Rare liver diseases

EnprEMA – PEDDCReN
workshop
8th Dec 2015

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Medizinische Hochschule
Hannover

Conclusion

Early recognition of rare disease is paramount for positive outcome

Diagnosis and management of rare liver diseases require high degree of specialisation and expertise

Networking and exchange between specialised centres are mandatory for optimal patient management

Rare disease – definition: 1 : 2000

COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 11.11.2008
COM(2008) 679 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS

on Rare Diseases: Europe's challenges

Rare diseases are diseases with a particularly low prevalence; the European Union considers diseases to be rare when they affect not more than 5 per 10 000 persons in the European Union. This still nevertheless means than between 5 000 and 8 000 different rare diseases affect or will affect an estimated 29 million people in the European Union.

Adult experience

Liver disease in Europe

A. BURROUGHS* & D. McNAMARA†
*Liver Transplantation Unit, Royal Free Hospital, London; †Department of Gastroenterology, Adelaide and Meath Hospitals, Dublin, Ireland

Table 1. Standard death rates for men and women per 10 000 from chronic liver disease in Europe

Country	Men	Women
Belgium	14.2	7.5
Denmark	18.2	7.7
Germany	30.0	11.9
Greece	7.0	2.4
Spain	23.3	7.9
France	23.4	9.3
Ireland	3.7	3.1
Italy	23.5	11.5
Luxembourg	26.7	12.9
Netherlands	6.2	3.6
Austria	37.9	12.6
Portugal	35.3	10.9
Finland	17.6	5.6
Sweden	7.0	2.8
UK	9.6	5.5
Iceland	0.9	2.0
Norway	5.9	2.6
Switzerland	3.5	5.1

Prevalence/Incidence of liver disease

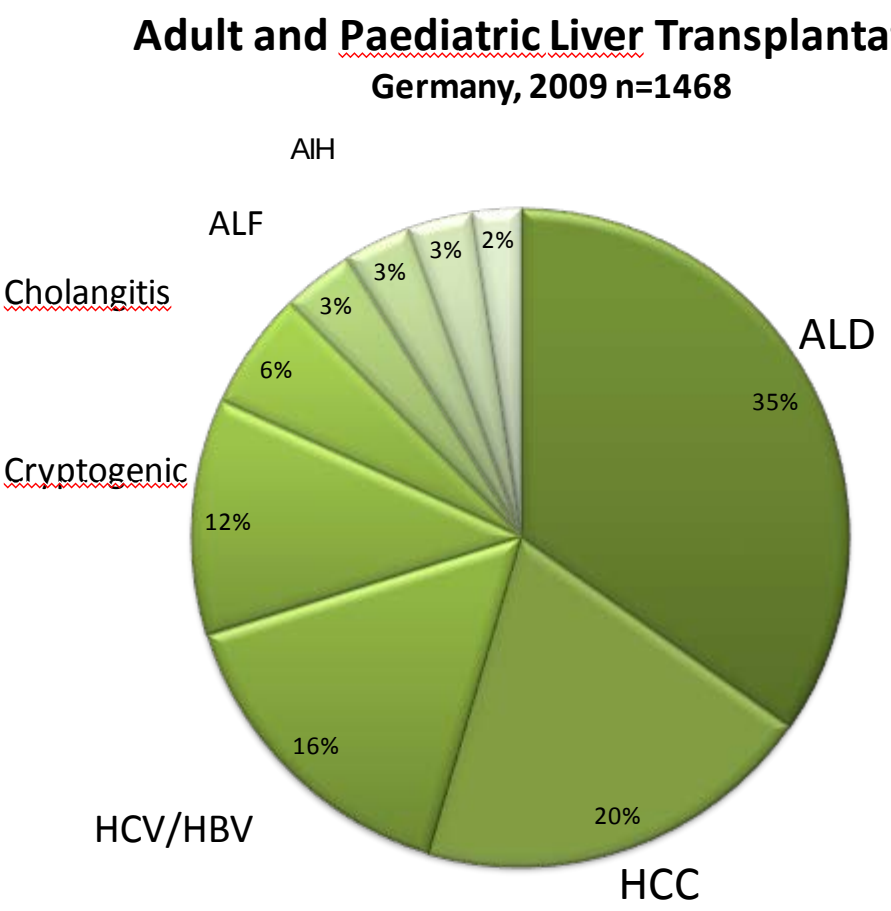
Alcoholic liver disease
4% Dionysos study, northern Italy

