (the child must be behind) to access supports

simply has to take a look at some of the family stories that are available in the public realm to appreciate the diversity of the family experience in raising a D/HH child.

A number of parent support organizations are available to families, some of which are organized around specific communication philosophies (see Table 55.3).

The pediatrician may be the first medical professional that families turn to if there is concern about language development and/or hearing. Although these physician/family relationships are often just as diverse as the families themselves, some universal concepts start to emerge when listening to parent stories (Table 55.5). Recognizing these themes and identifying ways to partner and support families is a critical role of the medical home.

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Chapter 56

Developmental Delay and Intellectual Disability

Meghan E. O'Neill and Bruce K. Shapiro

Intellectual disability (ID) refers to a heterogeneous group of disorders that have in common deficits of adaptive and intellectual function and an age of onset before maturity is reached. In Europe, the term *learning disability* is often used to describe ID.

DEFINITION

Contemporary conceptualizations of ID emphasize adaptive functioning and social interaction rather than test scores in isolation. The definition of ID requires significant impairment in general intellectual function (reasoning, memory, learning, problem solving) and adaptive behavior, with severity defined by limitations in adaptive functioning or levels of needed support. This focus encourages the development of individual treatment plans characterizing the supports needed to enhance functioning. Consistent across these definitions is onset of symptoms before adulthood (18-22 years of age). Children with ID have a nonprogressive disorder; loss of developmental milestones or progressive symptoms with a downward developmental trajectory suggest another disorder.

Significant impairment in adaptive behavior reflects the degree to which cognitive dysfunction directly contributes to impairments in daily functioning at home, at school and work, and in the community. **Adaptive behavior** refers to the skills required for people to function in their everyday lives, and individuals with deficits require more support than same-age peers for optimal participation. The American Association on Intellectual and Developmental Disabilities (AAIDD) and *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) classifications of adaptive behavior address three broad sets of skills: conceptual, social, and practical. **Conceptual skills** include language, reading, writing, time, number concepts, and self-direction. **Social skills** include interpersonal skills, personal and social responsibility, self-esteem, gullibility, naiveté, and ability to follow rules, obey laws, and avoid victimization. Representative **practical skills** involve performance of activities of daily living (dressing, feeding, toileting/bathing, mobility), instrumental activities of daily living (e.g., housework, managing money, taking medication, shopping, preparing meals, using phone and mail systems), occupational skills, and maintenance of a safe environment. For a deficit in adaptive behavior to be present, a significant delay in at least one of the three skill areas must be present. The rationale for requiring only one area is the empirically derived finding that people with ID can have varying patterns of ability and may not have deficits in all three areas.

The requirement for adaptive behavior deficits is the most controversial aspect of the diagnostic formulation. The controversy centers on two broad areas: whether impairments in adaptive behavior are necessary for the construct of ID and what to measure. The adaptive behavior criterion may be irrelevant for many children; adaptive behavior is impaired in virtually all children who have IQ scores <50. The major utility of the adaptive behavior criterion is to confirm ID in children with IQ scores in the 60-75 range, especially considering the historical overdiagnosis of ID among individuals of color with typical adaptive functioning and biased IQ testing results. It should be noted that deficits in adaptive behavior are often found in disorders such as autism spectrum disorder (ASD; see Chapter 58) and attention-deficit/hyperactivity disorder (ADHD; see Chapter 50) in the presence of typical intellectual function, often mediated by significant difficulties with executive functioning, self-directedness, or maladaptive behaviors. In contrast, deficits of adaptive functioning in ID are primarily attributable to the individual's overall cognitive limitations.

The issues of measurement are important as well. The independence of the three domains of adaptive behavior has not been validated. The relationship between adaptive behavior and IQ performance is insufficiently explored. Many adults with IQ scores in the 60-75 range do not have significant impairments in practical skills. Adaptive behavior deficits also must be distinguished from *maladaptive behavior* (e.g., aggression, self-injury, inappropriate sexual behavior).

Significant impairment in general intellectual function refers to performance on an individually administered test of intelligence that is approximately 2 standard deviations (SDs) below the mean. Generally, these tests provide a standard score that has a mean of 100 and SD of 15 points, so that IQ scores <70 would meet these criteria. If the standard error of measurement is considered, the upper limits of significantly impaired intellectual function may extend to an IQ of 75. Using a score of 75 to delineate ID might double the number of children with this diagnosis, but the requirement for impairment of adaptive skills limits the false positives. Children with ID often show a variable pattern of strengths and weaknesses. Not all their subtest scores on IQ tests fall into the significantly impaired range.

Onset before age 22 years or adulthood distinguishes dysfunctions that originate during the developmental period from those that begin in adulthood. The diagnosis of ID may be made after 22 years of age, but the cognitive and adaptive dysfunction must have been manifested before age 22 years. Age of onset may be relevant to qualification for certain benefits programs that require a diagnosis of ID.

Intellectual disability as nonprogressive. Individuals with ID will acquire new developmental milestones over time, although at a slower rate than unaffected children. A slowing trajectory is not uncommon as individuals with ID get older. This should be distinguished from *regression* of milestones, which involves true loss of previously acquired skills and demands additional and often more extensive etiologic workup. Sometimes regression is seen in the context of the child's larger medical picture, such as loss of mobility with increasing spasticity and contractures in children with comorbid cerebral palsy (CP) or loss of language skills in the setting of new seizures. Alternatively, regression could suggest a **progressive encephalopathy** caused by an *inborn error of metabolism* or a *neurodegenerative disorder* (see Chapters 104 and 639). Prompt identification is essential, as some of these conditions are treatable or modifiable and some necessitate conversations about future reproductive risk.

Global developmental delay (GDD) is a term often used to describe young children with delays across multiple domains of development that have not yet resulted in a diagnosis of ID. In DSM-5, GDD is a diagnosis given to children <5 years of age who display significant delay (>2 SDs) in acquiring early childhood developmental milestones in two or more domains of development. These domains include receptive and expressive language; gross and fine motor function; cognition, social and personal development; and activities of daily living. Typically, it is assumed that delay in two domains will be associated with delay across all domains evaluated, including cognitive and intellectual abilities. Longitudinal studies following outcomes of children with GDD are sparse but suggest that that upwards of 80% of children with early global delays continue to experience development challenges through the school-age years. However, not all children who meet criteria for a GDD diagnosis at a young age go on to meet criteria for ID later in childhood. Reasons for the lack of concordance between GDD and later diagnosis of ID include lower reliability and predictive validity of developmental testing in children under 5-6 years of age; a positive change in developmental trajectory with maturation or possibly with intervention; reclassification to a different disability category (autism, ADHD, developmental coordination disorder); or imprecise use of the GDD diagnosis initially. Conversely, in patients with more severe early delays, the GDD term is often used beyond the point when the child could be reclassified as having ID, such as when a child has persistently and markedly low developmental quotients on multiple assessments and despite intervention during the first few years of life.

It is important to distinguish the medical diagnosis of GDD from the federal disability classification of "developmental delay" that may be used by education agencies under the Individuals with Disabilities Education Act (IDEA). This classification requires that a child have delays in only one domain of development with subsequent need for special education. Each state determines its own precise definition and terms of eligibility under the broader definition outlined by IDEA, and many states use the label for children up to 9 years of age.

Table 56. 1 Genetic Testing Guidelines for ID/GDD and/or ASD

ORGANIZATION	RECOMMENDATION(S) FOR GENETIC TESTING

Autism and Intellectual Disability Committee of the American Academy of Child and Adolescent Psychiatry (AACAP)	• CMA in all individuals with ID/GDD and/or ASD
	• FMR1 repeat analysis in males and females with ID or a family history of ID
	• Depending on history and physical examination, consider:
	  • PTEN testing if head circumference (HCM) is more than 2.5 SD above the mean for age in a child with ID/GDD and/or ASD
	  • MECP2 testing for Rett syndrome in females with severe ID
	  • Karyotype if a chromosomal syndrome is suspected
	• If other investigations do not provide an etiology and there are unresolved clinical findings, consider ES and mitochondrial DNA testing

American Academy of Pediatrics (AAP)	• If a comprehensive history and exam are indicative of a specific syndrome or disorder, proceed with specific testing in patients with ASD and/or ID/GDD • In all individuals with ASD and ID/GDD without specific findings, consider CMA and FMR1 CGG repeat analysis • In females with ASD and/or ID/GDD without specific findings, consider MECP2 testing • In males with ID/GDD without specific findings, consider an X-linked ID panel (XLID) • If an etiology is not identified, consider a referral to genetics for additional workup, including possible ES
International Standard Cytogenomic Array (ISCA) Consortium	• CMA is the first-tier genetic test in patients with GDD/ID, ASD, and/or multiple congenital anomalies

American College of Medical Genetics (ACMG)	• After a detailed family history and physical examination, proceed with specific testing for patients with ASD if a syndrome is suspected or if features are suggestive of a mitochondrial or metabolic condition
	• If family history and physical exam are not suggestive of a specific diagnosis, metabolic, or mitochondrial condition, proceed with CMA for all patients with ASD and FMR1 repeat analysis for all males with ASD
	• If CMA (in males and females) and FMR1 repeat analysis (in males) are not diagnostic, consider:
	  • MECP2 sequencing in all females with ASD
	  • MECP2 duplication testing in males with ASD if phenotype is suggestive
	  • PTEN testing in patients with ASD if HCM is more than 2.5 SD above the mean for age
	  • FMR1 repeat analysis in females with ASD and additional features suggestive of fragile X (e.g., family history and phenotype)

American College of Medical Genetics (ACMG)	• CMA is the first-tier genetic test in patients with multiple congenital anomalies that are not indicative of a specific genetic syndrome and those with nonsyndromic ID/GDD and ASD
Multidisciplinary Expert Consensus Panel	• ES in all individuals with ID and/or ASD • If ES is nondiagnostic and does not include copy number variant analysis, proceed with CMA • If ES (and CMA if needed) is nondiagnostic, reanalysis of data from testing should be undertaken periodically
American Academy of Neurology (AAN) and Child Neurology Society (CNS)	• High-resolution karyotype and FMR1 repeat analysis for patients with ASD that also have ID, family history of fragile X and/or ID, or dysmorphic features • After obtaining a detailed medical, developmental, and family history for patients with ID/GDD, if a specific etiology is considered, perform appropriate testing such as single gene testing, metabolic testing, or XLID panel • If a specific etiology is not suspected, perform CMA (or, if not possible, karyotype and subtelomeric FISH) for all individuals with ID/GDD, MECP2 testing for females with moderate to severe ID/GDD, and FMR1 repeat analysis in all individuals with mild ID/GDD • If these and other etiologic workups are negative, consider a referral to genetics

From Savatt JM, Myers SM. Genetic testing in neurodevelopmental disorders. *Front Pediatr*. 2021;9:526779, Table 3.

ETIOLOGY

Numerous identified causes of ID may occur prenatally, during delivery, postnatally, or later in childhood. These include infection, trauma, prematurity, hypoxia-ischemia, toxic exposures, metabolic dysfunction, endocrine abnormalities, malnutrition, and genetic abnormalities. Most people with ID will not have a readily identifiable underlying diagnosis based on prenatal or perinatal history or dysmorphology, meriting further medical and genetic evaluation. Practice guidelines recommend that an etiologic workup be pursued in all children with ID or GDD when there is not a readily apparent explanation for the child's presentation (Tables 56.1 and 56.2). It is anticipated that these diagnostic guidelines change because genome sequencing studies have identified severe monogenic etiologies in previously difficult to diagnose developmental disorders despite extensive previous recommended evaluations.

Among children with milder GDD, yield of etiologic workup will likely be lower in comparison to children with more significant delays or disability. With increases in etiologic testing among all children with ID and advancement of technologic capabilities of testing, the number of identified biologic and genetic causes of ID is continuing to increase rapidly. There are slightly over 100 disorders (all of which are metabolic in nature) for which treatment may ameliorate the core symptoms of ID (see https://www.treatable-id.org/), but these conditions account for a relatively small percentage of children with ID (Table 56.3). However, there are several reasons beyond disease modification that should prompt providers to seek etiologic answers in patients with ID. These include insight into possible associated medical or behavioral comorbidities; information on prognosis and life expectancy; estimation of recurrence risk for family planning counseling, potential validation, and closure for the family; increased access to services or specific supports; and better understanding of underlying pathology with the hope for new treatment options. When surveyed, families of children with ID with no identified underlying etiology almost universally report that they would want to know of an etiologic diagnosis if given the choice. Expanded testing will contribute to the growing pathophysiologic understanding of how ID occurs mechanistically and serves as an opportunity for future targeted treatment opportunities and clinical trial development.

Mild and more severe forms of ID have different but overlapping risk factors and etiologies. Nongenetic risk factors that are often associated with mild ID include low socioeconomic status, low maternal education levels, residence in a developing country, malnutrition, and poor access to healthcare. The most common biologic causes of, or risk factors for, mild ID include intrauterine growth restriction; prematurity; perinatal insults; intrauterine exposure to drugs of abuse (including alcohol); postnatal exposure to neurotoxic substances (including lead); some sex chromosomal abnormalities; and some genetic syndromes with multiple, major, or minor congenital anomalies (e.g., 22q11 deletion syndrome, sex chromosomal abnormalities, Noonan syndrome). Familial clustering is common.

Table 56.2 Genetic Tests Commonly Used in Evaluation of Neurodevelopmental Disorders

TEST	RESULTS/VARIANTS DETECTED	DETECTION LIMITATIONS
Chromosomal microarray (CMA)	• Copy number variants (CNV) (generally >250 kb but could be smaller if region is specifically targeted) • Regions of homozygosity*	• Repetitive DNA sequences, including trinucleotide repeat expansions (e.g., *FMR1* repeat expansion) • Balanced chromosomal rearrangements • Sequence-level variants in the exome/genome • Mitochondrial variants • Epigenetics alterations (e.g., methylation abnormalities, uniparental heterodisomy) • Low-level mosaicism
Exome sequencing (ES)	• Sequence-level variants in the coding region (exome) • Copy number variants**	• Repetitive DNA sequences, including trinucleotide repeat expansions (e.g., *FMR1* repeat expansion) • Balanced chromosomal rearrangements • Smaller copy number variants, including deletions/duplications involving one to two exons • Mitochondrial variants • Epigenetics alterations (e.g., methylation abnormalities) • Intronic/noncoding variants • Variants in regions of the exome that are not well-covered by sequencing
FMR1 CGG repeat testing	• CGG repeat number in the *FMR1* gene	• Sequence-level variants in *FMR1* or elsewhere in the exome/genome • Copy number variants • Balanced chromosomal rearrangements • Exon-level deletions/duplications • Mitochondrial variants • Epigenetics alterations (e.g., methylation abnormalities)

*Single-nucleotide polymorphism–based chromosomal microarray (SNP-CMA)
**Several laboratories are now calling CNVs as a routine part of ES, and this trend will continue to expand.
From Savatt JM, Myers SM. Genetic testing in neurodevelopmental disorders. *Front Pediatr*. 2021;9:526779, Table 2.

Table 56.3 Conditions in Which Early Treatment May Significantly Improve the Course of the Disease

CONDITION	TREATMENT
Galactosemia	Lactose-free diet
Fructosemia	Fructose-free diet
Phenylketonuria	Phenylalanine-free diet
Maternal phenylketonuria	Phenylalanine-free diet during pregnancy
Maple syrup urine disease	Diet restricted in branched-chain amino acids + dialysis or exchange transfusion
Hypoglycemia from any cause	Prevent hypoglycemia and/or provide glucose
Lead intoxication	Separate child from source of lead; chelation therapy
Hypothyroidism	Thyroid replacement
Recurrent otitis media	Antibiotic prophylaxis, pressure-equalizing tubes
Malnutrition	Adequate nutrition
Increased intracranial pressure (e.g., hydrocephalus, neoplasm)	Shunt ventricles or cystic structure
Congenital HIV infection	Prenatal/postnatal treatment with AZT (zidovudine)
Congenital toxoplasmosis	Prenatal treatment with spiramycin, pyrimethamine, and sulfonamide
Dopa-responsive dystonia	Responds to levodopa; may be misdiagnosed as cerebral palsy
Biotinidase deficiency	Oral biotin
Biotin-thiamine–responsive basal ganglia disease	Biotin, thiamine
Wilson disease	Copper chelation; liver transplant
Cerebral folate disorder	Folinic acid

CONDITION	TREATMENT
Creatine disorders	Creatine monohydrate
Vitamin B_{12} deficiency	Vitamin B_{12}
Cerebral glucose transporter defect	Ketogenic diet
Metachromatic leukodystrophy	BMT
Niemann-Pick disease	BMT, liver transplantation, implanted amniotic epithelial cells
Adrenoleukodystrophy	BMT
Glycogen storage disease type IV	Liver transplantation
Menkes disease	Parenteral copper histidinate
Lesch-Nyhan syndrome	Allopurinol + BMT
Krabbe disease	BMT
α-Mannosidosis	ERT: velmanase alfa
Aspartylglucosaminuria	BMT
Gaucher disease type III	ERT: Ceredase; SRT: Cerdelga; PCT: Mucosolvan
Hunter syndrome (MPS II)	ERT: Elaprase
Hurler syndrome (MPS I)	ERT: Aldurazyme
Sanfilippo syndrome A (MPS IIIa)	SRT: Genistein
Sanfilippo syndrome B (MPS IIIb)	SRT: Genistein
Sanfilippo syndrome C (MPS IIIc)	SRT: Genistein
Sanfilippo syndrome D (MPS IIId)	SRT: Genistein
Sly syndrome (MPS VII)	ERT: Mepsevii
Neuronal ceroid lipofuscinosis type II	ERT: Brineura

BMT, Bone marrow transplant; ERT, enzyme replacement therapy; MPS, mucopolysaccharidosis; PCT, pharmacologic chaperone therapy; SRT, substrate reduction therapy.
From Muriello M. Neurocognitive and developmental regression. In: Kliegman RM, Toth H, Bordini BJ, Basel D (eds). *Nelson Pediatric Symptom-Based Diagnosis*, 2nd ed. Philadelphia: Elsevier; 2023: Table 28.10, p. 481.

Table 56.4 Identification of Causes in Children with Significant Intellectual Disability

CAUSE	EXAMPLES	% OF TOTAL
Chromosomal disorder	Trisomies 21, 18, 13 Deletions 1p36, 4p, 5p, 11p, 12q, 17p, others Microdeletions Klinefelter, 47,XXX, and Turner syndromes	~20
Genetic syndrome	Fragile X, Prader-Willi, Angelman, and Rett syndromes	~20
Nonsyndromic autosomal mutations	Variations in copy number; de novo mutations in *SYNGAP1*, *GRIK2*, *TUSC3*, oligosaccharyl transferase, and others	~10
Developmental brain abnormality	Hydrocephalus ± meningomyelocele; schizencephaly, lissencephaly	~8
Inborn errors of metabolism or neurodegenerative disorder	Phenylketonuria, ceroid lipofuscinosis, Tay-Sachs disease, other storage diseases	~7
Congenital infections	HIV, toxoplasmosis, rubella, cytomegalovirus, syphilis, herpes simplex, Zika virus	~3
Familial intellectual disability	Environment, syndromic, or genetic	~5
Perinatal causes	Hypoxic-ischemic encephalopathy, meningitis, intraventricular hemorrhage, periventricular leukomalacia, fetal alcohol syndrome	4
Postnatal causes	Trauma (abuse), meningitis, nutritional deficiencies, hypothyroidism	~4
Unknown		20

Adapted from Stromme P, Hayberg G. Aetiology in severe and mild mental retardation: A population-based study of Norwegian children. *Dev Med Child Neurol.* 2000;42:76–86.

In children with more severe ID, a biologic cause (usually with prenatal onset) can be identified in about three fourths of all cases. Causes include chromosomal (e.g., Down, Wolf-Hirschhorn, and deletion 1p36 syndromes) and other genetic and epigenetic disorders (e.g., fragile X, Rett, and Angelman syndromes), abnormalities of brain development (e.g., lissencephaly), and inborn errors of metabolism and mitochondrial disorders (e.g., mucopolysaccharidoses, mitochondrial respiratory chain complex disorders) (Table 56.4). *Nonsyndromic* severe ID may be a result of inherited or de novo gene mutations, as well as microdeletions or microduplications. Currently, >1,300 single genes have been associated with ID. Inherited genetic abnormalities may be mendelian (autosomal dominant de novo, autosomal recessive, X-linked) or nonmendelian (imprinting, methylation, mitochondrial defects; see Chapter 97). De novo mutations may also cause other phenotypic features such as seizures or autism; the presence of these features suggests more pleotropic manifestations of genetic mutations. Consistent with the finding that disorders altering early embryogenesis are the most common and severe, the earlier the problem occurs in development, the more severe its consequences tend to be.

EPIDEMIOLOGY

ID is one of the most common causes of disability in children globally. The prevalence of ID depends on the definition, method of ascertainment, and population studied, both in terms of geography and age. According to the statistics of a normal distribution, 2.5% of the population should have ID (based on IQ alone), and 75% of these individuals should fall into the mild to moderate range. Variability in rates across populations likely results from the heavy influence of external environmental factors and definitional differences on the prevalence of mild ID. The prevalence of severe ID is relatively stable. Globally, the prevalence of ID has been estimated to be approximately 16.4 per 1,000 persons in low-income countries, approximately 15.9/1,000 for middle-income countries, and approximately 9.2/1,000 in high-income countries. A meta-analysis of worldwide studies from 1980 to 2009 yielded an overall prevalence of 10.4/1,000. ID occurs more in boys than in girls, at 2:1 in mild ID and 1.5:1 in severe ID. In part this may be a consequence of the many X-linked disorders associated with ID, the most common being fragile X syndrome (see Chapter 59).

In the United States the prevalence of ID in school-age children ranges from 1.1% to 1.8%. There are several reasons why fewer children are identified as having mild ID than predicted from statistics. Professionals might miss or defer the diagnosis and "give the benefit of the doubt" to the child and await repeated confirmatory testing over time because it is more challenging to diagnose mild ID than the more severe forms. Other reasons that contribute to the discrepancy between predicted and observed prevalence are use of instruments that underidentify young children with mild ID, children diagnosed as having ASD without their ID being recognized or addressed, misdiagnosis as a language disorder or specific learning disability, and a disinclination to make the diagnosis in minoritized students because of concern about biased assessments that historically led to overdiagnosis. In some cases, behavioral disorders may divert the focus from the cognitive dysfunction.

Beyond potential under diagnosis of mild ID, the number of children with mild ID may be decreasing because of public health and education measures to prevent prematurity and provide early intervention and Head Start programs. However, although the number of school children who receive services under a federal disability classification of ID has decreased since 1999, when *developmental delay* is included in analysis of the data, the numbers have not changed appreciably.

The prevalence of *severe ID* has not changed significantly since the 1940s, accounting for 0.3–0.5% of the population. Many of the causes of severe ID involve genetic or congenital brain malformations that can neither be anticipated nor treated at present, though trends toward more expanded prenatal screening (and subsequent termination) may alter this balance, as seen with the decreasing incidence of Down syndrome. Additionally, expanded newborn screening with early treatment has virtually eliminated ID caused by phenylketonuria and congenital hypothyroidism. However, continued high prevalence of fetal exposure to alcohol and illicit drugs, improved survival of very low birthweight premature infants, and increasing overall maternal age during pregnancy (contributing to increased rates of genetic abnormalities) have counterbalanced this effect.

PATHOLOGY AND PATHOGENESIS

The limitations in our knowledge of the neuropathology of ID are demonstrated by the finding that 10–20% of brains of persons with severe ID appear normal on standard neuropathologic study. Many of the brains that appear abnormal show only mild, nonspecific changes that correlate poorly with the degree of ID, including microcephaly, gray matter heterotopias in the subcortical white matter, unusually regular columnar arrangement of the cortex, and neurons that are more tightly packed than usual. Only a minority of the brains show more specific changes in dendritic and synaptic organization, with dysgenesis of dendritic spines or cortical pyramidal neurons or impaired growth of dendritic trees. CNS maturation is defined by genetic, molecular, autocrine, paracrine, and endocrine influences. Receptors, signaling molecules, and genes are critical to brain development.

As the ability to identify genetic aberrations that correspond to particular phenotypes expands through the use of next-generation sequencing, more will be elucidated about the pathogenesis of ID at a genetic and molecular level. This expanding pathophysiologic knowledge base may serve as a framework with which to develop targeted therapies to bypass or correct newly identified defects. For example, use of histone deacetylase (HDAC) inhibitors has been shown to rescue structural and functional neural deficits in mouse models of Kabuki syndrome, a disorder of histone methylation that leads to variable levels of ID and characteristic facial features. Similarly, there is growing interest in the role of mammalian target of rapamycin (mTOR) inhibitor use preventing seizures, neurodevelopmental disabilities, retinal tumors, cutaneous tumors, and other manifestations seen in tuberous sclerosis (see Chapter 636.2).

CLINICAL MANIFESTATIONS

Early diagnosis of ID facilitates earlier intervention, identification of abilities, realistic goal setting, monitoring for potential comorbid conditions, easing of parental anxiety, and greater inclusion of the child in the community. Children with ID may first come to the pediatrician's attention because of dysmorphisms (often in infancy), associated developmental disabilities, or failure to meet age-appropriate developmental milestones (Tables 56.5 and 56.6). Physical exam findings are nonspecific, but constellations of dysmorphisms may be consistent with certain genetic syndromes. With the advent of more sophisticated genetic testing, the limitations of dysmorphology have become more apparent given the phenotypic variability seen with many genetic causes of ID.

