Congenital Hyperinsulinism International

Sant Joan de Déu

HOSPITAL MATERNOINFANTIL - UNIVERSITAT DE BARCELONA

The 2015 Barcelona Congenital Hyperinsulinism Family Conference

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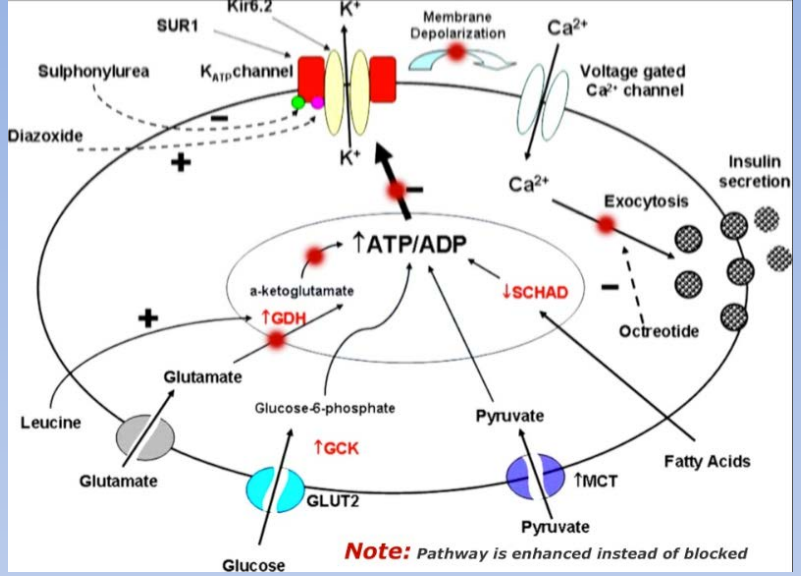
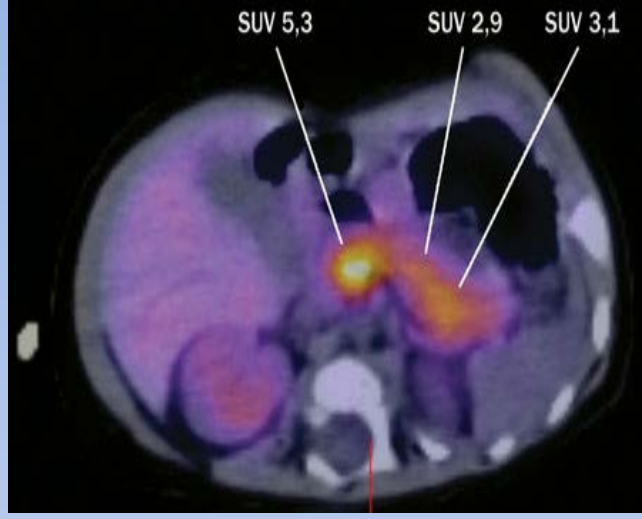
Congenital Hyperinsulinism: Spanish prespective





A decade of Change

DEMOGRAPHIC DATA

- Congenital hyperinsulinism is a rare disease, it has an estimated incidence between 1/25.000-1/ 50.000
- **Spain is the sixteenth most populated country in Europe with 46.507.760 and** 7 million children under the age of 15
- Spain has a National Health Service that attends every spanish resident

