UKGTN Testing Criteria

Name of Disease(s): GLYCOGEN STORAGE DISORDERS

Name of gene(s): 18 GSD GENES

Patient name: **Date of birth:**

Patient postcode: **NHS number:**

Name of referrer:

Title/Position:
Lab ID:

Referrals will only be accepted from one of the following:

Referrer	Tick if this refers to you.
Consultant Metabolic physician	
Consultant Hepatologist	
Consultant Cardiologist - paediatric/ adult	
Consultant Neurologist - paediatric/adult	
Consultant Clinical Geneticist	
Consultant Paediatrician	

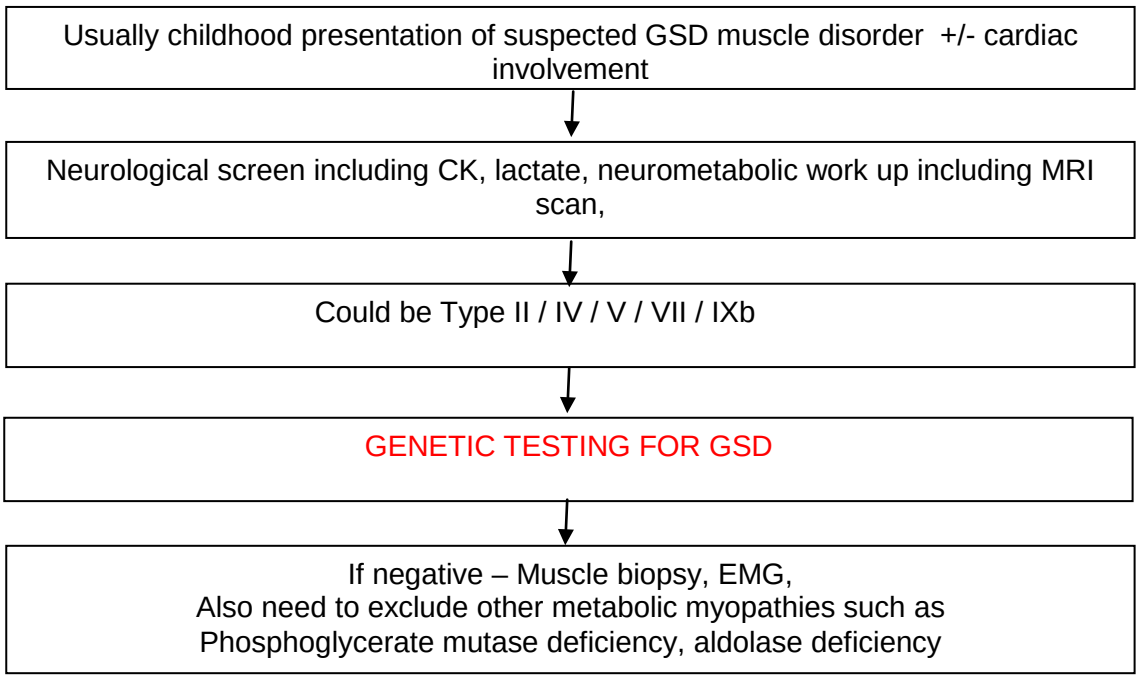
Minimum criteria required for testing to be appropriate as stated in the Gene Dossier:

Criteria	Tick if this patient meets criteria
Persistent hypoglycaemia with other metabolic causes excluded	
OR Persistent hepatomegaly in childhood	
OR Previous liver biopsy suggestive	
OR Neuromuscular presentation suggestive of GSD (see algorithm) **OR** previous muscle biopsy suggestive	
OR Affected 1st degree relative	
OR At risk family member where mutation is known	