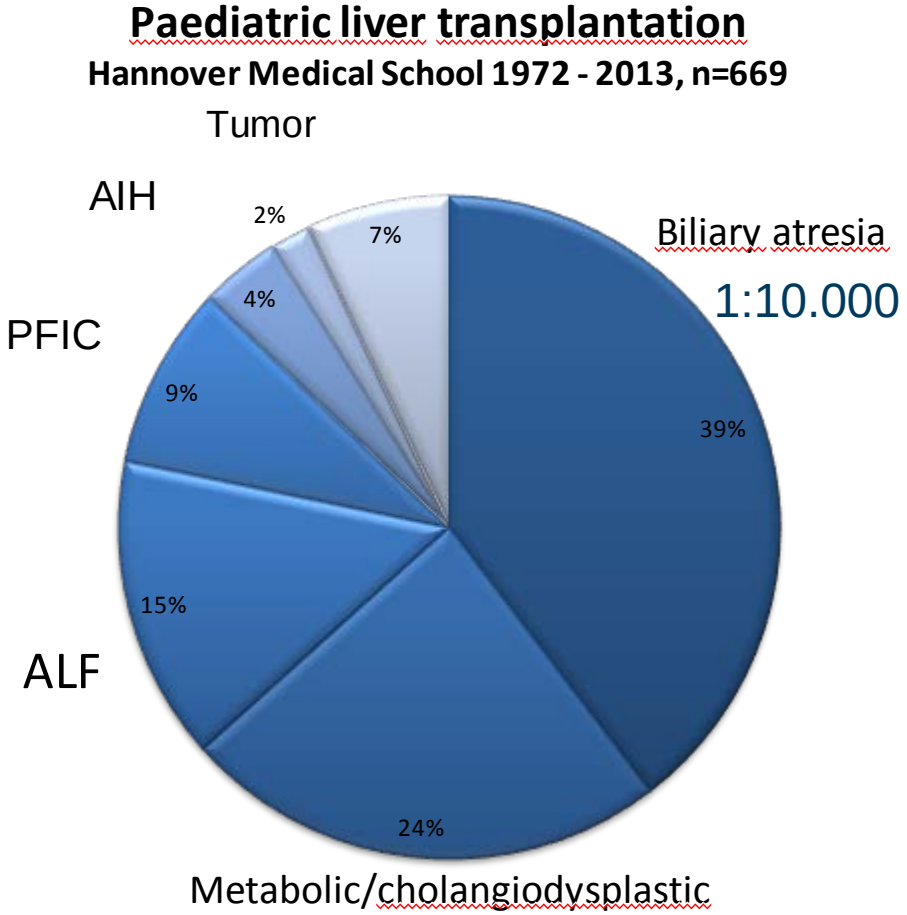
HCC: 25.000 new cases per in Europe

HCV 1 : 500
Hereditary hemochromatosis 1 : 1000

Aliment Pharmacol Ther 2003; 18 (Suppl. 3): 54–59.

Comparison: Indication for liver transplantation
adult and paediatric practice





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Comparison: Indication for liver transplantation
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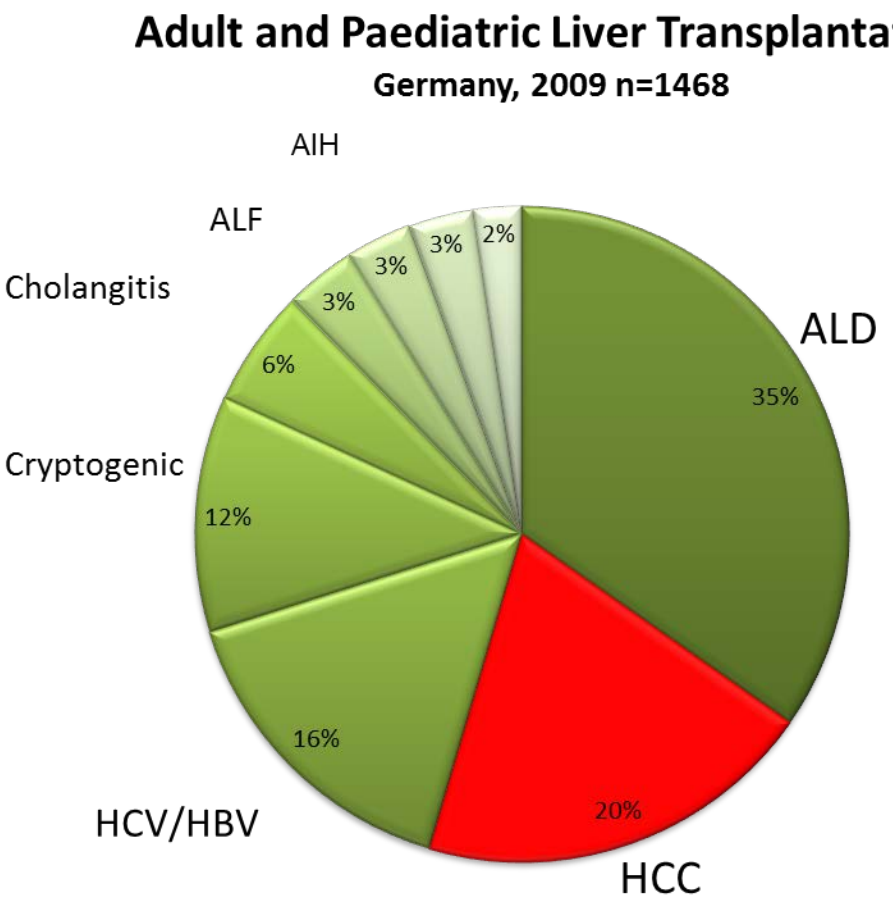