Hospital Santiago Compostela
H. General Coruña

Hospital Cruces Bilbao

Hospitals Barcelona
Sant Joan de Deu
Vall d´Hebron

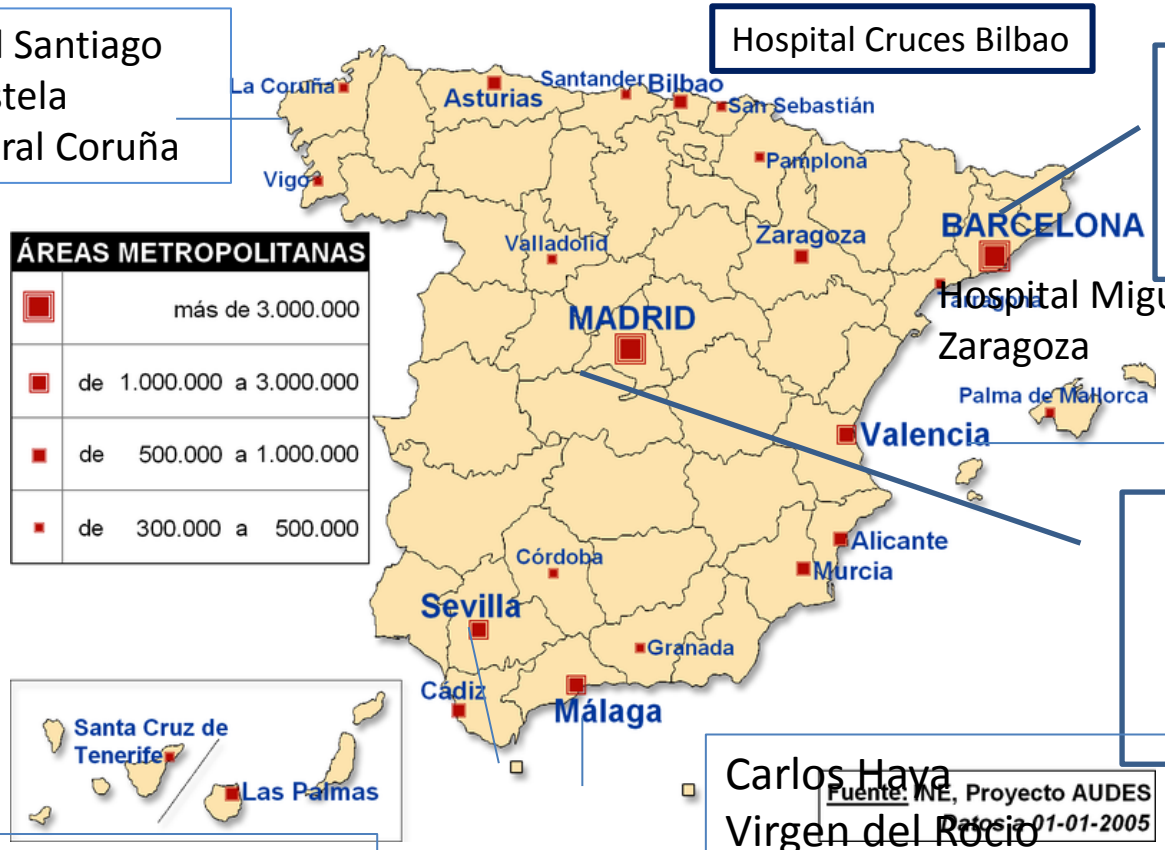
Hospital Miguel Servet Zaragoza

La Fe Hospital

Hospitals Madrid
La Paz Hospital
Niño Jesus
Gregorio Marañon
Ramon y Cajal

Carlos Haya
Virgen del Rocío

Hospital General Tenerife



SEEP Spanish Pediatric Endocrinology Society

Spanish Pediatric Endocrinology Society was founded in December of 1977
Actually it has a total of 248 members

We have two oficial scientific publications in spanish for pediatricians

Anales de Pediatria

(Index Medicus/Medline, EMBASE/Excerpta Medica e Índice Médico Español).

