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Carbohydrate Deficient Transferrin (CDT) and Alcoholism

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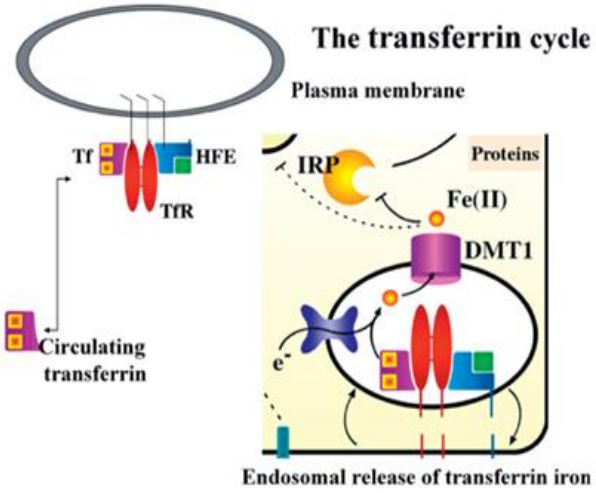
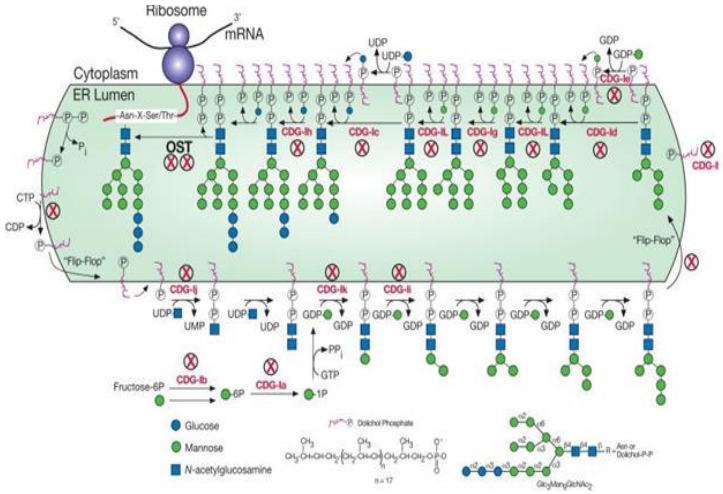
Abstract

Alcohol abuse is an important public health problem. This condition is usually identified on the basis of clinical judgement, alcoholism related questionnaires and laboratory tests i.e. Gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST) or mean cell volume (MCV.) The lack of sensitivity and specificity of these tests has led to a search for a specific marker. CDT has been shown to be more useful than any other currently available biochemical test for alcohol abuse. CDT represents the two isoforms of the iron transporting protein, transferrin with defective glycosylation. The same isoforms are also seen in higher concentration in the carbohydrate deficient glycoprotein syndrome (CDG)



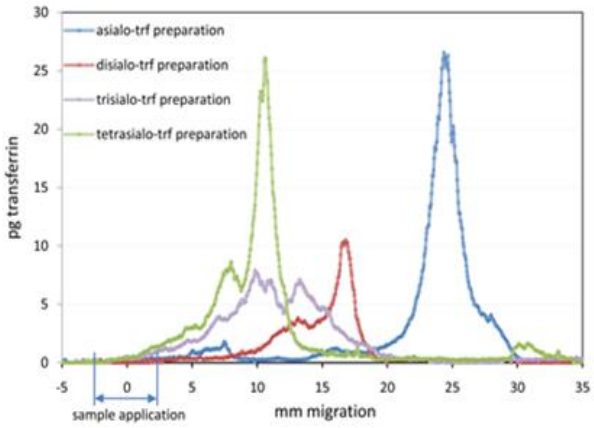
Other tests have recently been proposed, such as mitochondrial acetaldehyde adducts, b-hexosaminidase or phosphatidyl, but clinical experience is still limited. CDT is used for screening for hazardous alcohol consumption with negative results from interviews, but continued suspicion of alcohol abuse i.e. in liver disease.

