

GLYCOGEN STORAGE DISEASE TYPE 1B

Priority patient: must not wait in A&E / ED

Patient label

Risk of hypoglycaemic coma: NEVER LEAVE THE PATIENT WITHOUT A SUPPLY OF CARBOHYDRATES
Risk of neutropenia - gastrointestinal inflammatory disease

Do not wait for signs of hypoglycaemia, in all cases initiate management as set out below

1 EMERGENCY WORKUP

Capillary and venous **blood glucose**, blood gases and lactate, electrolytes, urea (BUN), creatinine, triglycerides, AST, ALT.
 + Tests depending on the triggering intercurrent illness. Must not delay treatment.

2 IF HYPOGLYCAEMIA < 60 mg/dL (=3.3 mmol/L)

- Administer **1mL/kg of 30% glucose** (max. 30 mL) **orally** or enterally if conscious or **3mL/kg of 10% glucose IV** if unconscious (30% glucose also possible via central line or intraosseous route, some teams allow 10mL of 30% glucose via a peripheral venous line for refractory hypoglycaemia).
- Check capillary blood glucose 5 minutes later.
- If still hypoglycaemic, administer a second dose of glucose and check capillary blood glucose 5 minutes later.
- **URGENTLY** set up an infusion (2 quick attempts at a peripheral venous line, otherwise intraosseous) **without delaying** the glucose administration.
- Immediately start an infusion even if blood glucose levels have been corrected: Infusion using **10% glucose** (= dextrose) in water with standard electrolyte additions* (never pure 10% glucose)

Age	0-24 months	2-4 years	4-14 years	>14 years - adult	MAX INITIAL RATE
Polyionic 10% glucose (glucose infusion rate)	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)

*e.g.: Bionolyte®, Glucidion®, etc. if no pre-made solution available, use 10% glucose in water + 4g/L NaCl (70 mEq/L) + 2g/L KCl (27 mEq/L)

If IV line is impossible => Nasogastric tube or gastrostomy: prepare the IV fluids listed above and pass them through the tube at the same rates.

- **CONTRAINDICATION to glucagon.**
- If there are no gastrointestinal disorders and if the preparation is available: instead of infusion, **emergency diet by continuous enteral feeding** using nasogastric tube or gastrostomy (use dietician sheet from parents)



NEVER clamp off the glucose infusion: neither in A&E, in theatre, nor when moving the patient (porter / nurse): NEVER, risk of hypoglycaemic coma/seizure.

3 CIRCUMSTANCES WITH A RISK OF HYPOGLYCAEMIA

- Any circumstance in which the patient is deprived of a carbohydrate supply, e.g. in case of **vomiting, food refusal, diarrhoea or fasting.**

=> Infusion via peripheral line, or continuous enteral feeding of "emergency diet" to be started **IMMEDIATELY**.

- **Failure to respect meal times (WARNING:** blood glucose levels can fall very rapidly within 5 minutes!). Hence, in the absence of hypoglycaemia or a situation creating a risk of hypoglycaemia: **Strictly respect** (within 5 minutes) the **meal times** of the patient's usual diet.

4 IF FEVER (> 38.5°C) WITH NEUTROPENIA

- If a viral source evident and no frank inflammatory syndrome: give symptomatic treatment.
- If bacterial cause suspected and/or neutropenia < 500/mm³:
 - Broad-spectrum IV antibiotherapy (e.g. PIPERACILLIN-TAZOBACTAM) while waiting for bacteriology results + G-CSF 5µg/kg/day by subcutaneous route.
 - If cellulitis or abscess: always treat with subcutaneous G-CSF 5µg/kg/day whatever the neutrophil count.

5 If gastrointestinal inflammatory flare-up : abdominal pain, diarrhoea, rectal bleeding

- Fasting with infusion as described above, plus analgesics. During working hours, refer with specialists treatments aimed at the gastrointestinal condition (mesalazine enemas, corticosteroids, etc.) and/or subcutaneous G-CSF 5µg/kg/day whatever the neutrophil count. Look for source of infection with stool virology and culture, and *C. difficile* detection.
- If abundant rectal bleeding with deglobulisation: consider endoscopic haemostasis.
- If severe flare-up with fever: treat with antibiotics for intestinal infections such as 3rd gen. cephalosporins + metronidazole

6 MONITORING

- Check capillary blood glucose 1 h after starting the infusion, then every 3 h.
- Adjust the rate of infusion of 10% glucose + electrolytes by +/- 5 mL/h. Target: capillary blood glucose between 60 and 120 mg/dL.
- If hyperlactataemia > 5 mmol/L: check blood gases - lactate every 4h. If hyperlactataemia > 10 mmol/L, add thiamine (B1) 100 to 200 mg/day orally or IV and STOP oral gliofosins (dapagliflozin).

