Neurodegenerative diseases:

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Metabolic diseases:

Inborn defects of carbohydrate metabolism :

Galactosemia **Fructosemia**	**UDPG deficiency (galactose-1-phosphate uridylyltransferase)** **aldolase B deficiency**	**The symptoms soon after birth** **- vomiting, diarrhea, hepatosplenomegaly, CNS damage, tubulopathy, cataract**
Glycogen storage diseases	Deficiency of enzymes involved in the synthesis and metabolism of glycogen	Symptoms in different ages: - hypoglycemia intracellular accumulation of glycogen: hepatomegaly, cardiomegaly, developmental delay, neurodegeneration

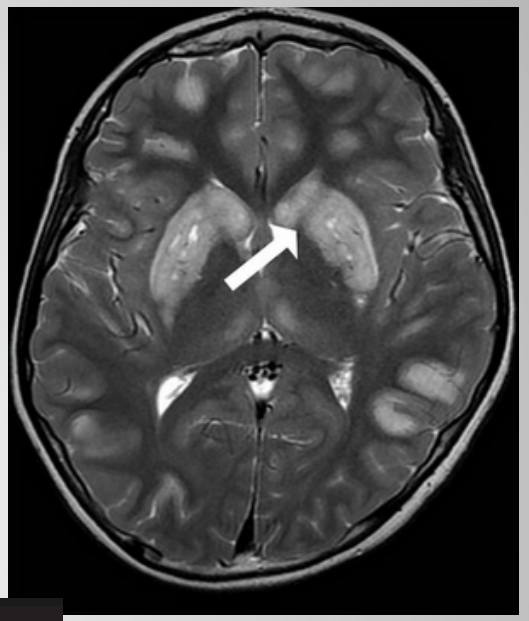
Amino acid metabolic disorders :

phenylketonuria	**phenylalanine hydroxylase deficiency**	**Early symptoms: vomiting, eczema, light skin, the smell of mouse urine, seizures, mental retardation,**
maple syrup disease(MSUD)	branched amino acids metabolism disorder	Early: hypoglycemia, severe general condition, coma, caramel -scented urine
nonketotic hyperglycinemia	Inborn error of glycine metabolism	Hypotonia, tremor, myoclonus, developmental delay

Hyperammonemia :

- Congenital enzymatic defects of urea cycle,
- The most common type II hyperammonemia - congenital deficiency of ornithine transcarbamylase (OTC) X- linked recessive inheritance (the most common symptoms in boys)
- Toxic ammonia rise
  Symptoms of intolerance of dietary protein
  vomiting,
  psychiatric and neurological symptoms
  (convulsions, disturbance of consciousness up to coma)

Mitochondrial diseases:



- Defects in the respiratory chain complex enzymes;
  mutations acquired or inherited, in mitochondrial DNA or in nuclear genes that code for mitochondrial components.

Symptoms: lactic acidosis, increased alanine (blood, CSF).

Leigh syndrome(vomiting, suppression of growth, seizures, hypotonia, nystagmus)

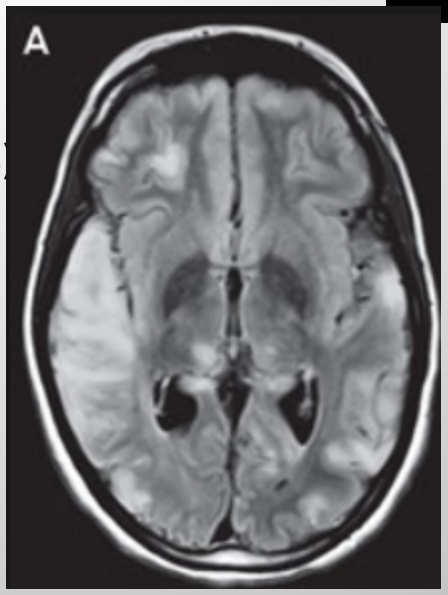
Leber syndrome (blindness, myoclonus, impaired development)

MERRF (myoclonal epilepsy, ragged red fibers)

Wolfram syndrome DIDMOAD (diabetes insipidus,diabetes mellitus,optic atrophy, deafness)

