



European
Reference
Network

MetabERN

European Reference Network
for Hereditary Metabolic Disorders

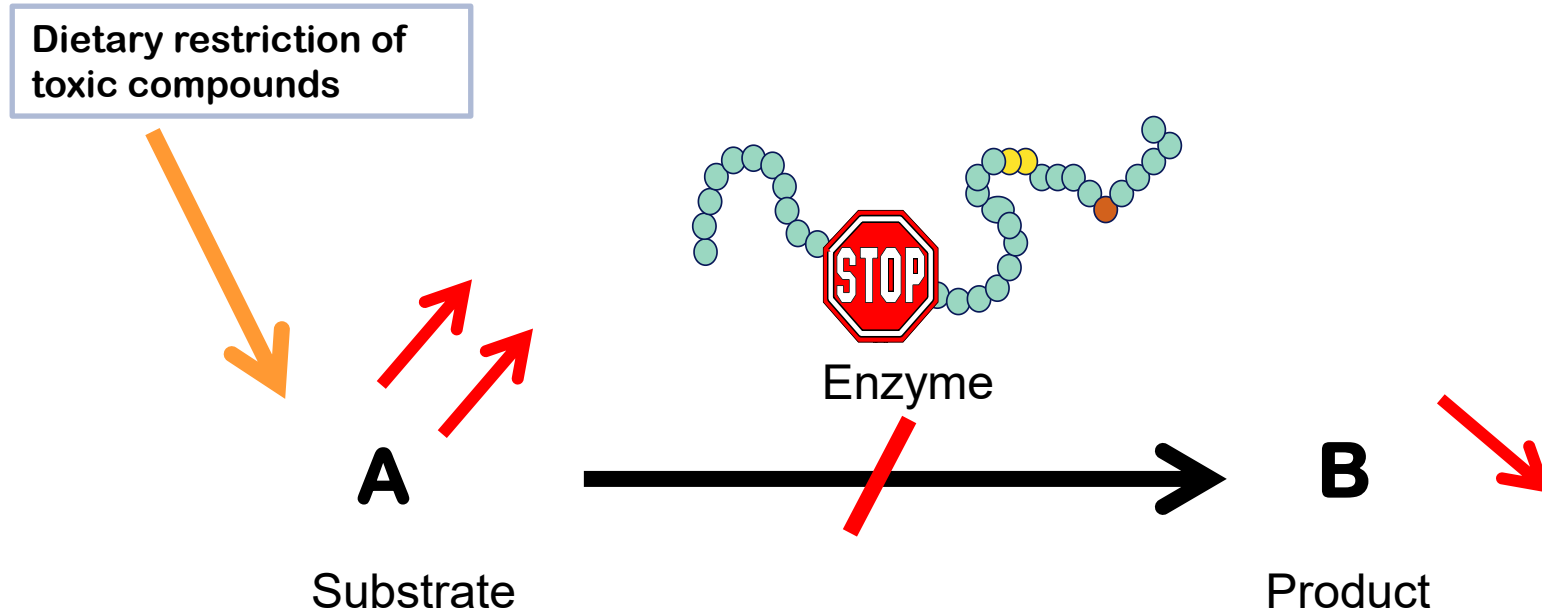
Diet, Drug therapies and Emergencies In Inborn Errors of Metabolism (IEM)

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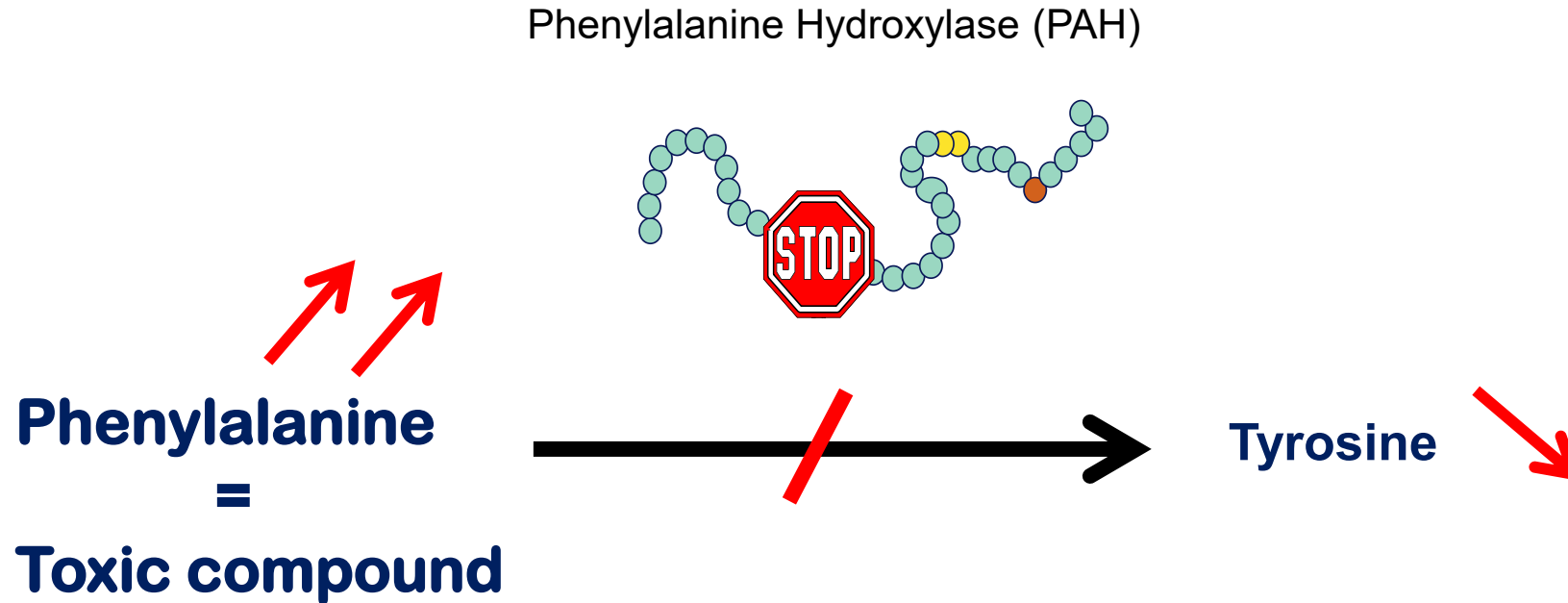
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Therapeutic strategies in IEM

Chronic Intoxication diseases < accumulation of small molecules



Phenylketonuria is the First Described First treated Metabolic Disease



Severity of the disease depends on
the severity of the enz deficiency (genotype/phenotype related)



Phenylketonuria is the First Treated Metabolic Disease

Phenylketonuria can be treated
with a phenylalanine (PHE) restricted diet

Horst Bickel (1953)



Principle of a phenylalanine restricted diet (ideally, should be initiate before the age of 10 days)

- Avoidance of high protein food
(milk, dairy products, meat, fish, chicken, eggs, beans,...)
- Control of **natural protein** intake
according to patient's tolerance in phenylalanine (PHE) intake
- **Low protein** food (manufactured hypoproteic bread, pasta, biscuits, ...)
- **Phenylalanine-free** formula (essential amino acids mixture + vitamins and oligoelements)

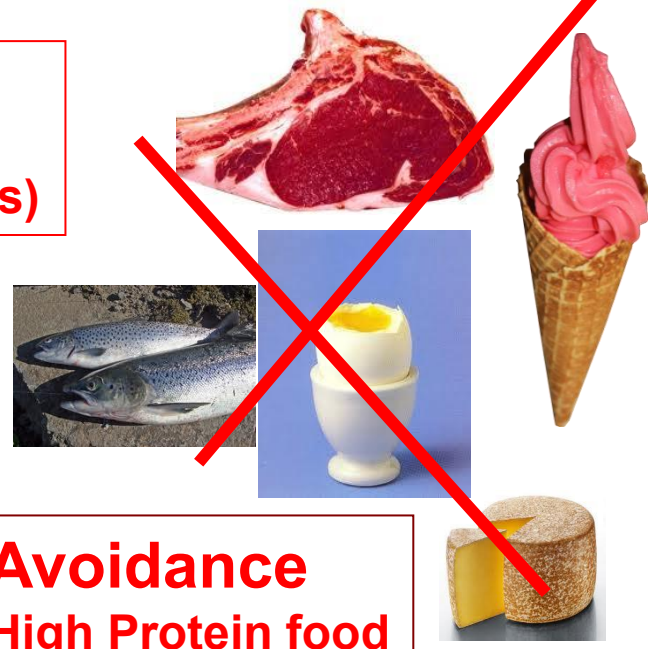
But no control of 'protein-free' food





Allowed
(sugar, lipids)

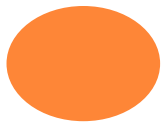
PHE-free
Amino acid supplements
(+Vitamines + Oligoelements)