Most children with ID lag behind peers in their acquisition of developmental skills. In early infancy, failure to meet age-appropriate expectations can include a lack of visual or auditory responsiveness, unusual muscle tone (hypotonia or hypertonia), or posture and feeding difficulties. Between 6 and 18 months of age, gross motor delay (lack of sitting, crawling, walking) is the most common concern. Language delay and behavior problems are common concerns after 18 months of age (see Table 56.6). For some children with mild ID, the diagnosis remains

Table 56.5 Physical Examination of a Child with Suspected Developmental Disabilities

ITEM	POSSIBLE SIGNIFICANCE
General appearance	May indicate significant delay in development or obvious syndrome
STATURE	
Short stature	Malnutrition, many genetic syndromes are associated with short stature (e.g., Turner, Noonan)
Obesity	Prader-Willi syndrome
Large stature	Sotos syndrome, Sotos-like syndromes
HEAD	
Shape	Flat occiput: Down syndrome, Zellweger syndrome; prominent occiput: trisomy 18 Delayed closure of sutures: hypothyroidism, hydrocephalus Craniosynostosis: Crouzon syndrome, Pfeiffer syndrome Delayed fontanel closure: hypothyroidism, Down syndrome, hydrocephalus, skeletal dysplasia
Macrocephaly	Alexander syndrome, Canavan disease, Sotos syndrome, gangliosidosis, hydrocephalus, mucopolysaccharidosis, subdural effusion
Microcephaly	Virtually any condition that can restrict brain growth (e.g., malnutrition, Angelman syndrome, Cornelia de Lange syndrome, fetal alcohol effects)
FACE	
Specific measurements may provide clues to inherited, metabolic, or other diseases	Midface hypoplasia: fetal alcohol syndrome, Down syndrome Triangular facies: Russell-Silver syndrome, Turner syndrome Coarse facies: mucopolysaccharidoses, Sotos syndrome Prominent nose and chin: fragile X syndrome Flat facies: Apert syndrome, Stickler syndrome Round facies: Prader-Willi syndrome Hypotelorism or hypertelorism; slanted or short palpebral fissure; unusual nose, maxilla, and mandible
Nose	Anteverted nares/synophrys: Cornelia de Lange syndrome Broad nasal bridge: fetal drug effects, fragile X syndrome Low nasal bridge: achondroplasia, Down syndrome Prominent nose: Rubenstein Taybi, Coffin-Lowry syndrome, Smith-Lemli-Opitz syndrome
Mouth	Long philtrum/thin vermilion border: fetal alcohol effects Cleft lip and palate: isolated or part of a syndrome Micrognathia: Pierre Robin sequence, trisomies, Stickler syndrome Macroglossia: hypothyroidism, Beckwith-Wiedemann syndrome
Teeth	Anodontia: ectodermal dysplasia Notched incisors: congenital syphilis Late dental eruption: Hunter syndrome, hypothyroidism Talon cusps: Rubinstein-Taybi syndrome Wide-spaced teeth: Cornelia de Lange syndrome, Angelman syndrome

Table 56.5 Physical Examination of a Child with Suspected Developmental Disabilities—cont'd

ITEM	POSSIBLE SIGNIFICANCE
EYES	
Set	Hypertelorism: fetal hydantoin syndrome, Waardenburg syndrome Hypotelorism: holoprosencephaly sequence, maternal phenylketonuria effect
Prominent	Crouzon, Seckel, Apert syndrome; Beckwith-Wiedemann syndrome and fragile X syndromes
Iris/sclera	Brushfield spots: Down syndrome Lisch nodules: neurofibromatosis Blue sclera: osteogenesis imperfecta, Turner syndrome, hereditary connective tissue disorders
Cataract	Galactosemia, Lowe syndrome, prenatal rubella, hypothyroidism
Cherry-red spot in macula	Gangliosidosis (GM_1), metachromatic leukodystrophy, mucolipidosis, Tay-Sachs disease, Niemann-Pick disease, Farber lipogranulomatosis, sialidosis type III
Chorioretinitis	Congenital infection with cytomegalovirus, toxoplasmosis, Zika virus, or rubella
Corneal cloudiness	Mucopolysaccharidosis types I and II, Lowe syndrome, congenital syphilis
EARS	
Low-set or malformed pinnae	Trisomies such as Down syndrome, Rubinstein-Taybi syndrome, CHARGE syndrome, cerebrooculofacioskeletal syndrome, Treacher Collins syndrome, fetal phenytoin effects
Hearing	Loss of acuity in mucopolysaccharidosis; hyperacusis in many encephalopathies
HEART	
Structural anomaly or hypertrophy	CHARGE syndrome, velocardiofacial syndrome, glycogenosis type II, fetal alcohol effects, mucopolysaccharidosis type I; chromosomal anomalies such as Down syndrome; maternal PKU; chronic cyanosis may impair cognitive development
LIVER	
Hepatomegaly	Fructose intolerance, galactosemia, glycogenosis types I-IV, mucopolysaccharidosis types I and II, Niemann-Pick disease, Tay-Sachs disease, Zellweger syndrome, Gaucher disease, ceroid lipofuscinosis, gangliosidosis
GENITALIA	
Macroorchidism	Fragile X syndrome
Hypogenitalism	Prader-Willi, Klinefelter, and CHARGE syndromes
EXTREMITIES	
Hands, feet; dermatoglyphics, creases	May indicate a specific entity such as Rubinstein-Taybi syndrome or may be associated with chromosomal anomaly Short limbs: achondroplasia, rhizomelic chondrodysplasia Small hands: Prader-Willi syndrome Clinodactyly: trisomies, including Down syndrome Polydactyly: trisomy 13, ciliopathies Broad thumb: Rubinstein-Taybi syndrome Syndactyly: de Lange syndrome Smith Lemli Opitz Transverse palmar crease: Down syndrome Joint laxity: Down syndrome, fragile X syndrome, Ehlers-Danlos syndrome Phocomelia: Cornelia de Lange syndrome
Joint contractures	Signs of muscle imbalance around the joints (e.g., with meningomyelocele, cerebral palsy, arthrogryposis, muscular dystrophy; also occurs with cartilaginous problems such as mucopolysaccharidosis) Williams syndrome
SKIN	
Café-au-lait spots	Neurofibromatosis, Legius syndrome, tuberous sclerosis, chromosomal aneuploidy, ataxia-telangiectasia, multiple endocrine neoplasia type 2b Fanconi anemia, Gaucher disease Syndromes: basal cell nevus; McCune-Albright, Silver-Russell, Bloom, Chediak-Higashi, Hunter, Bannayan-Riley-Ruvalcaba, Maffucci syndromes
Seborrheic or eczematoid rash	PKU, histiocytosis
Hemangiomas and telangiectasia	Sturge-Weber syndrome, Bloom syndrome, ataxia-telangiectasia; Klippel Trenaunay Weber
Hypopigmented macules, streaks, adenoma sebaceum	Tuberous sclerosis, hypomelanosis of Ito
Hair	Hirsutism: De Lange syndrome, mucopolysaccharidosis, fetal phenytoin effects, cerebrooculofacioskeletal syndrome, trisomy 18, Hurler syndrome Low hairline: Klippel-Feil sequence, Turner syndrome Sparse hair: Menkes disease, argininosuccinic acidemia, biotin deficiency Abnormal hair whorls/posterior whorl: chromosomal aneuploidy (e.g., Down syndrome) Hypertrichosis cubiti (elbows): Wiedemann-Steiner, MacDermot-Patton-Williams syndromes Abnormal eyebrow patterning: Cornelia de Lange syndrome

Continued

Table 56.5 Physical Examination of a Child with Suspected Developmental Disabilities—cont'd

ITEM	POSSIBLE SIGNIFICANCE
Nails	Hypoplastic or dysplastic: fetal alcohol, trisomies, Coffin Siris syndrome
NEUROLOGIC	
Asymmetry of strength and tone	Focal lesion, hemiplegic cerebral palsy
Hypotonia	Prader-Willi, Down, and Angelman syndromes; gangliosidosis; early cerebral palsy; muscle disorders (dystrophy or myopathy)
Hypertonia	Neurodegenerative conditions involving white matter, cerebral palsy, trisomy 18
Ataxia	Ataxia-telangiectasia, metachromatic leukodystrophy, Angelman syndrome
Spine	Sacral dimple/hairy patch: spina bifida
OTHER	
Neck	Webbed neck/low posterior hairline: Turner syndrome, Noonan syndrome
Chest	Shield-shaped chest: Turner syndrome Inverted nipples; congenital disorders of glycosylation

CHARGE, Coloboma, heart defects, atresia choanae, retarded growth, genital anomalies, ear anomalies (deafness); CATCH-22, cardiac defects, abnormal face, thymic hypoplasia, cleft palate, hypocalcemia, defects on chromosome 22; PKU, phenylketonuria.
Modified from Simms M. Intellectual and developmental disability. In: Kliegman RM, Lye PS, Bordini BJ, et al, (eds). *Nelson Pediatric Symptom-Based Diagnosis*. Philadelphia: Elsevier; 2018: Table 24.11, p. 376.

Table 56.6 Common Presentations of Intellectual Disability by Age

AGE	AREA OF CONCERN
Newborn	Dysmorphic syndromes, (multiple congenital anomalies), microcephaly Major organ system dysfunction (e.g., feeding, breathing)
Early infancy (2-4 mo)	Failure to interact with the environment Concerns about vision and hearing impairments
Later infancy (6-18 mo)	Gross motor delay
Toddlers (2-3 yr)	Language delays or difficulties
Preschool (3-5 yr)	Language difficulties or delays Behavior difficulties, including play Delays in fine motor skills: cutting, coloring, drawing
School age (>5 yr)	Academic underachievement Behavior difficulties (e.g., attention, anxiety, mood, conduct)

uncertain during the early years and becomes clearer as the demands of the school setting increase.

With increasing expectations for independence at home and socially, limitations among those with mild ID become more salient. Older school-age children and adolescents with mild ID are typically up to date on current trends and are conversant as to "who," "what," and "where." It is not until the "why" and "how" questions are asked that their limitations become apparent. If allowed to interact at a superficial level, their mild ID might not be appreciated, even by professionals such as healthcare providers. Because of the stigma associated with ID, adolescents may refer to themselves as learning disabled, dyslexic, language disordered, or slow learners. Some people with ID emulate their social milieu to be accepted. Adolescents with mild ID are both at high risk of being bullied and of being taken advantage of from a social perspective.

ETIOLOGIC EVALUATION

ID is one of the most frequent reasons for referral to pediatric genetic providers, with separate but similar etiologic evaluation guidelines (see Table 56.1). ID is a diagnosis of great clinical heterogeneity, with only a subset of syndromic etiologies identifiable through classic dysmorphology. If diagnosis is not made after conducting an appropriate history and physical examination, chromosomal microarray and testing for fragile X syndrome are often the recommended first steps in the etiologic evaluation of ID. Other testing to consider in the etiologic evaluation include exome or whole genome sequencing, neuroimaging, metabolic testing, and electroencephalography (Fig. 56.1).

Decisions to pursue an etiologic diagnosis should be based on the medical and family history, physical examination, and the family's wishes. Table 56.7 summarizes clinical practice guidelines and the yields of testing to assist in decisions about evaluating the child with GDD or ID. Yield of testing tends to increase with worsening severity of delays (see also Tables 56.1 and 56.2).

Microarray analysis has replaced a karyotype as first-tier testing, given that it discerns abnormalities that are far below the resolution of a karyotype. Microarray analysis will detect copy number variations but may result in identification of variants of unknown significance or benign variants and therefore should be used in conjunction with a genetic consultation. Karyotyping has a role when concerns for trisomy, inversions, balanced insertions, and reciprocal translocations are present. If microarray analysis is not diagnostic, whole exome sequencing (WES) increases the diagnostic yield in children with nonsyndromic severe ID, especially when associated conditions such as autism, epilepsy, or movement disorders are present. WES will identify nucleotide sequence variants within the coding region of genes which affect protein function, missing structural and noncoding variants, and trinucleotide repeat disorders. *Starting with WES may be more cost-effective and may substantially reduce time to diagnosis with higher ultimate yields compared with the traditional diagnostic pathway.* Whole genome sequencing, which identifies variants within both exons and introns, represents the most comprehensive sequencing option, providing roughly 3,000 times more data than a microarray. Multimodal genome-wide analysis has identified monogenic etiologies in difficult to diagnose patients when previous testing did not reveal a diagnosis.

Molecular genetic testing for fragile X syndrome is currently recommended, although a relatively low diagnostic yield has led some to suggest that this should not be considered a first-line test for all children with ID or GDD. Yields are highest in males with moderate ID, unusual physical features, and/or a family history of ID or for females with more subtle cognitive deficits associated with severe shyness and a relevant family history, including premature ovarian failure or later-onset tremor-ataxia symptoms (see Chapter 59). For children with a strong history of X-linked ID, specific testing of genes or the entire chromosome may be revealing. Testing for Rett syndrome (methyl CpG–binding protein 2 [MECP2]) should be considered in females with moderate to severe disability, though WES may supplant this.

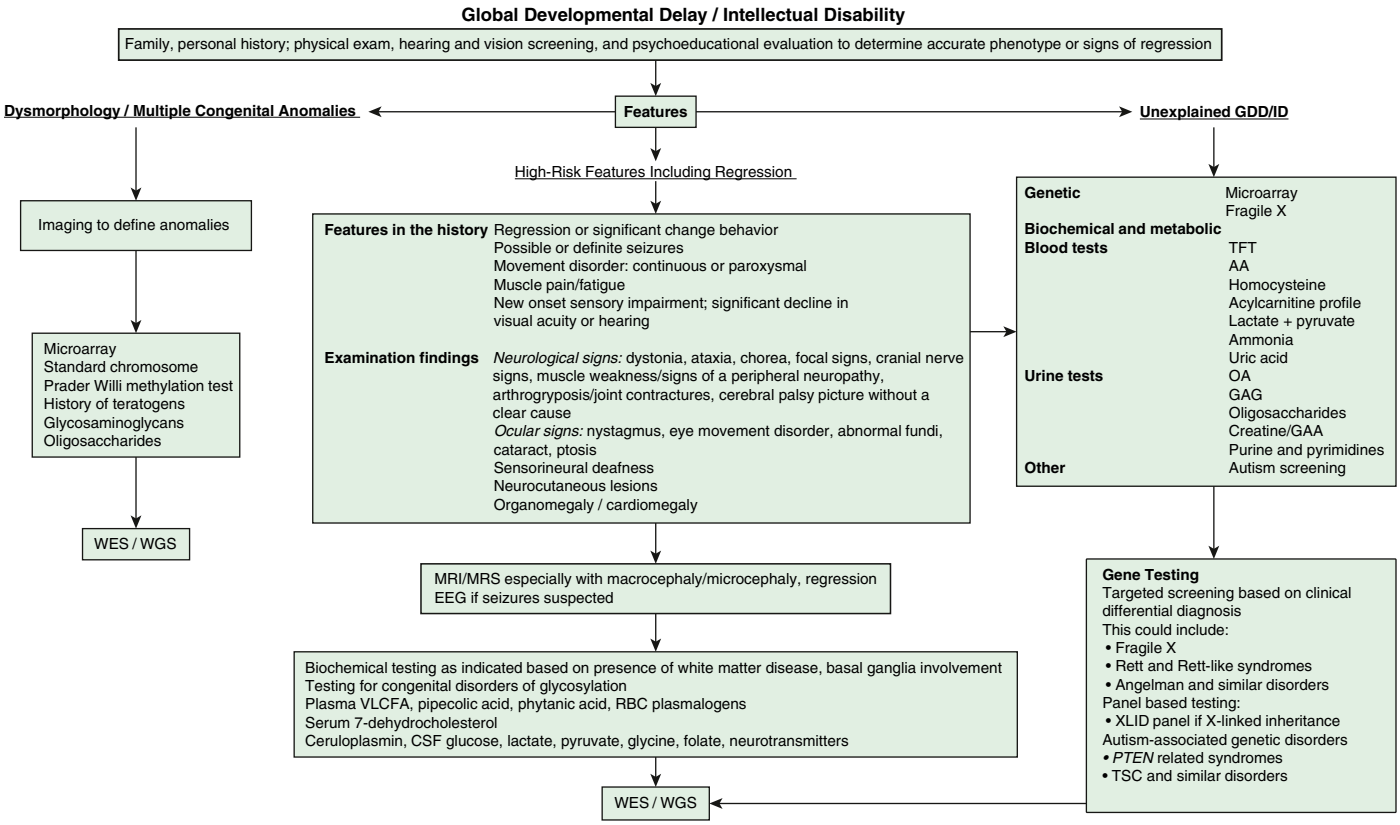

Fig. 56.1 Algorithm for the evaluation of the child with unexplained global developmental delay (GDD) or intellectual disability (ID). AA, Amino acids; ASD, autistic spectrum disorder; CK, creatine kinase; CSF, cerebrospinal fluid; FBC, full blood count; GAA, guanidinoacetic acid; GAG, glycosaminoglycans; LFT, liver function test; OA, organic acids; TFT, thyroid function tests; TSC, tuberous sclerosis complex; U&E, urea and electrolytes; VLCFA, very long-chain fatty acids; WES, whole exome sequencing; WGS, whole genome sequencing; XLID, X-linked intellectual disability genes.

A child with a **progressive neurologic disorder, developmental regression, or acute behavioral changes** needs metabolic investigation, as shown in Figure 56.1. Some advocate for metabolic testing to be done more frequently in children with ID because of the possibility of detecting a condition that could be treatable (Fig. 56.2, Tables 56.3 and 56.8), though with expanded newborn screening many of these conditions can be identified at birth. This is most relevant for children born in countries without widespread newborn screening initiatives, especially when there is a history of consanguinity. In the absence of a specific indication, an **electroencephalogram (EEG)** is typically of low diagnostic utility and should be reserved for evaluation of clinical events that may represent seizures or when significant language regression occurs, which may be concerning for Landau-Kleffner syndrome. **MRI of the brain** may provide useful information in directing the care of a child with microcephaly or macrocephaly, change in head growth trajectory, asymmetric head shape, new or focal neurologic findings, or seizures. MRI can detect a significant number of subtle markers of cerebral dysgenesis in children with ID, but these markers do not usually suggest a specific etiologic diagnosis, and the risk of anesthesia may outweigh the potential benefits in young children without any additional concerning signs or symptoms.

Some children with subtle physical or neurologic findings can also have determinable biologic causes of their ID (see Tables 56.5 and 56.6). How intensively one investigates the cause of a child's ID is based on the following factors:

- What is the degree of delay, and what is the age of the child? If milder or less pervasive delays are present, especially in a younger child, etiologic yield is likely to be lower.
- Is the medical history, family history, or physical exam suggestive of a specific disorder, increasing the likelihood that a diagnosis will be made? Are the parents planning on having additional children, and does the patient have siblings? If so, one may be more likely to intensively seek disorders for which prenatal diagnosis or a specific early treatment option is available.
- Is there a potentially treatable disorder?
- What are the parents' wishes? Some parents have little interest in searching for the cause of the ID, whereas others become so focused on obtaining a diagnosis that they have difficulty following through on interventions until a cause has been found. The entire spectrum of responses must be respected, and supportive guidance should be provided.

DIFFERENTIAL DIAGNOSIS

One of the important roles of pediatricians is the early recognition and diagnosis of cognitive deficits. Developmental surveillance should be multifaceted. Parents' concerns and observations about their child's development should be listened to carefully. Medical, genetic, and environmental risk factors should be recognized. Infants at high risk (prematurity, maternal substance abuse, perinatal insult) should be registered in newborn follow-up programs in which they are evaluated periodically for developmental lags in the first 2 years of life; they should be referred to early intervention programs as appropriate. Developmental milestones should be recorded routinely during healthcare maintenance visits. The American Academy of Pediatricians (AAP) has formulated a schema for developmental surveillance and screening at 9, 18, 24, and 30 months of age, including general developmental and autism screens (see Chapter 28).

Table 56.7 Suggested Evaluation of the Child with Intellectual Disability (ID) or Global Developmental Delay (GDD)

TEST	COMMENT
In-depth history	Includes prenatal, perinatal, and postnatal events (including seizures); developmental attainments; and three-generation pedigree in family history (focusing on neurologic or developmental abnormalities, miscarriages, consanguinity, etc.)
Physical examination	Particular attention to minor or subtle dysmorphisms; growth issues; neurocutaneous findings; eye and skull abnormalities; hepatosplenomegaly; and neurologic examination for focality Behavioral phenotype
Vision and hearing evaluation	Essential to detect and treat; can mask as developmental delay
Gene microarray analysis	A ~15% yield overall Better resolution than with karyotype; may identify up to twice as many abnormalities as karyotyping Often included in exome testing
Karyotype	No longer a first-line test Reserve use when concerned for trisomic/monosomic conditions, inversions and balanced insertions, or reciprocal translocations
Fragile X screen	Combined yield of 2%, preselection on clinical grounds can increase yield to 7.6%
Next-generation gene sequencing	Detects inherited and de novo point mutations, especially in nonsyndromic severe intellectual disability Whole exome sequencing gives an additional yield of about 30–40% Pilot studies of whole genome sequencing (WGS) reveal additional yield of about 15%
Neuroimaging	MRI preferred; positive findings increased by abnormalities of skull contour or microcephaly and macrocephaly or focal neurologic examination (30–40% if indicated, 10–14% if screening) Identification of specific etiologies is rare; most conditions that are found do not alter the treatment plan; need to weigh risk of sedation against possible yield
Thyroid (T_4, TSH)	Near 0% in settings with universal newborn screening program
Serum lead	If there are identifiable risk factors for excessive environmental lead exposure (e.g., low socioeconomic status, home built before 1950)
Metabolic testing	Yield of 0.2–4.6% based on clinical indicators and tests performed Urine organic acids, plasma amino acids, ammonia, lactate, and capillary blood gas Focused testing based on clinical findings is warranted if lack of newborn screen results or suggestive history/exam (e.g., regression, consanguinity, hepatosplenomegaly, course facies) Tandem mass spectrometry newborn screening has allowed for identification of many disorders in the perinatal period and has decreased yield in older children; other disorders have emerged, such as congenital disorders of glycosylation (yield 1.4%) and disorders of creatine synthesis and transport (yield 2.8%)
MECP2 for Rett syndrome	1.5% of females with criteria suggestive of Rett (e.g., acquired microcephaly, loss of skills) 0.5% of males
EEG	May be deferred in absence of history of seizures or significant language regression
Repeated history and physical examination	Can give time for maturation of physical and behavioral phenotype; new technology may be available for evaluation

EEG, Electroencephalogram; CGH, comparative genomic hybridization; MECP2, methyl CpG–binding protein 2; T_4, thyroxine; TSH, thyroid-stimulating hormone.
Data from Michelson DJ, Shevell MI, Sheer EH, et al. Evidence report. Genetic and metabolic testing on children with global developmental delay: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of Child Neurology. *Neurology*. 2011;77:1629–1635; Curry CJ, Stevenson RE, Aughton D, et al. Evaluation of mental retardation: Recommendations of a Consensus Conference: American College of Medical Genetics. *Am J Med Genet*. 1997;12:72:468–477; Shapiro BK, Batshaw ML. Mental retardation. In: Burg FD et al: *Gellis and Kagan's Current Pediatric Therapy,* 18th ed, Philadelphia: Saunders; 2005; and Shevell M, Ashwal S, Donley D, et al. Practice parameter: Evaluation of the child with global developmental delay. *Neurology*. 2003;60:367–380.

Before making the diagnosis of ID, other disorders that affect cognitive abilities and adaptive behavior should be considered. These include conditions that mimic ID and others that involve ID as an associated impairment. Sensory deficits (severe hearing and vision loss), communication disorders, refractory seizure disorders, poorly controlled mood disorders, or unmanaged severe attention deficits can mimic ID; certain progressive neurologic disorders can appear as ID before regression is appreciated. Approximately half of children with **cerebral palsy** (see Chapter 638.1) and one third of children with **autism spectrum disorder** (see Chapter 58) also have ID. Differentiation of isolated CP from ID relies on motor skills being more affected than cognitive skills and on the presence of pathologic reflexes and tone changes. Importantly, cognitive testing may be limited because of motor and communication impairments in CP such that an accurate diagnostic assessment often hinges on evaluation by a professional with experience with this population.

In ASD, social communication and social adaptive skills are more affected than nonverbal reasoning skills, whereas in ID, there are usually more equivalent deficits in social, fine motor, adaptive, and cognitive skills. The discrepancy between social communication abilities and overall developmental abilities and the presence, severity, and intensity of restricted and repetitive behaviors differentiates whether an individual has ID alone or a comorbid diagnosis of ASD. Among toddlers with ASD, those with lower verbal and nonverbal cognitive test scores in conjunction with poor adaptive skills have an 85–90% chance of being classified as having ID in adulthood. However, across all levels of cognition in ASD, there is a significant trend toward much lower adaptive functioning than would be expected otherwise.

