

FRUCTOSE 1,6-BISPHOSPHATASE DEFICIENCY**Priority patient: must not wait in A&E / ED**

Patient Label

**IN CASE OF VOMITING, DIARRHEA, FEVER, FASTING : RISK OF HYPOGLYCAEMIA,
SEVERE KETOTIC AND LACTIC ACIDOSIS, COMA**

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

1 EMERGENCY WORKUP

Capillary blood and venous glucose, capillary and/or urinary ketones (positive if $>0.8\text{mmol/L}$ or $1+$), blood gases, lactate, electrolytes with bicarbonate, urea (BUN), creatinine, liver enzymes, PT, factor V. ECG if abnormal potassium level.

Must not delay treatment.

2 TREATMENT TO BE STARTED URGENTLY, without waiting for lab results

- **Start an infusion in all cases** (even with normal glycaemia) : 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)	5mL/kg/h (8mg/kg/min)	4mL/kg/h (7mg/kg/min)	3.5mL/kg/h (6mg/kg/min)	2.5mL/kg/h (4mg/kg/min)	<u>120mL/h</u> (3L/24h)

*e.g.: Bionolyte®, Glucidion®, etc. if no pre-made solution available, use 10% glucose in water + 4 to 6g/L NaCl (70mEq/L) + 2g/L KCl (27mEq/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.

If hypoglycaemia $< 60\text{ mg/dL}$ (3.3 mmol/L): Administer **1mL/kg of 30% glucose** (max. 30 mL) orally or enterally. **If enteral route impossible: 10% glucose in water 3mL/kg by rapid IV injection** (IV 30% glucose is also possible via central line or intraosseous route; some teams allow 10 mL of 30% glucose via peripheral venous line for refractory hypoglycaemia).

- Check capillary blood glucose 5 minutes later. If still hypoglycaemic, administer a second dose of glucose and check 5 min later.



WARNING: do not treat low blood glucose with fruit juices, which contain fructose!

- If **hypovolaemia**, expand with **Normal Saline** at **10 mL/kg** (maximum 500 mL, avoid Ringer's lactate), reassess and continue if necessary.
- Continue with the patient's usual treatments orally or IV

Contraindication to Fructose: be aware, can be present in many oral rehydration solutions (check labels)

3 SEVERITY SIGNS = Consult / Transfer to Intensive Care

- **Coma** or **worsening** of mental status.
- **Circulatory failure.**
- **Ketoacidosis and severe lactic acidosis with $\text{pH} < 7.10$** An infusion of bicarbonate may be considered. Beware of hyperkalaemia with acidosis, adjust intakes accordingly.
- Signs of **severe hepatic insufficiency**: Prothrombin ratio $< 30\%$, factor V $< 50\%$.

4 MONITORING under treatment

- Electrocardioscope
- Capillary blood glucose q2h. If hyperglycaemia: adjust the rate of glucose intake (no lower than 50% of the initial rate). Acidosis and hyperlactacidaemia may be corrected more slowly.
- Urinalysis on every micturition and/or capillary ketones (positive if $>0.8\text{ mmol/L}$ or $1+$)
- Follow-up tests (blood gases, lactate, electrolytes, blood glucose):
 - If initial tests subnormal and clinically stable: follow-up tests between 12 and 24 hours
 - If $\text{pH} < 7.1$: every 3 hours initially, then reassess. Monitor liver function if initially abnormal. Monitor serum potassium and phosphate as acidosis is corrected (risk of hypokalaemia / hypophosphataemia).

PATHOPHYSIOLOGY

Hereditary fructose 1,6-bisphosphatase (or diphosphatase) deficiency is a disorder of the fructose metabolism, leading to deficient gluconeogenesis. Patients are at risk of hypoglycaemia, metabolic acidosis (ketotic and lactic), triggered by prolonged fasting or fructose load.

The usual treatment is (depending on the patient):

- Limitation of the fasting time at night, hence continuous enteral feeding at night or uncooked cornstarch in the evening for some patients.
- Limitation of fructose intake, either all the time, or solely in circumstances where there is a risk of decompensation: fruit, vegetables, sugary foods and drinks (see with parents).

CIRCUMSTANCES WITH RISK OF DECOMPENSATION

- Intercurrent infectious disease, fever, anorexia, vomiting, surgery, or any fasting state, insufficient caloric intake, weight loss or catabolic state.
- Dietary mistake (fructose load).
- In all these cases, the patient must be kept in hospital. These are emergency situations: do the workup on the patient in A&E before admitting them to the ward and implement the protocol overleaf. ACT QUICKLY to prevent hypoglycaemia and/or severe acidosis, which can have serious and irreversible neurological sequelae.

SIGNS OF DECOMPENSATION. Do not wait for these signs!

- Signs of hypoglycaemia, altered mental status, vomiting, acidotic dyspnea.
- Neurological deterioration and coma.
- Lactic and ketotic acidosis.

DRUG CONTRAINDICATIONS / GENERAL ADVICE

Prohibited: acetylsalicylic acid (aspirin)

Absolute contraindication for all drugs containing fructose, sucrose or sorbitol (check excipients and labels of rehydration solutions). For example:

- Oral rehydration solutions allowed: Fanolyte®, Novalac Hydranova®, Physiosalt®, Viatol®
- Oral rehydration solutions forbidden: Adiaril®, Picolite®, Ydrovit®

} Always check labels

- All vaccinations are recommended (particularly influenza).
- Prolonged fasting is contraindicated, never leave the patient without a supply of carbohydrate (infusion or CEF)

SURGERY:

WARNING: never leave the patient fasting without an infusion. Implement the emergency protocol with infusion as above, in preparation for surgery.

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

Certificate issued on :

Dr