Avoidance
High Protein food

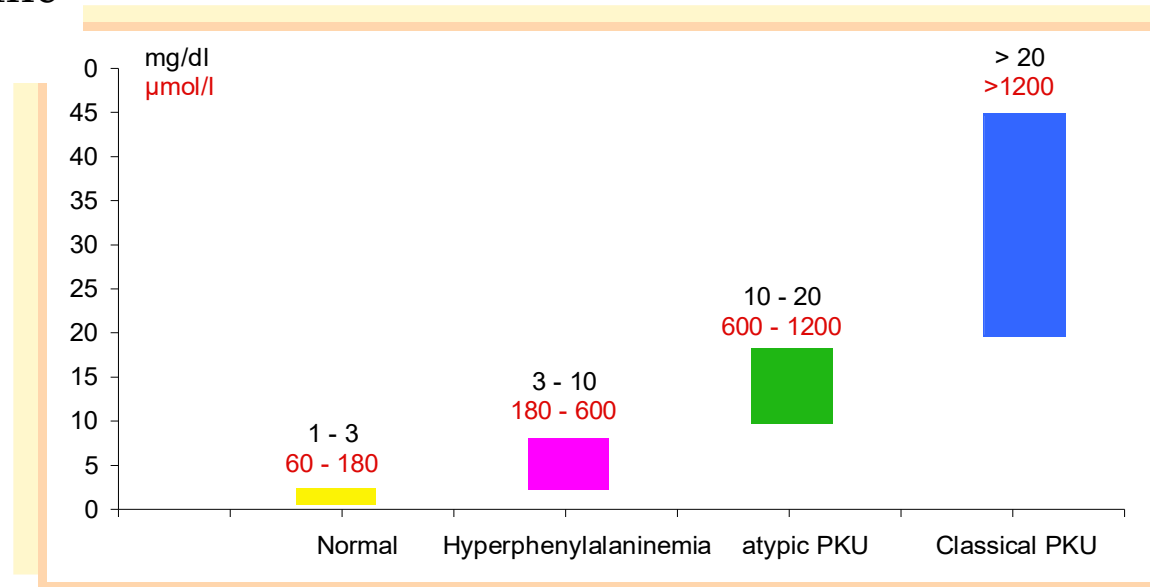
PHE-restricted diet

Control of
Natural Protein intake



Phe-tolerance depends on enzyme residual activity

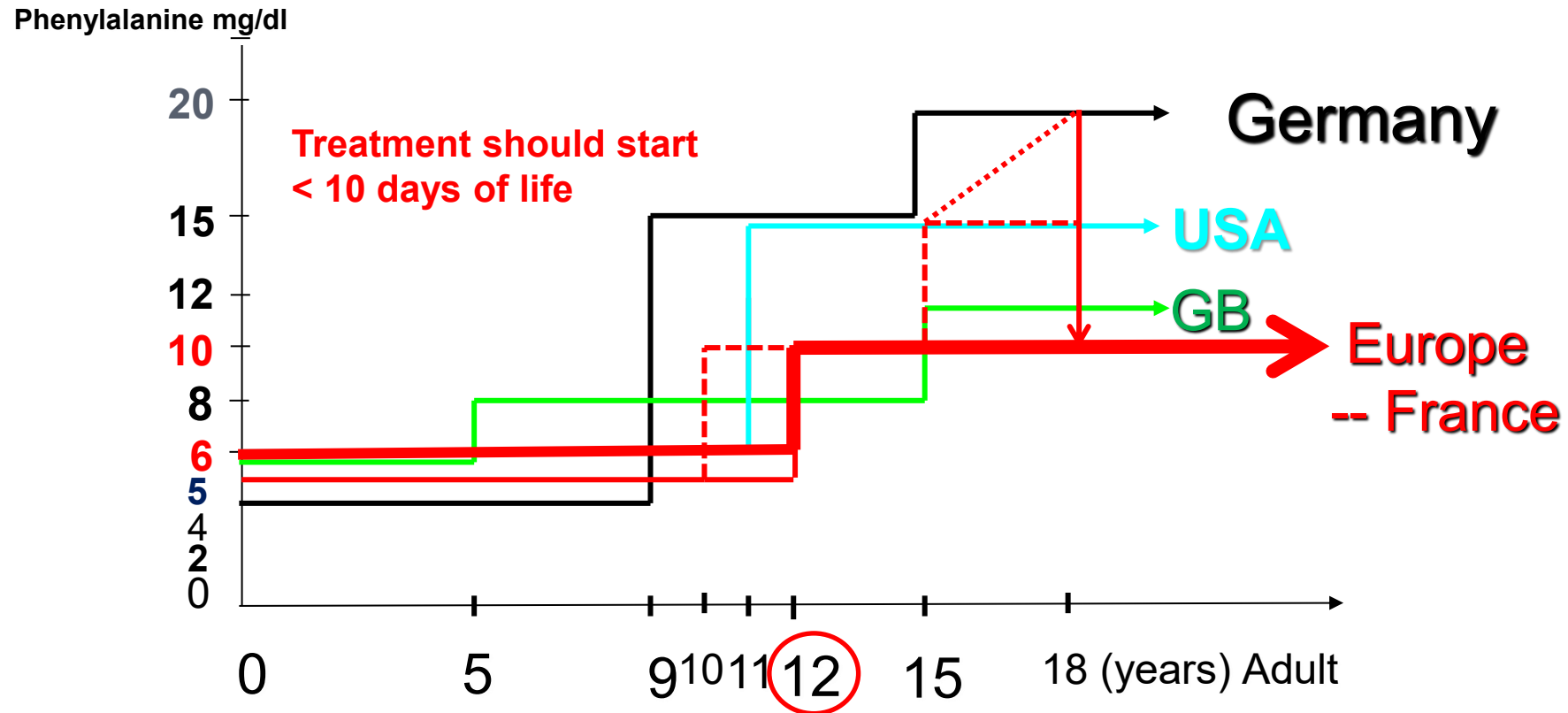
Phenylalanine
(PHE)



	PAH activity	PHE level without treatment	Daily PHE tolerance in food
Classical PKU	0-1 %	> 20 mg/dl > 1200 μmol/l	200 – 350 mg
Variant PKU or Atypical PKU	1-3 %	10 - 20 mg/dl 600-1200 μmol/l	350 - 850 mg
Hyperphenylalaninemia	3 - 5 %	6 – 10 mg/dl 360-600 μmol/l	> 850 mg



International recommendations for PHE control according to age / country – no universal consensus for years



Target PHE levels (European guidelines 2025)

< 12 years : 120 – 360 $\mu\text{mol/l}$ (2 – 6 mg/dl)

> 12 years : 120 – 600 $\mu\text{mol/l}$ (2 – 10 mg/dl)

Correlation between Phe metabolic control and IQ

Meta-analyses of within-study correlations: intelligence quotient (IQ) and concurrent^a blood phenylalanine (Phe) level

PKU population	<i>t</i>	<i>n</i>	<i>r</i> (95% CI) ^b
Early treated	29	666	−0.31 (−0.41, −0.20)*
Classic			
Total	23	499	−0.23 (−0.32, −0.14)
Early treated	21	473	−0.25 (−0.34, −0.15)
Mixed treatment history	3	32	0.04 (−0.35, 0.42)
Mixed/unspecified			
Total	14	310	−0.29 (−0.48, −0.07)*
Early treated	9	219	−0.42 (−0.60, −0.19)*
Mixed treatment history	5	91	0.02 (−0.27, 0.31)
Mild	1	8	−0.28 (−0.82, 0.53)
Hyperphenylalaninemia	1	16	−0.08 (−0.55, 0.43)

0-12 years : Each **100 μmol/l** Phe increase predicted a **1.3 to 3.1 IQ** point reduction

→PHE level is a predictive IQ indicator

A stronger association was observed between Phe levels during early childhood and later IQ.

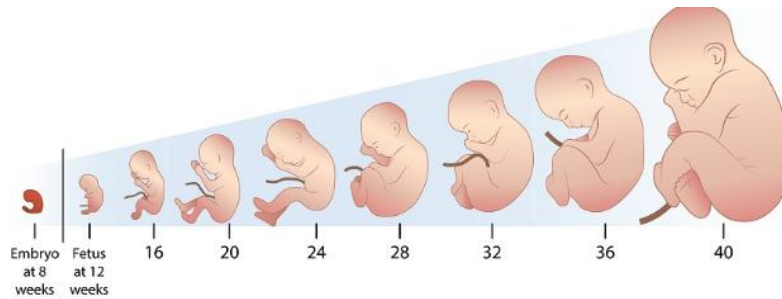


- **Lifelong low phenylalanine diet** (in males and females) to prevent : decrease in IQ scores, eczema, behavioral problems, seizures, decreased executive functioning, depression, irritability, headaches, impairment of short term memory,
- Important **in Females** who are willing to be pregnant, keep them on a **controlled diet**
- Recommendations to start a strict **low PHE diet** (Phe < 360 $\mu\text{mol/l}$) at least **3 months before planned conception** and **throughout** pregnancy because of **teratogenic** effects of Phenylalanine on fetus



