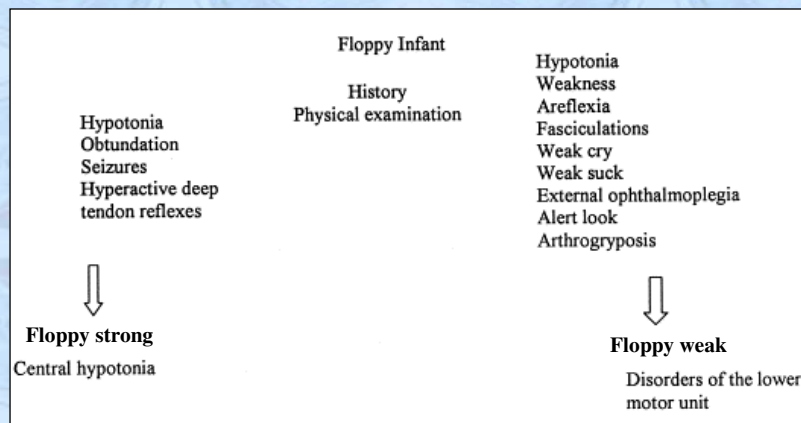


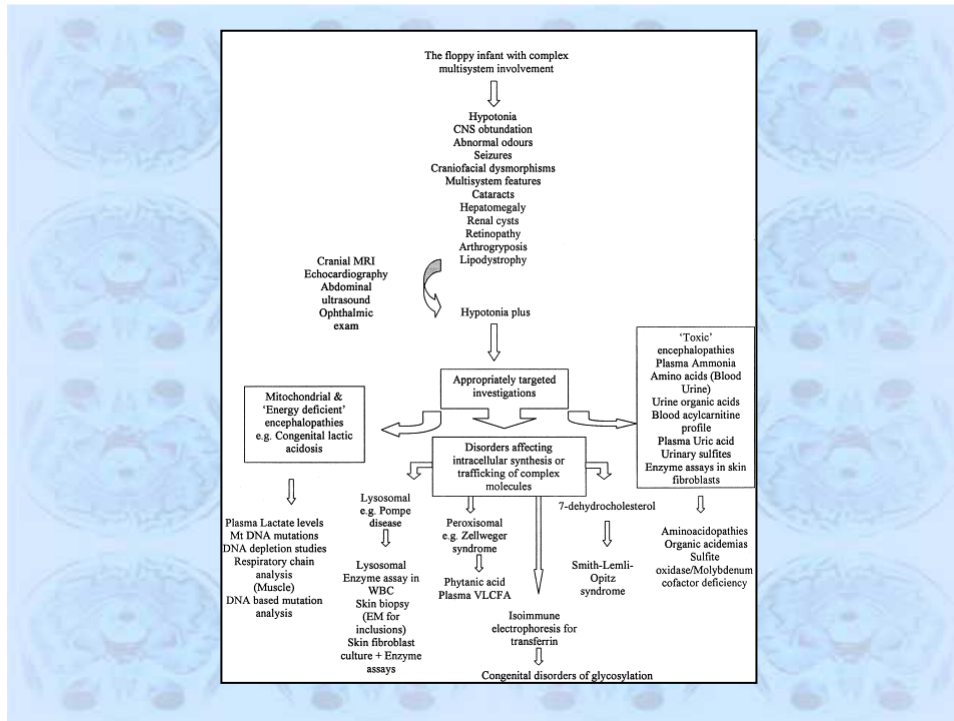
The floppy infant

Contribution of metabolic disorders



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Division of Pediatric neurology





Zellweger syndrome



Large fontanelle wide sutures
High forehead Hypertelorism
Broad nasal bridge
Epicanthus Shallow orbital ridges
External ear deformities.

