GLUTARIC ACIDURIA TYPE 1. EMERGENCY PROTOCOL

NAME:

REFERENCE HOSPITAL:

Metabolic Unit Contact Phones

Main Doctor: _____

Nurse: _____

Nutritionist: _____

Hospital Switchboard: _____

Emergency Department:_____

GLUTARIC ACIDURIA TYPE 1 (GLUTARYL-CoA DEHYDROGENASE DEFICIENCY)

Glutaric aciduria is an inherited disorder of the breakdown of certain amino acids, notably lysine. Any metabolic stress can lead to serious illness, with encephalopathy, a reduced level of consciousness and other neurological abnormalities. Following these episodes, patients often have **SEVERE PERMANENT NEUROLOGICAL IMPAIRMENT**, particularly a movement disorder. However with early aggressive treatment neurological complications can be prevented. The damage results from the accumulation of glutaric acid and other toxic metabolites.

Patients under 6 years of age are at HIGHEST risk of neurological damage so TREATMENT OF THESE CHILDREN **MUST BE VERY CAREFUL**.

Treatment aims to minimise the accumulation of toxic metabolites by preventing protein breakdown and to promote their excretion by the use of carnitine. The **EARLY SIGNS OF DECOMPENSATION MAY BE SUBTLE**, such as minor changes in tone and intake rejection. Vomiting and diarrhea are common symptoms and should always be taken seriously. However, the signs, such as irritability or just 'not feeling right,'may be difficult to assess.

Always listen to parents carefully, as they have been trained in recognizing early signs of decompensation.

Without decompensation patients doesn´t differ from a healthy child

DECOMPENSATION TRIGGERS (factors that cause protein breakdown)

1. Fasting
2. Insufficient intake
3. Typical childhood illnesses, particularly , particularly **VOMITING and DIARRHEA, WITH OR WITHOUT FEVER**
4. Fever (from any cause)
5. Intense physical exercise
6. High protein intake (dietary transgression)

TREATMENT

- REGULAR OR SLIGHTLY HIGH CALORIE LOW LYSINE/TRIPTOFAN DIET
- LOW TRIPTOFAN/LYSINE FREE AMINOACID SUPPLEMENTS
- CARNITINE SUPPLEMENT
- PREVENT ACUTE DECOMPENSATION

HOW TO PREVENT ACUTE DECOMPENSATION:

- ✓ AVOID HIGH PROTEIN INTAKE
- ✓ AVOID PROLONGED FASTING (5 hours in maintenance treatment, 2 hours in case of intercurrent febrile infection and risk situations).
- ✓ If at risk of acute decompensation, start outpatient **EMERGENCY TREATMENT** at the slightest suspicion and without delay.

OUTPATIENT EMERGENCY TREATMENT Use If the patient is clinically well despite intercurrent infectious disease or febrile reaction to vaccinations, the body temperature is <38.5 ˚C (101 ˚F), the diet is tolerated (at least 85%) and no alarming symptoms are found (i.e., alteration in level of consciousness, diarrhea, vomiting, irritability, hypotonia, dystonia) EVERY PATIENT HAS AN EMERGENCY DIETARY PLAN TAILORED TO HIS/HER NEEDS.

1- Reduce natural protein intake to 50 % or completely for a minimum of 24 h maximum of 48 h. Increase 10 % of regular calories, providing food high in carbohydrates. Ensure adequate fluids intake.
2- Feed the child every 2 hours day and night.
3- Use Low-protein special food, or protein-free dietary supplements (PFD, Energivit, Maltodextrin solution, Prozero.)
4- If tolerated, Lysine-free Amino-acid mixture should be administered according to maintenance therapy.
5- Double carnitine intake: e.g., 200 mg/kg per day in infants
6- Contact with your Metabolic specialist as soon as possible.
7- Gradually resume regular protein/lysine intake until reaching the daily treatment amount in 3–4 days.

IF ALARMING SYMPTOMS EVOLVE, SUCH AS RECURRENT VOMITING, RECURRENT DIARRHEA, REDUCED NUTRIENT INTAKE, SPIKING TEMPERATURE>38.5° C, OR SUSPICIOUS NEUROLOGIC SYMPTOMS, PATIENTS SHOULD IMMEDIATELY BE TRANSFERRED TO THE CLOSEST HOSPITAL OR METABOLIC CENTER TO START EMERGENCY TREATMENT

INPATIENT MANAGEMENT

1) Treatment is URGENT **even if the child seems to be in good overall condition.** Avoid long waiting times.