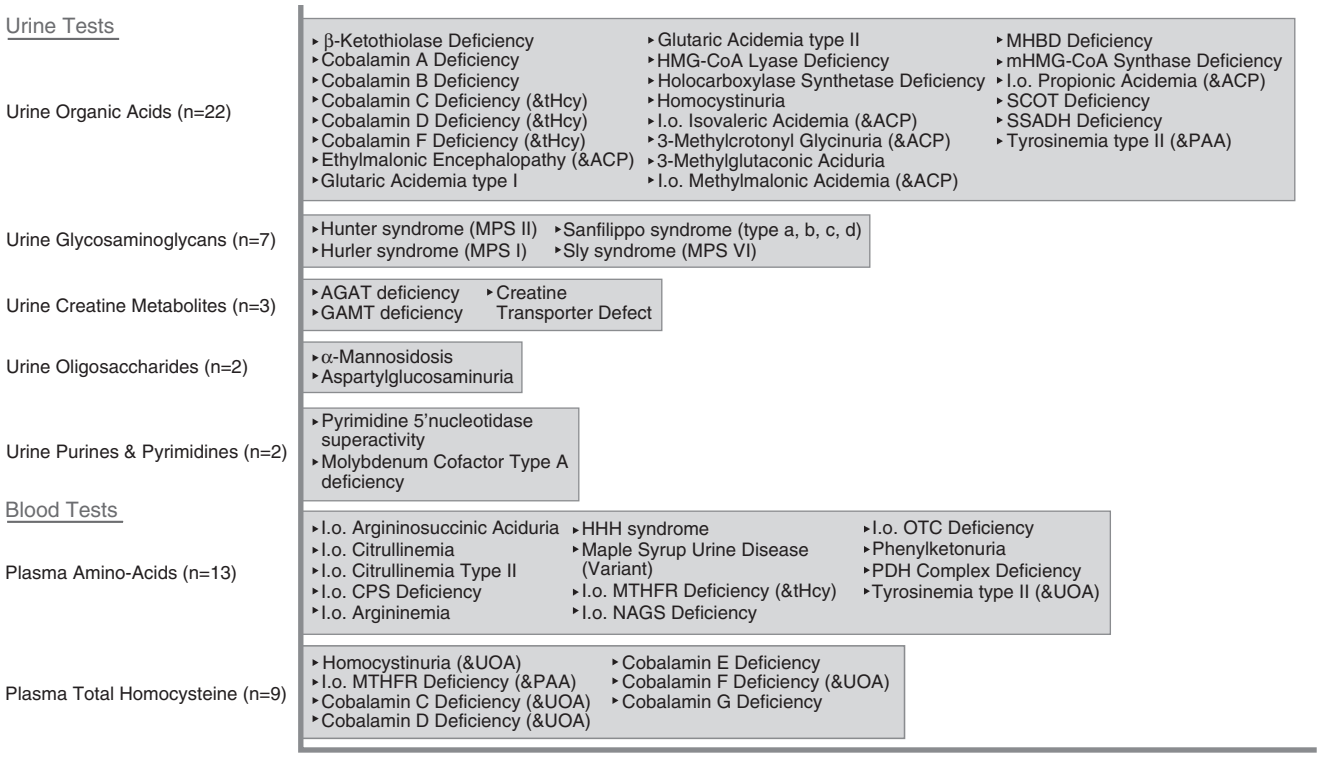

Fig. 56.2 Summary of treatable inherent errors of metabolism (IEM) that can be detected by metabolic tests in affected children, each of which is affordable and accessible and has the potential to identify at least 2 IEM (and up to 22). Each bar represents the yield of the specific screening test and lists the number and types of treatable IEM it can identify. PAA, Plasma amino acids; tHcy, total homocysteine; ACP, plasma acylcarnitine profile; UOA, urine organic acids. *(From van Karnebeek CD, Stockler S. Treatable inborn errors of metabolism causing intellectual disability: A systematic literature review. Mol Genet Metab. 2012;105:368–381, Fig. 1, p. 374.)*

Table 56.8 Treatable Intellectual Disability Endeavor (TIDE) Diagnostic Protocol

***TIER* 1: NONTARGETED METABOLIC SCREENING TO IDENTIFY 54 (60%) TREATABLE IEM**	
Blood	Plasma amino acids, total homocysteine, acylcarnitine profile, copper, ceruloplasmin
Urine	Organic acids, purine and pyrimidines, creatine metabolites, oligosaccharides, glycosaminoglycans, amino acids (when indicated)
***TIER* 2: CURRENT PRACTICE ADHERING TO INTERNATIONAL GUIDELINES* (ONE OR MORE OF THE FOLLOWING)**	
Blood	Cytogenetic testing (array CGH), thyroid studies, complete blood count, lead, metabolic testing, fragile X, targeted gene sequencing/molecular panel
Diagnostics	Brain MRI and 1H spectroscopy (where available)
Referrals	Audiology, ophthalmology
TIER 3: TARGETED WORKUP TO IDENTIFY 35 (40%) TREATABLE IEM REQUIRING SPECIFIC TESTING According to patient's symptomatology and clinician's expertise Use of digital tools (www.treatable-id.org)	
Blood	Plasma cholestanol, 7-dehydroxycholesterol:cholesterol ratio, pipecolic acid and urine α-amino adipic semialdehyde (AASA), very-long-chain fatty acids Plasma vitamin B_{12} and folate, serum lactate to pyruvate ratio, whole blood manganese
CSF	Lactate to pyruvate ratio, amino acids, neurotransmitters, CSF to plasma glucose ratio
Urine	Urine deoxypyridinoline
Other	Enzyme activities (leukocytes): arylsulfatase A, biotinidase, glucocerebrosidase, fatty aldehyde dehydrogenase CoQ measurement: fibroblasts Molecular analysis: *CA5A, NPC1, NPC2, SC4MOL, SLC18A2, SLC19A3, SLC30A10, SLC52A2, SLC52A3, PDHA1, DLAT, PDHX, SPR, TH* genes

*Low threshold for ordering tests.
IEM, Inborn errors of metabolism; CSF, cerebrospinal fluid; CGH, comparative genomic hybridization; CoQ, coenzyme Q (ubiquinone).
Adapted from Van Karnebeek CD, Stockler-Ipsiroglu S. Early identification of treatable inborn errors of metabolism in children with intellectual disability: The Treatable Intellectual Disability Endeavor protocol in British Columbia. *Paediatr Child Health.* 2014;19(9):469–471.

DIAGNOSTIC PSYCHOLOGIC TESTING

The formal diagnosis of ID requires the administration of individual tests of intelligence and adaptive functioning.

The *Bayley Scales of Infant and Toddler Development, Fourth Edition* (BSID-4), the most used infant intelligence test, provides an assessment of cognitive, language, motor, behavior, social-emotional, and general adaptive abilities between 16 days and 42 months of age. The BSID-4 correlates more strongly with other standardized tests of cognition and motor development than did prior versions of the test and permits the differentiation of infants with severe ID from typically developing infants, but it is less helpful in distinguishing between a typical child and one with mild ID.

The most used intelligence tests for children older than 3 years are the Wechsler Scales, although others are also used. The *Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition* (WPPSI-IV) is used for children with mental ages of 2.5-7.6 years. The *Wechsler Intelligence Scale for Children, Fifth Edition* (WISC-V) is used for children who function above a 6-year-old mental age. Both scales contain numerous subtests in the areas of verbal and performance skills. Although children with ID usually score low on all subscales, they occasionally score in the average range in one or more performance areas. Among children who have marked language or verbal limitations, tests like the *Differential Ability Scales-II (DAS-II)* or the *Leiter International Performance Scale,* Third Edition (Leiter-3) may be used to optimally capture nonverbal performance skills.

Several normative scales are used in practice to evaluate adaptive functioning, often through questionnaire or interview formats, with information being attained from caregivers and educators in multiple different environments when possible (home, school, work). For example, the *Vineland Adaptive Behavior Scale* (VABS-3) uses semi-structured interviews with parents and caregivers/teachers to assess adaptive behavior in four domains: communication, daily living skills, socialization, and motor skills. Other tests of adaptive behavior include the *Adaptive Behavior Assessment System* (ABAS-3), the *Woodcock-Johnson Scales of Independent Behavior–Revised,* and the *AAIDD Diagnostic Adaptive Behavior Scale* (DABS). There is usually (but not always) a good correlation between scores on the intelligence and adaptive scales in ID. However, it is important to recognize that adaptive behavior can by influenced by environmentally based opportunities and by family or cultural expectations. Basic practical adaptive skills (feeding, dressing, hygiene) are more responsive to remedial efforts than is the IQ score itself. The trajectory of adaptive skill acquisition may not be consistent over time because of the underlying condition, response to interventions, and environmental expectations.

COMPLICATIONS AND ASSOCIATED CONDITIONS

Children with ID have higher rates of vision, hearing, neurologic, orthopedic, and behavioral or emotional disorders than typically developing children (Table 56.9). These problems are often detected later in children with ID. If untreated, the associated impairments may adversely affect the individual's outcome more than the ID itself.

The more severe the ID, the greater the number and severity of associated impairments. Knowing the cause of the ID can help predict which associated impairments are most likely to occur. For example, fragile X syndrome (see Chapter 59) and fetal alcohol syndrome (see Chapter 146) are associated with a high rate of behavioral disorders and may be amenable to certain treatments. Children with fetal alcohol syndrome may have a less robust response to stimulant use, whereas preliminary data suggest that children with fragile X syndrome may see behavioral improvements with the use of metformin. Other genetic conditions may have well-established medical comorbidities that should be screened for throughout the life span. For example, Down syndrome (see Chapter 57) has many medical complications (hypothyroidism, hearing and vision impairments, obstructive sleep apnea, congenital heart disease, atlantoaxial subluxation). Such associated impairments can require ongoing physical therapy, occupational therapy, speech-language therapy, behavioral therapy, adaptive and mobility equipment, glasses, hearing aids, and medication or other medical management. Failure to identify and treat these impairments can hinder successful habilitation and result in difficulties in the school, home, and neighborhood environment.

Special attention should be given to screening for accidental injury, neglect, and abuse. Children with ID have a greater risk of preventable death from accidental injury. They are more likely to be victims of frequent, continual abuse at the hands of multiple abusers and are more frequently abused by unrelated or unfamiliar perpetrators compared to typically developing peers. Up to 15–30% of children with ID are victims of sexual abuse, with female teens with ID being at highest risk. Abuse may precipitate the onset of maladaptive behaviors and changes in mood. As such, a high index of suspicion must be maintained, with the knowledge that even individuals with severe ID may be able to reliably disclose victimization and abuse.

Table 56.9 Conditions Associated with ID

MEDICAL/PHYSICAL CONDITIONS	DEVELOPMENTAL/ PSYCHIATRIC CONDITIONS
Cerebral palsy/severe motor impairment	Attention-deficit/hyperactivity disorder
Seizures	Emotional disorders (anxiety, mood disorders, posttraumatic stress disorder)
Endocrine abnormalities (e.g., hypothyroidism, short stature)	Obsessive-compulsive disorder
GI issues (constipation, reflux)	Behavioral disorders (self-injurious behavior, aggression, adjustment disorder, disruptive behavior)
Dysphagia	Autism spectrum disorder
Other organ system anomalies (e.g., congenital heart disease, malformations)	Eating and feeding disorders
Hearing loss	Psychotic disorders
Vision impairment (refractive error, cataracts, strabismus)	Movement disorders (tics, stereotypies,)
Dental caries	Developmental coordination disorder
Lead poisoning from associated pica	Learning disabilities (difficulties not explained by cognition alone)
Sleep disorders (OSA, behavioral sleep dysfunction)	Substance abuse
Obesity	Victimization (bullying, sexual abuse, physical abuse)

GI, Gastrointestinal; OSA, obstructive sleep apnea.

PREVENTION

Examples of primary programs to prevent ID include the following:

- Increasing the public's awareness of the adverse effects of alcohol and other drugs of abuse on the fetus (the most common preventable cause of ID in the Western world is fetal alcohol exposure).
- Encouraging safe sexual practices, preventing teen pregnancy, and promoting early prenatal care with a focus on preventive programs to limit transmission of diseases that may cause congenital infection (syphilis, toxoplasmosis, cytomegalovirus, HIV).
- Preventing traumatic injury by encouraging the use of safety technologies (car seats, window locks, helmets, gun locks).
- Preventing poisonings by teaching parents about securing medications and potential poisons.

- Implementing immunization programs to reduce the risk of ID caused by encephalitis, meningitis, and congenital infection.

Presymptomatic detection of certain disorders can result in treatment that prevents adverse consequences. State newborn screening by tandem mass spectrometry (now detecting >60 rare genetic disorders in most states), newborn hearing screening, and preschool lead poisoning prevention programs are examples. Additionally, screening for comorbid conditions can help to limit the extent of disability and maximize the level of functioning in certain populations. Annual thyroid, vision, and hearing screening in a child with Down syndrome is an example of presymptomatic testing in a disorder associated with ID.

TREATMENT

Although the core symptoms of ID can be prevented in some conditions, they are generally not treatable once ID is diagnosed. Many associated impairments are amenable to intervention and therefore benefit from early identification. Most children with an ID do not have a behavioral or emotional disorder as an associated impairment, but challenging behaviors (aggression, self-injury, oppositional defiant behavior) and internalizing disorders (mood and anxiety disorders) occur with greater frequency in this population than among children with typical intelligence. These behavioral and emotional disorders are the primary cause for out-of-home placements, increased family stress, reduced employment prospects, and decreased opportunities for social inclusion. Some behavioral and emotional disorders are difficult to diagnose in children with more severe ID because of the child's limited abilities to understand, communicate, interpret, or generalize. Other disorders are masked by the ID. The detection of ADHD (see Chapter 50) in the presence of moderate to severe ID may be difficult, as may be discerning a thought disorder (psychosis) in someone with autism and ID.

Behavioral disorders in ID often result from a mismatch between the child's abilities and the demands of the situation, organic problems, and family difficulties. These behaviors may represent attempts by the child to communicate, gain attention, gain access to desired tangibles, escape certain demands, exert control, or avoid frustration. Determining the antecedents, functions, and consequences of behavior can help in developing an effective behavior intervention plan. The most formal iteration of this is a functional behavioral assessment carried out by a well-trained behavior analyst. In assessing the challenging behavior, one must also consider whether it is inappropriate for the child's *mental or developmental age,* rather than the *chronological age*. However, if the behavior is dangerous to the individual or the external world, intervention is required regardless of whether it is "appropriate" for their developmental age. When intervention is needed, an environmental change, such as a more appropriate classroom setting, may improve certain behavior problems. Behavior management techniques and parent training are valuable; psychopharmacologic agents may be appropriate in certain situations, such as aggression or self-injurious behaviors with high levels of intensity and frequency.

No medication has been found that improves the core symptoms of ID. However, several agents are being tested in specific disorders with known biologic mechanisms (e.g., mTOR inhibitors in tuberous sclerosis and PTEN disorder), with the hope for future pharmacologic options that could alter the natural course of cognitive impairment seen in patients with these disorders. Medication is most useful in the treatment of associated behavioral and psychiatric disorders that do not respond to initial behavioral approaches and environmental manipulation. Additionally, underlying medical disorders and abuse/neglect should be considered as part of the differential before medication initiation in patients with self-injury, aggression, irritability, or significant disruptive behaviors.

Medications used among individuals with ID generally target specific associated symptom complexes, including inattention, impulsivity, and hyperactivity (stimulant medications and alpha-agonists); self-injurious behavior and aggression (antipsychotics); anxiety, obsessive-compulsive disorder, and depression (selective serotonin reuptake inhibitors); and sleep-related dysfunction (melatonin, alpha-agonists, gabapentin, trazodone). Even if a medication proves successful, its use should be reevaluated at least yearly to assess the need for continued treatment of the target behaviors and improvements in functional goals. Generally, medications should be started at a low dose and increased slowly, with frequent assessments of whether benefits outweigh any adverse effects. Adverse effects and idiosyncratic responses to medications may be more common in this population.

PRIMARY CARE, SUPPORTIVE CARE, AND MANAGEMENT

Each child with ID needs a medical home with a primary care clinician who is readily accessible to the family to answer questions, help coordinate care, and discuss concerns. Healthcare clinicians can have effects on patients and their families that are still felt decades later. The role of primary care includes involvement in prevention efforts, early diagnosis, identification and management of associated deficits, longitudinal developmental surveillance and screening, referral for appropriate diagnostic and therapeutic services, interdisciplinary management, provision of anticipatory guidance (see Chapter 13), and advocacy for the child and family. The management strategies for children with an ID should be multimodal, with efforts directed at all aspects of the child's life: health, education, social and recreational activities, behavior problems, and associated impairments. Support for parents and siblings should also be provided (Table 56.10). A strengths-based approach focusing on optimizing participation in all aspects of life tends to be more beneficial than an exclusive focus on cognitive or academic skill attainment. Goals of overall care should include maximizing the individual's independent functioning, identifying effective communication strategies, preserving and enhancing physical fitness and well-being, supporting positive relationship building, and ensuring opportunities for the individual to participate fully in the community and find purpose and enjoyment in life activities. Goals should be individualized, flexible, appropriate, and attainable.

The AAP has published a series of guidelines and/or toolkits for health supervision of children with specific disorders associated with ID (Down syndrome, fragile X syndrome, Williams syndrome, fetal alcohol spectrum disorder). Another source for disorder-specific information can be found at https://www.medicalhomeportal.org/diagnoses-and-conditions.

Goals should be considered and programs adjusted as needed during the primary care visit. Decisions should also be made about what additional information is required for future planning or to explain why the child is not meeting expectations. Other evaluations, such as formal neuropsychologic or educational testing, can be helpful for diagnostic clarification, attaining more appropriate school-based supports, understanding strengths and challenges, or assisting with the process of transition at various time points.

Interdisciplinary Management

The primary care clinician has the responsibility for consulting with other disciplines to make the diagnosis of ID and coordinate treatment services. Consultant services may include speech-language pathology, physical therapy, occupational therapy, psychology, audiology, nutrition, nursing, and social work, as well as medical specialties such as neurodevelopmental disabilities, neurology, genetics, physical medicine and rehabilitation, psychiatry, developmental-behavioral pediatrics, and surgical specialties. Contact with early intervention and school personnel is equally important to help prepare and assess the adequacy of the child's individual family service plan or individual education plan. The family should be an integral part of the planning and direction of this process. Care should be family centered and culturally sensitive; for older children, their participation in planning and decision-making should be promoted to whatever extent possible. Goal setting should be appropriate, individualized, and achievable

Table 56.10 Resource List for Families by Category

Advocacy	Consortium for Citizens with Disabilities	http://www.c-c-d.org/
	The Arc	https://thearc.org/
	American Association on Intellectual and Developmental Disabilities	https://www.aaidd.org/
	Council for Exceptional Children	https://exceptionalchildren.org/
	The National Disability Rights Network	https://www.ndrn.org/
	Ollibean	https://ollibean.com/
	TASH	https://tash.org/
	National Association for Councils on Developmental Disabilities	https://www.nacdd.org/
Assistive Technology	Rehabilitation Engineering and Assistive Technology Society of North America	www.resna.org
	AT Network	www.atnet.org
	Association of Assistive Technology Act Programs (ATAP)	www.ataporg.org
	Guide to Software Accessibility for the Disabled	ithare.com/guide-to-software-accessibility-for-the-disabled/
Behavior and Mental Health	National Association for the Dually Diagnosed (NADD)	www.thenadd.org
	Behavior Analyst Certification Board	www.bacb.com
	Challenging behaviors in I/DD informational article	https://milnepublishing.geneseo.edu/instruction-in-functional-assessment/chapter/chapter-1-challenging-behaviors-of-individuals-with-developmental-disabilities/
	Challenging Behaviors Toolkit	https://www.autismspeaks.org/sites/default/files/2018-08/Challenging%20Behaviors%20Tool%20Kit.pdf
Early Intervention	Zero to Three	www.zerotothree.org/
	Pathways.org	https://pathways.org/
	First Signs Campaign	http://www.firstsigns.org/
	Early intervention overview	https://www.parentcenterhub.org/ei-overview/
	CDC Early intervention information	https://www.cdc.gov/ncbddd/actearly/parents/states.html
	CDC developmental milestones	https://www.cdc.gov/ncbddd/actearly/milestones/index.html
Special Education and Inclusion	Parent Training and Information Centers (PTIs)	https://www.parentcenterhub.org/find-your-center/
	Iris Center (Inclusion)	https://iris.peabody.vanderbilt.edu/
	Understood.org	https://www.understood.org/pages/en/learning-thinking-differences/
	WrightsLaw.com	http://www.wrightslaw.com/advoc/ltrs/inclusion_right_suzanne.htm
	Institute for Community Inclusion	http://www.communityinclusion.org
	Kids Included Together	https://www.kit.org/what-we-do/inclusion-resources/
	Kidstogether.org	http://www.kidstogether.org/
Postsecondary Education	PACER Center	www.PACER.org/transition
	National Center for College Students with Disabilities	https://www.nccsdonline.org/
	DREAM: Disability Rights, Education, Activism, and Mentoring	https://www.dreamcollegedisability.org/
	Guide to Paying for College for People with Disabilities	https://lendedu.com/blog/paying-for-college-for-people-with-disabilities/
	Affordable Colleges Online College Resources for Students with Disabilities	https://www.affordablecollegesonline.org/college-resource-center/resources-for-students-with-disabilities/

Table 56.10 Resource List for Families by Category—cont'd

Transition, Vocational Training, Employment, and Community Participation	The Arc	https://thearc.org/
	Best Buddies International	https://www.bestbuddies.org/
	Easter Seals	https://www.easterseals.com/EasterSeals.com
	Got Transition	https://www.gottransition.org/
	Project SEARCH	https://www.projectsearch.us/Project SEARCH
	Recruit Disability job listings	https://www.recruitdisability.org/
	Rehabilitation Services Administration	https://rsa.ed.gov/
	Work Incentives Planning and Assistance Project Fact Sheet	https://www.ssa.gov/disabilityresearch/wi/generalinfo.htm
	Respectability	https://www.respectability.org/resources/Job-Seekers-Disabilities/
	Employer assistance and Resource Network on Disability Inclusion	https://askearn.org/
	What Can You Do? Resources for Employers	https://www.whatcanyoudocampaign.org/where-to-learn-more/resources-for-employers/
Recreation	Special Olympics	https://www.specialolympics.org/
	Summer camp locator	https://www.veryspecialcamps.com/
Parent and Family Resources	Family Voices	https://familyvoices.org/lfpp/f2fs/
	Parents Helping Parents	https://www.php.com/
	Eparent.com	http://www.eparent.com
	Community Parent Resource Centers (CPRCs)	https://www.parentcenterhub.org/find-your-center/
	Summer camp options for siblings of children with I/DD	https://www.veryspecialcamps.com/summer/siblings-camps/
Government Initiatives and Services	Policy information on SSI for children with disabilities	https://www.cbpp.org/research/social-security/ssi-a-lifeline-for-children-with-disabilities
	Supplemental security income and social security disability insurance – beneficiaries with I/DD	https://www.ssa.gov/policy/docs/ssb/v77n1/v77n1p17.html
	Centers for Medicare and Medicaid Services	http://www.cms.gov
	Home- and community-based waiver programs	https://www.medicaid.gov/medicaid/home-community-based-services/index.html
	Achieving a Better Life Experience (ABLE) Accounts – ABLE national resource center	https://www.ssa.gov/ssi/spotlights/spot-able.htmlhttps://www.ssa.gov/ssi/spotlights/spot-able.html https://www.ablenrc.org/
	Association of University Centers on Disabilities	http://www.aucd.org/directory/directory.cfm
	Administration for Community Living	https://acl.gov/www.acl.gov/programs/aidd/index.aspx.
	Division on Developmental Disabilities (DDD)	http://daddcec.org/Home.aspxwww.acl.gov/programs/aidd/index.aspx.
	National Association of States Directors of Developmental Disabilities Services (NASDDDS)	http://www.nasddds.orgwww.nasddds.org http://daddcec.org/Home.aspx
	Division on Developmental Disabilities (DDD)	Individual state websites
Disorder-Specific Groups	Epilepsy	http://www.epilepsyfoundation.org
	Autism	www.autismspeaks.org www.autism-society.org
	Cerebral Palsy	https://www.yourcpf.org/
	There are other disorder-specific groups that are too numerous to list here, which include large national networks for more common syndromes such as Down syndrome (e.g., http://www.ndss.org, https://www.ndsccenter.org/) or fragile X syndrome (http://www.fragilex.org) and smaller support groups for more rare disorders (many of which can be located through the unique website at https://rarechromo.org/).	

Continued

Table 56.11 Severity of Intellectual Disability and Adult-Age Functioning

LEVEL	SUPPORT LEVEL	FUNCTIONAL AGE EQUIVALENT AS ADULT	ADULT ADAPTATION
Mild	Intermittent	9-11 yr	Reads at fourth- to fifth-grade level; simple multiplication and division; can write a simple list or letter; completes job application; basic independent job skills (arrive on time, stay at task, interact with coworkers); uses public transportation, might qualify for driver's license; keeps house, cooks using recipes; challenges with planning and money management; at risk of being manipulated by others; may need support for making decisions in healthcare, shopping, finances, and raising a family.
Moderate	Limited	6-8 yr	Sight-word reading; copies information (e.g., address from card to job application); matches written number to number of items; recognizes time on clock; communicates; some independence in self-care; housekeeping with supervision or cue cards; meal preparation, can follow picture recipe cards; job skills learned with much repetition; employment in a supported environment; use of public transportation with some supervision; successful friendships attained, but social judgment and life decisions require support.
Severe	Extensive	3-5 yr	Little understanding of written language or number, time, and money concepts; needs extensive supports for problem solving; trainable in some basic activities of daily living, but needs some level of continuous support and supervision for most activities; might communicate wants and needs with use of basic words, phrases, gestures, or with the use of augmentative and alternative communication techniques; trainable in some basic activities of daily living.
Profound	Pervasive	<3 yr	Dependent for self-care, continence, communication needs with supports required for all activities of everyday living; co-occurring physical and sensory limitations are common; may use objects in a goal-directed fashion for recreation or self-care; limited understanding of symbolic communication, but may understand some gestures and emotional cues; uses nonverbal expressions; might need complete custodial or nursing care.

Data from World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th revision. Geneva: WHO; 2011 and American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Washington, DC: American Psychiatric Association.

Periodic Reevaluation

The child's abilities and the family's needs change over time. As the child grows, more information must be provided to the child and family, goals must be reassessed, and programming needs should be adjusted. A periodic review should include information about the child's health status and the child's functioning at home, at school, and in other community settings. Other information, such as psychologic or educational testing, may be helpful. Reevaluation should be undertaken at routine intervals (every 6-12 months during early childhood), at any time the child is not meeting expectations, or when the child is moving from one service delivery system to another. This is especially true during the transition to adulthood, beginning at age 16, as mandated by the IDEA Amendments of 2004, and lasting through age 21, when care should be transitioned to adult-based systems and providers (see Chapter 152).