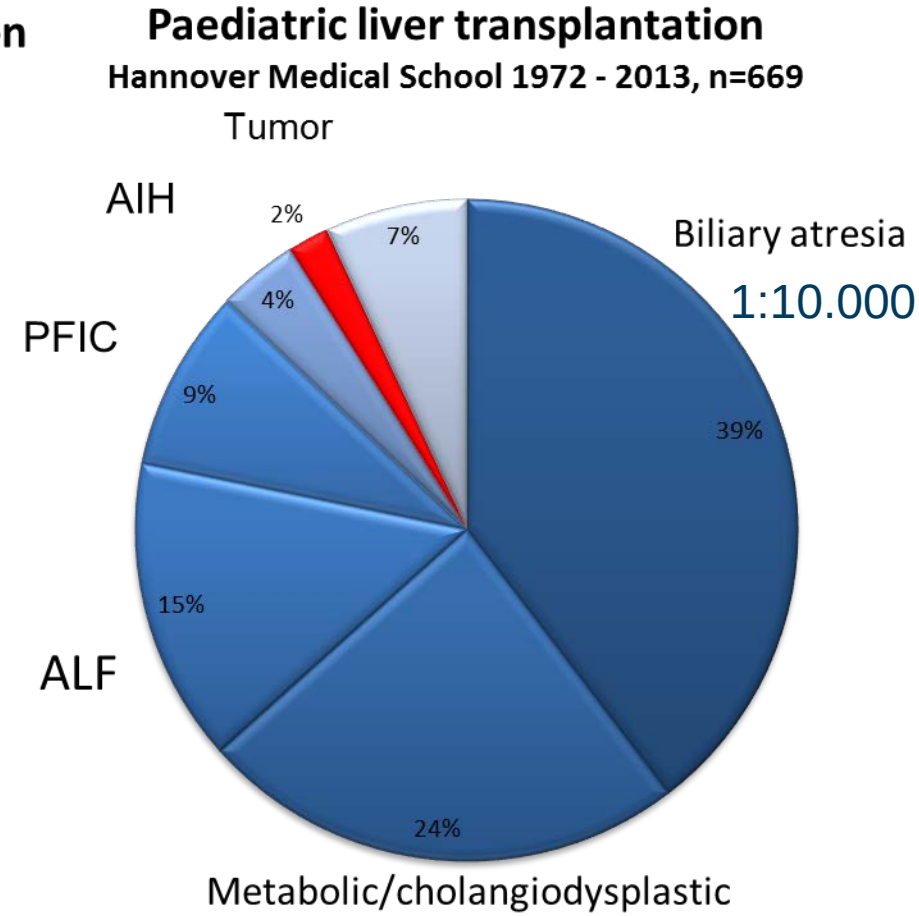

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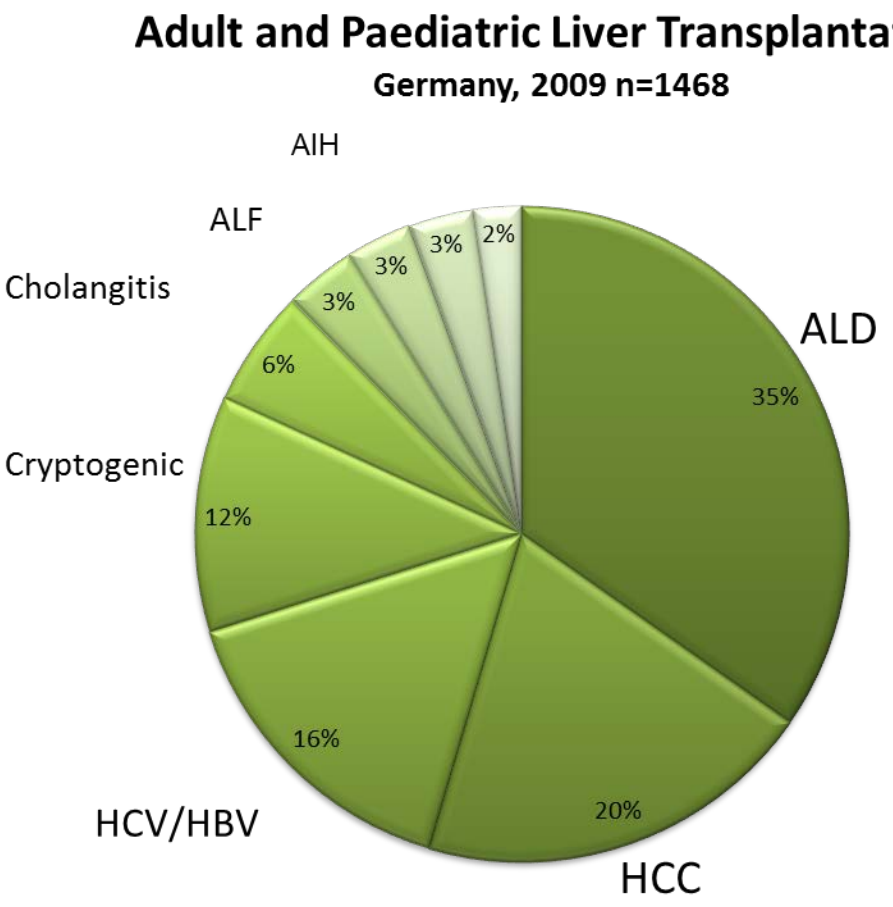