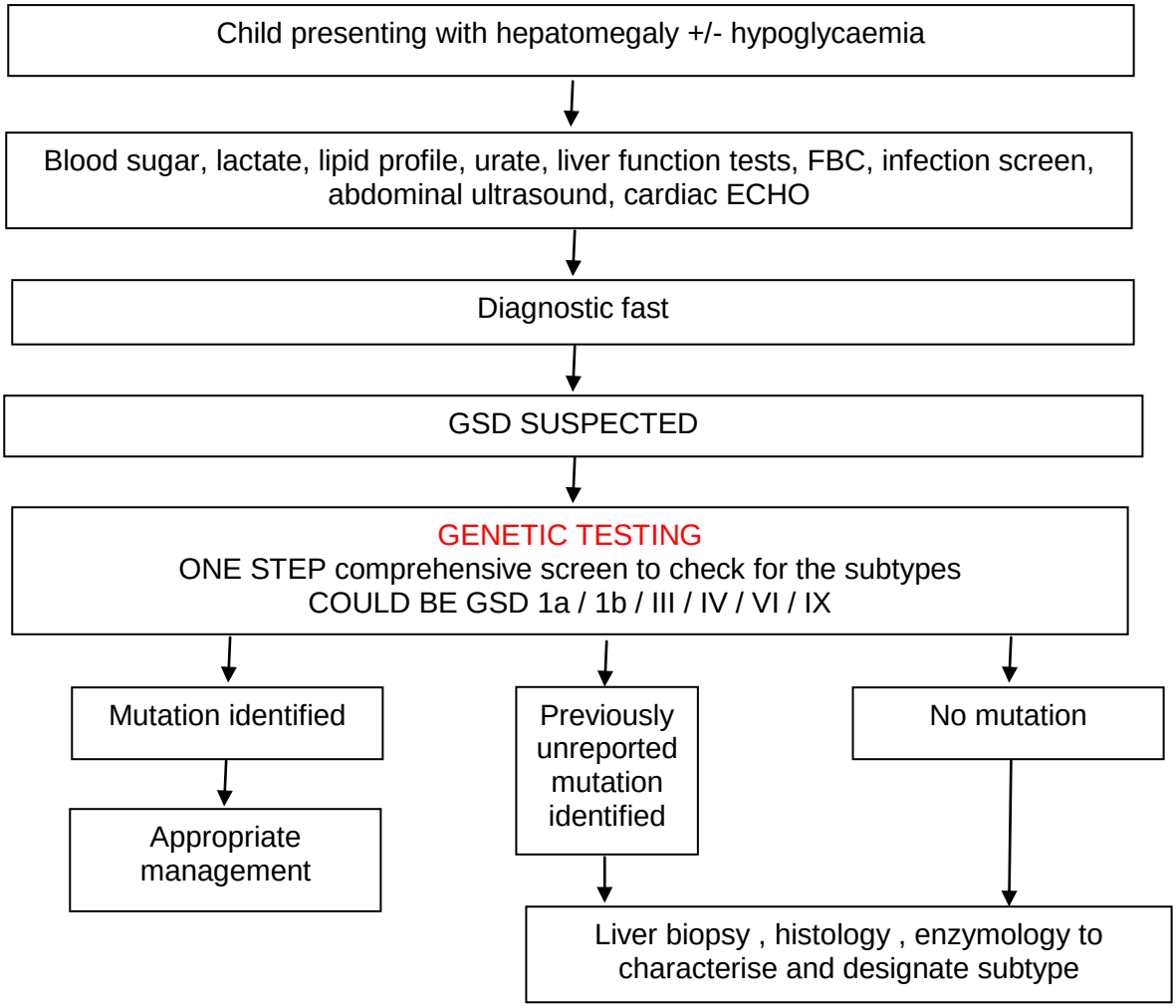
If the sample does not fulfil the clinical criteria or you are not one of the specified types of referrer and you still feel that testing should be performed please contact the laboratory to discuss testing of the sample.

CLINICAL ALGORITHMS FOR DIAGNOSIS OF GLYCOGEN STORAGE DISORDERS

Algorithm for diagnosis of muscle GSDs



Algorithm - Hepatomegaly (+/- neonatal hypoglycaemia)



EXAMPLE OF IMPACT ON THE NHS

Glycogen Storage Disorders (GSDS)

Case Study 1 (Patient 5)

Patient 5 in our initial study cohort was first referred to the metabolic physician at 3 years of age. He was seen by his local paediatrician for small stature and slow weight gain. Examination revealed hepatomegaly and nil else.

He had baseline biochemical tests that suggested a possible diagnosis of Glycogen Storage Disorder. Clinically, it was thought the presentation would be compatible with type III/ VI/ IX. Enzyme studies were performed on peripheral blood (£400) but were inconclusive. He was then reviewed regularly by the local team as well as the metabolic team and required intensive input from the dietician and the community paediatrics team. He remained small and hepatomegaly persisted. He then had repeat enzymology and as there was a delay in transit, the results could not be interpreted. It had to be repeated again but was still inconclusive (£800) He had a liver biopsy subsequently and histology (£800) as well as enzymology studies were done on liver tissue (£800). However, although a diagnosis of GSD was substantiated, it was not possible to assign the correct subtype.

He has remained under regular 6 monthly follow up with the metabolic team as well as his local paediatrician. This is because there is a high risk of cardiac complications with Type VI.

As molecular testing became available using conventional Sanger sequencing, he had mutation testing for all three GSD IX genes (£3000) but no mutation was identified. He is now 16 years old and remains without a definitive diagnosis. There was increasing concern by the family as his older sister was due to be married soon and they wanted accurate risks for her children.

Mutation analysis using the GSD NGS test has at last confirmed he has autosomal recessive GSD VI after 12 years. The total costs of tests alone for this patient exceed £8,000 over this period. This new test would have saved this as well as need for repeated hospital appointments, additional radiology investigations and invasive high risk procedure

Case Study 2 (Patient 15)

Patient 15 was seen in the metabolic clinic at 18 months with hepatomegaly. Clinical features as well as investigations including enzymology suggested this was GSD III. Mutation testing using conventional Sanger sequencing did not reveal any mutations in AGL (aka GDE) gene. This was disappointing as his mother was pregnant and enquired regarding a possible prenatal. Using the GSD NGS test we were able to identify the mutation in this patient confirming his clinical diagnosis but were not in time to offer a prenatal test. The sibling is due to be born shortly and will now be tested at birth.

We would have saved this patient's parents a lot of anxiety during the pregnancy and possibly avoid a recurrence had this test been available at the outset.