APPROACH TO DEVELOPMENTAL DELAY

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DEVELOPMENTAL MILESTONES

Newborn

-Gross motor

•Lies in flexed position

•Turns head from side to side; head sags on ventral suspension

-Social/communication

•Visual preference for human face

-Visual

•Able to fixate face on light in line of vision;

•Responds to visual threats by blinking

-Reflex

•Moro, stepping, placing, and grasp reflexes are all active

1 Month

-Gross Motor
•Legs more extended
•Head lifted momentarily to plane of body on ventral suspension
•Turns head in the supine position

-Fine motor
•Hands fisted near the face

-Social/communication/problem-solving
•Begins to smile
•Gazes at black-white objects
•Prefers human face; follows moving object
•Body movements following the sound of others

-Language
•Startles to voice or sound

2 Months

-Gross motor
•Raises head slightly further in prone position
•Head sustained in plane of body on ventral suspension
•Begins to push up when lying on tummy
•Head lags when pulled to sitting position

-Fine motor
•Hands unfisted 50% of the time
•Retains an object or finger if placed in the hand
•Brings hands to mouth, and may hold hands together

-Social/communication/problem solving
•Follows moving object 180°
•Able to fixate on the face and follow it briefly
•Stares momentarily where object disappeared
•Social smile to anyone
•Turns toward sounds

-Language
•Coos and makes gurgling sounds
•Begins to act bored (crying, fussy)

3 Months

-Gross motor

•Lifts head and chest with arms in prone position

•May roll to the side

-Fine motor

•Brings hands together in the midline and to the mouth

•Open hands

•Inspects their own fingers

-Social/communication/problem solving

•Expression of dislike for a taste or a loud sound

•Social smile to known people

-Language

•Regards and vocalizes to parents when talking

•Chuckles

4 Months

-Gross motor

- Holds head steady and no head lag when pulled from lying down to sitting position (Fig. 1.3)
- May be able to roll over from front to back
- Pushes tummy, with elbows lifting the head and chest (Fig. 1.4)

-Fine motor

- Brings hands to mouth
- Uses hands and eyes together, such as seeing a toy and

-Social/communication/problem solving

- Responds to affection
- Begins to babble
- Laughs out loud
- Recognizes familiar people and things at a distance
- Likes to play with people and might cry when playing stops

-Language

- Vocalizes when alone

- **Reflexes**
- Asymmetric tonic reflex is gone
- Palmar grasp is gone

Fig. 1.3 Holds head steady and no head lag when pulled from lying down to sitting position

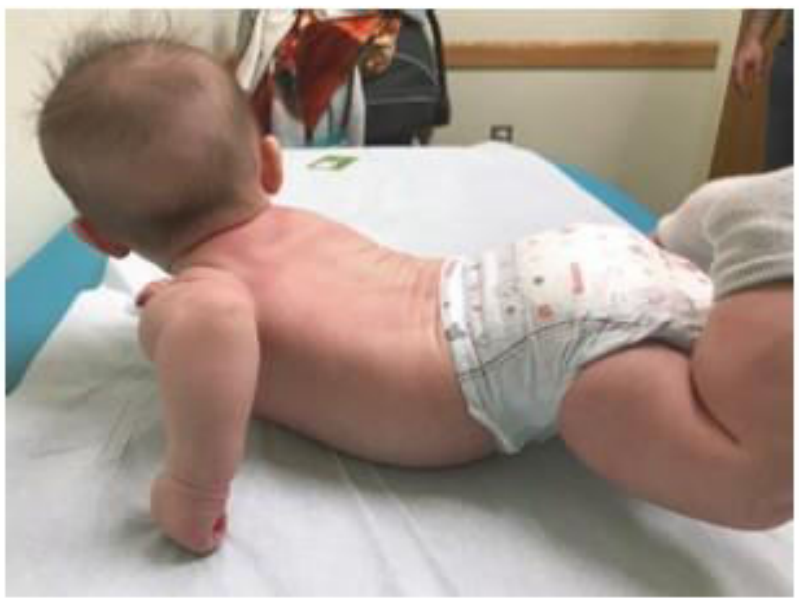


Fig. 1.4 Developmental milestone at 4 months: Pushes tummy, with elbows lifting the head and chest

6 Months

-Gross motor
- Begins to sit with minimal support
- Rolls over from back to front and front to back
- Supports weight on legs and might bounce

-Fine motor
- Transfers objects from one hand to another
- Brings objects or food to the mouth
- Places hands on the bottle
- Removes cloth on face

- Social/communication/problem-solving
- Stranger anxiety
- Responds to own name
- Responds to sounds by making sounds showing joy and displeasure

-Language
- Monosyllabic babble (babbles ba ,ma,da)
- Looks at self in mirror and smiles

7 Months

-Gross motor
- Sits steady without support (Fig. 1.5)
- Bounces when held upright
- Puts arms out to the side for balance

- Fine motor
- Radial palmar grasp

- Social/communication/problem-solving
- Explores different aspects of toy and observes toy block in each hand
- Finds partially hidden toys or objects
- Attends to sounds and music
- Prefers mother
- Inhibits to “no”

-Language
- More vowels and more variety of sounds

Fig. 1.5 Developmental milestone at 7 months: Sits steady without support

9 Months

-Gross motor

•Can get into sitting position from lying down
•Pulls to stand
•Begins to crawl (Fig. 1.6)
•Bears walk with all limbs straight

Fig. 1.6 Developmental milestone at 9 months: Begins to crawl

-Fine motor

•Radial-digital grasps of a block
•Bangs 2 blocks together
•Bites and chews cookie
•Inspects and rings a bell

-Social/communication/problem-solving

•Separation anxiety
•Recognizes familiar people
•May be afraid of strangers
•Uses sound to get attention
•Plays peek-a-boo
•Orients to name well

-Language

•Says “mamama” and “bababa” nonspecific
•Copies sounds and gestures of others

12 Months

-Gross motor

•Walks with one hand held
•Pulls up to stand, walks holding on to furniture (“cruising”)
•May stand alone and make a few steps without holding (Fig. 1.7)

-Fine motor

•Fine pincer grasps of pellet
•Holds crayon and scribbles after demonstration
•Attempts tower of 2 blocks
•Finger feeds part of a meal
•Takes off a hat
•Puts out arm or leg to help with dressing
•Rattles spoon in a cup
•Puts a toy in a container, takes it out of the container

-Social/communication/problem-solving

•Shows parents object to share interest
•Follows one-step command with a gesture
•Looks at the right picture or thing when it is named
•Points to get desired object (proto-imperative pointing) and to share interest
•Uses several gestures when vocalizing (e.g. waving , reaching)

-Language

•Says a few words, including “mama,” “dada,” +3 words

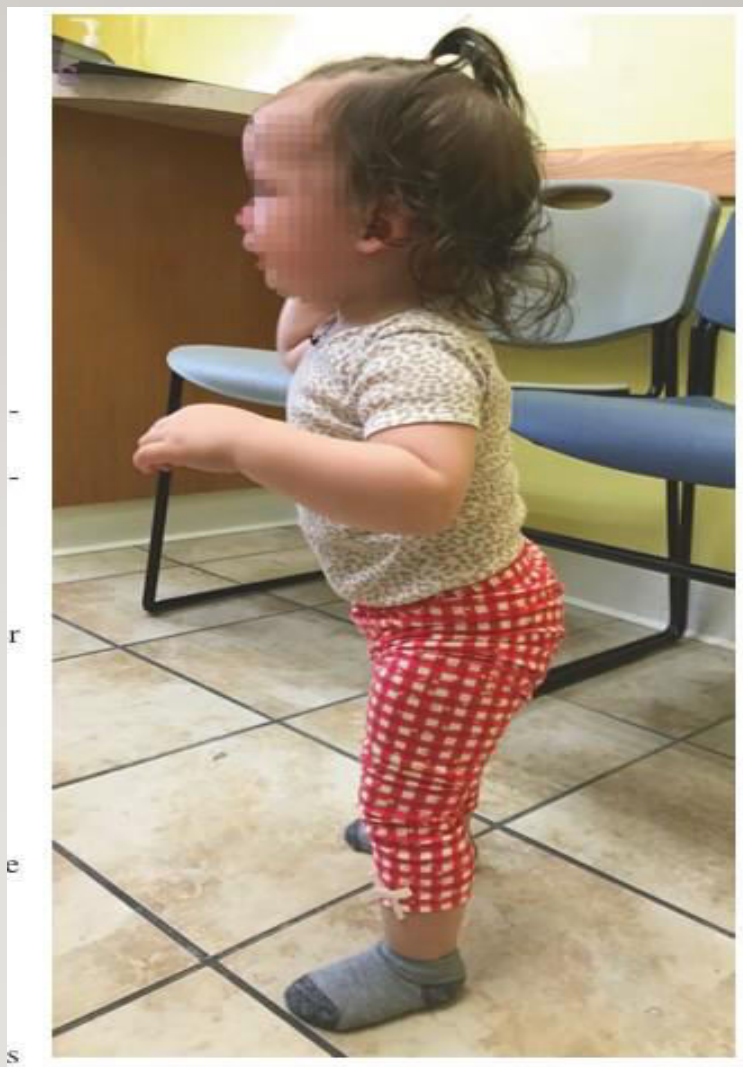


Fig. 1.7 Developmental milestone at 12 months: May stand alone and make a few steps without holding

14 Months

-Gross motor
- Walks well
- Stands without pulling

-Fine motor
- Imitates back and forth scribbling
- May add the third block to a 2-block tower
- Removes socks and shoes
- Chews well
- Puts a spoon in the mouth upside down

-Social/communication/problem-solving
- Points at an object to express interest (proto-declarative pointing)
- Purposeful exploration of toys through trial and error
- Follows one-step commands without gesture

- Language
- Names one object

15 Months

-Gross motor
- Stoops to pick up an object from the floor
- Runs stiff-legged
- Climbs on furniture and may be able to creep upstairs

-Fine motor
- Builds 3- to 4-block tower
- Places 10 blocks in a cup
- Drinks from a cup
- Eats with a spoon with some spilling
- Places circle in a single-shape puzzle
- Turns pages in a book

-Social/communication/problem-solving
- Hugs parents in reciprocation
- Shows empathy (may cry when someone else is crying)
- Recognizes without demonstration that a toy requires activation, then hands it to an adult if it cannot operate
- Points to one body part
- Gets an object from another room upon demand

-Language
- Uses 3–5 words

18 Months

-Gross motor
•Runs well
•Creeps downstairs
•Gets onto a chair without assistance

-Fine motor
•Throws a ball while standing
•Makes 4-block tower
•Can help undress him/herself
•Eats with a spoon
•Matches pairs of objects

- Social/communication/problem-solving
•Plays simple pretend, such as feeding a doll
•Points to 2 of 3 objects when named and 3 body parts
•Points to familiar people with the name
•Understands “mine”

-Language
•Uses 10–25 words
•Imitates animal sounds
•Names object in one picture on demand

24 Months

- Gross motor
•Walks upstairs and downstairs holding rail
•Kicks a ball
•Throws ball overhand
•Stands on tiptoes

-Fine motor
•Makes a single line of blocks
•In drawing, imitates horizontal line
•Begins to sort shapes and colors
•Opens door using the knob
•Takes off clothes without buttons
•Eats with a spoon without missing
•Builds a tower of 6 blocks
•Parallel play

-Social/communication/problem-solving
•Begins to mask emotions for social etiquette
•Follows 2-step instructions or commands such as “Sit on your chair and eat your food”
•Points to 5–10 objects in pictures
•Listen to stories

-Language
•Uses 2-word sentence
•Uses 50 or more words

3 Years

-Gross motor

•Walks up and down stairs, 1 foot on each step ,no rails
•Climbs well
•Ride a tricycle (3-wheeled bike)
•Balances on 1 foot for 3 seconds

-Fine motor

•Copies a circle with pencil or crayon
•Can work toys with buttons, levers, and moving parts
•Screws and unscrews jar lids and turns door handle
•Understands what “2” means
•Imitates bridge of blocks
•Independent eating
•Puts on shoes without laces and able to unbutton clothing
•Draws man with 2 to 3 parts

