

# Differential Diagnosis of Pediatric Neurodisorders

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## PREDOMINANT ETHNIC BACKGROUND

Ashkenazi Jews	Nova Scotia
Classic Tay-Sachs disease	Type D Niemann-Pick disease
Infantile Niemann-Pick disease	Japan
Juvenile Gaucher disease	Sialidosis with chondrodystrophy
Recessive dystonia musculorum deformans	Scandinavia
Mucopolysaccharidosis IV	Finnish (infantile) variant of ceroid lipofuscinosis
Canavan disease	Juvenile neuronopathic Gaucher disease
Dysautonomia	Krabbe disease
Juvenile non-neuronopathic Gaucher disease	Aspartylglucosaminuria
Saudi Arabia	Baltic myoclonus epilepsy (Unverricht-Lundborg syndrome)
Canavan disease	

## TYPICAL AGE AT ONSET

Neonatal or Early Infantile	Preschool Years
Aminoacidurias and organic acidurias Urea cycle disorders	Aminoacidurias, organic acidurias, urea cycle disorders with partial enzyme deficiency
Galactosemia	Aspartylglucosaminuria
Connatal Pelizaeus-Merzbacher syndrome	Marinesco-Sjögren syndrome
Connatal Alexander disease	Alexander disease
Congenital sialidosis	Ataxia telangiectasia
Early onset mitochondrial diseases	Xeroderma pigmentosum
Spongy degeneration (Canavan) (some cases)	Chediak-Higashi disease
Aicardi-Goutieres syndrome	Metachromatic leukodystrophy
Infantile Gaucher disease	Late infantile gangliosidoses
Infantile adrenoleukodystrophy	Niemann Pick--Nova Scotia variant
Zellweger syndrome and variants	Late infantile ceroid lipofuscinosis
Neonatal adrenoleukodystrophy	Sanfilippo syndromes
Chondrodysplasia punctata	Maroteaux-Lamy disease
Infantile Refsum syndrome	Mild Hunter disease
GM <sub>1</sub> gangliosidosis (infantile variant)	Leigh syndrome and other mitochondrial cytopathies
I-cell disease (mucopolysaccharidosis II)	Kearns-Sayre syndrome
Trichopoliodystrophy (Menkes)	Disintegrative psychosis
Neurocutaneous syndromes	Other autistic regression
Progressive spinal muscular atrophy (Werdnig-Hoffmann disease)	School Age or Adolescence
Seckel bird-headed dwarfs	Acute intermittent porphyria
Infantile	Juvenile ceroid lipofuscinosis
Aminoacidurias, organic acidurias, urea cycle disorders with partial enzyme deficiency	Adrenoleukodystrophy Late variants of gangliosidoses
Many sphingolipidoses, mucopolysaccharidoses, mucopolysaccharidoses Infantile ceroid lipofuscinosis	Niemann-Pick with vertical ophthalmoplegia
Leigh syndrome (early types)	Fabry disease
Other mitochondrial cytopathies	Cerebrotendinous xanthomatosis
Lesch-Nyhan syndrome	Leigh syndrome (some variants)
Sjögren-Larsson syndrome Spongy degeneration	Other mitochondrial cytopathies (e.g., MERFF, MELAS)
Wolman disease	Refsum disease
Alexander disease	Friedreich ataxia
Pelizaeus-Merzbacher disease	Bassen-Kornzweig disease
Neuraxonal dystrophy	Other spinocerebellar degenerations
Infantile Hallervorden-Spatz disease	Dystonia musculorum deformans
Infantile fucosidosis	Juvenile Huntington disease
Nephrosialidosis	Juvenile parkinsonism
Sialidosis	Classic Hallervorden-Spatz syndrome
Pompe disease	Lafora disease
Xeroderma pigmentosum	Baltic myoclonus
Cockayne disease	Subacute sclerosing panencephalitis (SSPE)
Infantile galactosialidosis	Wilson disease
Progeria	Sialidosis with cherry red spot-myoclonus (variants with and without chondrodystrophy)
Rett syndrome	

