Approach to developmental delay

Amira Masri
professor of child neurology
faculty of medicine
the university of Jordan

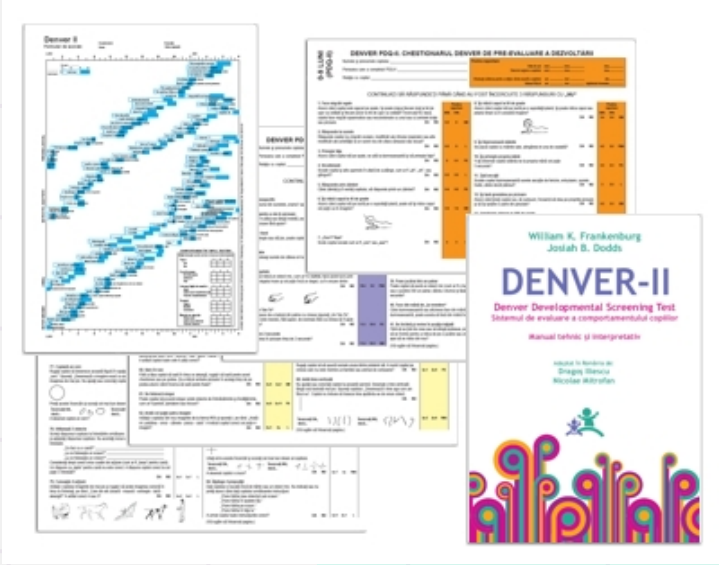
What is normal development

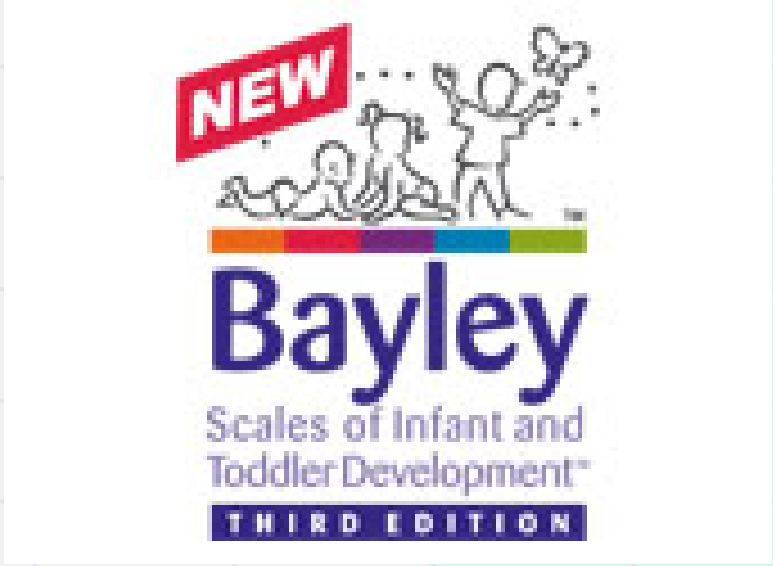
- humans develop through a dynamique sequential process since the early days of life as embryo and the process continues after birth

Child's development is a dynamic process

Developmental screening tools

- Provider
- Denver
- CAT/CLAMS
- Bayley
- Brigance
- DIAL-R
- Parent
- Ages and Stages Questionnaire
- Parent's Evaluations of Developmental Status





- Emerging patterns of development

Table 10-2	Emerging Patterns of Behavior During the 1st Yr of Life*
NEONATAL PERIOD (1ST 4 WK)	
Prone:	Lies in flexed attitude; turns head from side to side; head sags on ventral suspension
Supine:	Generally flexed and a little stiff
Visual:	May fixate face on light in line of vision; "doll's-eye" movement of eyes on turning of the body
Reflex:	Moro response active; stepping and placing reflexes; grasp reflex active
Social:	Visual preference for human face
AT 1 MO	
Prone:	Legs more extended; holds chin up; turns head; head lifted momentarily to plane of body on ventral suspension
Supine:	Tonic neck posture predominates; supple and relaxed; head lags when pulled to sitting position
Visual:	Watches person; follows moving object
Social:	Body movements in cadence with voice of other in social contact; beginning to smile
AT 2 MO	
Prone:	Raises head slightly farther; head sustained in plane of body on ventral suspension
Supine:	Tonic neck posture predominates; head lags when pulled to sitting position
Visual:	Follows moving object 180 degrees
Social:	Smiles on social contact; listens to voice and coos
AT 3 MO	
Prone:	Lifts head and chest with arms extended; head above plane of body on ventral suspension
Supine:	Tonic neck posture predominates; reaches toward and misses objects; waves at toy
Sitting:	Head lag partially compensated when pulled to sitting position; early head control with bobbing motion; back rounded
Reflex:	Typical Moro response has not persisted; makes defensive movements or selective withdrawal reactions
Social:	Sustained social contact; listens to music; says "aah, ngah"
AT 4 MO	
Prone:	Lifts head and chest, with head in approximately vertical axis; legs extended
Supine:	Symmetric posture predominates, hands in midline; reaches and grasps objects and brings them to mouth
Sitting:	No head lag when pulled to sitting position; head steady, tipped forward; enjoys sitting with full truncal support
Standing:	When held erect, pushes with feet
Adaptive:	Sees raisin, but makes no move to reach for it
Social:	Laughs out loud; may show displeasure if social contact is broken; excited at sight of food

AT 7 MO	
Prone:	Rolls over; pivots; crawls or creep-crawls (Knobloch)
Supine:	Lifts head; rolls over; squirms
Sitting:	Sits briefly, with support of pelvis; leans forward on hands; back rounded
Standing:	May support most of weight; bounces actively
Adaptive:	Reaches out for and grasps large object; transfers objects from hand to hand; grasp uses radial palm; rakes at raisin
Language:	Forms polysyllabic vowel sounds
Social:	Prefers mother; babbles; enjoys mirror; responds to changes in emotional content of social contact
AT 10 MO	
Sitting:	Sits up alone and indefinitely without support, with back straight
Standing:	Pulls to standing position; "cruises" or walks holding on to furniture
Motor:	Creeps or crawls
Adaptive:	Grasps objects with thumb and forefinger; pokes at things with forefinger; picks up pellet with assisted pincer movement; uncovers hidden toy; attempts to retrieve dropped object; releases object grasped by other person
Language:	Repetitive consonant sounds ("mama," "dada")
Social:	Responds to sound of name; plays peek-a-boo or pat-a-cake; waves bye-bye
AT 1 YR	
Motor:	Walks with one hand held; rises independently, takes several steps (Knobloch)
Adaptive:	Picks up raisin with unassisted pincer movement of forefinger and thumb; releases object to other person on request or gesture
Language:	Says a few words besides "mama," "dada"
Social:	Plays simple ball game; makes postural adjustment to dressing

