Autism Spectrum Disorder

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10.1 Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder, resulting from neurogenetic complex pathology that leads to significant developmental delays. Social communication impairment and stereotypic restrictive behaviors are the main symptoms. It ranges from severe form with children needing very substantial help for daily living to milder degree of impairments.

The word autism comes from the Greek word "autos," meaning "self." The term describes conditions in which a person is removed from social interaction, hence an isolated self. Leo Kanner, 1943, a doctor from Johns Hopkins University, used the term to describe the withdrawn behavior of several children he studied, which became the first description of cohort of cases with similar clinical presentation. "Infantile autism" was listed in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) for the first time in 1980; the condition was also officially separated from childhood schizophrenia. ASD was classified under a pervasive developmental disorders (autism, childhood disintegrative disorder, Rett syndrome, pervasive developmental disorder—not otherwise specified, and Asperger disorder), which has been changed in DSM-5.

Autism affects core areas of development, namely social skills, communication abilities, and behaviors of interest. Its first signs are usually observed in infancy. Although there may be warning signs before 1 year of age, most educated and attentive parents will first notice the delay or loss of any one of these skills by 15–18 months of age. No visible physical stigmata are present in autism, except if it is associated with some chromosome abnormality, like fragile X syndrome or

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tuberous sclerosis, where many abnormalities of the central and peripheral systems are present. It is estimated that 10–15% of known abnormal chromosomal conditions will have autism phenotype. In autism, intelligence may be within normal range in 50% of the cases. Regression of skills is an important characteristic of ASD; attribution of regression to environmental stressors, such as the birth of a new sibling, may delay the diagnosis of autism. Assessment of autism is clinical, and no laboratory or radiology investigations are required for diagnosis. Yet chromosomal analysis and metabolic screen may be done if clinically indicated; at the same time, all children suspected to have autism must have an objective hearing assessment [1].

10.2 Prevalence

There is a global increase in ASD prevalence, with variable case recognition; it is estimated that the overall prevalence is 1–2.4% of the population. Prevalence in the United States is estimated at 1 in 68 in children at the age of 8 years old, with an increase of 119.4% from 2000 (1 in 150) to 2010 (1 in 68) and by 137% by 2012; it has increased by 6–15% each year from 2002 to 2010. Autism is the fastest-growing developmental disability ever. This exceptional increase in prevalence has no obvious or known reason yet. ASD is four times more common in males than females and tends to be more severe in girls [2].

10.3 Risk Factors

Although knowledge is limited about the facts of ASD epidemiology, risks are based on statistical analysis and observational studies [3–5]. Table 10.1 highlights some risk factors and their significance.

10.4 Comorbid Conditions

ASD is associated with many conditions that may contribute to its morbidity and course; intellectual disability (ID) exists in around 47–75%, with varying degrees, but mostly mild ID. Seizures are found in 11–39% of cases, with increasing risk in individuals with severe intellectual disability. Less than 10–25% of cases of ASD are associated with a medical condition or known syndrome (e.g., phenylketonuria, fragile X syndrome). Children with tuberous sclerosis will manifest autism features in 17–60% of the cases, while only 0.4–4% of patients with ASD have tuberous sclerosis. Patients with comorbid tuberous sclerosis and ASD often have epilepsy [6].

10.5 Associated Behaviors

ASD is associated with many challenging behaviors that may not be consistently present in all individuals, and although some of these behaviors are easy to manage and dealt with, others may be severe and affect the prognosis negatively;