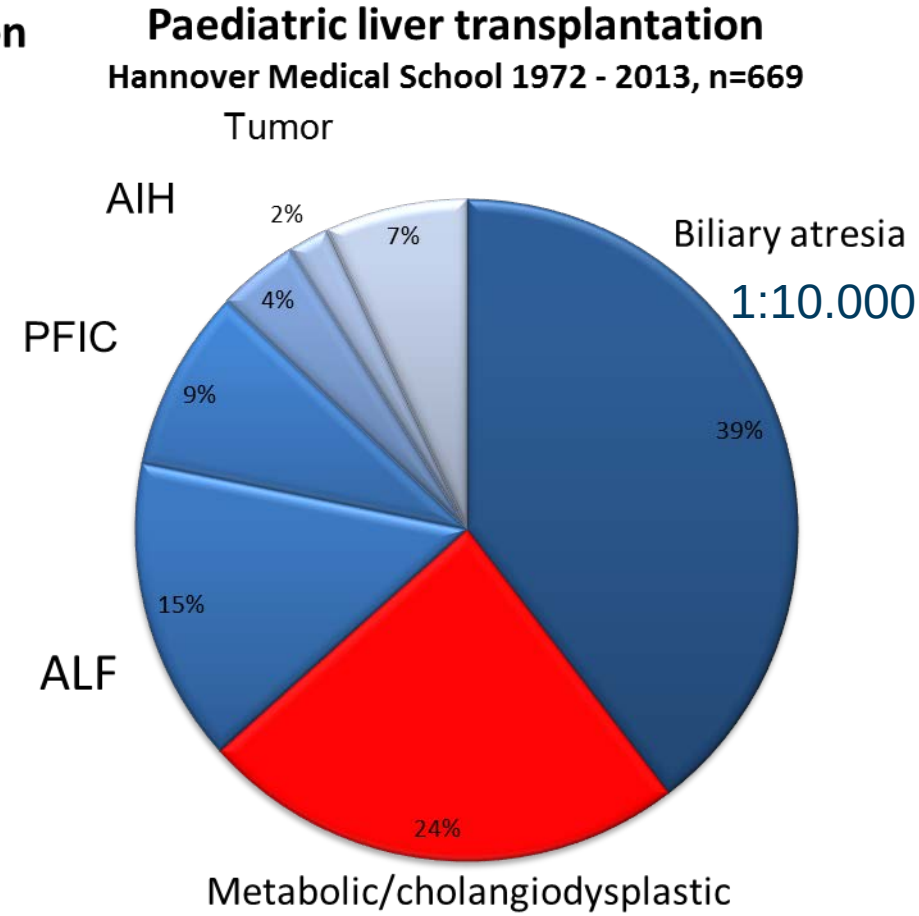

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Rare liver disease

- May be
  - metabolic
  - congenital
  - aquired
  - infectious
  - other

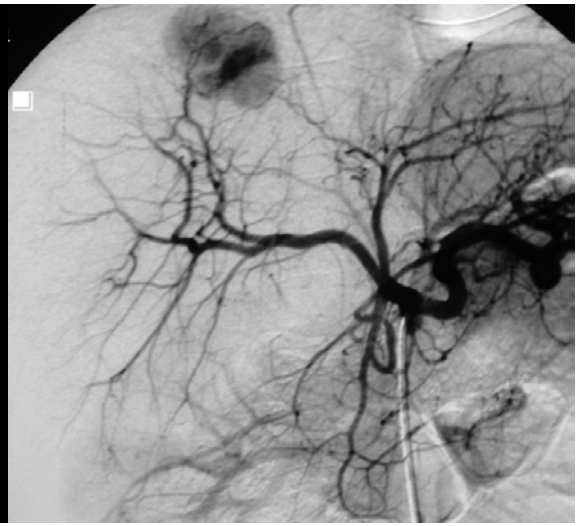
  is a diverse and heterogenous entity

How rare is rare….?

Biliary atresia
1 : 10.000

Tyrosinaemia Type 1
1 : 100.000

Crigler Najjar Syndrome
1 : 1.000.000



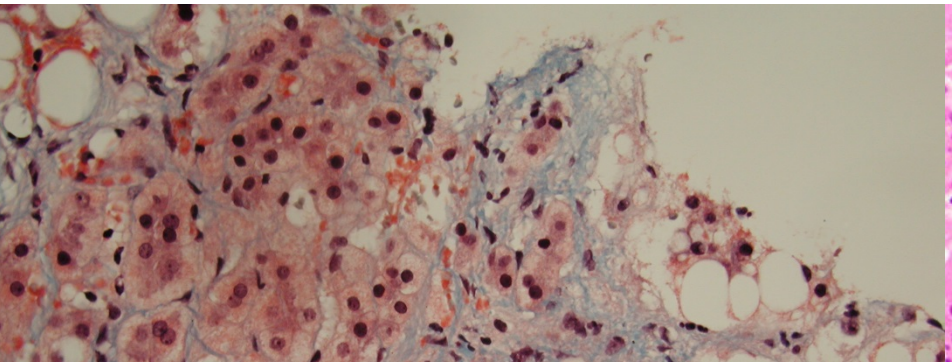
Liver-based metabolic disease

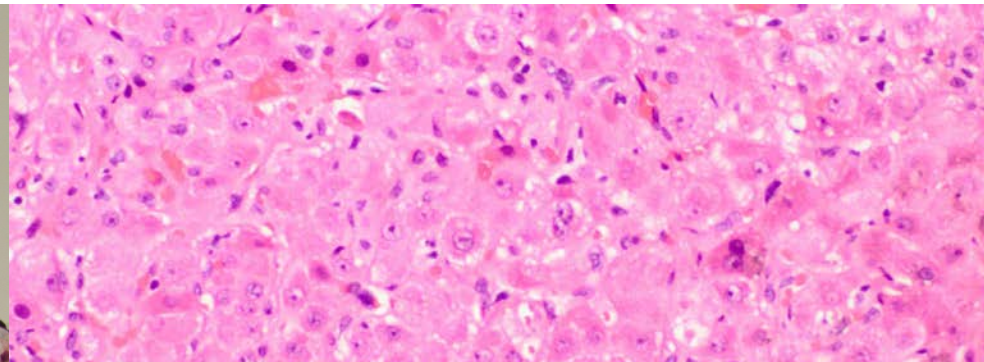
With structural damage to the liver

- Alpha-1-antitrypsin deficiency (1:2500)
- Tyrosinemia Type 1 (1:100.000)
- Bile salt export pump def.
- MDR3 deficiency (cumulative1:50.000)

