

Neurobehavioral Disorder Associated With Prenatal Alcohol Exposure

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Children and adolescents affected by prenatal exposure to alcohol who have brain damage that is manifested in functional impairments of neurocognition, self-regulation, and adaptive functioning may most appropriately be diagnosed with neurobehavioral disorder associated with prenatal exposure. This Special Article outlines clinical implications and guidelines for pediatric medical home clinicians to identify, diagnose, and refer children regarding neurobehavioral disorder associated with prenatal exposure. Emphasis is given to reported or observable behaviors that can be identified as part of care in pediatric medical homes, differential diagnosis, and potential comorbidities. In addition, brief guidance is provided on the management of affected children in the pediatric medical home. Finally, suggestions are given for obtaining prenatal history of in utero exposure to alcohol for the pediatric patient.

Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE) is a newly proposed mental health diagnosis associated with the teratogenic effects of in utero exposure to alcohol. This behavioral and mental health diagnosis is under the umbrella of fetal alcohol spectrum disorders (FASDs), which also includes fetal alcohol syndrome (FAS), partial FAS (pFAS), and alcohol-related birth defects; additional information is available at the American Academy of Pediatrics (AAP) Web site (<http://www.aap.org/fasd>).¹ ND-PAE was introduced into the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) of the American Psychiatric Association in 2013 as a “Condition for Further Study,” as well as a specified condition under “Other Specified Neurodevelopmental Disorder” (International Classification of Diseases, Ninth Revision code 315.8, International Classification of Diseases, 10th Revision code F88).² The intent of this new diagnostic designation

is to better capture the behavioral and mental health effects of in utero exposure to alcohol of individuals with and without the physical dysmorphism associated with prenatal alcohol exposure, in contrast to the term *alcohol-related neurodevelopmental disorder*, which applies only to individuals with neurobehavioral effects in the absence of physical dysmorphism effects.^{3,4} This report outlines the clinical manifestations of ND-PAE that are most salient for the pediatric medical home, including identification of children in need of evaluation, diagnosis, comorbid or differential diagnosis, referral, and management. Although they do not represent AAP policy, specific suggestions are provided for assessment of maternal use of alcohol during pregnancy at routine pediatric visits.

The most recent national data from the Centers for Disease Control and Prevention (CDC) indicate that alcohol consumption during pregnancy is not

abstract



Disclaimer: The guidelines/recommendations in this article are not American Academy of Pediatrics policy, and publication herein does not imply endorsement.

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TABLE 1 DSM-5 Proposed Criteria for Neurobehavioral Disorder Associated With Prenatal Alcohol Exposure

- A. More than minimal exposure to alcohol during gestation, including prior to pregnancy recognition. Confirmation of gestational exposure to alcohol may be obtained from maternal self-report of alcohol use in pregnancy, medical or other records, or clinical observation.
- B. Impaired neurocognitive functioning as manifested by one or more of the following:
1. Impairment in global intellectual performance (i.e., IQ of 70 or below, or a standard score of 70 or below on a comprehensive developmental assessment).
 2. Impairment in executive functioning (e.g., poor planning and organization; inflexibility: difficulty with behavioral inhibition).
 3. Impairment in learning (e.g., lower academic achievement than expected for intellectual level; specific learning disability).
 4. Memory impairment (e.g., problems remembering information learned recently; repeatedly making the same mistakes; difficulty remembering lengthy verbal instructions).
 5. Impairment in visual–spatial reasoning (e.g., disorganized or poorly planned drawings or constructions; problems differentiating left from right).
- C. Impaired self-regulation as manifested by one or more of the following:
1. Impairment in mood or behavioral regulation (e.g., mood lability; negative affect or irritability; frequent behavioral outbursts).
 2. Attention deficit (e.g., difficulty shifting attention; difficulty sustaining mental effort).
 3. Impairment in impulse control (e.g., difficulty waiting turn; difficulty complying with rules).
- D. Impairment in adaptive functioning as manifested by two or more of the following, one of which must be (1) or (2):
1. Communication deficit (e.g., delayed acquisition of language; difficulty understanding spoken language).
 2. Impairment in social communication and interaction (e.g., overly friendly with strangers; difficulty reading social cues; difficulty understanding social consequences).
 3. Impairment in daily living skills (e.g., delayed toileting, feeding, or bathing; difficulty managing daily schedule).
 4. Impairment in motor skills (e.g., poor fine motor development; delayed attainment of gross motor milestones or ongoing deficits in gross motor function; deficits in coordination and balance).
- E. Onset of the disorder (symptoms in Criteria B, C, and D) occurs in childhood.
- F. The disturbance causes clinically significant distress or impairment in social, academic, occupational, or other important areas of functioning.
- G. The disorder is not better explained by the direct physiologic effects associated with postnatal use of a substance (e.g., a medication, alcohol or other drugs), a general medical condition (e.g., traumatic brain injury, delirium, dementia), another known teratogen (e.g., fetal hydantoin syndrome), a genetic condition (e.g., Williams syndrome, Down syndrome, Cornelia de Lange syndrome), or environmental neglect.