Maternal Phenylketonuria

The teratogenic effects of Phenylalanine on fetus



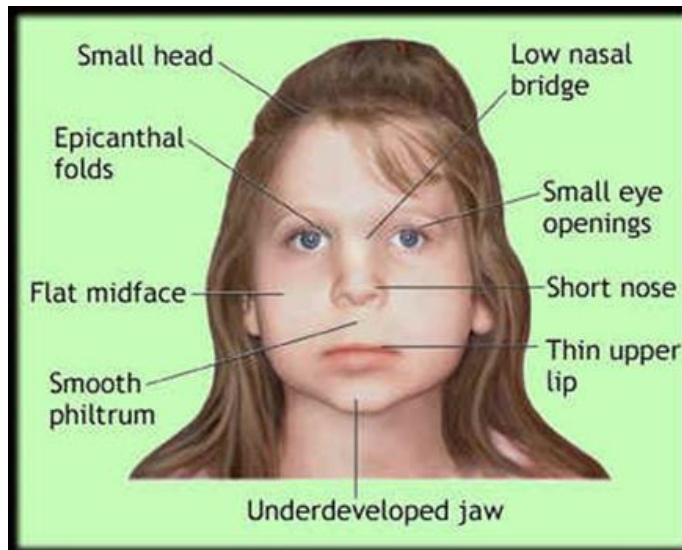
MATERNAL PKU : RISKS TO FETUS

Poor
metabolic
control in
mothers

May cause in fetus



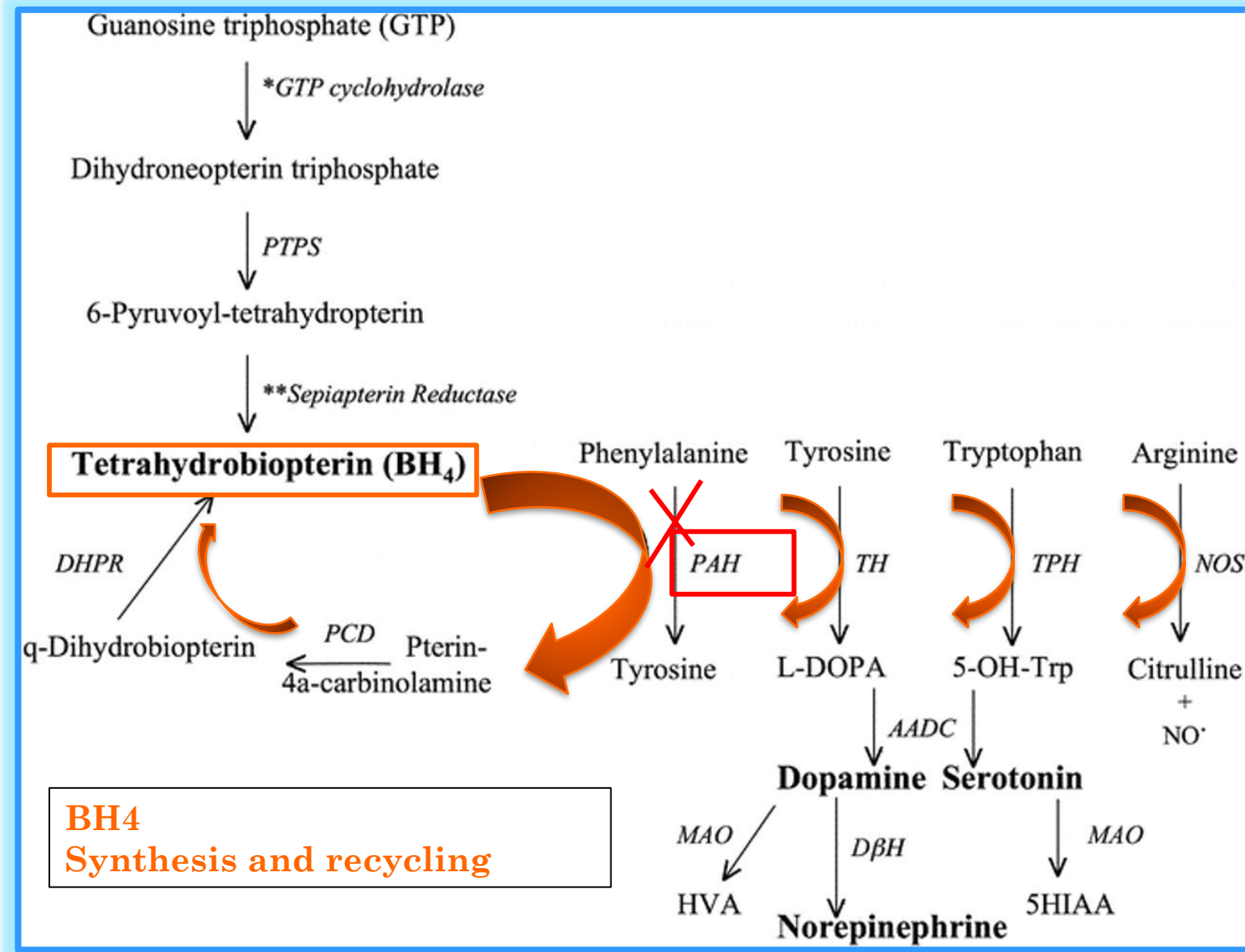
- Mental retardation 92 %
- Microcephaly 73 %
- Low birthweight 40 %
- Congenital heart disease 12 %
- Developmental delay



Maternal PKU Syndrome

- Dysmorphism (mimicking Fetal alcohol syndrome)

BH4: a natural cofactor of Phenylalanine Hydroxylase (PAH) system



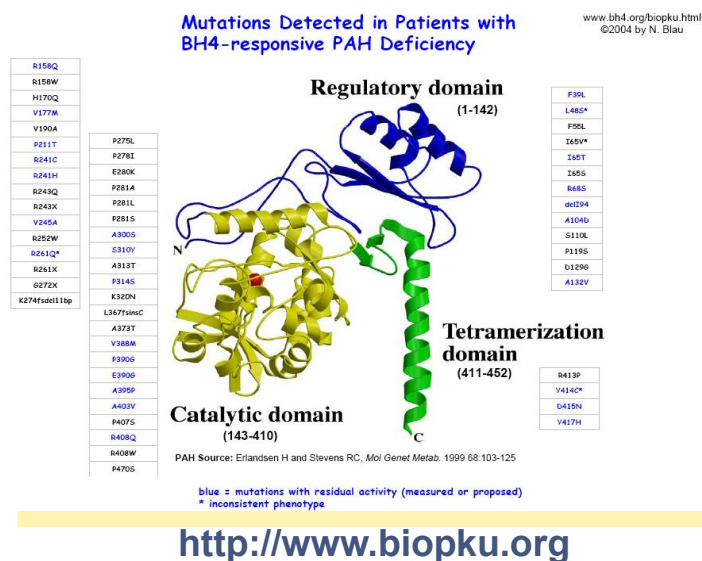
Better Response to cofactor BH4 in missense mutations

~ >1000 PAH mutations worldwide, most are missense mutations

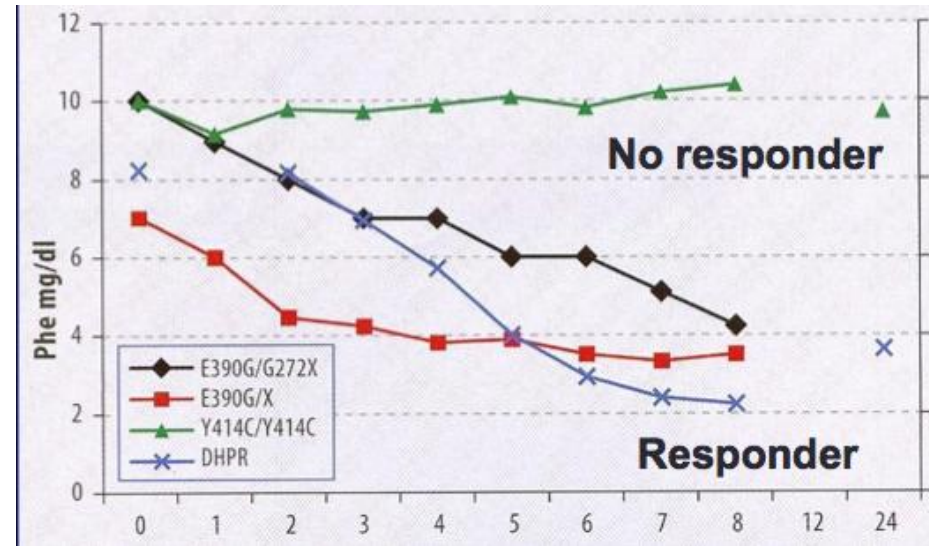
Mutation Type	N°	Graph	
Missense	308		61,85 %
Deletion	66		13,25 %
Splice	52		10,44 %
Silent	30		6,02 %
Nonsense	26		5,22 %
Insertion	8		1,61 %
Sil./Splice	3		0,60 %
Splicing	2		0,40 %
Silent ?	1		0,20 %
Unknown	1		0,20 %
Total	498		

- Missense mutations : Enzyme is synthesized but activity is null or decreased because of impaired conformation
- PKU as a model of « misfolding » enzyme ++

- BH4 = Natural cofactor of aromatic amino acid hydroxylases**
- Sapropterin (6R-BH4) synthetic form of tetrahydrobiopterin**
- Orphan drug (FDA and EMEA)
- Stabilization of the active tetramer forms of the mutant protein
- Protection from inactivation
- Acts as a « chemical chaperone », preventing misfolding and increase enzyme activity



Different responses to oral BH4 loading test (20mg/kg) according to genotype in PKU patients

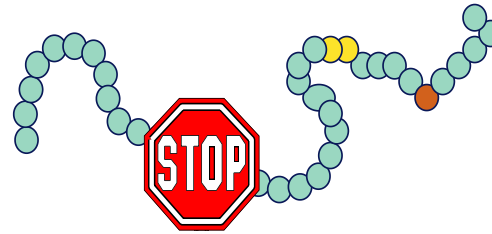


- About **70 %** of mild HPA and mild PKU patients proved to respond to BH4 therapy (reduced Phe level after loading test > 30 %).
- About **10 %** of classical PKU patient respond to BH4 (more severe mutations, null mutations)
- In PKU patients responsive to BH4, oral treatment could be used **in addition** to a restrictive low-phenylalanine diet to reduce blood phenylalanine and increase PHE tolerance, and might even replace the diet in some instances.

Therapeutic strategies in IEM

Intoxication diseases < accumulation in small molecules

Dietary restriction of
toxic metabolites



A



B

Decreasing metabolite toxicity

- Removing toxic metabolites
- Blocking the effect of toxic metabolites



Acute management in Intoxication diseases



Metabolic decompensation Triggers

- Prolonged fever
- Vomiting or diarrhoea
- Refusal to eat
- Prolonged fasting / protein overload
- Surgery



Early clinical signs may be subtle

- Lethargy,
- Loss of appetite,
- Change of behaviour or exacerbation of pre-existing neurological problems
- « Unwell »

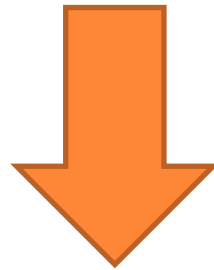


Management decisions should be based on clinical status and listening to parents



Principle of treatment in Intoxication diseases

- Control intake of precursors of toxic compounds (proteins, amino acids)
- Treat catabolic state with energy supply (glucose and lipids)
- Hydratation
- Epuration of accumulated toxic compounds with scavengers/extra renal epuration
- Stimulation of residual enzyme activity (with cofactors)



- **Emergency treatment**
- **Chronic treatment**



Acute management in Intoxication diseases

Decompensation	Mildly severe	Severe
Dehydration	< 10%	≥ 10%
Acidosis: pH HCO ₃	> 7.20 > 15 mEq/l	< 7.20 < 15 mEq/l
NH ₃	< 400 µM	> 400 µM
Glucose	N	N / ↑ / ↓
Lactate	N	> 5 mM
Calcium	N	↓
NFS	N	Neutropenia Thrombocytopenia



Acute management in Intoxication diseases

- Nutritional support

➡ 1. Stop protein intake **FIRST STEP !**

➡ 2. Provide adequate calories intake ≥ 100 Kcal/kg/d
to boost anabolism#reduce catabolism

- **Glucose** 10 mg/kg/min in neonate (oral/NGT/IV)
 - Isocaloric (1 ml = 1 kcal) orale route preferred if digestive tolerance
 - IV route Glucose 15 % (20 % with central catheter)
 - +/- Insuline 0,05 – 0,10 U/kg/H (if hyperglycemia)
- **Lipids** 0,5 g/kg/d up to 3g/kg/d (only contraindication FAO)



