Introduction : liver and liver cell transplantation for inborn errors of liver metabolism

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Inborn errors of metabolism affect around 1/900 life births. Most of these conditions are rare, but any physician will face patients affected by one or another of these diseases.

Management of patients with inborn errors of metabolism is often complex and includes orphan medications, very specific diets, special education. Beside life threatening conditions, a main concern is that long term intellectual prognosis of certain patients may be impaired, especially for diseases such as urea cycle disorders, organic aciduria and amino acidopathies.

Quality of life is often poor, due to anorexia, naso gastric feeding, poor variability of the diet and severe diet restriction, social eviction, special education requirements, frequent hospitalisations.

Liver transplantation has now become a very successful procedure, and more than 90% of the children survive on the long term. It remains however an heavy and radical procedure, and doctors and patients may be reluctant to undergo this operation for non vital indications. In addition, new hopes and perspectives such as emerging cell therapy and prospects of gene therapy are now being considered in the decision making process (1;2) (3).

Delaying the decision may however lead to sudden acute metabolic crisis and irreversible damages, most commonly to the central nervous system. Hepatocarcinoma occurrence is also a risk which may become a contra-indication to transplantation, as in mitochondrial diseases or tyrosinemia (4).

Transplantation for inborn errors of liver metabolism account for 15 to 25% off all indications in pediatric liver transplant series (5;6).

The most widely accepted indications are

- Progressive familial cholestasis
- Alpha 1 Antitrypsin deficiency, phenotype ZZ
- Decompensated Wilson disease
- Cystic Fibrosis

In these disorders, the liver itself undergoes progressive damage and cirrhosis, and the indication is more related to chronic liver disease than to systemic metabolic dysfunction

The following indications concern diseases with an intact liver or moderately abnormal parenchyma, but with distant organ damage.

Crigler Najjar Syndrome	➛ Brain damage
Primary Hyperoxaluria	➛ Kidney stones and insufficiency
Urea Cycle disorders	➛ Mental delay, hyperammonemic coma
Organic aciduria	➛ Metabolic crisis, mental delay, cardiac failure
Type I glycogenosis	➛ Hypoglycemic coma
Familial Hypercholesterolemia	➛ Cardiovascular disease
Aminoaciduria	➛ Intellectual delay

The aim of the 4th Brussels Orphan Conference is to establish guidelines to facilitate the decision process for patients who are potential candidates for both continued medical treatment and/or transplantation, with special attention for emerging cell therapy. Exchange of experience and viewpoints between metabolicians, hepatologists and transplant surgeons is mandatory and will improve patient's access to the most comprehensive information about alternative treatments.

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