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a rare event, with 10.2% of pregnant women reporting that they consumed alcohol in the past 30 days and 3.1% reporting binge drinking in the past 30 days.⁵ Furthermore, approximately half of pregnancies are unplanned, and a woman might not know she is pregnant until the sixth week of gestation or beyond, a period when she might still be consuming alcohol and causing damage.⁶ Thus, many pregnancies are alcohol-exposed and represent a population of children at risk for FASDs, especially ND-PAE. Recent studies including active, expert clinical assessment of school-aged children report estimates that ~2% to 5% of children in the United States have an FASD.^{7–10} Review of medical records indicates that most of these children are not identified or diagnosed.¹¹

Criteria for ND-PAE are based on extensive brain imaging and animal model studies of adverse effects of prenatal alcohol exposure despite the absence of physical features (ie, dysmorphia and growth restriction).^{3,12–14} In fact, only ~25% of children affected by in utero

exposure to alcohol exhibit physical features.¹⁵ In 2011, under the auspices of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders, the National Institute on Alcohol Abuse and Alcoholism and the CDC convened a panel of experts to evaluate the research on FASDs not associated with the typical physical features. (Information on these proceedings can be found at <http://www.niaaa.nih.gov/about-niaaa/our-work/ICCFASD/proceedings/2011>.) In their consensus statement, 3 major areas of impairment were identified: neurocognition, self-regulation, and adaptive functioning. These areas of deficit, along with evidence of in utero exposure to alcohol, formed the basis of the ND-PAE diagnostic criteria.^{3,13}

CLINICAL FEATURES OF ND-PAE

Diagnosis of ND-PAE is appropriate if a child presents with impairment in neurocognition, impaired self-regulation, 2 impairments of adaptive functioning, and a history of more than minimal exposure to alcohol in utero (Table 1), as long as the disorder is not better explained by other

factors (eg, genetic or teratogenic syndrome). Although these broad domains overlap with other disorders of childhood, specific deficits within them are indicative of ND-PAE. As with any developmental condition, impairments in these domains present differently as a child matures. To aid identification of patients with ND-PAE across development, age-specific traits in the framework for the continuous and comprehensive developmental screening included in *The Bright Futures Guidelines*, fourth edition, are presented in Fig 1A, Fig 1B, and Fig 1C.¹⁶

Impairment in Neurocognition

Criteria for neurocognitive impairment include evidence of 1 of the following: global impairment, executive dysfunction, deficits in learning, memory problems, or trouble with visual–spatial reasoning. These criteria may be assessed by standardized testing, clinical observation, or, more often, clinical history. To ensure the integrity of the diagnostic criteria for ND-PAE, findings based on clinical observation

A Neurocognitive Domains	0–11 Months	1–4 Years	5–10 Years	11–21Years
• General Cognitive Impairment	• Mild or global developmental delays	→	• Intellectual Impairment	→
		• Problems applying knowledge to new situations		→
		• Lack of elaborate imaginative play	• Difficulty with abstract reasoning	→
		• Difficulty transitioning from one activity to another		→
		• Problems learning sequential information - first to last, days of the week, least to most		→
		• Repeatedly making the same mistakes		→
		• Has trouble organizing himself/herself	• Poor planning and organization	→
		• Cannot describe events orderly or in a logical sequence	• Difficulty changing strategies or thinking about things in more than one way	→
• Executive functioning		• Is disorganized		
		• Is Inflexible		
		• Acts without thinking		
		• Gets stuck on things		
		• Poor understanding of consequences		
		• Poor linking of acts to consequences		
		• Difficulty thinking about things differently		
		• Does not plan to complete complex tasks		
		• Lies about things that don't make sense		
		• Requires repeated exposure to things to learn properly	• Lower academic achievement than expected for intellectual level	→
• Learning		• Struggles with learning early academic concepts	• Math learning disability	→
		• Struggles with early math concepts (one to one correspondence in counting objects; object constancy)		
		• Problems remembering something learned recently		→
		• Cannot hold information in their memory	• Difficulty with multi-step verbal instructions	→
		• Cannot carry out multiple step plans	• Frequently losing or misplacing possessions	→
• Memory		• Has poor recall of information or events	• Problems remembering personal information such as one's telephone number or other developmentally-appropriate information that should be well-known	
		• Frequently forgets things		
		• Difficulty constructing three-dimensional figures out of blocks	• Deficits in the perception and analysis of visual or spatial information	→
		• Has poor understanding of his/her body in space	• Problems understanding directionality like north or south	→
• Visual-spatial reasoning		• Difficulty copying simple visual patterns	• Problems aligning numbers in columns	→
		• Difficulty with learning spatial words (left, right, up, down)	• Disorganized or poorly planned drawings or constructions	→
			• Difficulty reading and following a map	→
			• Difficulty solving puzzles	→

FIGURE 1A
 ND-PAE Age-Dependent Symptom Diagnosis Guidelines: Neurocognitive Domain. (continued)

