Developmental and Behavioral Pediatrics Section

Autism Spectrum Disorder : Part 1

WHEC Practice Bulletin and Clinical Management Guidelines for healthcare providers. Educational grant provided by Women's Health and Education Center (WHEC).

In 1911, Swiss psychiatrist Paul Eugen Bleuler coined the German term *Autismus* to characterize the social withdrawal, he observed in people with schizophrenia. Rendered in English as *autism*, the term derives from the Greek word *autos* ("self"). Scholars have credited Grunya Sukhareva with making observations that, closely mirror Autism Spectrum Disorder (ASD), as described by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) and *International Classification of Disease* eleventh revision (ICD-11). Her work expanded on the definition throughout her career while making great strides in differentiating ASD and schizophrenia nearly 30 years, before the establishment of separate classifications of these diagnoses, with the publication of the DSM-III. Autism occurs in every country and demographic group. Most professionals believe that race, ethnicity, and socioeconomic background have limited effect on the occurrence of autism. The Centers for Disease Control's Autism and Development Disabilities Monitoring Network, reported that approximately 1 in 31 children in the United States (US) is diagnosed with autism, based on data collected in 2022.[1] For 2016 data, the estimate was 1 in 54, compared to 1 in 68 in 2010 and 1 in 150 in 2000. Diagnostic criteria for autism have changed significantly since the 1980s; for example U.S. special-education autism classification was introduced in 1994.[2] The World Health Organization (WHO) estimates that about 1 in 100 children were autistic between 2012 and 2021 with a trend of increasing prevalence over time. This may reflect an underestimate of prevalence in low- and middle-income countries.[3]

The purpose of this document / series, is to review the literature and discuss what the research say. Autism Spectrum Disorder (ASD) is a single disorder described in the recently released 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The diagnostic category no longer includes separate diagnoses for Asperger's Syndrome and Pervasive Developmental Disorder – Not Otherwise Specified. The DSM-5 also includes a related, but distinct, diagnostic category of Social Communication Disorder.

What is Autism?

Autism is a complex neurobehavioral disorder characterized by impairment in reciprocal social interaction, impairment in communication, and the presence of repetitive and stereotypic patterns of behaviors, interests and activities. The onset of symptoms is typically before the age of 3 years. The severity of impairment in the given domains as well as the pattern of impairments varies from individual to individual; that is why diagnosticians refer to a "spectrum" of disability.

Impairment in social interaction ranges from difficulty initiating and maintaining interaction, impaired ability to recognize and experience emotions, and difficulty processing and appreciating the thoughts and feelings of others. Communication deficits range from no useful form of communication to very advanced language abilities, but little ability to use language in a social manner. Repetitive and stereotypic behaviors include adapting to change and transition, and unusual movements such as hand flapping and whirling.

Diagnosis of Autism

Research indicates that early diagnosis is critically important. Therefore, parents and caregivers should be aware of some of the earliest signs of autism. Behaviors of concerns include:

- Regression (loss of) of previously achieved language milestones, including babbling;
- Lack of pretend play, or even imitative play, such as babbling on a toy telephone;
- Lack of pointing or looking toward where another points;
- Lack of response to one's name, or decreasing response to name; and
- Lack of pointing to indicate needs and lack of response to pointing behavior of others.

Once a suspicion is raised, the diagnosis is dependent on further assessment by an individual or team specializing in the diagnosis and treatment of Autism Spectrum Disorder (ASD). There is no single test that is diagnostic of autism. In order to have a diagnosis of Autism, an individual must satisfy the diagnostic criteria in the DSM-5. Historically, the basic triad of impairments underlying Autism has included:[4]

- Impairment of social interaction,
- Impairment of communication, and
- Restricted repetitive and stereotyped patterns of behavior.

