REFSUM DISEASE
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President and Founder of Global DARE Foundation & ULF Board Member
Discussion Topics

- Provide a high-level overview of Refsum Disease
- Kristie’s Refsum Journey
- Establishing Global DARE Foundation & Refsum Advocacy
- Discuss our Medical & Research objectives
What is Refsum Disease?

- Adult Refsum disease is a metabolic disorder caused by a few faulty genes (principally PHYH) which affects the pathway that breaks down phytanic acid.
- Phytanic acid is not produced in the body but found in many foods.
- The highest concentration of phytanic acid is found in dairy products, beef, lamb and some fish.
- In Refsum patients phytanic acid accumulates in nerves, liver and fat tissues.
- Refsum disease can be life threatening if undiagnosed. Therefore, early diagnosis is very important.
Pathophysiology of Refsum Disease

- Peroxisomal disorder
- Autosomal recessive (prevalence 1:10^6)
- 90% due to deficiency in phytanoylCoA hydroxylase (Chr 10p13)
- 5% due to variants of rhizomelic chondrodysplasia punctate (RCDP) due to defect in import of PTS-2 signal containing enzymes into the peroxisome
- 5% due to alpha-methyl-acyl racemase (AMARC) or PHARC deficiency or unknown
<table>
<thead>
<tr>
<th>What are the primary symptoms?</th>
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<tr>
<td><strong>Retinitis Pigmentosa</strong></td>
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<tr>
<td>(Loss of Vision)</td>
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<td><strong>Anosmia</strong></td>
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<td>(Loss of Smell)</td>
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<tr>
<td><strong>Peripheral Neuropathy</strong></td>
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<td>(Nerve pain, numbness)</td>
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<td><strong>Hearing Loss</strong></td>
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<td><strong>Cerebellar Ataxia</strong></td>
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<tr>
<td>(balance issues)</td>
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<td><strong>Skeletal Dysplasia</strong></td>
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<td>(Bone changes)</td>
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<tr>
<td><strong>Ichthyosis</strong></td>
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<tr>
<td>(itchy scaly skin)</td>
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<tr>
<td><strong>Cardiac Arrhythmias</strong></td>
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<td><strong>Weakness</strong></td>
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Disease Course in Refsum Disease

Wierzbicki AS et al, J Neurochem 2002
Clinical Features of Refsum Disease
What are the current treatments?

**Low Phytanic Acid Diet**

- A strict diet low in phytanic acid is used for long-term management. This diet includes the removal of foods that are high in phytanic acid such as dairy products, beef, lamb and some fish.
- Dietary restriction of phytanic acid intake helps lessen or resolve ichthyosis, sensory neuropathy, and ataxia. It is suspected to slow the progression of vision and hearing loss.

**Plasmapheresis or Lipid Apheresis**

- A dialysis-type process that is the direct removal of phytanic acid in the blood
- It is typically used in acute management of people hospitalized as a result of Refsum disease where it helps to resolve acute heart arrhythmias or extreme weakness.
- It may be done on a chronic regular basis in some patients whose phytanic acid levels do not fall sufficiently on diet.

**Symptom management**

- Symptom management could include cataract surgery, eye drops, hearing aids, cochlear implants, skin lotions, pain management, knee replacement, heart and liver transplant
Kristie’s Refsum Journey

Strong & Healthy
• 2010-2013 started a plan to lose weight and exercise. Lost 75lbs.
• No medical issues except minor hip pain and chronic migraines
• Became an Ironman level Triathlete
• Started a low carb nutrition plan in 2017

Deteriorating Health
• Neuropathy, leg pain & vision issues
• No longer able to ride & run
• 15 specialists and countless diagnostic tests plus surgery
• Something was “wrong”
• I never gave up on a diagnosis

Diagnosis & Navigating
• 2019 finally was diagnosed through genetic testing
• Struggled to navigate post diagnosis
• ULF, Global Genes and NORD were awesome resources
Global DARE Foundation's mission is to promote world-wide awareness and better quality of life for all who are diagnosed with Adult Refsum Disease.
Global DARE Foundation’s Board of Directors are part of the Refsum Disease Community and are highly motivated to do whatever it takes to find better therapeutic methods and ultimately a cure.
OUR KEY ACCOMPLISHMENTS TO DATE

**OCT 2019**
Launched Global DARE Foundation

**NOV 2019**
Website & 1st Fundraiser Launched

**JAN 2020**
Medical & Scientific Advisory Board Established

**MAR 2020**
Announced start of first research project

**JUN/JULY 2020**
Launched Webinar Series & Initiate Patient Registry

Success
2020 REFSUM ADVOCACY PLAN

The Global DARE Foundation Board has established a clear plan for 2020 aligned to the foundation’s mission.