Social/communication/problem-solving

•Understands long/short, big/small, more/less
•Knows own gender and age
•Follows 3-step instructions or commands
•Fears imaginary things
•Play with others

-Language

•Uses words to describe what someone else is thinking (“Dad thought I was crying”)
•Names body parts with function
•Uses 3-word sentences
•Says words like “I,” “me,” “we,” and “you” and some plurals (“cars”, “dogs,” “cats”)
•Names body parts by use

4 Years

-Gross motor

•Balances on 1 foot for 8 seconds
•Hops and stands on 1 foot up to 2 seconds

-Fine motor

•Throws ball overhand more than 3 yards
•Catches a bounced ball most of the time
•Copies a square
•Goes to the toilet alone
•Wipes after a bowel movement
•Draws man with 4 to 6 parts

-Social/communication/problem solving

•Group play
•Follows 3-steps commands and instructions
•Tells story and accurately counts 4 pennies

-Language

•Knows some basic rules of grammar, such as correctly using “he,” “she,” “his,” “her”
•100% intelligible speech

5 Years

-Gross motor
•Walks downstairs with rail, alternating feet
•Skips

-Fine motor
•Copies a triangle
•Cuts with scissors
•Builds stairs with blocks from model
•Dresses and undresses, ties shoes

-Social/communication/problem-solving
•Apologizes for mistakes
•Draws man with 8 to 10 parts
•Names 10 colors and counts to 10, counts 10 pennies correctly

-Language
•Knows right from left
•Asks questions about the meanings of words and responds to questions
•Repeats 6 to 8 words in sentences

6 Years

-Gross motor
•Tandem gait (heel-to-toe walks)

-Fine motor
•Builds stairs from memory
•Copies a diamond shape
•Writes first and the last name

- Social/communication/problem-solving
•Has a best friend of same gender
•Looks both ways at street when crossing
•Draws man with 12–14 parts
•Able to do simple additions and subtractions

- Language
•Knows days of the week
•Able to describe events in sequence

Primitive reflexes : are reflexes that are normally present during infancy and disappear with the development of inhibitory pathways to the subcritical motor areas (usually within the 1st year of life).

- Primitive reflexes persistence:
- In children; : indicates impaired brain development
- In adults; : suggests frontal lobe lesions .

Primitive reflexes

- **Moro** is absent around **3–4 months** of age
- **Palmar** grasp absent **around 2–3 months** of age
- **Parachute** starts around **6–9 months** of age

Hand Grip

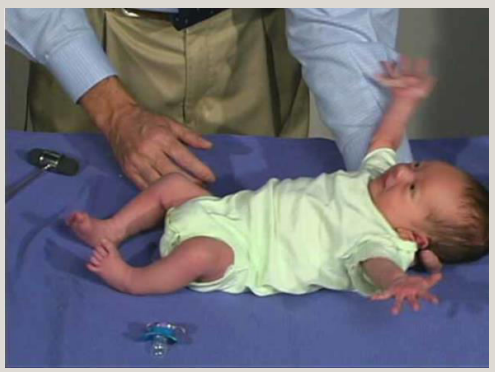
●Grasps object placed in palm/ 5-6 m

Sucking reflex

● when roof of mouth Is touched /4m

Moro reflex

●Extend arms when startled/ 5-6m



Rooting reflex

●Turn heard toward side of cheek stimulus / 2-3 m

Galant reflex

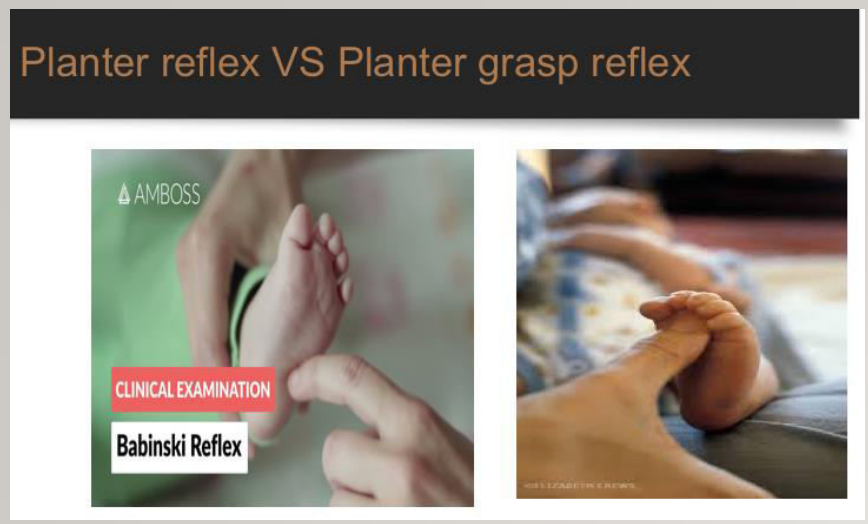
●Stroke spine on side, baby swings torso toward touch / 2-6 m

Parachute reflex

●when the child is held upright and the baby's body is rotated quickly to face forward (as in falling),The baby will extend their arms forward as if to break a fall

Landau reflex

●when held in a horizontal prone position, the infant maintains a convex arc with the head raised and the legs slightly flexed/ 12 –24 m.



Following objects

- 1 month: Follows to the midline
- 2 months: Follows past midline
- 3 months: Follows 180°
- 4 months: Circular tracking 360°

Speech intelligibility

- 50% intelligible at 2 years
- 75% intelligible at 3 years
- 100% intelligible at 4 years

Language: receptive

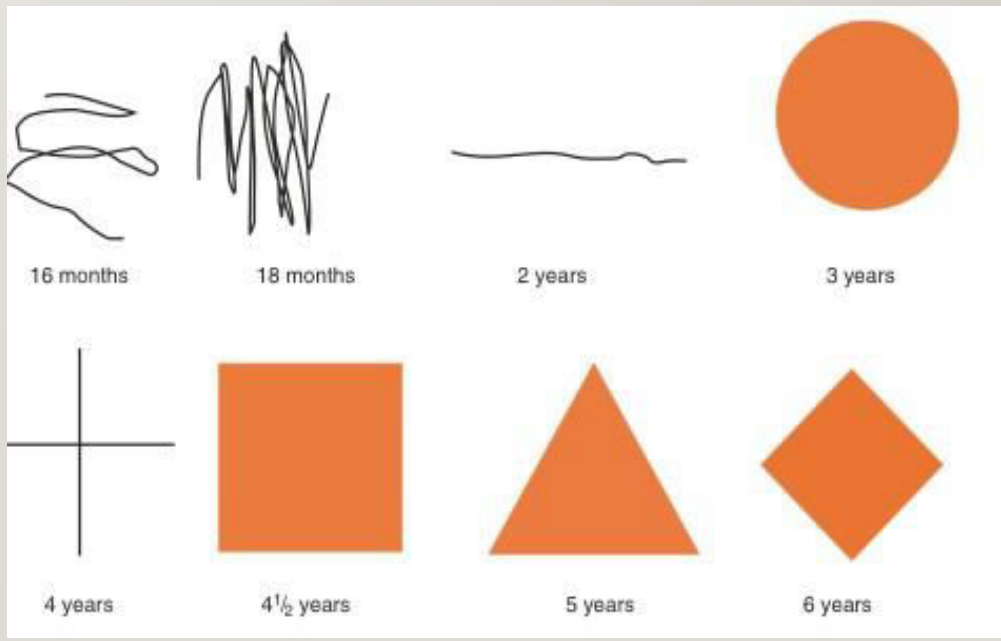
- 1 month– Startles to voice or sound
- 2 months– Alerts to voice or sound
- 4 months– Orients head to the direction of a voice or sound
- 8 months– Responds to parents
- 9 months– Orients attentively to his or her name
- 10 months– Waves “bye-bye” in return
- 12 months– Follows one-step command with a gesture
- 14 months– Follows one-step command without a gesture

Language: expressive

- Coos– 2 months (2–4 months)
- Laughs out loud– 4 months
- Babbles– 6 months
- “Mama” or “dada” non specific – 9 months
- “Mama” and “dada” specific , plus a few words– 12 months
- Vocabulary of 10–25 words– 18 months
- Two-word sentences– 2 years (18–24 months)
- Three-word sentences – 3 years (2–3 year)
- Four-word sentences – 4 years (3–4 year)

Drawing

- Scribbles spontaneously– 16 months
- Imitates vertical lines– 18 months
- Imitates horizontal lines– 2 years
- Circle– 3 years
- Cross– 4 years
- Square– 4.5 years
- Triangle– 5 years
- Diamond– 6 years



Social skills

•Reciprocal smiling– 2 months
•Follows the person who is moving across the room– 3 months
•Smiles spontaneously at a pleasurable sight/sound– 4 months
•Recognizes caregiver socially– 5 months
•Stranger anxiety– 6 months
•Separation anxiety; gaze follows caregiver's pointing to object, "Oh, look!"– 9 months
•Waves "bye-bye" in return– 10 months
•Shows objects to parents to share interests– 12 months
•Parallel play– 2 years
•Reduction in separation anxiety– 28 months
•Cooperative play– 3–4 years
•Ties shoelaces– 5 years
•Distinguishes fantasy from reality– 6 years

Walking and running

•Independent steps– 12 months
•Walks well– 14 months
•Runs stiff-legged– 15 months
•Runs well– 18 months
•Kicks ball without demonstration– 2 years
•Skips and walks backward heel-toe– 5 years
•Heel to toe walks (tandem gait)– 6 years

Climbing stairs

•Creeps upstairs– 15 months
•Creeps downstairs– 18 months
•Walks downstairs holding rail, both feet on each step– 2 years
•Goes up stairs, alternating feet, no rail– 3 years
•Walks downstairs with rail, alternating feet– 5 years

MOTOR RED FLAGS

Newborn
Hypotonia and feeding difficulty

2 months
Unable to hold head up when pushing up when on tummy

4 months
Unable to hold head steady
Unable to bring things to the mouth
Persistent fisting (a predictor of neurological dysfunction)

6 months
Unable to pass an object from one hand to another and does not try to reach an object Floppy like a rag doll

9 months
Unable to sit, not rolling

12 months
Unable to stand or bear weight on legs when supported Unable to crawl

15 months
Unable to do pincer grasps

18 months
Unable to walk

24 months
Unable to walk well

36 months
Unable to climb stairs well and frequent falling

4 years
Unable to jump in place

5 years
Unable to draw pictures, a cross, or a square Poor balance

6–12 years
Unable to skip or hop on one foot Unable to write name

All ages
Loss of skills they once had

LANGUAGE AND SOCIAL RED FLAGS

- Newborn
- Does not respond to loud sounds
- 2 months
- Does not alert to voice, lack of looking at faces Does not watch things as they move
- 4 months
- Does not coo or make sounds Does not smile at people
- 6 months
- Does not turn toward sounds; no smiling or laughing , or expression
- 9 months
- Does not babble (“mama,” “baba,” “dada”)
- 12 months
- Does not respond to name Does not understand “no”
- Indifferent or resistant attachment to the caregiver Does not look where caregiver points
- 15 months
- Does not use words “mama,” “papa,” “dada” Does not point to the desired object
- 18 months
- Does not gain new words Does not have at least 6 words
- Does not point to show things to other or share interest

24 months
Unable to use two-word phrases (e.g., “drink water”) Unable to follow simple instructions
Unable to imitate actions or words Unable to maintain eye contact

36 months
Unable to use a three-word sentence Unable to pretend, play, or make-believe

4 years
Unable to speak clearly
Unable to answer simple questions
Unable to use pronouns (“I”, “me”, “you”, “he”, and “she”) correctly Ignores other children or does not respond to people outside the family

5 years
Unable to use plurals or past tense properly Unable to recognize shapes, letters, colors
Unable to brush teeth, use toilet, wash and dry hands, or get undressed without help
Unable to distinguish between reality and fantasy
Shows extreme behavior (unusually fearful, aggressive, shy, or sad)

6–12 years
Unable retell or summarize a story Unable to name friends
Unable to recognize the feelings of others

All ages
Loss of skills they once had

DISORDERS OF DEVELOPMENT

- Developmental and behavioral problems are a common category of problems in pediatrics.
- In 2008, 15% of children ages 3-7 had a developmental disability and others had behavioral disabilities.
- It is necessary to monitor development and screen for the presence of these problems for the purpose of early detection and management.