Revista Endocrinologia Pediátrica

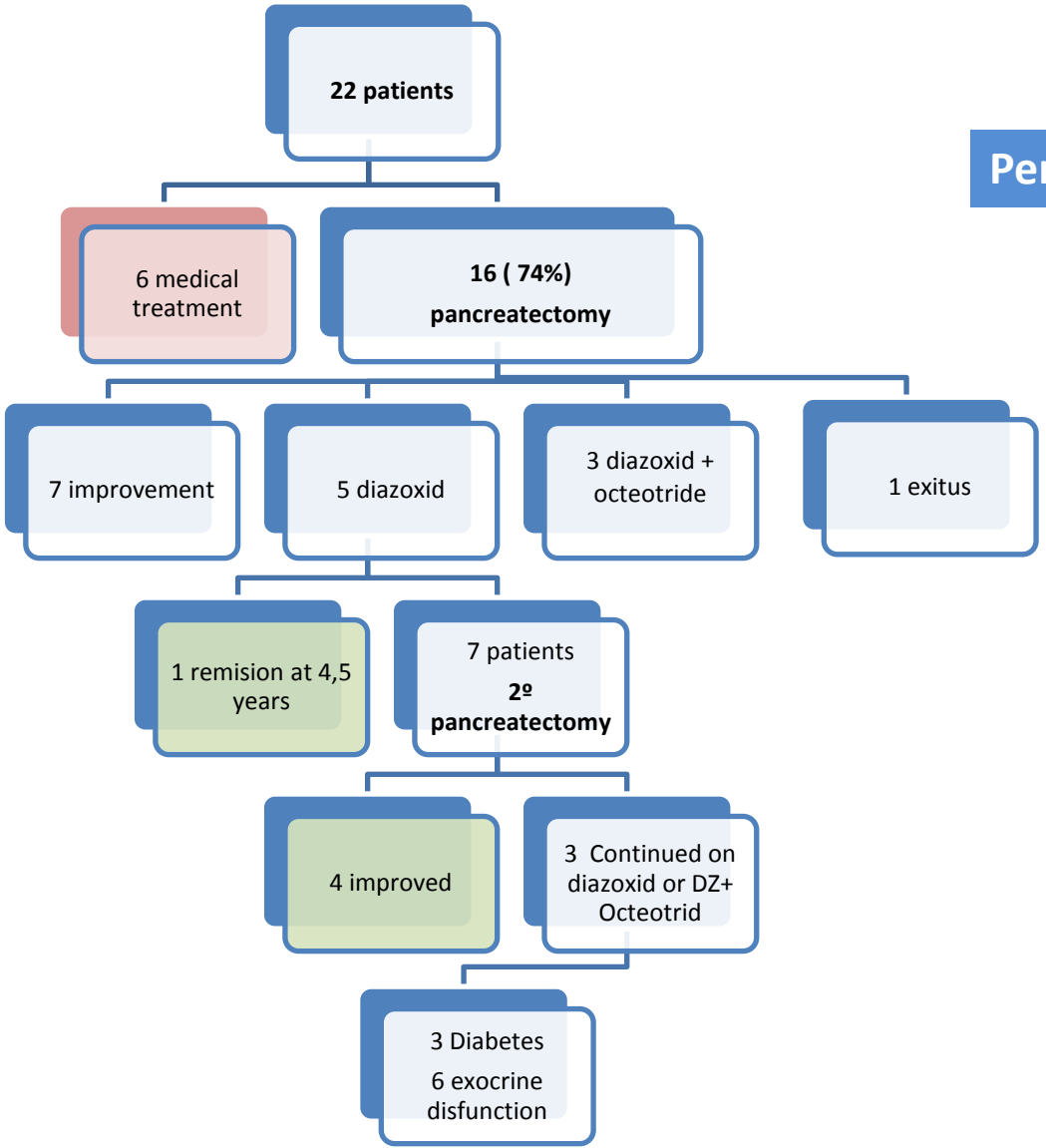
Sant Joan de Deu Hospital 1950

Historical data of Spanish patients with CHI

Hiperinsulinismo congénito. Revisión de 22 casos. Hospital de la Paz. Madrid

An Pediatr.2006;65:22-31

Guerrero-Fernándeza, I. González Casado, L. Espinoza Colindresa, R. Gracia Bouthelie



Period 1982-2004

Mutation spectra of ABCC8 gene in Spanish patients with Hyperinsulinism of Infancy (HI).

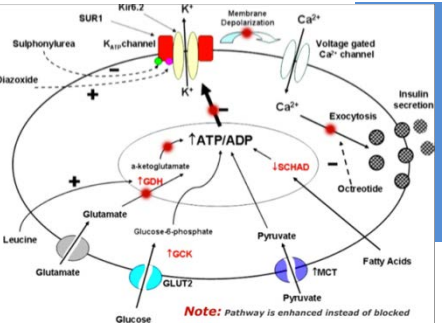
Fernández-Marmiesse A[1], Salas A, Vega A, Fernández-Lorenzo JR, Barreiro J, Carracedo A.

Hum Mutat. 2006 Feb;27(2):214.