Protein should be reintroduce **within 48-72 H** to avoid catabolism



Progressive protein reintroduction

From intraveinuous to oral route

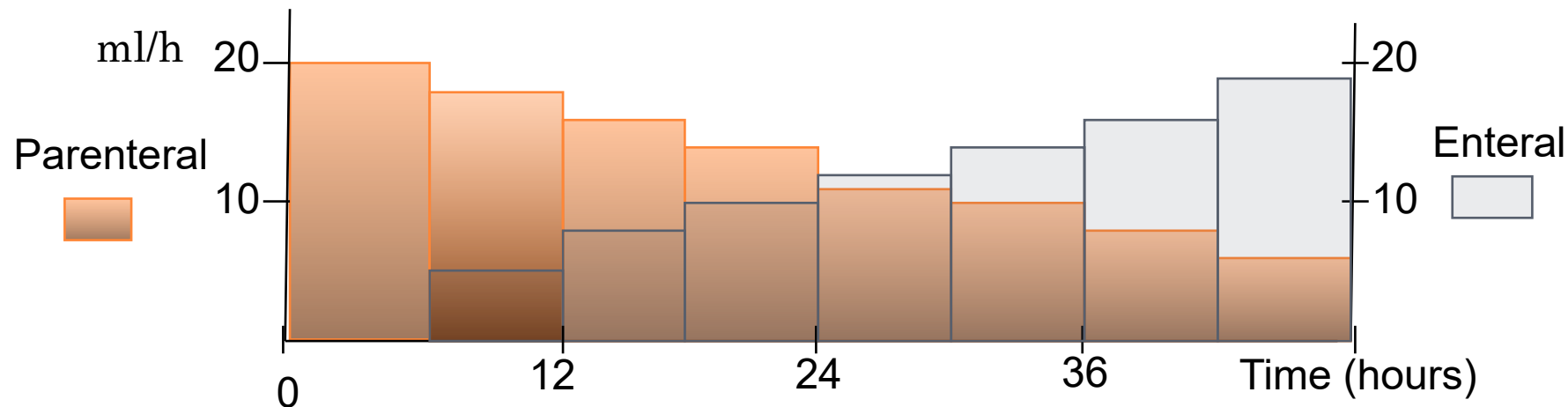
Without protein

- 120 – 130 ml/kg/d
- 90 – 100 Kcal/kg/d
70-75% Glucose
+ 25-30% lipids
- ions, Ca, Ph,
- vitamins, oligoelements



Protein Controlled diet

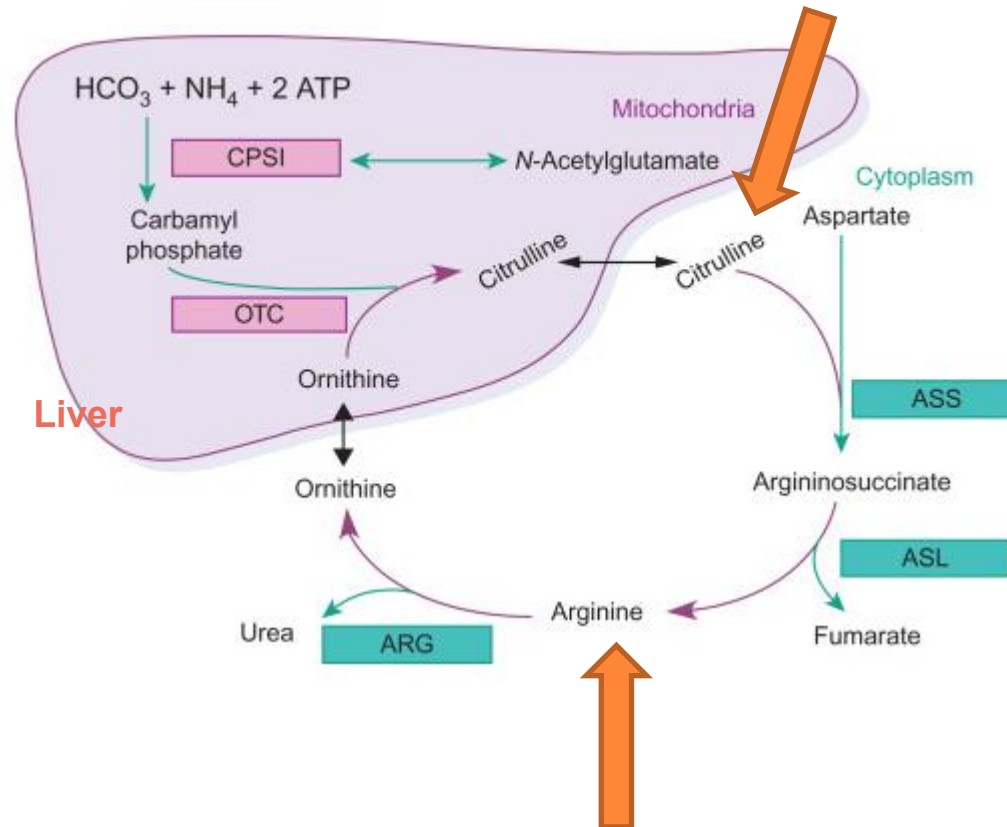
- IV Amino Acids / oral milk
- 120 – 130 ml/kg/d
- 90 – 100 Kcal/kg/d
70% Glucose
+ 25% lipids
- ions, Ca, Ph,
- vitamins, oligoelements



Management in Intoxication diseases

- Amino Acids supplements

Urea cycle defects (UCD)



Management in Intoxication diseases

- Amino Acids supplements

- In Urea Cycle defects = supplier



	Dosage	Route	IEM
L-Arginine HCL	200-600 mg/kg	IV/Oral	CPS, OTC ASS1, ASL
L-Citrulline	100-200 mg/kg	Oral	CPS, OTC

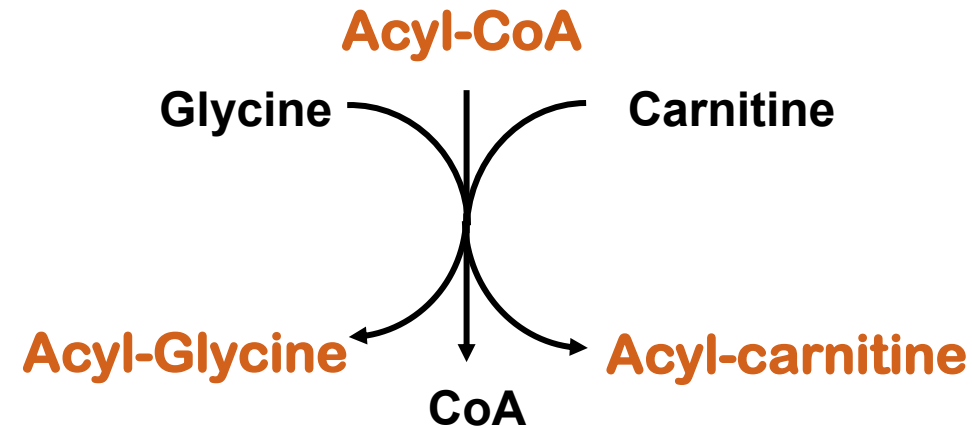
- In Organic Aciduria = scavenger

	Dosage	Route	IEM
L-Carnitine	100-400 mg/kg/d	Oral/IV	MMA, PA, IVA 3-MCC
L-Glycine	150-300 mg/kg/d	Oral	IVA, 3-MCG



Management in Intoxication diseases

- Amino Acids supplements



	L- Glycine	L – Carnitine
MMA	0	Methylmalonyl-carnitine + Propionyl-carnitine
PA	0	Propionyl-carnitine
IVA	Isovaleryl-glycine	Isovaleryl-carnitine
3- MCG	3-CH3-crotonyl-glycine	3-OH-isovaleryl-carnitine



Acute management in Intoxication diseases

- Pharmacologic epuration

- In UCD and OA



$\geq 110 \mu\text{Mol/L}$ in NN 1-7d
 $\geq 90 \mu\text{Mol/L}$ in NN 8-14d
 $\geq 50 \mu\text{Mol/L}$ in NN 15d - adult

➡ 1. Stop protein intake **FIRST STEP !**

➡ 2. Provide adequate calories intake $\geq 100 \text{ Kcal/kg/d}$

- Infuse Glucose 8 -10 mg/kg/min
- Infuse lipids 0,5 g/kg/d up to 3g/kg/d

☐ Protein should be reintroduce **within 48 H** after return of ammonia levels to 80–100 $\mu\text{mol/l}$ to avoid catabolism and nitrogen release

☐ Control blood $\text{NH}_4/3 \text{ H}$ (heparin tube on dry ice **within 15-30 min**)