2) Do not delay. Unless you are very confident and certain, treat with **intravenous fluids**.

3) If there is any doubt at all, the child **must be admitted**, even if only necessary for a short period of observation.

4) During hospital admission or stay at emergency department **protective isolation measures** should be adopted to avoid further infections.

5) **Stop natural protein intake during 24/48 hours.** Then reintroduce and increase gradually until the amount of maintenance treatment is reached within 3-4 days.

6) Start **intravenous fluids** with 10% glucose solution following the chart below. Energy intake should be 10-20% higher than everyday needs.

   Note: Enteral treatment is not recommended **instead of** IV fluids. It can be used only occasionally and supervised by a metabolic specialist. If the clinical status of the patient allows it, outpatient emergency diet can be administered bay nasogastric tube or gastrostomy.

AGE (years)	GLUCOSE (g/kg/day)	GLUCOSE (mg/kg/min)	VOLUME (ml/kg/day) 10% glucose solution
0-1	12-15	8-10	120-145
1-3	10-12	7-8	96-120
4-6	8-10	6-7	84-96
7-12	6-8	5-6	72-84
13-18	4-6	4-5	60-72
>18	2-4	3-4	60

If persistent hyperglycemia >150–180 mg/dl (>8–10 mmol/L) and/or glucosuria occurs, start with 0.025–0.05 IU insulin/kg per h IV instead of reduce glucose intake, and adjust the infusion rate according to serum glucose. MONITOR POTASSIUM.

If acidosis: alkalization of urine also facilitates urinary excretion of organic acids.
Add 25 ml of NaCl 1M and 10 ml of KCl 1 M to 500cc of 10% glucose solution.

7) If at all possible, **give the lysine free amino acid mixture** orally or via nasogastric tube, as drinks or as a continuous infusion. Initially it can be given at the rate of 1g/kg/d. If this is not tolerated, the quantity can be reduced to 0.5 g/kg/d but for as short a period as possible. Do not delay giving other treatment if the mixture is not immediately available.

8) **Carnitine:** 100 mg/kg per day IV (MAXIMUM 6g/daily) or CARNITINE 200mg/kg per day orally if intravenous is not available, in 4 doses.

9) Blood Tests:
- Metabolic parameters: glucose, blood gases, creatine kinase, amino acids (plasma) during the recovery phase, carnitine (plasma) Urine: ketone bodies, pH.
- Routine laboratory: Electrolytes, blood count, creatinine, C-reactive protein, blood culture (if indicated)
- In acute decompensation blood tests can be unaltered; CPK, liver enzymes and lactic acid are sometimes high. Ammonium is usually normal until advanced stages of acute decompensation. Is not necessary to measure it.

10) **It is important to control fever**. Ibuprofen, paracetamol or metamizole can be given at standard doses, especially if body temperature rises above 38.5°C (101°F)

11) If indicated, **Ondansetron** (0,15mg/kg) is preferred to other antiemetic.

12) **Avoid** Valproic Acid.

13) There are no contraindications for administration of ketamin, midazolam, diazepam or other drugs for analgesia or even anesthesia in painful procedures such as difficult venous line placement

14) **Parenteral nutrition:** If more than 3-5 days enteral feeding inability is predicted, parenteral nutrition must be considered within the first 24-48 hours. Initially only essential aminoacids 0,5 mg/kg per day. Add lipids according to the clinical situation.

15) **Nasogastric tube**: The parents are trained on outpatient nasogastric tube management. If clinical outcome allows it, with close supervision of the metabolic team, the patient can be discharged after placement of nasogastric tube.

16) Only allow the child to go home **if at least 85% of the intake is tolerated, you and the family are entirely content with the clinical outcome and you have discussed the problems with the consultant on call.**
THE FAMILY MUST HAVE A CLEAR MANAGEMENT PLAN AND BE PREPARED TO RETURN IF THE CHILD DOES NOT IMPROVE

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