Hepatomegaly and liver dysfunction
Kidney cysts

Zellweger syndrome



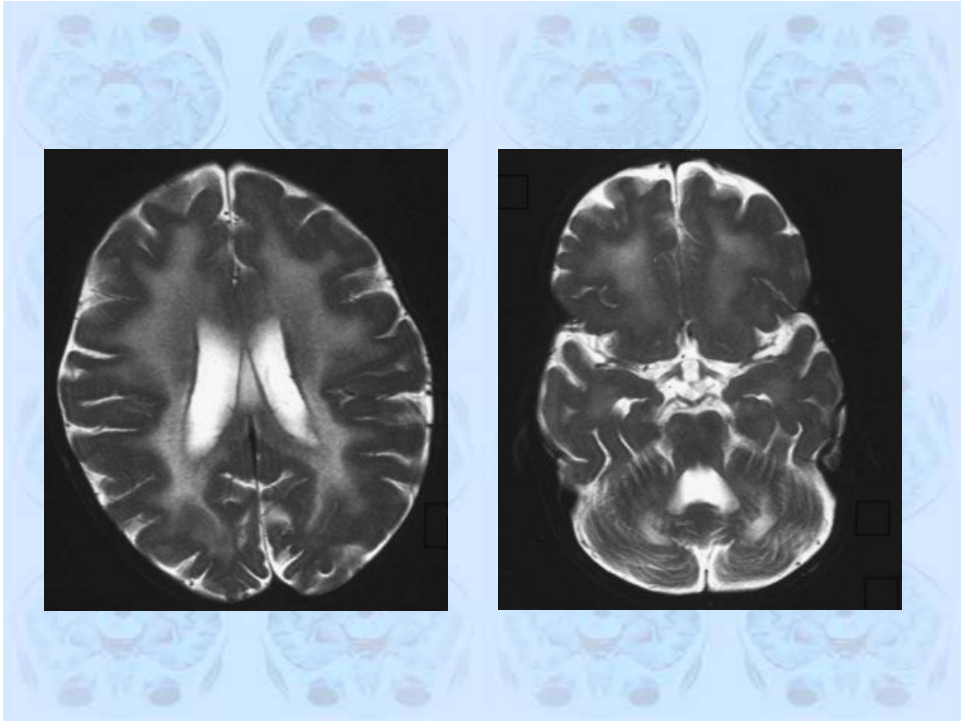
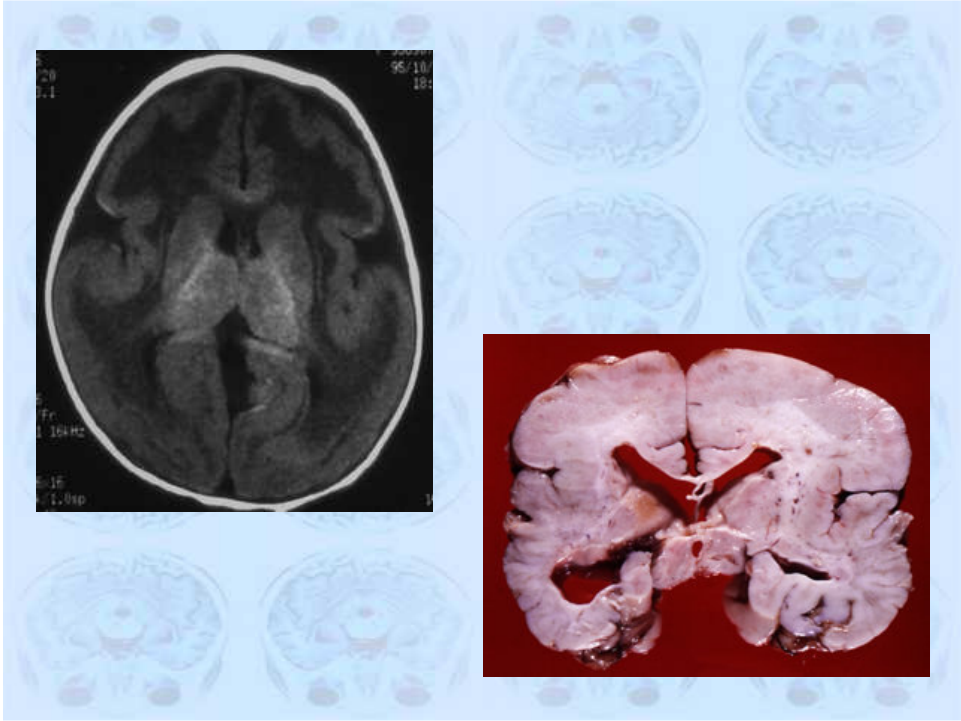
Neurological dysfunction