B Self-Regulation Domains	0–11 Months	1–4 Years	5–10 Years	11–21 Years
• Mood or behavioral regulation	• Difficulties going to sleep			
	• Difficulties staying asleep throughout the night			
	• Is a light sleeper			
	• Frequent meltdowns			
	• Moody			
	• Irritable			
	• Difficulty with adapting to changes			
	• Fussy			
	• Gets frustrated easily			
	• Has difficulty handling exciting events (parties, holidays, cannot be taken to a store or restaurant)			
	• Difficulty calming down or being soothed	• Difficulty calming down		
	• Overreaction to environmental events and stressors	• Becomes too upset		
	• Easily overwhelmed in stimulating environments	• Is easily overwhelmed		
		• Is easily overstimulated		
		• Problems calming self		
		• Cannot play independently		
		• Cannot entertain himself/herself		
		• Frequent behavioral outbursts		
		• Mood lability	• Frequently upset	
		• Is too intense at times		
	• Is hyperresponsive to things			
	• Gives up easily			
	• Negative affect or irritability	• Has problems fitting in with others		
		• Frequently loses things		
		• Gets angry easily		
		• Has a short fuse		
		• Grabs at things		
		• Often tests or pushes limits		
• Attention	• Difficulty shifting attention			
	• Difficulty maintaining focused play or exploration of toys	• Trouble staying focused		
		• Difficulty maintaining focus on task at hand		
		• Difficulty encoding new information		
		• Difficulty focusing on new information		
		• Difficulty sustaining mental effort		
• Impulse control	• Difficulty waiting			
	• Chaotic disorganized play	• Does not think before responding		
		• Difficulty complying with rules		
		• Engages in risky behavior		
		• Has poor impulse controls		
		• Difficulty delaying gratification		
		• Confabulating		
		• Taking possessions of others		
		• Frequently interrupting others		
		• Needs constant supervision		
	• Difficulty waiting turn			

FIGURE 1B
 ND-PAE Age-Dependent Symptom Diagnosis Guidelines: Self-Regulation Domain. (continued)

or history are best if based on specific examples of impairment and documented in the medical record.

For global deficits, comprehensive standardized testing results are the gold standard. This might require

referral for testing or coordination with school psychologists. However, for diagnosis it is important to

Adaptive Domains	0–11 Months	1–4 Years	5–10 Years	11–21 Years
• Communication	• Delayed acquisition of language	→	• Difficulty understanding jokes, idioms, or metaphors	→
	• Poor exploration of toys	• Difficulty using language to express self so that the listener understands	→	
		• Talking too much	→	
		• Problems linking words with feelings	→	
		• Making comments that seem out of context	→	
		• Reduced verbal fluency	→	
		• Difficulty following along in a conversation	• Difficulty understanding spoken language	
• Social	• Overly friendly with strangers	→		
		• Gullible or naive	→	
		• Is unaware of personal space	→	
		• Difficulty reading social cues	→	
		• Difficulty understanding social consequences	→	
		• Socially immature/acts too young	→	
		• Difficulty attending to facial or social cues	• Difficulty making and keeping friends	→
		• Difficulty interacting with friends/peers	• Superficial friendships but no close friends	→
		• Is not aware of his/her actions on others	• Poor judgment in choice of friends	→
			• Has friends who are much younger or much older	→
			• Makes inappropriate social overtures (may be sexual or intruding on boundaries of others)	→
		• Easily led by others	→	
		• Demands a lot of social attention	• Demands a lot of attention	
			• Difficulty attending to facial or social cues	
			• Is not aware of his/her actions on others	
• Daily living	• Delays in early feeding skills	• Struggles with understanding time	• Problems following rules of personal safety	→
	• Difficulties with adapting to environmental events	• Delayed toileting, feeding, or bathing	• Difficulty managing daily schedule	→
		• Persistent problems in carrying out common daily routines, such as getting dressed	• Slow to understand the function of money or to tell time	• Poor understanding of money values and time management
				• Difficulty keeping appointments
				• Problems managing finances
• Motor	• Delayed attainment of fine and gross motor skills	• Problems in coordination and balance	→	
	• Frequent falls or loss of balance	• Problems in integration of left and right motor activities	→	
	• Poor coordination	• Delayed attainment of gross motor skills	• Problems in visual motor integration	→
	• Poor motor skills	• Is accident prone	• Poor handwriting	• Difficulty learning coordinated motor skills
	• Struggles with using hands to complete tasks	• Poor fine motor skills (poor drawing and handwriting, difficulty manipulating buttons or zippers, difficulty using eating utensils)		
		• Difficulty learning coordinated motor skills		
		• Bumps into things frequently		
	• Falls frequently			

FIGURE 1C
ND-PAE Age-Dependent Symptom Diagnosis Guidelines: Adaptive Domains.

recognize that not all affected children perform in the range of intellectual disability. Clinical research has found that 86% of individuals with any of the FASDs have an IQ in the low average or borderline ranges.¹⁷ The important point is that the child under consideration is functioning below what would be expected relative to his or her peers.

Even if global delay or impairment is not present, specific deficits can indicate neurocognitive impairment consistent with ND-PAE. Impairment in executive function often presents as poor planning skills, inflexibility, or difficulty with behavior inhibition.¹⁸ Impaired learning or specific learning disabilities often manifest in the areas of math, visual-spatial reasoning, or abstract academic material. Finally, memory problems might be seen as problems remembering recently learned materials or repeatedly making the same mistake.¹⁹ These particular types of learning and memory problems often lead caregivers and educators to mistakenly assume the child is being defiant or willfully disobeying rather than having genuine difficulty, the “can’t vs won’t” error.^{2,20,21}

Self-Regulation

Impaired self-regulation might include difficulty regulating mood or behavior, attention deficits, or poor impulse control. Early signs of mood and behavior regulation problems might include sleep problems or severe reactions to discomfort for infants and extended tantrums for toddlers.²²⁻²⁵ For older children, increased incidence of externalizing behaviors and severe reactions to stress are most common.^{3,26,27} However, increased levels of anxiety and depression have been documented.²⁷ Attention problems are often associated with prenatal alcohol exposure. Children with ND-PAE can have

particular difficulty shifting attention, resulting in behavior problems. Poor impulse control is an additional impairment.^{28,29} These difficulties in all areas of self-regulation are particularly challenging for the entire family of a child with ND-PAE. The sleep problems and mood lability with frequent behavior outbursts, typically caused by frustration with task shifting, are often the presenting complaints to a pediatrician.³⁰⁻³²