Although the definition of Autism, as a neurodevelopmental disorder, has certainly evolved, studies predict a large change in prevalence rates from DSM-4 to DSM-5, should not be unexpected.[5] According to the Center for Disease Control and Prevention (CDC) key points for screening for ASD are:[6]

- Diagnosing ASD can be difficult because there is no medical test, such as a blood test, to diagnose the disorder. Healthcare professionals look at child's developmental history and behavior to make a diagnosis.
- Diagnosing ASD involves several steps
- Some people with ASD are not diagnosed until they are adolescents or adults. This delay means that they might not get the early help they need.

Severity rating reflects the impairment of the ASD symptoms and the resultant service needs of the individual. Severity rating is not a quantifiable score that can be used to monitor progress at this time; in clinical use, it often reflects the impact of cognitive limitations.[7] Measures have been published that attempt to capture severity of the core symptoms and allow for measurement of improvement with intervention. To date, no single measure adequately reflects the combination of medical, behavioral, and educational severity in a fashion that will help clinicians

and families determine progress with intervention across multiple functional domains. Co-existing medical disorders also affect the perception of severity and the prognosis for children with a diagnosis of ASD.

Autism Spectrum Disorder (ASD) Symptoms by Level of Severity

Severity Level	**Social Affective**		**Restricted and Repetitive Behaviors**
Level 1. "Requiring support"	Without support in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to social overtures of others. May appear to have decreased interest in social interactions.		Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.
Level 2. "Requiring substantial support"	Marked deficits in verbal and non-verbal social communication skills. Social impairments apparent even with support in place. Limited initiation of social interactions and reduced or abnormal responses to social overtures from others.		Inflexibility of behavior, difficulty coping with change, or other restricted and 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 3. "Requiring very substantial support"	Severe deficits in verbal and non-verbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others.		Inflexibility of behavior, extreme difficulty coping with change, or other restricted and repetitive behaviors markedly interfere with functioning in all spheres. Great distress and/or difficulty with changing focus or action.

Table 1. ASD (Autism Spectrum Disorder) severity levels. Source: DSM-5. (*Diagnostic and Statistical Manual of Mental Disorders, fifth edition).*American Psychiatric Association, 2013.

Patients with Rett Syndrome are no longer automatically considered to have a diagnosis of ASD according to DSM-5, although individuals with this neurogenic disorder may also meet diagnostic criteria for ASD. Specific genetic causes of ASD should be recorded as specifiers for individuals with ASD when identified. The DSM-5 promotes notation of all coexisting diagnoses as specifiers.

Social Pragmatic Communication Disorder

Social pragmatic communication disorder is a new diagnosis described within the DSM-5 that describes individuals who exhibit functionally impairing symptoms in social language use, but do not have habitual or repetitive behaviors.[4,8] Individuals who are affected must have deficits in using language for social purposes, impaired ability to match their communication style with the context for communication, difficulty following the conventional rules for conversation, and difficulty with idioms and unstated meaning in language. ASD and social communication disorder are similar and different in terms of etiology, prognosis, and treatment. Evaluation of pragmatic (social) language use by a speech-language pathologist provides additional information to consider this diagnosis.[9]

DSM-5 Social (Pragmatic Communication Disorder (DSM-5 315.39)

A. Persistent difficulties in the social use of verbal and non-verbal communication as manifested by all of the following:
    1. Deficits in using communication for social purposes, such as getting 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 the 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 sue verbal and non-verbal 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 attributed to another medical or neurological condition or to low abilities in the domains or word structure and grammar and are not better explained by ASD, intellectual disability (intellectual developmental disorders), global developmental delay, or another mental disorder.

Co-occurring Symptoms and Conditions

Co-occurring conditions are common in children with ASD and may have great effects on child and family functioning and clinical management. Examples include medical conditions such as sleep disorders and seizures; other developmental or behavioral diagnoses, such as attention-deficit/hyperactivity disorder (ADHD), anxiety, and mood disorders; and behavioral disorders, such as food refusal, self-injury , and aggression.[10] Approximately 30% of children with a diagnosis of ASD will also have intellectual disability, and 30% are minimally verbal.[11] Increasingly, researchers and clinicians recognize how co-occurring disorders help identify phenotypic differences within populations affected by ASD, which can influence prognosis and choice of interventions.