PATHOPHYSIOLOGY:

Inherited metabolic disease due to defect in glycogen use, characterised by:

- **Profound hypoglycaemia after a short period of fasting (2 to 4 h depending on the patient).** Usual treatment: Meals at precise times of day containing precise quantities of carbohydrates (starch without quick-acting sugars), with controlled lactose and fructose intake. Maizena/Glycosade (uncooked corn starch, not heated) intake and/or night time enteral feeding with a precise rate of carbohydrate intake. If intercurrent disease: emergency diet by continuous enteral feeding via NG tube / gastrostomy, with precise carbohydrate intake rate.
- **Disorder of platelet aggregation**, hence **risk of bleeding** during surgery.
- Permanent or cyclic **neutropenia** responsible for bacterial infections, particularly affecting the skin. In some cases, the patient has maintenance therapy with G-CSF and/or an antibiotic prophylaxis, or oral glifozins (dapagliflozin).
- An **inflammatory gastrointestinal disease, similar to Crohn's**: abdominal pain, mouth ulcers, diarrhoea which may contain mucus and blood, perianal abscess. Treatment can include: enteral feeding with Modulen®, 5-ASA, corticosteroids or TNF blockers (infliximab, etc.), G-CSF, and recently, glifozins.
- The possible **complications** during the course of the disease are: renal involvement (tubular disease, renal failure), hepatic involvement (hepatomegaly, cytolysis, adenomas), hypertriglyceridaemia, hyperlactataemia and hyperuricaemia.

- **DRUG CONTRAINDICATIONS / GENERAL ADVICE:**



Prohibited: antiplatelet drugs (acetylsalicylic acid, NSAIDs), **glucagon**, avoid Ringer's lactate

- All vaccinations are recommended (particularly influenza).
- **Never exceed the patient's usual fasting time: if admitted for a different reason, maintain the patient's usual diet (including quantities of carbohydrate), administration of uncooked cornstarch and the precise meal times (which the parents will know)**
- **If the patient has to be fasted (e.g. for surgery), give the infusion described overleaf.**
- Do not forget vitamins and trace elements when intake is exclusively parenteral.
- **In case of admission to hospital** (or attendance at A&E): patients must take with them their usual treatments and the special products that they have in order to prepare an emergency diet.
- The emergency treatment will be reassessed with the metabolic physician during the day.

SURGICAL PRECAUTIONS: THROMBOPATHY

Anaesthetic protocol: Contact the referring doctor in order to plan for precautionary measures.

- No risk of liver failure; no drug contraindicated apart from aspirin and NSAIDs; No additional risk with standard anaesthetic agents.
- **But: POTENTIAL RISK OF BLEEDING / THROMBOPATHY**

BEFORE SURGERY

- Investigation of haemostasis (platelet functions) prior to planned surgery and if any sign of bleeding: ecchymoses, haematoma, gingival bleeding, epistaxis
- **Glucose infusion** (10% glucose + electrolytes) as described overleaf, starting ideally 24 h before surgery.
- **The day before any surgical procedure: ORAL EXACYL** (tranexamic acid - antifibrinolytic) **20 mg/kg/day** divided into 3 doses (max 1g x 3/day). Warning: will lower the seizure threshold: If patient epileptic, consider the need for treatment.

DURING SURGERY

- **If surgery involves bleeding:** at induction administer **EXACYL IV 10mg/kg** (max 0.5-1g, slow IV over 15min)
- **In addition, if history of bleeding or known thrombopathy:**
 - **For minor surgery as outpatient: Desmopressin/OCTIM® nasal spray** (150µg per spray): **2 sprays** in one nostril 30 minutes before the operation. Contraindication: child under 2 years of age.
 - **If risk of bleeding, or actual bleeding: Desmopressin/MINIRIN® IV** by slow IV over 30 minutes, starting 1 hour before the surgical procedure: **0.3µg/kg** to be diluted in 50mL of normal saline, then after seeking haematologist's opinion, to be repeated after 12h and/or 24h if abundant bleeding. At the same time, restrict fluids for 24 h, hence the need for a central line to enable a concentrated glucose infusion (restrict to 20mL/kg/24h). If central line impossible, closely monitor the blood sodium level.
- **If severe bleeding complication: consider platelet transfusion.**

AFTER SURGERY

- Continue the glucose infusion in post-op until usual oral feeding is restored (normal quantities taken for 2 successive meals, respecting the patient's usual meal times and diet).
- **Monitor blood glucose and lactate every 3 h + ABG if lactate >4mmol/L** during and immediately after surgery.
- **Oral or IV EXACYL IN ALL CASES: 20 mg/kg/day** divided tid (max. 1g x 3/day) 5 to 15 days as long as the risk of bleeding persists.

REFERENCE PHYSICIANS 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 the outpatient office during the week or by email addressed to the patient's referring metabolic physician.

Certificate issued on :

Dr