Acute management in Intoxication diseases

- Pharmacologic epuration

- In UCD and OA

NH₃ ≥ 150 µMol/l

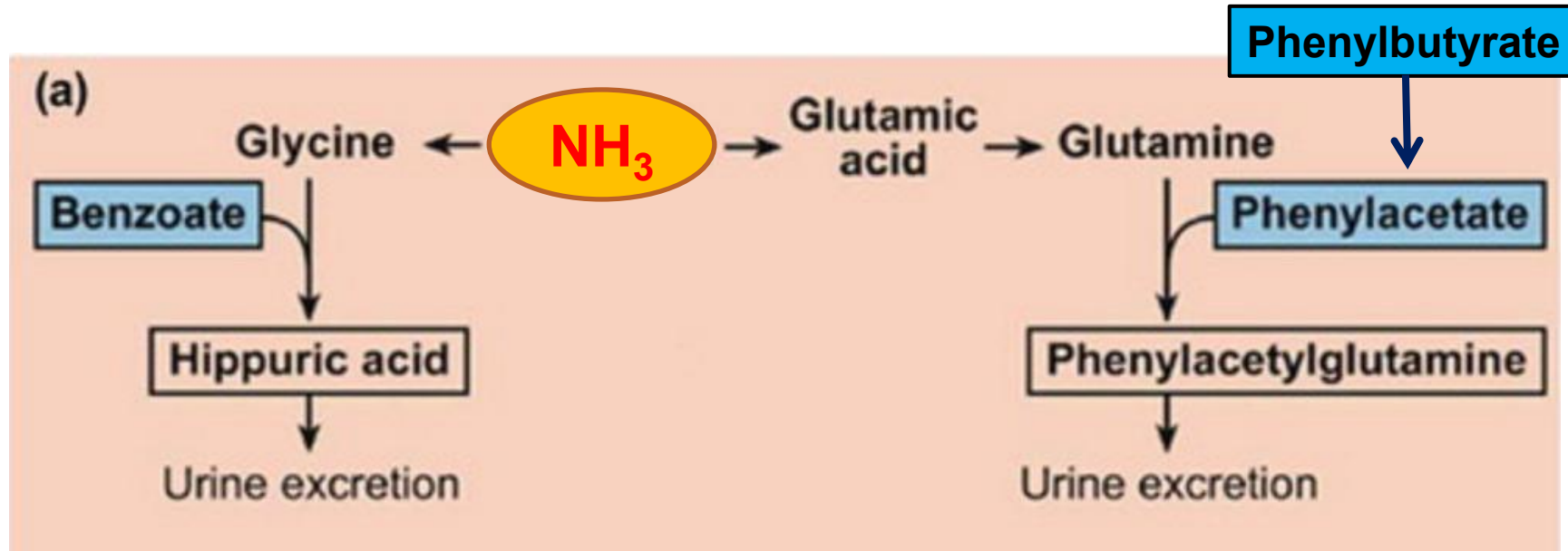


Nitrogen Scavengers	Dosage	Route	IEM
Sodium Benzoate	250 mg/kg	IV/oral	UCD, OA
Sodium Phenylacetate	250 mg/kg	IV	UCD, OA
Sodium Phenylbutyrate Ammonaps®	250 mg/kg	oral	UCD, OA
Glycerol Phenylbutyrate (Ravicti®)		oral	UCD
Carbamylglutamate (Carbaglu®)	100 -250 mg/kg/d	oral	NAGS, OA



Nitrogen Scavengers

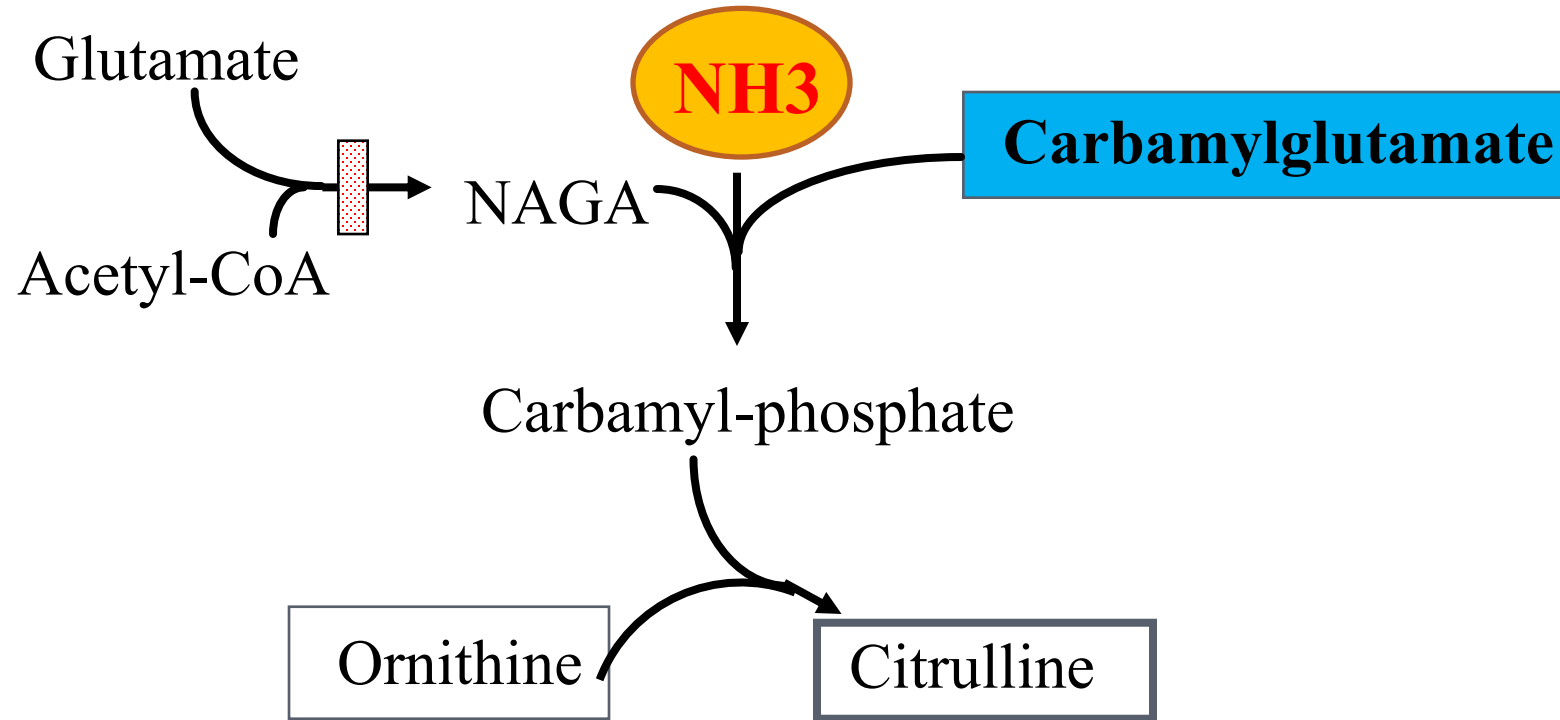
How they trap the toxic NH_3 and transform it into a non-toxic compound ?



1 mole Benzoate
=
1 mole NH_3 detoxification

1mole Phenylbutyrate
=
2 moles NH_3 detoxification

Nitrogen Scavenger Carbamylglutamate



The only form currently available is an oral preparation



Acute management in Intoxication diseases

Vitamins Cocktail

	Dosage	Route	IEM
Thiamine (B1)	100 (- 400) mg/d	Oral/IM/IV	Beri-Beri, PDH, MSUD
Riboflavine (B2)	50 mg/d	Oral	GA1, IVA, MADD, resp chain (CI and CII)
Biotin (B8)	10-20 mg/d	Oral/IM	PA, PC, MCD, BGBRD, MCG, resp chain
Hydroxocobalamine B ₁₂	1–2 mg/d	IM/IV	MMA, HCYST, CblC
Pyridoxine (B6)	0.5–1 g/d 100 mg/d (NN)	Oral/IV	HCYST (CBS) B ₆ -responsive seizures
Pyridoxal-P	30 mg/kg/d	Oral	PNPO
Folic acid	10–40 mg/d	IV	HCYST (MTHFR)
Folinic acid	5–15 mg/d	IV	HCYST (Remethylation), Cerebral folate transporter



Extrarenal epuration is the best way for a rapid ammonia decline



NN and children $\geq 200\text{-}300\text{ }\mu\text{Mol/l}$ if no response within hours
 $\geq 400\text{-}500\text{ }\mu\text{Mol/l}$ definitely

Adolescents and adults $\geq 200\text{ }\mu\text{Mol/l}$

Table 3 | Dialysis ammonia clearance and filtration fractions

Number of patients	Dialysis modality	Qb (ml/min)	Qd (ml/min)	Ammonia clearance (ml/min/kg body weight)	Ammonia filtration fraction (%)
3	CAVHD	10–20	8.3 (0.5 l/h)	0.87–0.97	12.5–14.3
3	CVVHD	20–40	33.3–83.3 (2–5 l/h)	2.65–6.80	53.0–58.0
2	HD	10–15	500	3.95–5.37	95.0–96.0

CAVHD, continuous arteriovenous haemodialysis; CVVHD, continuous venovenous haemodialysis; HD, haemodialysis; Qb, blood flow rate; Qd, dialysis fluid flow rate. Based on data from REF.³⁴.

Diet controlled in natural proteins and Amino acids mixtures supplements

1. Protein restriction Low protein diet,
minimal protein requirement/safe levels (FAO/WHO/UNU)

2. Specific AA mixtures

(not in all diseases, not in emergency situation, do not overload metabolism)

- For each disease, depending on affected metabolic pathway (PKU,
- Different forms (powder, gel, liquid)
- Different compositions (according to age : baby, infant or adult)
- Supplemented with trace elements, minerals and vitamins



Safe Protein levels and Energy needs in general population - FAO/WHO/UNU recommendations

PROTEIN INTAKE		
Age	Intake	
<i>months</i>	<i>g/kg bw/day</i>	
1	1.77	
2	1.50	
3	1.36	
6	1.31	
12	1.14	
<i>years</i>		
1.5	1.03	
2	0.97	
3	0.90	
4-6	0.87	
7-10	0.92	
	Females	Males
<i>years</i>		
11	0.90	0.91
12	0.89	0.90
13	0.88	0.90
14	0.87	0.89
15	0.85	0.88
16	0.84	0.87
17	0.83	0.86
18	0.82	0.85
> 18	0.83	0.83

ENERGY REQUIREMENTS				
Age	Females	Males	Females	Males
<i>years</i>	<i>kJ/kg bw/day</i>		<i>kcal/kg bw/day</i>	
0.5	340	335	81.3	80.0
2.5	334	348	79.8	83.2
5.0	305	315	72.9	75.3
10	248	275	59.3	65.7
15	193	230	46.1	55.0
Adults, moderate activity level, 70kg body weight				
18-29	159	183	38.0	43.7
30-59	148	175	35.4	41.8
Adults, moderate activity level, 50kg body weight				
18-29	180	212	43.0	50.7
30-59	183	212	43.7	50.7

Treat intercurrent illness as soon as possible at home first, according to emergency plan



To prevent metabolic decompensation during
poor feeding, vomiting, fever, etc

- Stop protein intake
- Give sufficient fluids (water, tea, ..) and calories (carbohydrates as glycose polymers/maltodextrin) with some salt every 2 H