Table 10.1 Autism risk factors

Factors	Risk for autism
Twins	Concordance rate: Identical twins: 36–95% Non-identical twins: 0–3% "Since concordance is not 100% in identical twins, it signifies an environmental influences"
Parents who have a child with ASD	2–18% Risk multiplies as more children are born with ASD
People who have certain genetic or chromosomal conditions	10–15% Known genetic conditions present with ASD phenotype
Intellectual ability	46% Higher risk for autism phenotype
Age of parent	Older parents Autism rates were 66% higher in children of fathers over 50 than in those fathering children in their 20s and 28% higher if they were in their 40s
Preterm born or low birth weight	20–30% greater risk Screening of premature babies for ASD is critical
Comorbidities	Co-occurrence with developmental conditions: 83% Co-occurrence with psychiatric conditions: 10% People with developmental and psychiatric conditions may manifest typical features of ASD

disruption and aggression may be seen in 15–64% of children or adolescents, and if severe, it will cause significant family dysfunction, impair regular intervention programs, and need a comprehensive team approaches to manage. Self-injurious behaviors are seen in 8–38%, and usually they may be means of communication in nonverbal children or attention-seeking behaviors, and careful approach is essential to establish cause and manage accordingly. Eating disorders, 25–50%, are common in children with ASD and may lead to nutritional deficiencies and parent frustrations. Sleep disturbances are seen in around 36% of children with ASD and my lead to disturbance in family routines and difficulties in educational programs [7].

10.6 Etiology

ASD has no known direct cause till now, and although many theories have been implicated, it is believed that it has strong genetic background. The following are some potential causes:

1. **Genetic factors**: More than 100 genes on different chromosomes may be involved in causing ASD to different degrees. ASD genetic causation is derived from unequal sex distribution 4:1 male predominance, high concordance rate among monozygotic twins, and relatedness 3% for cousins, 7% for paternal half siblings, 9% for maternal half siblings, 13% for full siblings and dizygotic twins, and 59% for monozygotic twins [3–5, 8].

2. **Neurobiological factors**: Neuroimaging and autopsy studies in patients with ASD suggest that brain abnormalities play an important role. These abnormalities include:
   (a) Diffuse differences in total and regional gray and white matter volumes, sulcal and gyral anatomy, brain chemical concentrations, neural networks, cortical structure and organization, brain lateralization, and cognitive processing compared with individuals without ASD.
   (b) Patients with ASD have accelerated head growth during infancy and increased overall brain size (by 2–10%), perhaps related to an increased number of neurons in the prefrontal cortex.
   (c) Functional MRI studies indicate that individuals with ASD use different patterns of connectivity, cognitive strategies, and brain areas to process information during tasks requiring social attribution or response to visual or auditory stimuli.
   (d) Positron emission tomography studies have shown that children with ASD have global and functional abnormalities in serotonin synthesis.
   (e) Brain electrophysiology studies indicate that individuals with ASD process information regarding faces differently and appear to have marked delay in the neural system processing eye gaze.
   (f) Individuals with ASD appear to have neural-based deficits in recognizing and understanding speech and attending to socially relevant sounds.
   (g) Neuropathologic studies demonstrate decreased numbers of Purkinje cells in the cerebellum (which modulates a variety of brain functions and impacts language processing, anticipatory and motor planning, mental imagery, and timed sequencing) and abnormal structure and organization in the prefrontal and temporal cortex (areas that mediate social, emotional, communication, and language). The cortical abnormalities appear to result from dysregulation of cortical layer formation and layer-specific neuronal differentiation during prenatal development.
3. **Environmental and perinatal factor**: Toxic exposures, teratogens, perinatal insults, and prenatal infections are implicated as potential causation factors. The effects of environmental exposures appear to depend on the timing and duration of exposure, concentration of the toxin, mechanism of action, and distribution in the central nervous system, yet none has been proven to be a direct cause of autism.

10.7 Symptoms and Signs

Children with ASD have abnormalities in social communication/interaction and restricted, repetitive patterns of behavior, interests, or activities. The clinical features are similar, whether the child is diagnosed with autism spectrum disorder using DSM-5 or a specific type of pervasive developmental disorder using ICD-10. One critical difference is that the ICD-10 requires symptoms to have onset before

age 3 years, whereas DSM-5 does not include an age cutoff, indicating that symptoms may not become manifest until high functional social demands exist.

1. *Impaired social interaction and communication* is a hallmark of autism spectrum disorder; delays in speech and language development are the most common presenting complaints of parents of children with ASD. In addition to delayed language skills, children with ASD often lack the intent to communicate.