15 MO	
Motor:	Walks alone; crawls up stairs
Adaptive:	Makes tower of 3 cubes; makes a line with crayon; inserts raisin in bottle
Language:	Jargon; follows simple commands; may name a familiar object (e.g., ball); responds to his/her name
Social:	Indicates some desires or needs by pointing; hugs parents
18 MO	
Motor:	Runs stiffly; sits on small chair; walks up stairs with 1 hand held; explores drawers and wastebaskets
Adaptive:	Makes tower of 4 cubes; imitates scribbling; imitates vertical stroke; dumps raisin from bottle
Language:	10 words (average); names pictures; identifies 1 or more parts of body
Social:	Feeds self; seeks help when in trouble; may complain when wet or soiled; kisses parent with pucker
24 MO	
Motor:	Runs well, walks up and down stairs, 1 step at a time; opens doors; climbs on furniture; jumps
Adaptive:	Makes tower of 7 cubes (6 at 21 mo); scribbles in circular pattern; imitates horizontal stroke; folds paper once imitatively
Language:	Puts 3 words together (subject, verb, object)
Social:	Handles spoon well; often tells about immediate experiences; helps to undress; listens to stories when shown pictures

30 MO

Motor:	Goes up stairs alternating feet
Adaptive:	Makes tower of 9 cubes; makes vertical and horizontal strokes, but generally will not join them to make cross; imitates circular stroke, forming closed figure
Language:	Refers to self by pronoun "I"; knows full name
Social:	Helps put things away; pretends in play

36 MO

Motor:	Rides tricycle; stands momentarily on 1 foot
Adaptive:	Makes tower of 10 cubes; imitates construction of "bridge" of 3 cubes; copies circle; imitates cross
Language:	Knows age and sex; counts 3 objects correctly; repeats 3 numbers or a sentence of 6 syllables; most of speech intelligible to strangers
Social:	Plays simple games (in "parallel" with other children); helps in dressing (unbuttons clothing and puts on shoes); washes hands

48 MO	
Motor:	Hops on 1 foot; throws ball overhand; uses scissors to cut out pictures; climbs well
Adaptive:	Copies bridge from model; imitates construction of "gate" of 5 cubes; copies cross and square; draws man with 2-4 parts besides head; identifies longer of 2 lines
Language:	Counts 4 pennies accurately; tells story
Social:	Plays with several children, with beginning of social interaction and role-playing; goes to toilet alone
60 MO	
Motor:	Skips
Adaptive:	Draws triangle from copy; names heavier of 2 weights
Language:	Names 4 colors; repeats sentence of 10 syllables; counts 10 pennies correctly
Social:	Dresses and undresses; asks questions about meaning of words; engages in domestic role-playing

Red flags worrisome if still not reached

babbling by 12 months

gesturing (e.g., pointing, waving bye-bye) by 12 months

single words by 16 months

two-word spontaneous (not just echolalic) phrases by 24 months

loss of any language or social skills at any age

Videos : how to perform developmental assessment

- https://mrcpch.paediatrics.co.uk/development/development-videos/

Developmental delay

Child not reaching developmental milestones at the expected age , even after allowing the broad variation of normality

Global developmental delay : when ≥2 domains in development are delayed

The earlier the identification of these children the better outcome(birth -2years)

Favorable environment: enhances + optimize brain development

Consequences of Early Childhood Developmental Problems

Developmental surveillance

5-10% of pediatric population have developmental disabilities

To identify these children : developmental surveillance:

1-observe infant

2-take developmental history

3-ellicit parental concerns

Developmental screen : necessary adjunct

Developmental delay

Developmental delay :Slow progress in the attainment of developmental milestones

Psychomotor regression: loss of developmental milestones previously attained.

Two important questions to answer

Is developmental delay restricted to specific areas or is it global (2 or more)?

Is it development delayed or is child regressing

Determine is the delay static or progressive

Predominant speech delay

- Hearing impairment
- Autism
- Bilateral hippocampal sclerosis
- Congenital bilateral perisylvian syndrome

Motor delay

Ataxia

Hemiplegia

paraplegia

Hypotonia

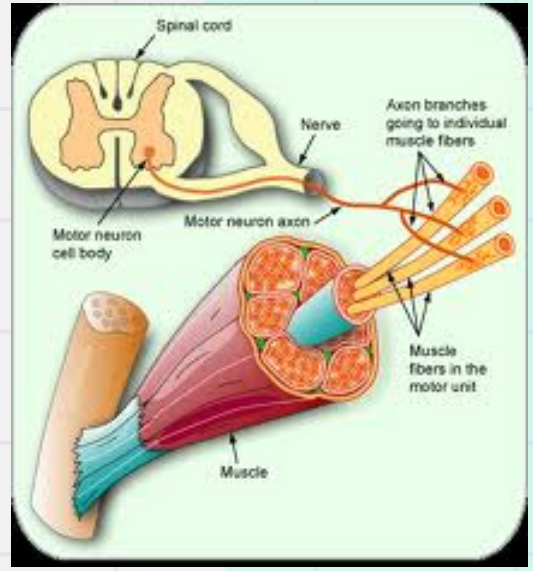
Neuromuscular disorders

Determine if the motor delay is due to central (upper motor neurone disorder) or peripheral (lower motor neurone disorder

Or combined : example Duchenne muscle dystrophy ,Cong muscle dystrophies ,Metachroamtic leukodystrophy

Peripheral

Central



Differentiating central from peripheral causes: hx and ex

- Normal or **Brisk reflexes**
- Other abnormal brain functions: delay, seizures
- Fisting

- Scissoring on vertical suspension
- Dysmorphic features
- Extra-cranial organ malformations

- **Absent** or Depressed reflexes
- Intact brain function
- Awake and alert
- Muscle atrophy
- Profound **weakness**
- Fasciculations
- No extra-cranial organ malformations

Global developmental delay (2 or more) : examples

- Perinatal insult : asphyxia , congenital infections, bilirubin toxicity
- Chromosomal /genetic
- Metabolic : hypothyroidism , neurometabolic disorders
- Cerebral malformations
- Progressive neurodegenerative disorders