DEVELOPMENTAL DELAY

- Developmental delay is defined as the failure to achieve the milestone at the limit age
- The limit age is the age at which a skill should have been achieved (2SD from the mean)

DEVELOPMENTAL DEVIANCE

- Developmental deviance is the acquisition of milestones in a sequence that is different from usual
- An example of this can be seen in conditions such as cerebral palsy, in which the infant rolls over early secondary to increased extensor tone

DEVELOPMENTAL DISSOCIATION

- Dissociations arise when a child has widely differing rates of development in different developmental domains.
- For example, children with autism often have typical gross motor development but significantly delayed language development; therefore language development has dissociated from gross motor development

DEVELOPMENTAL REGRESSION

- Developmental regression is when a child loses a certain developmental skill they previously acquired.
- It is less common than the other patterns
- It should cause greatest concern since it is often associated with serious neurological and inherited metabolic disorders

DEVELOPMENTAL DELAY

Can be:

1- Delay in a specific domain or global developmental delay (significant delay in 2 or more areas of development)

2- Transient of persistent

TRANSIENT DEVELOPMENTAL DELAY

- It can occur in extremely premature infants who may show delay for a period of time but then progress on at a normal rate
- Other causes of transient delay may be related to physical illness, family stress or lack of opportunities to learn.

PERSISTENT DEVELOPMENTAL DELAY

If the delay in development persists it is usually related to problems in one or more of the following areas:

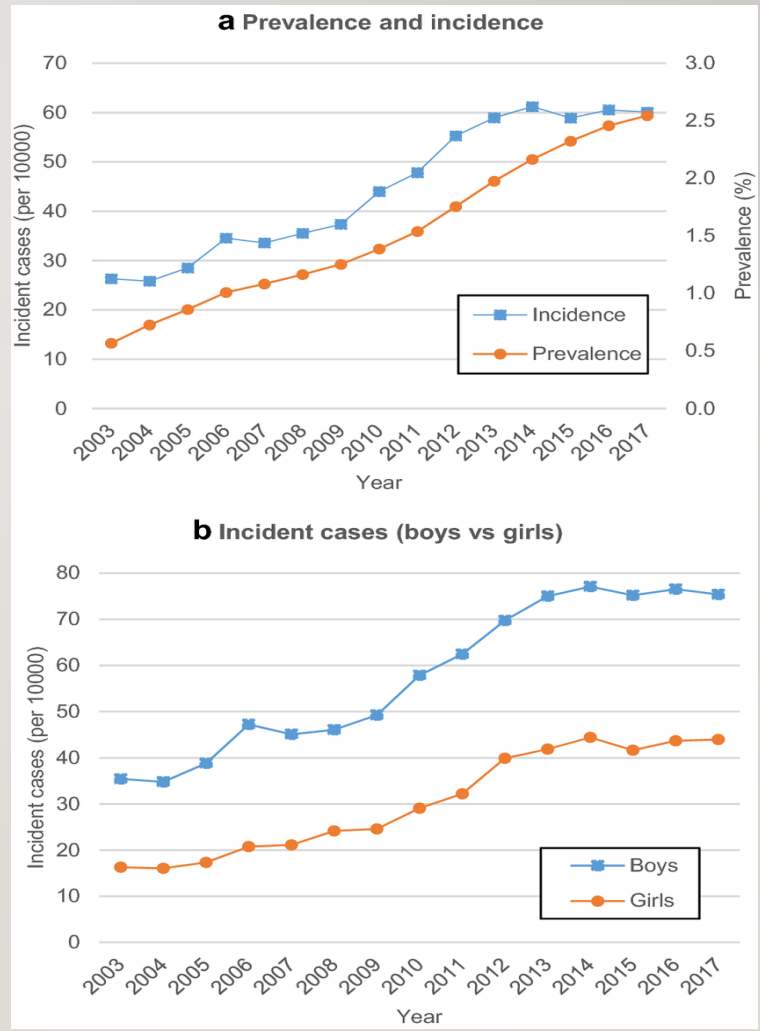
- ☐ understanding and learning
- ☐ moving
- ☐ communication
- ☐ hearing
- ☐ seeing.

◦ An assessment is often needed to determine what area or areas are affected.

◦ Disorders which cause persistent developmental delay are often termed developmental disabilities.

EPIDEMIOLOGY OF DEVELOPMENTAL DISORDERS

- This study identifies a trend in the presence and incidence, using nationwide population based data to analyse the characteristic of children with developmental disorders form 2003 to 2017
- The prevalence of developmental disorders has been increasing worldwide.
- The study showed that boys had higher incidence than girls throughout the period.



- In another study, prevalence of developmental disorders among children in the US between ages 3 and 17 increased by more than 2%, from 12.84 to 15.04%, over a period of 14 years.
- Although various causes, such as changes in diagnostic criteria, research methodology, environmental factors or diagnostic awareness, were suggested to explain this phenomenon, many researchers agree that the prevalence is increasing.

ETIOLOGY

- An etiology can be defined in 70% of patients with developmental disorders.
- In developed countries, antenatal factors predominate
- In the developing world, perinatal and postnatal factors are more common

WHY IS IT IMPORTANT TO FIND THE CAUSE?

- The family gains understanding of the condition, including prognostic information
- Lessens parental blame
- Prevents co morbidity by identifying factors likely to cause secondary disability that are potentially preventable e.g by surveillance of other systems such as hearing and vision
- Appropriate genetic counselling about recurrence risk for future children
- To address concerns about possible causes e.g events during pregnancy or delivery
- Potential treatment for a few conditions

ANTENATAL

- Syndromes (fragile X, Rett syndorme)
- Chromosomal disorders (down syndrome)
- Intrauterine infections (TORCH)
- Inborn errors of metabolism (aminoacidopathy, mitochondrial disorder, urea cycle disorder)
- Teratogen exposure
- Fetal alcohol syndrome

PERINATAL, NEONATAL

- Hypoxic ischemic encephalopathy
- Kernicterus
- Hypoglycaemic brain injury
- Hypothyroidism
- Post meningitis or encephalitis
- Post head trauma

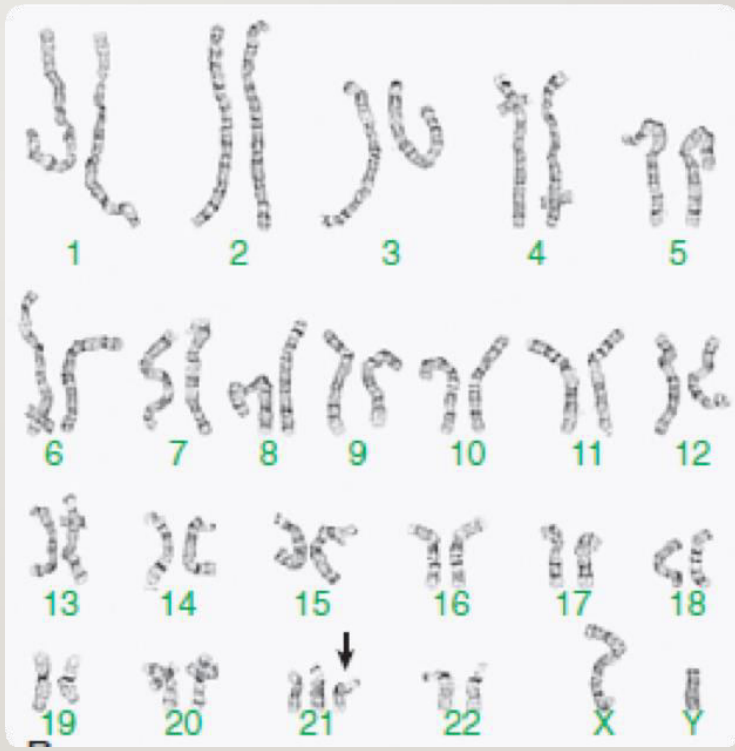
POSTNATAL

- Deficiency of vitamin B12, iodine
- Exposure to toxins (lead)
- Environmental causes; children in neglectful, abusive, under-stimulated environment may not show normal development

Disorders With Developmental Delay

- Down Syndrome
- Rett syndrome
- Fragile X-syndrome
- Congenital Hypothyroidism

Down syndrome
“ Trisomy 21 “



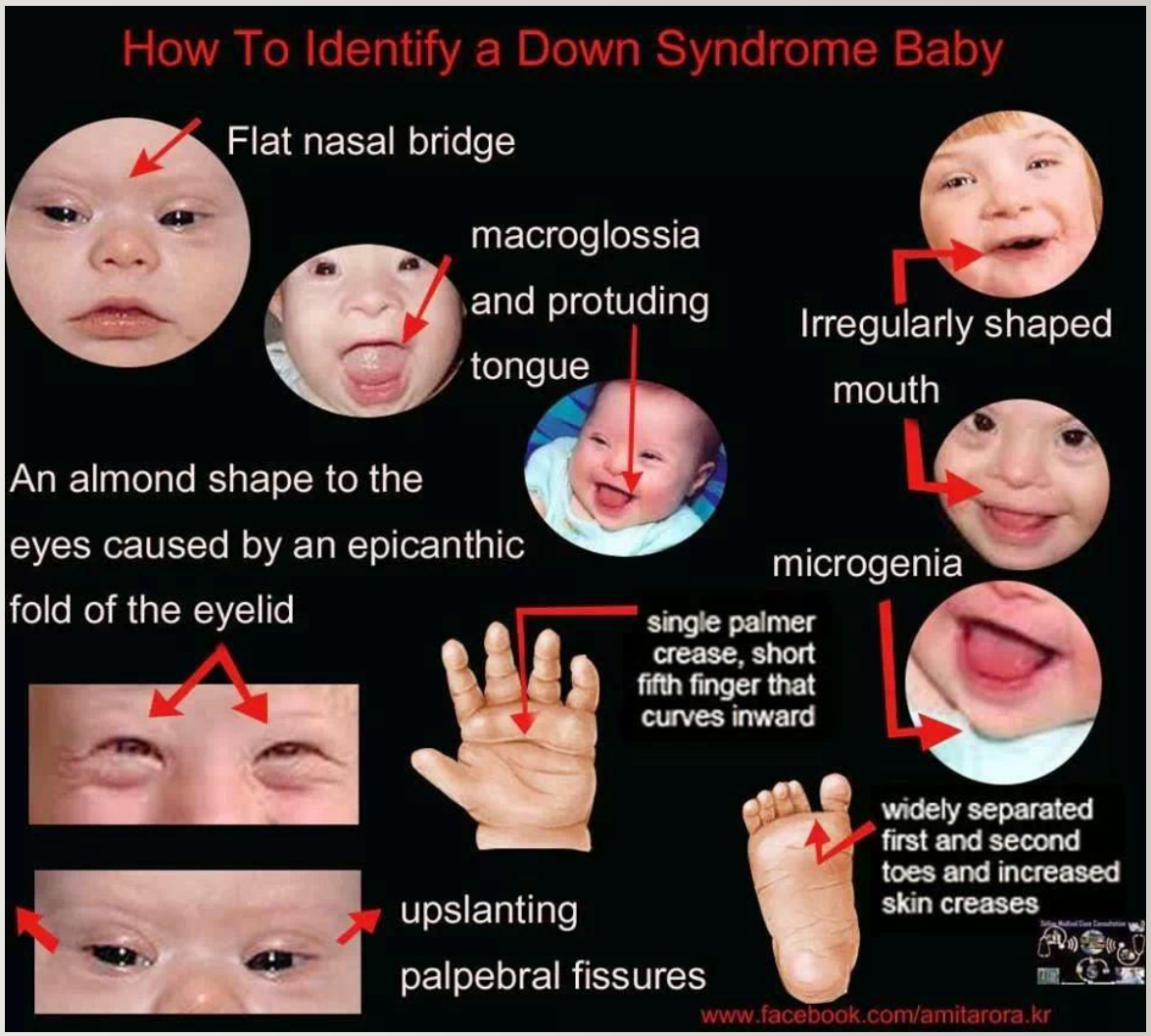
DOWN SYNDROME

1. The most common viable chromosomal disorder
2. Trisomy 21 is the most common genetic cause of moderate mental retardation.
3. The incidence of Down syndrome in live births is approximately 1 in 733
4. The life expectancy for children with Down syndrome is reduced (approximately 50-55 yr.)
5. Infants have normal birth weight and length
6. Usually have developmental delay, hypotonia, Poor Moro reflex
7. Developmental impairment becomes apparent in the first year of life. In general, the average age of sitting (11 months), creeping usually at (17 months), walking at 26 months which is approximately twice the typical age

