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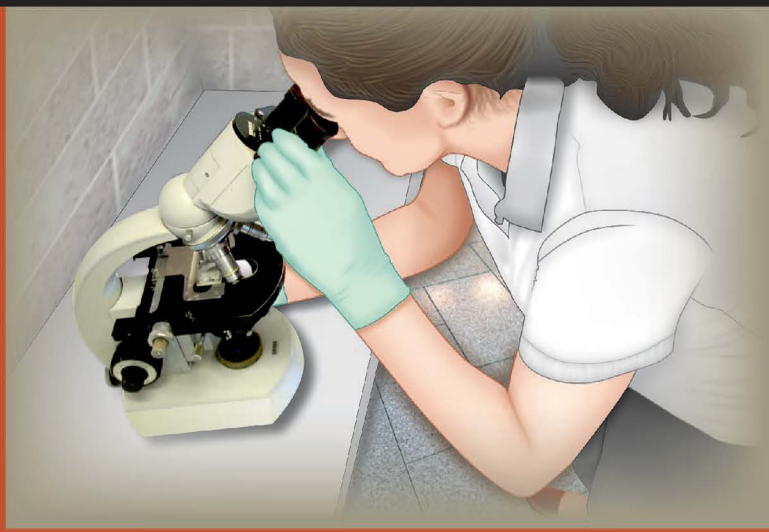

Celebrating 50 years
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Partha's Investigations and Interpretations in Pediatric and Adolescent Practice

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CHAPTER

2

Growth and Development

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2.1 GLOBAL DEVELOPMENTAL DELAY

Deepa Bhaskaran, MKC Nair

INTRODUCTION

Global delay can be defined as significant delay in two or more developmental domains: gross and fine motor; speech and language; cognition; personal and social development; or activities of daily living.[1]

Significant delay means performance of two or more standard deviations below the mean on developmental screening or assessment tests. The severity of delay can be classified as mild, moderate or severe, if the functional age is less than 33% below chronological age, 34–66% below chronological age, if functional age is more than 66% below chronological age respectively.[1]

The term GDD (global developmental delay) is used in children younger than 5 years in whom it is difficult to measure the IQ. The term "intellectual developmental disorder" is used in older children in whom IQ can be measured using standard tests (Table 2.1.1).[2]

Table 2.1.1: Investigations for inborn errors of metabolism.

Hematological investigations	*Urine*	*Neuroimaging*	*EEG*
Full blood count and ferritin: Iron deficiency	• Sialyl-oligosaccharides • Organic acids	*MRI:* If there are abnormal neurological examination findings, abnormal head size, seizures, and vision problems *MRI findings:* • Neurovascular diseases such as hypoxic-ischemic injury and non-specific findings: delayed myelination, hypoplasia of corpus callosum, ventriculomegaly. • Recognizable neurodegenerative diseases such as tuberous sclerosis, Sturge-Weber syndrome. • *Structural malformations:* Corpus callosum agenesis, heterotopia, Chiari malformations	EEG is done, if there are abnormal neurological findings, seizures, regression of language or suspected neurodegenerative disorder
Thyroid function tests: Hypothyroidism			
Uric acid level: To diagnose purine disorders			

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Creatinine kinase (CK): CK can help to distinguish between central (where there is normal CK) and peripheral (where CK may be elevated) causes of motor delay.			
Metabolic: Lactate • Ammonia • Amino acids • Homocysteine • Biotinidase estimation • LFT • Calcium • Acylcarnitine profile • VLCFA • White cell enzymes			
Genetics			
G-band karyotyping. Subtelomeric FISH, Microarray.			

(EEG: electroencephalogram; FISH: fluorescence in situ hybridization; LFT: liver function test; VLCFA: very-long-chain fatty acids)

INVESTIGATIONS IN A CASE OF GLOBAL DEVELOPMENTAL DELAY

The investigations considered in the literature fall into the categories of genetics, neuroimaging, electrophysiology, and biochemical including metabolic.

