

AUTISM
SPECTRUM
DISORDER



DEPARTMENT OF PAEDIATRICS

TOPICS

- ▶ Introduction
- ▶ Epidemiology
- ▶ Etiopathogenesis
- ▶ Clinical features
- ▶ Neuroimaging
- ▶ Differential diagnosis
- ▶ Treatment



INTRODUCTION

DEFINITION– Autism spectrum disorder is a neurobiologic disorder with onset in early childhood.

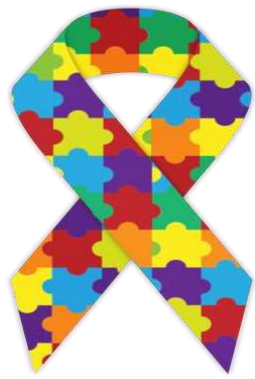
Key features are –

- 1) Impairment in social communication and social interaction
- 2) Restricted and repititive behaviours.

–Presentation of ASD can vary from one individual to another, as well as over the course of development for a particular child. –

Currently no diagnostic biomarker for ASD.

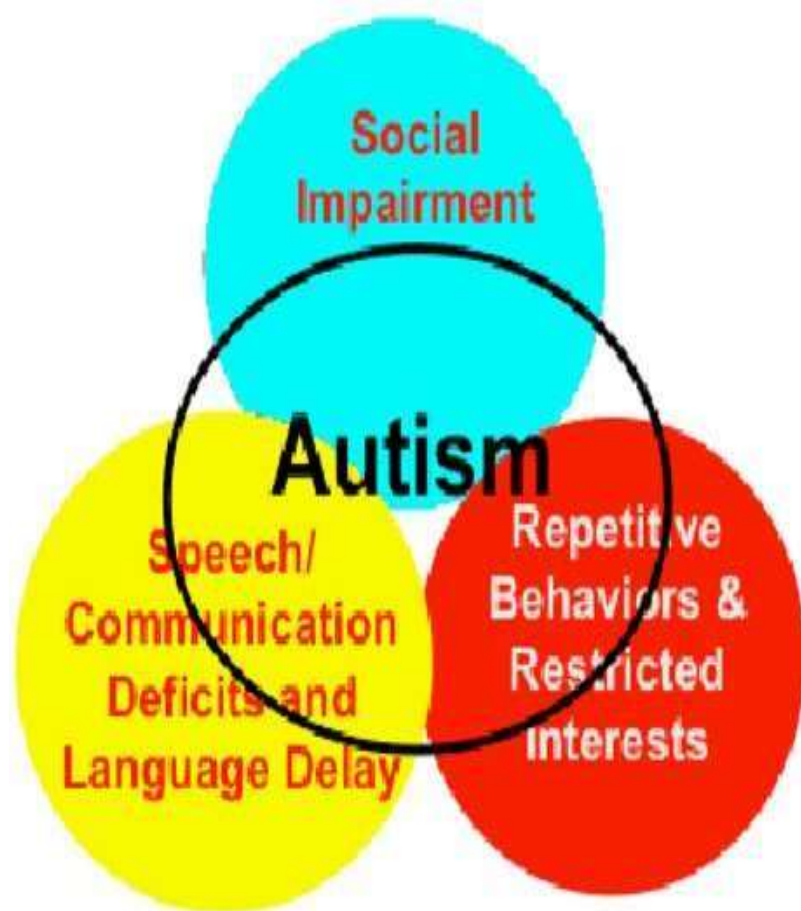
Diagnosis requires proper history and direct observation of the childs behavior.



A.

DSM IV:

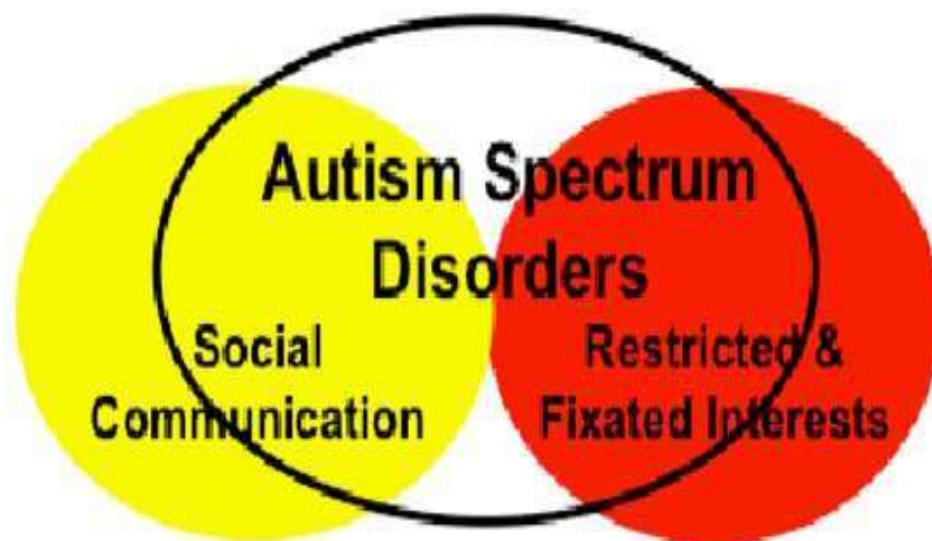
Pervasive Developmental Disorders:
Autism