- **The first mutations associated with HI were identified in the second nucleotide binding fold (NBF2) of SUR1 by Thomas et al. 1995**

- **The genetic causes of HI in Spanish population have not been completely studied and the molecular etiology of the condition remained unknown in most of Spanish patients**

- **The authors conducted extensive sequencing analysis of the ABCC8 (83.5Kb) and KCNJ11 (1.7Kb) genes in 34 Spanish HI Patients**

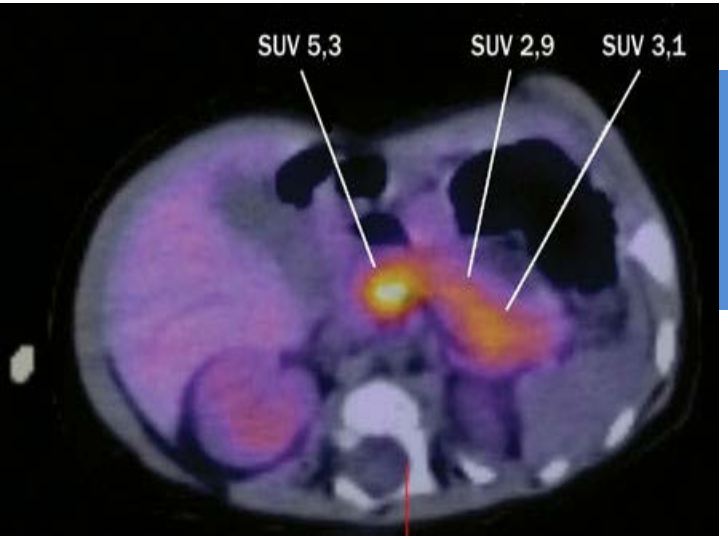


Mutation spectra of ABCC8 gene in Spanish patients with Hyperinsulinism of Infancy (HI).

- Origin: 6 from Galicia, 7 from Catalonia, 5 from Castella and 1 from Valencia, 1 Canarias, 1 Baleares, 1 Andalusian

- Mutations in ABCC8 were detected for both alleles in 13 patients while 10 patients carried only one mutation in one of the ABCC8 alleles.

- The authors suggested that some of these cases could be missed as focal forms of HI and pointed to an important underestimation of this HI type in our country (2006)



18 F-DOPA-PET-CT

18F-DOPA-PET/CT was first reported for the localisation of the focal lesion by Riberio et al in 2005 and Otonkoski et al in 2006

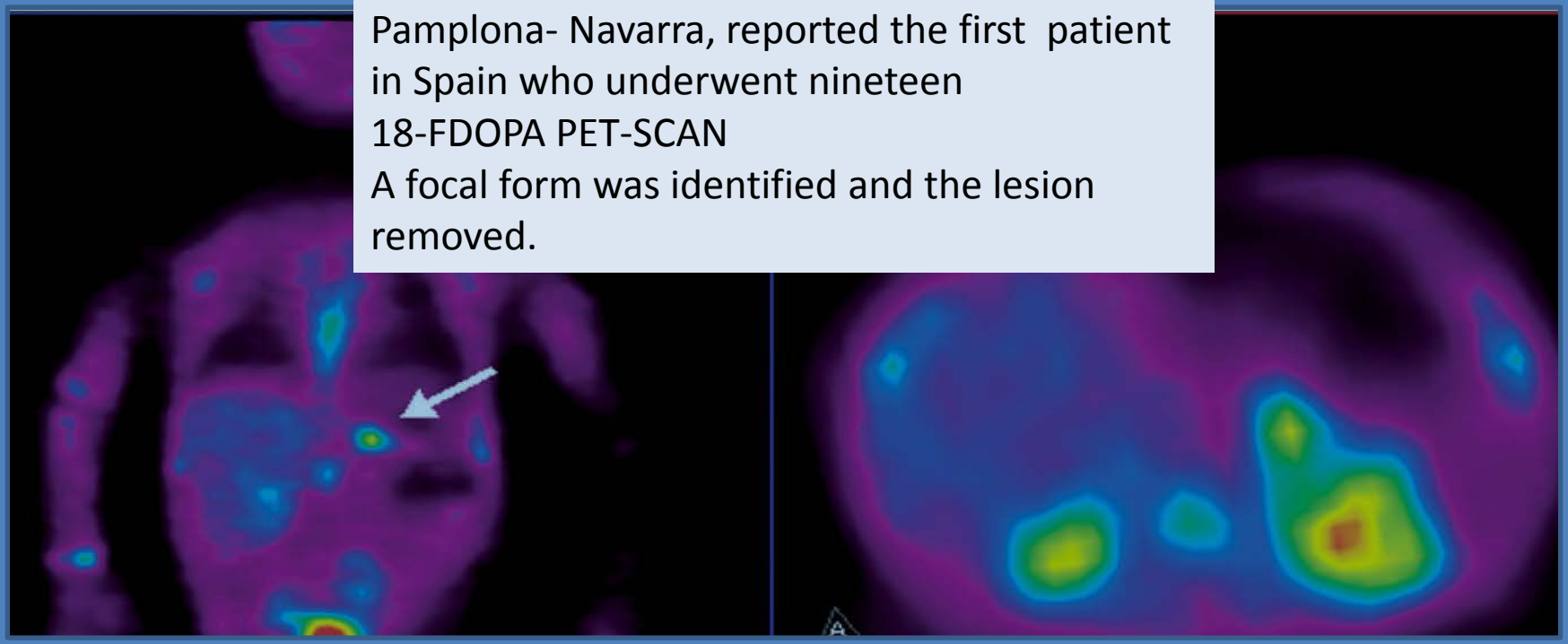
Sensitivity and specificity of 18 F-DOPA-PET/CT