   Impaired social reciprocity: ASD have deficits in social or emotional reciprocity, and younger children may be unaware of other children, and they may lack empathy for another's emotional perspective (e.g., unable to sense that another is in pain), and they are not interested in imitating others or in bringing a novel object to a trusted individual to show.

   Weak or absent joint attention: Individuals with ASD may lack or show reduced spontaneous seeking to share enjoyment, interests, or achievements with other people. Joint attention is a spontaneous behavior in which an infant or toddler tries to share interest, amusement, or apprehension about an object with a caretaker or playmate. The child does this by purposefully looking back and forth between the object of interest and the eyes of the caretaker or playmate (usually by 8–10 months of age) or by pointing to the object (protodeclarative pointing, usually by 14–16 months of age). Impairment of joint attention is believed to be pathognomonic for ASD [1, 9].

   Delayed nonverbal communication: Individuals with ASD have impaired ability to use and interpret nonverbal behaviors such as eye-to-eye gaze, facial expression, gestures, and body postures. They have difficulty reading nonverbal emotional cues. During infancy, parents may notice that the baby resists cuddling, avoids eye contact, or fails to spread the arms in anticipation of being picked up.

   Impaired social relationships: Children with ASD fail to develop and maintain peer relationships appropriate to their developmental level. Younger children may have little or no interest in other children. They may prefer solitary play to social play, involving others in activities only as tools or "mechanical" aid. Older children may become more interested in social interaction, but lack understanding of what behavior is appropriate in one situation but not another. Few children with ASD are so socially isolated that they fail to interact with a loved family member and may have intermittent interaction without the expected joy and reciprocity seen in typical peers.
2. **Restricted and repetitive behaviors, interests, and activities**: Restricted and repetitive and stereotyped patterns of behavior, activities, or interests and hyper- or hyposensitivity to sensory input are another core symptom of ASD.

   Stereotyped behaviors: stereotyped and repetitive motor mannerisms or complex whole-body movements (e.g., hand or finger flapping or twisting, rocking, swaying, dipping, walking on tiptoe) are feature of ASD. Children with ASD may line up an exact number of playthings in the same manner in a stereotyped ritual, without apparent awareness of what the toys represent. Other stereotyped

behaviors are echolalia and idiosyncratic phrases. Motor mannerisms are reported in 37–95% and often manifest during the preschool years. Stereotyped motor mannerisms appear to be self-stimulating and may also be self-injurious. Self-injurious behaviors are common among ASD patients with cognitive disability and include head-banging, face or body slapping, self-biting, or self-pinching. The triggers for these behaviors may be predictable (frustration, anxiety, excitement) or seemingly random.

Insistence on sameness: individuals with ASD have significant difficulty with transitions and may need the same routine identically every day. Apparently inflexible adherence to specific, nonfunctional routines or rituals is characteristic of ASD. These may manifest during various aspects of daily life, such as the need to always eat particular foods in a specific order or to follow the same route from one place to another without deviation. The insistence on sameness may manifest with distress at small changes in routines and difficulty with transitions.

Restricted interests: affected children may have encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal in either intensity or focus and persistent preoccupation with unusual objects.

Sensory perception: sensory processing abilities are aberrant in 42–99% of individuals with ASD, and these responses may include over-responsiveness, under-responsiveness, and paradoxical responses to environmental stimuli. Examples include visual gazing of objects out of the corner of the eyes; preoccupation with edges, spinning objects, or shiny surfaces, lights, or odors; refusal to eat foods with certain tastes or textures; or eating only foods with certain tastes and textures; dietary obsessions may be associated with gastrointestinal symptoms (e.g., weight abnormalities, abnormal stool patterns), preoccupation with sniffing or licking nonfood objects, resistance to being touched, or increased sensitivity to certain kinds of touch; light touch may be experienced as painful, whereas deep pressure may provide a sense of calm. This may include resistance to the feel of certain clothing textures or colors next to the skin, apparent indifference to pain, strong preferences for and/or compulsive touching of certain textures and strong aversions to others, and hypersensitivity to certain frequencies or types of sound (e.g., distant fire engines) with lack of response to sounds close by or sounds that would startle other children [1, 9, 10].