Age	Glycose polymers/ Maltodextrin %	Kcal/ 100 ml	Daily volume
0-1 y	10	40	150-200 mg/kg
1-2 y	15	60	95 ml/kg
2-10 y	20	80	1200-2000 ml/day
> 10 y	25	100	2000 ml/day

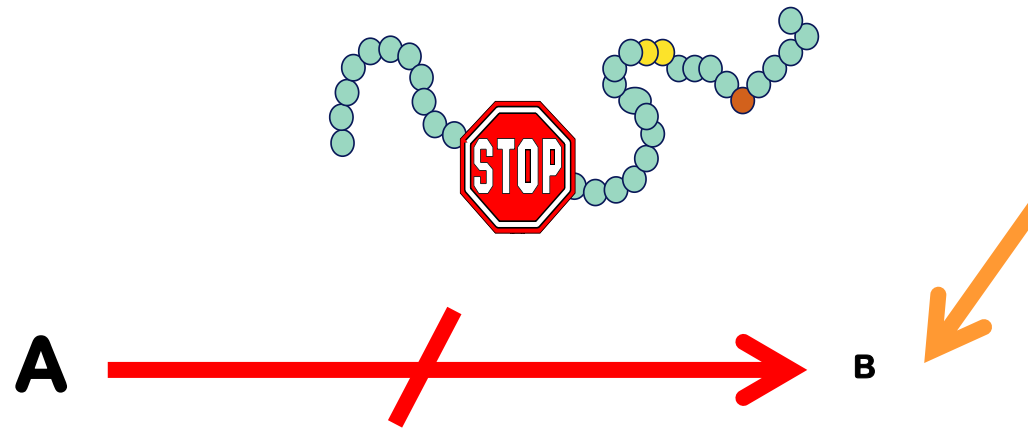


Product	Sachet size	Make up to final volume	Carbohydrate concentration provided	Recommended age group*
S-O-S10™	21g	200ml	10%	Birth - 1 year
S-O-S15™	31g	200ml	15%	1 - 2 years
S-O-S20™	42g	200ml	20%	2 - 10 years
S-O-S25™	52g	200ml	25%	10 years +



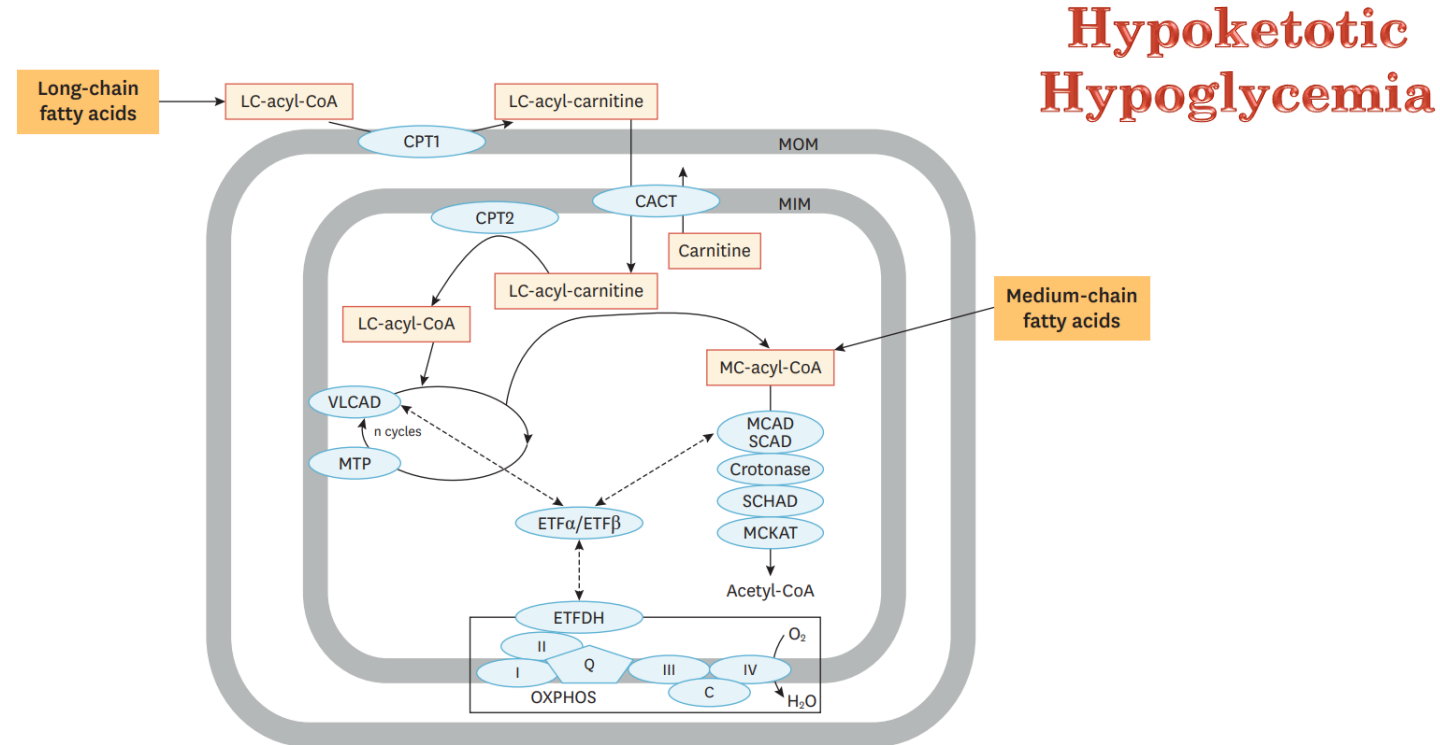
Therapeutic strategies in IEM

In Carbohydrate metabolism defects



Management in Carbohydrate metabolism is Based on diet and prevention of hypoglycemia

- In FAO defects



Avoid prolonged fasting; variable according to age

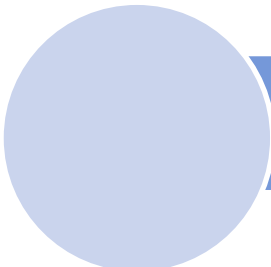
Provide high glucose amounts

Control lipids supply

Management in Carbohydrate metabolism is Based on diet and prevention of hypoglycemia

- In FAO defects

**Hypoketotic
Hypoglycemia**



Avoid prolonged fasting time; according to age

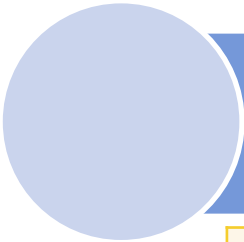
Age	Recommended fasting time	Maximal fasting time
Newborn	3 H	4 H
1 – 6 months	4 H	6 - 8 H
6 – 12 months	4 H (day)/ 6 – 8 H (night)	10 – 12 H (night)
1 – 6 years	4 H (day)/ 10 H (night)	12 H (night)
> 6 years	4 H (day)/ 12 H (night)	14 H (night)

Management in Carbohydrate metabolism is Based on diet and prevention of hypoglycemia

- In FAO defects in Emergency

If unwell, fever, vomiting, hospitalisation

**Hypoketotic
Hypoglycemia**



**Provide 120 – 200 % of daily glucose
Keep Glucose > 100 mg/dl**

Age	Recommended glucose IV/oral
Newborn	10 – 12 mg/kg/min
1 month – 6 y	8 – 12 mg/kg/min
6 y – 14 y	6 – 8 mg/kg/min
Adult	3 – 4 mg/kg/min

- Give enough glucose to block lipolysis
- Stop lipids

Routes : - Oral (mouth / nasogastric tube / gastrostomy)
- Depending on digestive tolerance (continuous or intermittent enteral feeding)
- IV if digestive intolerance



Management in Carbohydrate metabolism is Based on diet and prevention of hypoglycemia

- In FAO defects

Control Lipids in diet

IEM	LCFA in diet	MCT in diet	% Total Energy
VLCAD, LCHAD/MTP CPT-I, CPT-II CACT	Max 10 %	20 – 25 % 	25 – 30 %
MCAD		Contraindicated (e.g. coco milk/oil,..)	



In case of suspicion of FAO,
do not give IV lipids in emergency situations



Management in FAO

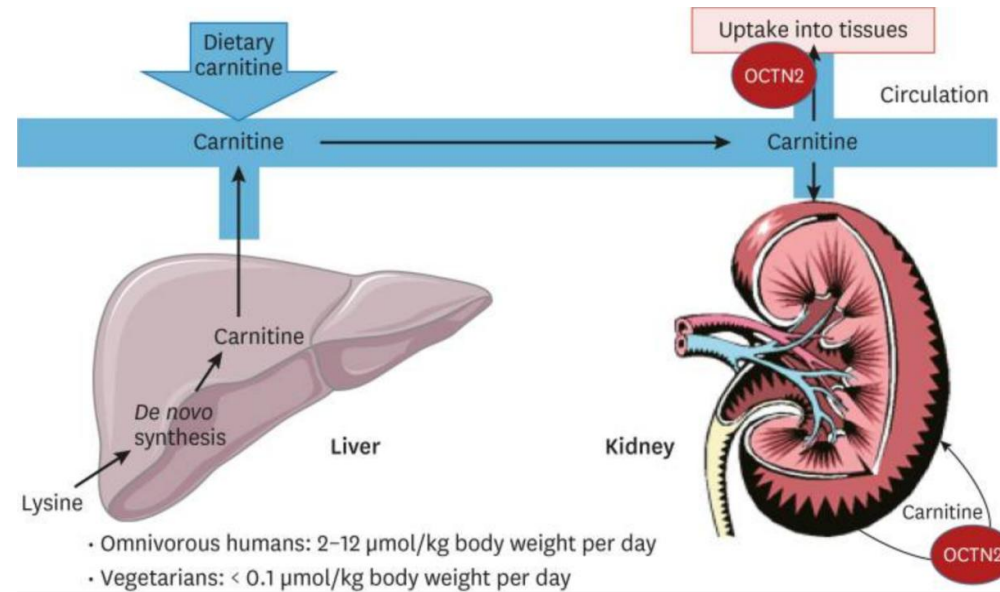
Based on diet - lipid restriction risks

- **Supply enough Polyunsaturated Fatty Acids (FA) :**
risk of omega-3 (EPA & DHA), omega-6 FA deficiency
in lipid- restricted diet
- **Control Fat-soluble vitamins (A, D, E, K)**