Federal and Education Services

Education is the single most important discipline involved in the treatment of children with an ID. In the United States, the IDEA, Part B, mandates a free and appropriate public education (FAPE) in the least restrictive environment (LRE) for all school-age children (3-21 years of age). Additionally, Part C mandates early intervention services from birth through 36 months of age to be delivered in a natural environment (usually home) for all qualifying infants and toddlers. The developmental and educational program for children with GDD or ID must be relevant to the child's unique needs and address the child's individual strengths and challenges. The child's developmental level, requirements for support, and goals for independence provide a basis for early intervention services to establish an **individualized family service plan (IFSP),** which focuses on the family's needs to help them optimize the development of their child. For children over 36 months of age, the school system develops an **individualized education program (IEP)**, which focuses on the child's educational needs. Inclusive education seeks to support the right of every child, regardless of ability, to participate in a broad range of activities and contexts as full members of families, communities, and societies with an effort to maximize access, participation, and supports. Research on inclusion reveals benefits for individuals with disabilities and for typically developing children. As such, to the maximum extent appropriate, children with disabilities should be educated with children who do not have disabilities. In general, removal from the regular educational environment should occur only when the nature or severity of the child's disability is such that education in regular classes with the use of supplementary aids and services cannot be achieved satisfactorily, not simply because significant curriculum modifications are needed. Children who are educated in more inclusive settings, regardless of overall developmental level, tend to have higher rates of community participation as adults. Behavioral challenges are the most limiting factor in terms of full inclusion, both in school and within the community, emphasizing the importance of implementing early and consistent behavior management strategies.

Beyond education services, families of children with ID often are eligible for federal or state-provided social services. All states offer developmental disabilities programs that provide home and

community-based services to eligible children and adults, potentially including in-home supports, care coordination services, residential living arrangements, vocational and employment support programs, and additional therapeutic options. A variety of Medicaid waiver programs are also offered for children with disabilities within each state. Children with ID who live in low-income-status households can qualify to receive supplemental security income (SSI), but many of these families do not receive the benefits to which they are eligible.

Leisure and Recreational Activities

The child's social and recreational needs should be addressed. Although young children with ID are generally included in play activities with children who have typical development, adolescents with ID often do not have opportunities for enriching social interactions. Community participation among adults with ID is much lower than that of the typical population even though these individuals tend to have the same preferences and wishes for leisure activities as their nondisabled peers. Individuals with ID experience high rates of marginalization, especially from involvement in formal recreational programs, often because of insufficient resources to accommodate participation, difficulties with expenses and transportation, and so forth. To reduce isolation, ideas for inclusion in leisure activities should be explored with families, including church group involvement, Boy and Girl Scout chapters, 4H clubs, local park district programs, and musical opportunities like choir and instrumental lessons. Participation in sports should be encouraged (even if the child is not competitive) because it offers many benefits, including weight management, development of physical coordination, maintenance of cardiovascular fitness, and improvement of self-image. Inclusion in class trips, dances, dating, and other social events should be encouraged. International programs such as Special Olympics and Best Buddies International seek to enhance inclusion and visibility of individuals with disabilities and can be a valuable resource.

Family Counseling

Many families adapt well to having a child with ID, but some have emotional or social difficulties. The risks of parental depression and child abuse and neglect are higher in this group of children than in the general population. The factors associated with good family coping and parenting skills include stability of the marriage, good parental self-esteem, limited number of siblings, higher socioeconomic status, lower degree of disability or associated impairments (especially behavioral), parents' appropriate expectations and acceptance of the diagnosis, supportive extended family members, and availability of community programs and respite care services. In families in whom the emotional burden of having a child with ID is great, family counseling, parent support groups, sibling support groups and camps, respite care, and home health services should be an integral part of the treatment plan.

Transition to Adulthood

The transition to adulthood can present a stressful and chaotic time for the adolescent with ID and their family (see Chapter 152). A successful transition correlates with better quality of life but requires significant advanced planning. The transition process for those with ID extends beyond medical care and needs to include education and employment, health and well-being, finances and independence, and social and community life. Specific issues include:

- Decision-making (supported decision-making, guardianship, power of attorney)
- Accessing and securing social benefits for which the person is eligible (e.g., SSI, Medicaid)
- The choice of living arrangements and necessary supports (independent living, shared living arrangements, or living with parents; community-integrated living arrangements; group homes)
- Estate planning for the parents (ABLE accounts, special needs trust)
- Postsecondary training (vocational choices, postsecondary education – pacer.org)
- Community participation and involvement in leisure activities (e.g., community service and volunteering activities, religious groups, Special Olympics, Best Buddies, local clubs)

Successful transition is difficult to achieve because of policies, systems, and services that are not comprehensive or coordinated. In moving from child to adult care, families tend to find that services are less readily available, more fragmented, and more difficult to navigate across multiple agencies and jurisdictions.

Transition planning is a required element of the IEP process by age 16 years, and options for continued education or entry into the workforce after high school should be thoroughly considered, with the greater goal of ultimate community-based employment. Postsecondary education possibilities might involve community college or vocational training. In 2008, the U.S. Higher Education Opportunity Act (HEOA) granted students with ID access to federal financial aid to attend colleges with **Comprehensive Transition Programs** (CTPs), which are designed for postsecondary students with ID to continue academic, career and technical, and independent living instruction to prepare for employment. As of 2019, more than 265 nondegree postsecondary programs for students with ID exist nationwide in the United States.

Although employment is a critical element of life adaptation for persons with ID, only 15% are estimated to have jobs, with significant gaps in pay and compensation compared to workers without disability. Employment selection should be "customized" to the individual's interests and abilities. Options may include participation in competitive employment, supported employment, high school–to–work transition programs, job-coaching programs, and consumer-directed voucher programs.

Self-Advocacy

The self-advocacy movement represents an important effort by persons with ID and other disabilities to advocate for maximal autonomy and self-determination in all aspects of life. This movement is a part of the greater disabilities rights movement and represents a resistance to historical systemic injustices experienced by individuals with ID, including neglect, abuse, nonautonomy, marginalization, incarceration, sterilization, and isolation. Self-advocacy stresses that individuals with ID should be able to speak for themselves, should be involved maximally in decision-making, should be treated as equal and fully included in society, and should be given as much control over their own self-direction as possible. This movement emphasizes the tenet of "nothing about us without us" and has led to nationwide changes in terms of policy and medical and legal nomenclature. Above all, the self-advocacy movement has sought to redefine the approach to disability, moving toward a social model of acceptance, equality, accommodation, and inclusion, putting the onus on society to change its attitudes and practices rather than calling on the individual with ID to change.

OUTCOMES

In children with severe ID or ID requiring significant supports, the prognosis is often evident by early childhood. Mild ID might not always be a lifelong disorder. Children might meet criteria for GDD at an early age, but later the disability can evolve into a more specific developmental disorder (language disorder, autism, ADHD, specific learning disability, or borderline intelligence). Others with a diagnosis of mild ID during their school years may develop sufficient adaptive behavior skills that they no longer fit the diagnosis as adolescents or young adults, or the effects of maturation and plasticity may result in children moving from one diagnostic category to another (from

moderate to mild ID). Conversely, some children who have a diagnosis of a specific learning disability or communication disorder might not maintain their rate of cognitive growth and may fall into the range of ID over time.

The apparent higher prevalence of ID in low- and middle-income countries is of concern, given the limitations in available resources. **Community-based rehabilitation (CBR)** is an effort promoted by the World Health Organization (WHO) over the past 4 decades as a means of making use of existing community resources for persons with disabilities in low-income countries, with the goal of increasing inclusion and participation within the community. CBR is now being implemented in >90 countries, although the efficacy of such programs has not been established.

The long-term outcome of persons with ID depends on the underlying cause; degree of cognitive and adaptive deficits; presence of associated medical, developmental, and behavioral impairments; capabilities of the families and schools; and availability of community supports, services, and training provided to the child and family (see Table 56.10). As adults, many persons with mild ID can gain economic and social independence with functional literacy, but they may need periodic support or supervision (especially when under social, economic, or health-related stress). Most live successfully in the community, either independently or in supervised settings. Many will marry, some will have children, and meaningful and long-lasting relationships can be expected.

For persons with moderate ID, the goals of education are to enhance adaptive abilities and "survival" academic and vocational skills, so they are better able to live and function in the adult world (Table 56.11). The concept of supported employment has been very beneficial to these individuals; the person is trained by a coach to do a specific job in the setting where the person is to work, bypassing the need for a "sheltered workshop" experience and resulting in successful work adaptation in the community and meaningful inclusion. These persons generally live at home with family or in a supervised setting in the community, such as a **community integrated living arrangement (CILA)** where different levels of supervision and support are provided depending on the needs of the individuals. There has been a strong movement away from institutionalized living, defined as residence in a facility of four or more people who did not choose to live together.

As adults, people with severe to profound ID usually require extensive to pervasive supports (see Table 56.11). These individuals often have associated impairments, such as CP, behavioral disorders, epilepsy, or sensory impairments, that further limit their adaptive functioning. They can perform simple tasks in supervised settings. Most people with this level of ID can live in the community with appropriate supports, though some may require a higher level of "institutional care" that is best provided though smaller community-run group home settings.

The life expectancy of people with mild ID is similar to the general population, with a mean age at death in the early 70s. However, persons with severe and profound ID have a decreased life expectancy at all ages, presumably from associated serious neurologic or medical disorders, with a mean age at death in the mid-50s. Given that persons with ID are living longer and have high rates of comorbid health conditions in adulthood (e.g., obesity, hypertension, diabetes), ID is now one of the costliest ICD-10 diagnoses, with an average lifetime cost of 1-2 million dollars per person. Thus the priorities for pediatric primary care are to improve healthcare delivery systems during childhood; facilitate the transition of care to adult providers; and ensure high-quality, integrated, community-based services for all persons with ID.

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Chapter 57

Down Syndrome and Other Abnormalities of Chromosome Number

Mary Pipan

PRINCIPLES OF CARING FOR CHILDREN WITH COMPLEX GENETIC DISORDERS

Down syndrome (trisomy 21) is the most common genetic cause of intellectual disability, with an incidence of 1 in 700 live births in the United States. Many of the principles of care for individuals with Down syndrome generalize to other complex genetic disorders. Genetic disorders generally affect all cells in the body, and hence tend to be multisystemic disorders. Trisomy 21's multisystem effects require monitoring of all organ systems for potential related issues.

Chromosome 21 is the smallest human autosome, which likely accounts for the relatively high fetal survival rate in trisomy 21. The clinical manifestations of *other* trisomies and aneuploidies are shown in Tables 57.1 and 57.2 and Figs. 57.1, 57.2, and 57.3. Fetuses with other

Table 57.1 Chromosomal Trisomies (13, 18) and Their Clinical Findings

TRISOMY 13	TRISOMY 18
HEAD AND FACE	
Scalp defects (e.g., cutis aplasia) Microphthalmia, corneal abnormalities Cleft lip and palate in 60–80% of cases Microcephaly Microphthalmia Sloping forehead Holoprosencephaly (arrhinencephaly) Capillary hemangiomas Deafness	Small and premature appearance Tight palpebral fissures Narrow nose and hypoplastic nasal alae Narrow bifrontal diameter Prominent occiput Micrognathia Cleft lip or palate Microcephaly
CHEST	
Congenital heart disease (e.g., VSD, PDA, ASD) in 80% of cases Thin posterior ribs (missing ribs)	Congenital heart disease (e.g., VSD, PDA, ASD) Short sternum, small nipples
EXTREMITIES	
Overlapping of fingers and toes (clinodactyly) Polydactyly Hypoplastic nails, hyperconvex nails	Limited hip abduction Clinodactyly and overlapping fingers; index over third, fifth over fourth; closed fist Rocker-bottom feet Hypoplastic nails
GENERAL	
Severe developmental delays and prenatal and postnatal growth restriction Renal abnormalities 1-year survival <10%	Severe developmental delays and prenatal and postnatal growth restriction Premature birth, polyhydramnios Inguinal or abdominal hernias 1-year survival <10%

ASD, Atrial septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect.
From Behrman RE, Kliegman RM. *Nelson Essentials of Pediatrics,* 4th ed. Philadelphia: Saunders;2002: 142.

Table 57.2 Other Rare Aneuploidies and Partial Autosomal Aneuploidies

DISORDER	KARYOTYPE	CLINICAL MANIFESTATIONS
Trisomy 8	47,XX/XY,+8	Growth and mental deficiency are variable. The majority of patients are mosaics. Deep palmar and plantar furrows are characteristic. Joint contractures are present.
Trisomy 9	47,XX/XY,+9	The majority of patients are mosaics. Clinical features include craniofacial (high forehead, microphthalmia, low-set malformed ears, bulbous nose) and skeletal (joint contractures) malformations and heart defects (60%).
Trisomy 16	47,XX/XY,+16	The most commonly observed autosomal aneuploidy in spontaneous abortion; the recurrence risk is negligible.
Tetrasomy 12p	46,XX[12]/46,XX, +i(12p)[8] (mosaicism for an isochromosome 12p)	Known as Pallister-Killian syndrome Sparse anterior scalp hair (more so temporal region), eyebrows, and eyelashes; prominent forehead; chubby cheeks; long philtrum with thin upper lip and cupid-bow configuration; polydactyly; streaks of hyperpigmentation and hypopigmentation

Fig. 57.1 Several physical manifestations of trisomy 18. **A,** Typical profile reveals prominent occiput and low-set, posteriorly rotated malformed auricles. **B,** Clenched hand showing typical pattern of overlapping fingers. **C,** Rocker-bottom feet. *(Courtesy Kenneth Garver, MD, Pittsburgh, PA.)*

Fig. 57.2 Trisomy 13 syndrome. Note sloping forehead with variable defect in facial development. *(From Jones KL, Jones MC, Del Campo M. Smith's Recognizable Patterns of Human Malformation, 8th ed. Philadelphia: Elsevier; 2022: Fig. 1 A-C, p. 16.)*

Fig. 57.3 Trisomy 13. A and B, Note hyperconvex nails and postaxial polydactyly. C, Aplasia cutis congenita over posterior occiput. D, Scrotalization of the phallus. *(From Jones KL, Jones MC, Del Campo M. Smith's Recognizable Patterns of Human Malformation, 8th ed. Philadelphia: Elsevier; 2022: Fig. 2, p. 17.)*

full autosomal trisomies are not always viable, but partial trisomy and quatrosomy (trisomy or quatrisomy of only part of the chromosome) or mosaic trisomy (only part of the cell lines contain the aneuploidy) can be viable.

The Down syndrome phenotype can occur as a result of full trisomy 21 (95%), partial trisomy 21 (part of the 21st chromosome in triplicate), mosaic trisomy 21, or translocation. Maternal nondisjunction in meiosis is the most common cause of trisomy 21. Paternal origin accounts for less than 10%.

Chromosome abnormalities affect not only the product and function of that particular group of genes but can have upstream and downstream effects on other gene products in linked pathways. The over 314 triplicate genes in Down syndrome are known to affect the products and metabolic activity of genes from every other chromosome. Possible phenotype (condition) gene relationships in trisomy 21 are noted in Figure 57.4.

The link between children's physical health, development, and behavior becomes obvious when caring for children with complex genetic disorders. Children with developmental disabilities often cannot adequately communicate the symptoms of illness. Challenging behaviors can also interfere with adequate assessment and intervention. Too often, sources of distress, developmental challenges, and behavioral issues are attributed to the genetic disorder and dismissed by family, medical, and educational caregivers. Providing care for genetically complex children requires health and other providers to consider a range of potential differential diagnoses when presented with a change in behavior, a plateau or regression in development, or a new physical complaint.

Trisomy 21 affects brain development across the life span, leading to differences in brain anatomy, neurotransmission, and connectivity that affect processing, glial cell function, infrastructure support, energy metabolism, and in adults, the formation of amyloid plaques leading to high risk for early Alzheimer disease. Alterations in brain development and functioning affect learning, behavior, and emotions, leading to an increased incidence of neurobehavioral and psychiatric disorders such as autism spectrum disorders (ASDs), attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, and depression.

It is important for the clinician to understand that children with genetic disorders are genetically more closely related to their biologic family than they are to other children with similar disorders. Children with Down syndrome will have similar patterns of familial heritability for heritable traits and medical conditions as their biologic siblings. Individuals with genetic disorders need to be seen as children/persons first who happen to have a genetic disorder. Using person-first language (child with Down syndrome, *not* Downs child) helps everyone focus on this principle.

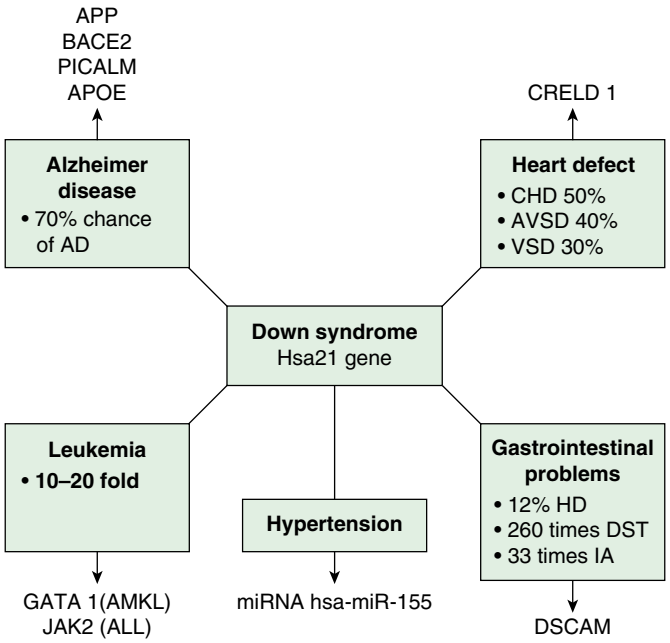

Fig. 57.4 Various conditions associated with Down syndrome with its causative genes. DST, Duodenal stenosis; IA, imperforate anus; HD, Hirschsprung disease; CHD, congenital heart disease; AVSD, atrioventricular septal defects; VSD, ventricular septal defect; AD, Alzheimer disease. *(From Asim A, Kumar A, Muthuswamy S, et al. Down syndrome: An insight of the disease. J Biomed Sci. 2015;22:41, Fig. 1.)*

CLINICAL CHARACTERISTICS

Children with Down syndrome are at increased risk for a variety of congenital anomalies and comorbid medical conditions. Typically, they have a characteristic facial appearance and other physical characteristics that allow clinical recognition of trisomy 21 in the newborn period (Figs. 57.5 and 57.6 and Table 57.3).

The increased risk for a variety of medical conditions continues throughout the life span (Table 57.4). The American Academy of Pediatrics (AAP) has developed Down Syndrome Health Supervision Guidelines for clinicians caring for children with trisomy 21 (Table 57.5). Individuals with Down syndrome often have significant communication deficits, which can result in difficulty reporting pain and discomfort; clinicians need to pay attention to the caregiver's observation of changes in behavior when evaluating the level of pain or illness. Paying close attention to subtle cues on exam

Fig. 57.5 Down syndrome in the neonatal period. **A,** Brushfield spots. **B,** Loose nuchal skin. **C,** Wide space between toes 1 and 2. **D,** Poor tone. **E** and **F,** Accentuation of typical face when crying. *(From Jones KL, Jones MC, Del Campo M. Smith's Recognizable Patterns of Human Malformation, 8th ed. Philadelphia: Elsevier; 2022: Fig. 3, p. 7.)*

Fig. 57.6 Appearance of two 2-year-old children with trisomy 21. The facial appearance of children with trisomy 21 is often characterized by a low nasal bridge, small nose, small ears, up-slanting almond-shaped eyes, and epicanthal folds. *(Photos courtesy of Children's Hospital of Philadelphia.)*

Table 57.3 Clinical Features of Trisomy 21 in the Neonatal Period

CENTRAL NERVOUS SYSTEM
Hypotonia*
Developmental delay
Poor Moro reflex*

CRANIOFACIAL
Brachycephaly with flat occiput
Flat face*
Upward slanted palpebral fissures*
Epicanthal folds
Speckled irises (Brushfield spots)
Three fontanels
Delayed fontanel closure
Frontal sinus and midfacial hypoplasia
Mild microcephaly
Short, hard palate
Small nose, flat nasal bridge
Protruding tongue, open mouth
Small dysplastic ears*

CARDIOVASCULAR
Endocardial cushion defects
Ventricular septal defect
Atrial septal defect
Patent ductus arteriosus
Aberrant subclavian artery
Pulmonary hypertension

MUSCULOSKELETAL
Joint hyperflexibility*
Short neck, redundant skin*
Short metacarpals and phalanges
Short fifth digit with clinodactyly*
Single transverse palmar creases*
Wide gap between first and second toes
Pelvic dysplasia*
Short sternum
Two sternal manubrium ossification centers

GASTROINTESTINAL
Duodenal atresia
Annular pancreas
Tracheoesophageal fistula
Hirschsprung disease
Imperforate anus
Neonatal cholestasis

CUTANEOUS
Cutis marmorata

*Hall's criteria to aid in diagnosis.

Table 57.4 Frequency of Medical Conditions in Trisomy 21

SYSTEM	CONDITION	ESTIMATED FREQUENCY (IF KNOWN)
EYE		
	Cataracts (birth/later)	1.4%/5–37 %
	Glaucoma	1%
	Nystagmus	18–30%
	Strabismus	19–34%
	Refractive errors	80%
	Astigmatism	67–74%
	Nasolacrimal duct obstruction	11–30%
ENT		
	Stenotic ear canals	50%
	Choanal atresia	
	Bifid uvula/mucosal cleft	5%
	Laryngomalacia	
	Middle ear effusions	50–90%
	Adeno/tonsillar hypertrophy	
	Hearing loss	37–78%
DENTAL		
	Tooth agenesis	54–58%
	Malocclusion	>70%
	Periodontal disease	~100% under 30 years
ENDOCRINE		
	Congenital hypothyroidism	1:113 to 1:141 live births
	Acquired hypothyroidism	13–34%
	Subclinical hypothyroidism	7–40%
	Hyperthyroidism	6.5%
	Type 1 diabetes mellitus	0.3–1%
CARDIAC		
	Congenital heart disease	44–54%
	AV canal defects	42% (of CHD)
	VSD	22–35%
	ASD	8–16%
	Tetralogy of Fallot	2–4%
	Acquired mitral, tricuspid, or aortic regurgitation PDA	5–7%

Table 57.4 Frequency of Medical Conditions in Trisomy 21—cont'd

SYSTEM	CONDITION	ESTIMATED FREQUENCY (IF KNOWN)
PULMONARY		
	Pulmonary hypertension	1–5%
	Subglottic stenosis	6%
	Tracheo/laryngomalacia	33% (of ENT-referred population)
	Tracheal bronchus	
	Obstructive sleep apnea	~50%
GASTROINTESTINAL		
	Esophageal atresia	0.5–0.9%
	Duodenal malformations	4%
	Rectoanal malformations	1%
	Hirschsprung disease	3%
	Celiac disease	5–9.8%
	GERD	14–40%
	Constipation	30–49%
GENITOURINARY		
	Renal/urinary tract findings	Up to 25%
HEMATOLOGY/ONCOLOGY		
	Transient myeloproliferative disease (TMD)	5–10%
	Acute megakaryoblastic leukemia (AMKL)	10–20% with TMD, first 4 years of life
	Acute lymphocytic leukemia	0.1–0.2%
ORTHOPEDICS		
	Atlantoaxial instability (AAI)	9–27%
	Symptomatic AAI	1–2%
	Recurrent joint dislocations (shoulder, knee, elbow, thumb)	1–7%
	Pes planus	91%
	Juvenile idiopathic arthritis	~1%
DERMATOLOGY		
	Alopecia/vitiligo	1–11%
	Hidradenitis suppurativa	2%
	Xerosis/eczema	
	Seborrheic dermatitis	
	Psoriasis	0.5–8%
NEUROLOGY		
	Infantile spasms	2–5%
	Seizure disorders	8% (lifetime)
	Strokes and moyamoya	
	Autism spectrum disorder	7–16%
	Early onset Alzheimer disease	~50% >50 yr
	Down syndrome disintegrative disorder	<1%

ENT, Ear/nose/throat; AV, atrioventricular; CHD, congenital heart disease; VSD, ventricular septal defect; ASD, atrial septal defect; PDA, patent ductus arteriosus; GERD, gastroesophageal reflux disease.

and asking direct questions about specific areas of pain or discomfort can be helpful (e.g., "Does your throat hurt?" while pointing to or touching their throat).

Ophthalmology

The red reflex should be evaluated in the newborn period with a thorough ophthalmologic exam in the first 6 months of life and then annually until age 5, then every 2-3 years thereafter. Children with DS are at higher risk for cataracts, glaucoma, nystagmus, strabismus, astigmatism, refractive error, accommodative error, blepharitis, and keratoconus. Visual acuity and visual processing are foundational for development.

Ear, Nose, and Throat

The pinna and external ear canals are often small with a predisposition to cerumen impaction. Middle ear effusion occurs in the majority of children, starting in infancy, and may require referral to an ear/nose/throat (ENT) specialist for better visualization because of stenotic ear canals. Chronic nasal congestion, choanal atresia, adeno/tonsillar hypertrophy, laryngo/tracheomalacia, subglottic stenosis, and laryngeal cleft all can affect feeding and breathing, including contributing to sleep apnea. Most children with DS require regular ENT follow-up.

Many children with DS have some degree of hearing loss (HL). Most commonly this is conductive HL associated with middle ear effusion. Smaller numbers have mixed or sensorineural HL. Hearing is foundational for speech development. Hearing should be screened in the newborn period and with audiologic assessment between 6 and 9 months and every 6 months thereafter until an accurate ear-specific audiologic evaluation is obtained, then annually. Hearing assessment through auditory brainstem responses (requiring sedation) may be needed if audiologic evaluation is inconclusive. Lack of parental concern about hearing should not preclude obtaining audiologic assessment. Aggressive treatment of otitis media and middle ear effusion reduces the frequency of hearing loss.