Adaptive Functioning

Adaptive functioning is the ability to acquire daily skills for personal and social sufficiency. Impairment in adaptive functioning can occur in communication, social communication and interaction, daily living skills, or motor skills for very young children. Adaptive functioning is an area of special concern of children with ND-PAE because these impairments are pervasive across domains and situations as children age.³ Therefore, meeting this criterion requires impairment across 2 domains of adaptive functioning. Although most language milestones (eg, babbling, first words, and syntax) are acquired on schedule,³³ individuals with ND-PAE might exhibit communication problems such as difficulty in understanding figurative language (eg, understanding idioms, jokes, or sarcasm) and social communication conventions (eg, how to effectively enter a conversation).^{30,34} Socially, they can be overly friendly with strangers, be at high risk of bullying, have difficulty learning social rules through experience (eg, how to join a group on the playground), or be highly susceptible to manipulation by others.³⁵ Because of attention and memory problems, a child with ND-PAE might initially learn daily skills such as hygiene or house rules, yet maintaining those skills and organizing daily activities present a challenge.^{36,37} Finally, motor skills can be impaired at the fine motor

level (eg, poor writing skills) or gross motor level (eg, poor coordination or balance).^{7,38}

In Utero Exposure to Alcohol

Unlike FAS, which can be diagnosed when information about history of prenatal alcohol exposure is unavailable, diagnosing other conditions along the continuum of FASDs, including ND-PAE, requires a confirmed history of in utero exposure. There are clear and strong research human and animal data documenting adverse neurodevelopmental outcomes from moderate to heavy levels of prenatal exposure to alcohol³⁶ and adverse reproductive (eg, prematurity) effects from even very low exposure levels.³⁹ Linking adverse neurodevelopmental outcomes to in utero exposure at these lower levels remains a challenge but can be revealed with more sensitive testing.⁴⁰ Despite clear evidence for the association between prenatal exposure to alcohol and the wide profile of strengths and weaknesses that might be observed across children with ND-PAE, the specificity of the profile is not yet known. Therefore, the criterion of *more than minimal gestational exposure* is required for the ND-PAE diagnosis. *More than minimal exposure* is defined as maternal consumption of ≥ 13 drinks per month during pregnancy (ie, any 30-day period of pregnancy). The “More than minimal” criterion is not intended to denote a threshold for safe consumption of alcohol during pregnancy. It is simply an acknowledgment of ongoing controversy about low levels of exposure and an attempt make sure the diagnosis was not overused because the base rate of drinking any alcohol among women of childbearing years is relatively high.⁵

Suggestions for obtaining a prenatal history of alcohol exposure are presented in the Appendix.

The primary care pediatrician needs to be aware that there is no known level of alcohol use during pregnancy that has been established as safe. The US surgeon general still advises that women who are pregnant, or are considering pregnancy, should abstain from consuming alcohol.⁴¹ Primary care pediatricians will want to provide this important health message to their adolescent patients and mothers-to-be and obtain information on prenatal exposure to alcohol for all patients.

DIFFERENTIAL AND COMORBID DIAGNOSES

As would be expected, symptoms associated with the diagnostic criteria of ND-PAE may be observed in children with other disabilities. The diagnosis must be applied with care and based on all available information, especially prenatal exposure history. It is important to keep in mind that the specific constellation of impairments and unique manifestations of the criteria are most relevant for recognition and diagnosis rather than the general symptom domains. Specifying co-occurring disorders can provide the most complete picture of the child's strengths and weaknesses to determine treatment or referral course.⁴²⁻⁴⁵ Differential diagnoses of ND-PAE can be particularly challenging because the disorder does not always present the same way in all children because of differences in timing and amount of prenatal alcohol exposure and difference in genetic predispositions or postnatal environment.^{33,46} Table 2 presents key differences between ND-PAE and several neurobehavioral conditions. The severity of presentation and the constellation of characteristics vary greatly from child to child.^{3,33,42-45} In a sample of children with FASDs, comorbid mental health conditions included (in descending order) mental retardation

(ie, intellectual disability), sleep abnormalities, reactive attachment disorder, anxiety, posttraumatic stress disorder, oppositional defiant disorder, language disorder, learning disability, depression, bipolar disorder, some features of autism, and specific phobias.^{45,47} Other conditions such as enuresis, encopresis, and eating disorders may be present depending on the age of the child.³²

FASDs

The diagnosis of ND-PAE encompasses the behavioral, developmental, and mental health aspects of FASDs. Other diagnoses along the spectrum, such as FAS or pFAS, focus on structural and neurophysiological central nervous system abnormalities (eg, microcephaly or neurologic soft signs). Physical features such as facial dysmorphism or growth restrictions (either prenatal or postnatal) are required for FAS and pFAS. Thus, for children with both physical findings and behavioral findings consistent with ND-PAE, it is appropriate that a comorbid diagnosis of FAS or pFAS also be used.³

