Pyruvate dehydrogenase (PDH) deficiency

In the event of vomiting, diarrhoea or fasting: **Administer infusion rapidly (see below)**
Risk of Leigh syndrome

1 PATHOPHYSIOLOGY

Energy metabolism disorder mimicking a mitochondrial cytopathy. Patients present with chronic neurological impairment: psychomotor delay, epilepsy, etc. The deficiency predisposes to Leigh syndrome and seizures/status epilepticus. Hyperlactataemia is common, with a low lactate/pyruvate ratio (around 10).
Treatment (which should never be stopped) consists of:
- A ketogenic diet, which may be strict depending on the patient: carbohydrate-restricted and lipid-enriched (specific Ketocal preparation for some patients)
- Thiamine (vitamin B1) supplementation

2 SITUATIONS WITH RISK OF DECOMPENSATION

As a general rule, any catabolic state: vomiting, fasting, risk of dehydration, severe infection.
If anaesthesia is required, ensure infusion is maintained.

- **Assessment**

Venous blood glucose, serum electrolytes with bicarbonate, lactate + additional tests depending on context (lactate is expected to be high in this condition)

3 MANAGEMENT

A– Treatments

- **Vitamin B1 (thiamine):** continue the usual dose (250–1000 mg/day) orally or IV. Must never be stopped.
- **In the absence of vomiting: continue the usual ketogenic diet** orally or via continuous enteral nutrition. If not provided by parents, Ketocal can be easily reconstituted:

  Define total intake according to age and weight recommendations.

Reconstitution	Ketocal	Maltodextrin	Water	Final volume	Energy intake
4/1	14 g	0	90 mL	100 mL	1.0 Kcal/ml
3/1	14 g	1 g	90 mL	100 mL	1.0 Kcal/ml
2/1	14 g	2 g	89 mL	100 mL	1.0 Kcal/ml
1/1	12 g	6 g	87 mL	100 mL	1.0 Kcal/ml
The reconstitution of Ketocal defines the lipid-to-carbohydrate ratio provided by feeding or nutrition. The higher the ratio (4/1), the stricter the ketogenic diet. In acute decompensation, the ketogenic diet may be increased (made stricter). Outside decompensation, respect the patient's usual ratio (known to the parents).					

- **If food intolerance:**
  - **2.5% glucose infusion** to avoid glucose overload (e.g. for 1 L of 2.5% glucose solution: add 500 mL of 5% glucose to a 500 mL bag of 0.9% NaCl) + electrolyte supplements according to serum electrolyte results.

    Daily volume: QSP usual intake for age and clinical condition.
  - **Via Y-set: IV lipids** if available: 1.5 g/kg/day or 0.3 mL/kg/hour (Medialipids 20%, Smoflipids 20%, Ivelip 20%, etc.).

If infusion is not possible → nasogastric tube. Administer the above IV solutions via the tube at the same rates, via Y-set (better tolerated than enteral feeding)

- **If lactic acidosis (lactate > 10 mmol/L)**: stop glucose and infuse saline only (0.9% NaCl). Avoid Ringer's lactate. Monitor capillary blood glucose.

B– Specific management

- **If status epilepticus:**
  - Usual antiepileptic treatments (benzodiazepines first-line, Dilantin second-line).
  - Also increase ketogenic diet, preferably continuous enteral tube feeding or IV if food intolerance (see table above)
- **If Leigh syndrome:**
  - Increase ketogenic diet, preferably continuous enteral tube feeding or IV if food intolerance (see table above).
  - To reduce cerebral oedema, discuss on a case-by-case basis: IV corticosteroids 2 mg/kg/day. Duration to be assessed during working hours, with gradual taper.

C – Other recommendations (all situations)

- Continue usual medication and diet
- Avoid glucose overload
- Treat cause of decompensation (infection, etc.) and symptoms

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

Prohibited: Acetylsalicylic acid (aspirin), valproic acid (Depakine®, unless already part of long-term treatment)

- **Vaccinations:** No contraindications. Annual influenza vaccination recommended.

IN THE EVENT OF ANAESTHESIA:

- **Avoid succinylcholine**. Most anaesthetics have depressant effects on mitochondrial function *in vitro*. However, general anaesthesia with intravenous agents, halogenated agents, and non-depolarising muscle relaxants has been reported safe.
- Relative overdosing (particularly with Propofol) has been observed, requiring **titration of the different anaesthetic agents and monitoring of their effects** (including local anaesthetics).
- **Avoid Ringer's lactate**
- **Systematic prevention of post-operative nausea and vomiting.** According to local protocols: Dexamethasone, Ondansetron (preferably 0.1 mg/kg in children), Droperidol (adults only, very low dose 0.625–1.25 mg)
- **Maintain homeostasis** (Safe Tots): pay close attention to maintaining normoglycaemia, normovolaemia, normothermia. Avoid prolonged use of tourniquets.
- **For minor surgery**, ketamine is a good alternative (ref.: PNDS MELAS, available on the HAS website).
- **Prolonged fasting contraindicated:** If surgery is required: systematic infusion (see above).

Refer to the **Emergency section** on the G2M

NUMBERS AND MEDICAL SPECIALISTS

On-call telephone numbers for metabolic emergencies:

At night, only 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. Whenever possible, calls should be made before nightfall.
Secretarial issues must be dealt with via the medical secretariat during the week, or by email addressed to the patient's metabolic medicine specialist.

Certificate issued on Dr