

**A Workshop Presentation given by
David A. Weinstein, M.D., M.M.Sc (University of Florida)
for the AGSD (UK) Conference October 2007**

Dr. Weinstein from the University of Florida joined the 2007 workshop for type Is and IIIs. He is the Associate Professor and of Paediatrics at the university and Director of the Glycogen Storage Disease programme. This was a joint workshop as many of the issues are relevant to both Is and IIIs.

Dr. Weinstein began his report with an explanation on treatment strategies. The guidelines for type III tend to be less formal than type I and there is significant variability between centres. Many centres, however, agree that it is important to avoid storage of excessive sugar and to provide enough fuel in the form of carbohydrates and protein to prevent hypoglycaemia. Some centres use exclusively cornstarch whereas others use just protein. Dr. Weinstein recommends a high protein intake with 3 – 4 grams/kg and the minimum amount of cornstarch possible to avoid hypoglycaemia. The dose is then adjusted based on home glucose, ketone and urine myoglobin monitoring. He has found that children (especially infants and toddlers) treated with just protein come in with low blood sugars.

FUTURE OF GSD III TREATMENT

Centres in Europe and North America are working together to answer this problem. A database of GSD III patients has been created Chris Peter Sentner and Professor Peter Smit to help analyze treatment strategies. The AGSD (US) has proposed sponsoring a consensus panel to create recommendations.

OVERVIEW OF COMPLICATIONS AND TREATMENTS

Despite improvements in therapy hypoglycaemia and long term complications are common. These are -

- Hepatic adenomas
- Liver cancer
- Liver fibrosis
- Muscle weakness
- Hypertrophic cardiomyopathy

MUSCLE DAMAGE

Patients with GSDIIIa often have progressive myopathy becoming severe by the fourth decade of life. Preliminary studies have demonstrated abnormal oxygen utilization by muscles during activity. It has also been shown that patients with GSDIII have a very low concentration of lactate during exercise - lactate causes oxygen to be released from muscles and it is a lack of oxygen that may be causing muscle damage. In order to understand the process and implications of this a GSD III exercise study is under way at the University of Florida.

GSD III EXERCISE STUDY

Aims of the Study:

- To characterise and evaluate the response to exercise in IIIa and IIIb patients
- To better understand what causes muscle damage in IIIa
- To try to find a method to prevent muscle damage

The study consists of a two day and night inpatient stay at the University of Florida. There are two exercise tests on consecutive days. On each day a lemonade drink is made with either sugar or Splenda (artificial sweetener). The aim of the sugar is to increase lactates prior to exercise and thus reduce muscle damage. Dr. Weinstein stressed that this is only a theory that is being tested and not a recommendation. Professor Smit in Holland has carried out similar studies where carbohydrates are given instead and similar results are being found. It was also mentioned that if too much sugar is given then lactates will spike too quickly and the patient will feel nauseous. It is anticipated the study will be finished by the summer of 2008. They may still be looking for volunteers.

ALTERNATIVE CORNSTARCH TRIAL

The search for an alternative cornstarch was partly prompted by a plea from the CureGSD foundation, a USA based charity. They wanted to sleep through the night! Arguably the traditional cornstarch in America does not last for many people through the night. Five products were identified and tested but were all found to be inferior to the present treatment. Eventually a product was identified and tested by Dr. Philip Lee. His initial studies were performed on 20 patients GSD I and III. The type I report contains a very good summary of the results of further trials carried out in Florida. It should be noted that studies of this type are much harder to do on type IIIs as the body can make its own sugars. A second study of the alternative cornstarch is presently underway, and investigations are being performed by Drs. Lee in England. In the United States, Dr. Weinstein will be performing the studies with Dr. Kishnani of Duke.

HEPATIC ADENOMAS

These occur in 20% of all type IIIs. The lesions usually develop during puberty with a mean average age of 14.8 plus or minus 4.2 years. They have also been seen in women taking contraceptives and men taking steroids. Adenomas can undergo a malignant transformation to hepatocellular carcinoma. With improved survival rates in GSD an increased risk has been noted and several cases have been reported in type III. However, Dr. Weinstein believes that this is not the normal progression of the disease. He pointed out that patients with this diagnosis had other precipitating factors such as hepatitis or poor control. There is no consensus on the management of adenomas. There is a summary of the management available in the type 1 report.

OSTEOPOROSIS

It is felt that ketone levels affect bone density in type III. Dr. Weinstein feels good control can help this problem. He advises against giving medication until after puberty as this is a time when bones strengthen. Women should wait until after childbearing.

ALCOHOL

Dr. Weinstein recommends that people with types III, VI, and IX do not drink at all. Alcohol makes the liver more inflamed, it also blocks the conversion of fats and protein to sugar – this means that blood sugars cannot recover as they normally do and severe hypoglycaemia with seizures can be the result. Type III also has the added risk of fibrosis which is only exacerbated by alcohol.

DELAYED PUBERTY

Dr. Weinstein feels this is due to lack of control. He stated that it is important to focus on ketones which indicate fat breakdown.

STATINS

It was pointed out that people with type III must not take statins as they have a side effect on muscles. Gemfibrosil is recommended to control triglycerides and good metabolic control for lipids.