## CLUES IN PHYSICAL EXAMINATION

<i>Big Head</i>	<i>Skin Abnormalities</i>
Tay-Sachs disease	<b>Thin atrophic skin:</b>
Alexander disease	Ataxia telangiectasia
Spongy degeneration (Canavan)	Cockayne disease
Hurler disease	Xeroderma pigmentosum
Other mucopolysaccharidoses with hydrocephalus	Progeria
<i>Small Head</i>	<b>Thick skin:</b>
Krabbe disease	I-cell disease
Infantile ceroid lipofuscinosis	Mucopolysaccharidoses I, II, III
Some infantile mitochondrial disorders	Infantile fucosidosis
Neuraxonal dystrophy	<b>Subcutaneous nodules:</b>
Incontinentia pigmenti	Farber disease
Cockayne disease	Neurofibromatosis
Rett syndrome	Cerebrotendinous xanthomatosis
Bird-headed dwarfs	<b>Xanthomas:</b>
	Niemann-Pick disease
<i>Hair Abnormalities</i>	<b>Blotching:</b>
<b>Stiff, wiry:</b>	Dysautonomia
Trichopoliodystrophy (Menkes)	
<b>Frizzy hair:</b>	<i>Enlarged Nodes</i>
Giant axonal neuropathy	Farber disease
<b>Hirsutism:</b>	Niemann-Pick disease
Infantile GM <sub>1</sub> gangliosidosis	Juvenile Gaucher disease
Hurler, Hunter, Sanfilippo syndromes	Chediak-Higashi disease
I-cell disease	Ataxia telangiectasia (lymphoma)
<b>Gray:</b>	<i>Stridor, Hoarseness</i>
Ataxia telangiectasia	Infantile-onset peroxisomal disorders
Cockayne disease	Farber disease
Chediak-Higashi disease	Infantile Gaucher disease
Progeria	Pelizaeus-Merzbacher disease
<i>Skin Abnormalities</i>	<i>Enlarged Orange Tonsils</i>
<b>Telangiectasia:</b>	Tangier disease
Ataxia telangiectasia	<i>Severe Swallowing Problems</i>
<b>Angiokeratoma:</b>	(Present late in course of all patients with severe bulbar, pseudobulbar, cerebellar, or basal ganglia pathology)
Fabry disease	
Juvenile fucosidosis	Infantile Gaucher disease
Galactosialidosis	Dysautonomia
<b>Ichthyosis:</b>	Hallervorden-Spatz syndrome
Refsum disease	Dystonia musculorum deformans
Sjögren-Larsson syndrome	Zellweger syndrome
<b>Hypopigmentation:</b>	<i>Heart Abnormalities</i>
Trichopoliodystrophy (Menkes)	Pompe disease
Chediak-Higashi syndrome	Hurler disease and other mucopolysaccharidoses
Tuberous sclerosis (ash leaf spots)	Fabry disease
Hypomelanosis of Ito	Infantile fucosidosis
Prader-Willi	Refsum disease
Phenylketonuria	Friedreich ataxia
<b>Hyperpigmentation:</b>	Zellweger syndrome
Niemann-Pick disease	Tuberous sclerosis
Adrenoleukodystrophy	Progeria
Farber disease	Abetalipoproteinemia (Bassen-Kornzweig disease)
Neurofibromatosis (cafe au lait spots)	
Xeroderma pigmentosum	
Incontinentia Pigmenti	
<i>Heart Abnormalities</i>	<i>Bone and Joint Abnormalities</i>
Disorders of carnitine metabolism	<b>Stiff joints:</b>
Duchenne muscular dystrophy	Mucopolysaccharidoses (all but type I-S)
Kearns-Sayre syndrome	Mucolipidoses (most types)
	Fucosidosis
<i>Strokes</i>	Farber disease
Fabry disease	Sialidoses (some forms)
Trichopoliodystrophy (Menkes)	Zellweger syndrome
Progeria	Rhizomelic chondrodysplasia punctata
MELAS	Cockayne disease
Homocystinuria	
Sickle cell diseases	<b>Scoliosis:</b>
	Friedreich ataxia
<i>Organomegaly</i>	Ataxia telangiectasia
Mucopolysaccharidoses (most types)	Dystonia musculorum deformans
Infantile GM <sub>1</sub> gangliosidosis	All chronic diseases with muscle weakness, especially anterior horn cell involvement
Niemann-Pick disease	Rett syndrome
Gaucher disease	
Generalized peroxisomal disorders	<b>Kyphosis:</b>
Galactosemia	Mucopolysaccharidoses
Pompe disease	<i>Endocrine Dysfunction</i>
Mannosidosis	<b>Adrenals:</b>
	Adrenoleukodystrophy
<i>Gastrointestinal Problems</i>	