Intellectual Disability

As mentioned, a majority of children with any of the FASDs score in the low range of normative intellectual functioning.¹⁵ The history of more than minimal in utero exposure to alcohol will be a major decision point between children with ND-PAE comorbid with intellectual disability and children with intellectual disability due to another etiology. However, deficits specific to ND-PAE are recognized. For example, even with repeated experience and an IQ within normal limits, the memory and learning impairments of a child with ND-PAE may mean that he or she has difficulty with previously learned skills, such as finding his or her locker at school on a routine basis despite repeated instructions

and practice^{48,49} or forgetting how to tie his or her shoes, despite previous mastery, and having to relearn that skill entirely. This is different from regression of emerging skills seen in some children with autism.³³

Finally, children with intellectual disability *without* prenatal alcohol exposure tend to have lowered functioning across all neurocognitive domains. In contrast, individuals *with* ND-PAE tend to have specific difficulty with nonverbal aspects of cognition such as visual-motor skills, learning and memory for recently learned skills, and executive functioning, resulting in behavioral problems.^{3,49} Cognitive impairment coupled with behavioral problems should prompt clinicians to consider a diagnosis of ND-PAE.

Attention Problems

Current research demonstrates differences in manifestations of attention-deficit/hyperactivity disorder (ADHD) and FASDs. Behaviorally, children with FASDs have higher rates of social behavioral problems resulting from difficulties in social cognition and emotional processing.⁵⁰ They might also be more likely to have problems dealing with overstimulation than children with simple ADHD.⁵¹ In contrast, children with ADHD due to etiology not attributable to alcohol have difficulty with focus and sustained attention.⁵² Medication for symptoms of ADHD can result in unexpected outcomes in children with a history of prenatal alcohol exposure.^{53,54} Stimulant medications are often ineffective for children with prenatal alcohol exposure.^{27,33} Care should be given to investigate whether in utero exposure to alcohol contributes to attention problems for any child because treatment and management plans could differ.²

Early Trauma

Children who experience early trauma (including physical events,

TABLE 2 Differential Diagnosis for ND-PAE

	Neurocognitive	Behavioral Regulation	Adaptive Functioning	Key Differential From ND-PAE
ND-PAE (formerly referred to as alcohol-related neurodevelopmental disorder)	Intellectual skills may be in the intellectually deficient range for some but not most. Deficits in executive functioning skills, learning, memory, and visual spatial reasoning are common.	Self-regulation impairments may take the form of poor mood or behavioral regulation skills, attention deficits, and poor impulse control. They are best characterized by arousal dysfunction involving slower gating of incoming stimulation and reduced capacity to inhibit attending to distracting stimuli. They respond to simplification of sensory input (fewer distracters and slower presentation).	Adaptive functioning skills often fall below that of their overall IQs, and often there are declines in their skills as they grow older relative to their peers. This decline may result in the standard scores being lower as they age. They often have impairments in the pragmatic communication skills, are socially disinhibited, and have poor motor skills or coordination, with the latter being a greater deficit in young rather than older children.	Not applicable.
Global developmental delay or intellectual disability	Children with global developmental delay by definition have impairments in multiple domains of functioning (eg, cognitive and motor functioning).	Behavioral regulation skills are variable, depending on the nature of the disorder causing the developmental delays or intellectual disability and the extent of the brain damage.	Adaptive functioning skills are also in the low or deficient range and are generally stable over the lifetime relative to peers and consistent with their levels of intellectual functioning.	<ul style="list-style-type: none"> • Overall development or IQ is often not delayed or intellectually impaired in ND-PAE. Early developmental problems in ND-PAE are often detected in motor functioning or quality of motor functioning. The cognitive deficits may not be detectable in the first year of life on measures of early childhood development. • Children with ND-PAE have behavioral regulation deficits, and those with intellectual disability may not.
ADHD	Intellectual skills are in the intellectually deficient range by definition. This often involves IQ score <70 on most standardized tests. Other cognitive skills general consistent with overall IQ.	ADHD is characterized by problems with sustaining attention and being impulsive or hyperactive. The disorder may be seen as being chronically underaroused, and individuals respond to stimulant medications and increases in arousal (exercise and movement or increasing arousal level of learning material).	Adaptive skill deficits are often present in untreated individuals with ADHD but with appropriate supports and medication may be age appropriate.	<ul style="list-style-type: none"> • Children with ND-PAE have adaptive skills below IQ or declining with age. • The extent of neurocognitive impairment is often greater in children with ND-PAE than those with ADHD. • Children with ND-PAE also demonstrate declines in adaptive skills with age. • Children with ND-PAE deteriorate under conditions of high arousal, but those with ADHD often improve.