First-line Investigations

Blood

- *Thyroid function tests*: Hypothyroidism is an easily treatable disorder, with significant implications if the diagnosis is missed. Many chromosomal abnormalities are associated with an increased risk of hypothyroidism, e.g. trisomy 21, 45X, and 22q11 deletion.
- *Uric acid level*: This is more stable than both ammonia and lactate, and is an easy way to diagnose purine disorders, which may present as isolated global delay.
- *Full blood count and ferritin*: Iron deficiency can be associated with developmental delay and can easily be detected and treated.
- *Creatinine kinase*: CK can help to distinguish between central (where there is normal CK) and peripheral (where CK may be elevated) causes of motor delay.

There are many peripheral neuromuscular conditions where the CK is always elevated from birth (e.g. in Duchenne and Becker muscular dystrophies, and in some of the congenital muscular dystrophies, and some limb girdle muscular dystrophies) and other conditions where CK is mildly elevated or normal (e.g. spinal muscular atrophy, neuropathies, and congenital myopathies).

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Second Line Investigations

Metabolic: These are considered, if the family history is suggestive, history of developmental regression or consanguinity. If the clinical examination reveals abnormal head size, organomegaly, coarse features, seizure, abnormal neurology, and metabolic work up is done.

Blood tests:

- Lactate, ammonia, amino acids, homocysteine, biotinidase estimation
- Liver function test, calcium, acylcarnitine profile
- Very-long-chain fatty acids white cell enzymes.

Urine:

- Sialyloligosaccharides
- Organic acids.

Neuroimaging

MRI: If there are abnormal neurological examination findings, abnormal head size, seizures, and vision problems.

MRI findings: Neurovascular diseases such as hypoxic-ischemic injury and nonspecific findings: delayed myelination, hypoplasia of corpus callosum, ventriculomegaly.

Recognizable neurodegenerative diseases such as tuberous sclerosis, Sturge-Weber syndrome.

Structural malformations: Corpus callosum agenesis, heterotopia, chiari malformations.

Metabolic diseases:[3,4]

- Diffuse cortical migration and sulcation abnormalities are seen in Zellweger's syndrome.
- Agenesis of the corpus callosum is seen in pyruvate decarboxylase deficiency, Menke's disease and nonketotic hyperglycinemia.
- Brainstem and cerebellar edema are seen in Maple syrup urine disease.
- Subdural hematomas and frontotemporal atrophy suggest Glutaric aciduria.
- Hunter's disease is a rare, X-linked mucopolysaccharidosis and it shows perivascular space enlargement, subarachnoid space enlargement, 3rd ventricle dilatation, pituitary sella abnormalities, cranial hyperostosis, craniosynostosis, enlarged cisterna magna, dens hypoplasia, periodontoid thickening, spinal stenosis, platyspondylia and disk abnormalities, which are frequently detected.

CT: Only where cerebral calcification is suspected, e.g. in perinatal infection or to look for abnormality of skull bones.

Neurophysiology

Electroencephalogram: Done if there are abnormal neurological findings, seizures, regression of language or suspected neurodegenerative disorder.

It is important to recognize subtle seizures, such as:

- Infantile spasms
- Drop attacks, head drops, atonic seizures
- Myoclonic seizures
- Staring spells

Electroencephalogram is of considerable value, if there is a history of regression in speech-language or regression in milestones to rule out.

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- Epilepsy aphasia syndromes—Landau Kleffner syndrome
- Epileptic encephalopathies—Dravet syndrome, etc.

Electroencephalogram yield in developmental delay without definite seizures is low and may reveal nonspecific epileptiform abnormalities.

GENETICS

Cytogenetic Testing

Genomic-wide testing for DNA rearrangements:

- *G-band karyotyping*: Detects chromosomal structural changes with a resolution of 3–5 million base pairs (3–5 mb)
- *Subtelomeric FISH testing*: Detect copy number changes (deletions or duplications) for which specific probes are constructed, resolution of 1 mb.
- *Microarray tests*:
  - Oligonucleotide probes
  - Resolution of 30,000–35,000 base pairs (kb)

Chromosomal microarray (CMA) testing is abnormal on average in 7.8% of subjects with GDD/ID and in 10.6% of those with syndromic features.

