Newborn Screening for Adrenoleukodystrophy in New York: Expect the Unexpected

Michele Caggana, Sc.D., FACMG
February 29, 2016
The Unexpected

1. Joe Orsini got travel approval at 10:47am Friday

2. He will be presenting on Pompe Disease!!
ALD Screening in NYS

- Aidan Seeger, a 7 year old from Brooklyn passes 4/29/2012
- Mrs. Seeger called in May 2012 to discuss screening
- Family garnered support: NY politicians; website; billboards
- Bill submitted August 2012
- Approved by Health Finance Committee 02/28/2013
- Became law 03/31/2013; start 01/01/2014 (actual 12/30/13)
Current New York State Assay
(Modified Krabbe and ALD)

Punch 3-mm specimen, add 200 µL methanol with d4-C26:0 LPC

1 hour extraction

Remove 50 µL of extract and combine with LSD extract

Analyze samples, 1.5 minutes per sample/Marker is C26:LPC

Follow screening algorithm
ALD Screening Algorithm

All specimens tested for C26:0 LPC

≥ 0.4 µM

< 0.4 µM

Second Tier HPLC C26:0 LPC

C26:0 LPC ≥ 0.4 µM

DNA testing
For information only

Screen
Positive/Referral

C26:0 LPC ≤ 0.24

Repeat < 0.24

Screen negative

Repeat C26:0
≥ 0.24 µM

C26:0 (0.24-0.39): Presumptive Positive/request repeat
Three Families Affected in Very Different Ways
Adrenoleukodystrophy Data


- 512,865 babies screened
- 262,499 males
- 250,366 females
Adrenoleukodystrophy Data

- 45 total referrals since 12/30/2013
- 22 girls and 23 boys

- 17 boys with ALD
- 19 carrier girls
- 1 carrier boy
- 5 Zellweger syndrome
- 1 Aicardi Goutieres syndrome
- 1 expired, likely PBD 1.79, 1.69
- 1 c.*8G>C only so far -- pending
Adrenoleukodystrophy Data

19 Mutations Known to Cause ALD

- p.Arg518Gln (carrier) – 2
- p.Arg591Gln (carrier) – 3
- p.Arg554His (ALD and carriers) – 2
- p.P623fs* – 2
- p.Q472Rfs*83 – 2

- 2 Polymorphisms -- *8G>C – very common
- 13 Novel (2 in one boy)
Hurry up, Burwell, lives are at stake

By Elisa Seeger

Sylvia Burwell, what are you waiting for?

Every 36 hours a baby in the U.S. is born with ALD or adrenoleukodystrophy, a treatable genetic disease that’s unnecessarily debilitating or fatal. It strikes one in 17,000 people, most severely boys and men, including my son Aidan.

He passed away on April 29, 2012 – just 11 months after being diagnosed too late. He was 7.

This mysterious and incurable brain disorder destroys myelin, the protective sheath surrounding the brain’s neurons, nerve cells that literally control our thinking and movement.

Initial symptoms are as common as withdrawal, vision and hearing problems, difficulty concentrating. Eventually, onset ALD results in blindness, deafness, seizures, progressive dementia, and eventually permanent paralysis or death.

The reason ALD’s ravages are so severe is because it’s usually not diagnosed in time, if at all.
THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

FEB 16 2016

Joseph A. Bocchini, Jr., M.D.  
Committee Chairperson  
Advisory Committee on Heritable Disorders in Newborns and Children  
5600 Fishers Lane  
Room 18W68  
Rockville, MD 20857

Dear Dr. Bocchini:

Thank you for your letter on behalf of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) regarding the ACHDNC’s recommendations to add X-linked Adrenoleukodystrophy (X-ALD) to the Recommended Uniform Screening Panel (RUSP) and the need for federal funding to support newborn screening for X-ALD.

However, I must bring to your attention a matter that has come to my attention. The coincidence of the date on which the RUSP was updated to include X-ALD on the very day that the Advisory Committee on Heritable Disorders in Newborns and Children met to discuss the matter is highly suspicious. This coincidence raises serious ethical and logistical concerns that must be addressed immediately. I request that you conduct a thorough investigation into this matter to ensure the integrity and fairness of the screening panel updates.

Sincerely,

[Name]

[Title]
Expected, But......
The Marty Luczak Story
The Unexpected

- Baby boy
- Long Island
- C26:0 – 0.38, 0.27
- DNA completed

c.-733G>C_c.-4_5delinsCCCCCGGCCCCT / *8G>C / Y
The Expected

- Boy undergoing surgery was spared adrenal crisis because providers knew he had ALD by screening
- Brothers were basis to identify other family members
- Sisters were basis to identify other family members
- We called referral for one family and they already had a strong family history
- Incidence is ~1/15,000 males; ~1/30,000 overall
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- Gerald Raymond, M.D.
- Ann Moser
- Inherited Metabolic Disease Specialty Care Center Directors
- Elisa Seeger
Thank You!!