<b>Malabsorption:</b>	Wolman disease
Wolman disease	<b>Hypogonadism:</b>
Bassen-Kornzweig disease	Xeroderma pigmentosum
<b>Nonfunctioning gallbladder:</b>	Ataxia telangiectasia
Metachromatic leukodystrophy	Some spinocerebellar degenerations
Infantile fucosidosis	<b>Diabetes:</b>
<b>Jaundice:</b>	Ataxia telangiectasia
Infantile Niemann-Pick disease	<b>Dwarfing:</b>
Zellweger disease	Morquio disease
Galactosemia	Other mucopolysaccharidoses
Niemann-Pick disease	Cockayne syndrome
<b>Vomiting:</b>	Progeria
Dysautonomia	Diseases with severe malnutrition
Urea cycle defects	<b>Hypothalamic dysfunction</b>
<b>Diarrhea:</b>	De Sanctis-Cacchione syndrome
Hunter syndrome	<i>Neoplasms</i>
<i>Kidney Problems</i>	Ataxia telangiectasia
Renal failure:	Xeroderma pigmentosum
Fabry disease	Neurofibromatosis
Nephrosialidosis	Von Hippel-Lindau disease
Cysts:	Tuberous sclerosis
Zellweger syndrome	<i>Hearing Loss</i>
Von Hippel-Lindau disease	Hunter disease
Tuberous sclerosis	Other mucopolysaccharidoses
Neonatal OPCA	Generalized peroxisomal disorders
Joubert syndrome	Refsum disease
Stones:	Cockayne disease
Lesch-Nyhan disease	Kearns-Sayre and Leigh syndromes
Aminoaciduria:	Other mitochondrial cytopathies
Aminoacidurias	Some spinocerebellar degenerations
Lowe syndrome	Usher syndrome
Wilson disease	

**PROMINENT SEIZURES OR MYOCLONUS**

Acute intermittent porphyria
Gangliosidoses (infantile types especially)
Ceroid lipofuscinoses (late infantile variant especially)
MERFF, MELAS
Trichopolydystrophy (Menkes)
Zellweger syndrome
Generalized peroxisomal disorders
Infantile Alexander disease
Krabbe disease
Lafora disease
Baltic myoclonus
Sanfilippo disease
Juvenile Huntington disease
Tuberous sclerosis
Juvenile neuropathic Gaucher disease
SSPE

**MOTOR SIGNS**

<i>Floppiness in Infancy</i>	<i>Prominent Cerebellar Signs</i>
Progressive spinal muscular atrophy	Neuraxonal dystrophy
Congenital myopathies	Metachromatic leukodystrophy
Zellweger syndrome	Ataxia telangiectasia
Pompe disease	Leigh syndrome
Trichopolydystrophy	Niemann-Pick disease (Nova Scotia variant)
Neuraxonal dystrophy	Some late-onset gangliosidoses
Gangliosidoses (early variants)	Some sialidoses
Fucosidosis (infantile variant)	Friedreich ataxia
Infantile ceroid lipofuscinosis	Bassen-Kornzweig disease
Spongy degeneration (early)	Cerebrotendinous xanthomatosis
Leigh syndrome (early variant)	Other spinocerebellar degenerations
Neonatal OPCA	Lafora disease
<i>Peripheral Neuropathy</i>	Baltic myoclonus
Acute intermittent porphyria	Chediak-Higashi disease
Metachromatic leukodystrophy	Usher syndrome
Fabry disease	Neonatal OPCA
Krabbe disease	DeSanctis-Cacchione
Neuraxonal dystrophy	<i>Abnormal Posture or Movements</i>
Refsum disease	Wilson disease
Tangier disease	Lesch-Nyhan disease
Bassen-Kornzweig disease	Hallervorden-Spatz syndrome