B.

DSM5:

Autism Spectrum Disorders





- ▶ adopted in 1999 as the universal sign of autism awareness
- ▶ The puzzle pattern reflects the complexity of the autism spectrum.
- ▶ The different colors and shapes represent the diversity of the people and families living with the condition.

EPIDEMIOLOGY

- ▶ ASD is typically evident during the second year of life
- ▶ However, in milder cases, the disorder is identified at a later age.
- ▶ Approximately 1/3 of children exhibit intellectual disability (ID).
- ▶ Children who exhibited severe language deficits received an ASD diagnosis, a year earlier.
- ▶ Children with ASD who exhibited repetitive behaviors such as hand- flapping, toe-walking, and odd play were also identified with ASD disorders at a younger age than those who did not exhibit such behaviors.



Prevalence

- ▶ Study estimated at 1 in 59 persons by the U.S. centers (CDC).
The prevalence increased over past 25 years primarily because of improved diagnosis and case finding .
- ▶ Because of the delay between onset and diagnosis, the prevalence rates increase with age.

Sex Distribution

- ▶ Four times more common in boys than in girls(4:1)
- ▶ In clinical samples, girls with autism spectrum disorder more often exhibit intellectual disability than boys.



Social class

- ▶ Although a few early studies supported Kanner's impression of an association between autism and upper socio-economic status, most epidemiological studies published in the 1990s have failed to reveal such association.
- ▶ Bias - more educated parents seek referral, families from disadvantaged backgrounds are still underrepresented in clinical samples.
- ▶ Autism clearly is seen in all social classes and in all countries.

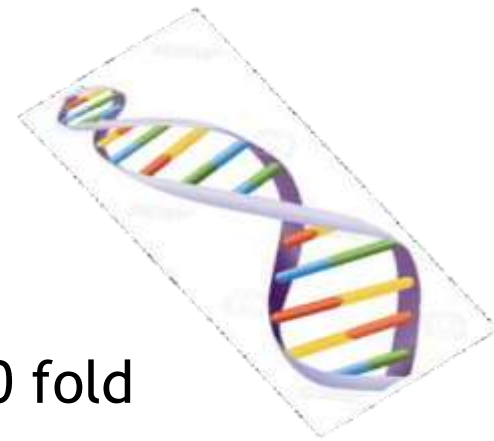


ETIOLOGY AND PATHOGENESIS

- ❑ Genetic factors
- ❑ Immunological factors
- ❑ Pre and perinatal factors
- ❑ Comorbid neurological disorders



GENETIC FACTORS



- ▶ First-degree relatives of ASD patient are 20 to 80 fold more likely to be affected.
- ▶ Family studies - increased rates of ASD in siblings of an index child, as high as 50 % in families with two or more children with ASD.
- ▶ Siblings of a child with autism are also at increased risk for impairments in communication and social skills, even when they do not meet criteria for ASD.



- ▶ The concordance rate of autistic disorder in two large twin studies was
 - More in monozygotic pairs as compare to dizygotic pairs.
- ▶ Neuroligins, shank3, contactin associated protein 2, and neurexin 1, and fragile X mental retardation 1 (FMR1) gene - critical role for synaptic formation and function.
- ▶ Genes that may contribute to ASD are present on chr 2,7,16,17



Biomarkers

- ▶ Several biomarkers, results from interactions of genes and environmental factors.

- ▶ Biomarkers results from
 1. abnormal signaling in the 5-HT system,
 2. the mTOR-linked synaptic plasticity mechanisms, and
 3. alterations of the GABA inhibitory system.

- ▶ The first biomarker identified was ↑ serotonin in platelets.
- ▶ Platelets acquire 5-HT through SERT (serotonin transporter), as they pass through the intestinal circulation.
- ▶ The genes that mediate SERT (SLC64A), and the 5-HT 2A receptor gene encode the **same protein** in the platelets and in the brain. Changes in 5-HT causes alterations in neuronal migration and growth in the brain.