MELAS – encephalopathy,lactic acidosis,stroke- like – episodes

Alpers syndrome – myoclonus, hypotonia, liver damage,



Lysosomal diseases :

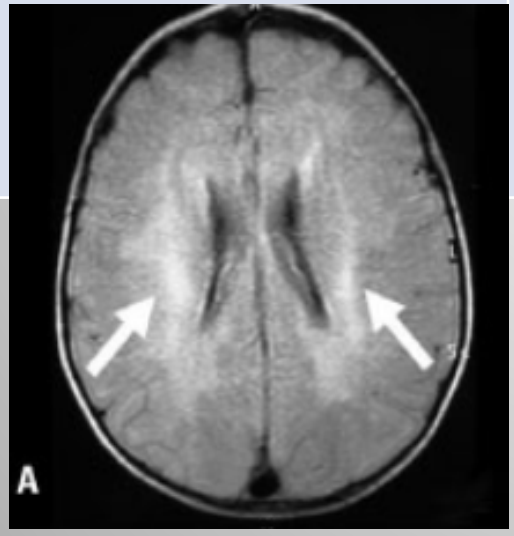
- The diseases associated with a deficit of enzymes involved in the synthesis and degradation of substances generated in the lysosomes: gangliosides,
  mukolipides, sphingolipides, cerebrosides

Mucopolysaccharidoses:

MPS I (Hurler syndrome) **MPS II (Hunter syndrome)**	**iduronidase deficiency** **deficit of idursulfase**	**Progressive neurodegeneration, dysmorphia, dwarfism, bone defects, deafness, hepatosplenomegaly**
MPS III (Sanfilippo syndrome)		neurodegeneration

Lipidoses:

Niemanna –Pick t.C disease	Intracellular transport of cholesterol impairment	Progressive neurodegeneration, epilepsy, hepatomegaly
Gaucher type II i III disease	Impairment of ceramide degradation	Neurodegeneration , hepatosplenomegaly
Krabbe disease	Beta galactosidase deficiency	Neurodegeneration, epilepsy, deafness, blindness, leukodystrophy



Sulfatydoses:

- **Metachromatic leukodystrophy** (deficit of sulfatase cerebroside) - peripheral neuropathy, demyelination, optic atrophy

Gangliosydoses:

Neurodegeneration, epilepsy, deafness, hepatosplenomegaly

- **GM I** (betagalaktosydase deficiency)
- **GM II** Tay – Sachs disease (deficiency of heksozamidase)

Glykoproteinoses:

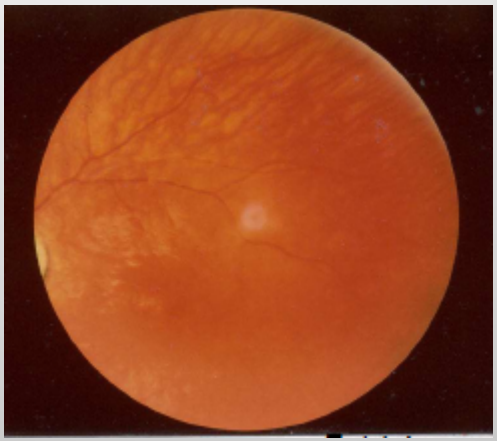
- **Neuronal ceroid lipofuscinosis (TPPI deficiency)**

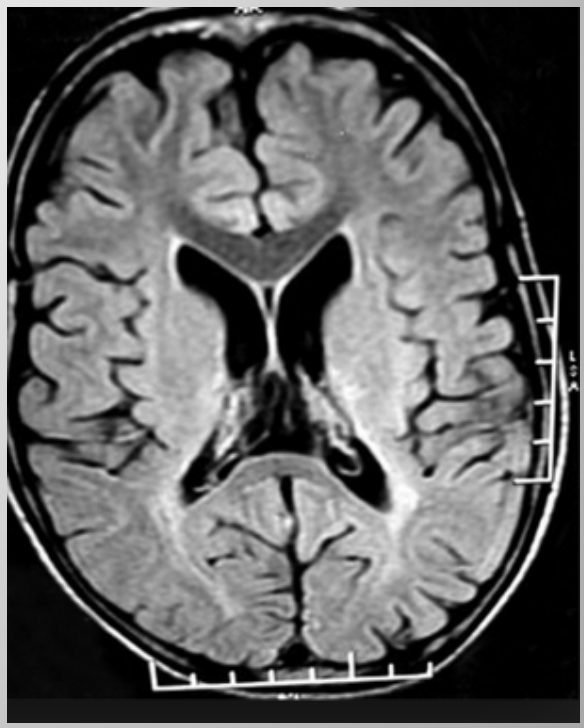
Symptoms:

