LSD	Enzyme Deficiency	Facies	Dysostosis Multiplex	Psychomotor retardation	Seizures	Peripheral Neuropathy	Muscular Involvement	Eye findings	Skin findings	Organomegaly and other significant features	Cardiac involvement	Diagnosis
Mucopolysaccharidosis (MPS)												
MPS1 (Hurler)	Alpha-L-iduronidase	Coarse	(+++)MPS1H	(+++)MPS1H	(+++)MPS1H	(+++) Carpal Tunnel Syndrome and myelopathies - MPS1H	-	(+++) Corneal clouding - MPS1H	Maculo papular erythematous	(+++) Hepatosplenomegaly- MPS1H	Hypertrophic cardiomyopathy and valvulopathies	Urinary MPS shows increased dermatan and heparan sulfate. α-L-iduronidase assay in WBC is diagnostic
MPS1H/S (Hurler-Scheie)*			(++) MPS1H/S and MPS1S	(++) MPS1H/S	(++) MPS1H/S	(++) Carpal Tunnel Syndrome and myelopathies -MPS1HS		(++) Corneal clouding - MPS1HS		(++) Hepatosplenomegaly - MPS1HS		
MPS1S (Scheie)*			(+) MPS1H/S and MPS1S	(+) MPS1S	(-) MPS1S	(+) Carpal tunnel and myelopathies - MPS1S		(+) Corneal clouding - MPS1S		(+) Hepatosplenomegaly - MPS1S		
MPS2 (Hunter syndrome) - neuropathic form (MPS2A)	Iduronate-2-sulfatase	Coarse	+++	(+++) MPS2A	+++(MPS2A)	(+++) Carpal Tunnel Syndrome	-	Optic atrophy and retinal degeneration and detachment	Pebbly, ivory-colored skin lesions	(+++) Hepatosplenomegaly - MPS2A	Hypertrophic cardiomyopathy and valvulopathies	Urinary MPS shows increased dermatan and heparan sulfate. Iduronate-2-sulfatase in WBC is diagnostic.
MPS8 - nonneuronopathic form			++	(-)MPS2B	- (MPS2B)	(++) Carpal Tunnel Syndrome				(++) Hepatosplenomegaly - MPS2B		
MPS3 (Sanfilippo disease	A: heparin-N-sulfatase B: N-acetyl-glucosaminidase C: Acetyl CoA glucosamine N-acetvl transferase D: N-acetyl-glucosamine-6-sulfatase	Coarse	++	+++	++	Carpal Tunnel Syndrome(+)	-	Optic atrophy and retinal degeneration		Hepatosplenomegaly (++)	+	Urinary MPS shows increased heparan sulfate. Each specific lysosomal enzyme (related to MPS-3) assay in WBC is confirmatory.
MPS4 (Morquio syndrome)	A: galactose-6-sulfatase B: β-galactosidase	Atypical	+++	(+++)MPS-IVB	(++)MPS-IVB	(++) Carpal tunnel and myelopathies	-	Corneal clouding	-	+	+	Urinary MPS shows increased keratan sulfate. The galactose-6-sulfatase and β-galactosidase assays in WBC are diagnostic
MPS6 (Maroteaux-Lamy syndrome)	Galactosamine-4-sulfatase	Coarse	++	-	-	(++) Carpal tunnel and myeloopathies	-	Corneal clouding	-	Hepatosplenomegaly	Hypertrophic cardiomyopathy and valvulopathies	Urinary MPS shows increased dermatan sulfate. The galactosamine-4-sulfatase is diagnostic
MPS7 (Sly disease)	β–glucoronidase	Coarse	+++	+++	++			Corneal clouding		Hepatosplenomegaly	Hypertrophic cardiomyopathy and valvulopathies	Urinary MPS shows dermatan and chondroitin sulfate. β-glucoronidase assay in WBC is diagnostic.