Immunological Factors

- ▶ Several reports have suggested that immunological incompatibility (i.e., maternal **antibodies directed at the fetus**) may contribute to autistic disorder.
- ▶ The lymphocytes of autistic children react with maternal antibodies, which raises the possibility that embryonic neural tissues may be damaged during gestation.
- ▶ This hypothesis is still under investigation.
- ▶ There also have been reports of autism associated with viral infections.
- ▶ Considerable controversy has arisen over the question of whether exposure to the **(MMR) immunization** might be a causative factor. The bulk of the available evidence does not support a causative association with immunization.



Prenatal and Perinatal Factors

- ▶ A higher incidence of prenatal and perinatal complications seems to occur in infants who are later diagnosed with ASD.

Prenatal factors

- ▶ advanced maternal and paternal age at birth,
- ▶ maternal gestational bleeding,
- ▶ gestational diabetes, and
- ▶ firstborn baby.



Perinatal risk factors

- ▶ birth trauma,
- ▶ fetal distress,
- ▶ low birth weight,
- ▶ low Apgar score,
- ▶ congenital malformation,
- ▶ ABO or Rh factor incompatibility and
- ▶ hyperbilirubinemia.

Many of the obstetrical complications that are which are risk for autism spectrum disorder are also risk factors for **hypoxia**, which may be an underlying risk factor itself.



Postmortem and Neuroimaging Studies

- ▶ The social, language, and behavioral problems suggest that the syndrome affects a functionally **diverse set** of neural systems. The initial insult is localized, branching off into more pervasive impairments.
- ▶ There is involvement **cortical** as well as **limbic** system.
- ▶ Postmortem studies - decrease in no. of Purkinje, granule cells in cerebellum.

These abnormalities, including a lack of gliosis indicates a prenatal origin.



- A series of MRI studies focusing on the cerebellar vermis revealed finding of a decrease in the midsagittal area of vermal lobules VI and VII.
- ▶ Limbic system - decreased neuronal size, decreased dendritic arborization, and increased neuronal packing density of neurons
- ▶ More recent studies - amygdala enlargement in autism and a decrease in total neuron number.
- ▶ One hypothesis is that autism is largely caused by abnormalities in the amygdala- cortical loops system that can regulate social-cognitive processes and social- perceptual processes.



DIAGNOSIS AND CLINICAL FEATURES



DSM-5 Diagnostic Criteria

- ▶ A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following,
 - 1 . Deficits in social-emotional reciprocity
 - 2 . Deficits in nonverbal communicative behaviors used for social interaction
 - 3 . Deficits in developing, maintaining, and understanding relationships
- ▶ B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following
 - 1 . Stereotyped or repetitive motor movements, use of objects, or speech
 - 2 . Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior
 - 3 . Highly restricted, fixated interests that are abnormal in intensity or focus
 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment



- ▶ C. Symptoms must be present in the early developmental period
- ▶ D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- ▶ E. These disturbances are not better explained by intellectual disability

Specify if:

- ▶ With or without accompanying intellectual impairment
- ▶ With or without accompanying language impairment
- ▶ Associated with a known medical or genetic condition or environmental factor
- ▶ Associated with another neurodevelopmental, mental, or behavioral disorder with catatonia



1. Persistent Deficits In Social Communication and Interaction.

- ▶ may not develop a social smile
- ▶ older babies may lack the anticipatory posture for being picked up by a caretaker.
- ▶ Less frequent and poor eye contact.
- ▶ The social development is characterized by atypical, attachment behavior.
- ▶ may not differentiate the most important persons in their lives-parents, siblings, and teachers
- ▶ may not react strongly when left with a stranger compared to others.
- ▶ often display extreme anxiety when their usual routine is disrupted.



By the School age,

- ▶ observable deficit in spontaneous play with peers.
- ▶ a lack of conventional back and forth conversation, fewer shared interests, and fewer body and facial gestures during conversations.
- ▶ Cognitively, more skilled in visuospatial tasks than verbal reasoning.
- ▶ an impaired ability to interpret the emotional state of others around them ("theory of mind").
- ▶ generally desire friendships, and higher functioning children may be aware that their lack of spontaneity and poor skills in responding to the emotions and feelings of their peers are major obstacles in developing friendships.