- Determine is it static or progressive
- Age of onset of symptoms
- Clues in history and examination

Evaluation of the child with global developmental delay

Look for the hints

- History :antenatal, birth history , past history
- Age of Onset of symptoms :static or progressive
- Family history (very detailed):consanguinity, similar cases , deaths in early infancy
- Examination : dysmorphysm
- systems involvement
- Results of investigations

Clues in the history

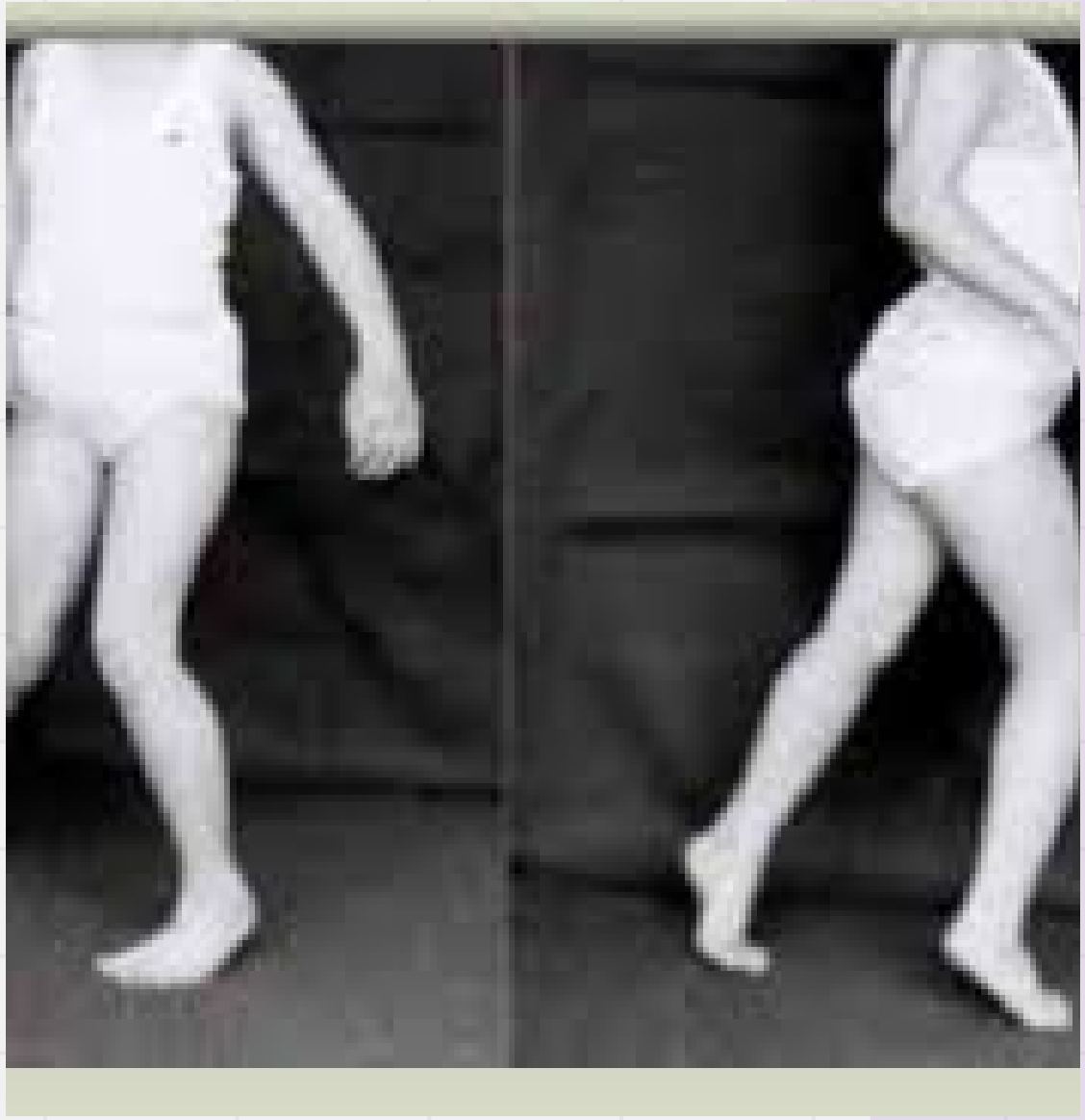
Antenatal history : trauma , infection, death of a twin , hypertension , diabetes ...

Birth history : weight , gestational age hyperbilirubinemia ..

Past : meningitis , encephalitis , epilepsy trauma ...

What is your most likely dx based on the clues

- 20 months old boy presented with history of delayed walking , he also has weakness of the right side of body
- Antenatal history revealed decreased fetal movement , he was born prematurely at 28 weeks of gestation



Cerebral palsy: definition

non progressive (static) disorder of motor function and movement that usually manifests early **in** life as a result of central nervous system damage to the developing brain

Incidence :1.5 to 2.5 per 1,000 live births

Most patients are identified by 2 years of age due to delayed motor milestones

More common in children who are born very prematurely or at term

Slightly higher prevalence in males M:F= 1.5:1

Poor prenatal care may increase the incidence of cerebral palsy

Onset

Prenatal

Perinatal

Post natal

Causes

In most cases, the exact cause is unknown but is most likely multifactorial

Majority of cases : not caused by hypoxic ischemic incidents occurring perinatally (as it was believed until recently.)

70-80% cases are prenatal in origin

Although prematurity is the most common known antecedent of CP, the majority of children who develop CP are born at term.

Causes

70% - 80% of cases of CP are due to antenatal factors

10% - 28% of cases are due to birth asphyxia in term and near-term infants

More than 1 etiologic factor is often identified.

The term CP is descriptive : different

etiologies and clinical presentations

1- According to the extremities involved

2-According to the characteristics of neurologic dysfunction.