10.8 Other Clinical Features

Children with ASD may manifest some features that are not consistently present like abnormal gait, clumsiness, toe walking, or other abnormal motor signs, such as hypotonia. Macrocephaly is another inconsistent feature with one-fourth of children with isolated ASD having head circumference greater than the 97th percentile. ASD and macrocephaly may have mutations in the PTEN gene, placing them at risk for hamartomatous tumor syndromes. Some children with ASD have special skills in memory, mathematics, music, art, or puzzles, despite profound deficiencies in other

domains. Other special skills include calendar calculation and hyperlexia. Some have super reading abilities, but it is usually concrete, with little comprehension or understanding of the purpose of reading [1, 9].

10.9 Differential Diagnosis

Missing the diagnosis of autism has disastrous consequences on overall prognosis, since delaying intervention minimizes optimal functional development and self-care. Developmental speech delay is the most common disorder to be confused with ASD; unfortunately families get reassured and send away with speech therapy prescription. Other differential diagnoses include global developmental delay; intellectual disability; genetic disease (fragile X syndrome, Rett disorder, Angelman syndrome, Prader-Willi syndrome, Smith-Lemli-Opitz syndrome, Landau-Kleffner syndrome); neurological conditions like seizures, tic disorders, and tuberous sclerosis complex; language-based learning disability; psychiatry disorders, e.g., anxiety, obsessive-compulsive disorders, extreme shyness, social phobia, mutism, mood disorders, and schizophrenia; severe early deprivation/reactive attachment disorder; and hearing impairment [1, 9, 11, 12].

10.10 Assessment

Evaluation for people with ASD should include a comprehensive assessment by a team that has expertise in the diagnosis and management of developmental and behavioral conditions and should be designed to achieve the following goals:

1. Establishment of definitive diagnosis of ASD.
2. Exclusion of conditions that may produce symptoms suggestive of ASD clinically or by diagnostic testing.
3. Identification of comorbid conditions that have implications for treatment or genetic counseling.
4. Determination of the child's level of functioning and profile of strengths and weaknesses.
5. Buildup of a multimodal comprehensive intervention plan.
6. Involvement of the family in the intervention process.

Assessment should include a complete history, careful physical examination, neurologic examination, and direct assessment of the child's social, language, and cognitive development. A standardized parent interview regarding current concerns and behavioral history as well as structured observation of social and communicative behavior and play are major components of the initial assessment by medical teams [1, 9].

Assessment of ASD takes two steps: developmental screening and comprehensive diagnostic evaluation.

10.11 Developmental Screening

The AAP recommends that all children be screened for autism at 18 and 24 months of age [1]. The sooner the autism is identified, and the sooner an intervention program can start, the better the outcomes.

In primary care practice, ASD-specific screening tool should be used for:

- Children with delayed language/communication milestones.
- Children who have a regression in social or language skills.
- Children with a sibling diagnosed with ASD.
- All children at 18 and 24 months of age.
- Children (regardless of age) whose parents, care provider, or clinician raises concerns regarding ASD (e.g., those with atypical behaviors, difficulty socializing, rigidity of behavior that interferes with function).

10.11.1 Screening Tools

1. Modified Checklist for Autism in Toddlers (M-CHAT): a 23-point questionnaire filled out by parents. Most families find it easy to fill out. Using this standardized screening, pediatricians can pick up children at risk for ASD and will be prompted to start conversations about language delay, concerns about behavior, or possible next steps for a toddler at risk with additional genetic, neurologic, or developmental testing. M-CHAT is the recommended tool by the APP.
2. Screening Tool for Autism in Toddlers and Young Children (STAT): a 20-min interactive screening measure that consists of 12 items and is designed to assess children of 24–36 months old.
3. Communication and Symbolic Behavior Scales (CSBS): standardized tool for screening of communication and symbolic abilities up to the 24-month level. The Infant Toddler Checklist is a one-page, parent-completed screening tool.

