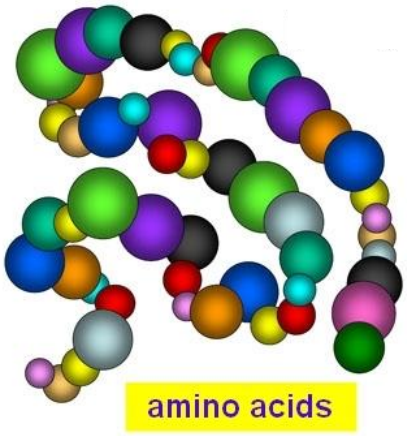
PROPIONIC ACIDEMIA

WHAT IS PROPIONIC ACIDEMIA?

Propionic acidemia is a **protein degradation disorder** which causes the accumulation of certain toxic products (propionic acid and its derivatives) in plasma, urine and tissues.

HOW DO PROTEINS DEGRADE?

Proteins are formed by a very long chain of **amino acids**. When proteins degrade, amino acids are released and can be used to form new proteins or to generate energy.



Each type of amino acid is formed, or degraded, via a specific chain of reactions known as a **metabolic pathway**. The reactions within a metabolic pathway are facilitated by specific proteins, the **enzymes**.

WHAT IS A METABOLIC ERROR?

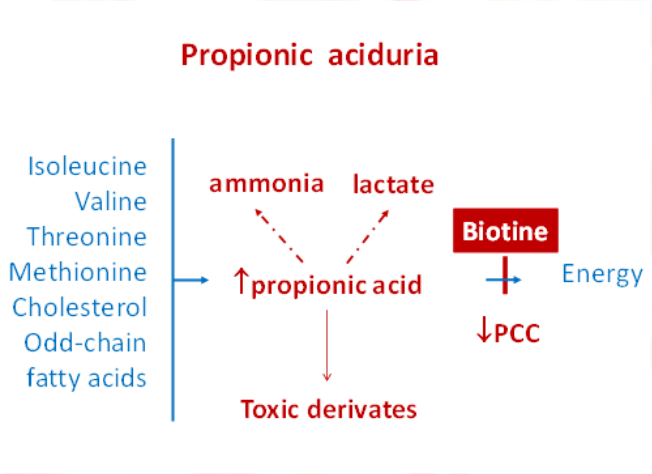
When a **metabolic error** occurs, one of the reactions within a metabolic pathway is unable to operate with its usual efficiency. This causes the compounds of previous reactions in the pathway to accumulate, while the products of subsequent reactions cannot be synthesized correctly. **Organic acidemias** are caused by **errors in the metabolism** of some amino acids resulting in the **accumulation of organic acids**.

WHAT HAPPENS IN PROPIONIC ACIDEMIA?

In propionic acidemia, deficiency of the enzyme **propionyl-CoA carboxylase (PCC)** causes the accumulation of **propionic acid and its derivatives**, most of which are toxic. Secondarily, accumulation of **ammonia and lactic acid**, both toxic, also occurs.

WHAT CAUSES PROPIONIC ACIDEMIA?

We all inherit genetic information from our parents that determines how each metabolic reaction within our body is carried out. In propionic acidemia, the deficient activity of PCC is due to mutations (stable, and hereditary changes) in the **genes *PCCA* or *PCCB***, which encode different subunits of the enzyme.



Propionic acidemia is an **autosomal recessive genetic disorder** and, although each parent is is a carrier of *PCC* gene mutations, they themselves do not suffer the effects of the enzyme deficiency. However, if both parents transmit a *PCC* gene mutation to their child, the child will suffer from **propionic acidemia**.

WHAT HAPPENS WHEN A CHILD IS BORN WITH PROPIONIC ACIDEMIA?

The foetus is able to fully develop without problems because, until the moment of birth, the mother's body metabolizes the fetal proteins. However, when the baby begins to feed after birth, milk proteins are digested to release amino acids. Certain of these amino acids will

not be degraded properly due to the defective PCC enzyme and a toxic accumulation of propionic acid, its derivatives, ammonia and lactic acids will occur. The baby will present with a loss of appetite, vomiting, dehydration, tone disorders, torpor, letargia and even coma. Complications can appear over the long term, such as mental retardation, movement disorders, pancreatitis and delayed cardiomyopathy.

Clinical presentation of propionic aciduria

Neonatal forms

Intoxication:
feed refusal
vomiting
Dehydration
hypotonus
hypertonus
letargia
coma

Late onset forms

Acute recurrent
Chronic-progressive

HOW IS A PROPIONIC ACIDEMIA DIAGNOSED?

Based on clinical suspicion of intoxication, a study of organic acids in the patient's urine is performed to demonstrate elevated levels of propionic acid and its derivatives. An enzymatic analysis and, above all, a mutational study of the genes *PCCA and PCCB* confirm the diagnosis and allow genetic counseling and prenatal diagnosis.

Diagnosis of propionic aciduria

clínical suspicion ? **Intoxication**

Biochemical study

↑ Lactate
↑ Ammonia
↑ Glycine

↑3OHpropionate, methylcitrate & derivates

↓ PCC

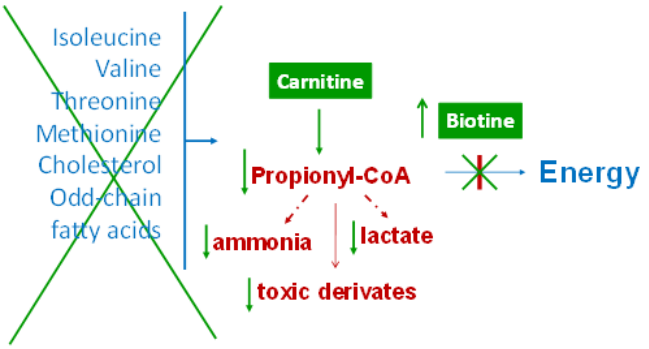
Genetic study

***PCCA y PCCB* mutations**

WHAT CAN YOU DO TO AVOID THE CONSEQUENCES OF PROPIONIC ACIDEMIA?

It is necessary to start treatment as quickly as possible. The aim is to avoid poisoning by the toxic products, and to prevent their future accumulation. This is initially achieved by restricting natural protein intake from the diet. However, as amino acids are indispensable for protein synthesis within the body, they need to be administered in a special formula which is free of the amino acid precursors of propionic acid (valine, isoleucine, methionine and threonine). In addition, carnitine is administered to convert the toxic products into non-toxic ones which are subsequently excreted in the urine.

Treatment of propionic aciduria



Propionic acidemia is an hereditary illness that, untreated, can cause severe consequences. Nevertheless, early diagnosis and treatment can improve the prognosis and quality of life of the patients affected.

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