Sialidosis (some variants)	Familial striatal necrosis
Mucopolipidosis III	Dystonia musculorum deformans
Cerebrotendinous xanthomatosis	Juvenile Niemann-Pick with ophthalmoplegia
Ataxia telangiectasia	Chronic GM <sub>1</sub> and GM <sub>2</sub> gangliosidoses
Adrenomyeloneuropathy	Pelizaeus-Merzbacher syndrome
Levy-Roussy syndrome	Crigler-Najjar disease
Mucopolysaccharidoses I, II, VI, VII (entrapment)	Ataxia telangiectasia
Cockayne syndrome	Juvenile ceroid lipofuscinosis
Some mitochondrial cytopathies	Juvenile Huntington disease
Giant axonal neuropathy	Juvenile Parkinsonism
<i>Prominent Cerebellar Signs</i>	Gilles de la Tourette syndrome
Wilson disease Late infantile ceroid lipofuscinosis	DeSanctis-Cacchione (Xeroderma pigmentosum with endocrine dysfunction)
Pelizaeus-Merzbacher disease	Dentato-rubro-luysial atrophy

**EYE FINDINGS**

<i>Conjunctival Telangiectasia</i>	<i>Macular and Retinal Pigmentary Degeneration</i>
Ataxia telangiectasia	Other mitochondrial cytopathies
Fabry disease	Hallervorden-Spatz syndrome (some types)
<i>Corneal Opacity</i>	Cockayne disease
Wilson disease (Kayser-Fleischer ring)	Sjögren-Larson syndrome (not always)
Mucopolysaccharidoses I, III, IV, VI	Usher syndrome
Mucopolipidoses III, IV	Some Other spinocerebellar syndromes
Fabry disease	Neurocutaneous syndromes
Galactosialidosis	<i>Optic Atrophy</i>
Cockayne disease	Krabbe disease
Xeroderma pigmentosum	Metachromatic leukodystrophy
Zellweger syndrome (inconstant)	Most sphingolipidoses late in their course
<i>Lens Opacity</i>	Adrenoleukodystrophy
Wilson disease	Alexander disease
Galactosemia	Spongy degeneration
Marinesco-Sjögren syndrome	Pelizaeus-Merzbacher disease
Lowe disease	Neuraxonal dystrophy
Cerebrocutaneous xanthomatosis	Neonatal mitochondrial cytopathies
Sialidosis (rarely significant clinically)	Leber congenital amaurosis
Mannosidosis	Some spinocerebellar degenerations
Zellweger syndrome	Diseases with retinal pigmentary degeneration
<i>Glaucoma</i>	<i>Nystagmus</i>
Mucopolysaccharidosis I--Scheie	Disease with poor vision (searching nystagmus)
Zellweger syndrome (infrequent)	Pelizaeus-Merzbacher syndrome
<i>Cherry-Red Spot</i>	Metachromatic leukodystrophy
Tay-Sachs disease	Friedreich ataxia
Sialidosis (usually)	Other spinocerebellar degenerations and cerebellar atrophies
Infantile Niemann-Pick (50% of cases)	Neuraxonal dystrophy
Infantile GM <sub>1</sub> gangliosidosis (50% of cases)	Ataxia telangiectasia
Farber disease (inconstant)	Leigh syndrome (inconstant)
Multiple sulfatase deficiency (metachromatic leukodystrophy variant)	Marinesco-Sjögren syndrome
<i>Macular and Retinal Pigmentary Degeneration</i>	Opsoclonus-myoclonus syndrome
Ceroid lipofuscinosis (most types)	Chediak-Higashi syndrome
Mucopolysaccharidoses I-H and I-S, II, III	<i>Ophthalmoplegia</i>
Mucopolipidosis IV	Leigh syndrome
Bassen-Kornzweig syndrome (abetalipoproteinemia)	Kearns-Sayre and Leigh syndromes
Peroxisomal disorders	Niemann-Pick variant with vertical ophthalmoplegia (type C)
Olivopontocerebellar variant	Bassen-Kornzweig syndrome
Refsum disease (all types)	Ataxia telangiectasia
Kearns-Sayre syndrome	Infantile Gaucher disease
Leber congenital amaurosis	Tangier disease