Chromosomal microarray has limitations. It can identify only unbalanced copy number changes. Not sensitive for:

- Inversions
- Balanced insertions
- Reciprocal translocations
- Polyploidy
- Low level mosaicism (<20–25%)
- Rearrangements in repeat sequences
- Point mutations
- Duplications/deletions undetectable test's resolution.

First Tier Genetic Testing

If a child has an identifiable or probable genetic syndrome such as Down syndrome or Turner syndrome for which genetic testing is available, karyotyping should be performed first.

If after a detailed clinical history, physical examination, and family history one cannot point at a specific disorder, then CMA should be considered first line for a diagnostic genetic evaluation of an individual with GDD or ID.

Chromosomal microarray permits genome-wide detection of copy number variants (CNVs) at a significantly higher resolution than G-banded karyotyping. Currently, available CMA platforms allow the detection of CNVs with a minimum resolution of 100 kb throughout the genome, compared with a lower limit of detection of 3–5 mb on G-banded karyotype. Therefore, CMA is superior in the detection of pathogenic microdeletions and microduplications, in addition to detection of cryptic genomic imbalances associated with apparently balanced chromosome rearrangements and more precise characterization of unbalanced chromosome rearrangements detected.

The two main types of CMA currently used are the comparative genomic hybridization array and the oligonucleotide array [including the single nucleotide polymorphism (SNP)-based array].

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Second Tier Genetic Testing

- Finding common single-gene syndromes in children with GDD or ID based on the clinical features. For example, Rett syndrome, Angelman syndrome, Prader-Willi syndrome.
- *Gene panels*: Multigene panels are available for the evaluation of GDD or ID; these panels are frequently focused on a subtype such as X-linked ID (XLID), or GDD or ID plus distinctive features including microcephaly, macrocephaly, seizures, or autism.
- *Most advanced genetic testing*: Whole exome sequencing (WES) or whole genome sequencing (WGS).

Whole exome sequencing: Here the sequence analysis of the areas of the genome that are primarily protein-coding (about 1% of the total genome) is done.

Whole genome sequencing: Here most of all DNA sequences in a person's genome are analyzed.

Whole exome sequencing has the advantage of being cheaper and less labor intensive than WGS.

Limitations of WES or WGS:

- All areas of the genome may not be captured and analyzed, even in WGS. Hence clinically significant genetic mutations may be missed.
- Epigenetic changes—heritable alterations in gene function that occur without a permanent change in DNA sequence—are not routinely detectable by either WES or WGS.

Third Line Investigations

- Metabolic
- Isoelectric focused transferrin
- 7-dehydrocholesterol
- Blood gas or chloride to calculate anion gap, if not done already
- Paired plasma creatinine and urine guanidinoacetate.

NONSYNDROMIC CHILD

In a consensus meeting[4] chromosome analysis and DNA testing for fragile X-syndrome have been recommended. While most children with chromosome abnormalities are dysmorphic, some are not, including most children with sex chromosome aneuploidy (XXX, XXY, XYY), as well as the increasing number of children found to have subtle deletions, duplications or other chromosome rearrangements with newer cytogenetic techniques. Fragile X may not be associated with specific dysmorphic features (long face, large ears, and large testes) especially in females or prepubertal males, and has been associated with 2–6% of males and 2–4% of females with undiagnosed intellectual disability.[5]

The prevalence of inborn errors of metabolism among children presenting with undifferentiated intellectual disability is extremely low.[4] In most of cases, children with metabolic disorders will have one or more other clinical features. These include developmental regression, ataxia, seizures, hypotonia, episodes of decreased level of consciousness, eye abnormalities, deafness, growth retardation and hepatomegaly among others. Therefore, routine metabolic screening is not recommended.[4]

The value of diagnostic imaging with computed tomography or magnetic resonance imaging (MRI) in a nondysmorphic, intellectual disability child who has a normal head circumference and no abnormal neurological symptoms or signs is unknown. In general, this should not be

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considered necessary unless there are other unusual features (e.g. neurological signs, macro- or microcephaly).