10.12 Diagnostic Evaluations

This is a comprehensive process that starts as soon as professionals encounter a child suspected to have autism, and care should be taken not to miss this first encounter since parents may not come back soon for evaluation specially if their concern is dismissed since 30% of family concerns about their children proven to be autistics had been dismissed by physicians.

10.13 History

The history for children who screen positive for ASD should include the following in form:

1. Review of the developmental history, with particular attention to early social-emotional and language milestones, play skills, behavior, and any regression.
2. Parental concerns regarding hearing, vision, and speech/language.
3. Specific information regarding early communicative behaviors, such as pointing, use of eye contact, and response to name.
4. History of repetitive, ritualized, or stereotyped behaviors, such as hand flapping, unusual visual behavior, or preoccupation with parts of toys.
5. Frequent tantrums and trouble tolerating change or transition.
6. History of possible seizures.
7. Self-injury.
8. Significant disturbance in eating (including pica) or sleep.
9. A three-generation family history should be reviewed thoroughly, since ASD has a strong genetic component.
10. The psychosocial history should include information regarding the family functionality, supports, and stresses including trauma.

10.14 Examination

Measurements of growth parameters, head circumference: One-fourth of children with isolated ASD have head circumference greater than the 97th. Height and weight measurements are necessary in children who are being evaluated for ASD, since dietary obsessions and compulsions can result in poor weight gain or obesity. Comprehensive neurological examination with special focus on identifying dysmorphic features is critical. Examination of the skin with a Wood's lamp may demonstrate the hypopigmented macules of tuberous sclerosis complex [1, 9, 11, 12].

10.15 Diagnostic Testing

There is no need to order any diagnostic lab tests to diagnose autism, since the most important tool for diagnosis is the skills of experienced physician. But some testing may be necessary to exclude conditions that may produce symptoms suggestive of ASD, to identify potentially treatable conditions associated with ASD, and to define the child's particular pattern of strengths and weaknesses for intervention planning. They include complete blood count, bone profile, iron study, lead screening, and genetic screening (chromosomal microarray (CMA) and DNA analysis for fragile X). Metabolic testing for disorders of amino acid, carbohydrate, purine, peptide, and mitochondrial metabolism accounts for less than 5% of cases of ASD. Although metabolic testing is not necessary in the routine evaluation of all children with ASD, it may be indicated if there are symptoms or signs of a metabolic disorder, like lethargy, limited endurance, hypotonia, early seizure, and dysmorphic or coarse features. Hearing measurement preferably by ABR is essential in all cases suspected to have autism. Neuroimaging is not routinely indicated; also electroencephalogram (EEG) is not indicated in the evaluation of all children with

ASD. Sleep-deprived EEG is indicated when there is a history of unusual spells or behaviors suggestive of seizures and to exclude Landau-Kleffner syndrome (acquired epileptic aphasia) in patients with a significant regression in language skills [1, 5, 8, 11, 13, 14].

10.16 Psychometric Assessment

There are various tools that specialists commonly use to diagnose autism. The only tool that currently fits the revised DSM-5 criteria is the Autism Diagnostic Observation Schedule (ADOS-2).

During an ADOS-2 assessment, the specialist interacts directly with your child in social and play activities. For example, the specialist will see whether your child responds to his or her name and how he or she performs in pretend play, such as with dolls. The specialist is looking for specific characteristics that are hallmarks of ASD. To be diagnosed with ASD, a child must have had symptoms since an early age [1, 3, 9, 15, 16] (Table 10.2).

10.17 Other Assessments

Typically children suspected to have autism should have comprehensive speech and language and occupational therapy assessments, and although this is not essential for diagnosis, they are of importance in understanding the child capabilities and challenges; also they carry significant importance in building up an intervention plan and for follow-up purposes.

10.18 Diagnosis

The diagnosis of ASD is made clinically, based upon history, examination, and observations of behaviors. It should be suspected in children with abnormalities in social interaction, social communication, and restricted, repetitive patterns of behavior, interests, and activities. Applying international diagnostic criteria (ICD-10 or DSM-5) is standard practice and is the mainstay of diagnosis. DSM-5 is used primarily in North America, while the rest of the world uses ICD-10 [1, 9].