2. Restricted, Repetitive Patterns of Behavior, Interests, and Activities.

From the first years of life, in a child with autism spectrum disorder,

- ▶ developmentally expected exploratory play is restricted and muted.
- ▶ Toys and objects are often manipulated in a ritualistic manner
- ▶ do not show the level of imitative play
- ▶ The activities and play are more rigid, repetitive, and monotonous than their peers. In early and middle childhood.
- ▶ often seem to enjoy spinning, banging, and watching water flowing.
- ▶ Frank compulsive behaviors, such as lining up objects, and
- ▶ may exhibit a strong attachment to a particular inanimate object.



- ▶ Children with autism spectrum disorder who are severely intellectually disabled have increased rates of self-stimulatory and self-injurious behaviors.
- ▶ Stereotypies, mannerisms, and grimacing emerge most frequently
- ▶ Often find transitions and changes intimidating. Moving to a new house, rearranging furniture in a room, may evoke panic, fear, or temper tantrums in a child with autism spectrum disorder.



ASSOCIATED BEHAVIORAL SYMPTOMS

- 1. Disturbances In Language Development and Usage.
 - ▶ Is characteristic of more severe subtypes of autism spectrum disorder.
 - ▶ Have significant difficulty putting meaningful sentences together, even when they have large vocabularies.
 - ▶ In the first year of life, a typical pattern of babbling may be minimal or absent.
 - ▶ Some children vocalize noises---clicks, screeches, or nonsense syllables in a stereotyped fashion, without a seeming intent of communication.
 - ▶ Speech may contain echolalia, both immediate and delayed, or stereotyped phrases that seem out of context.
 - ▶ Frequent pronoun reversals are present. A child with autistic disorder might say, "You want the toy" when she wants it



2. Intellectual Disability.

- ▶ About 30 % of children have Intellectual Disability.
- ▶ Of those, about 30 % - mild to moderate range, and about 45 to 50 % -severely to profoundly intellectually disabled.

3. Irritability.

- ▶ Irritability includes aggression, self-injurious behaviors, and severe temper tantrums.
- ▶ In children with intellectual deficits, aggression may arise unexpectedly without an obvious trigger, and self-injurious behaviors such as head banging, skin picking, and biting oneself may also be noted.

4. Instability of Mood and Affect.

- ▶ Some children with autism spectrum disorder exhibit sudden mood changes, with bursts of laughing or crying without an obvious reason.

5. Response to Sensory Stimuli.

- ▶ Overrespond to some stimuli and underrespond to other sensory stimuli.
- ▶ Some children have a heightened pain - even do not respond to an injury by crying or seeking comfort.

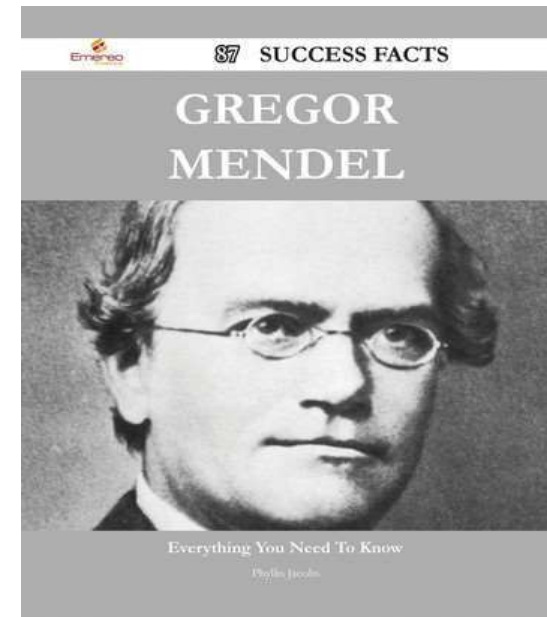
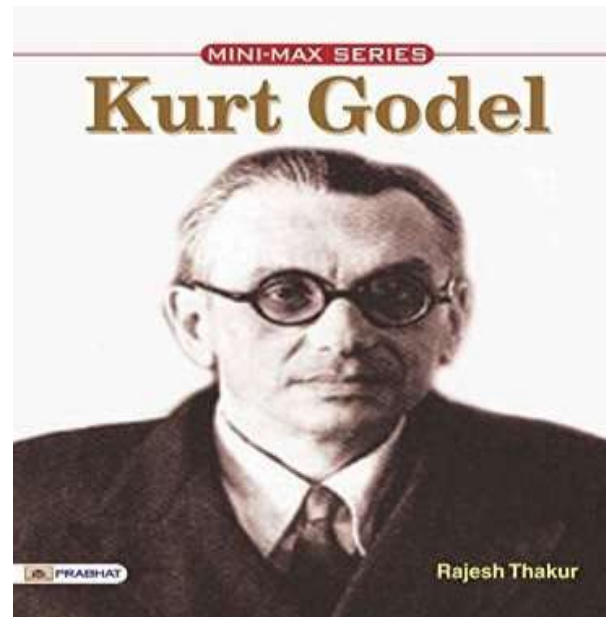
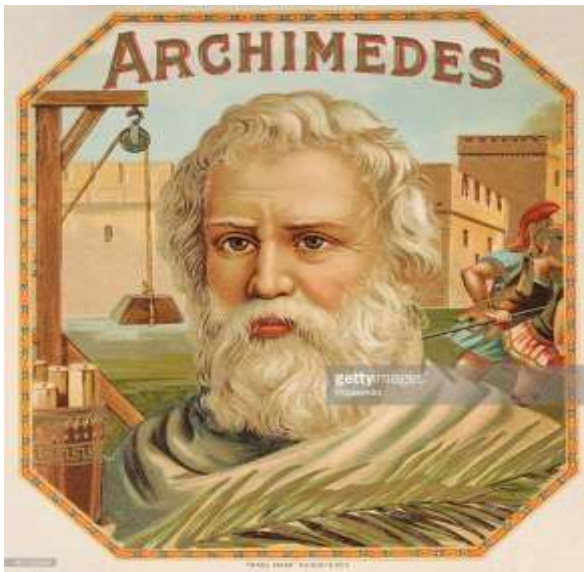