3- Functional classification

Hemiplegic CP

Arm > leg

walks : tip toes , swing the affected leg (semicircular arc)

Corticosensory impairment: common

Mental retard. : 1/3

Seizures : 1/3

vision

Spastic quadreplegic CP

- Generalized increase in muscle tone
- Legs > arms
- Opisthotonic posture (first year of life)
- Difficulties in swallowing and articulation
- Incoordination of oropharyngal m :recurrent pneumonia
- Seizures :50%
- Mental retardation : majority
- Auditory , visual abn : common

Diplegic

- Bilateral leg involvement
- Commonly *some* degree of UL involvement
- Infant : scissoring , older child : tip toewalk
- Seizures , MR , visual abn

According to neurological dysfunction:

- Spastic: most common type (70%-80%)
- Ataxic: with cerebellar involvement
- Dyskinetic (extrapyramidal, choreoathetoid): due to predominant basal ganglia involvement **in** patients with acute severe hypoxia and kernicterus. Symptoms consistent with a movement disorder may appear later **in** life
- Mixed

Diagnosis : HX + EX

Diagnosis : always a motor deficit

usual presentation :delayed motor milestones

hand preference < 3 years: relative weakness of 1 side.

History: the child is not losing function= the patient does not have a progressive disease.

Examination : hypotonia , spasticity, persistent primitive reflexes , underdevelopment of parachute reflex

Associated conditions

- Mental retardation :30- 50%
- Ophthalmologic defects : 30%
- Hearing impairment : 10%
- Speech and language disorders :40%
- Epilepsy : 30- 40 %

Mangement and ttt

Multidisciplinary team

goal for the treatment program : maximize function + optimize development = help them participate in as many activities as possible in multiple social settings

Types of interventions

- Physical therapy
- Orthopedic surgery (later)
- Muscle tone management
- orthosis

What is your diagnosis ? Clues in the family history

A 4 year old boy presented with history of global developmental delay , epilepsy and microcephaly

Parents are cousins , he has one cousin who was diagnosed to have phenylketonuria by neonatal screening

phenylketonuria

Error of amino acids metabolism

Autosomal recessive

No acute clinical symptoms

Untreated leads to mental retardation

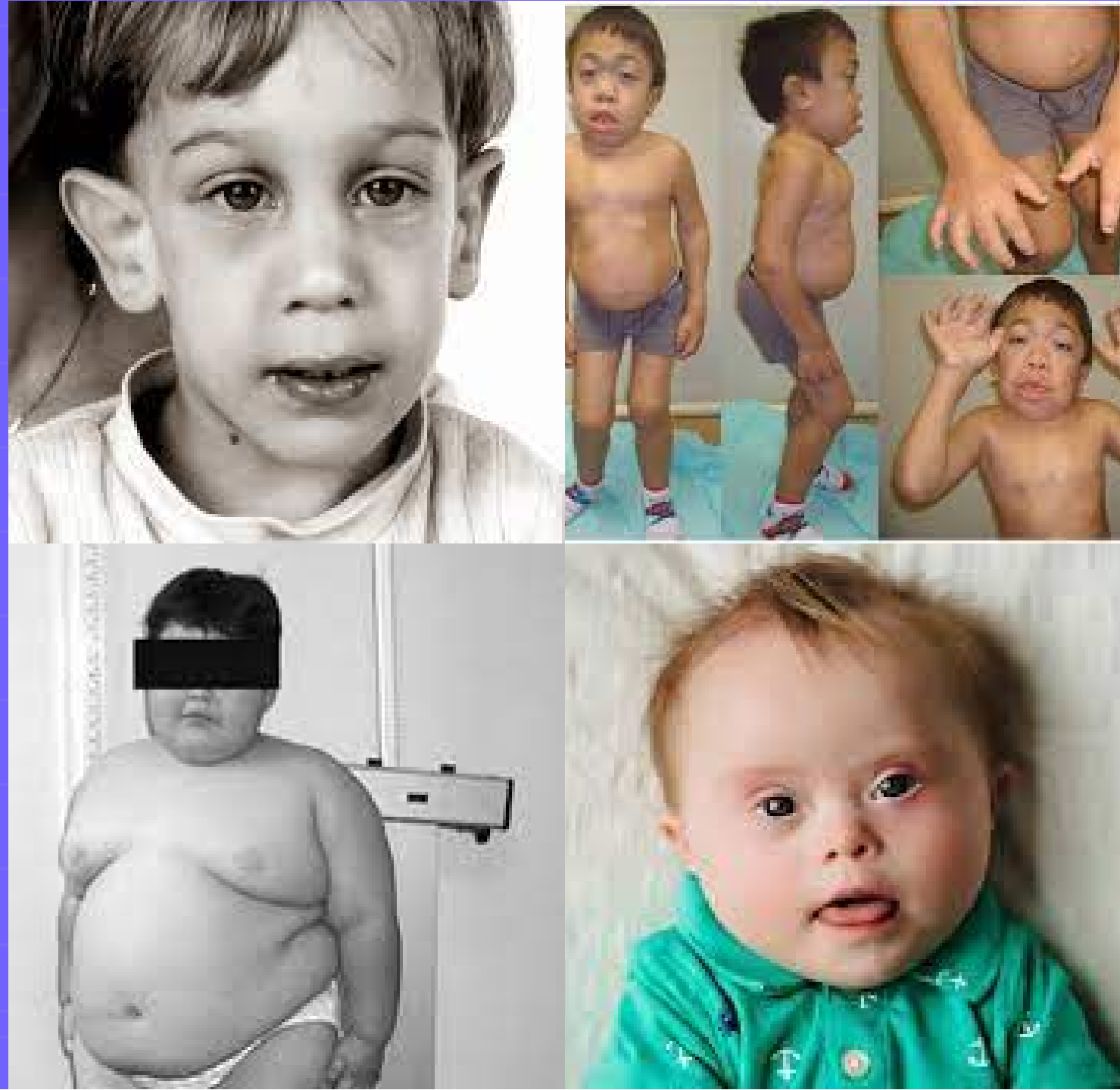
Associated complications: behavior disorders, cataracts, skin disorders, and movement disorders

First newborn screening test was developed in 1959

Treatment: phenylalaine restricted diet (specialized formulas available)

What is your diagnosis :