Dental

Children with DS often have delayed tooth eruption, malformed teeth, microdontia, permanent tooth agenesis, tooth impaction, malocclusion, and supernumerary teeth. Periodontal disease is

Table 57.5 Summary of Down Syndrome-Specific Care

Action	Pre-natal	Birth up to 1 mo	1 mo up to 1 yr	1 yr up to 5 yr	5 yr up to 12 yr	12 yr up to 21 yr
1. Confirm DS diagnosis with either CVS or amniocentesis prenatally or karyotype postnatally						
2. Review recurrence risk and offer the family referral to a clinical geneticist or genetic counselor.						
3. Offer parent-to-parent and support group information to the family.						
4. Use CDC DS-specific growth charts to monitor weight, length, weight-for-length, head circumference, or BMI. Use standard charts for BMI after age 10 years.		All healthcare visits				
5. Order an echo, to be read by a pediatric cardiologist.						
6. Feeding assessment or video study if any: marked hypotonia, underweight (<5th %ile weight-for-length or BMI), slow feeding or choking with feeds, recurrent or persistent abnormal respiratory symptoms, desaturations with feeds		Any visit				
7. Obtain objective hearing assessment (may be in NBS protocols) and follow EHDI protocols.			Up to 6 mo			
8. If TM can't be visualized, refer to otolaryngologist for exam with microscope until reliable TM and tympanometry exams are possible		Every 3-6 mo				
9. Car safety seat evaluation before hospital discharge.						
10. CBC with differential		By day 3				
11. If TAM, make caregivers aware of risk/signs of leukemia (e.g., easy bruising/bleeding, recurrent fevers, bone pain)						
12. TSH		At birth (if not in NBS)	Every 5-7 mo	Annually, and every 6 mo if antithyroid antibodies ever detected		
13. RSV prophylaxis based on AAP guidelines.		Annually		Through 2 yr		
14. Discuss cervical spine-positioning for procedures and atlantoaxial stability precautions.		All HMV		Biennially		
15. Assess for CAM use, discourage any unsafe CAM practices.		All HMV				
16. Refer children to early intervention for speech, fine motor or gross motor therapy.		Any visit	Up to 3 yr			
17. If middle ear disease occurs, obtain developmentally-appropriate hearing evaluation.			When ear clear	After treatment		
18. Rescreen hearing with developmentally-appropriate methodology (BAER, behavioral, ear-specific).			Start at 6mo, every 6 mo until established normal bilaterally by ear-specific testing, then annually			
19. Refer to ophthalmologist with experience and expertise in children with disabilities.			By 6 mo			
20. CBC with differential if easy bruising or bleeding, recurrent fevers, or bone pain			Any visit			
21. Assess for sleep-disordered breathing; if present, refer to physician with expertise in pediatric sleep disorders.			At least once by 6 mo, then all subsequent HMV thereafter			
22. Ensure child is receiving developmental therapies, and family understands and is following therapy plan at home.		All HMV				
23. CBC with differential and either (1) a combination of ferritin and CRP, or (2) a combination of serum iron and Total Iron Binding Capacity				Annually		
24. If a child has sleep problems and a ferritin less than 50 mcg/L, the pediatrician may prescribe iron supplement.				Any visit		
25. Vision screening			All HMV, use developmentally-appropriate criteria	Photoscreen (all HMV); if unable, refer to ophthalmologist annually	Photoscreen (all HMV); if unable, refer to ophthalmologist biennially	Visual acuity or photoscreening at all HMV, or ophthalmology-determined schedule
26. If a child has myelopathic symptoms, obtain neutral C-spine plain films (see text for details).				Any visit		
27. Obtain polysomnogram.				Between 3-5 yr		
28. Prepare family for transition from early intervention to preschool.				At 30 mo		
29. Discuss sexual exploitation risks.				At least once	At least once	At least once
30. Make developmentally-appropriate plans for menarche, contraception (advocate/offer LARC), and STI prevention.					As developmentally-appropriate, then all subsequent HMV	
31. Discuss risk of DS if patient were to become pregnant.					At least once	At least once
32. Assess for any developmental regression.			All HMV			
33. Discuss and facilitate transitions: education, work, finance, guardianship, medical care, independent living					All HMV starting at 10 yr	

	Do once at this age
	Do if not done previously
	Repeat at indicated intervals
(border)	See report for end point

Abbreviations: DS, Down syndrome; CVS, Chorionic villus sampling; HMV, Health Maintenance Visit; BMI, Body mass index; CDC, Centers for Disease Control; EHDI, Early Hearing Detection and Intervention; NBS, Newborn screen; CAM, Complementary and alternative medicine; BAER, Brainstem auditory evoked response; TM, Tympanic membrane; TAM: transient abnormal myelopoiesis

From Bull MJ, Trotter T, Santoro SL, et al. Health supervision for children and adolescents with Down syndrome. *Pediatrics*. 2022;149(5):e2022057010.

seen in the majority of individuals with DS. Starting oral health preventive programs young, close supervision and support of dental hygiene and chemical adjuvants improve outcomes. Children with DS should first see a pediatric dentist at age 1 year and follow up at least every 6 months. For children who do not tolerate dental examinations or procedures, sedated examinations may be necessary, preferably in a hospital with anesthesiologists familiar with caring for patients with DS.

Endocrine

Children with DS are at risk for congenital and acquired hypothyroidism (HT) and hyperthyroidism (Graves disease [GD]). Thyroid testing should be done at birth as part of newborn screening. Acquired HT and GD are autoimmune disorders with elevated thyroid antibodies. Thyroid-stimulating hormone (TSH) testing can detect both HT and hyperthyroidism and should be checked by 6 months, at 1 year, and then annually thereafter. Most cases of thyroid disorders are asymptomatic and would be missed without screening. Compensated HT refers to mild elevations in TSH with normal T_4, requiring continued monitoring. Low TSH can indicate Graves disease. Children with DS who have GD can develop HT, and those with HT can develop GD. Thyroid disorder should be considered as part of the differential diagnoses with mood or behavior changes, slowing of growth, exophthalmos, high blood pressure, or tachycardia.

Type 1 diabetes mellitus (DM) is more common in children with DS. Screening for type 2 DM, especially in obese individuals, should follow similar guidelines to the typically developing (TD) population.

Cardiac

Congenital heart disease (CHD) affects about half of all children with DS, including atrioventricular (AV) canal defects, atrial septal defect (ASD), ventricular septal defect (VSD), tetralogy of Fallot (TOF), patent ductus arteriosus (PDA), and patent foramen ovale (PFO). All children with DS should have an infant echocardiogram even with a normal physical examination. Cardiology follow-up will be based on echocardiogram findings. Signs of heart failure such as failure to thrive, tachypnea, easy fatigue, or sweating with feeds require expedited referral back to cardiology. Pulmonary hypertension can also occur in children with DS related to congenital heart defects or to respiratory illness. Later in adolescence and adulthood, clinicians should be aware of the increased risk for valvular heart disease and endocarditis.

Pulmonary

Respiratory infections are the most common cause for hospital admission of children with DS without CHD and are a common cause of mortality in children with CHD. Respiratory compromise may present with subtle signs of respiratory distress such as tachypnea, intercostal retraction, shortness of breath, and easy fatigue with exertion. The lack of overt distress may lead clinicians to underestimate the level of respiratory compromise. Both anatomy and immunodeficiency associated with DS can lead to increased risk for upper and lower respiratory infections. Macro and micro pulmonary structural anomalies have been reported. Gastroesophageal reflux disease, swallowing dysfunction, and upper airway differences (including transesophageal [TE] fistula) increase the risk of aspiration.

Sleep

The estimated prevalence of obstructive sleep apnea (OSA) ranges from 31% to 79%, and onset occurs from infancy through adulthood. A sleep study before the age of 4 years is recommended. Clinicians should consider ordering a sleep study at any age, with chronic signs of respiratory compromise when awake or asleep or daytime symptoms of nonrestorative sleep. There is some evidence that OSA causes difficulties in cognitive, behavioral, and adaptive functioning in children with DS. Obesity increases the risks for OSA in many children with DS.

Neurology

Children with DS ages 6-18 months are at increased risk for infantile spasms (IS). The outcome is often better with treatment than the non–DS population with ID but is variable, ranging from no obvious sequelae to ongoing seizure disorders, ASD, and more severe intellectual disability. In addition to the classic signs of IS, change in mental status in an infant or toddler or a plateau or regression in development should lead to prompt neurologic evaluation, including an electroencephalogram (EEG). Children with trisomy 21 are at increased risk for other seizure disorders. There is an increased risk for strokes possibly related to CHD, vascular malformations (including moyamoya syndrome), and other risk factors.

Gastrointestinal

Most children with DS have structural or functional gastrointestinal (GI) comorbidities, many of which can affect individuals across the life span. There is evidence of abnormalities in enteric nerves affecting microanatomy and nerve function. Congenital anomalies include esophageal atresia, TE fistula and duodenal atresia, stenosis, and webs, Hirschsprung disease, and anorectal malformations. Constipation and gastroesophageal reflux disease (GERD) are frequent causes of irritability, GI discomfort, feeding issues, toileting refusal, and incontinence. There appears to be a strong association between GERD, pneumonia, and OSA. Children with DS are also at higher risk of celiac disease, which can cause GI, nutritional, and behavioral issues. The AAP guidelines do not recommend routine celiac screening, but rather to maintain a high index of suspicion with GI complaints, growth faltering, or behavioral concerns. Many others, however, have performed routine screening because many patients with DS who have celiac disease are asymptomatic; there may be a lag of 2-3 years before symptoms appear.

Nutrition/Obesity

In infancy and early childhood, dysphagia, GI conditions, cardiac, and respiratory complications may cause failure to thrive. Weight faltering can continue for older children because of the same issues but may be more intermittent. Because of the high rates of dysphagia in infants with DS, video swallow studies should be considered when there is any sign of weight faltering, aspiration, feeding difficulties, or recurrent respiratory infections. Thickened formulas, low-flow bottles/nipples, or slower paced feeding may be required. Nasogastric (NG) or gastric tube (GT) supplementation to assure adequate nutrition may be needed. Many babies with DS can successfully breastfeed, and clinicians need to be encouraging but watchful for growth faltering.

Obesity becomes more prominent in early childhood and extending into adulthood. In school-age children with DS, those at 50% or greater on DS-specific BMI charts are in the obese range. Thus to gauge the level of overweight for children with DS, the Centers for Disease Control and Prevention (CDC) curves for BMI should be used. When children with DS gain more autonomy in feeding, overeating can become a problem. Many do not appear to satiate and will continue to eat as long as food is presented or will seek food. Caregivers therefore cannot rely on the child's satiety to determine caloric sufficiency. Decreased basal metabolic rates (reduced caloric needs) and lower physical activity can also contribute to obesity. Anticipatory guidance regarding healthy nutritional practices, meal and snack limits, and active lifestyle choices should be part of well-child visits from a young age.

Genitourinary

Renal and urinary tract abnormalities, including ureteropelvic junction obstruction, vesicoureteral reflux, renal hypoplasia, obstructive uropathy and posterior urethral valves, hypospadias,

Table 57.6 Neurodevelopmental, Neurobehavioral, and Psychiatric Characteristics of Trisomy 21

MOTOR SKILLS	
Gross motor skills	0-24 mo: Mild delays initially which widen with age At 2 years 25% walking
Oromotor	Dysphagia 0-6 mo: 50% Self-feeding delays: 70%
Fine motor skill	Early skills delays: ~75% Bimanual skill delays: 100%
SPEECH AND LANGUAGE	
Intelligibility	Frequently unintelligible (parent report): 5-21 yr: 54–57% Motor speech impairment: Delay: 27% Articulation: 60% Apraxia: 33% Dysfluency: Stuttering: 10–45% Cluttering (abnormally rapid or irregular pace or both): 80%
Language	Receptive: Similar to mental age–matched controls Expressive: More delayed relative to mental age–matched controls Syntax: More impaired than expressive vocabulary Pragmatics: Same variety of language functions as mental age–matched peers; may be less likely to ask for clarification
SOCIAL AND EMOTIONAL DEVELOPMENT	
	High sociability Joint attention compared with mental age–matched peers Strong imitation skills Pro-social empathetic responses to others in distress Underexpression of emotional distress Less frequent and shorter social referencing Reduced ability to read facial expressions More restricted repetitive behaviors and interests Average social motivation but lower social cognition
COGNITION	
	Intellectual disability: Mild: ~25% Moderate: ~50% Severe: ~25% Decline in IQ throughout childhood (slowing in developmental progress relative to same-age peers) Strengths: Implicit memory, visual spatial sequencing, visual spatial construction, and nonverbal memory Weaknesses: Working memory capacity, explicit memory, verbal processing, auditory short-term memory, complex visual spatial skills, executive functioning
Oppositional behaviors	70%
Aggression	4–15%
Self-injurious behavior	18%
Autism spectrum disorders	15–20%
ADHD	14–40%
Anxiety disorders	10–22%
Obsessive-compulsive disorders	0.5–4.5%
Depression	5–11%
Catatonia/Down syndrome disintegrative disorder	Multiple case series and case reports

IQ, Intelligence quotient; ADHD, attention-deficit/hyperactivity disorder.

asymptomatic renal pelvic dilatation, kidney ectopia, proteinuria and hematuria, immunoglobulin A (IgA) nephropathy, and focal segmental glomerulosclerosis, occur more frequently than in the general population. There are no current guidelines for regular surveillance, but clinicians need to maintain a high index of suspicion.

Sexuality and Reproductive Health

Males and females with DS undergo puberty at similar ages to peers. In males, after puberty, testicular volume decreases and gonadal dysfunction worsens with age. Males are infertile, with few exceptions. Females with DS are fertile, having a 33% chance of having a child with DS. Menstrual problems, including irregular periods, and premenstrual irritability are common reasons for use of oral contraceptives. Most females manage menstrual periods well, but there may be difficulties with hygiene. Menopause tends to occur early.

Individuals with DS are at increased risk for sexual abuse, and caregivers should discuss appropriate and inappropriate contact and relationships from an early age. Sexuality education should be included in their educational curriculum. Clinicians should discuss sexuality, birth control, and reproductive issues at health maintenance visits.

Hematology-Oncology

AAP guidelines recommend a complete blood cell count (CBC) with differential for all newborns with DS. Neonates with DS commonly have hematologic abnormalities, including peripheral blasts, neutrophilia, thrombocytopenia, or polycythemia. Five to ten percent of neonates with DS have transient myeloproliferative disorder (TMD) (also called *transient abnormal myelopoiesis* [TAM]), which is associated with pathologic variants in *GATA1*. Typically, this resolves spontaneously within the first 1-3 months of life, but 10–20% will develop acute megakaryocytic leukemia (AMKL) in the first 4 years of life. AMKL is sensitive to treatment in most cases and has a good prognosis.

Children with DS are ~20 times more likely to get acute lymphoblastic leukemia (ALL) (1 in 900-1,000) than the typical population, which is associated with pathologic variants in *JAK2*. Treatment trials show lower response rates, higher recurrence rate, and higher treatment-related mortality.

Annual hemoglobin screening for anemia is recommended throughout childhood with additional testing for ferritin and C-reactive protein (CRP) when iron deficiency is suspected. The incidence of anemia in DS may be similar or increased compared with the general population. Other common CBC findings include macrocytosis, low white blood cell (WBC) count, and polycythemia, the clinical significance of which is unknown.

Immunology/Allergy

Individuals with DS are more susceptible to infections because of mild to moderate T- and B-cell lymphopenia, with a decrease in naive lymphocytes, impaired mitogen-induced T-cell proliferation, reduced specific antibody responses to immunizations, and defects of neutrophil chemotaxis. Nonimmunologic anatomic factors also contribute to the increased risk of respiratory infections. Children with DS with significant numbers of serious infections or difficulty clearing infections need further immunologic evaluation.

Autoimmune disorders are also more common, including thyroid disorders, celiac disease, alopecia areata, vitiligo, type 1 DM, juvenile idiopathic arthritis, and systemic lupus erythematosus.

Musculoskeletal

Individuals with DS have short stature across the life span and stop growing sooner than typical peers, the mechanism of which is unclear. Growth hormone is rarely deficient. Ligamentous laxity is common, especially in the ankles and feet. Inflammatory arthritis is underrecognized, and scoliosis is more common. Joint instability is most apparent in the neck (atlantoaxial instability [AAI]), hips, and knees. Joint pain and impaired mobility can contribute to motor skills deficits, impede independence, and add to behavioral difficulties.

Radiographic screening for AAI is not recommended because flexion/extension neck x-rays are not predictive for future neurologic risk. Signs and symptoms of AAI occur because of compression of the spinal cord from slippage of the C1 or C2 vertebrae, which can occur after an injury or anesthesia but can also be seen spontaneously. Neck pain, stiffness, and/or myelopathic signs and symptoms (e.g., change in gait, bowel, or bladder pattern or weakness) should prompt referral to orthopedics or neurosurgery. Universal neck precautions are recommended for all children with DS, assuming that all are at risk for injury from AAI, including limited participation in any activities that would be associated with forcible neck movement such as contact sports, diving, and universal cervical precautions with intubation procedures/surgery. Children with DS should be secured in rear-facing car seats until 40 pounds and may need harness-style car restraints over 40 pounds.

Hip instability resulting in recurrent (often painless and voluntary) hip dislocation and patellar instability can impair ambulation and may require surgical interventions.

Dermatology

Although causing minor morbidity, dermatologic problems can be highly distressing to patients and families due to appearance (e.g., alopecia), discomfort (e.g., eczema, hidradenitis), or intractability (e.g., onychomycosis). Common conditions include folliculitis, hidradenitis suppurativa, eczematous and seborrheic dermatitis, autoimmune alopecia and vitiligo, fungal infections including tinea pedis and onychomycosis, angular cheilitis, and hyperkeratosis.

DEVELOPMENTAL AND BEHAVIORAL CHARACTERISTICS

Development and behavior concerns are almost universal. Some concerns are easily explained and remediated and are responsive to appropriate therapeutic or behavioral interventions, but others may indicate an underlying neurobehavioral disorder such as autism, ADHD, depression, or anxiety (Table 57.6). Thinking through the categories that follow will help clinicians understand this complexity and direct families to appropriate resources.

Motor Skills

Children with DS often have marked delays in motor skills in early development related to hypotonia, ligamentous laxity, and lack of coordination.

Acquisition of early gross motor skills is foundational for postural control, feeding, visual motor development, socialization, and communication. Without stimulation and support, infants with DS may persist in lax postural control, further adding to motor delays. Through toddler and childhood many gradually improve but have persistent deficits in motor control and coordination and more difficulty with speed and complex postural changes, as well as persistent hypotonia. **Physical therapy** in the first years of life concentrates on core strengthening and ensuring acquisition of adaptive motor planning that supports effective ambulation. Gait abnormalities and persistent low core strength often require ongoing physical therapy. Developing physical literacy in recreational fitness activities, such as swimming, and community sports can also support health and well-being in school-age and adult years.

Oromotor skills are often delayed, with dysphagia in half of infants, requiring feeding therapy, thickening of formula, low-flow nipples, pacing between swallows, and sometimes supplemental enteral feeding. **Feeding therapy** helps young children learn to handle food boluses, chew, and drink from a cup.

Fine motor skills are also delayed, although they seem to be acquired in the same sequence as typically developing peers, but with a wider age range of acquisition. Most unaffected children are able to write their name between 60 and 72 months, but in children with DS, this usually occurs between 120 and 216 months. **Occupational therapy** often helps remediate or compensate for motor difficulties interfering with independence in activities of daily living.

Speech and Language Skills

Individuals with DS often have difficulty speaking clearly enough to be readily comprehensible to listeners across the life span resulting in communication breakdowns, which can be frustrating to both parties. Typical children are 90–100% intelligible by age 4 years. In individuals with DS over 50% of parents reported frequent difficulties in intelligibility over the age of 5 years into adulthood, and almost all qualify for a diagnosis of a motor speech disorder. Differences in voice quality, articulation, phonology, fluency, prosody, and motor coordination (apraxia) all contribute to making speech hard to understand (see Chapter 53). The complexity of speech impairments in children with DS requires **speech therapy** evaluation with targeted interventions for each individual.

Children with DS relative to children matched for nonverbal skills show similar abilities in receptive vocabulary but impairments in expressive vocabulary, syntax, grammar, and verbal short-term

memory indicative of a specific language impairment (SLI). The frequency of such impairments requires comprehensive language assessment for all children with DS. The language impairment may be associated with decreased ability to express thoughts and feelings verbally and use of fewer words in answer to questions or to carry on a conversation.

Misunderstandings may occur if the individual refers to past events in the present tense or thinks that something described as a future event will happen immediately. Verbal short-term memory deficits affect comprehension of more complex language (e.g., multistep instructions, complex sentences, conversation, and narrative) and reading comprehension. Visual, contextual, and multisensory supports incorporated into both receptive and expressive language can be helpful.

Speech and language intervention has been shown to be effective, especially when of higher intensity; focused on individual needs and targeted skills; and when taking into account the individual's age, interests, and motivators. Use of **applied behavior analysis** to teach communication skills improves outcomes. Incorporating interventions across contexts (classroom, home, and community settings) and into pragmatic language situations outside of structured learning settings (e.g., peer interaction, conversation) supports generalization of skills learned in therapy. For some individuals with DS, speech and language intervention will be required through school and possibly into adulthood.

Social and Emotional Development

Social and emotional development occurs as a complex transactional process between the child and their social partners. Children with developmental delays will likely also have delays in their social interactions, social communication, and play. Children with DS often have a strong orientation toward sociability. From early infancy, mutual gaze in babies with DS emerges more slowly but once established tends to last longer, with sometimes strong preferences for looking at people as opposed to toys and other objects. Development of joint attention is commensurate with developmental age-matched peers and may be a relative strength. Strong imitation skills are noted in children with DS. Children with DS show stronger pro-social empathetic responses to others' distress, but their own expression of distress tends to be dampened (often described as high pain tolerance or, in older children, a perceived reluctance to acknowledge feelings of distress).

There are relative weaknesses in social development, which can help explain some of the social difficulties caregivers encounter. Children with DS have been shown to socially reference less frequently, with shorter glances toward others, and some have more difficulty interpreting the facial expressions of others. Older children with DS have more restricted repetitive behaviors and interests, including rigidity and insistence on sameness. Despite typical social motivation, they may have difficulties with social cognition and difficulty gaining and maintaining friendships. Having friends has been associated with improved quality of life in children with DS. Most adolescents are happy with their level of friendships, but friends may include helpers and adult companions. Leisure time is often spent at home with family or by themselves, and socializing with same-age peer-friends occurs predominantly in the context of common educational or community activities. Building healthy sustained friendships with both TD peers and those with developmental disabilities often requires active ongoing caregiver and community support to prevent social isolation and loneliness as children transition to adulthood.

Cognition

Individuals with DS have varied degrees of intellectual and learning disabilities. Intelligence quotient (IQ) scores of adults with DS are mostly in the 40s-60s, and tests of adaptive functioning typically have standard scores in the low 50s. In children with DS, IQ scores tend to decline with age because progress is slower than same-age peers, and deficits are more marked in higher-level thinking. Thus the gap between children with DS and same-age peers widens with age. An actual plateau in functioning before mid-adolescence or a decline at any age is not typical and should prompt thorough etiologic evaluation.

IQ scores are of limited value for intervention planning, as they provide limited information about relative strengths and weaknesses. Children with DS often have relative strengths in areas of imitation, implicit memory, visual spatial sequencing, visual spatial construction, and nonverbal memory. Relative weaknesses tend to occur in working memory capacity, explicit memory, verbal processing, auditory short-term memory, more complex visual spatial skills (mental rotation, closure, wayfinding), and executive functioning (see Chapter 49). Recognizing a child's individual learning profile and building on strengths while supporting weaknesses will help caregivers, teachers, and therapists work together to teach children effectively to their potential.

Children's reading skills are generally commensurate with their nonverbal mental age. Many children with DS can learn to read, some phonologically, some orthographically. Reading comprehension largely relies on language comprehension skills and is often more difficult.

Mathematics is much more difficult because of weak working memory, language deficits, and fine motor skills. Math interventions generally include direct instruction, modeling, guided and repeated practice, and use of concrete materials.

Neurobehavioral Challenges and Disorders

Autism Spectrum Disorder

Due to the sociability associated with children with DS, ASDs have been underrecognized in the past but are estimated to occur in 15–20% of children with DS. Studies also have shown that autism symptoms are not attributable to the degree of developmental disability and that individuals with DS and ASD are distinct from those with DS alone. *Children with DS who show high levels of repetitive behavior, maladaptive behaviors (e.g., aggression, self-injury, destructive behaviors), social isolation, or difficulty with reciprocal social interaction should be referred for further evaluation, even when overtly sociable.* Children with ASD require specialized behavioral and educational interventions with an emphasis on functional communication, social and play skills development, and sensory-based supports (see Chapter 58).

ADHD

The reported incidence of ADHD in children with DS varies greatly, from 14% to 44%. Inattention, impulsivity, and hyperactivity, the core symptoms of ADHD, are nonspecific, and it can be difficult to differentiate all the factors contributing to these symptoms in children with DS (see Chapter 50). From a clinical perspective, the diagnosis of ADHD relies on reports of ADHD symptoms from two different settings (usually parent and teacher) and dysfunction caused by the ADHD symptoms in areas such as learning, socialization, and safety. Medication use in ADHD has been shown to be effective in children with DS, but the response rates are lower than in typical peers with ADHD. Further, there are higher rates of significant side effects, with some children showing decline in behavior and cognitive performance on medication.