Multiple sulfatase deficiency	Formylglycine generating enzyme (FGE)	Coarse	+++	+++	+++	++	-	Corneal clouding and cherry-red spot	Dry skin; ichthyosis	Hepatosplenomegaly	Cardiomyopathy	Urinary sulfatides and molecular genetic analysis of SUMF1 *gene*
Oligosaccharidosis												
Sialidosis (also known as mucolipidosis type I)	Neuroaminidase	Coarse Type II - (infantile) Atypical (type I – juvenile)	(+++)infantile (-)juvenile	+++	+++ Myoclonus (juvenile)	(++)juvenile	-	Cherry-red spot and corneal clouding	Angiokeratomas (juvenile)	Hepatosplenomegaly and renal tubular dysfunction	Hypertrophic cardiomyopathy and valvulopathies	Urinary OLGs shows increased sialic acid. Neuraminidase assay in WBC is diagnostic
Galactosialidosis	Cathepsin A	Atypical	+/+++	+/+++	+/++	+	-	Cherry-red spot	Angiokeratomas	Hepatosplenomegaly	-	Urinary OLGs shows typical finding. Cathepsin A assay in cultured cells is diagnostic
α-fucosidosis	α-fucosidase	Atypical	++	+++	+++	-	-	Telangectasias	Angiokeratomas	Hepatosplenomegaly	Hypertrophic cardiomyopathy and valvulopathies	Urinary OLGs shows typical finding. α-fucosidase assays is confirmatory
α-mannosidosis	α-mannosidase	Coarse	++	+++	++ Myoclonus	-	-	Cataracts, corneal clouding	Angiokeratomas	Hepatosplenomegaly and early sensorineural hearing loss	Hypertrophic cardiomyopathy and valvulopathies	Urinary OLGs shows typical finding. α-mannosidase assay in WBC is diagnostic
Aspartylglucosaminuria	Aspartylglucosaminidase	Coarse	+	+++		-	-	Mild cataracts	Angiokeratomas, photosensitivity and acne	Early sensorineural hearing loss	-	Urinary OLGs shows typical finding. Aspartylglucosaminidase assay in WBC is diagnostic
Schindler's disease	N-acetyl-galactosaminidase	Atypical	-	+	-	-	-	-	-	Hepatosplenomegaly	-	Urinary OLGs shows typical finding. N-Acetylgalactosaminidase assay in WBC is diagnostic
Pycnodysostosis	Cathepsin K	Characteristic (large forehead midface hypoplasia and micrognathia and dental abnormalities)	(+++)osteosclerosis	-	-	-	-	-	-	-	-	Cathepsin K activity in cultured cells. Molecular analysis of *CTSK* gene
Mucolipidosis												
Mucolipidosis II (I-Cell disease) Mucolipidosis type III	N-Acetylglucosaminylphosphotransferase	(++) Coarse – MLP-II (+) Coarse (MLP-III)	(++) – MLP-II (+) – MLP-I	(+++) – MLP-II (+)-MLP-II	+++ -	-	-	(+) Corneal clouding (MLP-II) (-) MLP-III	-	Hepatosplenomegaly; Vacualoated lymphocytes	Hypertrophic cardiomyopathy and valvulopathies	Increased soluble lysosomal enzymes in plasma and decreased in leucocytes
Mucolipidosis IV	TRMPL1 (mucolipin 1, also known as MCOLN1)	Atypical	-	+++	+++	++	-	Corneal clouding and pigmentary retinopathy	-	Hepatosplenomegaly; elevated gastrin in serum	-	Molecular genetics diagnosis by detection of mutations in *MCOLN1* gene
Sphingolipidosis												
Gaucher Disease (type 1 - nonneuronopathic Type 2 (acute neuronopathic) Type 3 (chronic neuronopathic)	Glucocerebrosidase (β-glucosidase)	Atypical	Osteopenia, osteonecrosis, lytic lesison and fractures, avascular necrosis of femur, vertebral collapse(type I, II and III)	(-) type 1 – nonneuronopathic (++) type 3 chronic neuronopathic (+++) type 2 acute neuropathic	- (+++)type 2 (++)type 3	(+)type 1	-	Supra-nuclear palsy (type 3)	Ichthyosis (type 2)	Hepatosplenomegaly	Cardiomyopathy and arrhythmias (type 2)	Gaucher cells in histological studies (bone marrow, liver, bone); elevated chitotriosidase; glucoecerebrosidase in WBC is diagnostic