Screening and Diagnosis (Red Flags: Early Symptoms of ASD)

The American Academy of Pediatrics (AAP) recommends screening all children for symptoms of ASD through a combination of developmental surveillance at all levels and standardized autism-specific screening tests at 18 and 24 months of age in their primary care visits, because children with ASD can be identified as toddlers, and early intervention can and does influence outcomes.[12] This autism-specific screening complements the recommended general developmental screening at 9, 18, and 30 months of age. Some of these early symptoms that may alert the provider to the risk of ASD or "red flags."

Age	Symptom
By 12 months	Does not respond to name.
By 14 months	Does not point at objects to show interest.
By 18 months	Does not pretend play.
General	• Avoids eye contact and may want to be alone. • Has trouble understanding other people's feelings or talking about their own feelings. • Has delayed speech and language skills. • Repeats words or phrases over and over (echolalia). • Gives unrelated answers to questions. • Gets upset by minor changes. • Has obsessive interests. • Makes repetitive movements like flapping hands, rocking, or spinning in circles. • Has unusual reactions to the way things sound, smell, taste, look or feel.

Table 2. Red Flags – Early symptoms of Autism Spectrum Disorder (ASD)

Some of the signs of ASD may be noticed before the age of 1, although a reliable diagnosis by an autism specialist can be made in children as young as 18 months of age. Children who have less severe ASD, or are from minority backgrounds, tend to be diagnosed later than those with severe symptoms. There is no single scan or blood test that can independently diagnosed autism.

Autism Navigator might be helpful available @
https://navigatorcommunity.info/Early_Signs_of_Autism_Poster.pdf

Diagnostic Evaluation

Once a child is determined to be at risk for a diagnosis of ASD, either by screening or surveillance, a timely referral for clinical diagnostic evaluation and early intervention or school services, depending on his or her age, is indicated. Although most children will need to see a specialist, such as a developmental-behavioral or neurodevelopmental pediatrician, psychologist, neurologist, or psychiatrist, for a diagnostic evaluation, general pediatrician and child psychologists comfortable with application of the DSM-5 criteria can make an initial diagnosis. At this time, there are no laboratory tests that can be used to make a diagnosis of ASD, so careful review of child's behavioral history and direct observation of symptoms are necessary.[14] In the United States, early intervention services and school systems will evaluate children in these domains to assess educational needs. In some areas, initial evaluations are performed in clinical settings and paid for by insurance.

Cognitive Testing: A range of standardized measures are used to determine developmental levels of younger children and IQ (intelligent quotient) in children older than 3 years. The IQ test selected by the psychologist will depend on the age and language level of the child. Administration of a valid cognitive test is important in ascribing symptoms of ASD as part of the initial diagnosis but also helps to establish co-occurring diagnosis with ASD, such as intellectual disability.[15]

Language Testing: Inherent in the core symptoms of ASD are differences in the use of verbal and non-verbal communication for social interaction. Documentation of expressive and receptive language skills as well as the pragmatic or conversational use of language should be formally assessed.[16]

Adaptive Function Testing: Determining the extent that ASD affects daily functions is necessary to establish eligibility for some publicly funded programs as well as identify and monitor developmental goals for treatment. Adaptive behaviors are typically delayed in people who have intellectual disability with ASD but can be impaired in people with ASD and an average-range IQ. Commonly used adaptive measures include the Vineland Adaptive Behavior Scales and the Adaptive Behavior Assessment System.[17]

Motor Assessment: Children with ASD are more likely to have mild delays in gross motor skills and coordination compared with children in the general population and may meet DSM-5 criteria for developmental coordination disorder in addition of ASD.[18] A relationship of early motor delays and subsequent language and adaptive development in children with ASD has been proposed.