DOWN SYNDROME

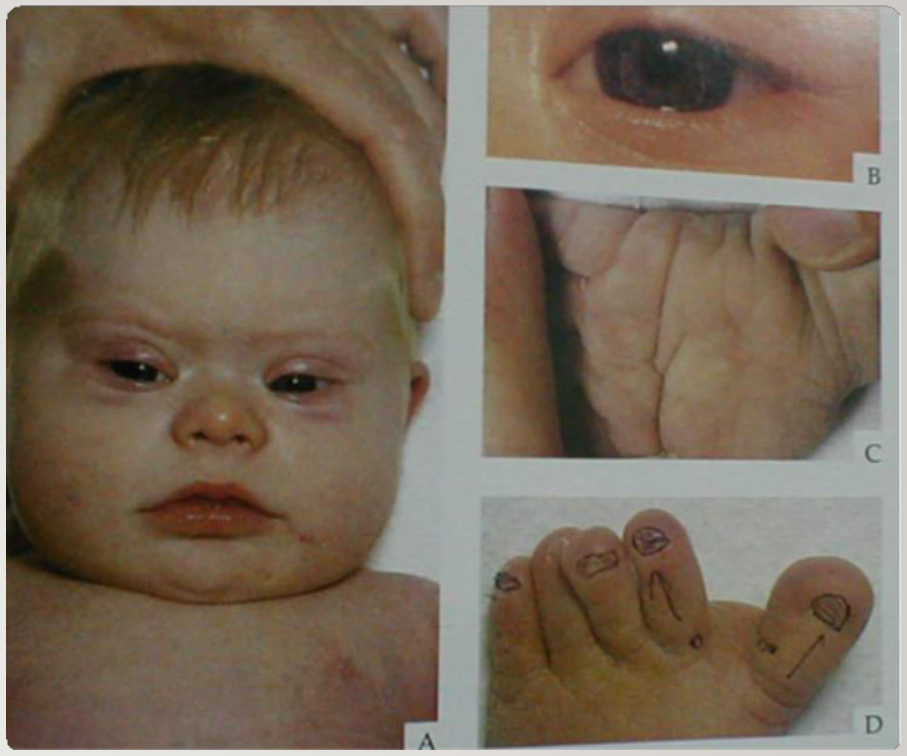
Common characteristics and facial appearance

- Brachycephaly
- Flattened occiput
- Hypoplastic midface
- Macroglossia
- Flattened nasal bridge
- Upward slanting palpebral fissures
- Epicanthal folds
- Small Low set ears
- Large protruding tongue
- Short broad hands often with a transverse palmar crease
- clinodactyly
- Wide gap between the first and second toes
- Severe hypotonia may cause feeding problems and decreased activity
- Brushfield spot in iris and Heterochromia

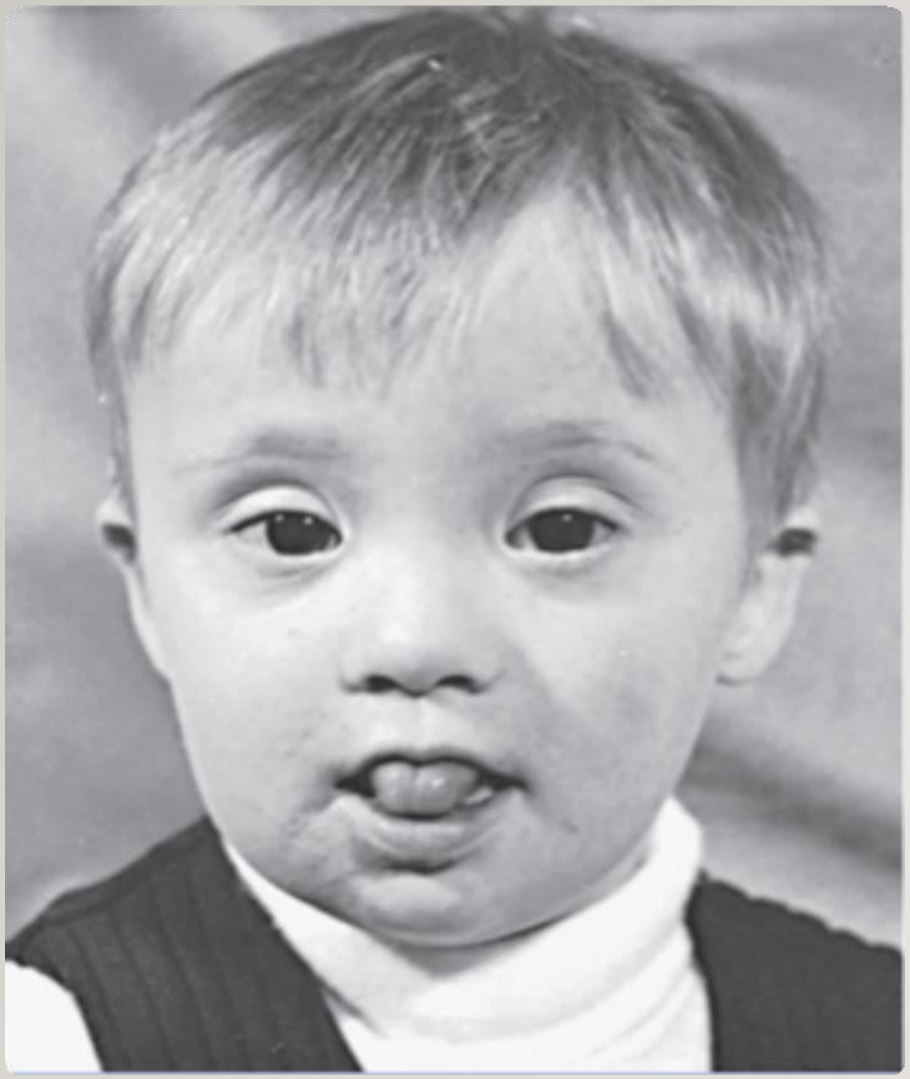


Complications:

- Neuropsychatric : (autism, disruptive behaviour, depression, alzheimer disease)
- Musculoskeletal : (atlantoaxial instability, hip dysplasia, Slipped capital femoral epiphyses, joints dislocations
- Congenital heart disease
- Endocardial Cushing defects
  - ASD, VSD
- Structural abnormalities of the bowel (eg. duodenal atresia)
- Central hypotonia
- Delayed closure of fontanels
- Statistically increased risk for leukemia, Alzheimer disease, hypothyroidism



Down syndrome



CENTRAL NERVOUS SYSTEM
Hypotonia*
Developmental delay
Poor Moro reflex*
CRANIOFACIAL
Brachycephaly with flat occiput
Flat face*
Upward slanted palpebral fissures*
Epicanthal folds
Speckled irises (Brushfield spots)
Three fontanels
Delayed fontanel closure
Frontal sinus and midfacial hypoplasia
Mild microcephaly
Short hard palate
Small nose, flat nasal bridge
Protruding tongue, open mouth
Small dysplastic ears*
CARDIOVASCULAR
Endocardial Cushing defects
Ventricular septal defect
Atrial septal defect
Patent ductus arteriosus
Aberrant subclavian artery
Pulmonary hypertension
MUSCULOSKELETAL
Joint hyperflexibility*
Short neck, redundant skin*
Short metacarpals and phalanges
Short 5th digit with clinodactyly*
Single transverse palmar creases*
Wide gap between 1st and 2nd toes
Pelvic dysplasia*
Short sternum
Two sternal manubrium ossification centers
GASTROINTESTINAL
Duodenal atresia
Annular pancreas
Tracheoesophageal fistula
Hirschsprung disease
Imperforate anus

Diagnosis:

- Through pregnancy
  - All women should be offered screening for Down syndrome in their 2nd trimester by quad screen : 4 maternal serum tests (free β-human chorionic gonadotropin (β-hCG), unconjugated estriol, inhibin, and α-fetoprotein).
  - Screening during the 1st trimester by fetal U/S of nuchal translucency thickness
  - Cytogenetic testing is diagnostic through chorionic villus sampling

Rett syndrome

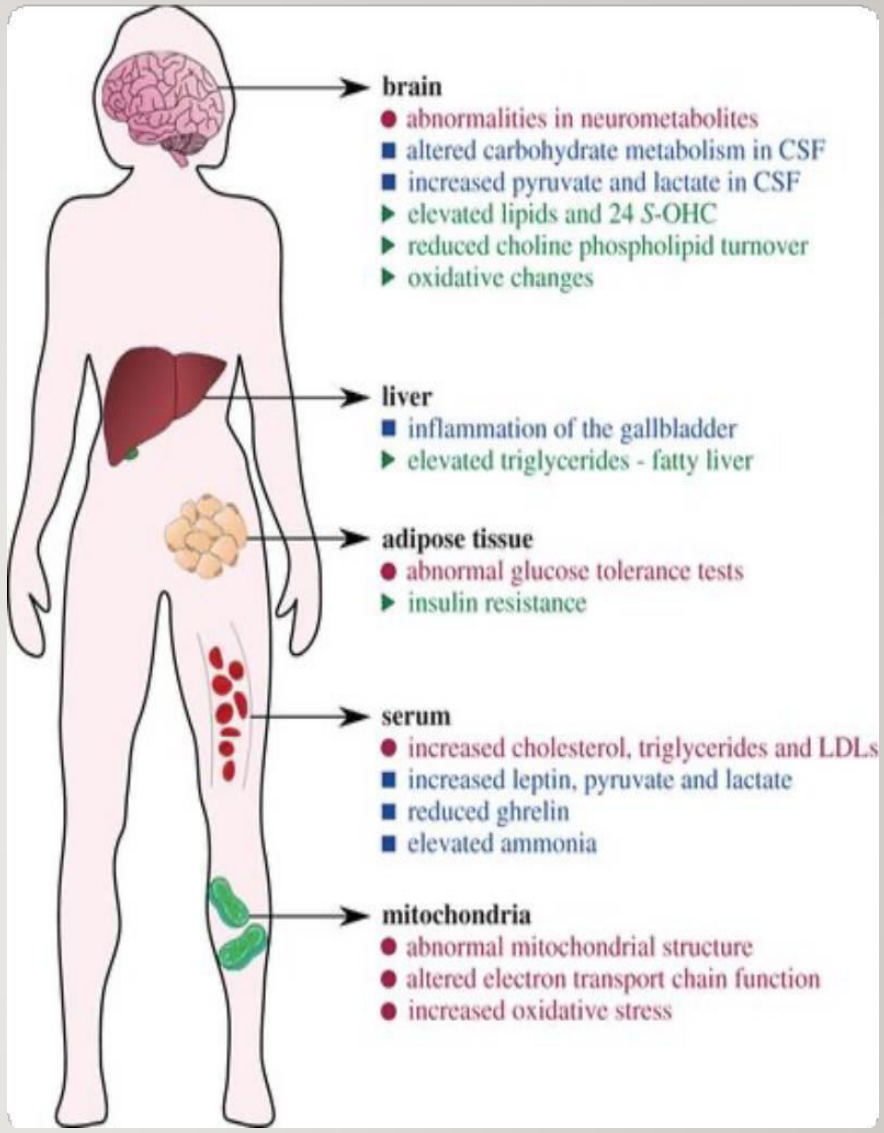
Rett syndrome is a neurodevelopmental disorder that affects girls almost exclusively.