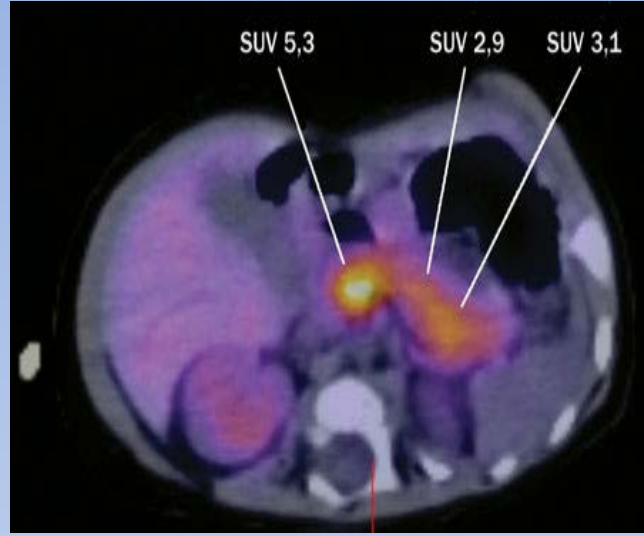
- A meta-analysis was performed and published recently by Yang J
- 10 studies were included involving 181 children
- The pooled sensitivity and the specificity in detecting focal CHI using ^{18}F DOPA PET and PET/CT was reported to be 88% (95%CI: 80%-94%) and 79% (95%CI: 69%-87%)

18F-fluoro-L-DOPA PET-CT imaging combined with genetic analysis for optimal classification and treatment in a child with severe congenital hyperinsulinism

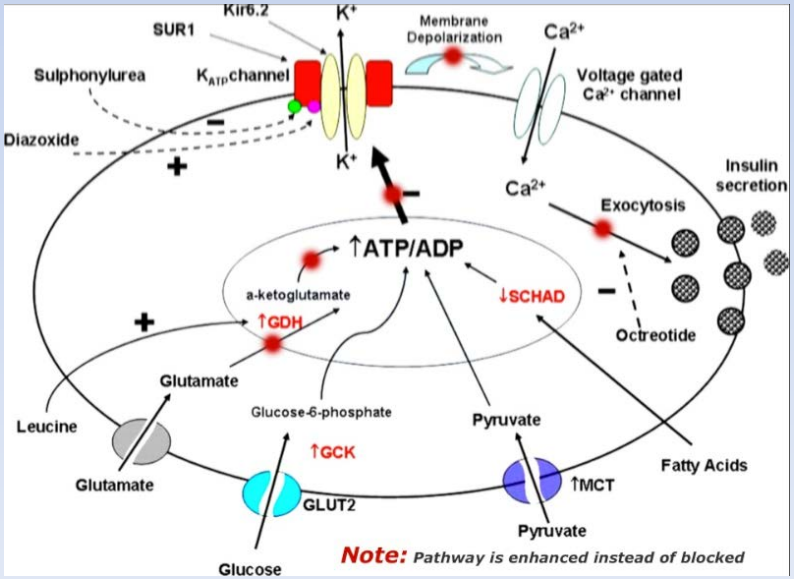
An Pediatr.2008;68:481-5 - Vol. 68 J. **Arbizu Lostaoa**,†, , A. Fernández-Marmiessec, P. Garrastachu Zumarrána, E. Martino Casadoa, C. Azcona San Julián, A. Carracedo, J.A. Richter Echevarría

Dr. Arbizu, radiologist from Clinica Universitaria Pamplona- Navarra, reported the first patient in Spain who underwent nineteen 18-FDOPA PET-SCAN
A focal form was identified and the lesion removed.