Fabry disease	α-galactosidase	Mostly atypical but coarse facies can be noted	-	Cerebrovascular disease can result in severe debilitation	May occur secondary to cerebrovascular disease	(+++)acroparesthesia	-	Corneal verticillata (corneal worms)	Angiokeratomas	Splenomegaly can occur	Hypertrophic cardiomyopathy and arrhythmias	Kidney biopsy Gb3 deposition in the glomerular endothelial, mesangial, intersticial cells and in podocytes; α-galactosidase assay in WBC is diagnostic
GM1 gangliosidosis	β-galactosidase	Coarse (severe form)	(+++) infantile form (++) juvenile and adult forms	(+++) infantile form (++) juvenile and adult forms	(+++)infantile (++)juvenile (-)adult	-	-	Corneal clouding and cherry-red spot	-	Hepatosplenomegaly	-	Urine OLGs can show abnormal pattern. β-galactosidase assay in WBC is diagnostic
GM2 gangliosidosis	β–hexosaminidase	Atypical	-	(+++) infantile form (++)juvenile and adult forms (+) psychiatric /behavior disturbances (adult form)	(+++)infantile (++)juvenile (-)adult	(++)juvenile and adult forms	-	Cherry-red spot	-	Hepatosplenomegaly (can occur in Sandhoff disease variant)	-	β–hexosaminidase assay in WBC is diagnostic
Krabbe disease	β-galactocerebrosidase	Atypical	-	(+++) infantile (++) juvenile and adult (+) psychiatric /behavior disturbances (adult form) Brain MRI shows severe leukodystrophy	(+++)infantile (++)juvenile (-)adult	(++)juvenile and adult forms	-	-	-	-	-	β–galactocerebrosidase assay in WBC is diagnostic
Niemann-Pick A and B	Sphnigomyelinase	Atypical	-	(+++)type A (++)type B	(+++)type A (++)type B	-	-	Cherry-red spot and corneal clouding	-	Hepatosplenomegaly; severe pulmonary infiltrative disease	-	Bone marrow aspirate and biopsy show sea-blue histiocytes: foam cells; Sphingomyelinase assay in WBC is diagnostic
Faber Disease (lipogranulomatosis, ceramidosis)	Ceramidase	Atypical	-	(++)type 1 (-)type 2 and 3 (+++)types 4, 5 and 6	+	(++)acroparesthesias	-	Corneal clouding; cherry-red spot can occur	Subcutaneous skin nodules in points of mechanical pressure and joints	Hepatosplenomegaly; pulmonary infiltration diseases; progressive hoarseness (laryngeal involvement)	-	Histology of skin subcutaneous nodules shows . Acid ceramidase assay in WBC is diagnostic
Metachromatic Leukodsytrophy	Arylsulfatase A	Atypical	-	(++)late infantile (+++) late-infantile (++) juvenile; (+) adult	(++) late infantile (+++) late infantile (++) juvenile	(++)acroparesthesias	-	Optic atrophy	-	-	-	Urine sulfatide measurement can be diagnostic. Arylsulfatase A activity is decreased (but high frequency of pseudopolymorphism in *ARSA* gene)
Lipid Storage Diseases												
Niemman-Pick type C	NPC1 and NPC2	Atypical	-	(+++) infantile (++) juvenile (+)adult	(+++)infantile (++)juvenile	-	-	Cherry-red spot	-	Hepatosplenomegaly; pulmonary infiltration diseases	-	Filipin cell staining is indicative for NPC1 but not diagnostic. Cholesterol esterification assay in cultured fibroblasts can be diagnostic; molecular genetic analysis of NPC1 and NPC2 are necessary
Cholesterol ester Storage Disease (CESD) and Wolman Disease	Acid lipase	Atypical	(+)Wolman disease	(++)Wolman disease (+)CESD	(++)Wolman disease (+)CEDS	-	-	Cherry-red spot	-	Hepatosplenomegaly; adremal calcifications (Wolman disease)	Ischemic cardiac disease; hypercholesterolemia and hypertriglycenemia	Histology of tissue specimens; acid lipase assay in WBC and cultured cells are diagnostic

Neuronal Ceroid Lipofuscinosis												
