COMA and Inherited Metabolic Diseases (New patient)

1 DEFINITION AND SYMPTOMS

Impairment of consciousness preventing awakening and eye opening, the depth of which is assessed using the Glasgow coma scale.

There are many causes of coma requiring specialist treatment, e.g. exogenous toxins, herpes encephalitis, severe infection, which will not be covered in this emergency certificate. However, it is useful to cover the inherited metabolic diseases (IMD) which can present alongside, or be complicated by, coma. Coma due to IMD can occur in the neonate (after a variable symptom-free interval), or at any age.

In general, **when an exogenous toxin is being considered, an endogenous toxin should also be considered.**

The main criteria pointing to an IMD are a coma with no obvious cause, or unusual progression towards coma in a clinical setting which does not account for it.

Investigate for non-metabolic causes of coma	Biological tests
Toxins : ethylen glycol, methanol Discuss with Neuro consult for other tests : brain imaging, lumbar puncture, EEG	• **Dextro/Blood glucose, Ketones,** • **Blood gases** • **Ammonia** • **Lactate** • **Serum electrolytes with Calcium, BUN, Creatinine, CK** • **Complete liver function tests** • **FBC** • **PT, Factors V, II, VII, X, Fibrinogen** • **Aminoacids (plasma)** • **Acylcarnitines (plasma)** • **Organic Acids (urine)**

** See emergency protocol for assistance with taking samples.*

Look up the **emergency**

2 SYSTEMATIC TREATMENT IN AN EMERGENCY SETTING

- **Start without awaiting lab results**
- **Stop feeding**
- **NO** amino acids, proteins or lipids (orally or IV)
- **If hypoglycaemia: correct until blood glucose returns to normal > 0.7 g/L: 10% glucose 3mL/kg by direct IV injection** (G30% can be done via a central line or via the intraosseous route; some teams allow G30% via peripheral line in cases of refractory hypoglycaemia). Check capillary blood glucose 10 minutes later. If still hypoglycaemic, give a second administration of glucose and check 10 minutes later; repeat as many times as necessary.
- **Infusion** via a peripheral line, while waiting for a central line: solution of 10% glucose (**G10%** or D10W) + 6 g/L NaCl and addition of KCl depending on serum potassium level and context (rhabdomyolysis?) (never pure G10%: risk of cerebral oedema)

Age	0 - 24 months	2 - 4 years	4 - 14 years	> 14 years / adult	MAX. FLOW RATE
G10% + added electrolytes*	6mL/kg/hr (10mg/kg/min)	5mL/kg/hr (8mg/kg/min)	3.5mL/kg/hr (6mg/kg/min)	2.5mL/kg/hr (4mg/kg/min)	**120mL/hr (3L/24 hrs)**

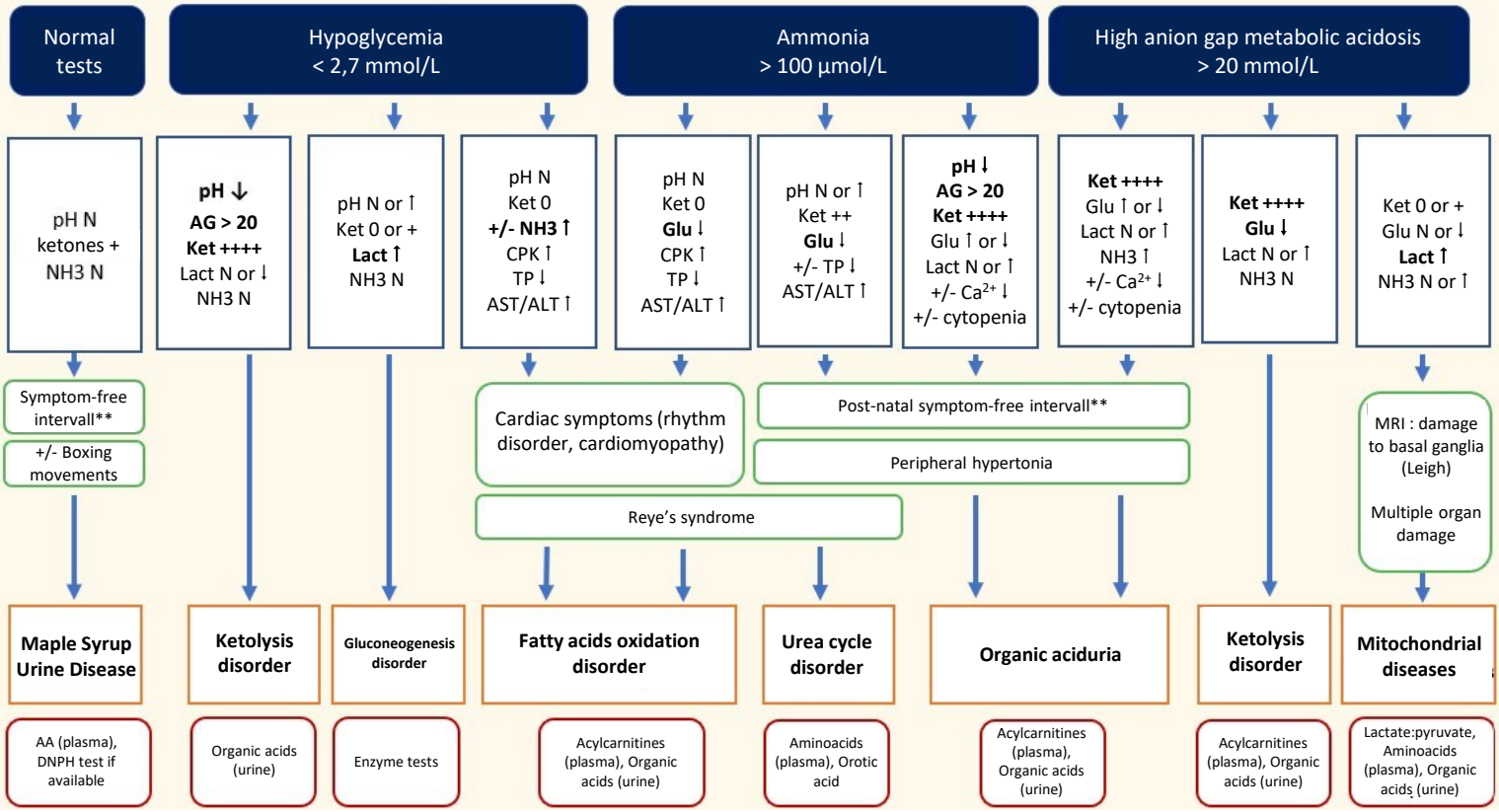
- **Preferably use a central line as soon as possible to concentrate the infusion** (risk of cerebral oedema) while maintaining glucose intake.
  Aims of the infusion:
  - NaCl 6 g/L (100meq/L), potassium and calcium, depending on the serum electrolyte results
  - Maximum total intake **1.5 L/m² of body surface area/day**