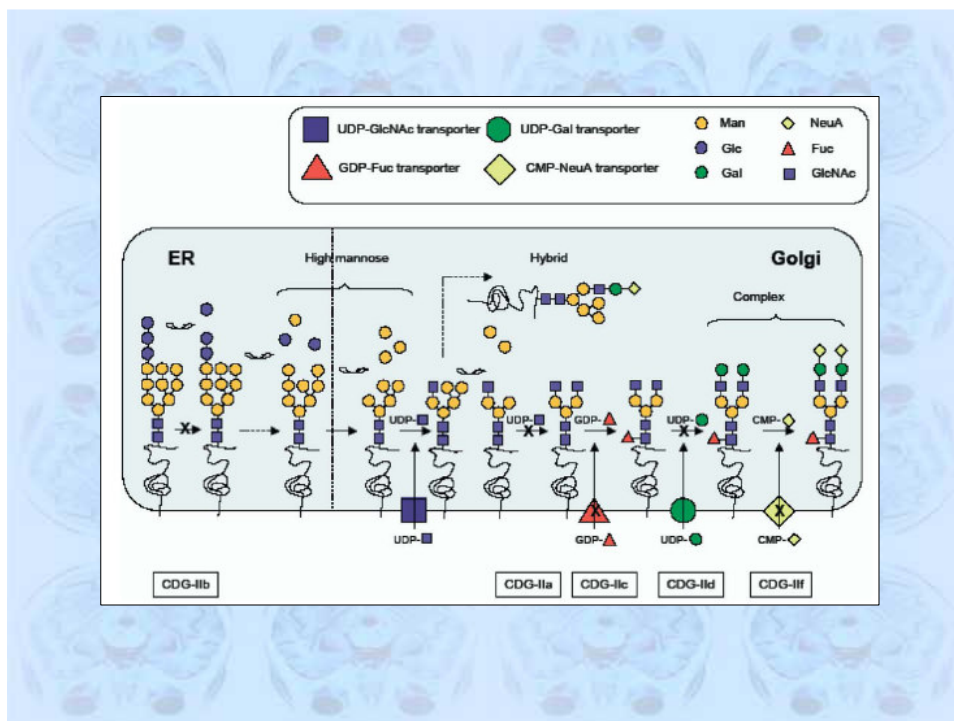
- Severe hypotonia
- Poor suck and swallow
- Seizures often from day 1
- Psychomotor retardation
- Cataract Retinitis pigmentosa
- Optic atrophy

Zellweger syndrome Diagnosis



- Plasma VLCFA
- Liver function tests
- Renal ultrasound
- Ophthalmology
- X-ray patella stippled calcifications
- PEX gene mutations
- Neuro imaging





Clinical characteristics of CDG

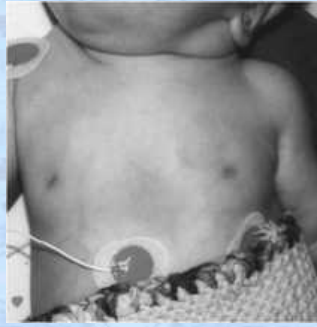
Suggestive features

Hypotonia
 Developmental delay in infancy
 Small cerebellum
 Early onset strabismus progressing to retinopathy
 Stroke-like episodes
 Seizures
 Pericardial effusions
 Inverted nipples
 Abnormal pubic fat distribution
 Lipodystrophic regions

Suggested laboratory features

Coagulopathy
 Elevated liver function tests
 Low Albumin
 Low thyroxine and thyroxine binding globulin levels.

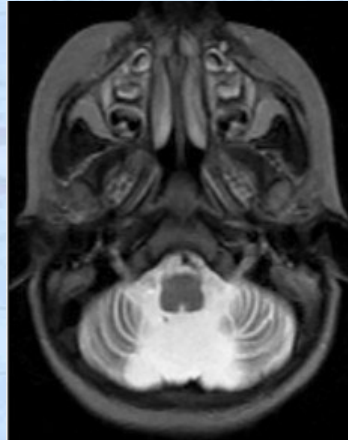
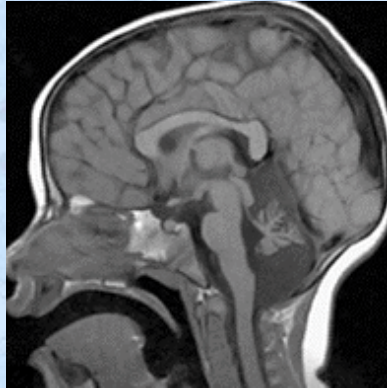
CDG Inverted nipples



CDG Abnormal fat distribution



CDG Small cerebellum



CDG Diagnostic testing

Analyse serum sample for deficiency transferrin glycosilation
(Isoelectric focusing, mass spectrometry or other methods.)