Neurodegeneration,

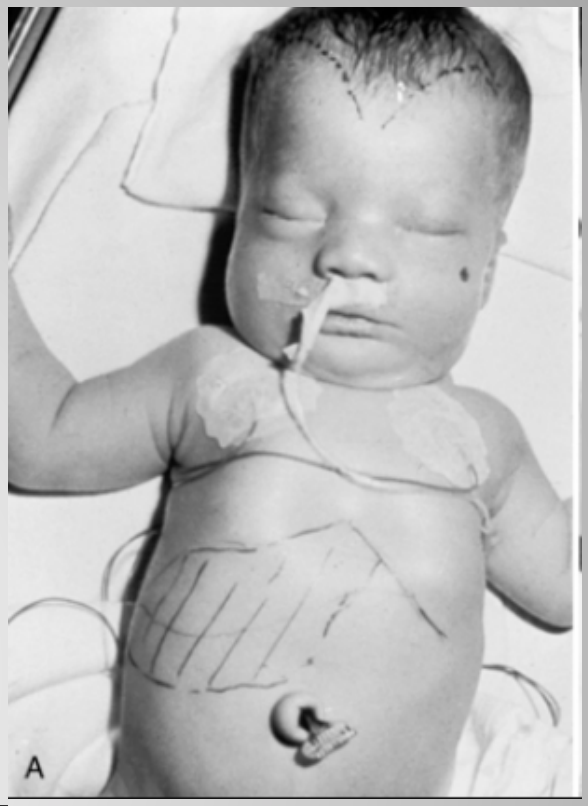
epilepsy,

Optic atrophy

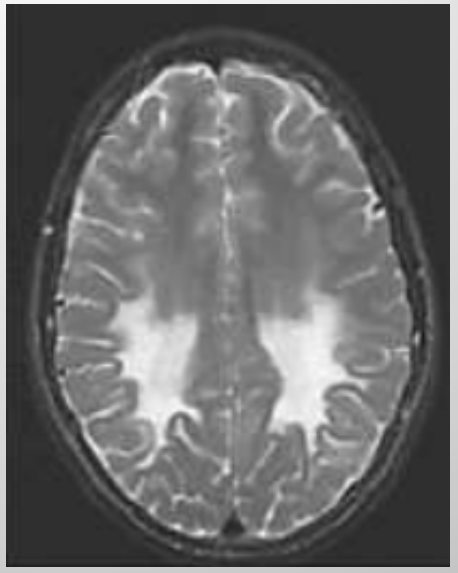




Peroksysomal diseases:



- **Zellweger syndrome** (cerebro-hepato-renal syndrome), cataracts, bone defects, retinitis pigmentosa
- **X – linked Adrenoleukodystrophy :** progressive leukodystrophy, adrenal insufficiency
  Diagnostics:
  increase VLCFA in blood

