



British Inherited Metabolic Disease Group

PATIENT NAME:

HOSPITAL:

DATE OF BIRTH:

EMERGENCY CONTACT:

**9-5pm Monday to Friday
Out of hours**

**ADULT EMERGENCY MANAGEMENT
METHYLMALONIC ACIDAEMIA**

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

Methylmalonic acidaemia is caused by a deficiency of methylmalonyl CoA mutase, an enzyme on the catabolic pathway of aminoacids (isoleucine, valine, threonine and methionine) and cholesterol side chains, odd chain fatty acids and free propionate from the gut. The co-factor for the enzyme is a derivative of vitamin B12 (hydroxocobalamin). Treatment is aimed at reducing the sources of the precursors so the patients are treated with a low protein diet and medicines - carnitine and metronidazole. **Note: Some patients respond to pharmacological doses of vitamin B12.**

SIGNS OF DECOMPENSATION

Decompensation is often triggered by metabolic stress such as febrile illness, particularly gastroenteritis, fasting, or constipation but an obvious cause is not always apparent. The early signs of decompensation may

be subtle, such as lethargy, worsening appetite or exacerbation of pre-existing neurological signs (movement disorder, etc). 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 some prescription low protein food products.
3. Carnitine replacement – generally 50-100mg/kg/day for an adult. 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 - may be treated orally using their [oral emergency regimen \(click here\)](#) but assess very carefully – generally give 200ml of a 25% glucose polymer (eg Maxijul) solution every 2 hours. If the patient is obviously unwell or clinical status is unsure - 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

Full blood count

Renal, liver, bone profiles

Amylase/lipase (if pancreatitis a possibility)

Ammonia

Lactate

Plasma and/or urine MMA levels (specialist test)

Urine culture - urinary tract infections are common and should be considered and treated

Other tests as clinically indicated (eg. CRP, blood cultures)

TREATMENT

1. Correct dehydration initially with 0.9% NaCl. Fluid balance is particularly important in this group of patients, particularly in patients with renal impairment – contact your renal team early for advice if needed.
2. Start intravenous 10% dextrose 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 (100mg/kg/day in divided doses) – if unable to tolerate then start carnitine 100mg/kg/day iv maintenance infusion.

4. Reduce oral protein intake initially (aim to restart protein intake by 24 hours after presentation – for further advice contact the metabolic dietitian).
5. Start metronidazole 400mg three times daily oral or intravenous.
6. Treat constipation (which increases propionate absorption from the gut).
7. If hyperammonaemic - start sodium benzoate 250 mg/kg/day either as a continuous infusion or enterally. Avoid the use of sodium valproate.
8. If B12 responsive continue to give hydroxocobalamin 1mg intramuscularly daily.
9. Treat any underlying infection or other clinical problem, including 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
 Full blood count
 Renal, liver, bone profiles
 Amylase / lipase
 Ammonia and lactate

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: Plasma potassium concentration should be monitored and corrected appropriately. Hyperkalaemia may occur secondary to renal impairment. Hypokalaemia may occur following glucose/insulin infusion.

COMPLICATIONS

If patients are not responding to treatment then consider the following early and institute appropriate treatment:

Dehydration – is common. Adjust fluid intake as needed.

Acidosis – pH and gases should be monitored carefully. If acidosis persists after perfusion deficits are corrected then consider the use of sodium bicarbonate. Severe acidosis may be associated with respiratory/cardiac arrest and consideration should be given to elective assisted ventilation.

Pancreatitis - should be suspected if there is abdominal pain, shock out of proportion to other symptoms or hypocalcaemia.

Cardiomyopathy - may develop at any time but for reasons not well understood may occur during recovery phase. Arrange echocardiography if there are signs of cardio-respiratory problems. Cardiac monitoring is advised.

Stroke-like episodes - may occur at any time, frequently of sudden onset and when the patient is appearing to recover. They often involve the basal ganglia and present as a movement disorder.

Failure of improvement of clinical state, ongoing acidosis, hyperammonaemia, fluid overload – consider haemofiltration (haemodialysis) and seek specialist help. Peritoneal dialysis is not as efficient.

Nutritional deficiencies – may be an issue if patients have had a poor appetite for some time, especially if not taking vitamin/mineral supplements. Consider supplements, particularly of thiamine.

RE-INTRODUCTION OF ORAL OR ENTERAL FEEDING

As the patient improves, oral or enteral feeds should be introduced as early as possible. Parenteral feeding can be used if enteral feeding is not possible. Protein intake should be reintroduced as early as possible and increased as tolerated. Anti-emetics may be needed. Consult your local metabolic dietitian or specialist centre for more details. See the BIMDG [oral emergency regimen \(click here\)](#) for more details.

MORE USEFUL INFORMATION

<http://www.bimdg.org.uk/> and click on the red tab for emergency guidelines.

Genereviews: <http://www.ncbi.nlm.nih.gov/books/NBK1116/>

Pubmed: <http://www.ncbi.nlm.nih.gov/pubmed/>