British Inherited Metabolic Disease Group

PATIENT NAME **HOSPITAL**

DATE OF BIRTH **EMERGENCY CONTACT**
9-5pm Monday to Friday
Out of hours

ADULT EMERGENCY MANAGEMENT

GLUTARIC ACIDURIA TYPE 1

(also known as Glutaryl-CoA dehydrogenase deficiency)

IMMEDIATE ACTIONS

Triage to high priority

Maintain glucose 6-10 mmol/L.

These guidelines are intended for immediate emergency management only. Please contact your local metabolic team early for specific advice on individual patients.

BACKGROUND

Glutaric aciduria type 1 is an inherited disorder of the breakdown of certain amino acids, notably lysine. Any metabolic stress can lead to serious illness, with encephalopathy and other neurological abnormalities. Following these episodes, patients often have severe permanent neurological disability, particularly a movement disorder. Patients are particularly at risk during early childhood. The damage results from the accumulation of glutaric acid and other toxic metabolites. Treatment aims to minimise the accumulation of toxic metabolites by preventing protein breakdown and to promote their excretion by the use of carnitine. Acute decompensation of GA1 is however relatively uncommon in adult patients – so that if an adult patient presents to a hospital unwell – then a thorough search should also be made for other underlying problems.

SIGNS OF DECOMPENSATION

Decompensation is often triggered by metabolic stress such as febrile illness, particularly gastroenteritis, or fasting, but an obvious cause is not always apparent. The early signs of decompensation may be subtle, such as minor changes in tone. **Vomiting** is common and should always be taken seriously. However, the signs may be difficult to assess such as **irritability** or just **'not right'**. Always listen to patients and their families carefully as they generally recognise early changes more quickly than medical professionals.

GENERAL TREATMENT

1. Avoidance of triggers of metabolic decompensation such as fasting – always ensure adequate carbohydrate intake – either orally or intravenously. Prompt treatment of fever and intercurrent illness.
2. Low protein diet – many adult patients self-impose a moderate reduction in protein intake with avoidance of high protein foods such as meat, fish and dairy. Some others are on a more formal low protein diet and use lysine-free amino acid supplements.
3. Carnitine replacement – generally 50-100mg/kg/day for an adult (eg. approximately 1g tds). Many patients have carnitine deficiency and carnitine replacement may prevent episodes of metabolic decompensation. Carnitine may not be available in every hospital pharmacy - further information is available from the pharmacy at Great Ormond Street Hospital for Children.

If there is any doubt at all, the patient should be admitted, even if only for a short period of observation.

INITIAL ASSESSMENT AND MANAGEMENT IN HOSPITAL

If the patient is shocked or clearly very ill arrange for admission to ITU / HDU.

Management decisions should be based primarily on the **clinical** status. If the patient is relatively well – they may be treated orally using their oral emergency regimen (click here) (generally give 200ml of a 25% glucose polymer solution every 2 hours) but assess very carefully. If the patient is obviously unwell then they must be treated with intravenous fluids.

Record the Glasgow Coma Scale (click here). This will allow early identification of encephalopathy and deterioration.

INITIAL INVESTIGATIONS

Blood pH and gases
Glucose
Urea, creatinine & electrolytes
Full blood count
Liver function tests
Other tests as clinically indicated (eg. amylase, CK, CRP, blood & urine cultures)

TREATMENT

1. Correct dehydration initially with 0.9% NaCl.

2. Start intravenous 10% dextrose started as soon as possible at a rate of 2mls/kg/hr, (e.g. 140 mls/hr in a 70 kg person).

3. Continue oral carnitine if possible (dose can be increased to 100mg/kg/day, in 4 divided doses). If unable to tolerate then start carnitine 100mg/kg/day intravenous maintenance infusion.

4. Reduce oral protein intake initially (aim to restart protein intake by 24 hours after presentation – for further advice contact your local metabolic dietitian). Some patients may be taking a lysine free aminoacid mixture – if so then this should be continued.

5. Treat any underlying infection or other clinical problem.

6. Give analgesia, anti-pyretic or an anti-emetic as required.

7. Consider the possibility of refeeding syndrome in susceptible patients.

MONITORING
Reassess regularly and if there is a change for the worse repeat the clinical assessment and blood tests:

Blood pH and gases
Glucose
Urea, creatinine & electrolytes
Liver function tests

Glucose: Hyperglycaemia can occur. If the blood glucose exceeds 10 mmol/L start an insulin infusion according to the local diabetic protocol rather than reducing the glucose intake. Avoid hypoglycaemia. National guidelines are available at:
(http://www.diabetes.org.uk/About_us/Our_Views/Care_recommendations/The-Management-of-Diabetic-Ketoacidosis-in-Adults/).

Potassium: Hypokalaemia may occur so plasma potassium concentration should be monitored and corrected appropriately.

RE-INTRODUCTION OF ORAL OR ENTERAL FEEDING
As the patient improves, oral or enteral feeds should be introduced as early as possible. Natural protein intake should be reintroduced gradually over a period of a few days before going back up to full requirements. See the BIMDG oral emergency regimen (click here) and / or contact your local metabolic dietitian for more details.

MORE INFORMATION
http://www.bimdg.org.uk/ and click on the red tab for emergency guidelines.
Pubmed: http://www.ncbi.nlm.nih.gov/pubmed/

Diagnosis and management of glutaric aciduria type I--revised recommendations.
Kölker S et al, J Inherit Metab Dis. 2011 Jun;34(3):677-94.