SYNDROMIC CHILD

In addition to the investigations listed above, a child who presents with unusual features, which may be related to disturbances in growth, specific birth defects, dysmorphic features, unusual behavior and so on, may warrant specific targeted investigations. They include:

Dysmorphic With or Without Congenital Anomalies

- Targeted fluorescence *in situ* hybridization analysis for specific chromosome microdeletion syndromes [e.g. velocardiofacial (VCF), Williams and Prader-Willi]
- Specific gene analysis or biochemical analysis (e.g. 7-dehydrocholesterol for Smith-Lemli-Opitz syndrome)
- Uniparental disomy studies (e.g. Prader-Willi syndrome, Angelman syndrome, balanced 13;14 translocation carrier)[5]
- High resolution banding chromosomes
- Chromosome studies from skin biopsy to search for somatic mosaicism, especially in the presence of unusual skin hyper- or hypopigmentation, or asymmetry of the body
- Search for occult congenital anomalies (e.g. renal ultrasound, cardiac echocardiogram)
- Central nervous system (CNS) and magnetic resonance imaging (MRI)
- Electroencephalogram (e.g. Angelman syndrome).

Overgrowth

- Bone age
- Abdominal ultrasound (e.g. in Beckwith-Wiedemann syndrome to look for organomegaly, tumors)
- CNS imaging (MRI) especially in Soto's syndrome.

Disproportionate Short Stature

- Skeletal survey radiographs
- Specific DNA analysis for suspected gene (e.g. FGFR3 for achondroplasia).

Unusual Head Shape (Craniosynostosis)

- Computed tomography (better than MRI for assessing cranial sutures)
- Specific gene analysis (e.g. TWIST for Saethre–Chotzen syndrome).

Coarse Facies

- Urine mucopolysaccharides and oligosaccharides
- Thyroid-stimulating hormone
- Skeletal survey.

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Hypotonia

- Creatinine kinase (especially in boys)
- Lactate
- Thyroid-stimulating hormone
- Neurological workup (e.g. electromyelogram or nerve conduction studies, muscle biopsy, CNS imaging)
- Specific DNA analysis for suspected gene (e.g. Prader-Willi syndrome, myotonic dystrophy, Duchenne and/or Becker muscular dystrophy).

In many cases, a genetic syndrome may not be obvious at birth or even in the first few years of life. As the child grows and develops, certain physical or behavioral features may appear that make the syndrome more recognizable. With the passage of time, new syndromes are described, and older syndromes are better delineated. Therefore, repeat assessments periodically over the years in a child with an undiagnosed syndrome may be warranted.

INVESTIGATING A CHILD WITH SUSPECTED INBORN ERROR OF METABOLISM[5]

History: The family history should be examined for consanguinity, unexplained neonatal or infantile deaths and for a three-generation pedigree.

Pregnancy and birth details: Children with inborn error of metabolisms (IEMs) are usually born of normal birth weight. Exceptions to this are disorders such as nonketotic hyperglycinemia and disorders of pyruvate metabolism which have intrauterine or immediate effects following birth.

Rule out a history of maternal acute fatty liver of pregnancy (AFLP) or hemolysis, elevated liver enzymes and low platelets (HELLP). This can be associated with several fatty acid oxidation disorders.

Useful clues in the past medical history of the child to an underlying IEM are a history of hypoglycemia, an episode of unexplained encephalopathy, or an extreme reaction requiring hospitalization to an otherwise supposed mild illness such as gastroenteritis. There may be unusual food behaviors such as protein aversion which is seen most commonly in the urea cycle disorders. A history of self-injurious behavior can be seen in Lesch-Nyhan syndrome and hyperammonemia; other psychiatric abnormalities can be associated with disorders of cobalamin and later onset lysosomal storage disorders.

History of regression makes an IEM much more likely. The pattern of delay is also important. Hypotonia with gross motor delay is seen in the organic acidurias, fatty acid oxidation disorders and urea cycle defects.

Sanfilippo syndrome (mucopolysaccharidosis type III) presents with speech delay as the first sign.

Generalized developmental delay with associated sensorimotor hearing loss suggests a mitochondrial disorder.