INCL (infantile); Santavuori-Hanti disease)	Palmitoyl-protein thioesterase (PPT1)	Atypical	-	+++	+++	-	-	Retinal dystrophy	-	-	Brain MRI reveals generalized cerebral atrophy	Skin or conjunctivae specimen showing granular osmiophilic deposits; PPT1 in WBC enzyme assays is diagnostic
LINCL (late infantile); Jansky-Bielschowlowsky)	Tripeptyl peptidase 1 (TTP1); Other causative variants with specific causative genes are: CLN5 (Finnish variant); CLN6 (early juvenile variant); CLN8; CTSD, MFSD8 (variants)	Atypical	-	+++	+++	-	-	Retinal dystrophy	-	-	Brain MRI reveals generalized cerebral atrophy	Skin or conjunctivae specimen shows lysosomal curvilinear bodies; TPP1 in assay is diagnostic. Mutation analysis for *CLN5*, *CLN6*, *CLN8*, *CTSD*, *MFSD8* and other variants are necessary
JNCL (juvenile); Batten disease or Spielmeyer-Vogt-Sjogren disease	CLN3 transporter (classic); variants(PPT1, TPP1, CLN9)	Atypical	-	+++	+++	-	-	Retinal dystrophy	-	-	Brain MRI reveals generalized cerebral atrophy	Skin or conjunctivae specimen shows intra-lysosomal finger print bodies; *CLN3* molecular gene analysis is diagnostic; PPT1 and TPP1 (WBC) assays and mutation analysis of *CLN9* gene maybe necessary
ANCL (adult); Kufs disease	CTSD, PPT1, CLN3, CLN5, CLN4	Atypical	-	(+)d ementia starts at adulthood – tvpe A (++) behavior/psychiatric disturbances (type B)	(++)type A (-)type B	-	-	Retinal dystrophy	-	-	Brain MRI reveals generalized cerebral atrophy	Skin or conjunctivae specimen shows intra-lysosomal finger print bodies; molecular analysis of specific causative genes is diagnostic
Lysosomal Transporter Defects												
Cystinosis	Cystine Transporter (CTNS)	Atypical	(+)nephropathic cystinosis, delayed bone age, hypophosphatemic rickets due to renal tubulopathy	(+)mild learning disabilities, but most individuals have normal cognition	-	-	-	Corneal cystine crystals causing corneal erosions (photophobia and blepharospasm can occur)	-	Renal tubular Fanconi syndrome	-	Cystine crystals in the cornea on slit lamp examination; and increased cystine content of leukocytes. Molecular analysis of CTNS gene is confirmatory
Sialic Acid Storage Disease (Salla disease)	Sialin (SLC17A5)	Atypical	-	(+++) severe form (-)mild form	+++	+	-	-	-			Urine OLGs shows increased free sialic acid. Mutations analysis in *SLC17A5* gene is confirmatory
Chediak-Higashi syndrome	LYST (lysosomal trafficking regulator)	Atypical	-	+	(+)mild cognitive impairment, ataxia, and tremors	(+) mild cognitive impairment, ataxia, and tremors	-	Partial oculocutaneous albinism	-	Hepatomegaly; giant cell inclusions (peroxidase-positive); immunodeficiencies and mild bleeding diasthesis	-	Giant inclusions in WBCs; molecular analysis of LYST gene is diagnostic
Lysosomal Glycogen Storage Disease												
Pompe Disease	α-glucosidase (acid maltase)	Full cheeks and macroglossia (infantile form); atypical (juvenile and adult forms)	-	-	-	-	(+++) infantile form (++) late onset form – proximal muscular dystrophy presentation	-	-	Hepatomegaly can be secondary to cardiac involvement; progressive pulmonary dysfunction	Progressive hypertrophic cardiomyopathy (infantile phenotype only)	Muscle biopsy shows accumulation of glycogen as stained with periodic acid-Schiff (PAS). Acid α-glucosidase is diagnostic and can be done in dried blood spots

*Both MPS1HS and MPS1S are currently known as attenuated forms of MPS1; MPS1H is the severe clinical form. OLG, oligosaccharides; MPS, mucopolysaccharides; WBC, white bloods cells.