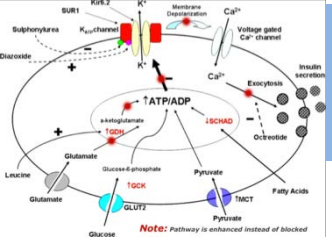
Congenital Hyperinsulinism: Present situation in Spain



Optimal strategy in CHI

The improvement in the understanding of the pathogenesis of CHI and the development of diagnostic modalities have helped in deciding the optimal management strategy for each patient

1) Molecular and pathological basis of CHI.
2) 18FDOPAPET/CT
3) Conservative treatment: diazoxide, octeotrid, lanreotide
4) Conservative surgery



European Journal of Endocrinology 2011
The contribution of rapid KATP channel gene mutation analysis to the clinical management of children with congenital hyperinsulinism

In 2011, Banerjee and colleagues from Manchester tried to identify prognostic factors

- for the probability of **remission**:

Positive correlation:

- responsiveness to diazoxide
- absence of identified gene mutations : 66 patients
  43 (65%) achieved remission, 22 (33%) were stable on medical treatment

- maternal heterozygous mutations were most likely to achieve remission (5/5, 100%).

No correlation:

- homozygous/compound heterozygous ABCC8/KCNJ11 mutations were more likely to require a subtotal pancreatectomy CHI (7/10, 70%)

Focal form: paternal heterozygous mutations were investigated with (18)F-Dopa PET-CT scanning and 7/13 (54%) had a focal lesion.

The probability of remission still remains difficult to predict despite having this deita

Therapeutical approach

Congenital Hyperinsulinism

Genetic analysis

Diazoxide Responsive

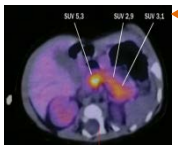
Diazoxide Unresponsive

Blood glucose monitoring at home
Nutritional management

Response
Octeotride +/-
Continous enteral dextrose

Unresponsive

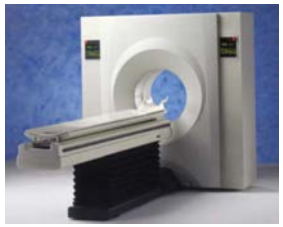
18 FDOPA



Focal o difuse

Surgery

PET-TC



For the realization of 18FDOPA PET/CT we need three elements:

- one a **PETSCAN**; currently we have one PETSCAN in nearly every principal city in SPAin

But we need two additional elements

- the isotope, **18FDOPA** is difficult to obtain due to its instability, its only procude in Pamplona and Malaga/Sevilla
- and the third and most important element is we need a **radiologist with experience in CHI**

ISOTOP 18 F DOPA

18 FDOPA PET- TC 2015

Distance between Madrid o Barcelona to Pamplona was 550 km with ambulance transport it requieres about 6 hours