a) Evidence of individuals at risk of developing chronic alcohol dependence.
b) Long term monitoring for early detection of relapse drinking during medical treatment which permits early intervention.
c) Aid in the assessment of reinstatement of a drivers license.
d) Identifying chronic alcoholics among traumatized patients *[1]*



a) Method of determination
b) These include
c) Amongst others
d) Mini columns
e) Chromatography

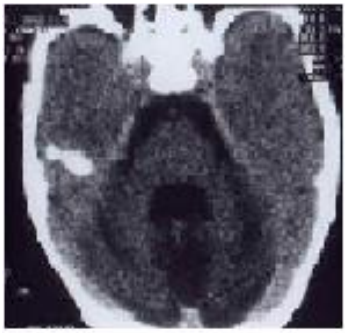
f) Radio immuno-assay
g) %CDT
h) Immunoblotting
i) Densitometry
j) Hplc (High Performance Liquid Chromatography)



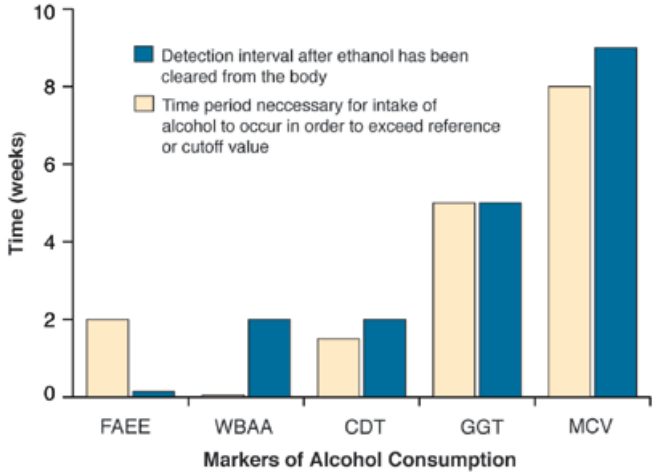
Clinical Significance

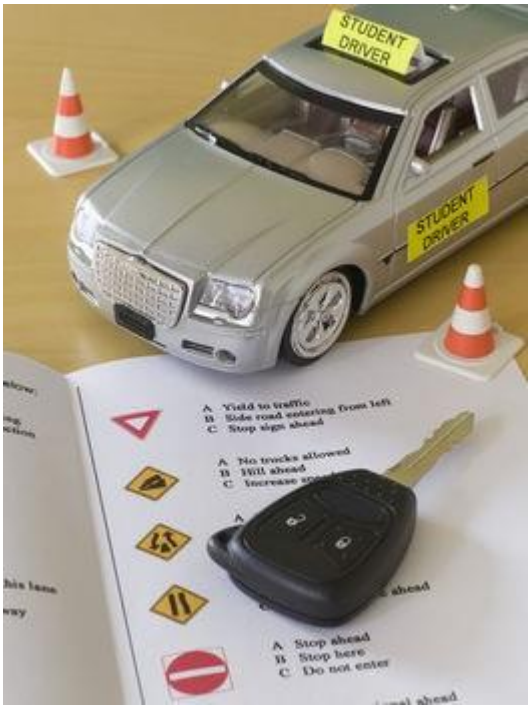
One looks specifically at the disialo and asialo forms *[5]* transferrin isoforms are separated out on HPLC at 460 nm.

These are asialo, disialo, trisialo ,tetrasialo and pentasialo transferrin isoforms *[2]*. Carbohydrate deficient transferrin (CDT) has been used as a test for excessive alcohol consumption in research ,clinical, and medico-legal settings , but there remains conflicting data on its accuracy ,with sensitivities ranging from <20% to 100% In studies published the results obtained with commercially available CDT assays were not significantly better than GGT (Gamma Glutamyl Transferase) as markers of excessive alcohol use in paired studies. Further high-quality studies comparing CDT ECT(modified) and other CDT assays with GGT in the same subjects are needed. In conclusion, the methods were in rather good agreement with each other. Diagnostic characteristics among heavy drinkers and correlations between methods differed slightly, probably depending on the ability of different methods to separate and detect asialo-,monosialo-, and disialotransferrin.