6. Hyperactivity and Inattention.

- ▶ Hyperactivity and inattention are both common behaviors in young children.
- ▶ Short attention span, poor ability to focus on a task, interfere with daily functioning

7. Precocious Skills.

- ▶ Some individuals with autism spectrum disorder have precocious or splinter skills of great proficiency, such as rote memories or calculating abilities, usually beyond the capabilities of their normal peers.
- ▶ Other potential precocious abilities include hyperlexia, an early ability to read well , memorizing and reciting, and musical abilities.



8. Insomnia.

- ▶ Insomnia occur in 44 to 83 percent of school-aged children.
- ▶ Behavioral interventions include modification of parental behaviour training, and removing reinforcers for remaining awake.
- ▶ Medication - melatonin in doses ranging from 1 mg fast-release to 4 mg controlled-release.

Minor Infections and Gastrointestinal Symptoms

- ▶ Have higher incidence of upper respiratory infections and other minor infections.
- ▶ Gastrointestinal symptoms - excessive burping, constipation, and loose bowel movements.
- ▶ Increased incidence of febrile seizures.



LABORATORY EXAMINATION

- ▶ A variety of EEG abnormalities may be seen in autism, including diffuse and focal spikes, paroxysmal spike-and-wave patterns, multifocal spike activity, and a mixed discharge.
- ▶ abnormal EEGs is significantly higher in mentally retarded autistic individuals.
- ▶ High incidence of EEG abnormalities and seizure disorders in autism was one of the first compelling evidence of a biological basis.
- ▶ Abnormalities of cognitive potentials, particularly the **auditory P300** (which represents the brain's processing of sensory stimuli), have been shown to be abnormal in autism. This presumably reflects abnormalities in higher auditory processing and neural pathways



ASSESSMENT TOOLS

- ▶ The Child Autism Rating Scale (CARS)
- ▶ The Autism Diagnostic Observation Schedule (ADOS)
- ▶ Autism Detection in Early Childhood (ADEC)
- ▶ The Autism Diagnostic Interview - revised (ADI-R)
- ▶ The Social Communication Questionnaire (SCQ).
- ▶ Ages and Stages Questionnaires (ASQ)
- ▶ Parent's Evaluation of Development Status (PEDS)
- ▶ Modified Checklist for Autism in Toddlers (M-CHAT)
- ▶ Screening Tool for Autism in Toddlers and Young Children (STAT)





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Mentally Handicapped**
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INDIAN SCALE FOR ASSESSMENT OF AUTISM

Name of the child:..... Gender:..... Date:.....