Genetic laboratories

Hospital Cruces
ABCC8/KCNJ11
GCK
GLUD1

Hospital Clínico
Universitario
Santiago de Compostela
ABCC8/KCNJ11

Hospital Clínic
Barcelona UB
ABCC8/KCNJ11
GCK

Hospital la Paz
Biologia Molecular
U. Complutentese
GCK
KCNJ11

Hospital Carlos Haya
GCK

2015 CHI Spanish patients

Galicia
Hospital Universitario
Santiago Compostela
Hospital General Coruña

País Vasco
Hospital de Cruces

Cataluña- Barcelona
Sant Joan de Déu
Vall d´Hebro

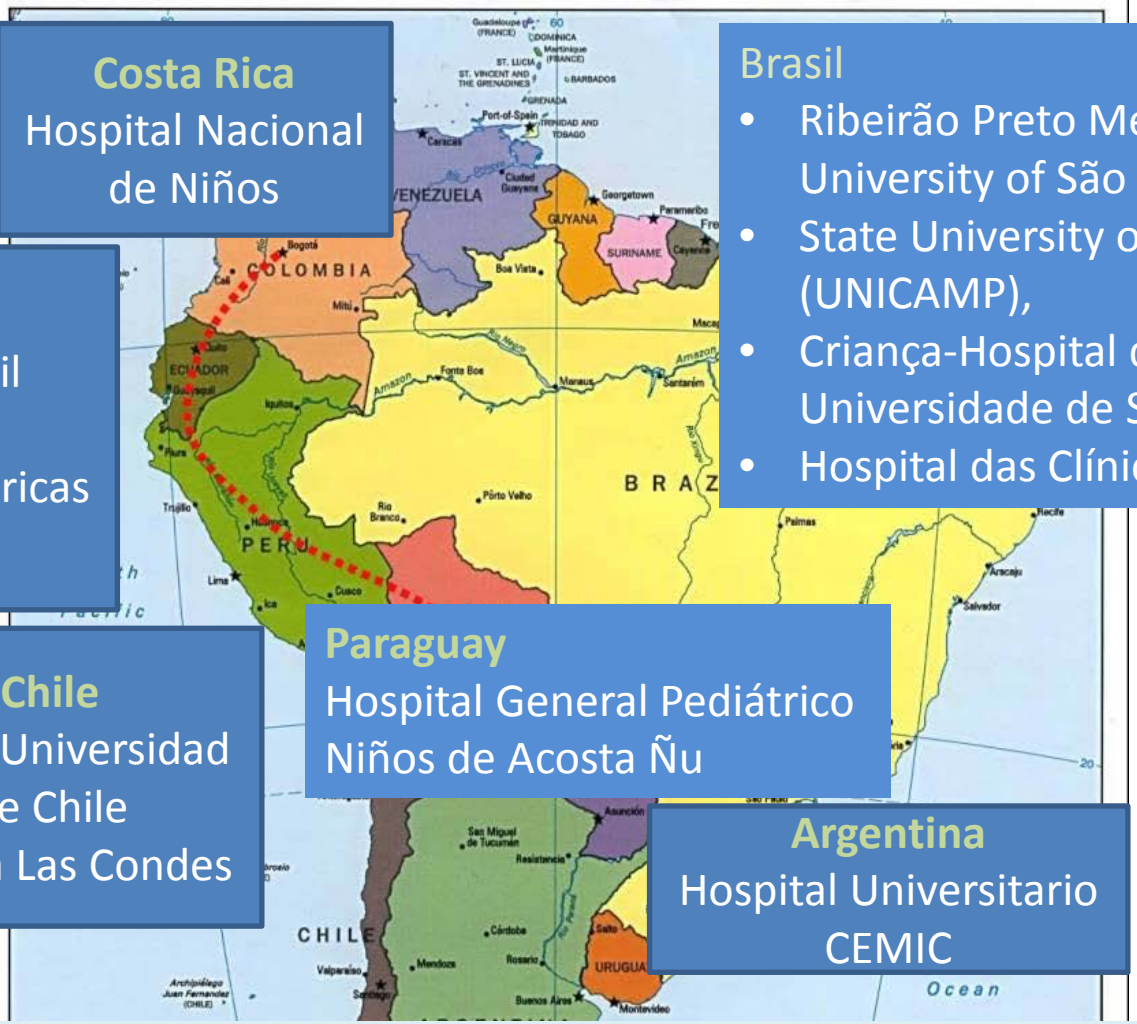
Madrid
Hospital La Paz
Niño Jesus

Islas
Baleares
Hospital Son Dureta

Islas Canarias
Hospital Universitario
De la Candelaria

Andalucía
Hospital Carlos Haya Málaga

At the moment we don´t have a national register of CHI in Spain, this meeting gives us the opportunity to share information between pediatric endocrinologist units. We have data from the biggest hospitals in Spain, some regional hospitals haven´t included their data, so a small number of



At present we have little information about CHi in South America. So we have invited our South American coligs to this meeting and they share some data with us.

In South America they haven't had the option of doing 18F DOPA PET-TC.

In Argentina Dra.Bastinello and coligs has started the realization of 18F PET-TC in Buenos Aires, they scanned 8 patients and identifed 2 focal forms

In addition, there are some economical restrictions in National Health Services to treat these patients and to do genetic studies

CHI Congenital Hyperinsulinism International

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SOUTH ATLANTIC OCEAN

WEDDELL SEA

THE WORLD