TABLE 2 Continued

	Neurocognitive	Behavioral Regulation	Adaptive Functioning	Key Differential From ND-PAE
ASD	Intellectual skills vary, with some being in the severely intellectually deficient range and others functioning within normal limits or gifted.	Easily overaroused and benefit from reducing sensory input during instruction.	Adaptive skills are often deficient, but typically they have relative deficits in the social and communication skills as compared with their independent living skills.	<ul style="list-style-type: none"> Children with ASD are characterized by being socially withdrawn, and children with ND-PAE are more likely to be socially disinhibited. In ASD, there is significant lack of social and emotional reciprocity, whereas in ND-PAE, the problem is socially inappropriate behavior that relates to their lack of cause-and-effect reasoning, slow and ineffective processing of what people say during conversation, and lack of visual-spatial skills that govern their ability to put their body at an appropriate distance from another. Children with ASD generally have stereotypes that are odd or very repetitive, which are not as common or may not be seen at all in some children with ND-PAE.
Early trauma exposure or PTSD	Intellectual skills would typically be within normal limits. For many, there may be deficits associated with environmental deprivation, but when removed from the adverse environment, young children often demonstrate dramatic gains in developmental functioning. Older children may have more persistent cognitive deficits, particularly in the area of memory functioning. The length of exposure to trauma and environmental deprivation typically relates to the extent of impairment.	Children with PTSD often have arousal dysfunction. They may have sleep problems, be anxious, and easily startle. They often have difficulty focusing on tasks and sustaining mental effort. Often these deficits are the result of anxiety or intrusive thoughts.	<p>Adaptive skills are often below their cognitive functioning skills. Some may have deficits associated with cues associated with the traumatic event. For many, these deficits may be associated with environmental deprivation, but when removed from the adverse environment and placed in a positive, nurturing environment, young children often demonstrate dramatic gains in developmental functioning. Older children may have more persistent adaptive deficits. The length of exposure to trauma and environmental deprivation typically relate to the extent of impairment.</p>	<ul style="list-style-type: none"> Young children with PTSD demonstrate quicker recovery of function in cognitive skills if placed into a stable, nurturing environment. Children with PTSD may have more anxiety symptoms.
				<ul style="list-style-type: none"> Children with PTSD may have difficulties forming positive relationships with caregivers. The extent of the cognitive impairment is typically not as great but may be in extreme abusive cases.

TABLE 2 Continued

Bipolar disorder	Neurocognitive	Behavioral Regulation	Adaptive Functioning	Key Differential From ND-PAE
	Intellectual skills typically are within normal limits.	The disorder is characterized by cyclic periods of depression and mania. During episodes of depression, the child's affect may be flat and he or she may lack interest in his or her preferred activities. During episodes of mania, the child may be extremely active and have difficulty organizing or regulating his or her thought patterns. Often children do not have the full pattern of cycling in the early stages of the disorder and may only become easily irritated or have significant mood lability.	Adaptive skill deficits may or may not be present but often are the result of the mood disturbance interfering with learning age-appropriate adaptive skills or being able to carry out the skills.	<ul style="list-style-type: none"> • Children with bipolar disorder typically do not have the same magnitude of cognitive impairment.

ASD, autism spectrum disorder.

psychological events, and abuse or neglect) often display serious behavioral problems, receiving a mental health diagnosis of conduct disorder, oppositional defiant disorder, anxiety, or depression. Because of overlap between these other behavioral disorders and ND-PAE, at a general level (especially for the self-regulation component) it is important for a clinician to consider these as both differential and comorbid diagnoses. Until additional data are available about the validity and reliability of all childhood behavior disorders, including ND-PAE, this will continue to be a tricky diagnostic issue. Furthermore, for some children a history of early trauma, abuse, neglect, or parental loss will be the only presenting problem because children with prenatal exposure to alcohol are at higher risk for these negative events. Therefore, it is particularly important to obtain prenatal exposure history in these situations.^{18,55} Such early trauma has been shown to drastically worsen the effects of prenatal alcohol exposure and must be taken into account.⁵⁵

Other Conditions

Children with diagnoses of conduct disorder, oppositional defiant disorder, or even posttraumatic stress disorder (PTSD) are often aggressive without appropriate provocation, whereas children with ND-PAE might have behavioral outbursts caused by situational frustrations they experience when interacting with others or by their own neurodevelopmental limitations.³⁵ Furthermore, children with other early trauma diagnoses might have inappropriate social interactions but tend to withdraw from others as self-protection, whereas children with ND-PAE are more likely to be overly friendly, seeking out companionship and social acceptance, although often in an inappropriate manner.^{35,56}

Foster Care and Adoption

A special issue regarding ND-PAE and early trauma is that among children in the child welfare system and children adopted internationally. Researchers have found disproportionately high rates of children with FASDs, including diagnoses without physical features such as ND-PAE, in these populations.^{57–60} Because these children also often experience early trauma, separation, and poor early caregiving, they are at elevated risk for a comorbid diagnosis of reactive attachment disorder or PTSD after abandonment.^{61–64} Obtaining information about, and documenting, possible prenatal exposures for all who have a current or history of involvement with the child welfare system is prudent clinical practice. Such information can inform assessments and evaluation at older ages.

Finally, although prenatal alcohol exposure does occur in various contexts and varying levels, the presence of ongoing alcohol or substance abuse in the home confers additional risk. Families with substance abuse problems are more likely to suffer from multiple forms of trauma, antisocial behavior, financial instability, and poverty.¹⁸ These factors can lead to additional comorbid conditions in a child with ND-PAE.

REFERRAL AND MANAGEMENT

Although providing appropriate diagnoses (including comorbidities) can make a positive impact by giving families and clinicians a framework for understanding a child's behavior, it is only a starting point. Ongoing care is the major role of the pediatric medical home.⁶⁵ Although specific and targeted early interventions have been shown to be most effective, more general special education and support services also improve outcomes.^{15,17,55,66,67}

Individuals with FASDs, including children without physical stigmata,

can experience a host of physical conditions and secondary disabilities including mental health problems, disrupted school experiences, trouble with the law, incarceration or confinement, inappropriate sexual behavior, alcohol or drug problems, dependent living, and problems with employment.¹⁷ In 1 study, only 8% of people diagnosed with FAS or a related condition did not have problems with independent living or employment. Even if this finding encompasses some amount of ascertainment bias because it is a clinical sample, the number of individuals with FASDs who do not achieve independent living is striking and cause for concern.¹⁵ Early diagnosis and treatment of children with FASDs, including ND-PAE, can reduce the risk of additional disabilities and adverse lifelong consequences. This protective effect of early diagnosis has been demonstrated in a number of studies.^{15,24,35,68} In addition, referral to other specialist may be warranted (eg, genetics, neurology, cardiology, nephrology).