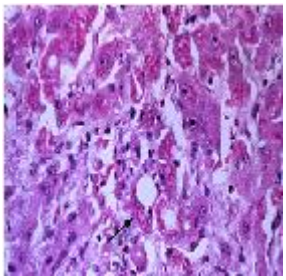
Another article focused on the sensitivity and specificity of ethanol and methanol concentration in plasma, and the 5-hydroxytryptonol (5htol) to 5-hydroxyindole acetic acid (55hiaa) ratio in urine as laboratory tests to identify acute alcohol consumption. Comparison was made with self reported drinking levels. This demonstrated that 5htol/55hiaa ratio was the most and ethanol the least sensitive indicator of recent alcohol consumption, and this was true for the different drinking categories as well as for the five study populations *[3]*.



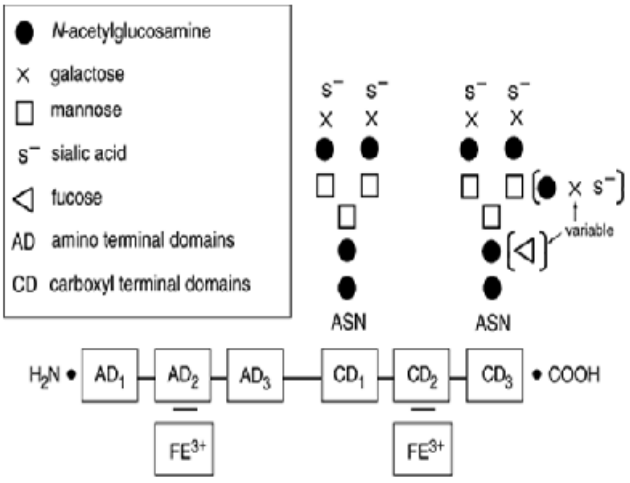


One of the biochemical characteristics of carbohydrate deficient glycoprotein syndromes is the presence of abnormal glycol forms in serum transferrin. both glycoform heterogeneity and variable site occupancy may ,in principle, lead to the generation of a range of glycoforms which contain different numbers of sialic acid residues, and therefore variable amounts of negative charge. Capillary zone electrophoresis was used to resolve the glycoforms of normal human serum transfer in and also a set of glycol forms which were prepared by

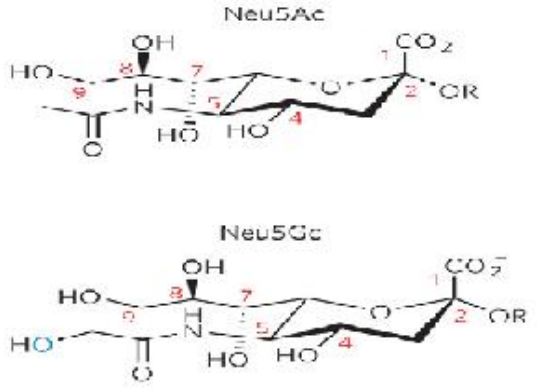
digesting the sugars on the intact glycoprotein with sialidase. The sugars on the intact glycoprotein were also modified by a series of neutral glycol forms which were also analyzed by a series of mixed exoglycosidase digests on the released glycan pool and quantified using a novel HPLC strategy.



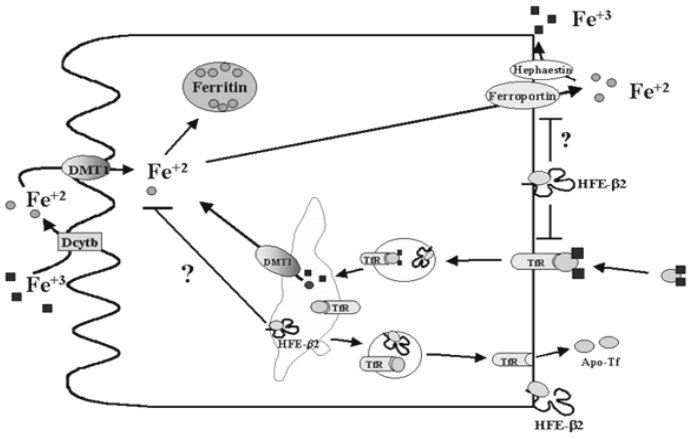
Transferrin was isolated from carbohydrate deficient glycoprotein syndromes type 1 serum and both the intact glycoforms and released sugars were resolved and quantified. The data presented here confirm the presence of a hexa-penta- and tetra-sialoforms of human serum transferrin in both normal and carbohydrate deficient glycoprotein syndrome type 1 serum samples. consistent with previous reports carbohydrate deficient glycoprotein syndrome type 1 transferrin also contained a di-sialoform,



