Severe rhabdomyolysis and Malignant hyperthermia (*RYR1* mutations and related genes)

Priority patient: must not wait in A&E

Label

In case of fever, vomiting, diarrhoea, muscle pain or **Anaesthesia:**
Risk of Acute Rhabdomyolysis and/or malignant hyperthermia

1 EMERGENCY

CPK, Blood glucose, serum electrolytes, **potassium**, calcium, phosphorus, urea, creatinine, blood gases, lactate, ASAT, ALAT, GGT, PT - **Factor V. ECG** on arrival**.** Note the **colour of the urine (myoglobinuria).** Tests depending on triggering intercurrent illness.

2 TREATMENT TO BE STARTED URGENTLY, without waiting for test results:

A- Management in all cases

- If **signs of hypoperfusion, replenish** with Ringer's Lactate or 0.9% NaCl at **10 ml/kg** (maximum 500 ml) if no cardiac signs - reassess and continue if necessary.
- Infusion for **IV hydration** for at least **6 to 12 hrs** even if initially normal CPK.
  - Serum Glucose **G10% + NaCl 6g/L WITHOUT POTASSIUM.** Intake **2L/m²/d** (maximum flow 150 ml/h). **Do not use pre-prepared solutes containing potassium** (polyionic, Glucidion, Bionolyte, etc.) [body surface area = (4P+7)/(P+90)]
  - If it is not possible to infuse the patient and clinical signs are reassuring: await the CPK. If CPK >6 000 U/L, install NG tube for hydration (infusion solute above given at same flow rate). If CPK<6 000 U/L, test again at H4.
- Initiate specific treatment for potential intercurrent infection

B– Adjustment depending on CPK

- **If CPK stable <6 000 U/L at H0 and H4** and serum potassium normal: infusion avec polyionic 10% glucosepossible (reintroduce K+), **to be continued** for at least **12 hrs** depending on the CPK kinetics.

- **If CPK falls between 6 000 and 20 000 U/L:** continue hydration described above 2L/m²/d WITHOUT POTASSIUM
  - **Injectable dantrolene (*RYR1* antagonist, see SFAR recommendations)**
    http://sfar.org/recommandations-dexperts-pour-le-risque-dhyperthermie-maligne-en-anesthesie-reanimation/

- **If CPK >20 000 U/L or from the outset if myoglobinuria:** plan for **transfer to Continuous monitoring unit/Intensive care,** and start **hyperhydration** as soon as possible, after agreement from reanimator:
  - Volume **3L/m²/day**
  - Preparation for 1 litre of solute: 200 ml of G30% + 400 ml of Bicarbonate 14 ‰ + 400 ml of NaCl 0.9%
    No potassium, nor calcium
  - **Injectable dantrolene (*RYR1* antagonist, see SFAR recommendations)**
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3 SEVERITY SIGNS = Consult / transfer to Intensive Care

- **CPK > 20 000 IU/L** (after installation of above infusion)
  - **Consider extrarenal purification** if serum potassium > 5mmol/L despite appropriate hyperhydration, an ECG anomaly of any nature, anuria/oliguria and positive electrolyte panel contraindicating the continuation of hyperhydration, renal damage (the creatinine figures do not express the degree of renal damage, since it is released by muscular necrosis, urea is more reliable)
  - **Intensive care monitoring:** Capillary blood glucose, Na, K/2h in the first 24h, Complete electrolytes with Ca, Ph, Mg, urea, creat, CPK / 6 hrs. Hourly urine flow monitoring > 2ml/kg/h, pHu and urinary density < 1005. Electrolyte panel / 3h to adjust hyperhydration. ECG in place, trace/h. Echocardiography.
- **Rhythm disorders, ECG signs** of hyperkalaemia, **hyperkalaemia > 7 mmol/L**
- **Oligo/anuria, "port wine" red coloured urine, renal failure.**
- **Neurological disorders, exhaustion,** (risk of hyperosmolar coma)

4 MONITORING (excluding severe rhabdomyolysis > 20 000 U/L in intensive care)

- Temperature (risk of malignant hyperthermia)
- **CPK, electrolytes, calcium, phosphorus, diuresis, and urine colour** every 4 hrs. Adjust the potassium intake to the serum potassium and renal function (in the absence of intake via the infusion, there is also a risk of hypokalaemia)
- **Electrocardioscope, ECG/4h if CPK > 6 000 U/L**
- If normal CPK, **keep the patient in hospital** for at least **12 hrs** to ensure the CPK does not increase secondarily.

PATHOPHYSIOLOGY:

RYR1 gene mutations (calcium channel gene in the skeletal muscle), and other related genes, are responsible for acute rhabdomyolysis, and episodes of malignant hyperthermia, **particularly during anaesthesia,** but also during situations of stress or catabolism (fever, fasting, diarrhoea, vomiting, prolonged effort). **This patient requires strict and urgent treatment in risky situations.**

CIRCUMSTANCES IN WHICH THERE IS A RISK OF DECOMPENSATION:

- **Surgery / Anaesthesia**
- Intercurrent infectious disease, fever, weight loss, vomiting, **or any fasting or catabolic state**.
- Unusual physical exercise

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

- Muscle pains (can precede the increase in CPK)
- Unable to walk, exhaustion
- Cardiac rhythm disorders, heart failure
- Impaired consciousness
- Hypovolemic shock
- Myoglobinuria (sign of severe rhabdomyolysis)

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

- Treatments contraindicated in the acute phase of rhabdomyolysis: NSAID, all hyperkalaemia-inducing drugs
- Statins (increased risk of rhabdomyolysis)
- Some anaesthetic agents: see below

- All vaccinations are recommended (particularly influenza).

IN CASE OF GENERAL ANAESTHESIA: RISK OF MALIGNANT HYPERTHERMIA

- **Contraindicated anaesthetic agents: Halogens (myocardium depressor), depolarising curares (succinylcholine, promotes muscle contraction), prolonged administration of propofol**
- ***RYR1* Mutation = Risk of malignant hyperthermia**
  - Ensure capnography and core temperature monitoring
  - Retrieve the injectable dantrolene protocol (*RYR1* antagonist, see SFAR recommendations) http://sfar.org/recommandations-dexperts-pour-le-risque-dhyperthermie-maligne-en-anesthesie-reanimation/
  - Prepare Dantrolene IV
  - CPK monitoring pre- and post-surgery

Consult the **Emergency page** on

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