Without structural damage to the liver

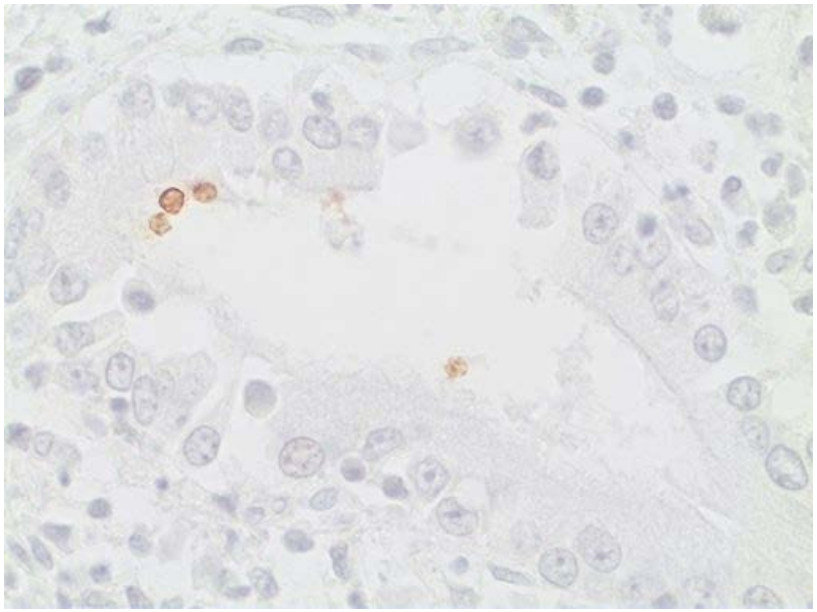
- Crigler Najjar Syndrome (1:100.000)
- Ornitine transcarbamylase def (1:14.000)
  Primary hyperoxaluria (1:100.000)

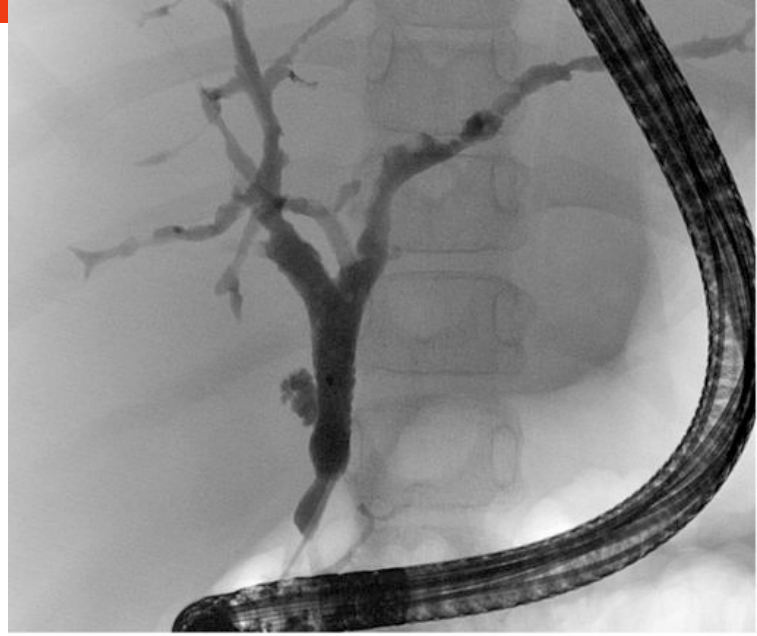


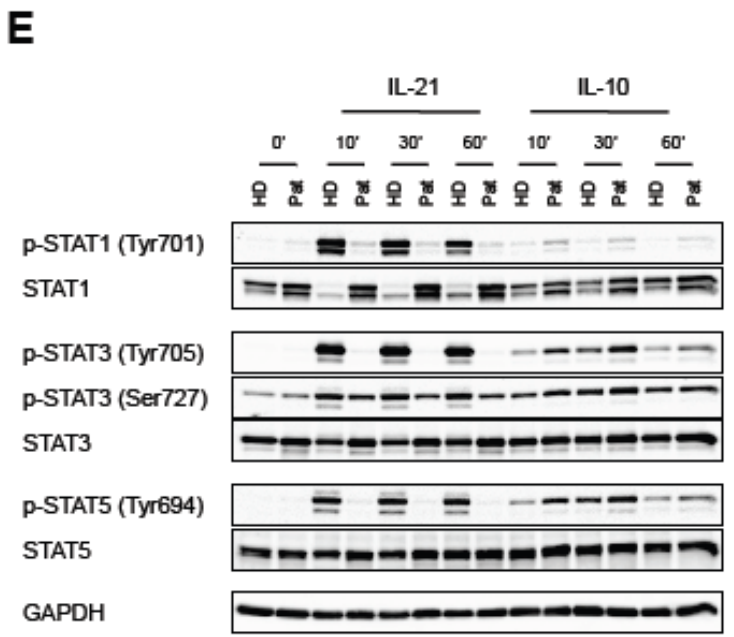


Once in a life time….?