Sensory Assessment: Hearing – Children with language delay or inattention to language should have an evaluation of their hearing as part of their initial assessment. Hearing loss may co-occur with ASD and needs to be considered in children with language delays, behavior problems, or inattention.[19]

Sensory Assessment: Vision – Visual function should be considered in the initial evaluation of children who are visually inattentive, have stereotypical (such as eye poking or close visual scrutiny), or do not make eye contact. Decreased visual acuity may affect interactive gaze and require accommodations in the educational setting.[20] Children with visual impairment may also demonstrate stereotyped motor behaviors.

Sensory Assessment: Sensory Processing – The DSM-5 does not include sensory processing disorder as a discrete diagnosis. Commonly used evaluation tools (such as the Short Sensory Profile and others) quantify parent perception of sensory differences relative to smell, taste, vision, hearing, and touch.[21] In addition, to capturing what is conventionally considered as a sensory disturbance, questionnaires that are used to assess sensory symptoms also capture motor hyperactivity as sensory seeking or sensory-avoiding behaviors.

Etiologic Evaluation

Children with a diagnosis of ASD should be assessed for potential etiology and common co-existing medical conditions. Suggested medical work-up of the child with ASD are:

Genetic Testing – Advances such as the development of chromosomal microarray (CMA) and next-generation sequencing technologies and the application of these technologies to well-characterized patient cohorts have led to progress in the understanding of the complex genetics of ASD and other neurodevelopmental disorders in the last decade. Identifying a genetic etiology provides clinicians with more information for families about prognosis and recurrence risk and may help to identify and treat or prevent co-occurring medical conditions, guide patients and families to condition-specific resources and support, and avoid ordering unnecessary tests. As research progresses, genetic testing my contribute to identifying effective interventions related to specific etiologies.

Potential benefits of establishing a genetic etiologic diagnosis are:[22]

I. Improving accuracy of counseling provided to patients and families:
    1. Prognosis or expected clinical course;
    2. Recurrence risk for the family and the individual affected.

II. Providing condition-specific family support, such as:
    1. Improving psychosocial outcomes for patients and their families (e.g., knowledge and sense of empowerment, parental quality of life).

III. Preventing morbidity and treating medical-conditions associated with genotype, i.e.:
    1. Conditions or anomalies likely to be present at diagnosis.
    2. Conditions that may develop later.

IV. Refining treatment options, including:
    1. Avoiding therapeutic-interventions based on unfounded etiologic-theories.
    2. Avoiding ineffective or potentially harmful treatments.
    3. Providing access to emerging etiology-specific treatments.

V. Facilitating acquisition of needed services and access to research treatment protocols.
VI. Avoiding additional diagnostic tests, which may be unnecessary, expensive, and/or uncomfortable.

The current estimate is that approximately 0.45% of individuals with ASD have the full mutation for fragile X syndrome, and many of them are female.[23] Because fragile X syndrome testing is relatively inexpensive and the condition has important genetic counseling implications, it is reasonable to consider testing both male and female patients with ASD, at least until more data become available to clarify the issue. When the history and physical examination, CMA, and fragile X analysis do not identify an etiology, the next step at this time in the etiologic evaluation for ASD is whole-exome sequencing (WES). WES technology allows for the identification of single-nucleotide variants, including pathogenic loss-of-function mutations and missense mutations, which have been found to be associated with ASD.[24]

Parents of a child with ASD should be counseled regarding recurrence risk in subsequent offspring, and the nature of the counseling depends greatly on whether a specific genetic cause of the child's ASD has been identified. For a couple with 1 child with ASD of unknown cause, the current best estimate of recurrence in a subsequent child is approximately 10% (range 4% to 14%).[25] If a couple already has >2 children with ASD of unknown etiology (idiopathic), the chance of a subsequent child having ASD may be as high as 32% to 36%.[25] However, the risk is not limited to ASD. Siblings of children with ASD who do not have ASD themselves may have a 20% to 25% risk for language disorders, and other neurodevelopmental- and psychiatric-disorders.