False negative results: very young & False positive results: secondary
glycosilation defects.

Confirmation by enzyme analysis in fibroblasts and leukocytes.
Mutation analysis.

All diagnostic tools for CDG (screening tests, expert analysis, tissue banking)

www.euroglycan.org

CDG Treatment

Only therapies available for 2 of the CDG subtypes.

CDG-Ib Failure to thrive, coagulopathy, liver fibrosis, hypoglycemia

No neuronal abnormalities (mentally spared)

Mannose supplementation

CDG-IIc Leukocyte adhesion deficiency type. High blood leukocyte count

Recurrent bacterial infections. Short stature. Facial abnormalities.

Mental deficiency.

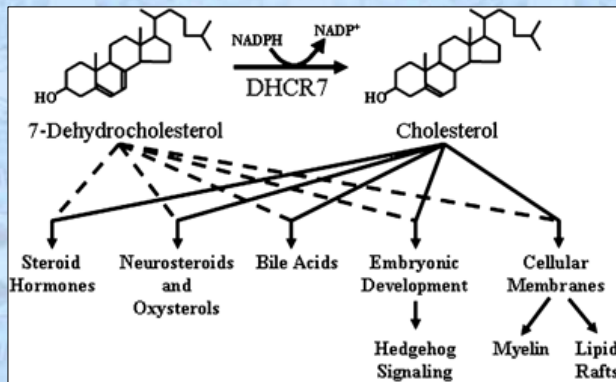
Fuctose supplementation.

Smith Lemli Opitz syndrome

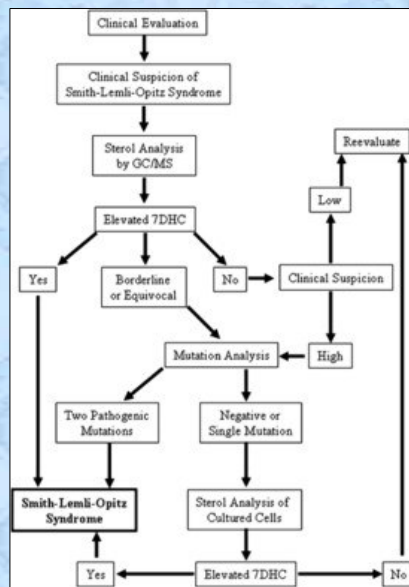
Second most common treatable recessive inherited error of metabolism causing mental deficiency.

Prevalence 1: 20 000 to 1: 40 000 births

First described 1964. Defect discovered 1994



Mutations of DHCR7 impair the reduction of 7-dehydrocholesterol to cholesterol in the final step of cholesterol biosynthesis. Cholesterol has multiple biological functions which may be disturbed due to the lack of cholesterol, toxic effects of 7DHC, or combination of these two factors.



Clinical indications for 7-dehydrocholesterol testing

Developmental delay of unknown cause and any of the following :

- Facial features suggestive of SLOS
- Syndactyly of the 2nd and 3rd toes
- Hand anomalies
- Genital anomalies
- IUGR and low birth weight
- Failure to thrive
- Cleft palate
- Autistic features
- Feeding difficulties necessitating enteral tube feeding
- Clinical diagnosis of Down syndrome but normal chromosomes
- Ambiguous genitalia

SLO Typical facial features



- Microcephaly
- Ptosis
- Broad nasal bridge
- Upturned nose
- Micrognathia
- Cleft palate

SLO Limb anomalies



Short proximally placed thumbs
Single palmar creases
Clinodactyly
Postaxial polydactyly

SLO Limb anomalies



Syndactyly of the 2nd-3rd toes is
the most frequent clinical finding.

SLO Treatment

Genetic counseling AR inheritance 25% RR

Prenatal diagnosis

Consider screening where triple test shows low unconjugated estriol.

Dietary cholesterol supplementation (restores both adrenal and bile salt deficiencies) No controlled trials to validate efficacy.

Photosensitivity and neuropathy improved not development.

Simvastatin (only case reports)

Medicolegal case

Male Term infant

Uncomplicated birth history.