D.O.B:..... Age: Examiner:

Directions:

Below are given 40 statements which are divided under six domains, please tick (✓) mark the appropriate rating for each item of the scale by observing the child and by interviewing the parents in order to assess Autism

Items		Rarely Upto 20% Score 1	Sometimes 21 – 40 % Score 2	Frequently 41 – 60% Score 3	Mostly 61- 80 % Score 4	Always 81-100% Score 5
I. SOCIAL RELATIONSHIP AND RECIPROCITY						
1	Has poor eye contact					
2	Lacks social smile					
3	Remains aloof					
4	Does not reach out to others					
5	Unable to relate to people					
6	Unable to respond to social/ environmental cues					
7	Engages in solitary and repetitive play activities					
8	Unable to take turns in social interaction					
9	Does not maintain peer relationships					
II. EMOTIONAL RESPONSIVENESS						
10	Shows inappropriate emotional response					
11	Shows exaggerated emotions					
12	Engages in self-stimulating emotions					
13	Lacks fear of danger					
14	Excited or agitated for no apparent reason					
III. SPEECH-LANGUAGE AND COMMUNICATION						
15	Acquired speech and lost it					
16	Has difficulty in using non-verbal language or gestures to communicate					
17	Engages in stereotyped and repetitive use of language					
18	Engages in echolalic speech					
19	Produces infantile squeals/ unusual noises					
20	Unable to initiate or sustain conversation with others					



Items		Rarely Upto 20% Score 1	Sometimes 21 – 40 % Score 2	Frequently 41 – 60% Score 3	Mostly 61- 80 % Score 4	Always 81-100% Score 5
21	Uses jargon or meaningless words					
22	Uses pronoun reversals					
23	Unable to grasp pragmatics of communication (real meaning)					
IV. BEHAVIOUR PATTERNS						
24	Engages in stereotyped and repetitive motor mannerisms					
25	Shows attachment to inanimate objects					
26	Shows hyperactivity/ restlessness					
27	Exhibits aggressive behavior					
28	Throws temper tantrums					
29	Engages in self-injurious behavior					
30	Insists on sameness					
V. SENSORY ASPECTS						
31	Unusually sensitive to sensory stimuli					
32	Stares into space for long periods of time					
33	Has difficulty in tracking objects					
34	Has unusual vision					
35	Insensitive to pain					
36	Responds to objects/people unusually by smelling, touching or tasting					
VI. COGNITIVE COMPONENT						
37	Inconsistent attention and concentration					
38	Shows delay in responding					
39	Has unusual memory of some kind					
40	Has 'savant' ability					

Classification	No Autism < 70	Mild Autism 70 to 106	Moderate Autism 107 to 153	Severe Autism > 153
Total score				



Table- M- CHAT R Scoring

1	If you point at something across the room, does your child look at it? (FOR EXAMPLE, if you point at a toy or an animal, does your child look at the toy or animal?)	Yes	No
2	Have you ever wondered if your child might be deaf?	Yes	No
3	Does your child play pretend or make-believe? (FOR EXAMPLE, pretend to drink from an empty cup, pretend to talk on a phone, or pretend to feed a doll or stuffed animal?)	Yes	No
4	Does your child like climbing on things? (FOR EXAMPLE, furniture, playground equipment, or stairs)	Yes	No
5	Does your child make unusual finger movements near his or her eyes? (FOR EXAMPLE, does your child wiggle his or her fingers close to his or her eyes?)	Yes	No
6	Does your child point with one finger to ask for something or to get help? (FOR EXAMPLE, pointing to a snack or toy that is out of reach)	Yes	No
7	Does your child point with one finger to show you something interesting? (FOR EXAMPLE, pointing to an airplane in the sky or a big truck in the road)	Yes	No
8	Is your child interested in other children? (FOR EXAMPLE, does your child watch other children, smile at them, or go to them?)	Yes	No
9	Does your child show you things by bringing them to you or holding them up for you to see – not to get help, but just to share? (FOR EXAMPLE, showing you a flower, a stuffed animal, or a toy truck)	Yes	No
10	Does your child respond when you call his or her name? (FOR EXAMPLE, does he or she look up, talk or babble, or stop what he or she is doing when you call his or her name?)	Yes	No

11	When you smile at your child, does he or she smile back at you?	Yes	No
12	Does your child get upset by everyday noises? (FOR EXAMPLE, does your child scream or cry to noise such as a vacuum cleaner or loud music?)	Yes	No
13	Does your child walk?	Yes	No
14	Does your child look you in the eye when you are talking to him or her, playing with him or her, or dressing him or her?	Yes	No
15	Does your child try to copy what you do? (FOR EXAMPLE, wave bye-bye, clap, or make a funny noise when you do)	Yes	No
16	If you turn your head to look at something, does your child look around to see what you are looking at?	Yes	No
17	Does your child try to get you to watch him or her? (FOR EXAMPLE, does your child look at you for praise, or say "look" or "watch me"?)	Yes	No
18	Does your child understand when you tell him or her to do something? (FOR EXAMPLE, if you don't point, can your child understand "put the book on the chair" or "bring me the blanket"?)	Yes	No
19	If something new happens, does your child look at your face to see how you feel about it? (FOR EXAMPLE, if he or she hears a strange or funny noise, or sees a new toy, will he or she look at your face?)	Yes	No
20	Does your child like movement activities? (FOR EXAMPLE, being swung or bounced on your knee)		

Scoring Algorithm

For all items except 2, 5, and 12, the response “NO” indicates ASD risk; for items 2, 5, and 12, “YES” indicates ASD risk. The following algorithm maximizes psychometric properties of the M-CHAT-R:

LOW-RISK: Total Score is 0-2; if child is younger than 24 months, screen again after second birthday. No further action required unless surveillance indicates risk for ASD.

