ACUTE CARDIAC PRESENTATIONS OF INBORN ERRORS OF METABOLISM (Unknown patient)

There are many causes of cardiomyopathy and arrhythmias, which we will not detail here. Symptomatic management and the diagnostic work-up must always be carried out in consultation with cardiologists and intensive care specialists if the patient's condition requires it.

Certain cardiac presentations should raise suspicion of inborn errors of metabolism, such as heart failure associated with hypertrophic or dilated cardiomyopathy, or certain arrhythmias. This is especially true in the presence of associated signs, as detailed below.

1 EMERGENCY TREATMENT TO BE IMPLEMENTED

Certain specific treatments should be started immediately, preferably after specific tests have been performed (plasma and urinary acylcarnitine profile)

- If a fatty acid oxidation disorder is suspected:
  - Glucose infusion: **10% glucose** + electrolytes according to clinical context

Age	0-3 mois	3-24 mois	2- 4 ans	4-14 ans	>14 ans - adulte	DEBIT MAX
Débit de perfusion	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)**

  /!\Caution: discuss fluid and sodium intake with cardiologists. If fluid restriction is necessary, concentrate glucose intake to maintain the above carbohydrate delivery rates.
  - IV lipids contraindicated
  - Levocarnil (L-carnitine): 10–50 mg/kg/day by continuous IV or in 4 doses per day (max 3 g/day)
  - Vitamin B2 (riboflavin): 100–200 mg/day PO
- If primary carnitine deficiency is suspected:
  - Levocarnil (L-carnitine): 100–200 mg/kg/day by continuous IV or in 4–6 doses (no maximum dose). To be started **after specific samples are taken** (plasma AND urinary carnitine levels, freeze samples outside working hours), without waiting for results.
- Cardiomyopathy with no obvious cause:
  - vitamin supplementation: B1 100–250 mg/day IV, B2 100–200 mg/day PO, B8 30–60 mg/day PO

The specific emergency management for each disorder is detailed in the dedicated emergency protocols, available on the G2M website: https://www.filiere-g2m.fr/

2 METABOLIC AETIOLOGIES

Cardiomyopathie Hypertrophique

Maladies énergétiques
- Déficits de la bêta-oxydation des AG
- Déficit primaire en carnitine
- Déficits de la chaine respiratoire mitochondriale

Maladies de surcharge
- Maladie de Pompe
- Glycogénose III, déficit AMPK
- Maladie de Danon
- Maladies lysosomales

Autres
- Déficits de glycosylation (CDG)
- Acidurie Propionique

Cardiomyopathie dilatée

- Déficit de la bêta-oxydation des AG
- Déficit primaire en carnitine
- Déficits de la chaine respiratoire mitochondriale
- Syndrome de Barth (garçon, neutropénie)
- Déficits de glycosylation (CDG)
- Acidurie Propionique
- Maladie de Danon

Troubles du rythme sans CM

- Déficit de la bêta-oxydation des AG
- Déficit primaire en carnitine
- Déficit en TANGO2
- Déficits de la chaine respiratoire mitochondriale (dont Kearn-Sayre)
- Déficit en phosphorylase kinase (Glycogénose IX)
- Déficit en AMPK (gène *PRKAG2*): aspect de WPW
- Carence en vitamine B1
- Déficits de glycosylation (CDG)

Details by disorder (suggestive clinical signs and possible management) are provided overleaf.

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

3 DIAGNOSTIC WORKUP

- CBC (neutropenia?)
- Liver function tests, PT, factor V, ammonia, CPK
- Blood glucose–lactate cycle ± redox points if hyperlactataemia
- Plasma acylcarnitine profile and free/total carnitine assay: 1 heparin tube. Centrifuge and freeze plasma
- urine: Organic acid chromatography (OAC) and free/total carnitine assay (1 frozen urine sample)
- CDG: Transferrin isoelectric focusing
- If Pompe disease suspected (< 1 year, hypertrophic cardiomyopathy, hypotonia, QRS hypervoltage): Acid maltase activity
- If lysosomal disease suspected: Urinary GAG, urinary oligosaccharides, WBC enzymes

This emergency protocol is proposed by the G2M network working group. The protocol may be modified under the responsibility of the specialist doctor. Under no circumstances can it replace the responsibility of the physician in charge of the patient in the emergency department.

4 DIAGNOSTIC GUIDANCE

Disorder	Suggestive elements	Diagnostic workup	Specific treatment
Fatty acid β-oxidation disorder	Isolated or associated with: - hypoglycaemia - rhabdomyolysis - hepatic involvement +/- hyperammonaemia (Reye)	Plasma acylcarnitine profile Urinary OAC	Glucose infusion Carnitine Vitamin B2 (MADD)
Primary carnitine deficiency	Mixed hypertrophic + dilated cardiomyopathy Isolated or associated with: - hypoglycaemia - hepatic involvement - rhabdomyolysis	Plasma and urinary carnitine /!\ Before treatment/!\	Carnitine
Mitochondrial respiratory chain defects	Mixed hypertrophic + dilated cardiomyopathy Isolated or associated with: -involvement of other organs - neurological involvement (Leigh syndrome) - Hyperlactataemia	Redox point Urinary OAC Brain MRI with spectroscopy Muscle biopsy Genetics	--
Pompe disease	Hypotonia with muscle involvement (elevated CPK) Macroglossia Suggestive ECG (major hypervoltage)	Acid maltase activity	Enzyme replacement therapy
Glycogen storage disease III & IX	Hypoglycaemia with low lactate. Hepatomegaly and hepatic cytolysis +/- Myopathy and elevated CPK	Enzyme activity Genetics	Glucose infusion then dietary management Ketone bodies for cardiac involvement
Lysosomal storage diseases	Other organ involvement (overload)	Urinary GAG & OS (glycosaminoglycans and oligosaccharides) Lysosphingolipids (lyso-Gb3) WBC enzymes Genetics	Disorder-specific
CDG	Isolated or associated with: - hypoglycaemia (PGM1) - rhabdomyolysis - haemostasis abnormalities (XI, ATIII)	Transferrin isoelectric focusing Genetics	Galactose for PGM1 deficiency
TANGO 2 deficiency disorder	- Arrhythmia: long QT syndrome, Brugada - chronic neurological impairment - hypothyroidism - rhabdomyolysis - hypoglycaemia - hyperammonaemia, Reye	Genetics	Vitamins B5 and B9 /!\ numerous drug contraindications

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