- Clues in the face



Clues : skin

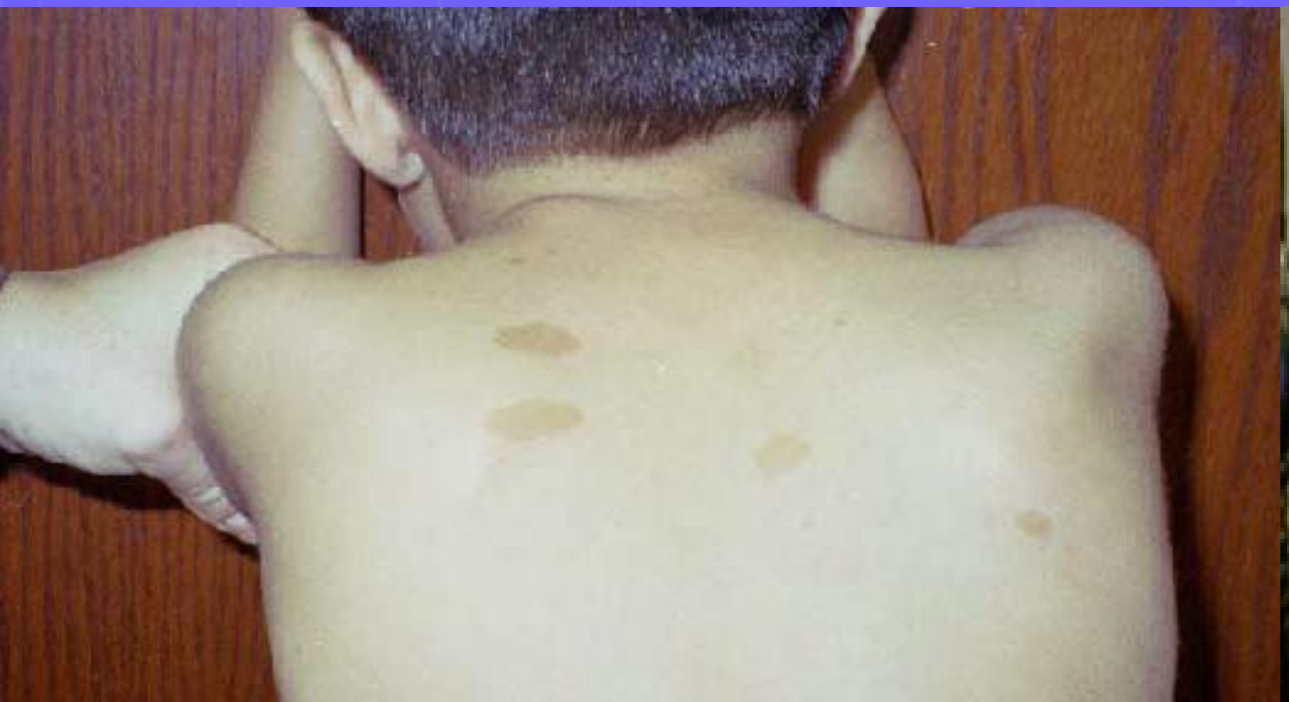
Neurocutaneous disorders : examples

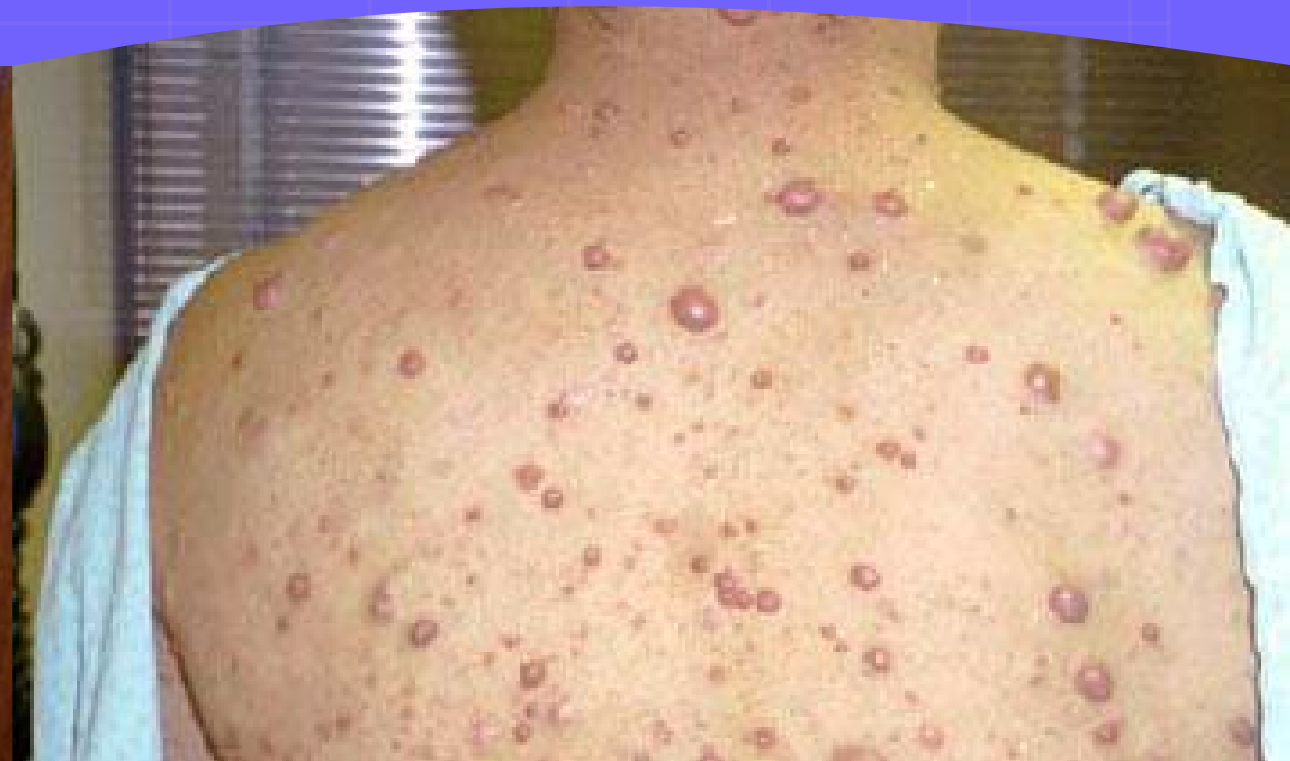
Neurofibromatosis type 1

Sturge weber syndrome

Tuberous scleoris

Clues in skin ??