- develop normally initially, then gradually loose speech, purposeful hand use after 18 months of age.
- deceleration in head growth.
- mutation in MECP2 gene.
- After Down syndrome, Rett syndrome is believed to be the most common cause of developmental delay in females.

Rett syndrome

Early signs usually appear from as early as the first 6-18 months, including:

- Low muscle tone (hypotonia)
- Difficulty feeding, swallowing typical size/texture food for their age
- Unusual, repetitive hand movements or jerky limb movements
- Delay with development of speech
- Mobility problems, such as problems sitting, crawling and walking
- Periods of distress, irritability, agitation, screaming for no obvious reason
- Constipation, causing stomach aches and distress
- Slowing of head growth compared to typical peers



DIAGNOSTIC CRITERIA

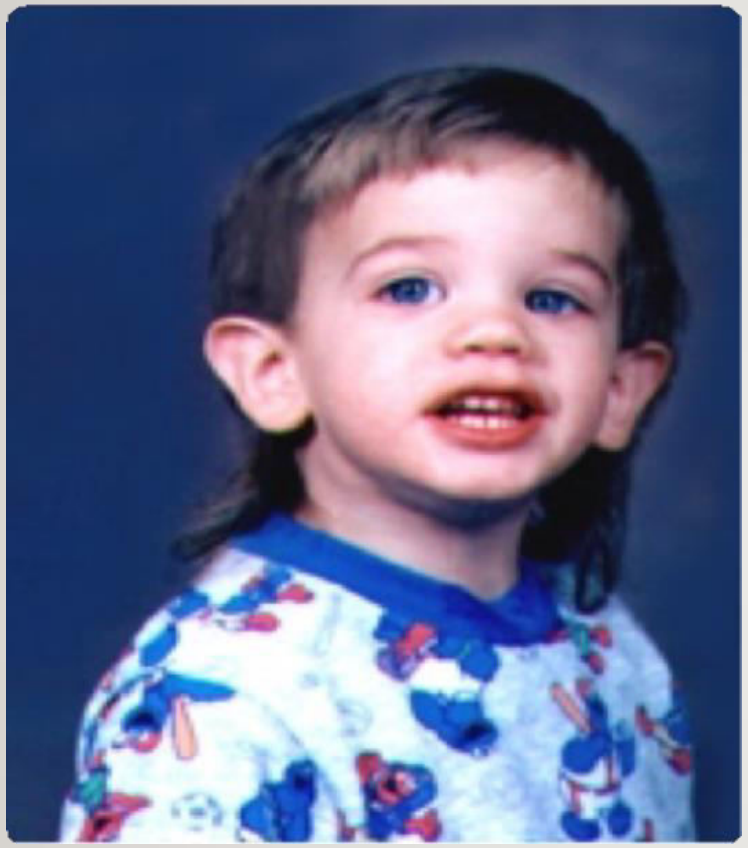
Main criteria	Supportive criteria
1. Partial or complete loss of acquired purposeful hand skills	1. Breathing disturbances
2. Partial or complete loss of acquired spoken language	2. Bruxism when awake
3. Gait abnormalities: dyspraxic gait or inability	3. Impaired sleep pattern
4. Stereotypic hand movements	4. Abnormal muscle tone
	5. Peripheral vasomotor disturbances
	6. Scoliosis/kyphosis
	7. Growth retardation
	8. Small cold hands and feet
	9. Laughing/screaming spells
	10. Diminished response to pain
	11. Intense eye communication
	Exclusion criteria
	• Brain injury secondary to trauma, neurometabolic disease, or severe infection
	• Grossly abnormal psychomotor development in first 6 months of life
Required for classical (typical) Rett syndrome	
• Regression followed by recovery or stabilization	
• All main criteria and exclusion of other etiology	
• Supportive criteria not required	
Required for variant (atypical) Rett syndrome	
• Regression followed by recovery or stabilization	
• At least two of the four main criteria	
• Five out of eleven supportive criteria	

Note: According to revised diagnostic criteria and nomenclature of RettSearch Consortium 2010.[3]

genetic testing (DNA analysis)

Testing for changes in the MEPC2 gene confirms the diagnosis.

FRAGILE X-SYNDROME

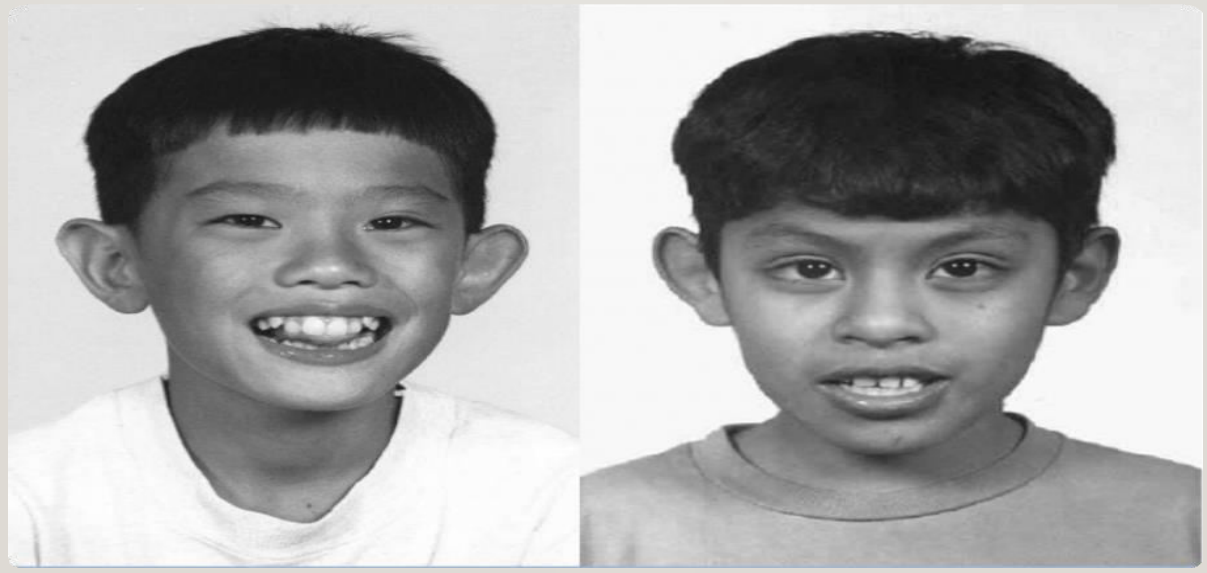


Fragile X- syndrome

- X linked dominant disorder
- Fragile X accounts for 3% of males with mental retardation.

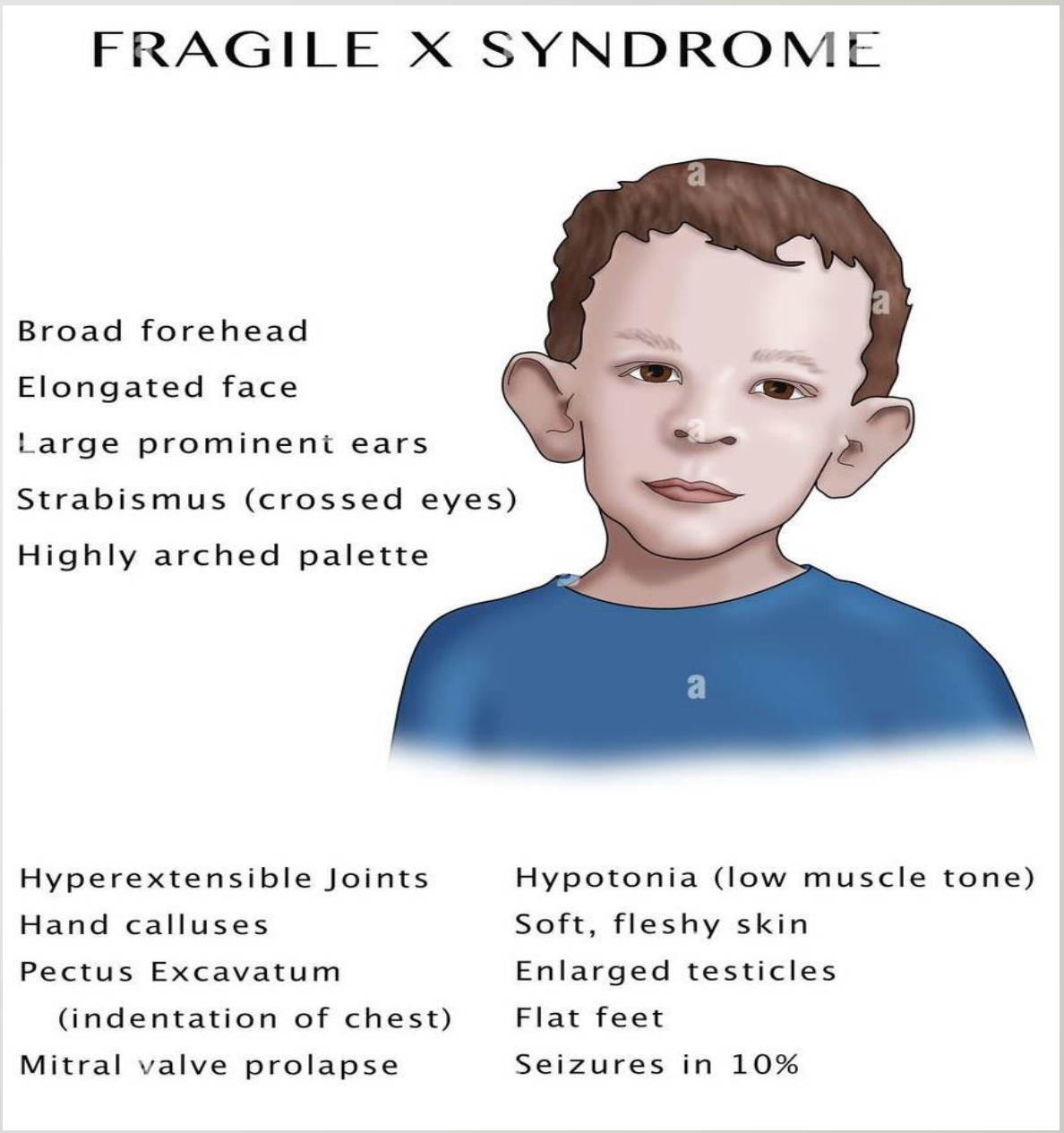
- The main clinical manifestations in affected males are mental retardation, autistic behavior, macro-orchidism (which may not be evident until puberty), and characteristic facial features

- Females affected with fragile X show varying degrees of mental retardation and/or learning disabilities.



