Comparative experience on Lysosomal diseases across Europe

VAINCRE LES MALADIES LYSOSOMALES
RARE MAIS PAS SEUL !

Membership Meeting 2013-DUBROVNIK 30 May -1June

EURORDIS
Rare Diseases Europe

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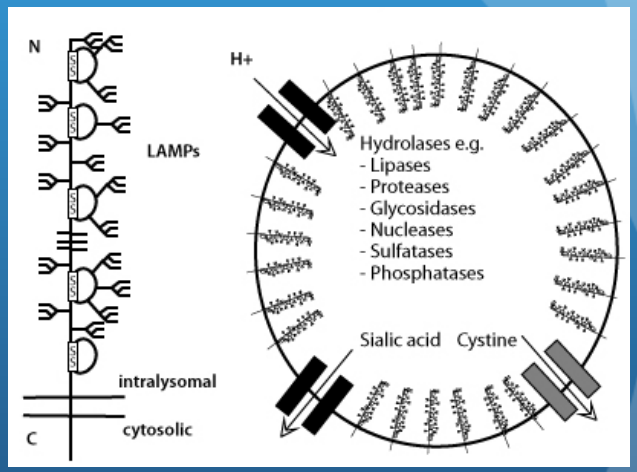
When should we screen?

- Important mortality and morbidity: cost of public health
- There are treatments
- Diseases have a recognizable latent or early symptomatic stage: improved survival
- Good screening tests: valid,reliable,efficient
- Acceptable: discomfort, cost of obtaining test
- Follow-up services: plan needed to deal with positiv results (Ann Jolly)

What are Lysosomal Storage Diseases (LSD)?

- More than 50 different genetic diseases
- Deficient activity of an enzyme in all the human cells or problem of transport across the lysosomal membrane
- Progressive conditions
- Usually asymptomatic at birth
- High morbidity
- Shortened life span



- Significant prevalence for LSDs together:1:4000-1:9000
- Diagnostic difficulties

Giugliani 2012

Why lysosomal disease could be a very good experiment field for screening ?

- **1990 : only 1 treatment, 2013 : 9 existing treatments (+ diverse ongoing trials to be completed)**

=> active and rapid research

- New protocols and **technologies that allow simplified screening (blood spot samples and tandem mass spectrometry)**
- **60 new cases in France every year, not too many, not too few**

=> important action, limited risks

- Degenerative aspects of lysosomal diseases

=> urgent actions **required**

- Cost of treating a patient vs cost of not detecting him

=> economic cost + patients quality of life

- Conclusion : ready to implement experiences on screening (newborn or genetic types) on lysosomal disease

LSD & NBS programs

- *R.Giuliani(2012) New born screening for lysosomal diseases: current status and potential interface with population medical genetics J Inherit Metab Dis 35:871-877*

Table 3 Selected pilot newborn screening programs carried out for lysosomal disorders

Disease	Country	Sample screened	Findings	Comments	Reference
Fabry	Italy	37,104 male newborns	12 affected (1/3,100) with α-gal A activity and GLA mutations	1 with the classic form, 11 with milder variants	Spada et al. 2006
Pompe	Taiwan	132,538 newbons	4 affected newborns detected	Similar number was detected on in the non-screened population (later diagnosis)	Chien et al. 2008
Fabry	Taiwan	90,288 male and 81,689 female newborns	73 males with low α-gal A activity and GLA mutations	86 % of affected males carry the late-onset cardiac variant mutation	Hwu et al. 2009
Fabry	Taiwan	110,027 newborns	45 neonates (3 females) with low α-gal A activity and GLA mutations	82 % of affected newborns carry the late-onset cardiac variant mutation	Lin et al. 2009
Krabbe	USA (New York)	555,000 newborns (data on Oct 2008, study ongoing)	10 with high to moderate risk for the early-onset form	4 considered high-risk for the early onset form	Duffner et al. 2009b
MPS VI	Brazil (Bahia)	298 newborns (data on August 2011, ongoing)	3 carriers detected by molecular analysis	High-incidence area with specific mutation	Bender et al. 2011 (personal communication)

LSD & NBS programs

LSD	Study in Austria N=34736	Previous selective studies
Gaucher	1/17 368 births	Ashkenazi Jews 1/800 births
Pompe	1/8684	Infantile: Taiwan,1/33000 Netherlands1/138000
Fabry	1 per 3859	northern Italy, 1/3100 for late-onset disease 1/ 37000 for the classic phenotype
Niemann-Pick A/B	Not found	1/250000