Neurofibromatosis type 1

- Autosomal dominant with variable expression
- Most common neurocutaneous syndrome
- Diagnosis: dx criteria
- Macrocepahly is common
- Learning disability
- Risk of neoplastic disorders
- Seziures
- Treatment : supportive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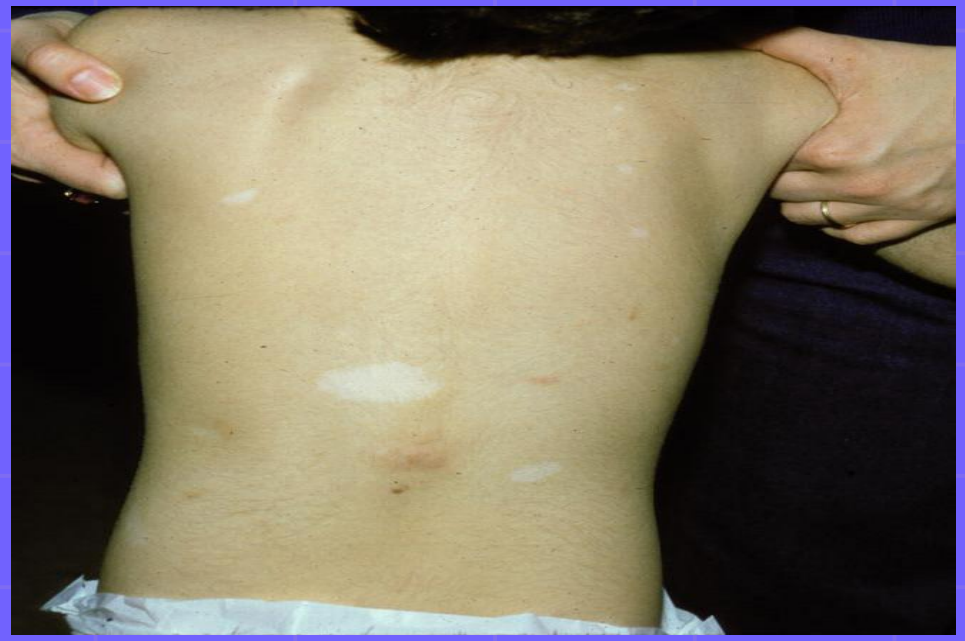
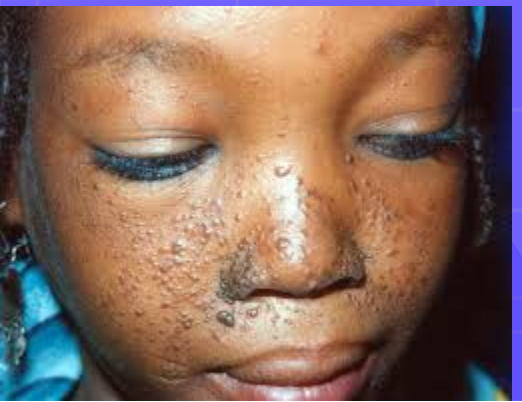
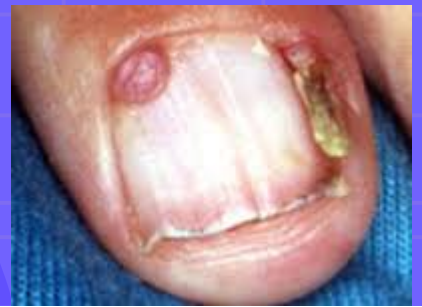






Tuberous sclerosis

Autosomal dominant

2 genes (TSC1 and TSC2)

Characteristic skin lesions (ash leaf , shagreen patches , achromic spots , sebaceous adenoma ....)

Epilepsy , developmental delay

Subependymal hamartomas

Dx : dx criteria

BOX 5-9 Clinical Diagnosis of Tuberous Sclerosis

Definite TSC: Two major features or one major feature plus two minor features
Probable TSC: One major feature plus one minor feature
Possible TSC: One major feature or two or more minor features

Major Features

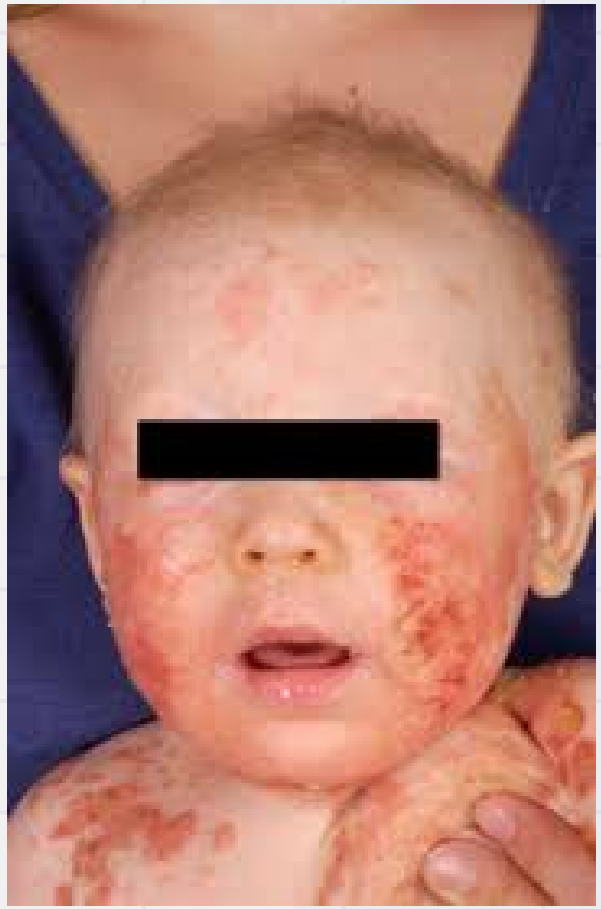
- Cardiac rhabdomyoma, single or multiple
- Cortical tuber[1]
- Facial angiofibromas or forehead plaque
- Hypomelanotic macules (three or more)
- Lymphangiomyomatosis[2]
- Multiple retinal nodular hamartomas
- Nontraumatic ungual or periungual fibromas
- Renal angiomyolipoma[2]
- Shagreen patch (connective tiss
- Subependymal nodule
- Subependymal giant cell astroc

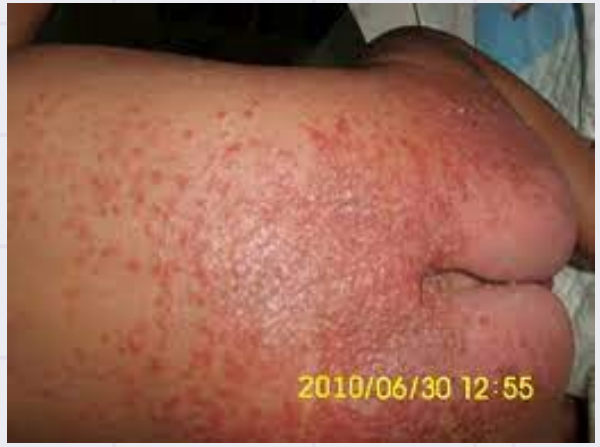
Minor Features

- Bone cysts[3]
- Cerebral white matter radi lines[1,3,4]
- "Confetti" skin lesions
- Gingival fibromas
- Hamartomatous rectal polyps[5]
- Multiple randomly distributed enamel
- Multiple renal cysts[5]
- Nonrenal hamartoma[5]
- Retinal achromic patch

clues in skin : rash, dermatitis

- Biotinidase deficiency
- Propionic acidemia(orgnic acidemia)
- Refsum disease(peroxysomal disorder)