10.19 ICD-10 Criteria for "Childhood Autism" [6]

A. **Abnormal or impaired development is evident before the age of 3 years in at least one of the following areas**:
   1. Receptive or expressive language as used in social communication.
   2. The development of selective social attachments or of reciprocal social interaction.
   3. Functional or symbolic play.

Table 10.2 Psychometric scales used for autism assessment

Test	Description	Sensitivity	Specificity
Childhood Autism Rating Scale (CARS)	Second Edition (CARS-2) is a 15-item direct observation instrument designed to facilitate the diagnosis of autism in children 2 years of age and older. Each of the items is scored on a four-point rating scale The CARS-2 is intended for use by a trained clinician and takes approximately 20–30 min to administer	82%	80%
Gilliam Autism Rating Scale (GARS)	Third Edition (GARS-3) consists of a checklist of 56 items for parents based on DSM diagnostic criteria The GARS-3 can be used for children and adolescents up to 22 years and was standardized on autism	97%	97%
Autism Behavior Checklist (ABC)	The (ABC) is a list of 57 questions to be completed by a parent or teacher It was designed primarily to identify children with autism from a population of school-age children with severe disabilities. However, it has been used with children as young as 3 years	38–58%	76–97%
Autism Diagnostic Interview-Revised (ADI-R)	A 2- to 3-h clinical interview that probes for autistic symptoms; it is a research tool, and not practical in clinical settings	82% in children <3 years and 91% in children >3 years	
Autism Diagnostic Observation Schedule (ADOS-2)	A semi-structured assessment of social interaction, play, communication, and imaginative use of materials; it is available for use in individual's age 12 months through adulthood. It takes 40–60 min to administer and requires substantial training for administration and scoring	Not published	Specificities of the first edition of the generic ADOS were 87% and 78%
Autism Diagnostic Observation Schedule-Toddler Module (ADSO-T)	A standardized research tool for use in children aged 12–30 months (or until phrase speech is acquired) It targets communication, reciprocal social interaction, emerging object use, and play skills	93%	95%

B. **A total of at least six symptoms from (1), (2), and (3) must be present, with at least two from (1) and at least one from each of (2) and (3)**.
   1. Qualitative impairment in social interaction are manifest in at least two of the following areas:
      (a) Failure to adequately use eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction.

(b) Failure to develop peer relationships that involve a mutual sharing of interests, activities, and emotions.
(c) Lack of socio-emotional reciprocity as shown by an impaired or deviant response to other people's emotions or lack of modulation of behavior according to social context or a weak integration of social, emotional, and communicative behaviors.
(d) Lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., a lack of showing, bringing, or pointing out to other people objects of interest to the individual).

2. Qualitative abnormalities in communication as manifest in at least one of the following areas:
   (a) Delay in or total lack of development of spoken language that is not accompanied by an attempt to compensate through the use of gestures or mime as an alternative mode of communication.
   (b) Relative failure to initiate or sustain conversational interchange (at whatever level of language skill is present), in which there is reciprocal responsiveness to the communications of the other person.
   (c) Stereotyped and repetitive use of language or idiosyncratic use of words or phrases.
   (d) Lack of varied spontaneous make-believe play or (when young) social imitative play.
3. Restricted, repetitive, and stereotyped patterns of behavior, interests, and activities are manifested in at least one of the following:
   (a) An encompassing preoccupation with one or more stereotyped and restricted patterns of interest that are abnormal in content or focus or one or more interests that are abnormal in their intensity and circumscribed nature though not in their content or focus.
   (b) Apparently compulsive adherence to specific, nonfunctional routines or rituals.
   (c) Stereotyped and repetitive motor mannerisms that involve either hand or finger flapping or twisting or complex whole-body movements.
   (d) Preoccupations with part objects of nonfunctional elements of play materials (such as their odor, the feel of their surface, or the noise or vibration).

