Outline

- Introduction to Niemann-Pick
- Etiology
- Genetic Factor
- Nutrition Component
- Intervention
- Conclusion
What is Niemann-Pick?

- Group of genetically inherited diseases
- Lipid Metabolism Disorder (Lysosomal Storage Disease)
- Prevalence

- 4 subtypes
  - Type A/B: Accumulation of sphingomyelin within the organs and CNS
    - **Type A:**
      - **Dx:** Infancy - 3 years, Death within 3 years of diagnosis
      - **Neurological Function**
      - **Physical Manifestations:** FTT
      - **Chronic features:** n/a
    - **Type B:**
      - **Dx:** mid-childhood but survive through adulthood
      - **Non-Neurological**
      - **Physical manifestations:** short stature and slowed bone mineralization (McGovern & Schuchman 2014).
      - **Chronic features:** lung infections and low number of platelets

Word of the Day

*Sphingolipid*
What is Niemann-Pick?

**Type C1/C2:** Different pathology than A & B
Accumulation of cholesterol absorption in the intestinal tract

*Increased synthesis of endogenous cholesterol & Increased absorption*
(via 3-hydroxy-3-methyl glutaryl co-enzyme A reductase) (Tomkin, 2015).

- **Dx**
  - Childhood through Adulthood
  - Develop into adulthood
  - Deteriorating quality of life

- **Physical Manifestations**
  - Ataxia & dystonia
  - Liver disease and pulmonary disease
  - Dysphagia & dysphasia
Etiology

- Autosomal recessive disease
  - Type A: Mutations in the SMPD1 Gene
    - Ashkenazi Jewish Population
    - Maternal Expression
  - Type B: Mutations in the SMPD1 Gene
    - Heteroallelic Variation
  - Type C1: Mutation in the NPC1 Gene on Chromosome 18
  - Type C2: Mutation in the NPC2 Gene on Chromosome 14
Genetic Factors- Type A & B

- **Type A**
  - Identifiable SNP’s (23andme)
  - Prenatal Testing/Infancy

- **Type B**
  - Heteroallelic R496L
  - 3 base deletion
  - Detectable in early childhood

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<thead>
<tr>
<th>Gene</th>
<th>Phenotype</th>
<th>Type/SNP</th>
<th>Genotype Risk</th>
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<tbody>
<tr>
<td>SMPD1</td>
<td>NPD A</td>
<td>i4000381/L302P</td>
<td>CC</td>
</tr>
<tr>
<td>SMPD1</td>
<td>NPD A</td>
<td>i4000383/fsP330</td>
<td>n/a</td>
</tr>
<tr>
<td>SMPD1</td>
<td>NPD A</td>
<td>i4000430/R496L</td>
<td>Heterozygous Mutation</td>
</tr>
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(Genetics Home Reference, 2018)
Genetic Factors - NPD Type C

- **Type C1**
  - Chromosome 18
  - Heteroallelic
  - Dx at any age
  - Proposed 40 SNPs

- **Type C2**
  - Chromosome 14
  - Homoallelic
  - Dx at any age

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<tr>
<td>NCPC1</td>
<td>NPD C1</td>
<td>rs1631685, rs1788799, Rs18050810, I1061T</td>
<td>Heterozygous Mutation</td>
</tr>
<tr>
<td>NCPC2</td>
<td>NPD C2</td>
<td>Rs8008640, Rs917394</td>
<td>Homozygous Mutation</td>
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Both forms of Type C are *diagnosable* by the Sanger *Sequencing* of the NPC gene.

- Polymerase chain reaction (PCR) to target the 30 coding exons, and intron-exon boundaries, of the NPC1 and NPC2 genes.
- Next-generation sequencing available
- *Not all variations have been documented to date*
NPC Suspicion Tool

(Papandreou & Gissen, 2016)
Nutrition Component

- Ultimate Goal: Holistic Care
- Management of Care in the Feeding Team:
  - GI (Constipation, GERD)
  - Speech/Oral Pathology
  - OT/PT
  - Genetic Counseling
  - Visits with an RDN!

Role of an RDN as part of the care team: Provide MNT and Improve Quality of Life

- Type A: Managing FTT, providing prescribed nourishment and nutrient delivery
- Type B: Proper Growth, feeding habits, monitor routine bloodwork
- Type C: Weight Maintenance, Altered Caloric Needs, Nutrient Delivery
Nutrition Intervention” Dietary Rx

- No known diets to prevent or manage disease

For a adult patient with NPD B/C and ability to self-feeding:
- Adequate intake of Energy-dense (plant-based) foods
- Lower cholesterol food
- High fruits and vegetable intake
- Proper Hydration
- Calcium and Vitamin E supplementation
- Cooking with Spices

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<th>Nutrient</th>
<th>Intervention &amp; Proposed Effect</th>
<th>Conclusion</th>
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<tr>
<td>Curcumin Supplementation</td>
<td>Elevates cytosolic calcium in vitro, normalize NPC1 disease cellular phenotypes</td>
<td>• prolong survival of NPC mice</td>
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<tr>
<td>Calcium Supplementation</td>
<td>Accumulation of excess cholesterol and glycosphingolipids in the acidic compartment of NPC cells may be caused by the depletion of calcium.</td>
<td>• effective</td>
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<td>Cholesterol Restriction</td>
<td>Dietary cholesterol restriction to lower accumulated cholesterol</td>
<td>• nontoxic</td>
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<td>Vitamin E Supplementation</td>
<td>Reduce the subcellular stress in NPC patients as NPC fibroblasts have higher levels of reactive oxygen species</td>
<td>• increases survivorship in NPC mice</td>
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<td>Ubiquinone (Co-enzyme Q10)</td>
<td>Markedly reduced in NP-C patients</td>
<td>• treatment delayed weight loss in female NPC mice</td>
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<td>• resulted in slight improvement in Rota-rod performance</td>
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<td>• results indicate the treatment has little benefit since CoQ10 barely passes the blood–brain barrier</td>
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Conclusion

- NPD has no current cure or medical nutrition therapy plan
- KEY: Early detection by of advancement screening and profiling
- RDN can provide a better quality of life to a patient with NPD by:
  - frequent assessment of caloric intake
  - delivery of nutrients
  - low cholesterol and supplementation
  - Prevention of Malnutrition
References