Fragile x syndrome may presents with :

- Post-pubertal marcroorchidism
- Long face with large jaw
- Large everted ears
- Autism
- Mitral valve prolapse
- Hypermobile joints

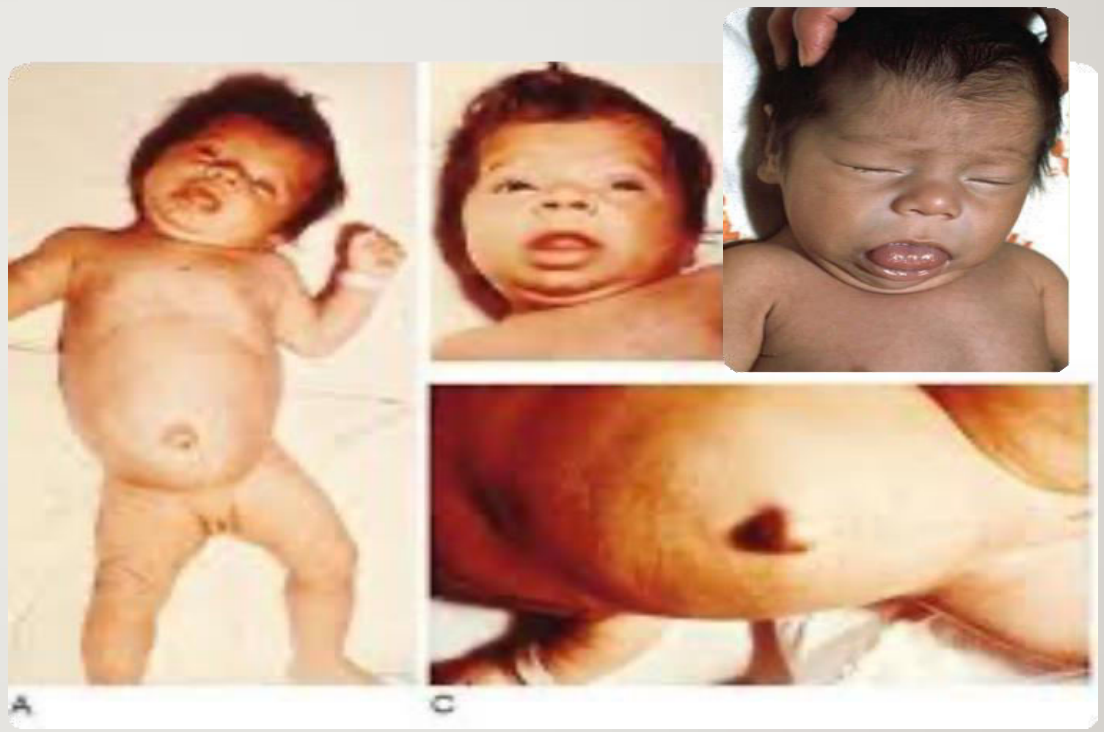


CONGENITAL HYPOTHYROIDISM

Congenital hypothyroidism is is one of the most common preventable causes of intellectual disability (mental retardation).As Thyroid hormones are essential for normal myelination and the development of CNS

Risk factors:

- Prematurity
- Multiple gestations
- Babies of old age mothers
- Asians and hispanics
- Down syndrome



Clinical manifestations:

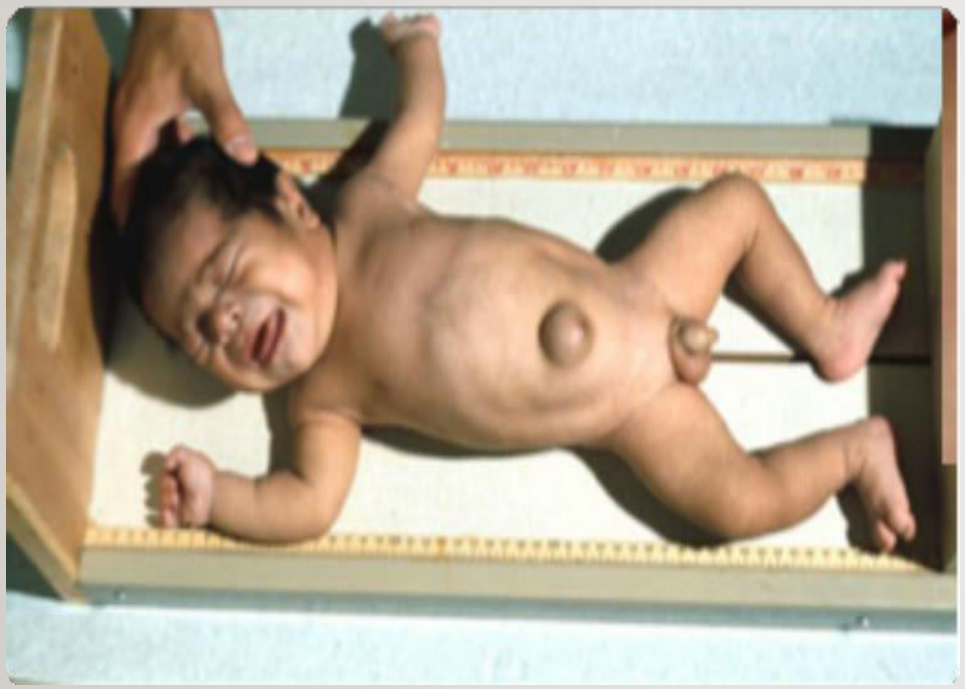
- Respiratory distress
- Large posterior fontanelle
- Abdominal distention
- Lethargy and poor feeding
- Prolonged Jaundice (may be the earliest sign)
- edema
- Umbilical hernia
- Mottled skin
- Constipation
- Dry skin
- Hoarse cry(cry little.sleep much,poor appetite)

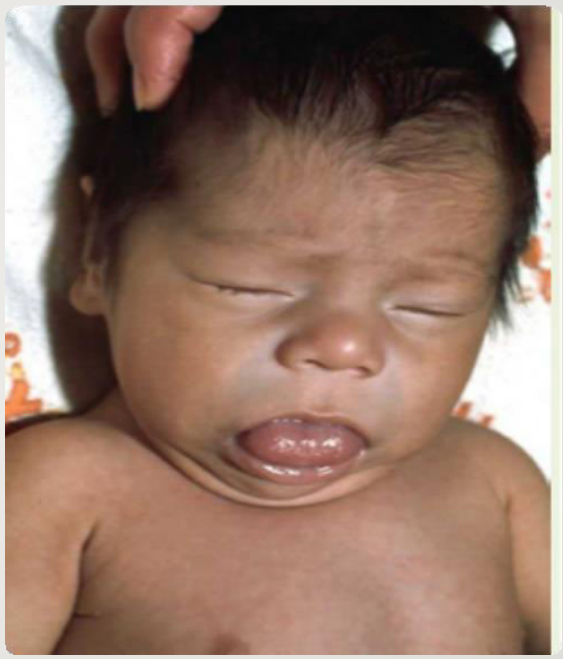
By age 3-6months the clinical picture is fully developed

- Growth is stunted,extremities are short. Head size normal or increased
- Open posterior fontanelle
- The mouth is kept open.and large tongue protruding
- Neck is short and thick

Clinical manifestations:

- Broad Hands , short fingers Skin is dry and scaly little perspiration Myxedema of the eyelids, dorsum of hands and ext genitalia Carotenemia :yellow skin white sclera
- Scalp is thickened hair is coarse brittle and scanty
- Low hair line





Diagnosis

- Sceening programs allow early detection
  T3 T4 LOW
  TSH HIGH more than 100 mU/l

- Serum level of prolactin are elevated
- Thyroid u/s
- thyroglobulin
- Skull x ray large fontanelle,wide sutures,wormian bones, sella turcica large and round
- THYROID SCAN detect presence or absence of thyroid tissue

Treatment

Sodium Thyroxine T4

- New born 10—15 ug/kg not mix with soy protein or iron
- Child hood 3-5 ug/kg
- Adults only 2 ug/kg

There is an inverse relationship between age at clinical diagnosis and treatment initiation and intelligence quotient (IQ) later in life,so that the longer the condition goes undetected, the lower the IQ.

APPROACH TO CHILD WITH DEVELOPMENTAL DELAY

- **APPROACH TO SURVEILLANCE** Developmental surveillance is the process through which children who may have a developmental delay or be at risk for a developmental delay are recognized through the milestones previously mentioned. Especially at the well-child visits:

- **9-month visit**
- **18-month visit**
- **24-month visit**
- **30-month visit**

- **Approach to screening** – Developmental-behavioral screening refers to the use of a standardized test to identify asymptomatic children at risk for a developmental disorder; children who screen positive should undergo developmental-behavioral evaluation.

  -risk factors: Prenatal exposures (eg, infections, alcohol, smoking)

- -Birth complications (eg, prematurity or low birth weight)
- -Perinatal infections (eg, herpes simplex virus, Zika virus)
- -Medical conditions (eg, lead poisoning, congenital heart disease
- -Genetic conditions (eg, Down syndrome, fragile X syndrome)
- -Adverse childhood or family experiences (eg, poverty, including housing or food insecurity; exposure to racism; abuse or neglect)
- -Parental/caregiver unemployment or mental health problems (eg, depression, anxiety, substance use)
- -Parents/caregivers with limited education/literacy
- -Teenage parents

WHEN TO SCREEN:

- For children of all ages, we provide developmental-behavioral or mental health screening any time a caregiver or clinician has concerns about development, behavior, or mental health.
- For children younger than four years who have no symptoms or signs of developmental-behavioral problem, screening is not strongly advised.
- At the four-year well-child visit, we focus developmental-behavioral screening on school readiness and motor skills
- For children ≥5 years who have no symptoms of mental health disorders, screening is not strongly advised