Other therapeutic options in FAO defects

- L-Carnitine

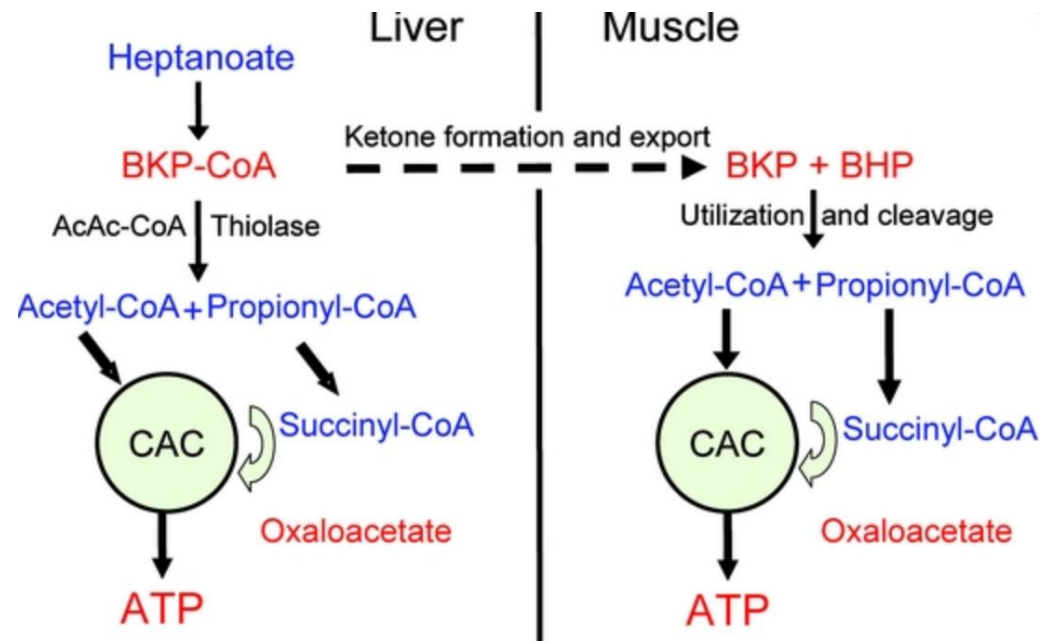


	Dosage	Route	IEM
L-Carnitine	50 – 100 mg/ kg	IV / oral	Systemic primary carnitine deficiency (OCTN2)
	20 – 50 mg/kg	IV / oral	MCAD
	10 – 50 mg/kg	IV / oral	CACT, CPT2, VLCAD, LCHAD & MTP, MAD

Controversial use in long chain FAO (cardiotoxicity)

Other therapeutic options in FAO defects

- **Triheptanoin (C7)** an anaplerotic therapy for Lc FAO



Triheptanoin (C7) produces 2 Acetyl-CoA and 1 propionyl-CoA units used by the Citric Acid Cycle (CAC)

- In studies, some improvements in cardiac parameters (decrease in LVM, small increase in ejection fraction)
- No effect on rhabdomyolysis crises in LcFAO (Vockley et al; 2020)



Management in Carbohydrate metabolism defects

Based on diet and prevention of hypoglycemia

Ketotic Hypoglycemia

- In Glycogenosis

- Prevent hypoglycemia to avoid neurologic and long term complications (hepatic, renal, ..)

- Monitor daily caloric intake

- Assure normal growth

- Avoid fasting; variable according to tolerance, to age

- Provide frequent Carbohydrate (CH) rich feeding (day time)

- Continuous nocturnal enteral supply of slow release (complex) CH

Nutritional Management in Glycogen Storage diseases

GSD 0a	Protein enriched diet (20%)
GSD Ia GSD Ib	High complex CH intake (55 – 70 %) Moderate fat restriction (20 – 30 %) Moderate protein restriction Galactose / Lactose restriction
GSD III	High complex CH intake (55 – 70 %) Moderate fat restriction (20 – 30 %) Protein enriched diet (20 %)



Management in Carbohydrate metabolism defects

Based on diet and prevention of hypoglycemia



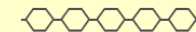
Provide frequent CH rich feeding

Glucose

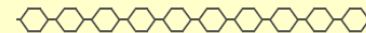


Only in an emergency!

Maltodextrin (industrially produced sugar)
Short chains of glucose



Starch (also uncooked – depot effect)
Long chains of glucose



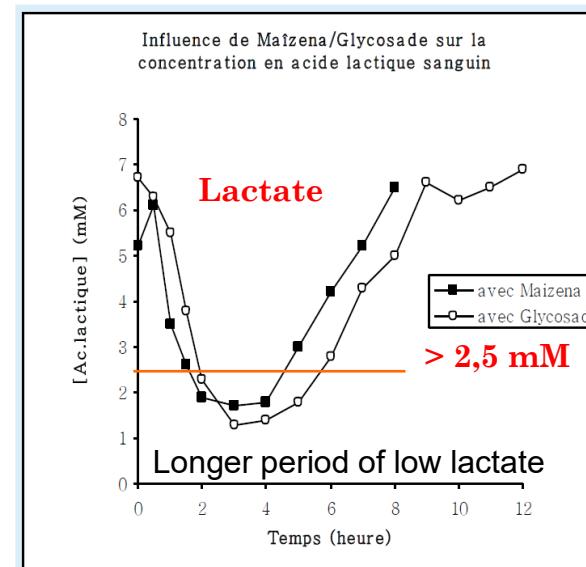
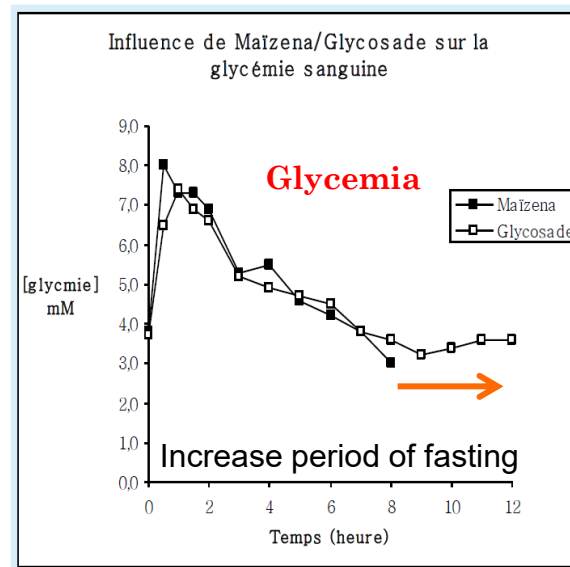
Management in Carbohydrate metabolism defects

Based on diet and prevention of hypoglycemia

Provide frequent CH rich feeding
to increase metabolic control



	Maizena	Glycosade ®
	Uncooked cornstarch	Modified cornstarch
Amylopectine	73 %	99,5 %
Resistant starch	60,5 %	68 %
From	6 months - 1 year	2 years



Management in Carbohydrate metabolism deficiency

Based on diet and prevention of hypoglycemia



Overnight Continuous enteral feeding of slow release Carbohydrate

- **Nasogastric or gastrostomy tube** or waking up every four to five hours to take cornstarch
- High-carbohydrate, lactose- and sucrose-free enteral formula (GSD I).
- An optimal infusion provides :
 - 8-10 mg/kg/min glucose in infants,
 - 6-8 mg/kg/min glucose in older children,
 - 3-7 mg/kg/min glucose in adults.
- Safety concerns (tube dislodgement, leakage, and pump failure) can cause serious hypoglycemia
- Safety precautions
 - bed-wetting devices (to detect formula leakage)
 - feeding pump alarms



Personalized Emergency card for every patient with metabolic decompensation risk

EMERGENCY CERTIFICATES - G2M NETWORK

V1 – May 2022

GLUTARIC ACIDURIA TYPE 1

Priority patient: must not wait in A&E / ED

If presenting with fever, vomiting, diarrhoea or fasting state
RISK OF ACUTE NEUROLOGICAL DISORDER with DAMAGE TO THE BASAL GANGLIA

Do not wait for signs of decompensation, in all cases initiate management as set out below

1 EMERGENCY WORKUP

Venous blood gases, lactate, electrolytes, blood glucose, CK, FBC, urea (BUN), creatinine. + Tests depending on the triggering intercurrent illness. Do not delay infusion. Normal test results do not exclude ongoing decompensation.

2 TREATMENT TO BE STARTED URGENTLY, without waiting for test results

- NO natural PROTEINS or IV amino acids : **stop feeding or specific low-protein nutrition.**
- If **hypovolaemia**, **expand** with Ringer's lactate or 0.9% NaCl at **10 mL/kg** (maximum 500 mL), reassess and repeat if necessary.
- Infusion using **10% glucose** with standard electrolyte additions* (never pure D10W)
- + Infusion using a Y-set of **20% lipids** (e.g. Medialipids, Intralipids),
- By peripheral line, at a rate depending on age:

Age	0-24 months	2-4 years	4-14 years	> 14 years / adult	MAX INITIAL RATE
Polyionic 10% glucose (glucose infusion rate)	6mL/kg/h (10mg/kg/min)	5mL/kg/h (8mg/kg/min)	3.5mL/kg/h (6mg/kg/min)	2.5mL/kg/h (4mg/kg/min)	120mL/h (3L/24h)
Lipids 20%	0.4 mL/kg/h (2g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	20mL/h (500mL/24h)

*e.g. Polyionic, Bionolyte, B45, Glucidon, etc. If no pre-made solution available, use 10% glucose in water + 4g/L NaCl (70 meq/L) + 2g/L KCl (27 meq/L)
If IV line is impossible => Nasogastric tube: prepare the IV fluids listed above and pass them through the tube at the same rates.

- If there are no gastrointestinal disorders and if the preparation is available: instead of infusion, **emergency diet by continuous enteral feeding** using nasogastric tube or gastrostomy (see diet sheet from parents)
- L-Carnitine**, orally divided into 3 to 4 doses or by continuous IV administration:
 - < 6 years of age: **200mg/kg/day**
 - > 6 years: **100 mg/kg/day**, max 12g/24h
- Continue any regular treatments
- Antipyretic and analgesic treatments if needed
- Treatment of intercurrent infection if needed

3 CRITERIA FOR HOSPITALISATION

- In all cases if under 6 years of age
- Over 7 years: return home if fever well tolerated and oral feeding possible with emergency diet.

