WHEN TO CONSIDER LYSINURIC PROTEIN INTOLERANCE (LPI)

Association and severity of symptoms vary greatly, depending on patients and intra-family variability. Secondary urea cycle deficit

Clinical signs

FIRST EARLY SYMPTOMS
Often occurs when the baby is weaned and when a range of foods is introduced

Digestive impairment
Mainly due to secondary urea cycle deficit

- **Recurrent vomiting**
- **Chronic diarrhoea**
- **Anorexia,** feeding problems
- **Aversion to high-protein foods**

Sometimes antenatal hyperechogenic colon

Other
- **Rupture in the growth curves for weight and height**
- **Hepatosplenomegaly**
- **Hypotonia**

EPISODES OF ACUTE/SUBACUTE DEGRADATION
Can occur at any age, aggravated by catabolism and high-protein meals

Hyperammonaemia[1]
Emergency treatment

Exacerbation of vomiting, anorexia, nausea

Acute neurological disorders:
impaired vigilance, confusion, sleepiness, impaired balance, behavioural issues, tremors, abnormal movements, etc.

Risk of degradation to **coma +/- convulsions** and risk of death and neurological sequelae

PROGRESSIVE ONSET OF SYMPTOMS / COMPLICATIONS
Sometimes, early onset when diagnosed, or only in adults

Growth issues and bone damage
Failure to thrive, severe osteoporosis (pathological fractures)

Lung damage
Progressive interstitial changes, **sometimes severe pulmonary alveolar proteinosis (life-threatening), pulmonary fibrosis**

Haematological/immunological diseases
Hepatosplenomegaly, cytopaenia, biological markers **of macrophage activation**

Predisposition to autoimmune diseases (ANF, anti-DNA antibodies, etc.)

Kidney disease (adolescents/adults)
Progressive proximal **glomerular and/or tubular** disease, kidney failure

Other
Acute pancreatitis
Psychomotor delay (possible consequence of episodes of hyperammonaemia)

Additional tests

Laboratory: **Sometimes high ammonia levels[1]** (particularly after meals or during decompensation), fluctuating liver cytolysis, **possible: cytopaenia (anaemia, thrombocytopaenia), signs of macrophage activation syndrome** (hyperferritinaemia, hypertriglyceridaemia, elevated LDH, low fibrin, etc.), coagulation disorders, signs of **tubulopathy**, microalbuminuria, proteinuria sometimes progressing to **kidney failure (frequent in adulthood)**

Thorax X-ray / scan: possible reticular interstitial syndrome

Specialist workup

Lysinuric protein intolerance?

Specialist workup in collaboration with Centre of Excellence
At the same time as looking for other potential differential diagnoses[2]

Plasma and urinary amino acid chromatography
Urinary orotic acid determination

→ Telltale abnormalities →

Confirmatory genetic analysis to be carried out subsequently by a specialist centre

Urgent specialist advice from a Centre of Excellence: Rare Disease Centre of Reference / Competence
https://www.filiere-g2m.fr/annuaire/

Start the parallel treatment, urgently depending on type of presentation

Refer to the **emergency protocols for each symptom and/or disease:**
https://www.filiere-g2m.fr/urgences

Specialist treatment coordinated by a Centre of Excellence

Genetic counselling, family screening in a specialist centre

For more information: PNDS French National Authority for Health - Urea Cycle Disorders (has-sante.fr)

Specialist medical opinion and reference laboratory

[1] **Pay attention to sample-taking conditions. Always perform tests but do not necessarily wait for test results to start treatment.**
Standard norms (vary depending on the laboratories): Neonates: ammonia <100 µmol/L, Non-neonates: ammonia <50 µmol/L, see: emergency protocol for hyperammoniaemia: https://filiere-g2m.fr/urgences.

[2] **Malabsorption (coeliac disease, etc.), haematological/immunological causes (malignant, auto-immune diseases), infectious causes, toxic causes and other metabolic diseases.**

Maladies rares Héréditaires du Métabolisme
Filière nationale de santé