MEDIUM-RISK: Total Score is 3-7; Administer the Follow-Up (second stage of M-CHAT-R/F) to get additional information about at-risk responses. If M-CHAT-R/F score remains at 2 or higher, the child has screened positive. Action required: refer child for diagnostic evaluation and eligibility evaluation for early intervention. If score on Follow-Up is 0-1, child has screened negative. No further action required unless surveillance indicates risk for ASD. Child should be rescreened at future well-child visits.

HIGH-RISK: Total Score is 8-20; It is acceptable to bypass the Follow-Up and refer immediately for diagnostic evaluation and eligibility evaluation for early intervention.

DIFFERENTIAL DIAGNOSIS

1. Social (Pragmatic) communication disorder

This disorder is characterized by

- ▶ cant understanding the rules of social communication through language,
- ▶ lack of conventional greeting others,
- ▶ Can't take turns in a conversation, and
- ▶ respond to verbal and nonverbal cues of a listener.
- ▶ found with greater frequency in relatives of individuals with autism spectrum disorder.
- ▶ This disorder does not include restricted or repetitive behaviors and interests, as autism spectrum disorder does.



2. Childhood Onset Schizophrenia

Criteria	Autism Spectrum Disorder	Schizophrenia (with Onset before Puberty)
Age of onset	Early developmental period	Rarely under 5 years of age
Incidence	1 percent	<1 in 10,000
Sex ratio (M:F)	4:1	1.67:1 (slight preponderance of males)
Family history of schizophrenia	Not increased	Likely Increased
Prenatal and perinatal complications	Increased	Not increased
Behavioral characteristics	Poor social relatedness; may have aberrant language, speech or echolalia; stereotyped phrases; may have stereotypies, repetitive behaviors	Hallucinations and delusions; thought disorder
Adaptive functioning	Impaired	Deterioration in functioning
Level of intelligence	Wide range, may be intellectually disabled (30 percent)	Usually within normal range, may be low average normal
Pattern of IQ	Typical higher performance than verbal	More even
Grand mal seizures	4 percent to 32 percent	Low incidence



3. Intellectual Disability with Behavioral Symptoms

- ▶ Display global impairments in both verbal and nonverbal areas, whereas children with autism spectrum disorder are relatively weak in social interactions compared to other areas of performance.
- ▶ Children with intellectual disability generally relate verbally and socially to adults & peers in accordance with their mental age.



4. Language Disorder

Impairments in processing of linguistic information

Criteria	Autism Spectrum Disorder	Language Disorder
Sex ratio (M:F)	4:1	1:1
Associated deafness	Infrequent	Frequent
Nonverbal communication	Impaired	Active
Language abnormalities (e.g., echolalia, stereotyped phrases out of context)	Present	Uncommon
Intellectual impairment	Impaired	Uncommon
Impaired social communication, restricted and repetitive behaviors	Present	Absent

- **5. Congenital Deafness or Hearing Impairment**

- ▶ infants with autism spectrum disorder may babble only infrequently, whereas deaf infants often have a normal babbling that gradually tapers off and stop at 6 months to 1 year of age.
- ▶ Deaf children generally respond only to loud sounds, whereas children with autism spectrum disorder may ignore loud or normal sounds and respond to soft sounds.
- ▶ Deaf children seek out nonverbal social communication
- ▶ audiogram or auditory-evoked potentials indicate significant hearing loss in deaf children.



TREATMENT



PSYCHOSOCIAL INTERVENTIONS

→ A. Early intensive behavioral and developmental interventions

- UCLA/Lovaas-based Model.
- Early Start Denver Model (ESDM)
- Parent Training Approaches



→ B. Social skills approaches

- Social Skills Training.



→ C. Behavioral interventions (bis) and cognitive behavioral therapy (cbt) for repetitive behaviors and associated symptoms

- Behavioral Therapy.
- Cognitive-Behavioral Therapy.