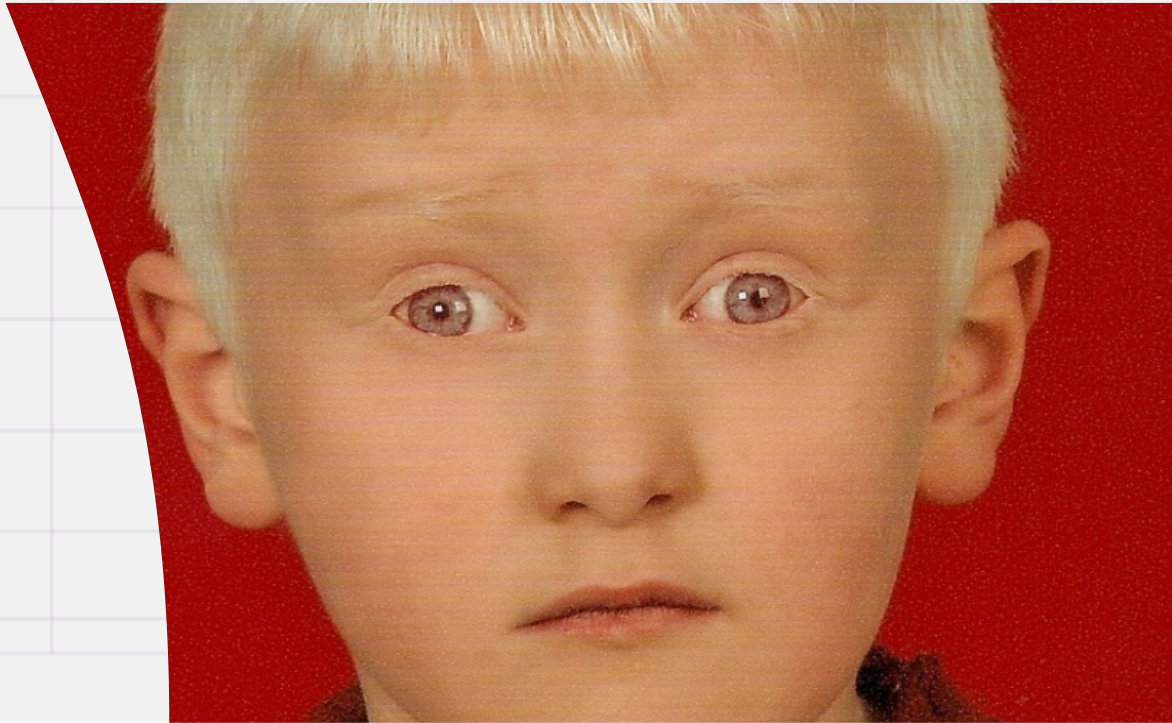




Clues in hair : Abnormal hair

- Eg:Menkes disease: global delay + hair coloreless , friable,kinky

Low cupper + cerulolasmin

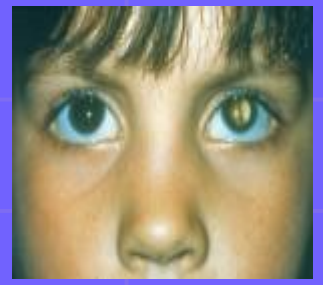


- Gricelli syndrome : Silvery hair

Clues in the eyes

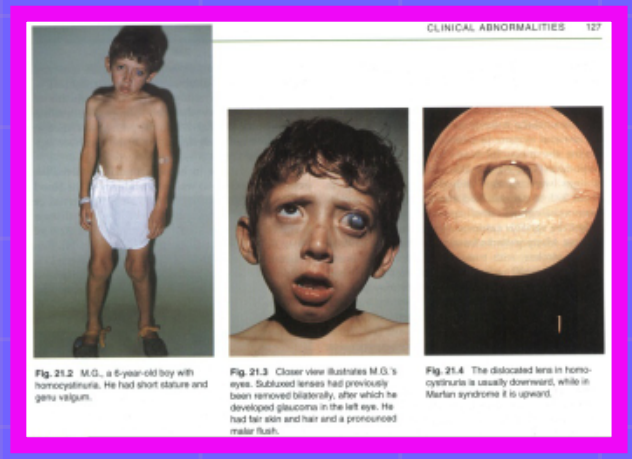
- **Cataracts :**

-Galactosemia
-Zellweger syndrome
- Lowe syndrome
-Other conditions



- **Dislocated lenses:**

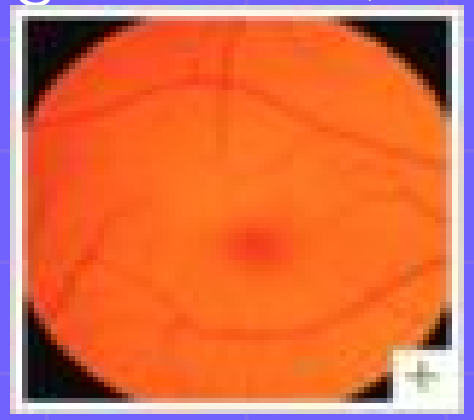
-Homocystinuria,
- Molybdenum co-factor deficiency
-Sulfite oxidase deficiency



- **Retinal degenerative changes**

-peroxisomal disorders
-others

Cherry red spot : (mainly lipid storage disease)
-Neimann pick
-Tay sack
-GM1 gangliosidosis
-Sandhoff disease
-Metachromatic leukodystrophy
-mucolipidosis



Then to summerize

History and examination : very important guides towards investigations and diagnosis

If there is no clinical features to suggest a specific diagnosis→ less likely to find a diagnosis

Lab investigations : necessary to reach for a final diagnosis

Lab investigations

If family history of specific disorder – screen for that disorder

If clue in examination : screen for that disorder

If no hint , what to do ?

