METABOLIC ACIDOSIS PROTOCOL (New patient)

1 DEFINITION AND SYMPTOMS

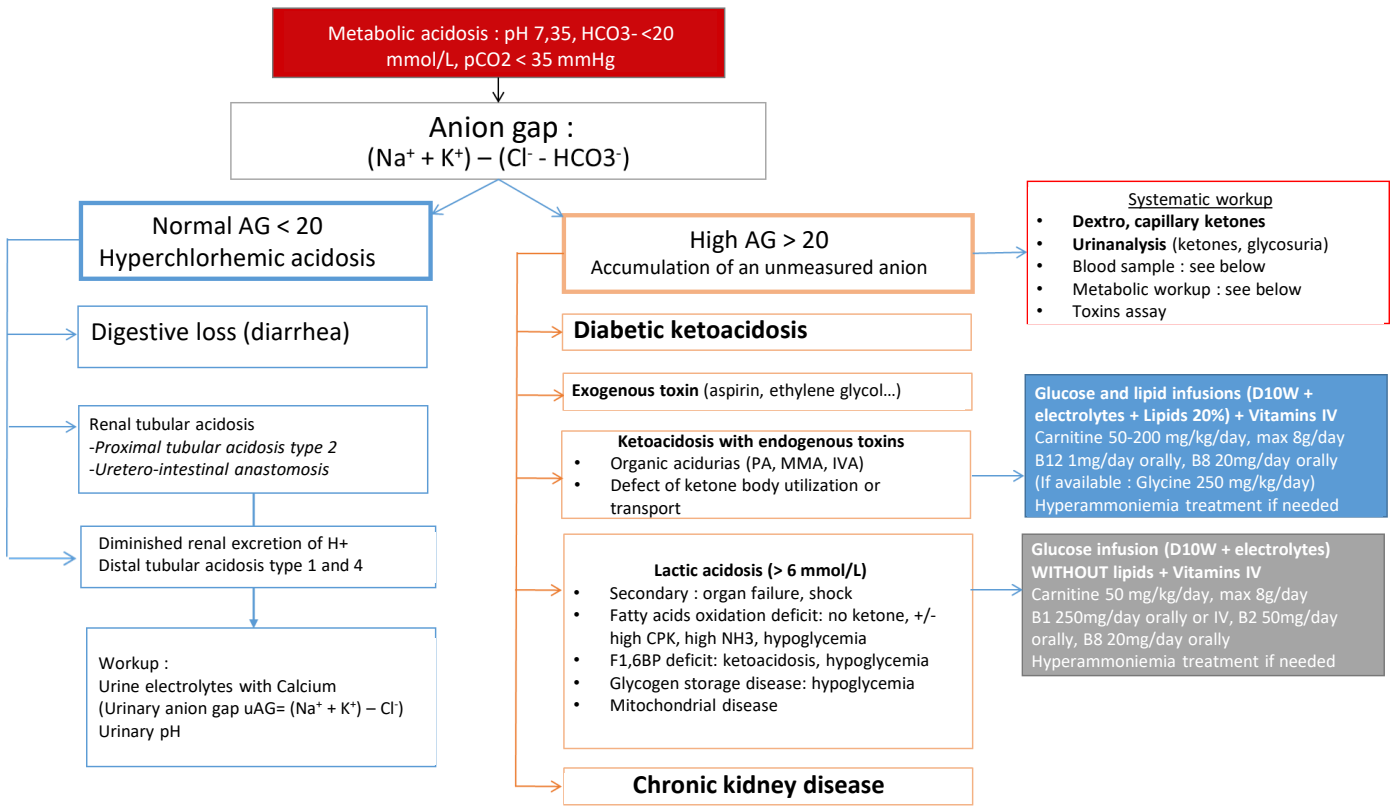
Acidosis is defined by venous blood pH < 7.35. Acidosis can be respiratory (increased PCO2 and bicarbonates), or metabolic (bicarbonate < 20 mmol/L and PCO2 < 35 mmHg as a result of respiratory compensation).

Clinically, metabolic acidosis can present as Kussmaul breathing. However, patients can also be asymptomatic.

In order to manage metabolic acidosis, its nature must be determined by calculating the **anion gap** (AG). The AG is calculated using the following formula: **AG = (Na+ + K+) – (Cl- + HCO3-)**. The normal range for AG is 16+/-4 mmol/L. It is considered to be heightened if it is greater than 20, which indicates accumulation of an unmeasured anion. Inherited metabolic diseases (IMD) must be considered in cases of metabolic acidosis with increased AG.

The unmeasured anions can be of **endogenous** origin (suggestive of IMD with accumulation of lactate, ketone bodies and/or organic acids) or **exogenous** (ethylene glycol, methanol, aspirin etc.). All of these accumulated compounds can be measured by specific assays, which should be carried out as soon as patient treatment is started.

When AG is normal (hyperchloraemic acidosis), gastrointestinal or renal loss of bicarbonate should be considered.