Neuroimaging – Specific clinical neuroimaging findings are not more prevalent in ASD compared with other neuro-developmental disorders, not do specific abnormalities correlate with clinical, etiologic or pathophysiological aspects of ASD.[26] Incidental findings are common, but rarely provide etiologic information or require intervention. MRI (magnetic resonance imaging) may be indicated in the evaluation of atypical regression, microcephaly, seizures, intracranial manifestations of genetic disorders, abnormal neurologic examination, or other clinical indications.

Metabolic Testing – The yield of routine metabolic testing for children with ASD is low and not recommended for regular use. Metabolic workup should be informed by history, family history, symptoms and examination and might include measurement of fasting plasma amino acid levels, urine organic acid levels, and acylcarnitine metabolite levels and other testing for specific metabolic disorders. Children who present with motor delay should be evaluated with creatine kinase and thyroid-stimulating hormone testing, according to AAP recommendations.[27] There is no evidence at this time for routine testing of hair, blood, or urine for environmental toxins or heavy metals outside of laboratory screening for lead exposure.

EEG (electroencephalogram) – Children with ASD have an increased risk for seizures, and EEG abnormalities are common in the absence of clinical seizures.[28] However, EEG is not recommended as a routine baseline evaluation in the absence of clinical concern about seizures, atypical regression, or other neurologic symptoms on history or examination that would suggest

EEG is indicated. Late or atypical loss of language, as might be observed in electrical status epilepticus of sleep with loss of language, should be evaluated with an overnight EEG.

The Biology of Autism Spectrum Disorder (ASD)

ASD is clinically and etiologically heterogenous yet highly heritable. The rate of ASD in siblings is much higher than the rate in the general population. Risk for ASD also is increased in the children of both older fathers and mothers.[29] Important aspects of the genetics of ASD are still poorly understood, including the role of common variants, epistasis (gene-gene interactions), and environmental modification of genotype effects. It is important to note that no specific mutation has been identified that is unique to ASD; there is substantial genetic overlap between ASD and other neurodevelopmental disorders, including intellectual disability, epilepsy and schizophrenia.

Environmental Exposures, Genetics and ASD – The potential environmental factors that may be related to increased reported prevalence of ASD is an area of active study, that as yet, is without firm conclusions. Environmental factors associated with ASD include in-utero exposure to medications such as valproate and thalidomide. It is prudent to limit exposure of children and pregnant women to known neurotoxicants.

Immunologic Exposures, Genes and ASD – It has been proposed that children with ASD-associated copy number variants (CNVs) may be more susceptible to environmental insult in the form of maternal immune activation. Unless otherwise indicated (e.g., history suggestive of autoimmune or immunologic disorder), no immune testing is recommended in the etiologic work up of a child with ASD.

Epigenetics – Epigenetics modifications, such as DNA methylation and post-translational histone modification, produce heritable changes in gene expression that do not involve a change in the DNA sequence. Some genetic disorders with ASD (e.g., Rett syndrome; CHARGE syndrome [coloboma, heart disease, choanal atresia, retarded-growth development – due to a novel mutation in the *CHD7* gene], 15_q duplication; Angelman syndrome, and fragile X syndrome), involve genes that either encode epigenetic regulators or are sensitive to alterations in their epigenetic regulation.[30]

Vaccines – **The scientific literature does not support an association vaccination as a factor that increases the risk of ASD.** Children with ASD should be vaccinated according to the recommended schedule. Vaccines used for children in the United States have not contained thimerosal since 2001. The overwhelming weight of evidence supports vaccine safety. Communicating information about vaccine safety is a critical component of pediatric practice.

