

GLUTARIC ACIDURIA TYPE 1

Priority patient: must not wait in A&E / ED

Patient label

If presenting with fever, vomiting, diarrhoea or fasting state
RISK OF ACUTE NEUROLOGICAL DISORDER with DAMAGE TO THE BASAL GANGLIA

Do not wait for signs of decompensation, in all cases initiate management as set out below

1 EMERGENCY WORKUP

Venous blood gases, lactate, electrolytes, blood glucose, CK, FBC, urea (BUN), creatinine. + Tests depending on the triggering intercurrent illness. Do not delay infusion. Normal test results do not exclude ongoing decompensation.

2 TREATMENT TO BE STARTED URGENTLY, without waiting for test results

- NO natural PROTEINS or IV amino acids : **stop feeding or specific low-protein nutrition.**
- If **hypovolaemia**, **expand** with Ringer's lactate or 0.9% NaCl at **10 mL/kg** (maximum 500 mL), reassess and repeat if necessary.
- Infusion using **10% glucose** with standard electrolyte additions* (never pure D10W)
 + Infusion using a Y-set of **20% lipids** (e.g. Medialipids, Intralipids),
- By peripheral line, at a rate depending on age:

Age	0-24 months	2-4 years	4-14 years	> 14 years / adult	MAX INITIAL RATE
Polyionic 10% glucose (glucose infusion rate)	6mL/kg/h (10mg/kg/min)	5mL/kg/h (8mg/kg/min)	3.5mL/kg/h (6mg/kg/min)	2.5mL/kg/h (4mg/kg/min)	120mL/h (3L/24h)
Lipids 20%	0.4 mL/kg/h (2g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	20mL/h (500ml/24h)

*e.g. Polyionic, Bionolyte, B45, Glucidion, etc. if no pre-made solution available, use 10% glucose in water + 4g/L NaCl (70 meq/L) + 2g/L KCl (27 meq/L)

If IV line is impossible => Nasogastric tube: prepare the IV fluids listed above and pass them through the tube at the same rates.

- If there are no gastrointestinal disorders and if the preparation is available: instead of infusion, **emergency diet by continuous enteral feeding** using nasogastric tube or gastrostomy (see diet sheet from parents)
- **L-Carnitine**, orally divided into 3 to 4 doses or by continuous IV administration:
 - < 6 years of age: **200mg/kg/day**
 - > 6 years: **100 mg/kg/day**, max 12g/24h
- **Continue** any regular treatments
- Antipyretic and analgesic treatments if needed
- Treatment of intercurrent infection if needed

3 CRITERIA FOR HOSPITALISATION

- In all cases if under 6 years of age
- Over 7 years: return home if fever well tolerated and oral feeding possible with emergency diet.

4 SEVERITY SIGNS = consult / admit to Intensive Care

- Comatose or rapid neurological deterioration.
- Dystonic crisis

5 MONITORING

- Clinical: altered consciousness, change in findings on neurological examination, dystonia.
- Repeat laboratory tests depending on initial abnormalities.
- Blood glucose every 4 h: target range 1-1.8g/L. If blood glucose >2g/L and glycosuria, consider insulin 0.01 units/kg/h with subsequent dose adjustment every hour. Consider reducing sugar intake (25 to 50%) if persistent hyperglycaemia despite insulin therapy at 0.05 IU/kg/h and/or onset of hyperlactataemia > 3mmol/L.

PATHOPHYSIOLOGY:

Glutaric aciduria type 1 is a cerebral organic aciduria due to deficiency of glutaryl-CoA dehydrogenase. This disease exposes the patient to a risk of neurological damage (damage to the basal ganglia). There is a major risk of neurological deterioration during catabolic states (fever, vomiting, fasting), essentially in children under 6 years of age.

The usual treatment is :

- Carnitine supplementation (100 mg/kg/day up to 6 years of age, 30-50 mg/kg thereafter), orally or IV in case of fasting.
- Limited proteins diet (fruit and vegetable diet +/- amino acid substitution); strict diet up to 6 years of age. See "Maintenance diet" sheet. This type of diet totally excludes meat, fish and eggs.
- "Emergency diet" of carbohydrates and lipids without protein via NG tube or IV in situations where there is a risk of increased catabolism.

CIRCUMSTANCES WITH RISKS OF DECOMPENSATION: Do not wait for these signs!

Intercurrent infectious disease, fever, anorexia, vomiting, surgery, excess protein intake, **or any fasting state, insufficient caloric intake, weight loss or catabolic state.**

In all these cases, the patient must be kept in hospital. They represent an emergency: Do the workup on the patient in A&E before admitting him/her to the ward. **ACT QUICKLY** to prevent neurological sequelae.

CLINICAL SIGNS OF DECOMPENSATION:

Acute neurological disorders (altered mental status, confusion, drowsiness, gait disorder, ataxia, behavioural disorders, dystonia, abnormal movements, apathy, etc.) or exacerbation of preexisting disorders.

DRUG CONTRAINDICATIONS / GENERAL ADVICE

Prohibited: valproic acid (depakin). Corticosteroid therapy: consider the need if duration > 3 days. Use hydrocortisone if necessary in intensive care.

- All vaccinations are recommended (particularly influenza).
- Prolonged fasting is contraindicated, never leave the patient without a supply of carbohydrate (infusion or continuous enteral feeding) or carnitine.
- Do not forget vitamins and trace elements when intake is exclusively parenteral.
- **Do not leave the patient without proteins for more than 3 days.** The emergency treatment should be reassessed with the metabolism clinician during the day.
- **In case of admission to hospital** (or attendance at A&E): patients must take with them their usual treatments and the special products that they have in order to prepare an emergency diet.

SURGERY under General Anaesthesia:

WARNING: never leave the patient fasting without an infusion. Implement the emergency protocol with infusion as above in preparation for surgery, and continue until appropriate nutrition has been resumed (consult with referring service)

ASSISTANCE WITH PRACTICAL ADMINISTRATION OF TREATMENTS:

- LEVOCARNIL IV (vials 1g = 5mL), given neat or diluted in normal saline, using a Y infusion set
- LEVOCARNIL orally (vials 1g = 10mL), divided into 3 oral doses/day

ASSISTANCE WITH DIET:

- If exceptionally a feeding bottle / meal is missed during a hospital stay: give an emergency, protein-free meal (low-protein pasta, low-protein bread with butter and jam) or, if by bottle: PFD1® / Energivit®: 1 measuring spoon per 30 mL of water (0.7 kcal/mL)
 - If the composition of the ongoing emergency diet is unknown: prepare an isocaloric solution with [100g of PFD1® or Energivit® or Duocal® + 430mL of water] or [80g of maltodextrin + 20ml of oil + 425 ml of water]: equivalent preparations 500mL = 500kcal, adjust total intake according to the patient's needs. Review during working hours with a dietician, especially for calcium and electrolytes (Na, K etc.) intake.

REFERENCE PHYSICIANS AND CONTACT DETAILS

On-call telephone numbers for metabolic emergencies of:

At night, only the medical teams can call in emergency situations and only if the emergency certificate has not been understood or if the clinical state or test results are worrying. As far as possible make calls before night-time.

Secretarial issues must be dealt with the outpatient office during the week or by email addressed to the patient's referring metabolic physician.

Certificate issued on : Dr