Aggression and Self-Injurious Behaviors

Aggressive behavior is more common in children with many genetic disorders, including DS. The estimated incidence in DS is 4–15%, which is higher than the general population but less than many other genetic syndromes. Aggression disproportionately affects quality of life for the individual and family members and may result in the use of medications and more restrictive educational placements. These behaviors occur more often in males and in individuals with ASD, ADHD, or poor communication skills. Self-injurious behavior (SIB) occurs in

~18%. Individuals with DS who engage in SIB are likely to have lower cognitive and communication ability (may be nonverbal), more repetitive behaviors, higher levels of activity and impulsivity, and fewer social interactions. Assessment of aggression or SIB should include a functional behavioral analysis (FBA) along with overall skills assessment with emphasis on communication. New onset or escalation of aggression or SIB should also include careful assessment for potential sources of pain or discomfort that may exacerbate these behaviors. Behavioral interventions designed based on the results of the FBA should be the initial intervention. Medications may be needed to address symptoms of ADHD, irritability, mood, or anxiety.

Oppositional Behaviors

Disobedience and stubbornness are common. In some cases, this behavior may relate, at least in part, to differences in cognitive processing. Children with DS have difficulty shifting attention or disengaging from activities. They often desire sameness and resist changes to routine or to the way they think things should be done. Difficulties with language comprehension or frustration with a task or trying to express oneself may result in behaviors that are seen as oppositional. When combined with difficulty problem solving, low frustration tolerance, and emotional dysregulation, disruptive or sometimes verbally or physically aggressive behaviors may result. Before diagnosing a child as having oppositional defiant disorder (see Chapter 42), clinicians should try to understand potential comprehension or skill deficits that may be contributing to the behavior. If the child has difficulty with transitions, interventions to help them shift activities more easily such as transition routines, warnings, or countdowns may be most helpful. Visual schedules can also be helpful to prepare the child for what is next, as can providing some additional time for the transition. Simplifying language can help avert communication frustration.

Anxiety

There is an increased prevalence of anxiety disorder in children with DS compared with typical peers. Generally, anxiety disorders are diagnosed based on verbal descriptions of fear or worry and the impact of the fear or worrying on functioning or individual distress. Whereas some individuals with DS have the language skills to describe these experiences, others do not. Clinicians often need to rely on the history from caregivers and contextual cues. Behavioral reactions to anxiety can result in flight-or-fight responses. Thus anxiety could manifest with aggressive or escape/avoidance behaviors. Cognitive-behavioral therapy or exposure therapies can be helpful, and medication management is sometimes needed when anxiety is overwhelming or affects sleep or daytime functioning. Evidence for effectiveness of intervention in DS specifically is sparse.

Obsessive-Compulsive or Perseverative Behaviors

Children and adults with DS often need specific things to be a certain way or may have repetitive patterns of behavior that can seem obsessive or compulsive. They may spend many minutes arranging pillows on their bed, need all doors in the house to be shut, make long lists, or perseveratively ask about upcoming events. These behaviors can be associated with anxiety, and the possibility of increased anxiety should be investigated if there are sudden increases in intensity or frequency of these behaviors.

Depression

The prevalence of depression in DS ranges from 4% to 11%, with most studies being done in adults. This may be an underestimation, as depression in individuals with intellectual disability can be difficult to diagnose because of limited abilities to self-report internal mood states. Behavioral symptoms can include anxiety, increases in obsessive-compulsive behaviors, depressed affect, crying for no reason, lack of emotion, social isolation, anhedonia, irritability with increases in outbursts or aggression, sleep disturbance, psychomotor retardation, low self-esteem, catatonia, and psychosis. Clinicians need to consider potential contributing factors, including medical factors, recent life stressors, trauma, and family history. Anecdotally, interventions that involve reengagement in previously enjoyed activities and treatment with selective serotonin reuptake inhibitors (SSRIs) can be effective.

Catatonia (Also Known as Down Syndrome Disintegrative Disorder or Down Syndrome Regression Disorder)

Older children and young adults can experience a sudden regression in communication, socialization, and daily living skills associated with psychomotor retardation, negative mood or mood lability, refusal to participate in activities, social withdrawal, and insomnia with signs and symptoms of catatonia on the Bush Frances Catatonia Scale (see Chapter 47.3). Patients should undergo a medical evaluation for mental status change. Contributing etiologic factors include stressful events, depression, anxiety, or high physiologic stress. Treatment consists of addressing the underlying suspected cause and may include a trial of Ativan and then electroconvulsive therapy (ECT) if Ativan is unsuccessful.

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Chapter 58

Autism Spectrum Disorder

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DEFINITION

Autism spectrum disorder (ASD) is a neurobiologic disorder with onset in early childhood. The key features are impairment in social communication and social interaction and restricted and repetitive behaviors. The presentation of ASD can vary significantly from one individual to another, as well as over the course of development for a particular child. There is currently no diagnostic biomarker for ASD. Accurate diagnosis therefore requires careful review of the history and direct observation of the child's behavior.

DIAGNOSTIC CRITERIA AND SYMPTOMS

The diagnostic criteria in the *Diagnostic and Statistical Manual, Fifth Edition* (DSM-5) focus on symptoms in two primary domains: (1) social communication and social interaction and (2) restricted interests and repetitive behaviors (Table 58.1). To meet criteria for ASD, the symptoms need to have been present since the early developmental period, significantly affect functioning, and not be better explained by the diagnosis of intellectual disability (ID) or global developmental delay (GDD; Chapter 56). Table 58.2 provides associated features not included in the DSM-5 criteria.

Symptoms can present in infancy, with reduced response to name and unusual use of objects being strong predictors for risk of ASD. However, symptoms before age 12 months are not as reliably predictive of later diagnosis. Individuals with milder severity may not present

Table 58.1 DSM-5 Diagnostic Criteria for Autism Spectrum Disorder

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history:
   1. Deficits in social-emotional reciprocity.
   2. Deficits in nonverbal communicative behaviors used for social interaction.
   3. Deficits in developing, maintaining, and understanding relationships.

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two 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 interest in sensory aspects of the environment.

C. Symptoms must be present in the early developmental period (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.

From the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. (Copyright 2013). American Psychiatric Association, pp. 50–51.

Table 58.2 Associated Features of Autism Not in DSM-5 Criteria

Atypical language development and abilities
- Age <6 yr: frequently disordered and delayed in comprehension; two thirds have difficulty with expressive phonology and grammar
- Age ≥6 yr: disordered pragmatics, semantics, and morphology, with relatively intact articulation and syntax (i.e., early difficulties are resolved)

Motor abnormalities: motor delay; hypotonia; catatonia; deficits in coordination, movement preparation and planning, praxis, gait, and balance

For version with full references, see American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Washington DC: American Psychiatric Association; 2013. Adapted from Lai MC, Lombardo MV, Baron-Cohen S. Autism. *Lancet*. 2014;383:896–910.

until preschool or school age, when the social demands for peer interaction and group participation are higher.

Social Communication and Social Interaction

Individuals with ASD have difficulty understanding and engaging in social relationships. The problems are pervasive and affect three major areas: social-emotional reciprocity, nonverbal communication, and understanding of social relationships. The presentation can vary with severity and developmental functioning. A diagnosis of ASD requires the presence of symptoms from all three categories (Table 58.3).

Social-Emotional Reciprocity

Reduced social interactions in ASD may range from active avoidance or reduced social response to having an interest in, but lacking ability to initiate or sustain, an interaction with peers or adults. A young child with ASD may not respond when their name is called, may exhibit limited showing and sharing behaviors, and may prefer solitary play. In addition, the child may avoid attempts by others to play and may not participate in activities that require taking turns, such as peek-a-boo and ball play. An older child with ASD may have an interest in peers but may not know how to initiate or join in play. The child may have trouble understanding the rules of conversation and may either talk at length about an area of interest or abruptly exit the interaction. Younger children often have limited capacity for imaginative or pretend play. Older children may engage in play and conversation but lack flexibility and may be highly directive to peers. Some children with ASD interact well with adults but struggle to interact with same-age peers.

Nonverbal Communicative Behavior

Difficulties with nonverbal communication may manifest as reduced or overly intense use of eye contact and gestures such as pointing. Children may also show reduced awareness or response to the eye gaze or pointing of others. They may use eye contact only when communicating a highly preferred request or may have difficulty coordinating the use of nonverbal with verbal communication. Children with ASD may have limited range of facial social-communicative expression or expressed emotion.

Developing, Maintaining, and Understanding Relationships

Children with ASD have limited insight regarding social relationships. They may have difficulty understanding the difference between a true friend and a casual acquaintance, and even when the definitions are well understood, there may still be difficulty in developing and maintaining more intimate relationships They have trouble picking up on the nuances of social interactions and understanding social expectations for polite behavior. They may have reduced understanding of personal boundaries and may stand too close to others. In addition, they can have trouble understanding and inferring others' emotions and are less likely to share emotion or enjoyment with others. Adolescents and young adults have difficulty engaging in group interactions and navigating romantic relationships.

Restrictive and Repetitive Behavior

A diagnosis of ASD requires the presence of two of the four symptoms of restrictive and repetitive patterns of behavior discussed next.

Stereotyped Motor Movements or Speech

Stereotyped (or stereotypic) movements and repetitive behaviors may include hand flapping, finger movements, body rocking and lunging, jumping, running and spinning, and repetitive speech such as echoing words immediately after they are said. Repetitive patterns of play may be present, such as lining up objects, repetitively turning light switches on and off or opening and closing doors, spinning objects, or arranging toys in a specific manner. These repetitive patterns may not be seen in very young toddlers but may develop as they get older. Stereotyped movements can change over time and in older children are seen more often in individuals with lower cognitive functioning.

Insistence on Sameness

Children with ASD have difficulty tolerating transitions or change. They may insist on certain routines or schedules and can become very distressed with unexpected events or new situations. They may repeat scripts from shows or movies or watch the same portion of a video repeatedly. Intolerance for change can cause significant impairment and irritability and have an effect on child and family function.

Restricted Interests

This symptom may manifest as interests that seem of greater intensity when compared to same-age peers. Younger children may play with a limited range of toys or may insist on retaining a small object in each hand. Older children may have a strong preference for a particular story or movie. The area of interest may be shared by peers (e.g., Disney movies, Legos, Thomas the Train) but *unusual* in its intensity. Other affected children may have interests that are both intense and

Table 58.3 Signs and Symptoms of Possible Autism in Preschool Children (or Equivalent Mental Age)

Spoken Language
- Language delay (in babbling or using words; e.g., using <10 words by age 2 yr).
- Regression in, or loss of, use of speech.
- Spoken language (if present) may include unusual features, such as vocalizations that are not speechlike; odd or flat intonation; frequent repetition of set words and phrases (echolalia); reference to self by name or "you" or "she" or "he" beyond age 3 yr.
- Reduced and/or infrequent use of language for communication (e.g., use of single words, although able to speak in sentences).

Responding to Others
- Absent or delayed response to name being called, despite normal hearing.
- Reduced or absent responsive social smiling.
- Reduced or absent responsiveness to other people's facial expressions or feelings.
- Unusually negative response to the requests of others ("demand avoidance" behavior).
- Rejection of cuddles initiated by parent or caregiver, although the child may initiate cuddles.

Interacting with Others
- Reduced or absent awareness of personal space, or unusually intolerant of people entering their personal space.
- Reduced or absent social interest in others, including children of own age—may reject others; if interested in others, child may approach others inappropriately, seeming to be aggressive or disruptive.
- Reduced or absent imitation of others' actions.
- Reduced or absent initiation of social play with others; plays alone.
- Reduced or absent enjoyment of situations that most children like (e.g., birthday parties).
- Reduced or absent sharing of enjoyment.

Eye Contact, Pointing, and Other Gestures
- Reduced or absent use of gestures and facial expressions to communicate (although may place an adult's hand on objects).
- Reduced and poorly integrated gestures, facial expressions, body orientation, eye contact (looking at people's eyes when speaking), and speech used in social communication.
- Reduced or absent social use of eye contact (assuming adequate vision).
- Reduced or absent "joint attention" (when one person alerts another to something by means of gazing, finger pointing, or other verbal or nonverbal indication for the purpose of sharing interest). This would be evident in the child from lack of:
  - Gaze switching
  - Following a point (looking where the other person points to—may look at hand)
  - Using pointing at or showing objects to share interest

Ideas and Imagination
- Reduced or absent imagination and variety of pretend play.

Unusual or Restricted Interests and/or Rigid and Repetitive Behaviors
- Repetitive "stereotypic" movements such as hand flapping, body rocking while standing, spinning, and finger flicking.
- Repetitive or stereotyped play (e.g., opening and closing doors).
- Overfocused or unusual interests.
- Excessive insistence on following own agenda.
- Extremes of emotional reactivity to change or new situations; insistence on things being "the same."
- Overreaction or underreaction to sensory stimuli, such as textures, sounds, or smells.
- Excessive reaction to the taste, smell, texture, or appearance of food, or having extreme food fads.

Adapted from Baird G, Douglas HR, Murphy MS. Recognizing and diagnosing autism in children and young people: Summary of NICE guidance. *BMJ*. 2011;343:d6360, Box 1, p. 901.

unusual, such as an interest in brands of vehicles, license plate numbers, or fans and heating systems. These interests interfere with social interactions; a child may only want to talk about their area of interest or may insist that peers act out a particular story in a rigid and inflexible manner.

Hyporeactivity or Hyperreactivity to Sensory Input

Children with ASD may be overly sensitive to sensory input, such as noise, smells, or texture. Children may scream or react strongly when they hear a siren or vacuum and may gag and choke with certain foods or odors. They may refuse to wear certain clothing or may become very distressed with bathing or with cutting nails and hair. Conversely, some affected children seem to crave sensory input. They may engage in repetitive jumping or hugging and may smell or lick objects or people. Young children may inappropriately touch the face or hair of others.

Diagnosing ASD with DSM-5 criteria can be challenging in very young children because of reduced expression of repetitive behaviors, particularly stereotyped behavior and intense interests. Studies monitoring development in high-risk young children who have an older sibling with ASD indicate these additional symptoms may emerge over time. This creates a dilemma for specialty clinicians evaluating very young children for ASD, because they may not be able to endorse sufficient symptoms to make an early diagnosis and access specialized intervention services.

Severity Levels Defined in DSM-5

Severity levels in ASD are based on the level of support the individual requires in each of the major domains impacted—social communication and restricted interests and repetitive behavior. Levels range from "needing support" (level 1), to "needing substantial support" (level 2), to "needing very substantial support" (level 3) (Table 58.4).

Specifiers Defined in DSM-5

A formal diagnosis of ASD also includes documenting associated conditions, including whether the individual has cognitive and/or language impairment; any related medical, genetic, or environmental factors; and any other neurodevelopmental or behavioral health conditions, including catatonia (Table 58.5). This process helps to better characterize the presentation in an individual child and ensures that the diagnosis has been made by considering the symptoms in the context of the child's current cognitive and language abilities.

EPIDEMIOLOGY

The prevalence of ASD is estimated at 1 in 36 persons by the U.S. Centers for Disease Control and Prevention (CDC). This information comes from prevalence data of 8-year-olds derived from 11 sites participating in the Autism and Developmental Disabilities Network (ADDM) and shows a greater than 300% increase in prevalence since systematic surveillance began in the year 2000. The increased prevalence relates, at least in part, to improved diagnosis and case finding, as well as inclusion of less severe presentations within the autism *spectrum*. There is a 4:1 male predominance, although new emerging information suggests that the prevalence in females may be higher than previously believed. Females with ASD often use "camouflaging," which is intentionally or unconsciously hiding social communication difficulties by mimicking the facial expressions of others, having more effective compensatory behaviors, and displaying less clearly unusual preoccupying interests. All of these things, including clinician bias, may decrease girls with ASD being diagnosed. The prevalence is increased in siblings (up to 18% recurrence rate) and particularly in identical twins. There are no racial or ethnic differences in prevalence. Individuals from racial minorities and lower socioeconomic status are at risk for later

Table 58.4 DSM-5 Severity Levels for Autism Spectrum Disorder

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

From the Diagnostic and Statistical Manual of Mental Disorders, 5th ed (Copyright 2013). American Psychiatric Association, p. 52.

diagnosis, although the most recent prevalence data suggest that this gap is closing.

ETIOLOGY

The etiology of ASD is thought to result from disrupted neural connectivity and is primarily impacted by genetic variations affecting early brain development. Animal models and studies of individuals with ASD indicate changes in brain volume and neural cell density in the limbic system, cerebellum, and frontotemporal regions. One study documented changes in early brain development, characterized as "hyperexpansion of cortical surface area," at age 6-12 months on brain MRI, which correlated with later development of impaired social skills. Functional studies show abnormalities of processing information, particularly related to foundational social skills such as facial recognition. The disruptions in early brain development likely are responsive to treatment. Early developmental therapies in young children with ASD have demonstrated the capacity for normalization of electrophysiologic response to visual stimuli, including faces.

Numerous genes involved in brain development and synaptic function have been associated with ASD. Pathogenic variants that include large genetic deletions or duplications and small sequencing changes have been implicated; these can be inherited or occur de novo. Heterozygous mutations in genes, such as present in deletion or duplication of 15q11.2 or 16p11.2, may have variable expression within a family. Rare recessive mutations have been implicated in some populations with high levels of consanguinity. Patients with a number of genetic syndromes (e.g., fragile X, Down, Smith-Lemli-Opitz, Rett, Angelman, Timothy, Joubert), as well as disorders of metabolism and mitochondrial function have higher rates of ASD than the general population (Tables 58.5, 58.6, and 58.7).

There is also possible evidence for environmental contributions to ASD. Older maternal or paternal age may increase the risk of ASD. In addition, factors influencing the intrauterine environment, such as maternal obesity or overweight, short interval from prior pregnancy, premature birth, and certain prenatal infections (e.g., rubella, cytomegalovirus), are associated with ASD. Population-level associations have been investigated for environmental toxins such as organophosphates, pesticides, air pollution, and volatile organic compounds. An epigenetic model is considered one explanation for the etiology; individuals with genetic vulnerability may be more sensitive to environmental factors influencing early brain development.

Despite frequent concerns from families that vaccines or the preservatives in vaccines lead to ASD, *there is no evidence to support this claim.* Multiple research studies and meta-analyses have failed to show an association of vaccines with ASD.

No biomarkers are available yet, but there is emerging evidence from neuroimaging findings, electrophysiologic testing, and eye tracking that hold the promise for presymptomatic detection along with accurate clinical diagnosis and prognostic assessment.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of ASD is complex because many conditions in the differential can also occur with ASD. The most important conditions to consider in young children are language disorder (see Chapter 53), ID or GDD (Chapter 56), and hearing loss (Chapter 55). Children with **language disorder** may have impairments in social communication and play; their social and play skills, however, are typically on par with their language level. In addition, they do not have associated restricted and repetitive behavior or atypical use of language, such as scripting. The diagnosis of **social communication disorder** is also distinguished from ASD by the lack of restrictive and repetitive behaviors. Children with **ID** or **GDD** may have delays in social and communication skills as well as stereotyped behavior. However, social and communication skills are typically commensurate with their cognitive and adaptive functioning. Children with **hearing loss** may present with some "red flags" for ASD, such as poor response to name. However, they typically develop nonverbal communication and play skills as expected and do not have stereotyped or restricted behavior patterns.

In older children, disorders of attention, learning, and mood regulation must be considered in the differential diagnosis of ASD. Children with **attention-deficit/hyperactivity disorder (ADHD)** may present with reduced eye contact and response to name caused by poor attention rather than lack of social awareness. Children with ADHD, however, do not have associated impairments in shared enjoyment and social reciprocity or repetitive behaviors. Children with **social anxiety** or other anxiety disorders may present with some symptoms suggestive of ASD. Shy children may have reduced eye contact and social initiation. Anxious children can be resistant to change and prefer familiar routines. Children with anxiety, however, typically will have preserved social interest and insight and will not exhibit high levels of stereotyped behaviors. **Reactive attachment disorder** can be difficult to distinguish from ASD, particularly in younger children with a history of prolonged

Table 58.5 Common Co-occurring Conditions in Autism Spectrum Disorder (ASD)

COMORBIDITY	INDIVIDUALS WITH AUTISM AFFECTED	COMMENTS
DEVELOPMENTAL DISORDERS		
Intellectual disability	~45%	Prevalence estimate is affected by the diagnostic boundary and definition of intelligence (e.g., whether verbal ability is used as a criterion). In individuals, discrepant performance between subtests is common.
Language disorders	Variable	An autism-specific language profile (separate from language disorders) exists, but with substantial interindividual variability.
Tic disorders	14–38%	~6.5% have Tourette syndrome.
Motor abnormality	≤79%	See Table 58.2.
GENERAL MEDICAL DISORDERS		
Epilepsy	35-46%	Increased frequency in individuals with intellectual disability or genetic syndromes. Two peaks of onset: early childhood and adolescence. Increases risk of poor outcome.
Gastrointestinal problems	9–70%	Common symptoms include chronic constipation, abdominal pain, chronic diarrhea, cyclic vomiting, and gastroesophageal reflux. Associated disorders include gastritis, esophagitis, gastroesophageal reflux disease, inflammatory bowel disease, celiac disease, Crohn disease, and colitis.
Immune dysregulation	≤38%	Associated with allergic and autoimmune disorders.
Genetic disorders	10–20%	Collectively called *syndromic autism.* Examples include fragile X syndrome (21–50% of individuals affected have autism), Rett syndrome (most have autistic features but with profiles different from idiopathic autism), tuberous sclerosis complex (24–60%), Down syndrome (5–39%), phenylketonuria (5–20%), CHARGE syndrome* (15–50%), Angelman syndrome (50–81%), Timothy syndrome (60–70%), and Joubert syndrome (~40%).
Sleep disorders	50–80%	Insomnia is the most common.
BEHAVIORAL HEALTH DISORDERS		
Any behavioral health disorder	70–90%	
ADHD	40–70%	
Anxiety	~40%	Common across all age-groups. Most common are social anxiety disorder (13–29% of individuals with autism) and generalized anxiety disorder (13–22%). High-functioning individuals are more susceptible (or symptoms are more detectable).
Catatonia	Unknown	Autism shutdown disorder similar to Down syndrome disintegrative disorder (see Chapters 47.3 and 57).
Depression	12–70%	Common in adults, less common in children. High-functioning adults who are less socially impaired are more susceptible (or symptoms are more detectable).
Obsessive-compulsive disorder (OCD)	7–24%	Shares the repetitive behavior domain with autism that could cut across nosologic categories. Important to distinguish between repetitive behaviors that do not involve intrusive, anxiety-causing thoughts or obsessions (part of autism) and those that do (and are part of OCD).
Psychotic disorders	12–17%	Mainly in adults. Most commonly recurrent hallucinosis. High frequency of autism-like features (even a diagnosis of ASD) preceding adult-onset (52%) and childhood-onset schizophrenia (30–50%).
Substance use disorders	≤16%	Potentially because individual is using substances as self-medication to relieve anxiety.
Oppositional defiant disorder	16–28%	Oppositional behaviors could be a manifestation of anxiety, resistance to change, stubborn belief in the correctness of own point of view, difficulty seeing another's point of view, poor awareness of the effect of own behavior on others, or no interest in social compliance.
Eating disorders	10-21%	Avoidant/restrictive food intake may lead to nutrient deficiencies and poor growth.
PERSONALITY DISORDERS†		
Paranoid personality disorder	0–19%	Could be secondary to difficulty understanding others' intentions and negative interpersonal experiences.
Schizoid personality disorder	21–26%	Partly overlapping diagnostic criteria.
Schizotypal personality disorder	2–13%	Some overlapping criteria, especially those shared with schizoid personality disorder.
Borderline personality disorder	0–9%	Could have similarity in behaviors (e.g., difficulties in interpersonal relationships, misattributing hostile intentions, problems with affect regulation), which requires careful differential diagnosis. Could be a misdiagnosis of autism, particularly in females.
Obsessive-compulsive personality disorder	19–32%	Partly overlapping diagnostic criteria.
Avoidant personality disorder	13–25%	Could be secondary to repeated failure in social experiences.

Continued

Table 58.5 Common Co-occurring Conditions in Autism Spectrum Disorder (ASD)—cont'd

COMORBIDITY	INDIVIDUALS WITH AUTISM AFFECTED	COMMENTS
BEHAVIORAL DISORDERS		
Aggressive behaviors	≤68%	Often directed toward caregivers rather than noncaregivers. Could be a result of empathy difficulties, anxiety, sensory overload, disruption of routines, and difficulties with communication.
Self-injurious behaviors	≤50%	Associated with impulsivity and hyperactivity, negative affect, and lower levels of ability and speech. Could signal frustration in individuals with reduced communication, as well as anxiety, sensory overload, or disruption of routines. Could also become a repetitive habit. Could cause tissue damage and need for restraint.
Pica	~36%	More likely in individuals with intellectual disability. Could be a result of a lack of social conformity to cultural categories of what is deemed edible, or sensory exploration, or both.
Suicidal ideation or attempt	11–14%	Risks increase with concurrent depression and behavioral problems and after being teased or bullied.

*Coloboma of the eye; heart defects; atresia of the choanae; retardation of growth and development, or both; genital and urinary abnormalities, or both; and ear abnormalities and deafness.
†Particularly in high-functioning adults.
DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.
Adapted from Lai MC, Lombardo MV, Baron-Cohen S. Autism. *Lancet*. 2014;383:896–910.