Representing a glycoform in which one of the two n-glycosylation sites is unoccupied and a non-glycosylated form where both remain unoccupied. this study demonstrates that capillary zone electrophoresis can be used to resolve quantitatively both sialylated and neutral complex type glycoforms, suggesting a rapid diagnostic test for the carbohydrate deficient glycoprotein syndromes group of diseases *[4]*. Transferrin is a protein that carries iron through the bloodstream to the marrow, where red blood cells are manufactured, as well as to the liver and spleen. Structurally, transferrin is a polypeptide with two n-linked polysaccharide chains. These polysaccharide chains are branched with sialic acid residues. sialic acid is a monosaccharide carbohydrate.

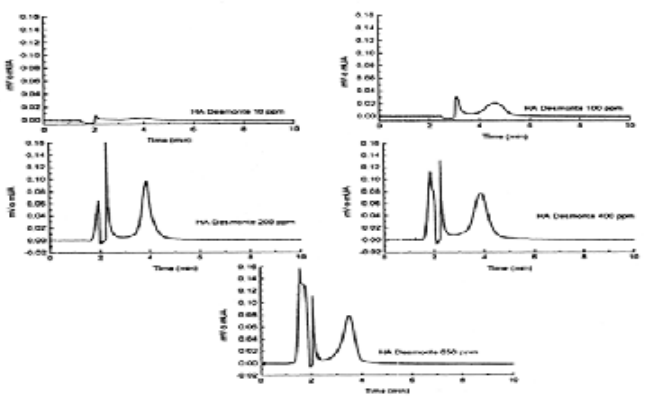


Various forms of transferrin exist, with differing levels of sialylation. The most common form is tetrasialotransferrin, with four sialic acid chains. In persons who consume significant quantities of alcohol (usually more than 4 or 5 alcoholic beverages a day for two weeks or more), the proportion of transferrin with zero, one or two sialic acid chains is increased. These are referred to as carbohydrate deficient transferrin. These carbohydrate-deficient transferrins can be measured in the bloodstream, and are an important marker for alcohol abuse. Used with other tests, such as gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT), carbohydrate deficient transferrin can be a useful tool in identifying problem drinking, such as alcohol abuse or alcoholism.

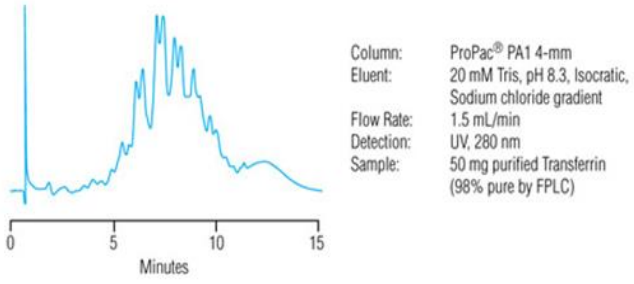


CDT is measured by taking a sample of a patient's blood. Apparently healthy individuals with no or low reported alcohol

consumption and a negative alcohol use disorder test will have a % CDT <3.0 (95th percentile for the social drinking population). Elevated levels of CDT suggest recent alcohol abuse, especially if other liver-associated enzymes (such as GGT) are elevated. Although, recent alcohol use is most commonly associated with elevated CDT, certain rare liver disorders can also increase levels of CDT *[5]*.