10.20 Severity Level

The DSM-5 recommends that clinicians specify the severity level of ASD, recognizing that severity may vary with context and over time. Severity should be assessed separately for each domain and should help in building up the management plan and in counseling parents regarding prognosis (Table 10.3).

Table 10.3 DSM-5 severity levels of ASD

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

10.21 Management

After establishing a diagnosis of autism, all effort must be focused on starting an intervention plan as soon as possible, involving parents and reliable family members in all stages of building the intervention plan and outlining clearly their role and expectations from them. At the same time, parents have to be informed about what to expect from the intervention team and should be advised to monitor progress and discuss concerns as they arise on a timely manner. Intervention plans must have agreed-upon goals like minimizing core features of autism, maximizing

functional independence, and maximizing quality of life. We have to note that all children with developmental delays must have proper therapeutic interventions as soon as possible regardless of the diagnosis [1, 11, 17].

10.22 Main ASD Interventions

10.22.1 Early Intervention Programs (EIP)

The mainstay, evidence-based interventions of autism are behavioral and educational therapies, as early as possible. And no other interventions can replace them. Supportive therapies include speech and occupational therapies. Medications are not needed unless indicated to control behavioral and co-occurring conditions. As soon as children are diagnosed or strongly suspected to have autism, they should be referred to an early intervention program (EIP) depending on priority (severity level). EIP is an intensive (20–40 h per week), structure intervention strategies that are systematically planned and developmentally appropriate educational activities aimed to maximize children's abilities and functionality. Children should be enrolled as early as they are flagged to have delayed development and expected to have behavioral modification therapies, speech therapy, occupational therapy, and physical therapy with investment in parent/family training. Each child will have his/her own individual intervention plan (IIP), which may take up to 2 years, and each IIP should be discussed and communicated very well with parents and all members in the management team. Early intervention plans should prepare child to inclusion schooling as primary outcome, which is a very important driving goal for intervention teams and parents, who should assess preset periodic goals every 1–3 months to recognize and address challenges as early as possible [1, 9, 18].

With early intervention, between 3% and 25% of children with autism make so much progress that they are no longer on the autism spectrum when they are older. Many of the children who later go off the spectrum have something in common: they were diagnosed and treated at younger ages, have higher intelligence quotient (IQ) than the average child with autism, and have better language and motor skills.

10.22.2 Behavioral Management Therapy (BMT)

BMT helps to reinforce wanted behaviors and reduce unwanted behaviors. It also directs caregivers what to do before, during, after, and between episodes of problem behaviors. Behavioral therapy is often based on applied behavior analysis (ABA), a widely accepted approach that tracks a child's progress in improving his or her skills. Different types of ABA commonly used to treat ASD include:

- *Positive Behavior and Support (PBS)*: Aims to understand reasons for a child particular problem behavior and works to change the environment, teach skills, and make other changes to correct behaviors. It supports and encourages the child for positive behaviors.

- *Pivotal Response Training (PRT)*: Its goal is to improve a few "pivotal" skills, such as motivation and taking initiative to communicate. These help the child to learn many other skills and deal with many situations and take place in the child's everyday environment.
- *Early Intensive Behavioral Intervention (EIBI)*: Provides individualized, behavioral instruction to very young children with ASD. It requires a large time commitment and provides one-on-one or small-group instruction.
- *Discrete Trial Teaching (DTT)*: Teaches skills in a controlled, step-by-step way. The teacher uses positive feedback to encourage the child to use new skills [12, 19].

10.22.3 Cognitive Behavioral Therapy

Cognitive behavioral therapy focuses on the connection between thoughts, feelings, and behaviors. Together, the therapist, the person with autism spectrum disorder, and/or the parents come up with specific goals for the course of therapy. Throughout the sessions, the person with autism learns to identify and change thoughts that lead to problem feelings or behaviors in particular situations. It is designed for older children, adolescents, and adults. Cognitive behavioral therapy is structured into specific phases of treatment. However, it is also individualized to patients' strengths and weaknesses. Research shows that this therapy helps some people with ASD deal with anxiety, social situations, and better recognition of emotions.