→ D. Interventions for comorbid symptoms

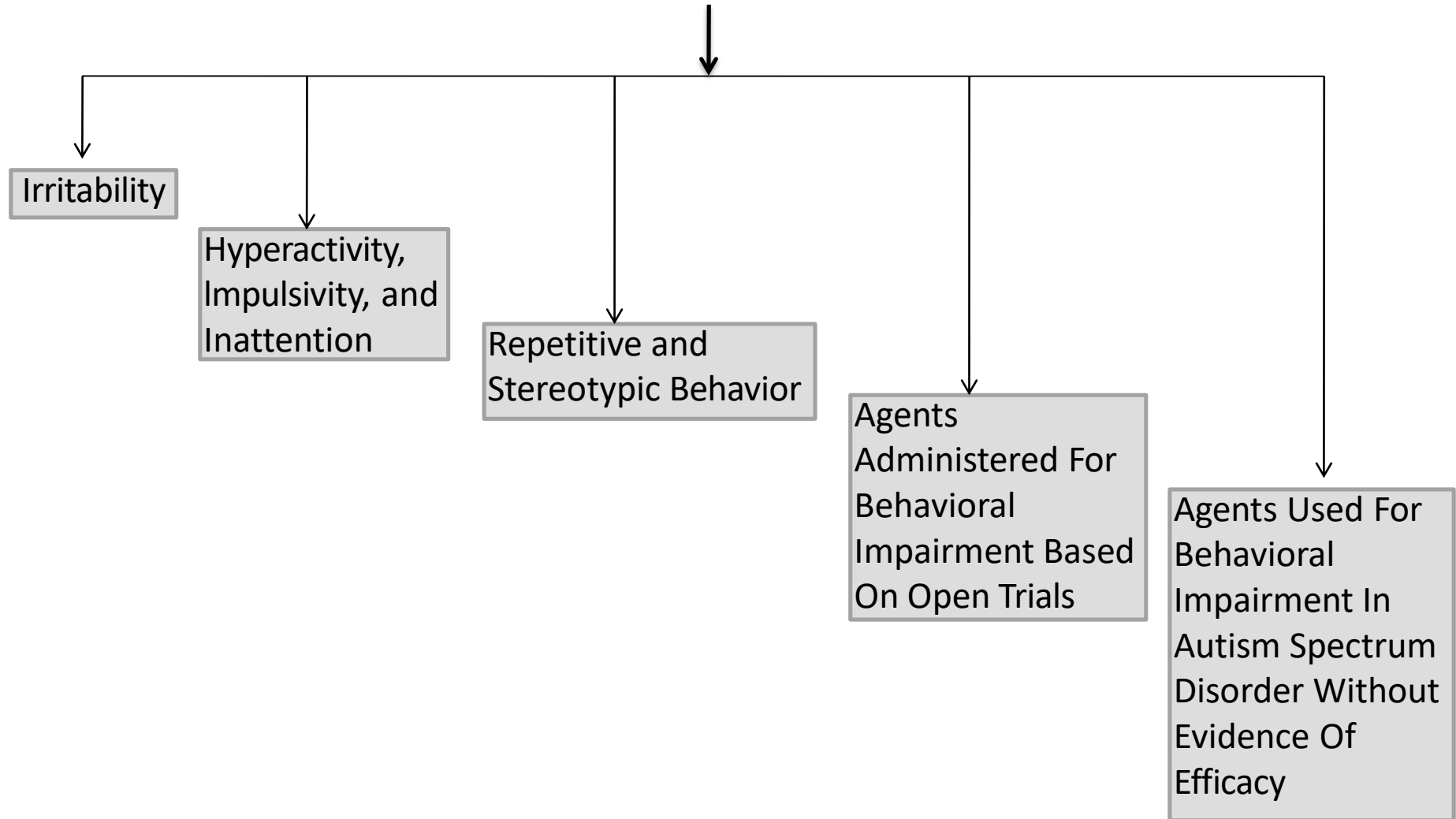
- Neurofeedback
- Management of insomnia in autism spectrum disorder

→ E. EDUCATIONAL INTERVENTIONS

- Treatment and Education of Autistic and Communication related Handicapped children (TEACCH).
- Computer-based approaches and virtual reality.



PSYCHOPHARMACOLOGICAL INTERVENTIONS



Complementary and Alternative Medicine (CAM) Approaches

- ▶ Safe interventions that have been applied to target both core and associated behavioral features include :
- ▶ music therapy, to promote communication and expression; and
- ▶ yoga, to promote attention and decrease activity level.
- ▶ Melatonin reduces sleep-onset latency in children that is deemed safe and shown to be efficacious.



THANK YOU