Neuropathology – No uniform neuropathology has been identified in people with ASD. MRI have highlighted a few brain regions that are structurally distinct in people with autism. **Hippocampus**: children and adolescents with autism often have an enlarged hippocampus, the area of brain responsible for forming and storing memories. **Amygdala:** the size of amygdala also seem to differ between people with and without autism, although researchers from different labs have turned up conflicting results. Some find that with autism have smaller amygdalae than people without autism, or that their amygdalae are only smaller if they also have anxiety. Others

have found that autistic children have enlarged amygdalae early in development and that the difference levels off over time.[31] **Cerebellum:** Autistic people have decreased amounts of brain tissue in the parts of cerebellum, the brain structure at the base of the skull, according to a meta-analysis of 17 imaging studies.[32] Scientists long thought the cerebellum mostly coordinates movement, but it is now believed it plays a role in cognition and social interaction as well.

Corpus callosum: People who lack all or part of one white matter tract called the corpus callosum, which connects the brain's two hemispheres, have and increased likelihood of being autistic or having traits of the condition.[33] The corpus callosum contains many of the long-range connections that extend throughout the brain; the fact that disrupting those connections may lead to autism traits supports the connectivity theory of autism.

There may be epigenetic effects, environmental influences, and other factors that contribute to the mechanisms and affected neural pathway(s). The underlying neuropathology of the disorder has been evolving in the literature to include specific brain areas in the cerebellum, limbic system, and cortex. Genetic testing can be a powerful diagnostic and predictive tool that can help people understand more about the biological basis of a health condition they may already have or may be at an increased risk to develop in the future.

Part(s) of structures appear to be affected most rather than the entire structure, for example, select nuclei of the amygdala, the fusiform face area, and so forth. Altered cortical organization characterized by more frequent and narrower minicolumns and early overgrowth of the frontal portion of the brain, affects connectivity. Abnormalities include cytoarchitectonic laminar differences, excess white matter neurons, decreased numbers of GABAergic cerebellar Purkinje cells, and other events that can be traced developmentally and cause anomalies in circuitry.[33]

Biomarkers

Objectively measured biological characteristics, or biomarkers, of ASD could potentially be used to predict ASD risk, enhance screening, and permit presymptomatic detection. Their use could improve the reliability and validity of clinical diagnosis (identifying clinically meaningful subgroups that would allow for prediction of prognosis or treatment responses), identifying mechanisms for developing treatment, and confirm the need for a specific intervention.[34]

Early Brain Growth: an accelerated brain growth before 2 years of age, leads to significantly above-average health circumferences and MRI brain volumes in toddlers, followed by a plateau in brain growth, with brain volumes in adolescence and adulthood similar to those of controls. Almost 16% of young children with ASD have a head circumference greater than the 97th percentile. A preliminary study suggested that infant siblings of children with ASD who exhibited a larger head circumference at 12 to 24 months had an increased chance of demonstrating symptoms of ASD.[35] It is possible that a large head size is unrelated to ASD and/or may be part of general somatic overgrowth.

Neuroimaging Patterns Associated with ASD in Research Studies: Diffusion tensor imaging has been used to identify altered patterns in white patterns in white matter by 6 months of age in infants later diagnosed with ASD. Functional MRI has demonstrated differences in people with

ASD relative to controls in efficiency of visual processing, executive function, language, and basic and complex social processing skills.[36] In research this settings demonstrate differences in the mechanisms of attention to social stimuli, modulation in response to task demands or intensity of stimuli, and executive function in people with ASD. Functional underconnectivity has also been demonstrated across a wide variety of the brain regions that support language, executive function, social cognition, emotion processing, and motor tasks, especially for long-range, frontal-posterior networks.

Electrophysiologic Testing and Measurement of Eye Tracking: Continuous measures of resting-state and task-related quantitative EEG are used to calculate and describe spectral power, complexity, and coherence. Although promising, the clinical utility of these measure as biomarkers requires additional studies.[35,36] Eye tracking has been used to determine if infants who are younger siblings of children with ASD, and therefore at increased risk for ASD exhibit differences in fixation on faces. Preliminary evidence suggests that infants later diagnosed with ASD exhibit a decline in gaze fixation from age 2 to age 6 months.