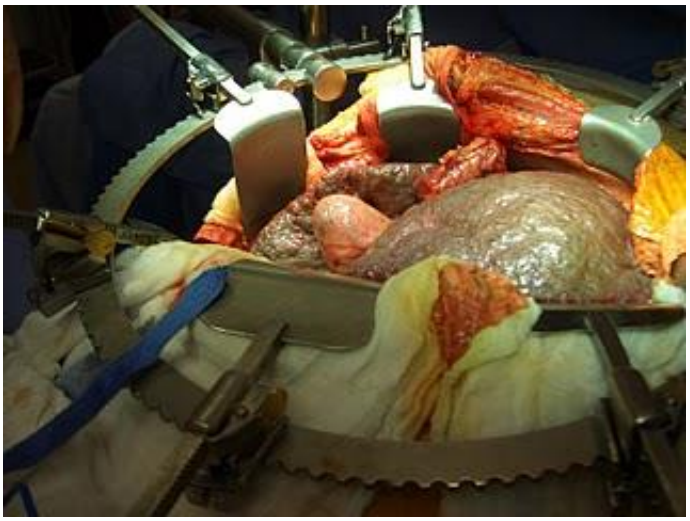


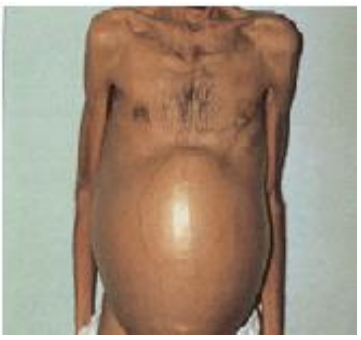
Perhaps we are even reaching a stage where the CDT value as a percentage may even be a predictor of who would be a good candidate for a liver transplant? A value of greater than 6.5 for example! Not that it will obviate liver function tests or histology of a liver biopsy, but the CDT value may give one a good indication of impending liver failure and the need for a transplant! this is because alcoholic liver disease is probably still the biggest cause of liver disease globally beating hepatitis of all causes into second place

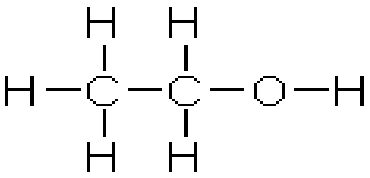


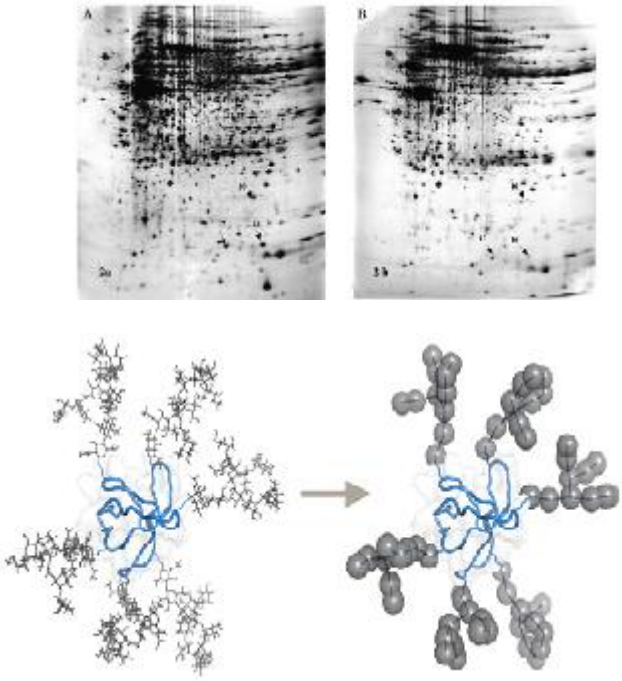
Summary of Liver Function Test Abnormalities

Disease	ALT	AST	GGT	ALP
Viral hepatitis	+++	+++	++	N/+
Drug induced hepatitis	++	++	++	N/+
Chronic active hepatitis	++	++	++	++
Infectious mono-nucleosis hepatitis	++	++	++	N
Primary biliary cirrhosis	++	++	+++	++
Alcoholic cirrhosis	N	++	+++	N/+
Intrahepatic cholestasis	++	++	+++	++
Extrahepatic cholestasis	++	++	+++	+++
Hepatoma	N/+	++	++	++









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