NEONATES ACUTE ONSET

From 24 to 72 hours of life

SYMPTOM-FREE INTERVAL



Rapidly-worsening neurological impairment

Impaired consciousness up to coma ± convulsions

Hyper or hypoventilation Axial hypotonia, peripheral hypertonia



Digestive and liver impairment Vomiting / Nausea / Anorexia Cytolysis /

Liver failure

Other

Peripheral circulation disorders Temperature instability



ONSET REVEALED BY ACUTE ATTACK OR CHRONIC ILLNESS, BOTH TYPES ARE OFTEN ASSOCIATED Association and severity of symptoms vary depending on patients

ACUTE LATE ONSET

Paroxysmal episodes (metabolic decompensation)

Triggering factors: infections, fever, anorexia, vomiting, diarrhoea, excessive protein intake, fasting, insufficient calorie intake, catabolism, surgery, weight loss

Risk of multiorgan failure, death or severe disability during decompensation



Neurological impairment

Impaired consciousness, up to coma ± convulsions Hyper or hypoventilation, Pyramidal syndrome



Psychiatric disorders

Hallucinations, paranoia, manic episodes, emotional disorders, personality changes, post-partum psychosis



Digestive and liver impairment Vomiting / Nausea / Anorexia Cytolysis / Liver failure / Reye Syndrome

CHRONIC PRESENTATION



Digestive and liver impairment

Chronic vomiting and anorexia



Aversion to protein **Growth retardation**

Hepatomegaly

Cholestasis in some deficiencies



Neurological impairment

Learning disabilities Intellectual disability **Headaches** Tremors, ataxia, dysarthria Progressive spastic diplegia or quadriplegia



Psychiatric disorders

Hyperactivity, Mood and behavioural disorders and autistic spectrum disorders

Non-specialist laboratory workup

Possible: cytolysis, cholestasis, hepatocellular insufficiency. hypokalaemia

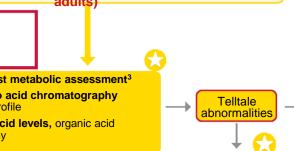
Standard metabolic assessment¹

HYPERAMMONAEMIA 2 + initial alkalosis then +/- acidosis

Hyperammonaemia = ammonia levels above the norm: Norm: Neonate ammonia < 100 µmol/L, Non-neonate ammonia < 50 µmol/L

Severe hyperammonaemia

if >200 µmol/L (Neonates, infants)/>150 umol/l (children and



Specialist treatment coordinated by a Centre of Excellence

https://www.filiere-g2m.fr/urgences

received: https://www.filiere-a2m.fr/annuaire/

Start the parallel treatment urgently: Refer to the

Genetic counselling, family screening in a specialist

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

Urgent specialist advice from <u>Centre of Excellence: Rare</u> Disease Centre of Reference / <u>Competence</u>, as soon as

emergency protocols for each symptom and/or disease:

the results of the standard metabolic assessment are

Specialist medical opinion and reference laboratory

Urea cycle disorder?

No specific anomalies

> Secondary causes of hyperammonaemia

Specialist metabolic assessment³

Plasma: amino acid chromatography acylcarnitine profile

Urine: orotic acid levels, organic acid chromatography

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

¹ Standard metabolic assessment - Blood: ammonia levels, blood gases, blood sugar, lactates, ketosis test (urine dipstick test and/or capillary blood ketones). To be performed immediately where there is no obvious cause, at the same time as looking for other causes: sepsis (neonates), brain damage: trauma-related, vascular, infection-related, encephalitis etc., drug toxicity, other metabolic diseases. Refer to the emergency protocol for coma 2 Pay attention to sample-taking conditions. Always perform tests but do not necessarily wait for test results to start treatment. Ammonia level norms may vary depending on the laboratory.

The severity and impact of hyperammonaemia may vary depending on age and/or presentation type. Treat severe cases of Hyperammonaemia in intensive care.

3It is important to take samples during the acute phase, and as soon as possible, ideally before starting any treatment, though this should not be delayed. The samples that are essential for diagnosis are in bold, while the others may be useful to interpret the metabolic assessment and eliminate certain differential diagnoses.

4 Hepatocellular insufficiency, drugs (valproate,etc.), portosystemic shunts (portocaval shunts, some infections including bacterial urease in urine +, some tumours, etc.), others (severe malnutrition, etc.)