Medications

The evidence base for pharmacologic treatment in this population is limited,^{53,69,70} with no medications indicated specifically for ND-PAE. Studies on human and animal models are inconclusive at this time, and more data are needed for proper guidance. However, findings from small pilot studies suggest that ADHD stimulant medication can improve hyperactive symptoms but not attention and impulsivity.^{71,72} And another small study found that neuroleptics can be more beneficial than psychostimulants for improving social skills.⁵⁶ A poor or adverse clinical response to stimulants (ie, ineffective clinical response or significant side effects) can occur, and clinicians should plan to adjust medications as necessary. Such medication failure also might be an indicator to consider a diagnosis under the umbrella of FASDs.

Behavioral, Mental Health, and Academic Referrals

By definition ND-PAE is a behavioral or mental health diagnosis, and therefore such patients will benefit from referral to specialties that can address these needs.^{3,73,74} In addition, academic problems are a natural sequela of these primary disabilities. An overview of interventions developed specifically for these children found that effective interventions include explicit teaching techniques, repetitive presentation, and caregiver instructions about specific strengths and weaknesses associated with prenatal alcohol exposure.^{73,75,76} As with many aspects of ND-PAE, additional systematic research is needed to develop new intervention strategies and to get a clearer picture of the long-term effectiveness of available programs.^{24,73,74,77,78} However, a sample of currently available evidence-based and evidence-informed interventions are described in the online Supplemental Information.

It is important to remember that all aspects of the ND-PAE diagnosis (ie, neurocognition, self-regulation, and adaptive behavior) are developmental processes, and the type of specialty needed might change across development. For younger children, allied health referrals, such as physical or occupational therapies, might be most appropriate. Early intervention might focus on general developmental skills for the infant or preschooler. Occupational therapy is often recommended for fine motor impairments, sensory integration problems, and emerging self-regulation problems.⁷⁹ For older school-age children, several evidence-based interventions targeting specific skills and adapted for children with FASDs are available and can be recommended to school-age children. Several of these interventions are described in the online Supplemental Information.⁷³ More information on such interventions is available at the National Organization

on Fetal Alcohol Syndrome (www.NOFAS.org).

Older children with ND-PAE might need more traditional mental health services and can begin to benefit from modified insight-based therapies.^{27,80} Referral to a psychiatrist or psychologist can be appropriate. Referral for substance abuse evaluation or treatment also might be warranted.^{15,27} For the medical home provider, however, it is most effective to provide background information on the strengths and weaknesses of a child with ND-PAE in addition to child specific symptoms when making such a referral.

Of special note for this population is that many affected children and adolescents do not qualify for special education under standard criteria, yet they still need services.^{17,81} This gap must be addressed at the individual patient or student level. Psychoeducational testing (by school personnel or private psychologists) might be required for diagnostic confirmation and treatment planning. Creative solutions and closely engaging with the family, school, and community by the pediatric medical home can facilitate meaningful results (see the AAP FASD Toolkit at www.aap.org/fasd).^{82,83}

Family Support

Parental education about ND-PAE, and even about FASDs in general, is particularly effective.⁸⁴ For parents there might be fears about stigma or the legal implications of the child's diagnosis. It is important that clinicians ask the difficult questions to screen for prenatal alcohol exposure when they suspect a child might have been prenatally exposed to alcohol.

Caregivers appreciate information about how the behavioral difficulties they experienced with their child were directly related to their child's exposure to alcohol in utero.^{17,73,84} Instruction on the use of explicit explanations that avoid idioms or other figurative

language, the value of routines, and the need to relearn some skills and obtain repeated instruction is a practical technique. Furthermore, such instruction provides reassurance and support.^{64,73} It often helps to explain to parents that structural brain abnormalities and the resulting neurobehavioral manifestations their child has (eg, problems with poor problem solving and executive dysfunction) might make him or her less responsive to pharmacotherapy than other children with a developmental disability. The pediatric medical home is an ideal setting to provide such education and reassurance that the child's primary care pediatrician will be available to work with the family to address problems as they arise.⁶⁵ It is especially helpful for the clinician to explain that the vulnerabilities of a child with ND-PAE might not be readily recognizable by others. For example, the child's good structural language skills and friendly nature can give a false impression of competence, and forgetting previously learned material might give a false impression of a defiant or oppositional disorder.⁷⁴ Additionally, the medical home provider caring for the child with ND-PAE can help explain how the needs of the child change across development and provide anticipatory care.

SUMMARY AND PEDIATRIC MEDICAL HOME PRACTICE SUGGESTIONS

The value of the medical home starts at the identification and diagnostic stage and continues through treatment planning and ongoing care. Although barriers to diagnosis and treatment remain,⁸⁵ the AAP endorses the identification, diagnosis, referral, and management of all children and adolescents with FASDs, including ND-PAE. The brain damage that is caused by prenatal alcohol exposure is permanent and irreversible, resulting in impaired neurocognitive functioning regardless of IQ; however, interventions can improve function.