2 EMERGENCY METABOLIC WORKUP

The following workup should be carried out as a minimum in all cases of metabolic acidosis in order to eliminate the possibility of an inborn error of metabolism:

- **Blood gases, lactate, electrolytes, blood urea nitrogen, creatinine,**
- **blood glucose, ketones. Urine dipstick to test for ketonuria.**
- **Blood ammonia, CPK, liver function tests (AST, ALT, GGT, ALP, total and conjugated bilirubin),**
- **FBC-platelets, PT, factors V, II, VII, X, fibrinogen.**
- Tests for tubular disease (if AG normal): as a minimum, urine electrolytes with urinary glucose, chloride and pH

Specialist biochemical tests are also justified in this situation, including:

- **plasma amino acids (quantitative)**
- **plasma acylcarnitines**
- **urinary organic acids**
- **lactate:pyruvate ratio**

It is important to draw samples during the acute phase, and they should be drawn as soon as possible during patient treatment.

If exogenous toxins are suspected, assays for specific toxins should be carried out.

Look up the emergency

3 TREATMENT TO BE STARTED URGENTLY

If a metabolic disorder is suspected

A. Baseline infusion

- No IV amino acids, no oral proteins: **stop feeding**
- **Infusion** of **10% glucose** (D10W) with standard electrolyte additions* (never pure 10% glucose), via peripheral catheter.

e.g.: Polyionique, Bionolyte, B45, Glucidion etc. with addition of 2 g/L NaCl (6 g/L in total) or, if pre-made solutions not available, 10% glucose in water + 6 g/L NaCl and 2g/L KCl

Age	0 - 24 months	2 - 4 years	4 - 14 years	> 14 years / adult	MAX. FLOW RATE
G10% + added electrolytes *	5mL/kg/hr (8mg/kg/min)	4.2mL/kg/hr (7mg/kg/min)	3.5mL/kg/hr (6mg/kg/min)	2.5mL/kg/hr (4mg/kg/min)	120mL/hr (3L/24 hrs)

- No lipids initially, until fatty acid oxidation deficit has been excluded. If indicated, 20% lipids given via a Y-set

Age	**0 - 24 months**	**> 2 years**	**MAX. FLOW RATE**
20% lipids (if needed)	0.4 ml/kg/hr (2g/kg/day)	0.3ml/kg/hr (1.5g/kg/day)	**20ml/hr (500ml/24 hrs)**

B. Additional treatments

- **Detoxification treatments if NH3 >100 µmol/L**
  - **Sodium benzoate** by continuous IV infusion: Start with a **loading dose** of 250 mg/kg over 2 hours (**max. 8g over 2 hours**), then 250 to 500 mg/kg/24 hrs (**max. 12g/24 hrs**) (give orally or via NG tube if no venous access available). Draw another sample for blood ammonia just before starting the loading dose, without waiting for the results, then again at the end of the loading dose.
  - **Carbaglu®** (N-carbamyl-glutamate) if available: oral loading dose 50-100 mg/kg then maintenance dose 50 mg/kg/6 hours orally or via NG tube (Max 8g over 24 hrs).

  Give the sodium benzoate straight away, then add the Carbaglu if available.

  For the ongoing treatment of hyperammonaemia in the ICU, refer to the hyperammonaemia protocol.
- **L-Carnitine (Levocarnil):**
  - **If ketoacidosis is found:** 200mg/kg/day without exceeding 12g/24 hrs by continuous IV infusion, or in 4 fractionated oral or IV administrations, depending on the child's state of consciousness and whether there is vomiting.
  - If there is hypoglycaemia, rhabdomyolysis, cardiac or hepatic disorders (suggestive of fatty acid oxidation deficiency): 50 mg/kg/day by continuous IV infusion or as 4 fractionated doses, orally or via IV.
- **Glycine** if ketoacidosis suggestive of isovaleric acidaemia (IVA) (sweaty feet odour): 200 mg/kg/day in 3 or 4 doses orally or via NG tube, if available (max. dose a priori 10g/day)
- ***Vitamin therapy:***
  - ***If lactic acidosis is found: B1 250 mg/day for a child (1g/day for an adult) orally or IV, B8 20 mg/day orally***
  - ***If ketoacidosis (suspected organic aciduria): B12 (cyanocobalamin) 1 mg/day orally and B8 20mg/day orally***
  - ***If hypoglycaemia is found (suspected fatty acid oxidation deficit) B2 orally 100 to 200 mg/day***

If there is no certainty of the indication: start treatment with all 4 vitamins from the outset.

- **If an exogenous toxin is suspected,** start specific antidote treatment, without waiting for the toxicology results (formepizol for ethylene glycol etc.) Prescribing should be discussed with a specialist toxicology team.

4 SEVERITY SIGNS / MANAGEMENT IN ICU

- **If pH < 7.20, consider management in ICU or HDU**
- If there is persistent severe acidosis, renal replacement therapy may be considered
- **If there is cerebral oedema, it is preferable to administer fluids on a central line in order to concentrate the infusion**: maintain glucose and sodium intake: [for example: 30% glucose (enough to provide the same glucose intake as above), NaCl 6 g/L (100meq/L), potassium and calcium according to serum electrolyte results + normal saline (NaCl 0.9%) in parallel via a Y-set, for a total intake of **1.5 L/m² of body surface area/day** *(Body surface area = (4 x Weight in kg + 7) / (Weight in kg + 90))*

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. As far as possible, make calls before nighttime.
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