4 SEVERITY SIGNS = consult / admit to Intensive Care

• <https://www.bimdg.org.uk/site/guidelines.asp>

• https://www.orpha.net/consor/cgi-bin/Disease_Emergency.php?Ing=EN

• <https://www.filiere-g2m.fr/parcours-patients/urgences-et-voyages>

• <https://metab.ern-net.eu/emergency-protocol/>

• Should explain the disease, and management of risks

• For intercurrent illness management at home/in hospital

Your Emergency Letter

The emergency letters created through this website can help patients and families in home managing of metabolic emergencies and in the communication with local doctors in the first hour of in-hospital management until expert metabolic support is secured. The online protocol has been reviewed and approved by medical doctors from centres of expertise that are part of the MetabERN network.

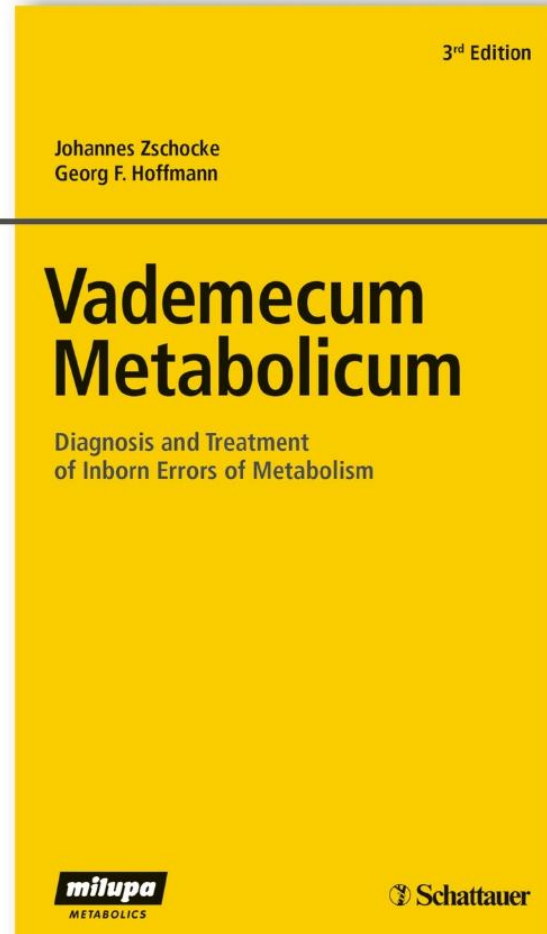
[Generate your emergency letter](#)

The following details are requested to generate the protocol:

- name of the patient
- specific disease the patient has,
- patient's weight in kg,
- language,
- possible sick-day regimen
- details of metabolic specialists and healthcare providers, and phone

A book to have in your pocket !

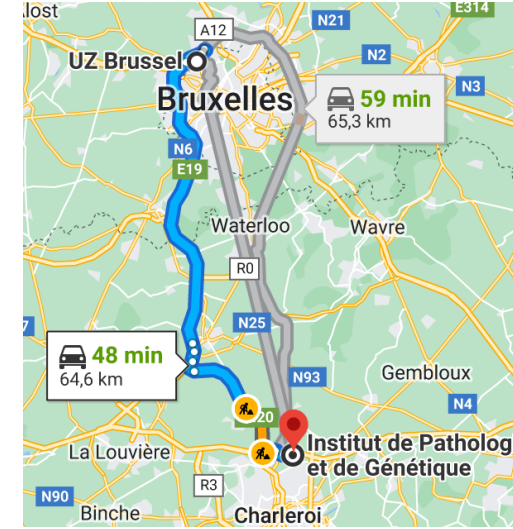
<http://www.vademetab.org/>





Institut de Pathologie et de Génétique

25 Avenue Lemaître, 6041 Gosselies (Charleroi)



Centre Agréé des Maladies Héréditaires du Métabolisme

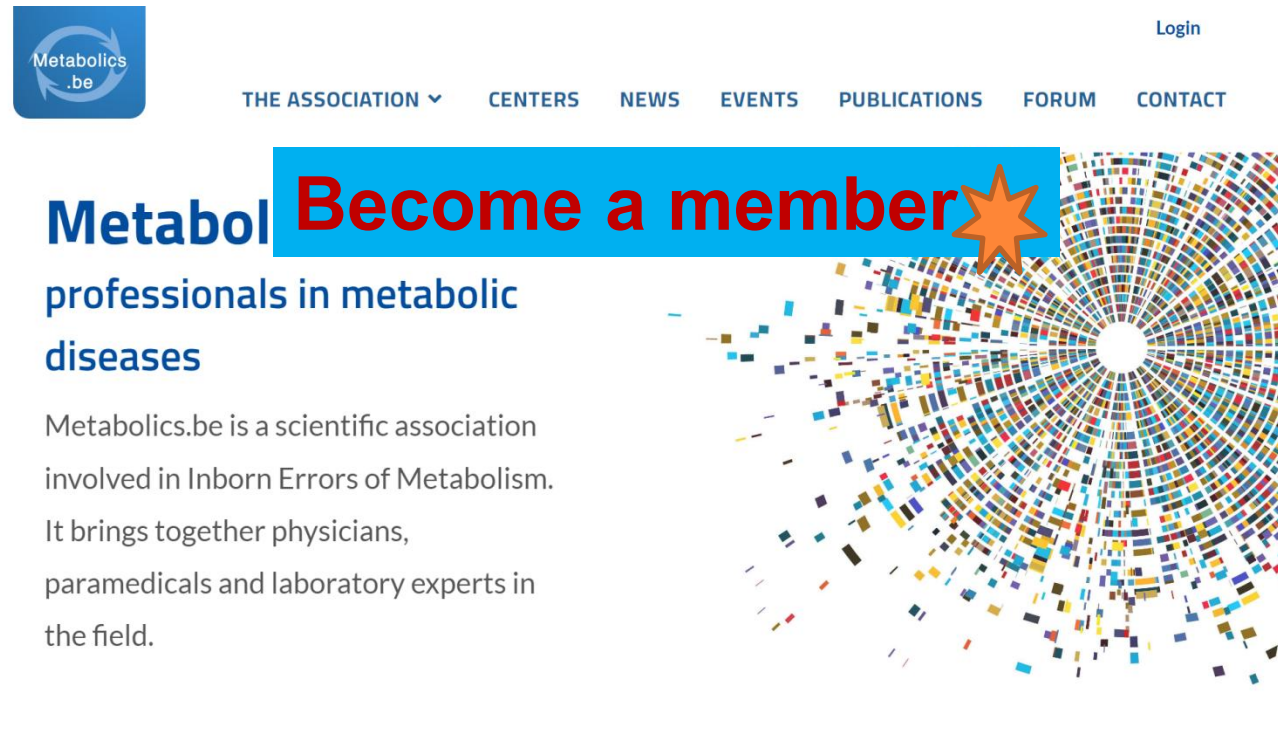
Département de Génétique Humaine

Dr Dominique Roland (Clinical Geneticist and Metabolism)
Pr Christine Verellen-Dumoulin (Clinical Geneticist)
Dr Hendrica Belge (Clinical Geneticist and Nephrologist)
Dr Marie Deprez (Neuropediatrician)
Mrs Ilaria Joly (Dietitian)
Mrs Stéphanie Dubruille (Psychologist)
Mrs Valérie Deville (Psychologist)
Mrs Nathalie Bercy (Social Nurse)
Mrs Camille Rouyer (Social Nurse)



CONTACT YOUR LOCAL METABOLIC TEAM

8 belgian centers for IEM – see their contacts on www.metabolics.be



The screenshot shows the homepage of the Metabolics.be website. At the top left is the Metabolics.be logo, which consists of a blue square with a white circular arrow and the text 'Metabolics .be'. To the right of the logo is a navigation menu with the following items: 'THE ASSOCIATION' (with a dropdown arrow), 'CENTERS', 'NEWS', 'EVENTS', 'PUBLICATIONS', 'FORUM', and 'CONTACT'. In the top right corner, there is a 'Login' link. The main content area features a large blue banner with the text 'Metabol' in white and 'Become a member' in red, followed by a large orange star. Below the banner, the text 'professionals in metabolic diseases' is displayed in blue. To the right of this text is a large, colorful, circular graphic made of many small squares, resembling a molecular structure or a complex network. Below the banner and text, there is a paragraph of text: 'Metabolics.be is a scientific association involved in Inborn Errors of Metabolism. It brings together physicians, paramedicals and laboratory experts in the field.'

Metabolics
.be

THE ASSOCIATION ▼ CENTERS NEWS EVENTS PUBLICATIONS FORUM CONTACT

Login

Metabol **Become a member** ★

professionals in metabolic diseases

Metabolics.be is a scientific association involved in Inborn Errors of Metabolism. It brings together physicians, paramedicals and laboratory experts in the field.



LEXICAL

CblC, cobalamin C deficiency;

FAO, Fatty acid oxydation defects

GA1, glutaric aciduria type 1;

GSD 1, glycogenosis storage disease type 1

HCYST (CBS), hyperhomocystinuria due to cystathionine beta synthase;

HCYST (MTHFR), hyperhomocysteinemia due to methyltetrahydrofolate deficiency;

IEM, Inborn error of metabolism

IVA, isovaleric acidemia;

MADD, multiple acyl CoA dehydrogenase def;

MMA, methylmalonic aciduria;

Resp chain (CI and CII), mitochondrial respiratory chain complex I and II deficiency;

MCD, multiple carboxylase deficiency;

MCG, methylcrotonyl CoA carboxylase def;

MSUD, Maple Sirup Urine Disease;

NGT, nasogastric tube

PA, propionic aciduria;

PC, pyruvate carboxylase deficiency;

PDH, pyruvate dehydrogenase deficiency;

PNPO, pyridox(am)in 5' phosphate oxidase

UCD, urea cycle disorders