IL-21 receptor mutation

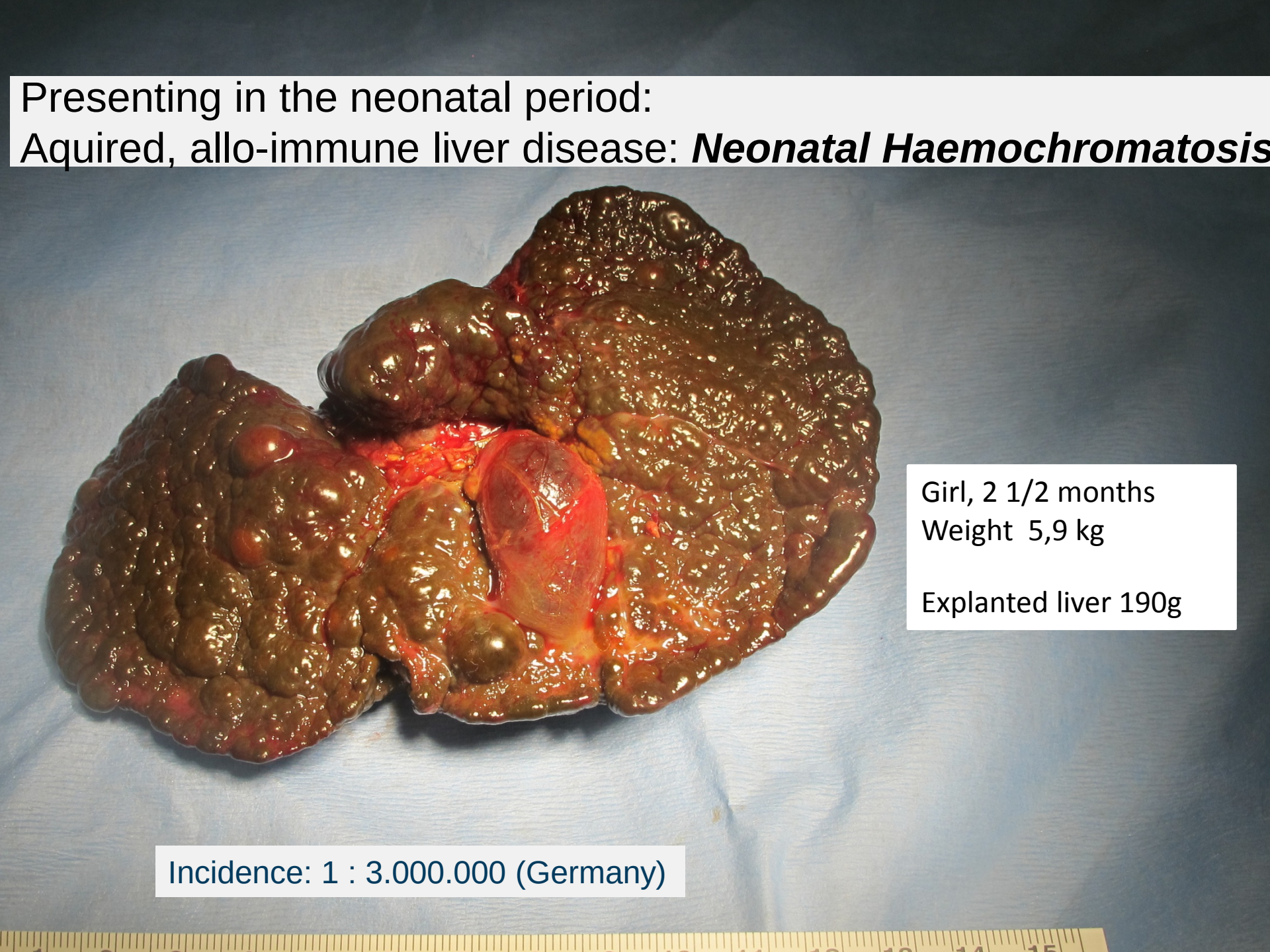






Kotlarz et al., 2011

Presenting in the neonatal period:
Aquired, allo-immune liver disease: ***Neonatal Haemochromatosis***