10.22.4 Social Skills Training

This training teaches children the skills they need to interact with their peers and can help improve relationships. It includes repeating and reinforcing certain behaviors. The Children's Friendship Training intervention 2, for instance, helps elementary school-age children improve several social skills such as conversation, handling teasing, being a good sport, and showing good host behavior during play dates [11, 19].

10.22.5 Parent-Mediated Therapy

Parents learn therapy techniques from professionals and provide specific therapies to their own child. This approach gives children with autism spectrum disorder consistent reinforcement and training throughout the day. Parents can also conduct some therapies with children who are at risk of autism but are too young to be diagnosed. Several types of therapies can be parent-mediated, including joint attention therapy, social communication therapy, and behavioral therapy.

10.22.6 Joint Attention Therapy

People with autism usually have difficulty with joint attention. This means that they have trouble following someone's gaze or pointed finger to look at something. Joint

attention is important to communication and language learning. Joint attention therapy focuses on improving specific skills related to shared attention such as pointing, showing, and coordinating looks between a person and an object. Improvements from such treatments can last for years [12, 19].

10.22.7 Educational and School-Based Therapies

Individualized Educational Program (IEP) is the most important intervention in school-age children; special education teachers with the help of psychologists, parents, and other team members will design a written document that lists individualized educational goals for the child, specifies the plan for services the child will receive, lists the developmental specialists who will work with him/her, and will outline the monitoring and role of every team member. The school environment must be adjusted to meet the child's needs.

10.22.8 Medication Treatment

There is no medication that can cure ASD or all of its symptoms. But in many cases, medication can help treat some of the symptoms associated with ASD. Healthcare providers often use medications to deal with a specific behavior, such as to reduce self-injury or aggression. Once a symptom is no longer a problem, other intervention strategies will be much easier to implement and sustain. Some of the medications used in autism care are listed in Table 10.4.

Table 10.4 Indications of pharmacotherapy in autism spectrum disorders

Symptoms	Medications
Hyperactivity, impulsivity, distractibility	Stimulants (Ritalin, Adderall, etc.), non-stimulants (Strattera, tricyclic, and antidepressants), antipsychotic agents (occasionally)
Aggression	Antipsychotic drugs, mood stabilizers, beta blockers (rarely)
Self-injurious behavior	Mood stabilizers, antipsychotic drugs, naltrexone
Extreme difficulty with transitions	Clomipramine, SSRI antidepressants
Extreme compulsive behaviors	Clomipramine, SSRI antidepressants
Irritability	Antidepressants
Mood swings	Mood stabilizers (lithium, anticonvulsants (Depakote), antipsychotics)
Anxious and phobic symptoms	Antidepressants
Psychotic behavior	Antipsychotic drugs
Sleep disturbance	Benadryl, trazodone, clonidine, antipsychotics
Ties and Tourette syndrome	Antipsychotic drugs, clonidine
Seizures	Anticonvulsants

10.23 Complementary and Alternative Treatments

To relieve the symptoms of ASD, some parents and healthcare professionals use treatments that are outside of what is typically recommended by the pediatrician. These types of treatments are known as complementary and alternative treatments (CAM). They might include special diets, chelation (a treatment to remove heavy metals like lead from the body), biologicals (e.g., secretin), or body-based systems (like deep pressure). These types of treatments are very controversial. Current research shows that as many as one-third of parents of children with an ASD may have tried complementary or alternative medicine treatments and up to 10% may be using a potentially dangerous treatment.

Almost all CAM have no effect on core features of autism and are not recommended by the international scientific bodies like the APP, American Psychiatric Association (APA), and CDC [2].

10.24 Role of Primary Care

The primary care clinician should listen to parents and take their concerns seriously. Children identified by primary care providers to be at risk for ASD should be referred for a comprehensive specialty evaluation. Primary care physicians must be familiar with DSM-5 and ICD-10 diagnostic criteria and should be able to have a provisional diagnosis. Children with ASD need to be missed or delayed for extended periods, and primary care clinicians should be familiar with the components of the comprehensive evaluation and all types of interventions. At the same time, follow-up and family support is key component of primary care services [20, 21].

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