Seizures with developmental delay: Severe seizure disorder in the newborn period occurs in nonketotic hyperglycinemia, peroxisomal disorders and in sulfite oxidase/molybdenum cofactor deficiency.

Beyond infancy: Epilepsy is quite common in mildly delayed children and would not specifically indicate an IEM. A severe seizure disorder and delay is seen in many of the lysosomal storage disorders, but in these cases there is usually neurological regression giving stronger indication

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of IEM. The group of creatine deficiency disorders can cause seizures and developmental delay, although more usually there are extrapyramidal movements and hypotonia.

BASELINE INVESTIGATIONS IN GLOBAL DELAY WITH NO SPECIFIC ASSOCIATED FINDINGS

Blood

- Full blood count
- Urea, sodium, potassium, calcium
- *Liver function tests*: ALT, ALP, cGT, albumin
- Lactate
- Creatine kinase
- Thyroid function tests (TSH, free thyroxine)
- Ammonia
- Urate
- Amino acids.

Urine

- Organic acids
- Amino acids
- Glycosaminoglycans.

Serum Lactate

Disorders of energy metabolism such as disorders of gluconeogenesis, disorders of pyruvate metabolism and respiratory chain mitochondrial disorders can be screened with blood lactate estimation.

Increase in lactate with associated hypoglycemia is suggestive of gluconeogenic disorders. Blood lactate level may be erroneously elevated when associated with excessive screaming, tourniquet pressure or hemolysis. Hence, mildly elevated lactate levels (up to 3 mmol/L) may be difficult to interpret.

Increased lactate along with elevated plasma alanine and proline suggests a chronic lactic acidemia. CSF lactate is a more reliable indicator of elevated lactate. It can be elevated when plasma lactate is normal, especially if the clinical presentation is largely neurological.

Serum Ammonia Level

This may also be elevated erroneously such as lactate. Elevated ammonia is indicative of a urea cycle disorder. This may be due to a primary urea cycle defect or secondary to liver disease, drugs such as sodium valproate, or another inborn error.

Urine Organic Acids

- This helps to detect nearly all organic acid defects and some fatty acid oxidation defects.
- If the index of suspicion is high but the preliminary tests are negative repeat testing during acute illness is important.

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Creatine Kinase

Duchenne muscular dystrophy can present with delay in more than one developmental domain (e.g. Language and motor delay) especially in boys. Hence CK is measured as a first-line investigation in boys with global developmental delay. CK measurement is considered in girls with severe global (and especially motor) developmental delay. Raised creatine kinase is a nonspecific finding in fatty acid oxidation defects.

Urate Measurement

Low urate level may indicate a defect of purine metabolism or molybdenum cofactor deficiency and a high concentration is seen in several IEMs such as Lesch-Nyhan syndrome and glycogen storage disorders.

Electrolytes and urea are first-line investigations to rule out renal disorders.

Calcium Measurement

It can assist in the diagnosis of Velocardiofacial and Williams syndromes, and pseudohypoparathyroidism.

Urinary Glycosaminoglycans

This is indicative of mucopolysaccharidosis type III (Sanfillipo disease) as it presents solely as developmental delay. In sanfillipo disease, the coarse facial dysmorphism typically associated with MPS disorders is generally absent. Hence a diagnosis of an MPS disorder as a cause of pure developmental delay may not be considered.

Serial review in children with developmental delay is important. With time new symptoms such as the repetitive hand movements of Rett syndrome, or a protein aversion may become clearer as the child reaches an age where they would eat a more varied diet. Organomegaly becomes more obvious as the disorder progresses, and slowly evolving regression is only obvious as time elapses. In patients with a high index of suspicion of IEM, they should be reviewed for two assessments in the first year of life, thereafter annually until school age, and once more at puberty.

Specific Investigations for Inborn Error of Metabolism[5]

In situations where developmental delay is associated with a specific finding, i.e. hypotonia, regression, eye abnormalities, hepatosplenomegaly, or dysmorphism it is valuable to carry out investigations specific to those IEM which can present with these factors (Table 2.1.2).

Table 2.1.2: Developmental delay plus disorder test.