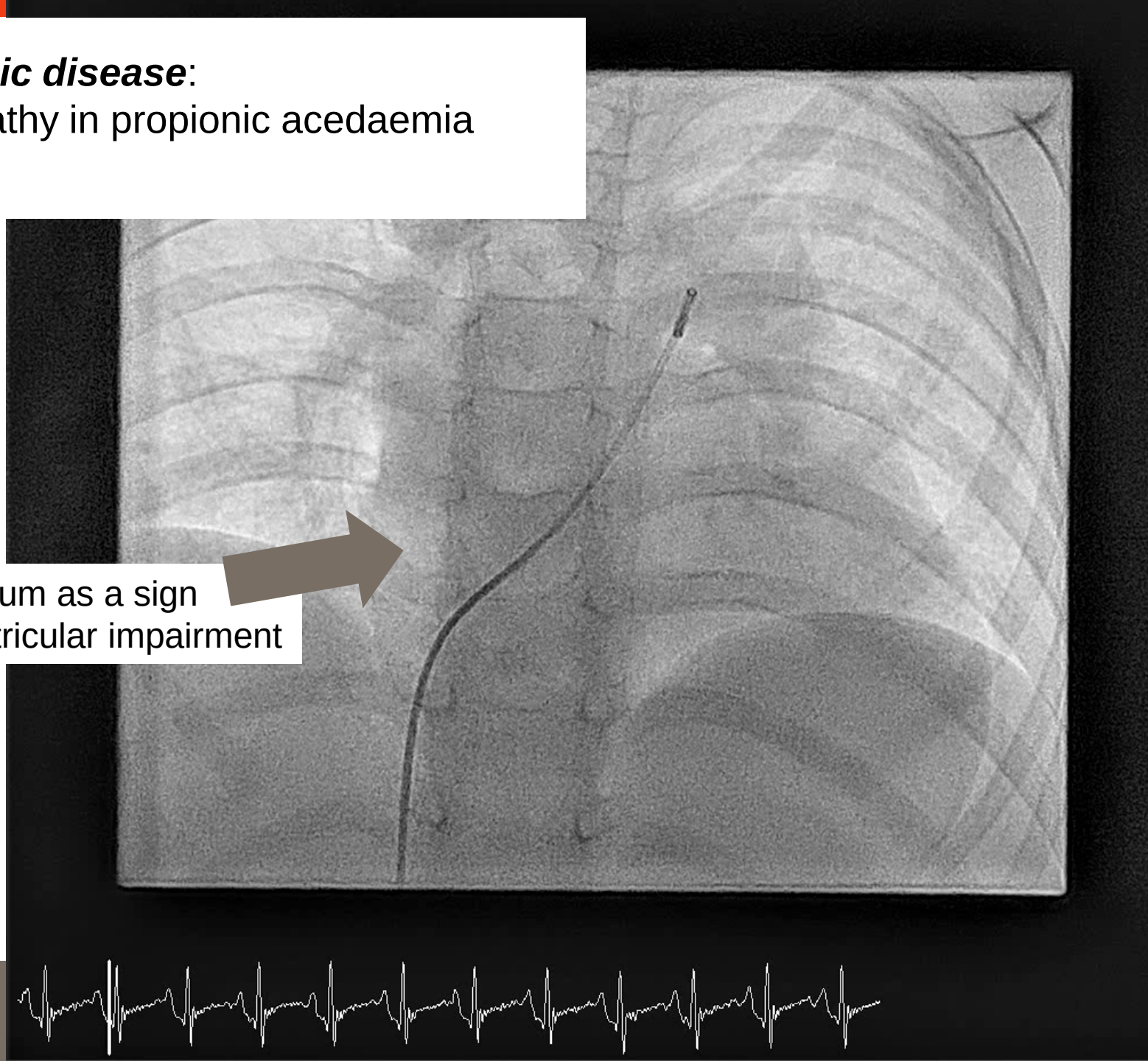


Girl, 2 1/2 months
Weight 5,9 kg

Explanted liver 190g

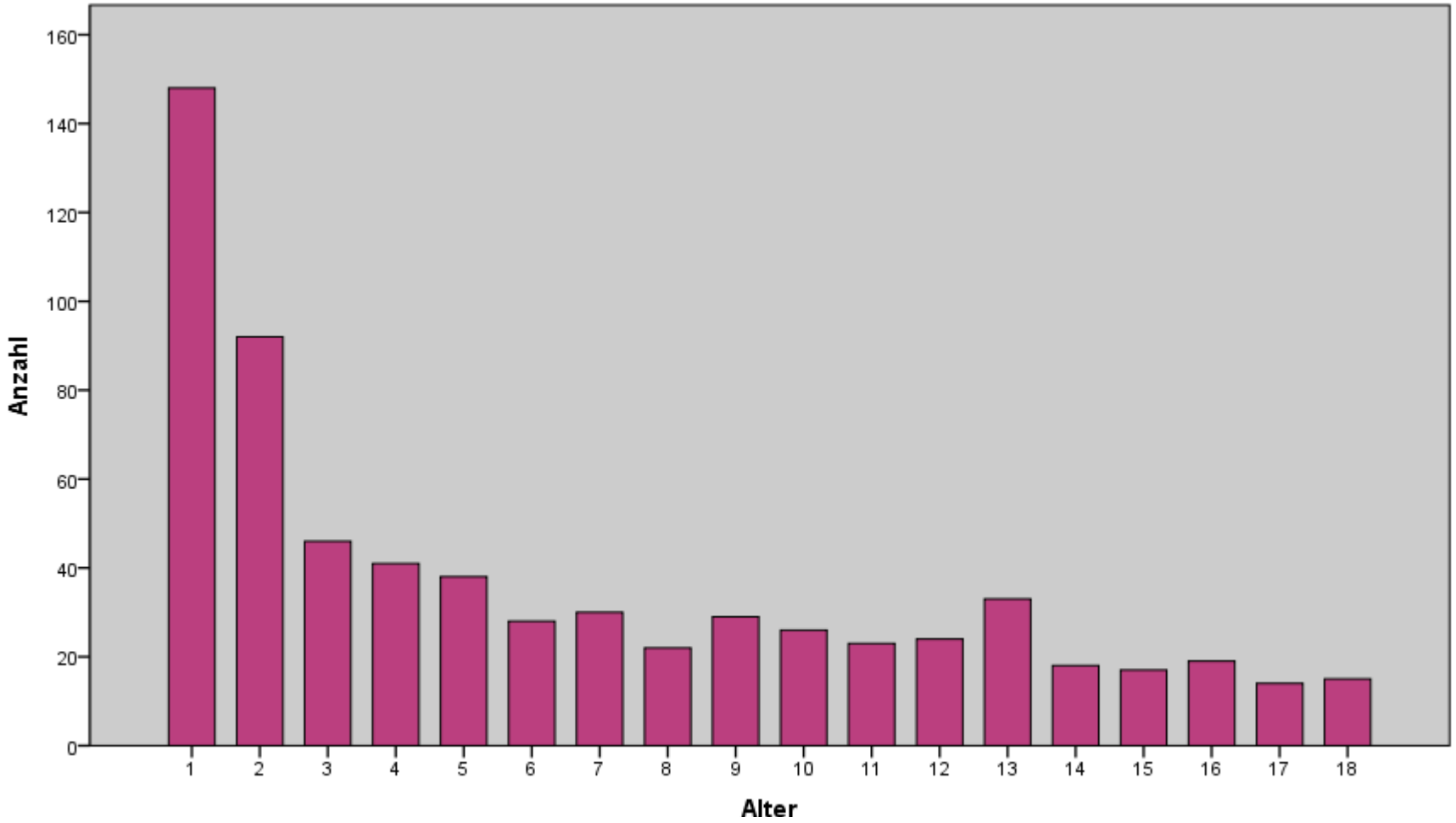
Incidence: 1 : 3.000.000 (Germany)

Multisystemic disease:
Cardiomyopathy in propionic acedaemia
1:150.000



Enlarged atrium as a sign
of right venntricular impairment

Age at liver transplantation, single centre experience
1972-2013 (n=669)



Transplantationsmedizin
2011, 23. Jahrgang

E.-D. Pfister, T. Becker, F. Lehner, U. Baumann
Die Auswirkungen der Organallokation auf die Wartezeit zur Lebertransplantation bei Kindern und ...