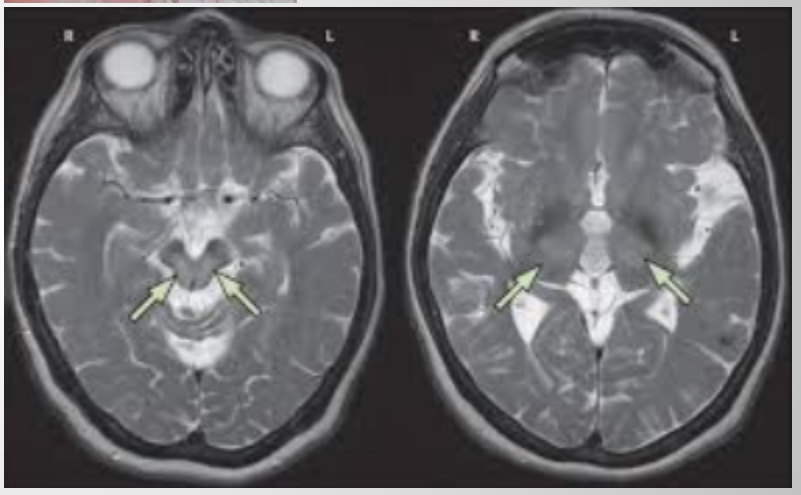


Metal related disorders:

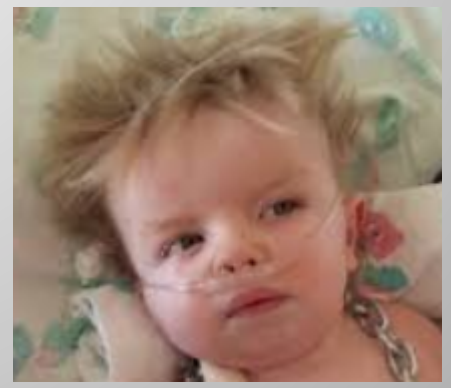
- **Wilson disease** (hepato – lenticular degeneration) defect of transmembrane transport of copper involves liver and CNS , autosomal recessive inheritance

Symptoms: liver failure, slurred speech, tremor, Kayser- Fleischer ring, hemolytic anemia

Diagnosis: MRI, Cu and ceruloplasin decrease in serum , increased urinary excretion of Cu

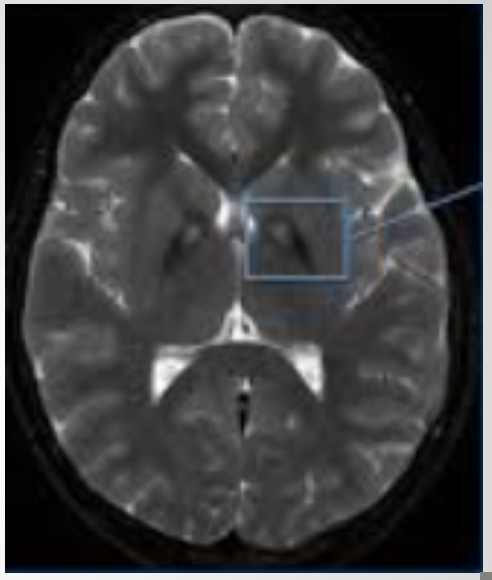


- **Menkes disease:** X- linked inheritance, malabsorption of Cu
  Symptoms: decrease copper and ceruloplasmin in serum, neurodegeneration, laxity, „kinky" hair



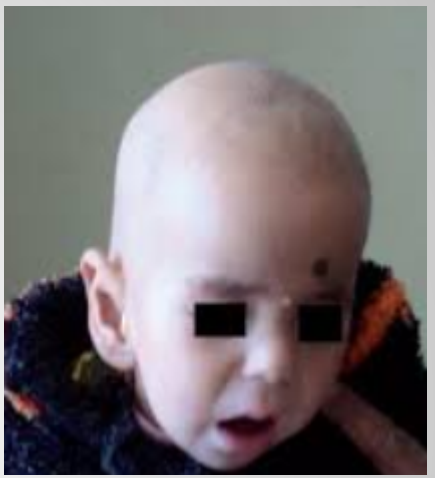
Metal related disorders:

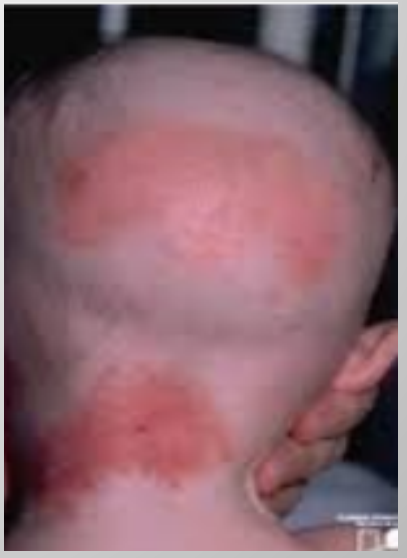
- **NBIA** (formerly Hallervorden – Spatz disease)
  - deficiency of pantothenic kinase, iron deposition in the globus pallidus "tiger eye"
  Symptoms:
  neurodegeneration
  optic atrophy, dystonia