- **Routine vitamin therapy:**
  - Vitamin B1 (Thiamine): 250 mg/day orally or IV (1g for an adult), vitamin B8 (Biotin): 20 mg/day orally
  - Vitamin B12 (cyanocobalamin): 1 mg/day orally
  - Vitamin B2 (Riboflavin): 50 mg/day orally
- **Prevention of secondary cerebral injury of systemic origin**

3 IMD DIAGNOSTIC ALGORITHM

*AG = $(Na^+ + K^+) – (Cl^- + HCO3^-)$

The algorithm below assists with diagnosis. There is an **emergency protocol for every IMD.**



If IMD is suspected, the table below provides a guide to diagnosis.

Inherited metabolism disorder	Symptom free intervall	pH	Ketonuria	NH3	Lactate	Glycemia	Lab investigations
Urea cycle disorder	Yes	N or ↑	0	↑ ↑ ↑	N	N	Aminoacids (plasma), Orotic acid (urine)
Organic acidurias	Yes	↓↓↓	++++	↑ ↑	N or ↑	↑ or N or ↓	Organic acids (urine)
Maple syrup urine disease	Yes	N	++	N or ↑	N or ↑	N	Aminoacids (plasma), DNPH
Mitochondrial diseases	No	N or ↓	0 to ++	N	↑ to ↑↑↑	N or ↓	Organic acids (urine), Redox (lactate:pyruvate)
Fatty acids oxidation deficit	No	N	0	N or ↑	N	↓ to ↓↓↓	Acylcarnitines (plasma)
Gluconeogenesis disorder	No	N or ↑	0 to ++	N	↑ to ↑↑↑	↓ to ↓↓↓	Enzyme studies
Ketolysis disorder	No	↓↓↓	++++	N	N	↓ to ↓↓↓	Organic acids (urine)

Glu: Blood glucose; Lact: lactate; N: normal, Ket: ketones, AG: anion gap, NH3: blood ammonia level, Ca2+ : blood calcium,

DNPH test: mix 1 mL of urine with 1 mL of DNPH. Test positive if mixture becomes cloudy.

4 TREATMENTS DEPENDING ON LABORATORY RESULTS

These treatments must be started after taking samples for specialist biochemical testing: aminoacids, acylcarnitines (plasma), organic acids (urine)

- **Detoxification treatments if NH3 >100 µmol/L**
  - **Sodium benzoate** by continuous IV infusion. Start with a **loading dose** of 250mg/kg over 2 hours (**Max. 8 g over 2 hours**). Draw another ammonia blood sample just before administering the loading dose. Do not wait for the result and start sodium benzoate. Then, **maintenance dose** over 24 hrs : 250 to 500 mg/kg/24hrs (**Max 12g/24 hrs**) (*switch to NG tube if no venous access).*
  - Carbaglu (carbamylglutamate) if available*:* Start with a **loading dose** of 100 mg/kg orally, then a maintenance dose over 24 hrs of 50 mg/kg/6h (orally) (max 8g/24 hrs)
  - Possible loading dose of Ammonaps/Ravicti: 250 mg/kg orally (max 10g) in combination with sodium benzoate.
  - **If ineffective, consider:**
    - Possibility of a loading dose of Ammonaps: 250mg/kg orally (max 10g)
    - **Ammonul®** (250 mg/kg/day) ideally via central line, max. 12g (stop benzoate and phenylbutyrate)
    - **Consider haemodialysis**

Refer to the hyperammonaemia emergency protocol (https://www.filiere-g2m.fr/urgences)

- **L-carnitine (Levocarnil):**
  - **If ketoacidosis: L-Carnitine 50 mg/kg/day max 6 g/24 hrs by continuous IV infusion while awaiting specialist metabolic medicine opinion**
  - **If hypoglycaemia, rhabdomyolysis, cardiac or hepatic disorder: L-Carnitine 10mg/kg/day max 1 to 2 g/24 hrs by continuous IV infusion.**

For subsequent management of metabolic acidosis, refer to the metabolic acidosis protocol (https://www.filiere-g2m.fr/urgences)

NUMBERS AND MEDICAL SPECIALISTS

For any question relating to this emergency certificate or the metabolic treatment of the patient, you can contact the nearest reference centre or skill centre. You will find the list on the G2M web site: https://bit.ly/3OvIW4I