	Ages & Stages - Social and Emotional, Second Edition[1]	Conners - 3[2]	Moods and Feelings Questionnaire[3,4]	Pediatric Symptom Checklist - 17[5,6]	Pediatric Symptom Checklist - 35[6-8]	Pediatric Symptom Checklist - Youth Report[6,9]	Strengths and Difficulties Questionnaire[10]
Considerations related to patient population							
Ages	▪ 1 to 72 months	▪ Caregiver and teacher questionnaires – 6 to 18 years ▪ Self-report – 8 to 18 years	▪ 8 to 18 years	▪ 6 to 18 years	▪ 3 to 5 years (with some questions removed) ▪ 6 to 18 years	▪ 11 to 18 years	▪ 3 to 16 years
Domains	▪ Self-regulation ▪ Compliance ▪ Communication ▪ Adaptive functioning ▪ Autonomy ▪ Affect ▪ Interactions with people	▪ Inattention ▪ Hyperactivity/impulsivity ▪ Learning problems ▪ Executive functioning ▪ Defiance/aggression ▪ Peer/family relations ▪ DSM-5 symptoms scales: ▪ ADHD inattentive ▪ ADHD hyperactive-impulsive ▪ Conduct disorder ▪ Oppositional defiant disorder	▪ Depression	▪ Emotional and behavioral problems	▪ Emotional and behavioral problems	▪ Emotional and behavioral problems	▪ Emotional symptoms ▪ Conduct problems ▪ Hyperactivity/inattention ▪ Peer relationship problems ▪ Prosocial behavior
Time to complete	▪ 10 to 15 minutes	▪ 20 minutes	▪ 5 to 10 minutes	▪ 2 minutes	▪ Under 5 minutes	▪ 2 minutes	▪ 10 minutes
Reading level	▪ Fourth to sixth grade	▪ Caregiver and teacher – Fourth to fifth grade ▪ Self-report – Third grade	–	▪ Fifth to sixth	–	–	–
Available languages	▪ English ▪ Spanish ▪ French ▪ Arabic	▪ English ▪ Spanish ▪ French	▪ Arabic (Modern Standard) ▪ Arabic (Iraq) ▪ Filipino ▪ Finnish ▪ German ▪ Norwegian ▪ Portuguese ▪ Spanish	▪ Chinese ▪ English ▪ Spanish ▪ Vietnamese ▪ Norwegian	▪ English and multiple other languages	▪ English ▪ Spanish ▪ Haitian-Creole ▪ Setswana ▪ French ▪ Portuguese (Brazilian American)	▪ English and multiple other languages
Additional information	▪ Can be used with ASQ3 for comprehensive developmental-behavioral screening	–	▪ Also available as adult self-report	–	▪ Pictorial version with subtitles available in English, Spanish, and Filipino	▪ 17 question youth self-report in English and Spanish available, but has not been validated	–
Considerations related to practice characteristics							
Description	▪ Approximately 30 questions (varies with age)	▪ Full length – 99 to 115 items ▪ Short form – 41 to 45 items ▪ ADHD index – 10 items	▪ Descriptive phrases with 3-point Likert scale ▪ Long form – 33 to 34 phrases ▪ Short form – 13 phrases ▪ Includes child self-report (long and short forms) and caregiver report (long and short form)	▪ 17 items	▪ 35 items	▪ 35 items (self-report)	▪ 25 questions completed by parent, teacher, or self-report in 11- to 16-year olds
Determination of positive/negative result	▪ 3 results: ▪ No or low risk – Development appears appropriate ▪ "Monitor" zone – Review concerns and monitor ▪ "Cutoff" – Above the cutoff means referral recommended	▪ Provides T-scores*	▪ Suggested long form cutoffs: ▪ Child – ≥29 ▪ Caregiver – ≥27 ▪ Suggested short form cutoffs: ▪ Child – ≥12 ▪ Caregiver – ≥11	▪ Total score of 15 or higher – Significant behavioral or emotional problems ▪ Internalizing subscale – Cutoff 5 or more items ▪ Attention subscale – Cutoff 7 or more items ▪ Externalizing subscale – Cutoff 7 or more items	▪ For children ages 6 to 18 years, cutoff score is 28. ▪ For children ages 3 to 5 years, the scores on elementary school related items 5, 6, 17, and 18 are ignored and a total score based on the 31 remaining items is computed. The cutoff score for younger children is 24.	▪ Cutoff score of 30 recommended	▪ Classification system: ▪ Close to average ▪ Slightly raised ▪ High ▪ Very high
Validity and test performance	▪ Concurrent validity – 84% ▪ Test-retest reliability – 89% ▪ Sensitivity – 81% overall ▪ Specificity – 83% overall	▪ Sensitivity and specificity vary based on predictor scale and target group (ADHD inattentive, combined, hyperactive-impulsive, learning disorder, disruptive behavior disorder)[22] ▪ Sensitivity range – 55 to 96% ▪ Specificity range – 22 to 91%	▪ Child self-report: ▪ Sensitivity – 68% ▪ Specificity – 88% ▪ Caregiver report: ▪ Sensitivity – 75 to 86% ▪ Specificity – 73 to 87%	▪ Total PSC-17 scale: ▪ Sensitivity – 82% ▪ Specificity – 81%	▪ Cutoff score of 28: ▪ Sensitivity – 95% ▪ Specificity – 68%	▪ Cutoff score of 30: ▪ Sensitivity – 94% ▪ Specificity – 88%	▪ Sensitivity – 63 to 94% ▪ Specificity – 88 to 98%
Who can deliver	▪ Professionals ▪ Paraprofessionals ▪ Clerical staff	▪ Anyone can deliver ▪ Health care provider interprets results	▪ No training requirement	▪ Anyone can deliver ▪ Health care provider interprets results	▪ Anyone can deliver ▪ Health care provider interprets results	▪ Self-administered ▪ Health care provider interprets results	▪ Self-administered
Time to score and interpret	▪ 1 to 3 minutes	▪ 20 minutes (administration and scoring time)	▪ 3 to 5 minutes (short) ▪ 5 to 10 minutes (long)	▪ 2 minutes	▪ 3 to 5 minutes	▪ 2 minutes	▪ 10 minutes (total administration and scoring)
Cost to purchase¶	▪ Starter kit in one language – $295	▪ Online Software Kits with DSM-5 Update start at $899 ▪ Manual Scoring Kits with DSM-5 Update start at $599	▪ Free from Duke University	▪ Free from: ▪ Massachusetts General Hospital ▪ Brightfutures.org	▪ Free from: ▪ Massachusetts General Hospital ▪ Brightfutures.org	▪ Free from: ▪ Massachusetts General Hospital ▪ Brightfutures.org	▪ Free (with permission) at www.sdqinfo.org
Ease of integration into EMR	▪ Online management and questionnaire completion options	▪ Online software available	▪ Can be digitized	▪ Online software available	▪ Online software available	▪ Online software available	▪ Online scoring and report generation available

HISTORY

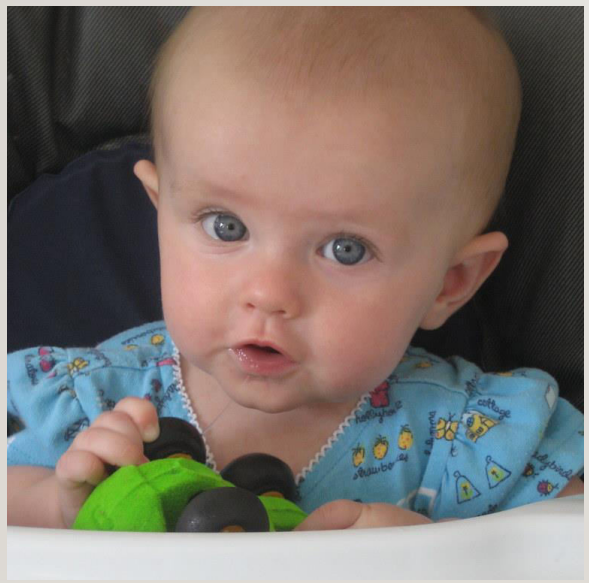
- A description of the child's developmental progress, stagnation, or regression.
- ●Results of prior developmental, psychologic, and psychiatric evaluations.
- ●A description of the child's language development.
- ●History of medical problems, including seizures, ataxia, or weakness; infections; and/or congenital abnormalities.
- ●Prenatal, perinatal, and postnatal problems, including alcohol intake in pregnancy or other environmental exposures, prenatal diagnosis, any complications during delivery, trauma, infections, prematurity, LBW, encephalopathy...
- ●Medication history.

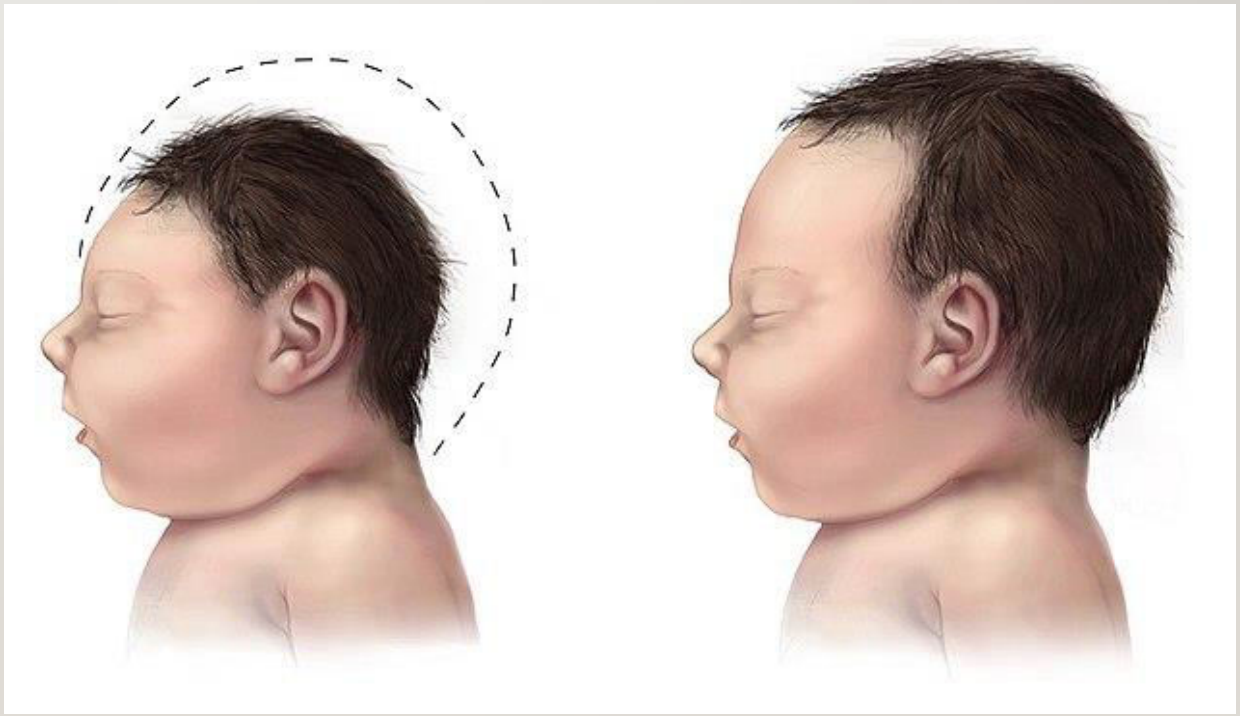
HISTORY

- Results of previous newborn, metabolic, thyroid, lead, iron, vision, and hearing screening tests.
- Review of growth charts.
- Review of previous neuroimaging, if performed.
- A three-generation family history, assessing for neurodevelopmental and genetic disorders, miscarriages, stillbirths, neonatal deaths, and/or consanguinity.
- Questions regarding quality of life, community or recreational participation, friendships, family psychosocial needs, and parental stress/depression.

PHYSICAL EXAMINATION

- Measurements of height, weight, and head circumference, including growth velocity and use of syndrome-specific growth charts. (macrocephaly : hydrocephalus , microcephaly : rett's disorder)

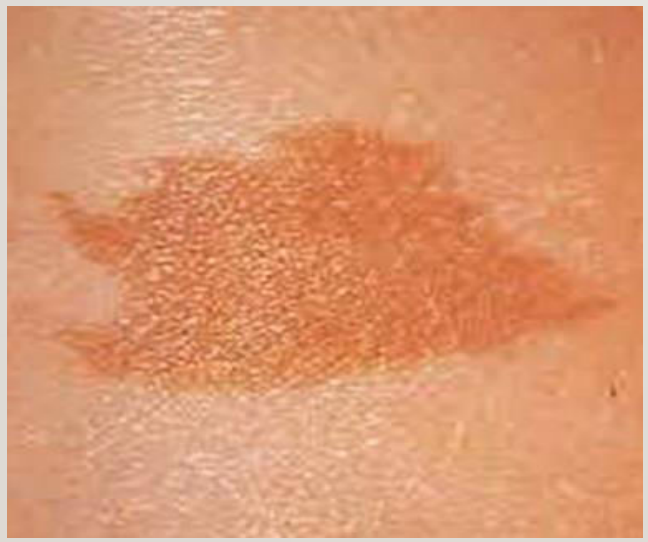


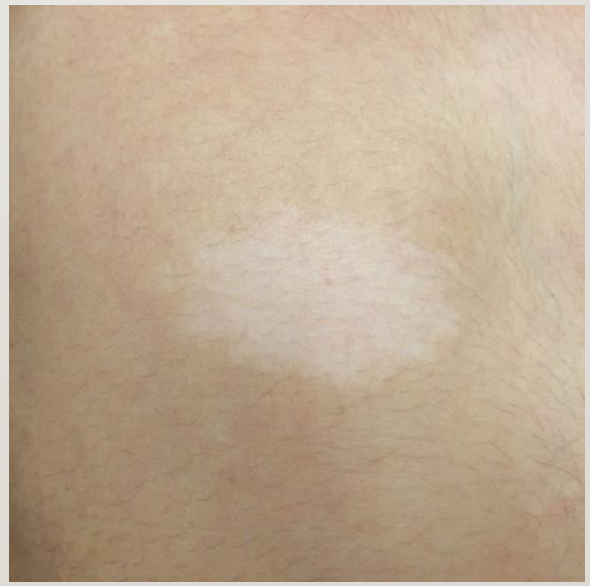


- Dysmorphic features that may suggest genetic or syndromic etiology and guide selection of genetic tests