Birth weight 3570g Head circumference 35cm Apgars 9 10

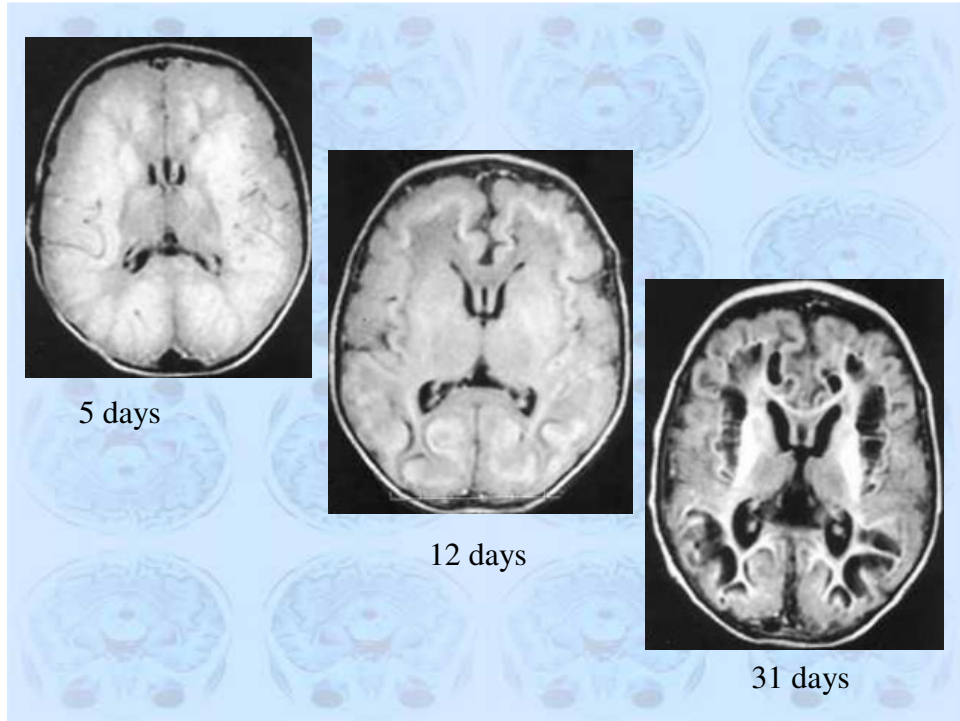
Prior to leaving the nursery BCG and OPV → 5 minutes later high pitched screaming, cyanosis and tachypneas.

Readmitted later same day with fever, lethargy and seizures.

Full septic screen negative, serum NH₃ CUEG acid base analysis LFT.

Neuro imaging performed.

Subsequently: Spastic quadriplegia Cortical blindness intractable seizures acquired microcephaly .



Conclusion Medico legal report

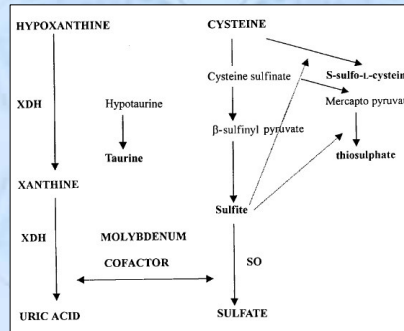
Brain injury of hypoxic-ischemic origin. Only explanation is that due to the shock-like picture/anaphylaxis that developed after the vaccination.

At age 4 years: Low hair molybdenum levels

Molybdenum Cofactor deficiency

Molybdenum cofactor is a constituent of 3 enzymes: sulfite oxidase, xanthine dehydrogenase and aldehyde oxidase.

Inactivation of sulfite oxidase oxidizes toxic sulphites



Clinical manifestations

- Early and late presenters.
- Early infantile encephalopathy
- Neonatal seizures unresponsive to anti epileptic drugs.
- Coarse facial features.
- Progressive mental retardation.
- Microcephaly
- Spastic quadriplegia
- Lens dislocation (later)
- Urinary Xanthine stones



Diagnosis

MRI /CT findings reminiscent of hypoxic-ischemic encephalopathy.

Urine sulphite dipstick test (fresh)

Absence of uric acid in plasma and urine (hypouricaemia)

Quantitative amino acid analysis (S-sulfo-L-cysteine, hypoxanthine, xanthine and thiosulfate)

Fibroblast culture (Sulphite oxidase activity)