Other Potential Biomarkers: Although some studies have attempted to differentiate people with ASD and without ASD on the basis of differences in laboratory profiles of platelet serotonin, plasma melatonin, urine melatonin sulfate, redox status, placental trophoblast inclusions, and immune function, currently no diagnostic laboratory tests have been approved for ASD. To date, none of these potential biomarkers under study has sufficient evidence to be recommended.

Future Directions of Biomarkers: The search for biomarkers is a major research focus. Biomarker research has important ethical issues, and concerns have appropriately been raised regarding premature translation of research data into commercially available tests marked to patients and families. However, the capabilities to screen large numbers of bioactive compounds, examine the entire genome, and simultaneously analyze large data sets have accelerated into the neurobiology of ASD and may result in the identification of valid biomarker.

Prognosis

The prognosis and trajectory of development for a young child diagnosed with ASD typically cannot be predicted at the time of diagnosis.[33] However, most children with ASD (>80%) who are diagnosed with ASD after comprehensive evaluation at less than 3 years have retained their diagnosis. It may be more difficult to recognize mild symptoms of ASD in children younger than 3 years of age, especially if they have average or above-average cognitive abilities. Across early childhood development, communication skills and social affective symptoms may improve, whereas repetitive behaviors may change, possibly reflecting maturation and/or intervention. In general, young children with ASD with language impairment appear to have more social difficulty than do children with ASD with language impairment. Children with ASD and intellectual disability have the most difficulty developing social competence.

Approximately 9% of children who are diagnosed with ASD in early childhood may not meet diagnostic criteria for ASD by young adulthood. Severity scores are most likely to improve in youth who have had the greatest increase in tested verbal IQ.[37] Measured IQ and language ability

in childhood tend to predict outcome in adulthood. However, reported quality of life in high-functioning adults with ASD was associated more with the presence of family and community support than their symptoms related to ASD.

Interventions

The goals of treatment of children with ASD are:

1. Minimize core deficits (social communication and interaction and restricted or repetitive behaviors and interest), and co-occurring associated impairments;
2. Maximize functional independence by facilitating learning and acquisition or adaptive skills; and
3. Eliminate, minimize, and prevent problem behaviors that may interfere with functional skills.

Treatments should be individualized, developmentally appropriate, and intensive, with performance data relevant to treatment goals to evaluate and adjust interventions. All interventions should be based on sound theoretical constructs, rigorous methodologies, and objective scientific evidence of effectiveness. Early intervention services under part C of IDEA (Individuals with Disabilities Education Improvement Act of 2004) provides for assessment and intervention for children younger than 3 years with developmental delays, including ASD. Advocacy is often necessary to obtain desired services through schools or through mechanisms paid for by insurance. It is noted that many of the interventions in common use do not have a strong evidence base. Some types of intervention may not be paid for by insurance.

Two common theoretical approaches to intervention for symptoms of ASD are: applied behavior analysis (ABA) and developmental models. There is considerable regional variation in the availability of various interventions. Characteristics of effective interventions are:[38]

I. Assessment and Goals

1. Systematically assess skills;
2. Include input of family (shared decision-making);
3. Select individualized measurable goals and instructional procedures on the basis of objective assessment of each child;
4. Use assessment-based, empirically supported instructional methods to build, generalize, and maintain skills and reduce problem behaviors.

II. Instructional Methods

1. Address core symptoms in social communication and restricted and repetitive behaviors as well as skill deficits;
2. Provide a student / teacher ratio low enough to address the child's individualized goals;
3. Interventions should be by providers who are properly trained and should maintain fidelity with the treatment approach selected;
4. Ensure that multiple providers work collaboratively.

III. Services and Supports

1. Individualize services and support;
2. Make use of the child's interests and preferences in determining reinforcement systems;
3. Incorporate preferred activities to increase engagement in activities.

IV. Environment

1. Provide a structured learning environment that helps children anticipate transition between activities, including a predictable routine and visual activity schedules;
2. Organize workspaces to minimize distraction and promote task completion;
3. Limit access to things that may distract a student;
4. The environment should promote opportunities for the student to initiate communication and interact with peers.