Disorder	Clinical features	Targeted tests
Down syndrome	▪ Characteristic dysmorphic features ▪ Wide range of cognitive impairment ▪ Cardiac defects and multiple congenital anomalies	G-banded karyotype analysis
Fragile X	▪ Males with moderate to severe ID, macrocephaly, large ears, enlarged testes after puberty, perseverative speech, and poor eye contact ▪ Males and females with family history of ID	*FMR1* DNA analysis
Rett syndrome	▪ Females with normal early development followed by regression to moderate or severe ID ▪ Stereotypic hand movements	*MECP2* testing
Klinefelter syndrome	▪ Males with mild ID, hypogonadism, tall stature, gynecomastia, reduced body hair	G-banded karyotype analysis
Prader-Willi syndrome	▪ Mild to moderate ID, behavior difficulties, food-seeking behavior and obesity, hypogonadism, neonatal hypotonia, delayed motor milestones	Methylation analysis to detect abnormal parent-specific methylation on chromosome 15q11.2-13
DiGeorge (22q11.2 deletion) syndrome	▪ Mild to moderate ID, multiple congenital anomalies (including cardiac defects, hypoplastic thymus, palatal abnormalities), immunodeficiency	FISH for 22q11.2 deletion
Metabolic disorders	▪ Severity of ID varies ▪ Episodic decompensation (eg, with febrile illnesses or periods of starvation) ▪ Family history of metabolic disorders or parental consanguinity ▪ Seizures, developmental regression, failure to thrive	Metabolic screening (typically this includes measurement of plasma amino acids, urine organic acids, serum ammonia, and lactate; more selective testing can be performed based on the patient's specific characteristics). Further metabolic testing is guided by a specialist.
Muscular dystrophy	▪ Mild ID ▪ Proximal muscle weakness	Measure serum creatinine kinase as initial screen; if elevated, perform additional evaluation (refer to UpToDate topics on muscular dystrophy for details).
Congenital hypothyroidism*	▪ Decelerating growth velocity/short stature, cold intolerance, feeding problems, puffy facies, macroglossia, large fontanels, hypotonia, dry skin, prolonged jaundice	Thyroid function tests (serum TSH free T4)
Lead poisoning¶	▪ Mild to moderate ID, language delay, and behavior problems ▪ Vomiting, colicky abdominal pain, fatigue, renal insufficiency ▪ Exposure history (eg, persistent mouthing behavior, living in a house or child care facility built before 1950, recent immigration or home renovation, folk remedies, and some parental occupations [smelting, soldering, and auto body repair])	Blood lead level

- Cutaneous findings that are important to note include café-au-lait macules (suggestive of neurofibromatosis) (, ash-leaf spots (suggestive of tuberous sclerosis) , and bruises or other signs suggestive of neglect and physical abuse (including intraoral examination)





- Detailed observation of the child's behavior, including attention, impulsivity, activity, affect, motor mannerisms, social skills, communication, and mood.

- Complete neurologic and neurodevelopmental assessment
- **Cranial nerves**
- **Motor examination (**The patient should be observed for abnormalities of posture and movements, including asymmetry at rest, fisting of the hand, frog-legged position suggesting hypotonia, tremor, myoclonus, or tics and Muscle tone)
- **Sensory examination (**A sensory examination in young children is often imprecise, and only gross deficits can be detected. In children older than five to six years, sensory function is evaluated in the same manner as in an adult.)
- **Developmental reflexes**
  and deep tendon reflexes

COMPREHENSIVE NEURODEVELOPMENTAL EVALUATION — REFERRAL TO A DEVELOPMENTAL PEDIATRICIAN, PEDIATRIC NEUROLOGIST, AND/OR PSYCHOLOGIST IS USUALLY NEEDED FOR A COMPREHENSIVE NEURODEVELOPMENTAL EVALUATION.

Examples of commonly used instruments	Applicable ages
Infants and young children <2 years	
Cognitive and adaptive testing	
Bayley Scales of Infant and Toddler Development 4th Edition (Bayley-4)*¶ (2019)	16 days to 42 months
Griffiths Scales of Child Development 3rd Edition (Griffiths III)Δ¶ (2015)	Birth to 72 months
Adaptive testing	
Vineland Adaptive Behavior Scale 3rd Edition (Vineland-3)◇ (2016)	Birth to beyond 21 years
Adaptive Behavior Assessment System 3rd Edition (ABAS-3)§ (2015)	Birth to beyond 21 years
Preschool age	
Intellectual testing	
Wechsler Preschool & Primary Scale of Intelligence 4th Edition (WPPSI-IV) (2012)	2 years, 6 months to 7 years, 7 months
Stanford-Binet Intelligence Scales, 5th Scales, 5th Edition (SB-5) (2003)	2 to beyond 21 years
Differential Abilities Scales 2nd Edition (DAS-II) (2007)	2 years, 6 months to 17 years
Kaufman Assessment Battery for Children 2nd Edition (KABC-II) (2004)	3 to 18 years
Leiter International Performance Scale 3rd Edition (Leiter-3) (2013)	3 to beyond 21 years
Adaptive testing	
Vineland Adaptive Behavior Scale 3rd Edition (Vineland-3)◇ (2016)	Birth to beyond 21 years
Diagnostic Adaptive Behavior Scale (DABS)§¥	4 to 21 years
Adaptive Behavior Assessment System 3rd Edition (ABAS-3)§ (2015)	Birth to beyond 21 years
School age and beyond	
Intellectual testing	
Wechsler Preschool & Primary Scale of Intelligence 4th Edition (WPPSI-IV) (2012)	2 years, 6 months to 7 years, 7 months
Stanford-Binet Intelligence Scales, 5th Scales, 5th Edition (SB-5) (2003)	2 to beyond 21 years
Wechsler Intelligence Scales for Children 5th Edition (WISC-V) (2014)	6 to 16 years, 11 months
Differential Abilities Scales 2nd Edition (DAS-II) (2007)	2 years, 6 months to 17 years
Kaufman Assessment Battery for Children 2nd Edition (KABC-II) (2004)	3 to 18 years
Leiter International Performance Scale 3rd Edition (Leiter-3) (2013)	3 to beyond 21 years
Test of Nonverbal Intelligence 4th Edition (TONI-4) (2010)	6 to beyond 21 years
Wechsler Adult Intelligence Scale 4th Edition (WAIS-IV) (2008)	16 to beyond 21 years
Adaptive testing	
Vineland Adaptive Behavior Scale 3rd Edition (Vineland-3)◇ (2016)	Birth to beyond 21 years
Diagnostic Adaptive Behavior Scale (DABS)§¥	4 to 21 years
Adaptive Behavior Assessment System 3rd Edition (ABAS-3)§ (2015)	Birth to beyond 21 years

VISION AND HEARING SCREENING — CHILDREN WITH GDD AND/OR ID ARE AT HIGH RISK FOR SENSORY IMPAIRMENTS. THIS MAY INCLUDE A COMPLETE OPHTHALMOLOGIC EXAMINATION AND AUDIOMETRY, PREFERABLY USING BRAINSTEM AUDITORY EVOKED RESPONSE.

- Also check for language delay or abnormal speech

- **Other assessments** — Additional evaluations may include:
- ●A genetic evaluation should be offered to children who have syndromic findings or unexplained GDD or ID. This is discussed separately.
- ●Occupational and physical therapists can assist in assessing functional impairments, strengths, needs, and supports.
- ●If there are complex psychiatric comorbidities, a child psychiatrist can help evaluate the child's need for psychopharmacologic therapy.
- ●A social worker can assist in assessment of the family and child-family needs, provide counseling, generate access to social supports, and contribute to long-term planning.

DIAGNOSIS

- **Diagnosis** – The diagnosis of ID is based upon identifying impairments in **both** adaptive and intellectual functioning, with onset before the age of 18 years. Assessment of intellectual and adaptive functioning should be performed using standardized, valid, and reliable instruments. The instrument used should be appropriate for the child's level of functioning and take into account the child's age, language, culture, communication, socioeconomic status, and disability profile. Other factors such as ease of administration and examiner experience may also be considered.

- **Testing for specific disorders** — Children with dysmorphic features or other characteristics that suggest a particular syndrome or disorder should undergo specific testing to confirm or rule out that disorder

Disorder	Clinical features	Targeted tests
Down syndrome	▪ Characteristic dysmorphic features ▪ Wide range of cognitive impairment ▪ Cardiac defects and multiple congenital anomalies	G-banded karyotype analysis
Fragile X	▪ Males with moderate to severe ID, macrocephaly, large ears, enlarged testes after puberty, perseverative speech, and poor eye contact ▪ Males and females with family history of ID	*FMR1* DNA analysis
Rett syndrome	▪ Females with normal early development followed by regression to moderate or severe ID ▪ Stereotypic hand movements	*MECP2* testing
Klinefelter syndrome	▪ Males with mild ID, hypogonadism, tall stature, gynecomastia, reduced body hair	G-banded karyotype analysis
Prader-Willi syndrome	▪ Mild to moderate ID, behavior difficulties, food-seeking behavior and obesity, hypogonadism, neonatal hypotonia, delayed motor milestones	Methylation analysis to detect abnormal parent-specific methylation on chromosome 15q11.2-13
DiGeorge (22q11.2 deletion) syndrome	▪ Mild to moderate ID, multiple congenital anomalies (including cardiac defects, hypoplastic thymus, palatal abnormalities), immunodeficiency	FISH for 22q11.2 deletion
Metabolic disorders	▪ Severity of ID varies ▪ Episodic decompensation (eg, with febrile illnesses or periods of starvation) ▪ Family history of metabolic disorders or parental consanguinity ▪ Seizures, developmental regression, failure to thrive	Metabolic screening (typically this includes measurement of plasma amino acids, urine organic acids, serum ammonia, and lactate; more selective testing can be performed based on the patient's specific characteristics). Further metabolic testing is guided by a specialist.
Muscular dystrophy	▪ Mild ID ▪ Proximal muscle weakness	Measure serum creatinine kinase as initial screen; if elevated, perform additional evaluation (refer to UpToDate topics on muscular dystrophy for details).
Congenital hypothyroidism*	▪ Decelerating growth velocity/short stature, cold intolerance, feeding problems, puffy facies, macroglossia, large fontanels, hypotonia, dry skin, prolonged jaundice	Thyroid function tests (serum TSH free T4)
Lead poisoning¶	▪ Mild to moderate ID, language delay, and behavior problems ▪ Vomiting, colicky abdominal pain, fatigue, renal insufficiency ▪ Exposure history (eg, persistent mouthing behavior, living in a house or child care facility built before 1950, recent immigration or home renovation, folk remedies, and some parental occupations [smelting, soldering, and auto body repair])	Blood lead level

- **Unexplained ID** — If no specific disorder is clinically suspected or if initial testing for specific disorders is nondiagnostic, then genetic testing for idiopathic or unexplained ID is recommended, starting with a chromosomal microarray analysis (CMA)

- Chromosomal microarray analysis (CMA) is a technology used for the detection of clinically-significant microdeietions or duplications, with a high sensitivity for submicroscopic aberrations.
- CMA is preferred over G-banded karyotype analysis or subtelomeric fluorescence in situ hybridization (FISH) as the first-line genetic test for unexplained ID due to its higher sensitivity and thus greater diagnostic yield

- **Karyotype analysis** — G-banded karyotype analysis should be reserved for the following circumstances :
- ●A common aneuploidy is suspected based on clinical findings (eg, Down syndrome, trisomy 18, or a sex chromosome aneuploidy).
- ●There is concern for balanced translocation (eg, maternal history of frequent miscarriages, or a family history of translocation).
- ●CMA is unavailable.

- **Metabolic testing**
- To perform metabolic screening, concentrations of plasma amino acids, urine organic acids, serum ammonia, and lactate are most often measured; very long-chain fatty acids and carnitine may also be measured on blood samples [23]. Electrolytes are measured to detect acidosis.

- And TSH, FREE T4 should be preformed

- **Whole exome sequencing**
- Whole-exome sequencing is a widely used next-generation sequencing (NGS) method that involves sequencing the protein-coding regions of the genome.
- WES should be considered for patients with moderate to severe ID in whom other standard tests (including CMA) have failed to identify the cause
- Due to the falling costs of sequencing and its high diagnostic yield, WES is rapidly becoming a clinical tool for the evaluation of ID, especially at specialty centers

- **Fluorescence in situ hybridization (FISH) to detect** Chromosomal rearrangements ; however, CMA has replaced FISH as the test of choice

- **Other tests**
- **Lead screening**
- **Neuroimaging** :We suggest neuroimaging be obtained (preferably with magnetic resonance imaging [MRI]) if there are concerning features in the history (eg, seizures, progressive or degenerative neurologic symptoms) or abnormal findings on physical examination (eg, microcephaly, macrocephaly, focal neurologic deficits). Consultation with a pediatric neurologist may be warranted in these cases.

THANK YOU