Paediatric Hepatology

- Small sub-subspecialty – distinct differences to adult hepatology
- Metabolic and congenital disease - with emerging new challenges
- Many small children – impact on interventions
- Focus on transplantation – centre based medicine
- Need for collaboration and networking

ESPGHAN

www.espghan.org

European Society of Paediatric Gastroenterology, Hepatology and Nutrition

Strengthening collaborative research

European Paediatric Liver Transplantation Network
EPLTN

ESPGHAN

European Paediatric Liver Transplantation Network EPLTN

EnprEMA

A network of European specialist centres for paediatric liver transplantation

Funding:

- Network grant ESPGHAN 2012

Aims:

- To foster excellence in research and clinical practice
- To obtain meaningful patient numbers

Current projects:

ChilSFree study

PLTQL study

Cardiovascular commorbidity trial

Adeno-associated virus vector-mediated liver gene therapy for Crigler-Najjar Syndrome

Bosma P[1], Junge N[2] , Labrune P[3], d'Antiga L[5], Brunetti-Pierri N[6], Ott M[2], Beuers U[1], Baumann U[2], Muro A[7], Mingozzi F*[4]

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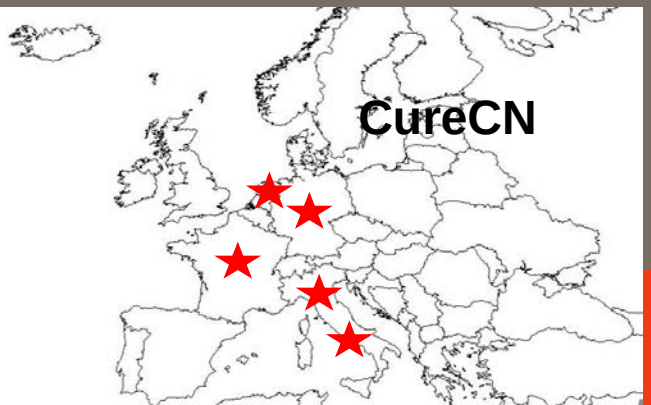
[4] Genethon, Evry, France; [5]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo;
[6]Department of Translational Medicine Federico II University, Napoli;
[7]International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

GPGE Jahrestagung Berlin 2015



Medizinische Hochschule Hannover

European reference networks

17.5.2014 EN Official Journal of the European Union L 147/71

COMMISSION DELEGATED DECISION

of 10 March 2014

setting out criteria and conditions that European Reference Networks and healthcare providers wishing to join a European Reference Network must fulfil

(Text with EEA relevance)

(2014/286/EU)

Conclusion

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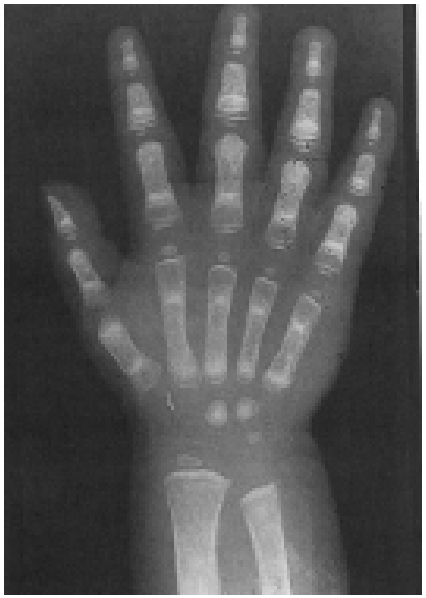
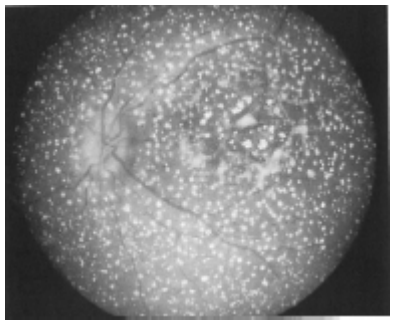
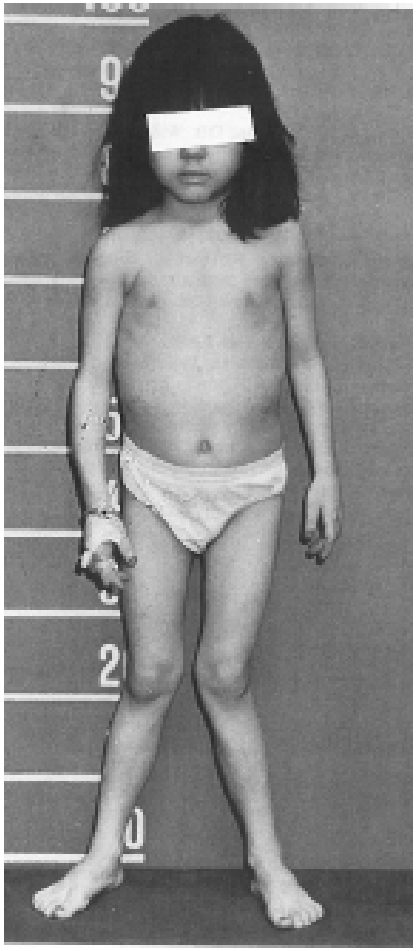
Primary hyperoxaluria, 1 : 100.000







Debilitating multisystemic oxalate deposits

Haffner et al., 1995