British Inherited Metabolic Disease Group

PATIENT NAME **HOSPITAL**

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

ADULT EMERGENCY MANAGEMENT
PROPIONIC 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

Propionic acidaemia is caused by a deficiency of propionyl CoA carboxylase, an enzyme on the catabolic pathway of aminoacids (isoleucine, valine, threonine and methionine) as well as cholesterol side chains, odd chain fatty acids and free propionate from the gut. 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. Some adult patients may have a later-onset form of disease which tends to be easier to manage and may not require such rigid protein restriction.

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, even worse appetite than usual or exacerbation of pre-exiting 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 – they 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 – 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
Full blood count
Renal, liver, bone profiles
Amylase / lipase (if pancreatitis a possibility)
Ammonia
Lactate
Plasma or blood spot acylcarnitines (specialist test)
Urine culture and ketones
Other tests as clinically indicated (eg. CRP, blood 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 (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. Do **not** use sodium valproate.

8. Treat any underlying infection or other clinical problem, including refeeding syndrome in susceptible patients.

A number of cases of severe cardiac complications in patients with decompensated propionic acidaemia have now been described: dilated cardiomyopathy, prolonged QTc interval and arrhythmia. Patients should therefore be placed on a cardiac monitor whilst in hospital and have an urgent cardiac assessment.

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

COMPLICATIONS

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

Acidosis – pH and gases should be monitored carefully. If acidosis persists after perfusion deficits are corrected then consider 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
Stroke-like episodes - may occur at any time, frequently of sudden onset and when patient 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. Parentral 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 general 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/