Biotynidase deficiency:

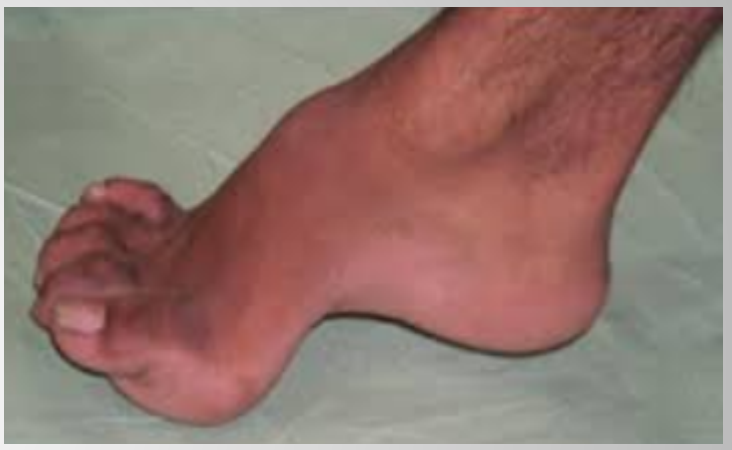
- Biotynidase- involved in the cyclic reproduction of biotin (vitamin H)
  Symptoms: muscular hypotonia, developmental delay, seizures, eczema, hair loss, ataxia, blindness, deafness
  Treatment: Biotin (vitamin H)





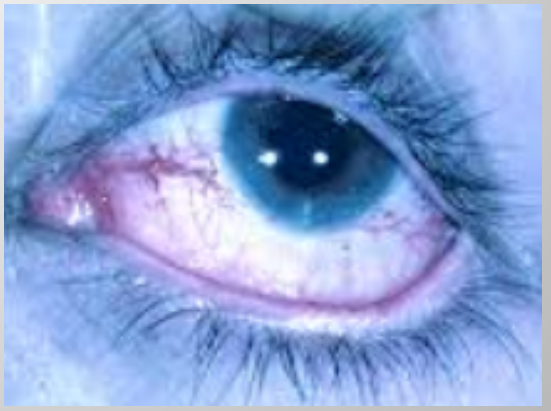
Neurodegeneration with ataxia:

- **Friedreich's ataxia**; AR inheritance,gene coding frataxine (increased number of repetitions of GAA, mitochondrial protein)
  Symptoms in adolescence:
  - Gait and limbs ataxia and limbs, hollowed feet
  - Lack of tendon reflexes
  - Babinski sign (+)
  - dysarthria
  - Numbness deep

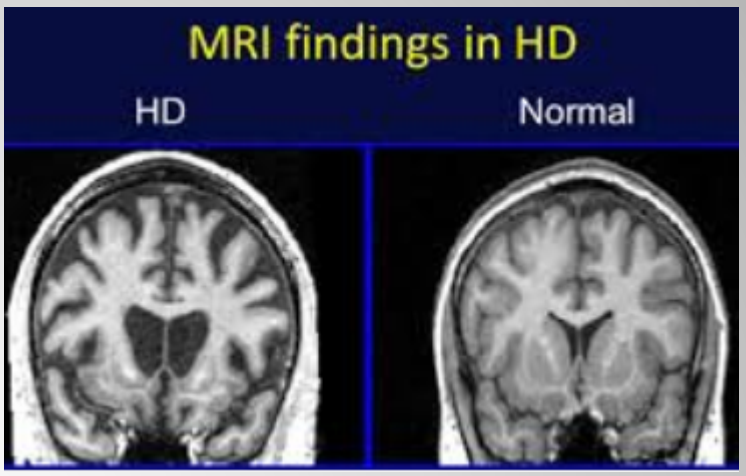


- **Ataxia telangiectasia**; AR inheritance , gene ATM

(involved in regulation of DNA repair)
Symptoms: 1-4 years of age
- cerebellar symptoms:
-apraxia, ophtalmoplegia (nystagmus, dysmetria)
-blurred speech
-hipomimia
-telangiectasias
-Ig deficiencies (IgA, IgG)
-increased concentration of AFP