Table 58.6 Syndromes with Autistic-Like Behaviors

CHROMOSOME DELETIONS
1q21
7q11.28
16p11.2
17q12
2q23.1 (*MBD5**)
12q24.3
Cri-du-chat (5p15.2-p15.33)
22q deletion syndrome
Jacobsen (11q23.2)
Phelan-McDermid (*SHANK3*; 22q13)
Pitt-Hopkins (18q21.2)

CHROMOSOME DUPLICATIONS
15q11.1-q13.3
7q11.23
18q12.2
16p11.2
1q21.1
22q11.2
Potocki-Lupski (17p11.2)

EPILEPSY ENCEPHALOPATHIES, EPILEPSY
Cortical dysplasia focal epilepsy
SCN1A-related syndromes (Dravet, Lennox Gastaut, others)
Early myoclonic encephalopathies (Ohtahara: *STXBP1*, *ARX*, *SIK1*)
SCN2A-related syndromes (West, others)
SLC6A1 myotonic-atonic epilepsy
HCN1-related epilepsies
CDKL5
SCN8A
PCDH19
SCL35A2-related disorders
Epilepsy-aphasia spectrum (Landau-Kleffner; *GRIN2A*; continuous spike wave during low-wave sleep)
Juvenile myoclonic epilepsy (*RING2*)

OTHER SYNDROMES
2q37 monosomy
Angelman
Bardet-Biedl
Cardiofaciocutaneous
CHARGE association
Cohen
Congenital rubella
Cornelia de Lange
Costello
FOXG1 variants
Fragile X
Hypomelanosis of Ito
Joubert
Kleefstra (*EHMT1*)
Lujan-Fryns
Moebius sequence
Muscle-eye brain disease
Myotonic dystrophy
Neurofibromatosis
Nonsyndromic intellectual disability due to *SYNGAP1* variants
Noonan
Oculoauriculovertebral spectrum (including Goldenhar)
Partial monosomy 1p36
Partial tetrasomy 15
Prader-Willi
PTEN variants
Rett complex (female >> male)
Ring chromosome 14
SETD1B variants
Sex chromosome aneuploidies
Sashi-Pena (*ASXL2*)
Smith-Lemli-Opitz
Smith-Magenis
Sotos
Timothy
Tolchin-Le Caignec (TOLCAS)
Trisomy 21
Tuberous sclerosis
WAGR
Wiedemann-Steiner (*KMT2A*)
Williams

*Italics denoted affected gene
Modified from Kliegman RM, Toth H, Bordini BJ, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis*, 2nd ed. Philadelphia: Elsevier; 2023: Table 32.6, p. 537.

Table 58.7 Inborn Errors of Metabolism with Autistic-Like Behavior

Adenylosuccinate lyase deficiency
Biotinidase deficiency
Cerebral creatinine deficiency
Cerebral folate deficiency
Ceroid lipofuscinosis (infantile)
Cystathionine β-synthase deficiency
Dihydropyrimidinase deficiency
Disorders of creatine transport or metabolism
Homocystinuria
Lesch-Nyhan syndrome
Methylenetetrahydrofolate reductase deficiency
Mitochondrial disorders
Mucopolysaccharidosis
Phenylketonuria (untreated)

Modified from Kliegman RM, Toth H, Bordini BJ, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis*, 2nd ed. Philadelphia: Elsevier; 2023: Table 32.8, p. 539.

neglect or trauma. However, social behaviors in these children generally improve with positive caretaking.

The differentiation of ASD from **obsessive-compulsive disorder (OCD)**, tics, and stereotyped behaviors can sometimes be challenging. In general, stereotyped behaviors may be calming or preferred, whereas tics and compulsive routines generally are distressing to the individual. Children with OCD have intense interests, as well as repetitive behaviors and rituals, but do not have impairment in social communication or interaction. Children with **stereotypic movement disorder** will not have impaired social skills or other types of restricted and repetitive behaviors. Children with **Landau Kleffner syndrome (LKS)** present with a loss of skills in language comprehension (auditory verbal agnosia) and verbal expression (aphasia) associated with onset of epileptic seizures during sleep (see Chapter 53). In contrast to ASD, children with LKS usually present with typical early development followed by loss of language function at age 3-6 years.

CO-OCCURRING CONDITIONS

Between 35% and 50% of individuals with ASD have ID, ranging in severity from mild to severe (see Table 58.5). An additional 23% of children have intellectual functioning in the borderline range (IQ = 71-85), and approximately 40% of individuals with ASD are nonverbal. ID is associated with higher rates of both identified genetic conditions and epilepsy. Children with ASD often have associated language impairments, including delays in expressive, receptive, and pragmatic (social) language skills. Language function can range

widely from nonverbal status to age appropriate. Gastrointestinal (GI) problems such as cyclic vomiting, constipation, esophagitis, and gastroesophageal reflux disease (GERD) are reported in up to 70% of children with ASD. Epilepsy occurs in up to 35–46% of children with ASD and presents in two peaks: in early childhood and in adolescence. Children with ID, female gender, and lower gestational age are at higher risk for having seizures.

Overall, between 70% and 90% of children with ASD are identified as having a co-occurring behavioral health condition, with ADHD being the most common, occurring in between 40% and 70% of children with ASD. There are higher rates of anxiety (~40%) and mood disorders in ASD, particularly during adolescence. Children with ASD are also at increased risk for being bullied and may present with secondary irritability, anxiety, or depression. Adolescents may develop gender-nonconforming roles, gender variance, and transgender identities; this may also lead to being bullied. Children with ASD are at high risk for suicidal ideation and attempts. **Catatonia** can also occur, most commonly developing during the teenage years, and may present with changes in activity level, unusual movements, and behavioral regression or loss of skills (Chapter 47.3).

Sleep problems, including delayed sleep onset, frequent night waking, and abnormal sleep architecture, are reported in 50–80% of children with ASD. There is some evidence for baseline abnormalities in melatonin secretion. The use of screen-based activities such as television, computers, or tablets before bedtime can inhibit melatonin secretion.

Children with ASD commonly have high rates of feeding and toileting problems resulting from resistance to change, sensory sensitivity, and repetitive behavior patterns. Many children with ASD have **restrictive feeding patterns** and food selectivity. DSM-5 introduced the diagnosis of avoidant and restrictive food intake disorder (ARFID) that, although not specific to children with ASD, describes a pattern of a severely disturbed eating experience resulting in nutritional deficiency or inadequate weight gain and may affect as many as 21% of children with ASD. Restrictive eating patterns may lead to nutritional deficiencies, such as scurvy, rickets, anemia, or protein malnutrition. Children with ASD also have higher rates of overweight, possibly because of diets higher in carbohydrates, reduced physical activity, use of food rewards to regulate behavior, and side effects from medications used for managing mood and behavior. As many as 25% of preschool-age children with ASD have pica (eating of nonfood items), and this tends to persist in children with co-occurring ID.

Self-injury and aggression are common in ASD patients, but most common in individuals with lower cognitive function and limited language. Sleep deprivation, nutritional deficits, pain, epilepsy, and medication side effects may contribute to these behaviors.

Wandering frequently co-occurs with ASD, with nearly 50% of children between 4 and 10 years of age reported as trying to elope. In children who were missing long enough to call the police, approximately 66% were at risk for traffic-related injury and nearly 30% had near-drowning events, which is the leading cause of death in children who wander.

SCREENING

The American Academy of Pediatrics recommends screening for ASD for *all* children at age 18 months and 24 months (see Chapter 28). Screening should also occur when there is increased risk for ASD, such as a child with an older sibling who has ASD, or whenever there is concern for possible ASD. Screening can be done by a parent checklist or direct assessment. The most frequently used screening tool is the *Modified Checklist for Autism, Revised/Follow-Up Interview* (MCHAT-R/FU), a 20-item parent report measure, with additional standardized parent interview completed for intermediate scores. The MCHAT-R/FU can be used from age 16-30 months. Children who score ≥8 or between 3 and 7 after the parent interview are at high risk for a diagnosis of ASD or some developmental delay. The Parent's Observation of Social Interaction (POSI) is another commonly used autism specific screener. It includes seven items.

ASSESSMENT

Diagnostic assessment optimally should include medical evaluation and assessment of the child's cognitive, language, and adaptive function. Developmental-behavioral pediatricians, neurodevelopmental disability specialists, neurologists, psychiatrists, and psychologists are qualified to make a formal diagnosis of ASD. Other specialists, including speech-language pathologists and occupational therapists, should also be included depending on the child's age and the presenting concerns.

Assessment of ASD includes direct observation of the child to evaluate social-communicative skills and behavior. Informal observation can be supplemented with structured diagnostic tools such as the *Autism Diagnostic Observation Schedule, Second Edition* (ADOS-2) or the Toddler module (ADOS-T). These structured play-based assessments provide social prompts and opportunities to evaluate the frequency and quality of a child's social responsiveness to, initiation, and maintenance of social interactions, the capacity for joint attention and shared enjoyment; the child's behavioral flexibility; and the presence of repetitive patterns of behavior and preoccupying interests. These measures also provide some understanding of a child's insight about social relationships and emotional awareness. The ADOS-2 and ADOS-T are not required for accurate diagnosis and do not stand alone, but rather can be used to augment a careful history and observation. The *Childhood Autism Rating Scale, Second Edition* (CARS-2) is a 15-item direct clinical observation instrument that can assist clinicians in the diagnosis of ASD. The *Autism Diagnostic Interview-Revised* (ADI-R) is a lengthy clinical interview tool that is used primarily in research settings because it takes several hours to administer. Other tools include standardized rating scales, such as the Social Responsiveness Scale or the Social Communication Questionnaire, that parents and teachers can complete to report on the child's social skills and behaviors. There is an emergence of the use of telehealth to assess children with ASD, and preliminary studies have suggested that 80% of children could be determined to have or not have ASD with reasonable certainty.

Medical evaluation should include a thorough history and detailed physical examination of the child, including direct behavioral observations of communication and play. In addition, the examination should include measurement of head circumference, careful evaluation for dysmorphic features, and screening for tuberous sclerosis with Wood lamp exam. Children with ASD should have genetic testing, an audiology examination to rule out hearing loss, and in children with pica, a lead test (Table 58.8).

There are currently several specialty-specific clinical guidelines for genetic evaluation of children diagnosed with ASD. Genetic testing is shown to impact clinical decision-making, but no studies have evaluated the impact of genetic testing on the outcome for the child. The American College of Medical Genetics recommends a tiered approach to genetic testing.

Initial Etiologic Assessment

All children with ASD should have a **chromosomal microarray (CMA)**. CMA will be positive in 10–15% of individuals with ASD. The rate is increased to almost 30% in individuals who have complex presentations, such as associated microcephaly, dysmorphic features, congenital anomalies, or seizures. CMA technology will identify copy number variants but not DNA sequencing errors, balanced translocations, or abnormalities in trinucleotide repeat length. *Fragile X DNA testing is recommended for all males with ASD.* Fragile X testing should also be considered in females with physical features suggestive of fragile X syndrome or with a family history of fragile X, X-linked pattern of ID, tremor/ataxia, or premature ovarian failure (see Chapter 59).

Second Tier Etiologic Assessment

Females with ASD should have testing for pathologic variants in the *MeCP2* gene. Males who have hypotonia, drooling, and frequent respiratory infections should have *MeCP2* deletion/duplication testing. All individuals with ASD and a head circumference greater than 2.5

Table 58.8 Medical and Genetic Evaluation of Children with Autism Spectrum Disorder

PHYSICAL EXAMINATION
Dysmorphic physical features
Muscle tone and reflexes
Head circumference
Wood lamp examination for tuberous sclerosis
DIAGNOSTIC TESTING
Chromosomal microarray (CMA) in all individuals
Fragile X DNA test in males
Audiology and vision evaluation
Lead test in children with pica
ADDITIONAL TARGETED GENETIC TESTING
Fragile X DNA test in females with symptoms suggestive of fragile X, family history of X-linked intellectual disability, tremor, ataxia, or premature ovarian failure
MeCP2 sequencing in females
PTEN testing if head circumference >2.5 standard deviations (SD) above the mean
MeCP2 deletion/duplication testing in males with significant developmental regression, drooling, respiratory infections, and hypotonia
Karyotype if unable to obtain CMA or if balanced translocation suspected
ADDITIONAL TARGETED DIAGNOSTIC TESTING
Electroencephalogram (EEG) in children with seizures, staring spells, or developmental regression
Brain MRI in children with dysmorphology, microcephaly, focal neurologic findings, seizures, severe hypotonia, or developmental regression
Metabolic testing in children with developmental regression, hypotonia, seizures, food intolerance, cyclic vomiting, lethargy, hearing loss, ataxia, or course facial features
Exome or genome sequencing if atypical features are present (behavioral or dysmorphic) (see Table 56.1)

Data from Schaefer GB, Mendelsohn NJ. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. *Genet Med.* 2013;15(5):399–407 and Lord C, Charman T, Havdahl A, et al. The Lancet Commission on the future of care and clinical research in autism. *Lancet.* 2022;399:271–326.

standard deviations (SD) above the mean should have testing for pathologic variants in the *PTEN* gene because there is a risk for hamartoma tumor disorders (Cowden, Proteus-like, Bannayan-Riley-Ruvakaba syndromes) in these individuals. Cytogenetic testing (karyotype) has a lower yield than CMA. Karyotype is recommended if microarray is not available and in children with suspected balanced translocation, such as history of multiple prior miscarriages.

Further medical diagnostic testing is indicated by the child's history and presentation. Brain imaging (MRI) is indicated in cases of microcephaly, significant developmental regression, seizures, or focal findings on neurologic examination. Because of the high rate (up to 25%) of macrocephaly in ASD, imaging is not indicated for macrocephaly alone. MRI is not recommended for minor language regression (loss of a few words) during the second year of life that is often described in toddlers with ASD. Children with concern for seizures, spells, or developmental regression should have an electroencephalogram (EEG). Metabolic screening is indicated for children with signs of a metabolic or mitochondrial disorder, such as developmental regression, weakness, fatigue, lethargy, cyclic vomiting, or seizures (see Table 58.7 and Chapters 56 and 104).

Next-Generation Sequencing

Whole exome sequencing (WES) can identify single-nucleotide variants, including pathogenic loss of function mutations and missense mutations; studies have identified a molecular diagnosis in nearly 30% of individuals tested because of the presence of a neurodevelopmental disorder. If the initial genetic testing is negative, clinicians should consider ordering this test in conjunction with genetic counseling to aid in understanding results.

TREATMENT AND MANAGEMENT

Approaches to Intervention

The primary treatment for ASD is done outside the medical setting and includes developmental and educational programming (Fig. 58.1). Numerous resources have been developed that can help families in the complex process of treatment planning (Table 58.9). Intensive behavioral therapies have the strongest evidence to date. Earlier age at initiation of treatment and higher intensity of treatment are associated with better outcomes, although recent studies comparing two different treatments at different levels of intensity (15 vs 25 hr/wk) did not show significant differences between groups in any of the outcomes assessed. Programming must be individualized, and no approach is successful for all children. In addition, research treatments are often conducted with a high level of intensity and fidelity that is difficult to scale up or reproduce in community settings. Higher cognitive, play, and joint attention skills and lower symptom severity at baseline are predictors for better outcomes in core symptoms, intellectual function, and language function.

There are many evidence-based approaches to treating children with ASD, with three main approaches identified. The intervention with the strongest evidence base is **applied behavioral analysis (ABA)**, which is based on the principles of direct incremental teaching of skills within a traditional behavioral framework using reinforcement of desired behavior, careful data collection, and analysis and adjustment of the treatment program based on review of data. The second is **developmental relationship-based intervention (DRBI)**, which includes parent-mediated interventions that focus on building warm, meaningful interaction to improve communication, learning, and problem solving. The best-known approach in this category is **Floortime.** The third approach is the **naturalistic developmental behavioral intervention**, which builds upon ABA to incorporate more choices for children and is implemented in natural situations. Comprehensive models integrating behavioral and developmental approaches that build on key foundational skills, such as joint attention, shared enjoyment, and reciprocal communication, show strong evidence of efficacy for young children, particularly toddlers, with ASD. Examples include the *Early Start Denver Model* (ESDM), *Joint Attention Symbolic Play Engagement and Regulation* (JASPER), and *Social Communication/Emotional Regulation/Transactional Support* (SCERTS).

Educational approaches such as the *Treatment and Education of Autistic and Communication Handicapped Children* (TEACCH) incorporate structured teaching, visual supports, and adjustment of the environment to the individual needs of students with ASD, such as difficulty with communication, understanding time, and need for routine. These approaches have demonstrated efficacy for improved cognitive and adaptive skills. For older children with more severe symptoms, approaches that use behavioral principles in addition to adjusting the environment may be most effective.

Speech and language therapy can help build vocabulary, comprehension, and pragmatic skills. Children with ASD benefit from visual supports for comprehension, understanding expectations, and communicating their needs. **Augmentative communication** approaches using photographs or picture icons can improve comprehension and ability to communicate (see Chapter 54). There are a range of options with varying levels of complexity, flexibility, and technology. Using augmentative communication does not inhibit acquisition of verbal language. On the contrary, supporting a child's language development with augmentative supports can facilitate the development of spoken language, even in older children.

Additional strategies to build social skills are used for school-age children and adolescents and may be administered in the school or community setting by a variety of specialists, including speech therapists, psychologists, and counselors. **Social skills programs** that include training peer mentors have higher rates of efficacy.

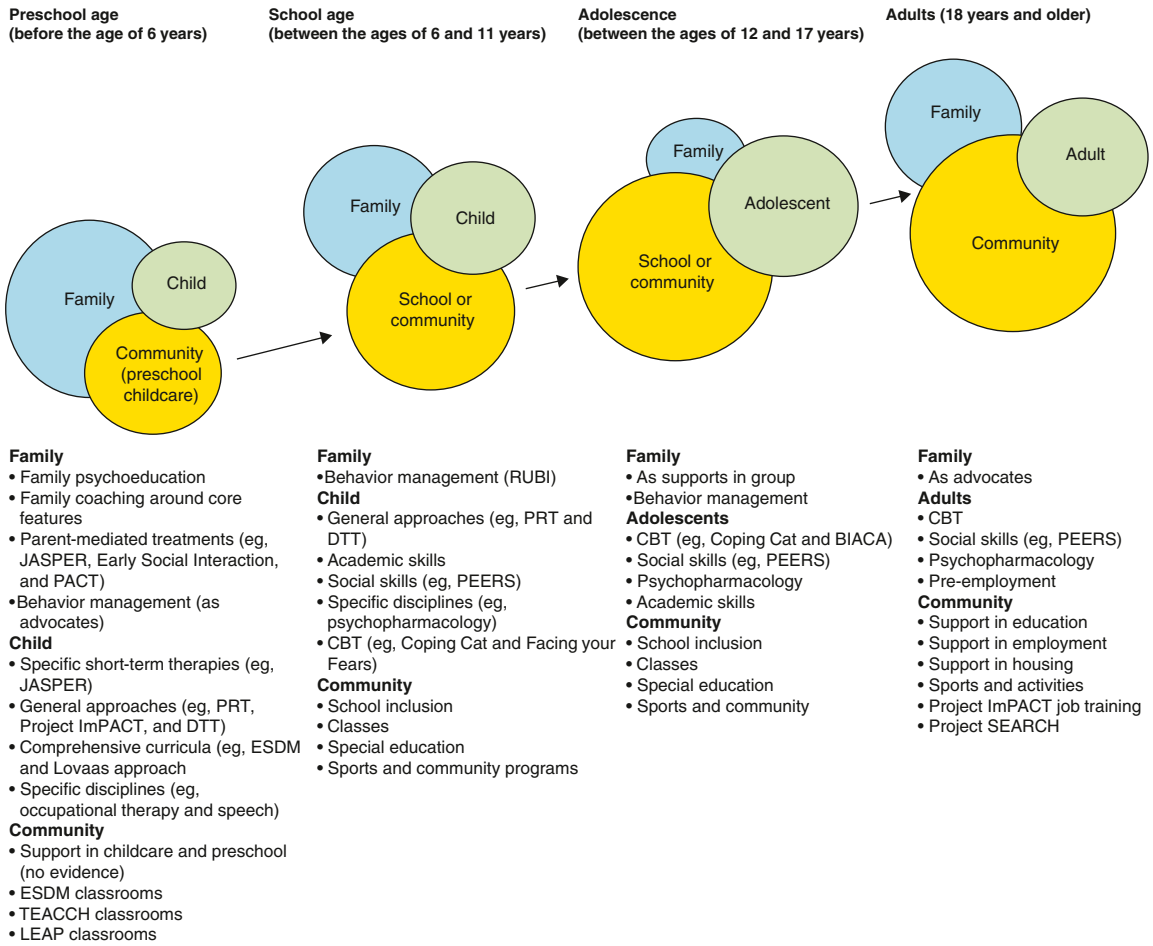

Fig. 58.1 Sources of support and locations of treatment. The size of each ellipse represents the extent of care or intervention received. BIACA, Behavioral Interventions for Anxiety in Children with Autism; CBT, cognitive-behavioral therapy; DTT, discrete trial training; ESDM, Early Start Denver Model; ImPACT, Improving Parents as Communication Teachers; JASPER, Joint Attention, Symbolic Play, Engagement, and Regulation approach; LEAP, Learning Experiences and Alternative Program for Preschoolers and their Parents; PACT, Preschool Autism Communication Trial; PEERS, Program for the Education and Enrichment of Relational Skills; PRT, Pivotal Response Treatment; RUBI, Research Units in Behavioral Intervention; TEACCH, Treatment and Education of Autistic and Related Communication Handicapped Children program. *(From Lord C, Charman T, Havdahl A, et al. The Lancet Commission on the future of care and clinical research in autism. Lancet. 2022;399:271–326, Fig. 6, p. 287.)*

Table 58.9 Autism Resources for Families

Autism Speaks First 100 Days kit https://www.autismspeaks.org/family-services/tool-kits/100-day-kit
Autism Speaks Toolkits–dental, transition, guardianship https://www.autismspeaks.org/family-services/tool-kits
AACAP Autism Spectrum Disorder Parent's Medication Guide https://www.aacap.org/App_Themes/AACAP/Docs/resource_centers/autism/Autism_Spectrum_Disorder_Parents_Medication_Guide.pdf
Sexuality information for individuals with developmental disability http://vkc.mc.vanderbilt.edu/healthybodies/

Occupational and physical therapy may be indicated for individuals with motor delay and difficulty acquiring adaptive skills such as dressing and toileting.

For some high school students with ASD, training in life skills and vocational skills is critical for maximizing independence in adulthood. Training may focus on basic self-care (e.g., dressing, hygiene), functional academics (e.g., money management, banking skills), learning to fill out a job application, and understanding how to behave with strangers and in work settings. Social skills and job coaching may be needed even for adolescents with strong cognitive and academic function, because they may struggle with social perception and may be vulnerable to exploitation by others.

There continue to be disparities in regard to accessing care, with racially and ethnically minoritized groups and children from low-income families showing less access to acute care and specialized, community and educational services, when compared with higher-income and White families.

Co-occurring Conditions

Additional medical or behavioral health treatment is often required for the management of co-occurring conditions in ASD. Seizures occur in up to 35% of children with ASD and should be managed with appropriate antiepileptic therapy (see Chapter 633). GI problems (e.g., cyclic vomiting, constipation, esophagitis, GERD) may present with nonspecific irritability, sleep disturbance, self-injury, aggression, and signs of pain or discomfort, such as crying, and can be managed with the same approaches used in typically

Table 58.10 Common Pharmacologic Treatments in Autism Spectrum Disorder (ASD)

TARGET SYMPTOM	MEDICATION CLASS*	EFFECTS	SIDE EFFECTS	MONITORING
Hyperactivity and/or Inattention	Stimulants	Decreased hyperactivity, impulsivity, improved attention	Activation, irritability, emotional lability, lethargy/social withdrawal, stomach ache, reduced appetite, insomnia, increased stereotypy	Height, weight, BP, HR
	α_2-Agonists	Decreased hyperactivity, impulsivity, improved attention	Drowsiness, irritability, enuresis, decreased appetite, dry mouth, hypotension	Height, weight, BP, HR
	Selective norepinephrine reuptake inhibitor	Decreased hyperactivity, impulsivity, improved attention	Irritability, decreased appetite, fatigue, stomach ache, nausea, vomiting, racing heart rate	Height, weight, BP, HR
Anxiety	Selective serotonin reuptake inhibitors	Decreased anxiety	Activation, hyperactivity, inattention, sedation, change in appetite, insomnia, stomachache, diarrhea Citalopram: prolonged QTc interval	Weight, BP, HR
Irritability	Atypical antipsychotics (risperidone, aripiprazole)	Decreased irritability, aggression, self-injurious behavior, repetitive behavior, hyperactivity	Somnolence, weight gain, extrapyramidal movements, drooling, tremor, dizziness, vomiting, gynecomastia	Weight, BP, HR Monitor CBC, cholesterol, ALT, AST, prolactin, glucose or hemoglobin A_{1c}
Insomnia	Melatonin	Shortened sleep onset	Nightmares, enuresis	—

*Specific medication names are provided in parentheses when there is a Food and Drug Administration (FDA)–approved indication for the use of the medication to treat the symptom in children with ASD. Further information about these medications is available in Chapter 33.
BP, Blood pressure; HR, heart rate; CBC, complete blood count; ALT, alanine transaminase; AST, aspartate transaminase.

developing children. Children with pica should have lead and iron levels monitored.

Management of co-occurring attention and mood disorders is similar to that for typically developing children. Strategies to increase structure and organization in the environment and use of visual supports (e.g., schedules) can improve attention and reduce anxiety. Some children with ASD benefit from modified cognitive-behavioral therapy to address anxiety and OCD. (see Chapter 31).

Strategies to promote **sleep hygiene** and use of behavioral approaches, such as structured bedtime routines, can address delayed sleep onset. Other medical problems, such as epilepsy or GERD, can also contribute to poor sleep and should be treated directly. In cases refractory to behavioral approaches, medications may be used.

Structured behavioral approaches for delayed toilet training in concert with treatment to prevent constipation are often needed for children with ASD. For children with highly restrictive diets, nutrition counseling and behaviorally based feeding therapy may be needed to address poor caloric intake or lack of nutritional quality. Because of limited diets, children with ASD may be at risk for low levels of calcium, vitamins C and D, and iron. Children who are overweight may still have poor nutrition as a result of restrictive diets.