Hearing+ vision assessment

- Should be done **for all** developmentally delayed children

Metabolic work up including test for thyroid

High resolution chromosomal microarray

Karyotype : if microarray not available (yield is 3.7%): it is indicated in the evaluation even in the absence of dysmorphic features

Testing for fragile X (yield 2.6%)

Females : frequently affected , may also be considered for testing

Advancement in genetic testing

High resolution chromosomal microarray have a diagnostic yield of 15%-20%.

Targeted gene panels has 11-32% diagnostic rate

Whole exome sequencing :has a diagnostic yield of around 40%

whole genome sequencing : 42 %

EEG

- Not recommended in the routine evaluation if child does not seize

Neuroimaging

- MRI brain : abn detected in 48-65% of cases

Identified aetiology

- Traditional tests : diagnostic yield 40% - 60%

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Brain & Development 33 (2011) 810–815

DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Profile of developmental delay in children under five years of age in a highly consanguineous community: A hospital-based study – Jordan

Amira Masri [a,*], Hanan Hamamy [b], Amal Khreisat [a]

[a] *Department of Pediatrics, Division of Child Neurology, Faculty of Medicine, The University of Jordan, P.O. Box 1612, 11941 Amman, Jordan*
[b] *Department of Genetic Medicine and Development, Geneva University Hospital, Geneva, Switzerland*

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Diagnostic rate 44.5%

Abstract

Aim: To assess etiologies and risk factors for global developmental delay (GDD) in children.

Patients and methods: Between January 2006 and 2007, a retrospective study was carried out at the Child Neurology Clinic of Jordan University Hospital on all 229 children under five years of age presenting with GDD. To assess risk factors for GDD, 229 age-matched healthy children were included as controls.

Whole exome sequencing (WES

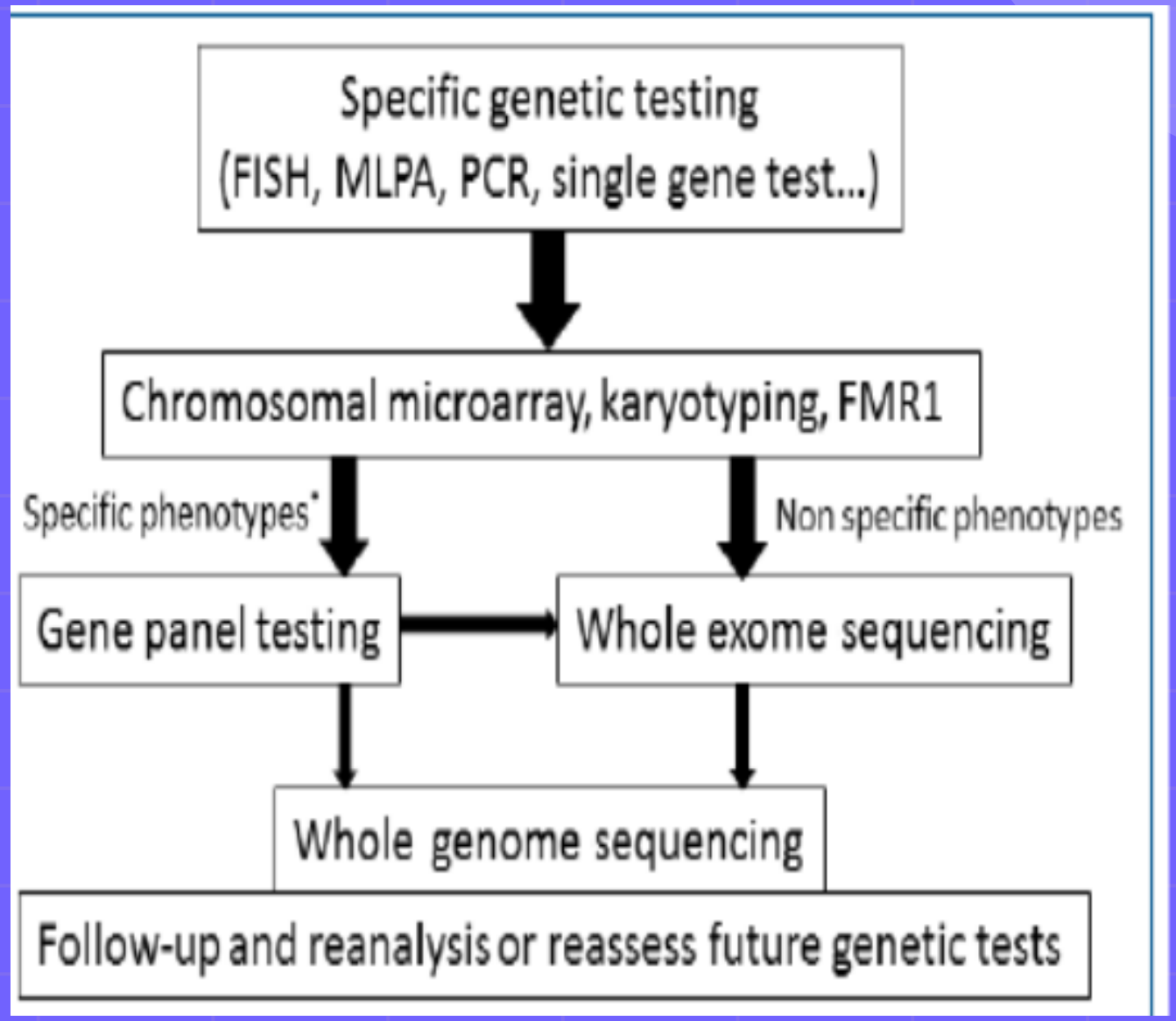
Powerful tool for etiological discovery in neurodevelopmental disorders

A high-throughput genetic sequencing method that focuses on the protein-coding regions of the genome

While protein-coding genes constitute only 1% of the human genome, they are home to 85 % of mutations underlying monogenic disorders

Diagnostic rate :40-60%

Should be done if all of the previous investigations did no t reveal any cause


Specific genetic testing
(FISH, MLPA, PCR, single gene test...)
Chromosomal microarray, karyotyping, FMR1
Specific phenotypes*
Non specific phenotypes
Gene panel testing
Whole exome sequencing
Whole genome sequencing
Follow-up and reanalysis or reassess future genetic tests

Conclusion

Developmental assessment is very crucial

History and examination are very helpful

Tremendous improvement in genetic progress gives hope to many families

Thank you