Although additional taxometric research on ND-PAE is needed, an extensive scientific literature already provides support for its constellation of symptoms and criteria. Several efforts are under way to obtain appropriate taxometric data, with results forthcoming (J. Kable, PhD, personal communication, 2015); our understanding may require modification once tested in a sizable cohort of children with developmental disabilities. Children and adolescents with ND-PAE can reach their full potential with proper identification, diagnosis, and treatment if clinicians and families work as a team, especially toward early identification, treatment, and family support.^{24,73} Diagnosis and care of the patient with ND-PAE provides the child, family, and pediatric clinician with a lens through which to help that child reach his or her developmental potential. Specific points to consider are presented in Table 3.

Clinical and research evidence clearly indicates that children affected by ND-PAE and their families face substantial challenges. Although these recommendations do not represent AAP policy, early recognition in the medical home can capitalize on neural plasticity, early intervention, and ongoing support systems to maximize the developmental potential of these children. Thus the pediatric medical home plays a central role in maximizing the developmental outcomes of children with ND-PAE.

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APPENDIX: SUGGESTED SCREENING FOR PRENATAL EXPOSURE TO ALCOHOL

Maternal self-report remains the major approach for identifying alcohol consumption during

TABLE 3 ND-PAE Points for the Pediatric Medical Home

Universally screen for prenatal alcohol exposure, prenatally, in the newborn period, at the time of adoption, and for new patients; the diagnosis should be considered throughout childhood (especially at developmental transitions).

Document the presence and, if possible, the amount of prenatal alcohol exposure in the child's medical chart.

Perform frequent developmental screening with early referral to developmental specialist if concerns are identified.

Identify comorbid diagnoses to effectively manage ND-PAE or, if appropriate, identify as a comorbid diagnosis.

Treat ND-PAE as a chronic condition in a medical home.

Educate women about the risks of alcohol use during pregnancy and advise them to avoid alcohol consumption while pregnant or when conception is possible.

pregnancy, even though women might be reluctant to reveal prenatal alcohol use.⁸⁶ More accurate reports about alcohol use are elicited when screening is conducted in a nonjudgmental and nonconfrontational manner, respecting confidentiality.^{87,88} Use of alcohol by a mother during pregnancy should be assessed, avoiding questions that require “yes/no” answers (eg, “Do you drink alcohol?”). Because of the stigma associated with alcohol use during pregnancy, asking patients about prepregnancy drinking can improve accuracy of the screening. Questions about alcohol use can be imbedded in a general conversation about health behaviors during pregnancy (eg, smoking, diet, current medications). Furthermore, single binge drinking questions have been shown to be effective at identifying women at risk for alcohol use during pregnancy and are consistent with current CDC and National Institute on Alcohol Abuse and Alcoholism recommendations.⁸⁹⁻⁹¹

Based on international work that involved minimal questioning and clinical experience, the ND-PAE workgroup suggests beginning screening with an introductory statement, such as “I ask all patients standard health questions to understand factors that may affect health of their child and their health.”^{89,92} To approach the topic of alcohol and quickly determine whether prenatal exposure occurred, the following sets of questions are

suggested in the newest edition of *Bright Futures*¹⁶:

- “How often do you drink beer, wine or liquor in your household?” (Continue for any response other than “never”)
- “In the 3 months before you knew you were pregnant, how many times did you have 4 or more drinks in a day?”
- “During the pregnancy, how many times did you have 4 or more drinks in a day?”

If positive responses are given to any of the above questions, the clinician can follow up to determine frequency and extent of consumption by asking,

- “During the pregnancy, on average, how many days per week did you have a drink?”
- “During the pregnancy, on a typical day when you had an alcoholic beverage, how many drinks did you have?”

Any affirmative answer indicates maternal at-risk drinking; a brief intervention or referral is indicated. *The Bright Futures Guidelines* (4th ed) suggests that these questions be asked at the prenatal visit, at an initial postnatal well visit, for all new patients, based on clinical suspicion, and if a caregiver describes cognitive or behavioral concerns consistent with ND-PAE criteria.¹⁶ Documentation of findings is very important because not all criteria for a ND-PAE diagnosis might present in

a single visit or might have emerged at the time of screening. For example, executive function deficits often do not become apparent until school age, but documentation of prenatal exposure to alcohol would put those deficits in the proper context.

One concern expressed by some clinicians is that obtaining exposure information will trigger scrutiny by child welfare agencies. The Child Abuse Prevention and Treatment Act does *not* require clinicians to report to Child Protective Services if a child has been prenatally exposed to alcohol. Referral to Child Protective Services is required if the child has been diagnosed with an FASD in the period between birth and 3 years. The intent of this referral is to develop safe care and possible treatment plans if needed, not to initiate punitive actions.^{93,94}

Although discussing prenatal alcohol exposure with patients might be a challenge, and some providers express discomfort about discussing alcohol use with their patients, it is an important component of both prenatal and postnatal care and is necessary for diagnosing FASDs.⁹⁵

ABBREVIATIONS

AAP:	American Academy of Pediatrics
ADHD:	attention-deficit/hyperactivity disorder
CDC:	Centers for Disease Control and Prevention
DSM-5:	<i>Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition</i>
FAS:	fetal alcohol syndrome
FASDs:	fetal alcohol spectrum disorders
ND-PAE:	neurobehavioral disorder associated with prenatal alcohol exposure
pFAS:	partial fetal alcohol syndrome
PTSD:	posttraumatic stress disorder

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