Neurodegeneration with movement disorders:



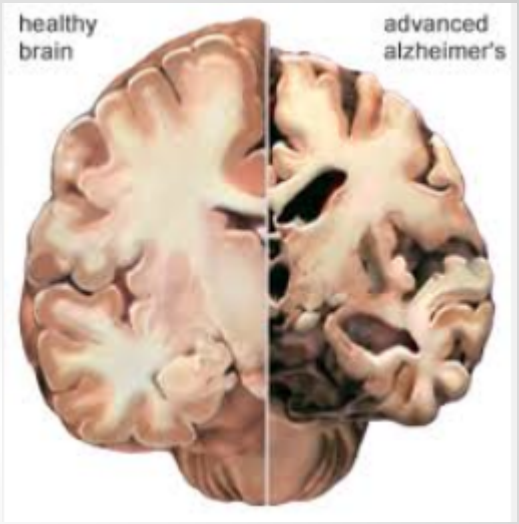
Huntington disease AD, increased number of CAG repeats, mutation of huntingtin protein
Symptoms 35-40years old (also juvenile form):
-involuntary movements (choreiform)
-personality disorders,
-dementia

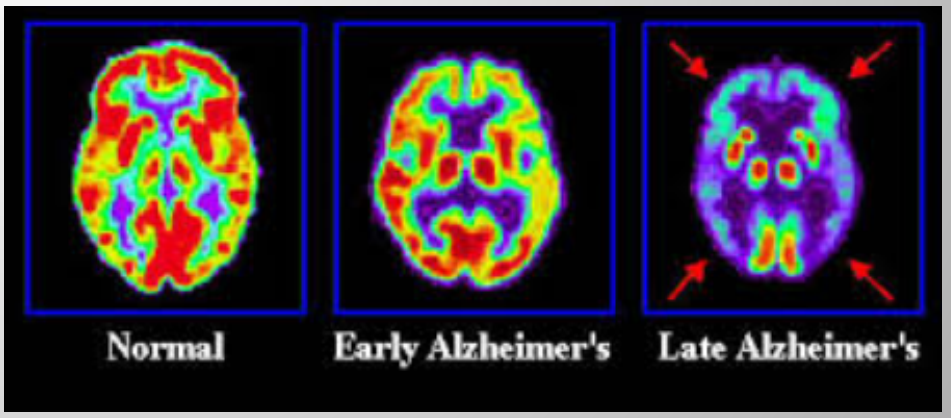
Parkinson disease - the most common gene PARK 1 (protein α-synuclein), PARK 2 (parkin)
Symptoms:
-movement disorders (resting tremor, rigidity, hypokinesia, stooped posture, freezing, slurred speech)
-attention deficit ,
-personality disorders
- bradyfrenia

Neurodegeneration with dementia:

- **Alzheimer's disease** AD?, deposits of β-amyloid in brain

Symptoms:
- recent memory disturbances,
- disturbances of abstract thinking,
- depression
- initially without other neurological disorders (then extrapyramidal symptoms, abnormal posture, gait problems)





Neurodegeneration – diagnostic:

- Metabolic screening after birth:
  TANDEM MS - profile of acylcarnitines in the blood
  Other: AA serum
- Cerebro-spinal fluid examination (lactate concentration)
- GCMS - profile of organic acids in urine
- Ammonia concentration in the blood
- Oligosaccharides in urine
- Biotynidase dry blood drop
- Lysosomal enzymes in the blood
- VLCFA (very long chain fatty acids in the blood)
- Genetic diagnosis
- Neuroimaging (MRI head, spinal cord)
- Ophthalmological examination