THE CDG DIAGNOSTIC ROADMAP

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Marisa Girós - Spain

WHAT IS CDG?

Congenital disorders of glycosylation (CDG) is an umbrella term for a rapidly expanding group of rare metabolic disorders due to genetic defects in complex biochemical processes known as glycosylation. ①

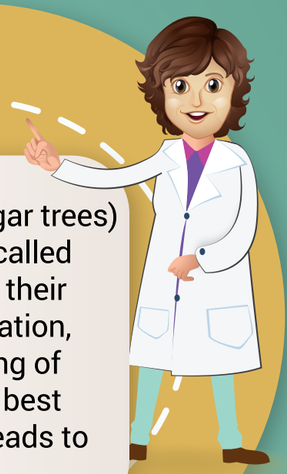
CAUSES OF CDG

Glycosylation is carried out by many specific enzymes and transporters that are defective in CDG.
As a result, the glycans are either completely missing (CDG-I) or structurally abnormal or incomplete (CDG-II).


Celia Perez Cerda - Spain

GLYCOSYLATION: WHY IS IT IMPORTANT?

Glycosylation is the assembly of glycans (or sugar trees) and their binding to certain proteins and lipids (called glycoproteins and glycolipids). It is essential for their many biological functions in cell-cell communication, intracellular signalling, protein folding or targeting of proteins a.o. The importance of glycosylation is best illustrated by the fact that its disruption often leads to multisystem and serious diseases.


Dulce Quelhas - Portugal

BECAUSE OF THE GREAT VARIETY OF CDG SYMPTOMS AND THE RESEMBLANCE TO OTHER DISEASES, THE DIAGNOSIS OF CDG IS VERY DEMANDING. THUS, THE MOST IMPORTANT STEP IS TO SUSPECT A CDG! ①

WHEN SHOULD WE SUSPECT A CDG

COMMON NEUROLOGICAL SYMPTOMS INCLUDE:
Hypotonia, seizures, developmental disability, cognitive impairment, cerebellar hypoplasia, which can cause problems with balance and coordination.

ABNORMAL FAT DISTRIBUTION SUCH AS:
Fat pads, “orange peel” skin.

DEFECTS IN BLOOD CLOTTING:
That can cause abnormal bleeding or clotting (coagulation defects).

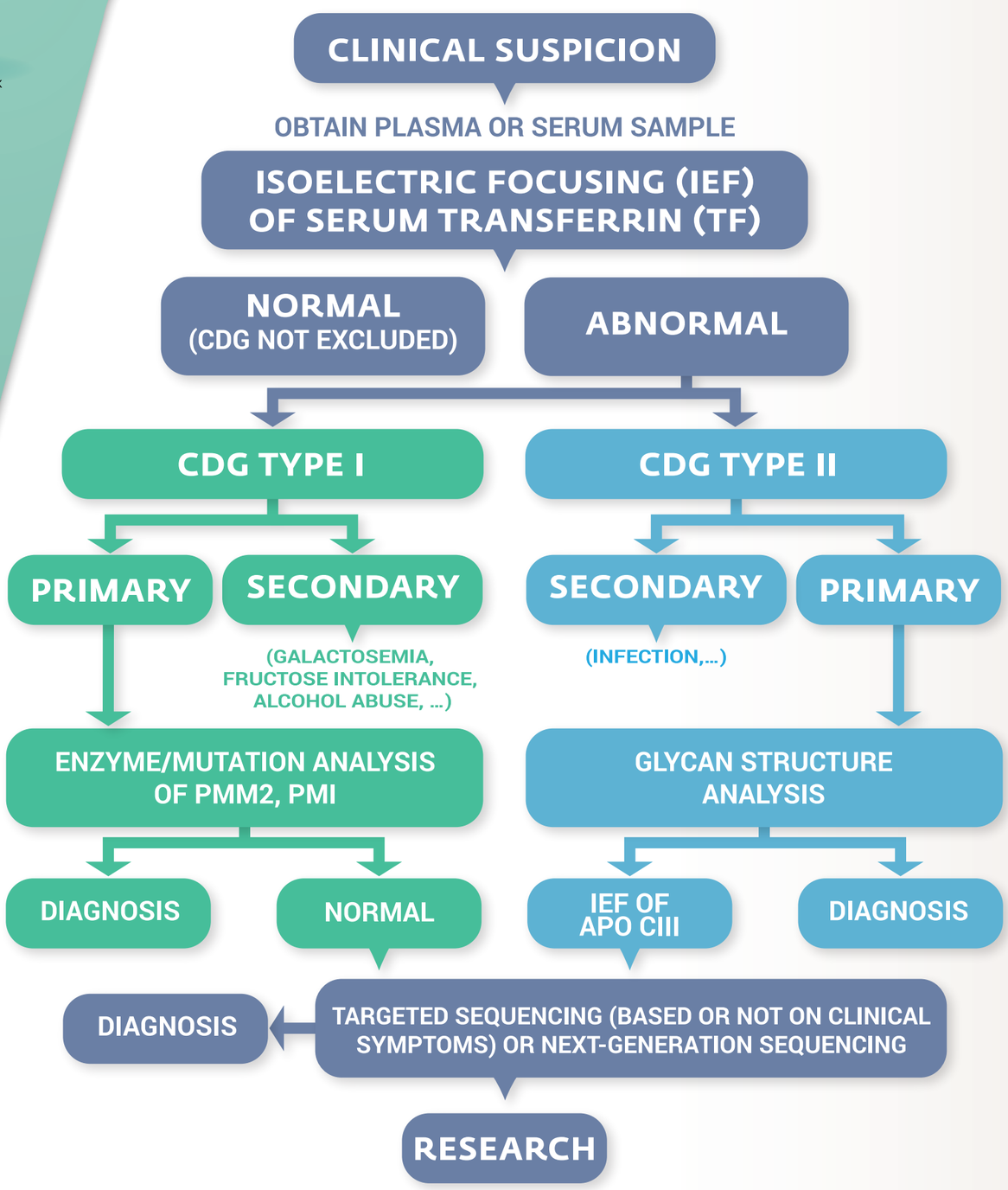
GASTROINTESTINAL SYMPTOMS:
Vomiting and diarrhea, feeding difficulties leading to failure to thrive is also common.

EYE ABNORMALITIES SUCH AS:
Crossed eyes (strabismus) and retinal degeneration.

OTHER SYMPTOMS MAY BE CONSIDERED.


Stephanie Grunewald - UK

STRATEGY FOR THE LABORATORY DIAGNOSIS OF CDG



WHAT IS THE NEXT STEP AFTER SUSPICION OF A CDG?


Dirk Lefeber - Netherlands

The next step is to perform a blood test to analyze the glycosylation status of transferrin (serum transferrin isoelectrofocusing or IEF). This test is able to diagnose only CDG due to an N-glycosylation defect.
Thus not all CDG can be detected by this assay.
Some O-glycosylation defects can be diagnosed by IEF of another serum protein namely apoprotein CIII.

IMPORTANT

Sometimes the defect is not found because it is in a gene that has not yet been implicated in CDG. In that situation research will be started. This can be a difficult time – emotionally and psychologically – for the patients and particularly their families.

PITFALLS

Transferrin glycosylation patterns may initially be normal. Repeat testing is thus warranted in patients with a strong clinical suspicion. Many referral centers offer diagnosis of CDG. Contact us if you wish to liaise with one center:

sindromecdg@gmail.com

① Jaeken J. Congenital disorders of glycosylation. NORD report available at: https://rarediseases.org/rare-diseases/congenital-disorders-of-glycosylation/. Accessed 01/08/2015.

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