**Research & Care**
- Establish and mature a Medical & Scientific Advisory Board.
- Research patient registries for deployment in 2020 to collect patient data for research.
- Conduct Research on Phytanic Acid in Foods
- Drive forward treatment guidelines for Adult Refsum Disease
- Define and prioritize research priorities

**Raising Awareness**
- Create and mature a Refsum Website
- Create a Refsum video showing the impact of Refsum Disease on patients.
- Develop and mature social media sites
- Find more patients through outreach efforts with clinicians at medical facilities and on social medial platforms.
- Run two to three fundraisers in 2020 with the goal of raising $25,000.

**Collaboration**
- Mature the Foundation
- Create a Collaborative Network of Patients, Clinicians, Researchers and Supporters to drive Refsum Advocacy
- Conduct a 2020 Refsum Conference connecting Patients, Clinicians Researchers, and Supporters
- Partner with other foundations to find synergies.
Our Medical & Scientific Advisory Board

The Global DARE Foundation is fortunate to have an advisory board made up of the foremost researchers and clinicians in the field of Refsum Disease, peroxisomal disorders and Retinitis Pigmentosa. In their roles as medical and scientific advisers, members collaborate with each other and with our Board of Directors to drive forward better quality of life for those diagnosed with Refsum Disease.
MEDICAL & RESEARCH OBJECTIVES

Our Medical & Scientific Advisory Board has set focused medical & research objectives aligned to DARE’s mission

**Treatment & Care**
- Develop, publish and maintain treatment guidelines for the care of ARD patients
- Yearly updates to the diet and nutrition guidelines
- Publish guidelines on nutritional approaches and exercise to minimize fat burning
- Participate in the educational activities of DARE including assistance with content on the website and other outreach opportunities

**Research**
- Collaborate in establishing a patient registry and Natural History Study for ARD
- Provide advice and recommendations to the DARE Board on short-term and long-term planning for better therapeutic approaches and a potential cure for ARD
- Assist the DARE board in the review of scientific proposals for support and funding
- Recommend research on nutrition, diet and physical activity (e.g. phytanic acid in food, exercise, fat mobilization)

**Collaboration**
- Advocate within the research and medical field for focused work on areas that may improve the quality of life of patients diagnosed with ARD.
- Assist DARE in interactions and connections with sponsors and industry.
- Help plan, promote, and generate presentations for the annual Conference.
- Promote and expand cooperation with other research and rare disease organizations.
- Raising awareness with the medical community to promote earlier diagnosis of Refsum Disease
**UPCOMING REFSUM WEBINARS**

Global DARE Foundation will be holding webinars throughout the summer. Registration can be accessed through our website at [https://www.defeatadultrefsumeverywhere.org/dare-events](https://www.defeatadultrefsumeverywhere.org/dare-events)

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<tr>
<th>Date</th>
<th>Time</th>
<th>Title</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>7/1/20</td>
<td>7:00AM EST</td>
<td>Science behind Refsum Disease</td>
<td>Ronald JA Wanders, PhD &amp; Sacha Ferdinandussa, PhD from Academic Medical Center, UMC</td>
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<td>7/24/20</td>
<td>7:00AM EST</td>
<td>Refsum Diet Overview &amp; Discussion</td>
<td>Eleanor Baldwin &amp; Sarah Firman, the clinical dietitians at Guy's &amp; St. Thomas Hospital in London</td>
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<td>8/7/20</td>
<td>8:00 PM EST</td>
<td>Gene Therapy - A Potential Therapy for Refsum Disease</td>
<td>Ryan Butler, PhD from UT Southwestern will provide an overview of Gene Therapy as a potential future therapy for Refsum Disease</td>
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Q&A

For more information contact:

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www.defeatadultrefsumeverywhere.org