

## **2002 Workshop - Type III & IX**

Presentation by Dr Helen Mundy to the October 2002 Conference workshops of (AGSD)UK Types 3 and 9

The objectives of Dr H. Mundy's first session in the morning which was well attended by representatives of both Type 3 and type 9 were to review the glycogen metabolism, to focus on the clinical features of types 3 and 9, and to discuss aspects of their current management.

Her initial slides showed the complex metabolic process involved in the production of glycogen, and the role played by the enzymes in type 3.

She described the chemical reasons for the effects of exercise on types 3a and 3b, and the clinical features of type 3.

She noted that in adulthood there is reason to believe that type 3 can become normalised, with better fasting tolerance. However there is also evidence that some cirrhosis can occur, less likely in 3a, and rarely, a condition known as hyperuricaemia (not gout) where muscles produce uric acid. Other issues may present via heart, cramps in fingers and arms, and again rarely, some respiratory myopathy.

Thickening of the Heart (see also Workshop report by Dr. Eli Hershkovich in 2000)  
Looking at the incidence of adulthood heart problems in type 3 patients, Dr. Mundy noted surveys by Moser (20 patients) Labrune (18) and Lee (5 with GSD and 10 with other forms of metabolic disorder). Dr Mundy works with Dr Lee. They have found that of 25 adult type III patients 5 have heart related problems. Their research measured heart thickening and found that thickening from GSD 3 did not bring the same risks as other causes of heart thickening.

This is particularly important for those managing the condition, both patients and clinicians. A cardiologist with no knowledge of GSD 3 might otherwise say from the apparent evidence that the myopathy is much more of a problem than it actually is.

### GSD Type 9 (IX)

As she had for type 3, Dr Mundy outlined the metabolic processes and clinical features surrounding type 9.

The aims of the management of all the GSDs under discussion were to normalise biochemistry, to improve clinical problems and long term implications, and to empower both patients and families in the management process.

Treatments are still primarily dietary. Whilst there are drugs for cardiomyopathy, the future was really all about super starches and novel therapies. One type one patient with type 1 in Italy had had hepatocyte transfer (liver cell transplant) and this had led to slight improvements, though it still carried the risk of organ rejection and was only to be considered in the most extreme circumstances.

In the afternoon Dr Mundy took us through some of the current research

The first concerned cardiomyopathy and the use of cardiac MRI studies to identify changes to the heart. At present regular echocardiograms carried out on type 3a patients have a poor predictive value and are not particularly sensitive to changes. Current research is looking at the feasibility of cardiac MRIs though this is a noisy and invasive test which requires patience on the part of the participant. It could however pick up those at risk.

An exercise study (type 1, 3 and 9 adults) was concentrating on the degree of exercise intolerance experienced. A treadmill is used with increasing speeds and gradients and the cardio-respiratory and metabolic responses documented. Another aim is to determine whether cardio pulmonary exercise testing will be useful and acceptable for any possible future therapies and their testing. So far it has been noted that all of the GSD subtypes have

less cardiovascular fitness than average. It has been wondered whether regular cornstarch or protein /alanine improves fitness or exercise tolerance.

Body composition in this study the aim is to measure the amount of fat, muscle and bone in people with GSD, with the aim of answering:

whether biochemical abnormalities may cause demineralisation of bone;  
if treatment (cornstarch) causes an abnormal fat/muscle ratio;

to assess the effect of treatment on muscle bulk.

It has been discovered that a significant number of people with type 3 have a low bone mineral density, especially adults. Also it has been shown that those in the research program would appear to carry more fat to muscle than the average person.

The question is, is this a consequence of diet or disease?

Superstarch

Uncooked cornstarch has revolutionised treatment, and ways are being explored of improving this, particularly with the aim of improving fasting tolerance and dosage. Five different types of starch have been tested on one adult and two in particular have been particularly effective. The best response has been shown to be from a mixture of these two substances. The major hurdle at present is palatability , and it is hoped that there will be answers to this problem within the year.

All present thanked Dr Mundy for her very informative and helpful sessions which with question and answer sessions had covered much ground.

A.Arthur, AGSD(UK) Type III Representative