Irritability is a nonspecific symptom and can be a reflection of pain, anxiety, distress, or lack of sleep. Children with ASD are prone to irritability because of their difficulty tolerating change and their limited communication skills. Management of irritability includes evaluating carefully for medical problems that may be causing pain and for any factors in the child's home or school environment that may be causing distress. Possible causes of distress range from common experiences such as changes in the routine to undisclosed abuse or bullying. Treatment should be targeted first at any underlying cause. Medications are often used to treat irritability in ASD, but should only be used after appropriate behavioral and communication supports have been implemented.

Pharmacology

There are currently no medications that treat the core symptoms of ASD. Medications can be used to target specific co-occurring conditions or symptoms (Table 58.10; see also Table 58.5). Families should be cautioned, however, that the effect size may be lower and the rate of medication side effects higher in children with ASD.

Preliminary data suggested that intranasal therapy with neuropeptide oxytocin may improve social functioning in children with ASD, particularly those with low pretreatment oxytocin levels, but a recent randomized trial did not demonstrate any effect of oxytocin on social or cognitive functioning.

There is evidence to support the use of stimulant medications, atomoxetine, and α-agonists for ADHD in ASD. Selective serotonin reuptake inhibitors (SSRIs) can be used for anxiety and OCD and in adolescents may also be useful for depression. Benzodiazepines may be useful for situational anxiety, for example, triggered by dental and medical procedures or air travel. Medications used to treat ADHD and anxiety may result in activation or irritability in ASD and require careful monitoring.

Melatonin can be used to improve sleep onset but will not address night waking. Clonidine or trazodone may be used for sleep onset and maintenance. No medications are specifically labeled for treatment of insomnia in ASD.

The α-adrenergic agonists may be helpful in children who present with significant behavioral dysregulation. There are two atypical antipsychotic medications that have U.S. Food and Drug Administration (FDA) recommendation for irritability and aggression in children with ASD. Both risperidone and aripiprazole have several studies documenting efficacy for reducing irritability, aggression, and self-injury. Secondary improvements in attention and repetitive behavior were also noted. Side effects include weight gain and metabolic syndrome, as well as tardive dyskinesia and extrapyramidal movements. Careful laboratory monitoring is recommended. Mood-stabilizing antiepileptic medications have also been used to treat irritability.

Complementary and Alternative Medicine

Families of children with ASD often use complementary and alternative medicine (CAM) approaches. These treatments can include supplements, dietary changes, and body or physical treatments. There is limited evidence to inform families, who often learn about these treatments from friends and family members, alternative medicine providers, or the internet. For most therapies, evidence is insufficient to show benefit. There is strong evidence that secretin and facilitated communication are not effective. Some therapies, such as hyperbaric oxygen, chelation, and high-dose vitamins, are potentially harmful. For children with restrictive diets, taking a daily multivitamin and 400 IU vitamin D may be indicated, although there is no evidence to support megadoses of vitamins. Similarly, for children with evidence of gluten sensitivity, a trial of a gluten-free diet may be indicated. However, current evidence does not support this as a treatment for all children with ASD. There is an interest in the use of cannabidiol (CBD) to treat core autism symptoms or co-occurring problems such as anxiety, ADHD, or sleep problems, but there is currently no evidence to support this therapy.

When discussing CAM with a family, it is best to use open and collaborative communication, encouraging them to share their current practices and any questions. Specifically ask if they use any herbal treatments, supplements, or other therapies, such as acupuncture, massage, or chiropractic treatment, and what they have observed since trying the treatment. Provide accurate information regarding potential benefit and risk for any treatment. Educate about "red flags" such as treatments that are marketed as a cure for multiple conditions, that report no risk of side effects, or that are marketed by the clinician recommending the treatment. Encourage families to identify a target symptom, "try one thing at a time," and monitor response carefully.

Transition

Navigating a successful transition to adult care is a key role for the pediatric provider. This process should ideally start as early as age 12-13 years. Parents are faced with a complex and disconnected system of diverse agencies that they need to navigate. Use of structured-visit templates and care coordinators can help ensure that families and their youth with ASD are able to make appropriate decisions about secondary and postsecondary educational programming, vocational training, guardianship, finances, housing, and medical care. High school educational programming should include individualized and meaningful vocational training, as well as instruction regarding sexuality, relationships, safety—particularly internet safety and abuse prevention—finances, travel training, and general self-advocacy. More than half of young adults with ASD remain unemployed and unenrolled in higher education 2 years after high school graduation. Individuals with ASD who are of average cognitive intellectual functioning will need help accessing supports for college or postsecondary skills training and may benefit from referral to their state vocational rehabilitative services and personal life coaches or counselors. Families who have adult children with more significant cognitive disability need information about the range of adult disability services; how to apply for supplemental security income (SSI); and the process for considering guardianship, medical and financial conservatorship, or supported decision making for their adult child. These decisions are complex and must be individualized for the adult with ASD and the family.

OUTCOME

ASD is a lifelong condition. Although a minority of individuals no longer meet criteria for the diagnosis, most will make progress but continue to have some impairment in social, behavioral, learning, language, or emotional functioning as adults. Adult outcome studies are sobering, indicating that many adults with ASD are socially isolated, lack gainful employment or independent living, and have higher rates of depression and anxiety. It is not clear if these data can be extrapolated to younger children currently receiving intensive educational therapies. There is a growing network of adult self-advocates who promote the unique strengths in individuals with ASD. Outcome, as measured by developmental progress and functional independence, is better for individuals who have higher cognitive and language skills and lower ASD severity at initial diagnosis.

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Chapter 59

Fragile X Syndromes

Amanda E. Bennett and Marcy Schuster

Fragile X syndrome (FXS) is a genetic disorder associated with intellectual, learning, and behavioral symptoms and some specific physical characteristics. In FXS an expansion of >200 CGG repeats on the distal long arm of chromosome Xq27.3 silences the *FMR1* gene, which leads to a deficiency in fragile X mental retardation protein (FMRP) and affects synaptic function throughout much of the brain. It is the most common heritable cause of intellectual disability and has a prevalence rate of approximately 1 in 4,000 males and 1 in 7,000 females. Like many X-linked disorders, males with fragile X tend to present with more features and more significant impairments than females.

On average, unaffected individuals have 30 CGG repeats in the untranslated region of the *FMR1* gene. Those with 55-200 repeats are described as having the premutation. Females with the premutation are at increased risk of expansion of the number of CGG repeats causing FXS in their children (Table 59.1). When males with the premutation alleles pass them to daughters, they typically remain as premutation alleles. Those with premutation alleles may also have clinical manifestations (Tables 59.2 and 59.3).

Fragile XE syndrome (FRAXE) resembles FXS and manifests within a variable spectrum of intellectual and learning disabilities. The involved gene *(AFF2)* results in an expansion of CCG trinucleotide repeats and is inherited as an X-linked disorder. Symptoms also include aggressive behaviors, agitation, autistic behaviors, clumsiness, and delayed speech and language development. *This form of FXS will not usually be detected with standard fragile X testing.*

EVALUATION AND DIAGNOSIS

The phenotype of FXS early in life can be nonspecific with symptoms such as developmental delay, including motor and language delays, and autistic-like behaviors, such as repetitive motor mannerisms, sensory sensitivities, and deficits in eye contact. Manifestations in early to middle childhood often include problems with learning, attention-deficit/hyperactivity disorder (ADHD), anxiety, and aggressive behaviors. The physical features become more pronounced during or after puberty and include macroorchidism, hyperextensible finger joints, and characteristic facial features, including a long face, large ears, and a prominent square jaw (Fig. 59.1). Females affected with FXS show varying degrees of intellectual disability and/or learning disabilities, and they may present with symptoms of ADHD and anxiety as well.

Children with FXS are at increased risk for ophthalmologic, feeding, and orthopedic problems, as well as recurrent otitis media in early childhood. Females are at increased risk for precocious puberty.

Adolescents should be monitored for seizures and heart murmurs, and adults with FXS are at increased risk for mitral valve prolapse. Adults are also at risk for intention tremor and ataxia and premature menopause, which can also occur in those with the premutation. Table 59.3 includes phenotypic features, clinical signs, and their typical age of onset.

Family History and Premutation Carriers

Collecting a detailed family history can help identify potential risk factors for FXS. Individuals with premutation triplet repeat expansions have been found to have a variety of clinical manifestations. **Fragile X–associated tremor/ataxia syndrome (FXTAS) is a progressive neurodegenerative disorder** that most commonly affects males over age 50 years. Females are less commonly affected and tend to have mild disease. Symptoms include an intention tremor followed by ataxia that may manifest as needing support when walking or with a wide-based gait. Females with premutation triple repeat expansions are at risk for developing **fragile X–associated premature ovarian insufficiency (FXPOI)**. Women with this condition undergo menopause approximately 5 years earlier than women without the condition, but symptoms are variable, with the most severely affected experiencing irregular or absent menstrual periods before age 40 and often infertility. A variety of neuropsychiatric symptoms, including anxiety, ADHD, social deficits, or autism spectrum disorder (ASD), have also been associated with the premutation. Asking about family members for a history of developmental, behavioral, or learning problems or adult family members with early menopause, fertility challenges, or adult-onset neurologic problems may help to identify risk for a positive fragile X test in a child with developmental or behavioral concerns. Asymptomatic siblings or other family members may benefit from testing to determine premutation status, which can also be associated with the symptoms noted earlier. See Table 59.3 for additional information about clinical symptoms in **premutation carriers**.

Table 59.1 Risk of Expansion of a Premutation to a Full Mutation in Male Offspring Based on Maternal Number of CGG Triplet Repeats

MATERNAL CGG TRIPLET REPEAT NUMBER	RISK FOR EXPANSION OF PREMUTATION TO FULL MUTATION
59-69	37%
70-79	65%
80-89	70%
90-99	95%
100 or more	100%

CGG triplet repeat, Cytosine-guanine-guanine trinucleotide repeat.
From Fragile X Syndrome. *Clinical Overview. Elsevier Point of Care*. https://www.clinicalkey.com/#!/content/clinical_overview/67-s2.0-c9588237-6031-4f21-b273-34970f89cd2e. Updated June 14, 2021. Copyright Elsevier. All rights reserved; with data from Hersh JH et al. Health supervision for children with fragile X syndrome. *Pediatrics*. 2011;127(5):994–1006, Table 1; and Saul RA et al. FMR1-related disorders. In: Pagon RA et al, eds. *GeneReviews [internet]*. University of Washington; 1993–2018.

Diagnostic Testing

A diagnosis of FXS is possible through PCR and Southern blot analysis of a patient's blood. Positive DNA testing shows an expansion of >200 trinucleotide CGG repeats inside an area of the *FMR1* gene on the X chromosome. Diagnostic testing that reports methylation status of the gene region is preferred because methylation status is inversely correlated with cognitive functioning. Because the physical features of FXS are not always apparent in early childhood, diagnostic testing is recommended for any child who presents with global developmental delay, intellectual disability, or ASD (see Chapters 56 and 58). Any positive test for fragile X should include genetic counseling to inform of inheritance risk, phenotypic variability, and medical conditions associated with FXS and premutation status. Specific gene (*AFF2*) testing for FRAXE should be considered if CGG repeat testing is negative.

Table 59.2 Phenotypic and Genetic Effect of Number of CGG Repeats

VARIATION TYPE	CGG ALLELE SIZE	TYPICAL PHENOTYPE	GENETIC CONSEQUENCES
Full mutation	More than 200 repeats	Males are affected with fragile X syndrome About 50% of females are affected with fragile X syndrome	Repeat expansion and methylation typically result in partial or complete silencing of *FMR1* Females usually benefit from having two X chromosomes, because usually one of them is unaffected (i.e., no expanded CGG repeats) and X-inactivation does not silence all copies of it
Premutation	About 55-200 repeats	Patients typically have normal intellect, and some may have mild manifestations associated with fragile X syndrome Carriers may be at increased risk for fragile X–associated tremor ataxia syndrome and *FMR1*-related primary ovarian insufficiency	FMRP expression is usually not significantly impaired; however, larger mutations may have lowered expression Alleles are at risk for CGG expansion during maternal gametogenesis, and offspring are at risk for fragile X syndrome
Intermediate (gray zone)	About 45-54 repeats	Patient does not have fragile X syndrome caused by CGG repeats	A minority of intermediate/gray zone alleles may have minor instability; however, expansion of CGG repeats is unlikely, and if it occurs, it will not reach full mutation number within a single generation
Normal	About 5-44 repeats	Patient does not have fragile X syndrome caused by CGG repeats	No meiotic or mitotic instability is present; alleles are transmitted without any change in repeat number

FMR1 gene, FMRP translational regulator 1; FMRP, fragile X mental retardation protein.
From Fragile X Syndrome. *Clinical Overview. Elsevier Point of Care*. https://www.clinicalkey.com/#!/content/clinical_overview/67-s2.0-c9588237-6031-4f21-b273-34970f89cd2e. Updated June 14, 2021. Copyright Elsevier. All rights reserved; with data from Hersh JH et al. Health supervision for children with fragile X syndrome. *Pediatrics*. 2011;127(5):994–1006, Table 1; and Saul RA et al. FMR1-related disorders. In: Pagon RA et al, eds. *GeneReviews [internet]*. University of Washington; 1993–2018.

Table 59.3 Clinical Features of Fragile X Syndrome and Premutation Carriers

COGNITIVE, BEHAVIORAL, AND PHYSICAL CHARACTERISTICS	AGE REPORTED
FULL MUTATION FRAGILE X SYNDROME (>200 CGG REPEATS)	
Hypotonia	Infancy
Reflux	Infancy
Poor suck	Infancy
Developmental delay/intellectual disability (96% males, 64% females)	Early childhood
Autism (46% males, 16% females)	Early childhood
Attention problems (84% males, 67% females)	Early childhood
Hyperactivity (66% males, 30% females)	Early childhood
Anxiety (70% males, 56% females)	Early childhood
Aggression (38% males, 14% females)	Early childhood
Self-injurious behaviors (41% males, 10% females)	Early childhood
Depression (12% males, 22% females)	Early childhood
Recurrent otitis media (>60%)	Early childhood
Seizures (18% males, 7% females)	Early childhood
Strabismus (20%)	Early childhood
Sleep disturbances	Early childhood
Flat feet	Early childhood
Low muscle tone	Early childhood
Hyperextensible joints	Early childhood
Large prominent ears	Early/middle childhood
Elongated face	Early/middle childhood
Large testes	Adolescence
Obesity (30%)	Adolescence
Mitral valve prolapse	Adulthood
Cognitive decline/parkinsonism (17%)	Adulthood
Perseveration	Adulthood
PREMUTATION CARRIERS (55-200 CGG REPEATS)	
Attention problems	Early childhood
Autism spectrum disorder	Early childhood
Seizures	Early childhood
Anxiety	Adolescence
Depression	Adulthood
Hypertension	Adulthood
Sleep disturbances	Adulthood
Migraine	Adulthood
Fibromyalgia	Adulthood
Hypothyroidism	Adulthood
Fragile X–associated primary ovarian insufficiency (FXPOI) (~20%)	Adulthood
Fragile X–associated tremor ataxia syndrome (FXTAS) (40% males, 16% females)	Later adulthood

Data from National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention. Data and Statistics on Fragile X Syndrome, 2021; Hagerman RJ, Berry-Kravis E, Hazlett HC, et al. Fragile X syndrome. *Nat Rev Dis Primers.* 2017;3:17065; Hersh JH, Saul RA; Committee on Genetics. Health supervision for children with fragile X syndrome. *Pediatrics.* 2011;127(5):994–1006; Wheeler A, Raspa M, Hagerman R, Mailick M, Riley C. Implications of the FMR1 Premutation for Children, Adolescents, Adults, and Their Families. *Pediatrics.* 2017;139(Suppl 3):S172–S182.

MANAGEMENT OF FRAGILE X SYNDROME

Management of FXS in children often requires a multidisciplinary approach focused on monitoring for and managing developmental and/or behavioral symptoms. In addition to health supervision visits with a primary care clinician, many children with FXS benefit from ongoing care with a medical professional with experience or knowledge of FXS. Families will also benefit from accessing educational and behavioral health resources in the community.

Educational

Many individuals with FXS will require educational support to meet their needs starting from a young age. **Early intervention** services, including speech therapy, occupational therapy, physical therapy, and special instruction, are often vital components of addressing developmental delays. As a child ages and ongoing assessment occurs, special education support through an **individualized education plan (IEP)** may be warranted (See Chapter 49). There are interventions shown to be specific to the learning needs of individuals with FXS. Biologic males typically demonstrate strengths in receptive language, verbal labeling, simultaneous processing, imitation, and daily living activities. Biologic females typically demonstrate areas of strength in vocabulary, comprehension, reading, writing, spelling, and short-term visual memory. These advantages should be explored when educational interventions are being developed. Areas often in need of interventions for individuals with FXS include improving complex problem solving, maintaining attention, improving impulse control, understanding spatial relationships, and math concepts.

Environmental modifications and adaptive technologies can be an asset for an individual with FXS. This can include a modified keyboard and/or mouse and touch-screen computer options integrated into classroom lessons. A quiet environment with minimal distractions can help improve focus on tasks. Small group and one-on-one instruction for teaching new tasks can minimize anxiety and improve generalization of skills to the larger classroom. Teaching students to request breaks when feeling overwhelmed can minimize overall frustration. Visual schedules, manipulatives, clutter-free areas, and social stories are all interventions to improve compliance and learning.

Behavioral

Individuals with FXS can present with a variety of cognitive and behavioral challenges. ASD is diagnosed in between 50% and 60% of individuals with FXS. ASD is characterized by deficits in communication and social skills along with restricted interests and/or repetitive behaviors that interfere with one's daily life (see Chapter 58). Individuals with FXS can struggle with making eye contact, engaging in conversations, and expressing wants and needs. Often individuals with FXS want social contact but may avoid it due to anxiety. Hyperarousal is a common behavioral symptom, particularly in social situations where eye contact is expected, suggesting the presence of significant sensory aversions. Behavioral interventions that include skill development and anxiety management can be helpful in addressing social skills deficits. Other sensory-aversive behaviors can be related to auditory, visual, or tactile stimuli. Tantrums, and occasionally aggression, can emerge when children with FXS are overstimulated.

Sensory-seeking behaviors can also be present in individuals with FXS. These may include repetitive movements, narrowed interests, rigid routines, and atypical sensory exploration. Behaviors such as rocking, pacing, and jumping could occur to obtain sensory input. Individuals with FXS can become extremely anxious if a routine is changed or if a preferred activity is interrupted. Teaching coping strategies along with the recognition of triggers for anxiety can be helpful as a behavior management strategy.

Individuals with FXS can present with deficits in attention and focus, impulsivity, and/or hyperactivity, particularly during childhood. This can lead to a diagnosis of ADHD (see Chapter 50). These deficits can affect learning in school and require specialized

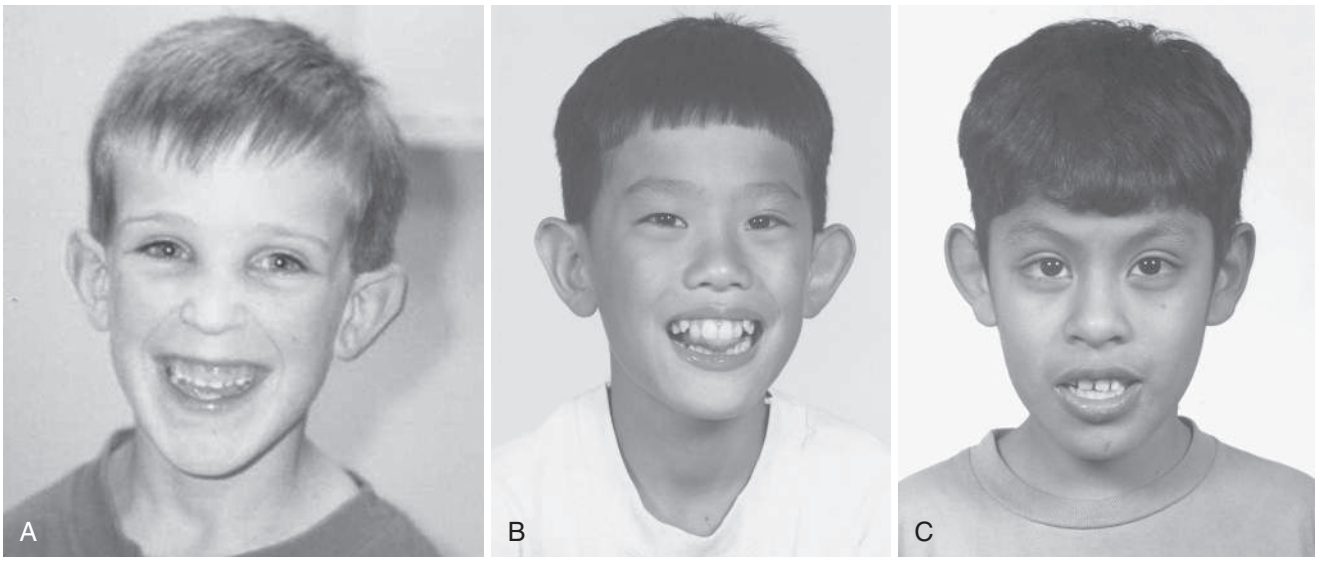

Fig. 59.1 Boys with fragile X syndrome. Note the long faces, prominent jaws, and large ears and the similar characteristics of children from different ethnic groups: European (**A**), Asian (**B**), and Latin American (**C**). *(From Jorde, LB, Carey JC, Bamshad MJ. Medical Genetics, 6th ed. Philadelphia: Elsevier; 2020: Fig. 5.20.)*

instruction or classroom accommodations to help improve focus and participation.

Individuals with FXS can present with aggressive behavior directed toward themselves and toward others. These behaviors are seen in approximately 50% of males with FXS and tend to increase with age. Individuals who exhibit ongoing aggression also typically present with more significant intellectual impairment, communication delays, and anxiety. Aggression can put a strain on caregivers or lead to injury and therefore often emerges as a primary focus of treatment.

Behavior management techniques vary depending on a child's needs. If an ASD diagnosis is present, applied behavioral analysis (ABA) programs are often integrated into treatment. ABA promotes multiple areas of development, including language, emotion, and cognition. ABA focuses on tracking specific behaviors through observation and data collection, learning their antecedents (the event or environment before the behavior occurred), and managing their consequences (the response others have after the behavior occurs) through a structured approach. Most interventions for unwanted behaviors (e.g., aggression or self-injury) aim to change the antecedents to reduce the likelihood of the behavior occurring or to change the consequence in order to make the behavior less rewarding for the individual. Interventions that aim to increase a desired behavior (e.g., complying with an instruction or toilet training) will incorporate environmental changes to remind and encourage the behavior and identify rewarding consequences that can be delivered after the behavior has occurred. ABA interventions delivered during daily living activities, community participation, and family interactions allow for optimal skill development. Special education programs often include similar behavior management techniques throughout the early childhood for individuals with FXS.

Medical

In addition to educational and behavioral management, many children with FXS may present with certain medical conditions and may require additional monitoring or care by a specialist (see Table 59.3). Monitoring in infancy and early childhood should emphasize assessment for orthopedic, growth, and/or feeding concerns. Because young children with FXS are more susceptible to otitis media and may lack communication skills to convey discomfort, a full physical examination, including ear examination, is recommended if a child presents with acute behavior changes. Young children should also be routinely screened for ophthalmologic problems, such as strabismus or astigmatism, and monitored for symptoms related to connective tissue problems, such as hypermobile joints or inguinal hernias. Seizures are more prevalent in children with FXS; symptoms concerning for any type of seizure should be investigated with electroencephalogram (EEG) when the child is both awake and asleep. Although risk for mitral valve prolapse is not typically increased until adulthood, examination for murmurs, clicks, or changes in blood pressure should be performed regularly. Sleep disturbances commonly reported among children with FXS include delayed sleep onset, frequent night waking, and occasionally obstructive sleep apnea. Screening for sleep concerns should be done at every visit, and parents should be counseled on behavioral strategies to address sleep onset and waking challenges (see Chapter 31). Concerns for apnea or snoring may require further evaluation by a sleep specialist or with polysomnography. Medications to help address sleep concerns may include melatonin or clonidine, neither of which is currently approved by the Food and Drug Administration (FDA) for use in children with FXS.

There are currently no approved treatments for the core symptoms of FXS, but many individuals will benefit from medication to address some of the commonly co-occurring behavioral symptoms associated with absence of FMRP. If behavioral strategies are not sufficient to address hyperactivity or impulsivity, a young child (<5 years) may benefit from a trial of an α_2-adrenergic agonist, such as clonidine or guanfacine. School-aged children with FXS often show improvements in hyperactivity, impulsivity, and/or attention problems when treated with a stimulant, but side effects such as irritability or aggression may occur. Selective serotonin reuptake inhibitors (SSRIs) can be safe and effective in reducing anxiety, obsessive-compulsive symptoms, and sometimes aggression in young children with FXS; one trial of sertraline in young children with FXS demonstrated improvements in visual reception and fine motor coordination in 2- to 6-year-olds. Additional analyses demonstrated improvements in expressive language skills for children with FXS and ASD. Treatment with an atypical antipsychotic, such as risperidone or aripiprazole, may be needed in cases of severe anxiety, aggression, or mood instability that have not responded to other medications.

Neurobiologic studies of FXS have identified overactivation of brain glutamate pathways and underactivation of gamma-aminobutyric acid (GABA) pathways leading to studies of

medications targeting these pathways in the hopes that they would improve cognitive outcomes. Although some studies in animal models were encouraging, human trials have yet to demonstrate consistent benefits. Some clinical trials are ongoing.

In addition to continued monitoring for cardiac, seizure, sleep, and behavioral symptoms, health supervision in late childhood and adolescence should also include discussion of adult transition issues, including vocational training, accessing state-specific adult disability services, and transition to adult medical care.

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