Disorder	*Test*
Hypotonia	
• Peroxisomal disorders • Biotinidase deficiency • Purine/pyrimidines disorders	• Very long chain fatty acids (P) • Biotinidase assay (P) • Urate (B) and (U) Purine/pyrimidines (U)

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• Neurotransmitter deficiencies • Fatty acid oxidation defects • Organic acid disorders	• Biopterins (B) + (C) Neurotransmitters (C) • Acylcarnitines (P) • Organic acids (U)
Neurological regression	
• Biotinidase deficiency • Mucopolysaccharidoses • Neuronal ceroid lipofuscinosis • Other lysosomal disorders • Mitochondrial disorders • Neurotransmitter deficiencies	• Biotinidase (P) • Urine glycosaminoglycans (U) White cell enzymes (B) • Vacuolated lymphocytes, NCL enzymes, mutations (B) • White cell enzymes (B) Oligosaccharides (U) • Lactate (B) and (C) • Respiratory chain enzymes (muscle and skin) Mitochondrial mutations/deletions (B and muscle) • Neurotransmitters (C) Biopterins (B) and (C)
Organic acid disorders	
• Eye signs • Peroxisomal disorders • Disorders of cholesterol synthesis	• Organic acids (U) Acylcarnitines (P) • Very long chain fatty acids (P) 7-dehydrocholesterol, cholesterol (B)
Mitochondrial disorders	
• Congenital disorders of glycosylation • Sulfite oxidase deficiency • Homocystinuria • Lysosomal storage disorders • Cerebrotendinous xanthomatosis	• Lactate (B), CSF lactate • Transferrin isoforms (B) • Urate (P), sulfites (U) • Homocysteine (P) • Amino acids (homocystine) (U) • Glycosaminoglycans (U) • White cell enzymes (B) • Bile acids (U)
Severe seizure disorder	
• Sulfite oxidase deficiency/molybdenum cofactor deficiency • Biotinidase deficiency • Neuronal ceroid lipofuscinosis • Nonketotic hyperglycinemia • Creatine deficiency	• Urate (P) Sulfites (U) • Biotinidase • Vacuolated lymphocytes, NCL enzymes, mutations (B) • Amino acids (P and U) • 24-hour creatine: creatinine, specific metabolites, MRS brain
Hepato(spleno)megaly	
• Lysosomal storage disorders • Urea cycle disorders • Bile acid disorders • Glycogen storage disorders	• Glycosaminoglycans (U) White cell enzymes (B) Oligosaccharides (U) • Ammonia Amino acids (P) and (U) Orotic acid (U) • Bile acids (U) • Lactate (B), glucose profile, cholesterol, triglycerides

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Developmental delay plus dysmorphism	
• Smith-Lemli-Opitz • Peroxisomal disorders • Congenital disorders of glycosylation • Mucopolysaccharide disorders and other storage disorders	• 7-dehydrocholesterol, cholesterol (P) Cholesterol precursors (P) • Very long chain fatty acids (P) Plasmalogens (XR epiphyses) • Transferrin isoforms (P) • Glycosaminoglycans (U) White cell enzymes (B)

[B: blood; P: plasma; U: urine; C: CSF (cerebrospinal fluid)]

REFERENCES

1. Majnemer A, Shevell MI. Diagnostic yield of the neurologic assessment of the developmentally delayed child. J Pediatr. 1995;12(7):193-9.
2. Banerjee M. An Approach to Global Developmental Delay in Children. In: Meschino WS (Eds). The child with developmental delay: An approach to etiology. Paediatr Child Health. 2003;8(1):16-9.
3. Kachewar SG, Sankaye SB, Kulkarni DS, et al. The role of radiodiagnosis in inborn errors of metabolism. J Clin Diagnostic Res. 2011;(Suppl-2)5(7):1467-72.
4. Cleary MA, Green A. Developmental delay: when to suspect and how to investigate for an inborn error of metabolism. Arch Dis Child. 2005;90:1128-32.
5. Curry CJ, Stevenson RE, Aughton D, et al. American College of Medical Genetics. Evaluation of mental retardation: Recommendations of a consensus conference. Am J Med Genet. 1997;72:468-77.

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