## WHEN TO CONSIDER ISOVALERIC ACIDEMIA (IVA)-TYPE OF ORGANIC ACIDURIA

## **Neonatal screening in France since 1st January 2023:**

This clinical picture should no longer be seen in children born in France after January 2023 who have been screened<sup>1</sup>



# **NEONATES**

Starting at 48 to 72 hrs, but can be several days/weeks



### Rapidlyworsening neurological impairment

**Impaired** consciousness up to coma,

**Axial hypotonia** 

**Peripheral** hypertonia

Signs of cerebral œdema

**ACUTE ONSET** 

**Symptom-free interval** 



#### **Digestive signs** Unusual smell

Refusal to drink Sweaty feet smell

Nausea

Anorexia

Vomiting Dehydration

Weight loss Sometimes moderate hepatomegaly





# INFANTS, CHILDREN, ADOLESCENTS, ADULTS: ONSET REVEALED BY ACUTE OR CHRONIC IMPAIRMENT, WITH **BOTH KINDS OFTEN BEING ASSOCIATED**

Association and severity of symptoms vary depending on patients

#### **ACUTE IMPAIRMENT**

Paroxysmal episodes (metabolic decompensations) Triggering factors: infections, fever, anorexia, vomiting, diarrhoea, excessive protein intake, fasting, insufficient calorie intake, catabolism, surgery

Risk of multiorgan failure, death or severe disability during decompensation



## **Neurological impairment**

Altered consciousness leading to coma

Abnormal movements



### **Digestive impairment**

Anorexia, nausea, vomiting, pancreatitis

#### CHRONIC IMPAIRMENT



#### Neurological impairment

Inconstant and variable depending on patients Hypotonia,

Neurodevelopmental disorders Intellectual disability Autistic spectrum disorder Learning disabilities Abnormal movements, Dystonia



#### Digestive impairment and feeding/eating disorders

Chronic anorexia, nausea and



vomiting, aversion to high-protein foods, oral fixation, growth retardation



Specialist medical opinion and reference laboratory



High anion gap metabolic acidosis

- +/- frequent hypocalcaemia
- +/- hyperglycaemia or hypoglycaemia,
- +/- neutropaenia, pancytopaenia,
- +/- cytolysis and high lipase

Standard metabolic assessment<sup>2</sup> High anion gap metabolic acidosis With hyperammonaemia<sup>3</sup> +/- Hyperlactataemia

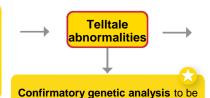
**Isovaleryl-CoA** 

dehydrogenase deficiency?



Plasma: acylcarnitine profile, amino acid chromatography

Urine: organic acid chromatography (uOAC)



carried out subsequently by a specialist

Seek urgent specialist advice from a Centre of Excellence: Rare Disease Centre of Reference / Competence

as soon as the results of the standard metabolic assessment are received: https://www.filiere-q2m.fr/annuaire/

Start the parallel treatment urgently:

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 under preparation: French National Authority for Health - French National Diagnosis and Treatment Protocols (has-sante.fr)

<sup>3</sup> Pay attention to sample-taking conditions. Always perform tests but do not necessarily wait for test results to start treatment. Standard norms (may vary depending on the laboratories): Neonate: ammonia < 100 µmol/L, Non-neonate am It 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 some differential diagnoses.



Neonatal screening (https://depistage-neonatal.fr/) makes it possible to identify affected neonates and initiate treatment at an early stage to prevent the onset of clinical symptoms.

<sup>&</sup>lt;sup>2</sup> Standard metabolic assessment - Blood: ammonia levels, blood gases, blood sugar, lactate levels, ketosis test (urine dipstick test and/or capillary blood ketones). To be performed immediately where there is no obvious cause, at the same 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.