Thomas P Mechtler, Lancet 2012; 379: 335-41

The ongoing process of screening

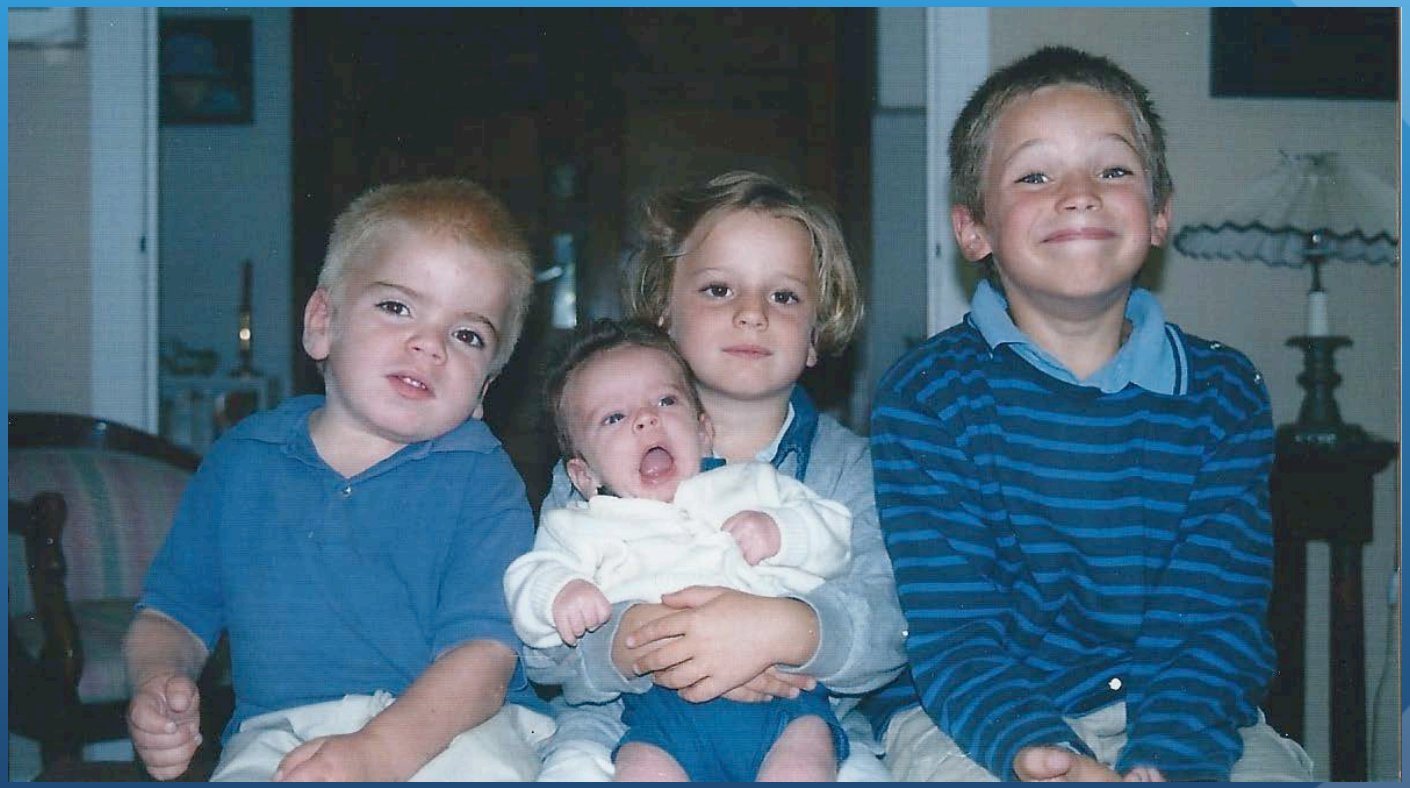
- Speed of scientific research,
- Society evolutions, laws and rules,
- Medical education for patients and doctors
- => The process has to be ruled but not constrained
  - Scientific research may accelerate
  - Society may be transformed under certain rules (Wilson and Jungner criteria)
  - Education in medical field is a long process
- => LSD are again a good experimental field (collaboration between patient organizations, centers of expertise, laboratories,multidisciplinary team)

How could we develop Rare Diseases screening in Europe?

- European level is the ultimate objective,
  - European Reference Networks (ERNs), standardization of international data bases, Community strategy to support member states, development of European guidelines on diagnostic tests or population screening, access for the treatments (equity)
- National level is a way to progress efficiently with coordination (EUROPLAN)
  - Adoption before the end of 2013 of national plans and strategies
- The process will have to include many fields such as ethical impact (informed consent for informed decision…), health economy, medicals and scientifics aspects, identification of areas with higher risk (customized screening program), genotype vs phenotype,biomarkers….
- Individual, society, humanity are the long term objectives
- => LSD might help us on this difficult path

Our childrens: they give sense to our engagement

M**ERCI**



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