Genetics and Ethical Dilemmas in Newborn Screening: A Case Of Isovaleric Acidemia

Maria C. Reyes
NURS 6033 & BIOL6903
December 8, 2010
Overview of IVA

• Background
• Organic Acid Disorder
• Build up of organic acids
• Organic acidemia
• Organic aciduria
• Prevalence
• (OMIM 243500)
• ICD-9-CM Code: 270.3
Overview

• Break down of Proteins
• Amino Acids
• Leucine
Nearly 3000 genetic disorders have been identified. Of the ... babies born in the United States each year, 2-3% have a major genetic or congenital disease. The average person has 4-8 potentially harmful genes." - Jerry L. Northern & Marion P. Downs
History of NBS

• 1957: Dr. Centerwall
• 1961: Dr. Guthrie
• 1963: NBS legislation in MA and OR
• 1965: Texas 59th Legislator
• 1997: NC begins piloting MS/MS
• 1999: NC and MA begin NBS with MS/MS
• 2000: WI begins MS/MS
• 2005: Texas HB790
Characteristics of the Disorder

- Poor feeding
- Vomiting
- Fussiness
- Seizures
- Lethargy
- Coma
- Death
Characteristic Signs of IVA

- Hallmark sign “Sweaty feet” Odor
- During Acute Illness
- Build up of Isovaleric Acid
- S/S in Childhood
- Development
- Triggers
- Asymptomatic
Pathogenesis of IVA

- $IVD$ Gene
- Leucine
- Isovaleryl-CoA Dehydrogenase Deficiency
IVD Gene

- Isovaleryl-CoA dehydrogenase
- Function
- Results
Location of the *IVD* Gene
Chromosome 15
Chromosome 15
Isovaleric Acidemia (IVA)

Normal

Protein from food

Protein from muscles

Amino Acids

Leucine

Other amino acids

Isovaleric acid

Isovaleryl CoA dehydrogenase enzyme

Energy Growth

IVA

Protein from food

Protein from muscles

Amino Acids

Leucine

Other amino acids

Isovaleric acid

Isovaleryl CoA dehydrogenase enzyme

Build up of Isovaleric acid + other harmful substances

Energy Growth

Health Problems
Genetic Inheritance

- Autosomal Recessive
- Mutations
- Chromosome 15
Autosomal Recessive

Autosomal Recessive Inheritance
Chances for each child when both parents are carriers

Carrier Father

Carrier Mother

Rr
Rr
Rr
Rr

R.R
R.r
R.r
r.r

Normal (25%)
Carrier (50%)
Has the disorder (25%)

Keys:
- R = working gene
- r = non-working gene
Recessive Mutation

mutation

No Disease

mutation

mutation

Disease
Diagnosis

- NBS
- MS/MS
- C5
- Isovaleryl-CoA Dehydrogenase
- 2-MethylButyryl-CoA Dehydrogenase
- Isovalerylglycine
- Prenatally
Second mass separation of fragment ions

Fragmentation of molecular ions

First mass separation of molecular ions

Ionization

Detection

Collision cell

Source

MS1

MS2
Mass Screening
How does MS/MS work?
Treatment

- Dietary Control
- Acute Therapy
- Glycine
- Carnitine
- Pediatric Metabolic Disease Specialist
- Dietician
Case Study

Jonathan Martinez 4 yrs 4mons. white Hispanic male
DOB: June 6, 2006
Ht: 41” 25%tile
Wt: 37 lbs 25%tile
Assessment: Isovaleric Acidemia-stable
Mom: Jennifer
Father: Juan
No siblings
Medical Home: Parra Pediatric Clinic
Specialist: UT Metabolic Clinic
Case Study Cont’d

PMH: Jonathan was diagnosed with Isovaleria Acidemia shortly after birth via NBS

Meds: Glycine po qd

SH: lives with parents, only child, attends prekindergarten 3 days a week

HPI: Well child exam; 4 yr old immunizations delayed due to URI last visit; Mom anxious about Jonathan starting all day prekindergarten in August

Plan: Kinrix, MMR, Varicella

Referral: psychology clinic
Cultural Considerations

- Cross-cultural care
- Hispanic culture
Ethical Principles of Newborn Screening

• Seriousness of genetic disorder
• Accuracy of Screening
• Treatment available
• Cost proportional to the benefit
• No unreasonable burden
Ethical Principles

• Quality of life
• Fair allocation of resources
• Beneficence
• Decision-making
• Autonomy
Stakeholders

- Child
- Parents
- Siblings
- School
- Healthcare Provider
Arguments For

• Benefits of NBS
• Quality of life
Arguments Against

- Expansion of NBS
- Reasonable allocation of resources
- Parental decision-making
- Eugenics
My Personal Stance

Beneficence
National Registry
Identification of genes that are responsible for inherited disorders has become commonplace, if not mundane; and genetic factors in common disorders are coming to light. The promise of genetics in medicine is still largely unappreciated, but this...is changing. Genetics used to be viewed as the discipline that studied rare disorders. Now genetics is recognized as an integral part of oncology,... cardiology and neurology; eventually it will leave no area untouched." -Bruce R. Korf
• National Newborn Screening Status Report
• Updated 08/02/10
• The U.S. National Screening Status Report lists the status of newborn screening in the United States.
• Dot "□" indicates that screening for the condition is universally required by Law or Rule and fully implemented
• A = universally offered but not yet required, B = offered to select populations, or by request, C = testing required but not yet implemented
• D = likely to be detected (and reported) as a by-product of MRM screening (MS/MS) targeted by Law or Rule
Resources

- Organic Acidemia Association
  http://www.oaanews.org
- Save Babies Through Screening Foundation
  http://www.savebabies.org/
- CLIMB (Children Living with Inherited Metabolic Disorders)
  http://www.climb.org.uk
- National Coalition for PKU and Allied Disorders
  http://www.pku-allieddisorders.org/
- Genetic Alliance
  http://www.geneticalliance.org/
- Isovaleric Acidemia: A Guide for Parents (PacNoRGG publication)
  http://www.westernstatesgenetics.org/pacnorgg/PDFs_all-081409/isovaleric_eng.pdf
Expanded Newborn Screening Using Tandem Mass Spectrometry
Financial, Ethical, Legal and Social Issues (FELSI)
Newborn Screening: Toward a Uniform Screening Panel and System > Report for Public Comment > Executive Summary
Effect of Expanded Newborn Screening for Biochemical Genetic Disorders on Child Outcomes and Parental Stress
Resources

- **MORE INFO ABOUT IVA**

  *Isovaleric Acidemia: A Guide for Parents*
  Sponsored by the Pacific Northwest Regional Genetics Group (PacNoRGG). Univ of WA, Seattle.
  *'Acidémia Isovalérica - Una Guía para los Padres'*

Other publications by PacNoRGG Organic Acidemia Association (OAA)
- **IVA Support Organization**

  *Isovaleric Acidemia: An Organic Acid Disorder*
  Supplied by Save Babies Through Screening.

**PEDBASE: Isovaleric Acidemia**

**Is Isovaleric Acidemia Treatable?**
Answers to a few questions about IVA and its ability to be treated.
References

Genetics Home Reference: Isovaleric acidemia

Isovaleric Acidemia: A guide for parents. n.d. Regional Genetics Group

Newborn Screening Coding and Terminology Guide: Isovaleria Acidema


References
