

Mitochondrial fatty acid β -oxidation disorders - MCAD

Label

Priority patient: must not wait in A&E

If presenting with vomiting, diarrhoea or fasting state: **Risk of hypoglycaemia if prolonged fasting**
Rarely, cardiac rhythm disorders / heart failure / myolysis

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

1 EMERGENCY WORKUP

Capillary and venous blood glucose, AST, ALT, GGT, PT, CPK, serum electrolytes, potassium, calcium, urea, creatinine, blood gases, lactate, blood ammonia. **If cardiac signs** or abnormality on electrocardiogram: ECG, BNP, Troponin +/- echocardiogram. **Do not delay infusion.**

2 ON ARRIVAL AT A&E

If vomiting / refusal to eat / diarrhoea: see next paragraph.

If consulting for another reason: ensure that the food intake is correct. In case of simple difficulty with feeding, parents are advised to split up the meals and/or to give a **sugary solution** divided into doses every 2 - 3 hours (Maltodextrin / Maxijul in water or oral rehydration solution), to be continued in A&E. No need for routine use of infusion, but **never leave the patient fasting** and manage the disease as usual.

3 IN CASE OF VOMITING / REFUSAL TO EAT: INFUSION TO BE STARTED URGENTLY, without waiting for test results

- If **blood sugar < 3mmol/L**, raise blood sugar with 1ml/kg of 30% glucose orally (max. 30ml) or 2-3 ml/kg of 10% glucose by direct intravenous injection and start the glucose infusion below. (30% glucose possible via central line or intra-osseous route)
- Set up an infusion without waiting for the test results in order to ensure a **continuous glucose supply**:
 Infusion using 10% glucose with standard electrolyte additions* (not pure 10% glucose)
- IV lipids are contraindicated

Age	0-3 months	3-24 months	2-4 years	4-14 years	>14 years - adult	MAX FLOW RATE
Infusion flow rate	7ml/kg/h (12mg/kg/min)	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)

*e.g.: Polyionic, Bionolyte, B45, Glucidion, etc. if no solutes available, 10% glucose + 4g/L of NaCl (70 meq/L) and 2g/L of KCl (27 meq/L)

If unable to infuse the patient => Nasogastric tube: prepare the IV fluids listed above and pass them through the tube at the same rate

- Continue usual treatments (including levocarnil if given long-term), if no rhythm disorders.
- Specific treatment for potential intercurrent infection
- If NH₃ > 150 μ M (children) or >100 μ M (adults): do a check, and without waiting for the result, start sodium benzoate continuous IV infusion (or orally / by NG tube if no IV line available): loading dose of 250 mg/kg over 2 hours (Max. 8g) then 250 mg/kg/24h (Max. 12g/24h).

4 SEVERITY SIGNS = Consult / transfer to Intermediate Care Unit / Intensive Care

- Neurological disorders, exhaustion, coma, severe hyperammonaemia: Newborn >200 μ M – Child & adult >150 μ M
- Cardiac rhythm disorder: stop the levocarnil
- ECG signs of hyperkalemia, hyperkalemia > 7 mmol/L: stop the potassium, give potassium-lowering treatments
- **CPK > 15 000 IU/L**: review hydration, 3L/m²/day if no cardiac failure, see rhabdomyolysis protocol
- **Haemodynamic insufficiency and/or renal failure**
- **Severe hepatic insufficiency**: Prothrombin ratio < 50%, **factor V < 30%**
- **In all cases, take care to maintain glucose intake**

5 MONITORING

- Scope, ECG - Echocardiogram if signs indicative of cardiac failure
- Blood glucose every 4 h: target 1 to 1.8g/L. If blood glucose > 2g/L with glycosuria, consider insulin 0.01 IU/kg/h with subsequent dose adjustment every hour. Consider reducing sugar intake (20 - 25%) if hyperglycaemia despite insulin therapy at 0.05 IU/kg/h
- Laboratory workup to monitor CPK, electrolytes, NH₃, PT, liver function:
 - if initial tests normal and clinically stable: follow-up tests between 12 hours and 24 hours
 - in all other situations: close monitoring, and reassessment of fluid and electrolyte intake

PATHOPHYSIOLOGY

MCAD deficiency is a fatty acid oxidation (FAO) disorder. FAO is a major route of energy production by the body, particularly when fasting and in inflammatory states, in the heart, muscles, liver and brain.

The long-term treatment of MCAD deficiency is based on:

- Limiting fasting time depending on age:

Age	0-1m	1-4m	4-8m	8-10m	10-12m	1-6 years	>6 years and adults
Maximum fasting period if in good health	3-4h	4-6h	6-8h	8-10h	10-12h	12h	14h

- Carnitine supplements (LEVOCARNIL 10- 50 mg/kg/day as 2 oral doses) if necessary
- No specific diet, but avoid milk or oil containing medium chain triglycerides (MCT).

ASSISTANCE WITH PRACTICAL ADMINISTRATION OF TREATMENTS:

- LEVOCARNIL IV (amp. 1g = 5ml), given neat or diluted in normal saline, using a Y infusion set
- LEVOCARNIL orally (amp. 1g = 10ml), divided into 3 to 4 oral doses/day
- SODIUM BENZOATE IV (amp. 1g = 10ml), for dilution 1:1 by volume with 10% glucose. Given via a second peripheral venous line. Warning: contains 7 meq of sodium per gram of benzoate.

CIRCUMSTANCES IN WHICH THERE IS A RISK OF DECOMPENSATION

- Prolonged fasting, intercurrent infection, fever, anorexia, vomiting, surgery, dehydration, **or any fasting state, weight loss or catabolic state**. Rarely strenuous exercise.
- In all these cases, the patient will be kept in hospital. They represent an emergency:** do the workup on the patient in A&E before admitting him/her to hospital. **ACT QUICKLY** to prevent severe hypoglycaemia or cardiac damage.

CLINICAL AND BIOLOGICAL SIGNS OF DECOMPENSATION: Do not wait for these signs!

- Hypoglycaemia without ketosis, liver failure, hyperammonaemia
- Impaired consciousness, exhaustion, coma
- Cardiac rhythm disorders, haemodynamic disorders
- Rhabdomyolysis, muscular pain

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

Prohibited: acetylsalicylic acid (aspirin), valproic acid (Depakin®, etc.), Corticosteroid therapy: weigh up the need if duration > 3 days. No bar to using hydrocortisone hemisuccinate if necessary in intensive care.
MCAD deficiency: avoidance of MCTs (contained in milk or oils)

- All vaccinations are recommended (particularly influenza).
- Prolonged fasting is contraindicated, never leave the patient without a supply of carbohydrate (infusion or continuous enteral feeding)**
- Do not forget vitamins and trace elements when intake is exclusively parenteral. If intravenous lipids needed: use Intralipids or Numetah (which do not contain MCT)
- 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
- The emergency treatment will be reassessed with the metabolic medicine specialist during the day.

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)

- Continuous infusions of propofol and etomidate are to be avoided because they come in the form of a lipid emulsion (but can be used as a single injection for induction); anaesthetic gases can be used.

REFERENCE DOCTORS 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 via the medical secretariat during the week or by email addressed to the patient's referring metabolic doctor.

Certificate issued on

Dr