V. Behavioral Management

1. Implement a functional behavioral analysis to identify the reasons why challenging behaviors occur and develop a behavior improvement plan based on this assessment (IDEA-mandated approach);[39]
2. Instruct children more appropriate responses using the behavior improvement plan.

VI. Progress

1. Systematically measure and document the individual child's progress;
2. Adjust instructional strategies as necessary to enable acquisition of target skills;

VII. Family Support

1. Involve and educate families so they can use the behavioral strategies at home and in the community.

VIII. Transition Planning

Plan for transitions in school settings and to adulthood (e.g., from home-based early intervention to preschool services, preschool to elementary school, elementary school to middle school to high school, high school to work or post-secondary education, and home to community living).[40]

Suggested Areas for Future Research, Funding and Collaboration

The Women's Health and Education Center (WHEC) recommends these 7 areas of research, funding and collaborations:

1. Early detection;
2. Underlying biology;
3. Genetic and environmental risk factors;
4. Treatments and interventions;
5. Services and implementation science;
6. Life-span services and supports, and

7. Epidemiological surveillance and infrastructure.

It is important that multiple levels of inquiry be pursued simultaneously to inform evidence-based clinical care, such as: basic and translational services, clinical trials, epidemiological surveillance to gather data important for planning for current and future needs. Health services research should provide guidance for comprehensive, accessible and culturally appropriate medical, educational, and behavioral care for children, youth, adults and families affected by ASD.

Summary

Key Facts:[41]

- Autism – also referred to as autism spectrum disorder – constitutes a diverse group related to development of the brain.
- In 2021 about 1 in 127 persons had autism.
- Characteristics may be detected in early childhood, but autism is often not diagnosed until much later.
- The abilities and needs of autistic people vary and can evolve over time. While some people with autism can live independently, others have severe disabilities and require life-long care and support.
- Evidence-based psychosocial interventions can improve communication and social skills, with a positive impact on the well-being and quality of life of both autistic people and their caregivers.
- Care for people with autism needs to be accompanied by actions at community and societal levels

Autism spectrum disorder (ASD) is a common neurodevelopmental disorder with reported prevalence and significantly influences the lives of affected children and families because they need extensive behavioral, educational, health and other services. Primary care providers play a critical role in identifying, diagnosing, and managing ASD in children and providing support for their families. ASD is more commonly diagnosed than in the past, and the significant health, educational, and social needs of individuals with ASD and their families constitute an area of critical need for resources, research, and professional education. Timely diagnosis, early identification, evidence-based intervention and training caregivers are helpful steps to ensure satisfactory outcomes. It is recommended for children with ASD. Stakeholders include families and affected individuals, scientists, clinicians, and public health agencies.

Approaches to Intervention; Educational Interventions; Medical Interventions; Psychopharmacology Approaches to Management; Other Interventions and Future Areas of Research, are discussed in Autism Spectrum Disorder – Part 2.

Suggested Reading

1. American Academy of Pediatrics (AAP)
   Autism Toolkit

https://publications.aap.org/toolkits/pages/Autism-Toolkit

2. Centers for Disease Control and Prevention (CDC)
   Myths vs. Facts: Developmental Screening
   https://www.cdc.gov/autism/hcp/diagnosis/myth-busters.html

3. American Psychiatric Association (APA)
   Frequently Asked Q & A: Autism Spectrum Disorder
   https://www.psychiatry.org/patients-families/autism/what-is-autism-spectrum-disorder

4. World Health Organization (WHO)
   Global Report on Children with Developmental Disabilities
   https://www.who.int/publications/i/item/9789240080232

5. (U.S.) Individuals with Disabilities Education Improvement Act of 2004 (IDEA)
   Public Law 108-446 and No Child Left Behind Act of 2001
   Every Student Succeeds Act of 2015
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