**USEFUL LABORATORY TESTS**

<p><b>Urine</b></p> <ul style="list-style-type: none"> <li>Amino acids, organic acids</li> <li>Galactose, other sugars</li> <li>Mucopolysaccharides, sialylated oligosaccharides</li> <li>N-Acetyl aspartic acid</li> <li>Copper excretion</li> <li>Porphyryns</li> <li>Metachromatic granules</li> <li>Oxalate, cysteine crystals</li> </ul> <p><b>Blood Chemistry</b></p> <ul style="list-style-type: none"> <li>Ammonia (urea cycle disorders)</li> <li>Lactate-pyruvate ratio (Leigh syndrome, other mitochondrial cytopathies)</li> <li>Amino acids, organic acids and other special metabolites</li> </ul>	<p><b>Cultured Skin Fibroblasts</b></p> <ul style="list-style-type: none"> <li>Enzymatic assays for most diseases with known deficits</li> <li>Lipid and other inclusions (in mucopolipidosis IV, I-cell disease, mucopolysaccharidoses, Chediak-Higashi) DNA repair after ultraviolet or irradiation exposure (ataxia telangiectasia, Cockayne syndrome, xeroderma pigmentosum)</li> <li>Restriction fragment length polymorphisms</li> <li>DNA tests for genetic mutations</li> </ul> <p><b>CSF Protein</b> Increased</p> <ul style="list-style-type: none"> <li>Metachromatic leukodystrophy, Krabbe, infantile adrenoleukodystrophy (not always in classic variant), Friedreich ataxia and other spinocerebellar degenerations (inconstant), Zellweger disease (sometimes), Refsum disease,</li> </ul>
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<p>C26/C22 very long chain fatty acid ratio (adrenoleukodystrophy, Zellweger disease, infantile Refsum disease)                      Phytanic acid                      Pipecolic acid  <b>White Blood Cells</b>                      Lysosomal enzymes and other enzymatic assays                      DNA tests for genetic mutations                      Lipid and other inclusions (ceroid lipofuscinoses, gangliosidoses)  <b>Red Blood Cells</b>                      Enzymatic assays for galactosemia, porphyria</p>	<p>Cockayne syndrome  <b>CSF Lactate/Pyruvate</b>                      Mitochondrial cytopathies  <b>Amniotic Cells</b>                      Enzymatic assays for disease of known enzymatic defect                      Abnormal inclusion in mucopolipidosis IV                      Karyotype in X-linked disease                      C26/C22 very long chain fatty acid ratio                      Restriction fragment length polymorphisms                      DNA tests for genetic mutations  <b>Intradermal Histamine test</b>                      Dysautonomia</p>
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**ELECTRODIAGNOSIS**

<b>EMG and nerve conduction velocity</b>	To detect neuropathy, anterior horn cell disease, or muscle involvement
<b>Electroretinography</b>	To detect retinal degeneration
<b>Visual evoked responses</b>	Giant potentials in late infantile ceroid lipofuscinosis; delayed latency and decreased amplitude in leukodystrophies or optic atrophy.
<b>Brain stem auditory evoked responses</b>	Diagnosis of hearing loss; prolonged latency in leukodystrophies; delayed waves with decrease of amplitude in leukodystrophies and other disease of brain stem
<b>Somatosensory evoked responses</b>	Giant potentials in sialidosis with cherry-red spot myoclonus; decreased amplitude in peripheral neuropathy; delayed waves with decreased amplitude in diseases of white matter and peripheral nerves

**BIOPSIES**

Skin	Nerve
Ceroid lipofuscinosis	Neuraxonal dystrophy
Mucopolysaccharidoses	Metachromatic leukodystrophy
Mucopolipidosis IV	Other diseases with neuropathies
Neuraxonal dystrophy	Liver
Lafora disease	Wilson disease (copper content)
Conjunctiva	Generalized peroxisomal disorders (absent peroxisomes, cirrhosis)
Mucopolysaccharidoses	
Mucopolipidoses	Lafora disease
Neuraxonal dystrophy	Glycogenesis
Bone Marrow	Brain (rarely needed except possibly for following)
Niemann-Pick disease	Atypical ceroid lipofuscinosis
Gaucher disease	Alexander disease
Mucopolysaccharidoses	Neuraxonal dystrophy
Sea-blue histiocyte syndrome	Undiagnosed disease with probable cortical involvement
Muscle	Rectum
Lafora disease	
Glycogenoses	Sphingolipidoses
Other myopathies	Ceroid lipofuscinoses
Neuraxonal dystrophy	Sialidoses
Mitochondrial myopathies (Kearns-Sayre, Leigh syndrome)	

BIBLIOGRAPHY for ch. "Pediatrics" → follow this [LINK >>](#)