

# Adrenoluekodystrophy (ALD) Newborn Screening Advisory Committee Recommendations

Dr. Diana Yu, Board Sponsor  
Tara Wolff, Policy Advisor

# Adrenoleukodystrophy

- Frequency  $\approx$  1:20,000 births
- X-linked peroxisomal disorder
- Defect in ABCD1 gene; many described mutations
- Defective metabolism of very long chain fatty acids (VLCFA)
- Affected boys have high plasma VLCFA; establishes the diagnosis

# X-ALD Phenotypes and their Relative Frequency

- Cerebral (35–40%)
  - Diffuse inflammatory demyelination with rapid progression.
  - Childhood form (onset 4–8 years) most common
- Adrenomyeloneuropathy (AMN) (40–45%)
  - Distal axonopathy mainly in spinal cord.
  - Paraparesis in young adults and progresses over decades
- Addison Disease only (20–30% at onset)
  - Most develop AMN later
- Asymptomatic
- >50% of heterozygous women develop ‘AMN’ in adult years

# Phenotypes: ALD

|  |                 |
|--|-----------------|
| Childhood Cerebral ALD (C-ALD)<br>2.75–10 years at onset; median age 7.2 years | 30 – 35%        |
| Adolescent Cerebral ALD; 11–21 years at onset                                  | 4 – 7%          |
| Adrenomyeloneuropathy (AMN)<br>Spinal cord disease (40% develop C-ALD)         | 40 – 46%        |
| Adult C-ALD alone  | 2 – 5%          |
| Addisonian Disease alone   | 50%             |
| Asymptomatic: Decreases with age   | Rare <40 of age |

# Childhood Cerebral ALD

- Initial normal development
- Onset between 4–10 years
  - Earliest 2.75 years,
  - Peak 7 years
- Initial presentation often subtle
  - May resemble ADHD and respond to stimulants
- Progresses rapidly to vegetative state
  - 1.9 years  $\pm$  2 years
- Adrenal insufficiency 85%



# Adrenal insufficiency (Addison disease)

- Primary adrenocortical dysfunction
- May present acutely or chronically
- Hypoglycemia
- Difficulty fighting infections
- Dehydration
- Hyperpigmentation (elevation in ACTH)
- Rarely low Na, high K
- A leading cause of adrenal insufficiency in males
- Majority will develop neurologic manifestations

# Current ALD Therapies

- Adrenal hormone replacement
  - Not to be overlooked
  - Life-saving and once instituted is life long
  - Stress dosing at times of illness and surgeries
- Preventative therapy with Lorenzo's oil
- Hematopoietic stem cell transplant (HSCT)
  - Early cerebral disease
- Gene therapy

# NY Experience to date

- Screened ~410,000 babies
- ~200, 000 boys
- 39 referrals
- 14 boys with ALD
- 18 female carriers
- 6 non-ALD cases

Questions?