NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 25 • Fall 2017

The National Cell Repository for Alzheimer's Disease (NCRAD) is a data and specimen collection source for families affected by Alzheimer's disease (AD) or serious memory loss. Families having two or more living individuals with memory loss are encouraged to participate. We would like to thank the hundreds of families nationwide who already contribute to the National Cell Repository for AD. Many family members have provided blood samples, which researchers use to study AD and other related diseases. Our hope is that through the efforts of our participants, we will one day unravel the mystery of devastating diseases like AD and other related dementias. We are always eager to accept new families who wish to help us move toward this goal.

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An assignment, a family, and a journey: How *Pathways* led to *The Inheritance*

By Niki Kapsambelis — On a drizzly spring day in April 2009, I walked into the elaborate lobby of the historic William Penn hotel in downtown Pittsburgh, notebook in hand, for a group interview with a family from North Dakota. I had no notion of the impact that interview would have on my life, nor how important these people would become to me.

I was there because the Alzheimer's Disease Research Center at the University of Pittsburgh had hired me to write an article for *Pathways* about the DeMoes of Tioga, North Dakota, who were longtime contributors to a study headed by Dr. William Klunk. I knew relatively little about Alzheimer's and next to nothing about the family, beyond some background information I had been given in advance. When you're a freelance journalist, you typically don't pick and choose the topics you write about; there's a lot of on-the-job learning involved. It's actually one of my favorite things about my profession: I truly do learn something new every day.

Gail DeMoe surrounded by her children, Summer 2005.

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But nothing in my prior experience could have prepared me for what that day would bring. I didn't know how deep a dive I would take into the world of Alzheimer's, one of the great medical mysteries of our time. I would trace the steps of doctors who rode through the mountains of Colombia and poured over church records in rural Italy; I would learn about the rogue geniuses – half-neuroscientists, half-anthropologists – who lived among the people they studied to better understand their mysterious afflictions; of young scientists who dedicated their careers to understanding a disease of the old.

Karla, the de facto DeMoe family spokesperson, met me in the lobby and took me up to their suite. Inside were Karla's mother, Gail; her sister, Lori; her brothers, Dean and Doug; her niece, Kassie; and Kassie's husband and young daughter. I walked into the chaos and scribbled furiously as they talked:

Dean – memory testing. Worst part.

Their dad had it. Autopsy confirmed it, but it was so rare.

Lori – "You know you're going down eventually."

Kassie has not been tested yet. "I think about it every day anyway. I repeat things and wonder if I have it."

And boy, did they hate the MRI scans they did as part of the study.

Dean – "The night before, you try to stay up as late as possible."

Doug – "You just lay there like you're dead."

Their story was astonishing. Gail DeMoe and her husband, Galen, had six children: Brian, Karla, Lori, Doug, Dean, and Jamie. Galen died from early onset Alzheimer's, but nobody thought much about the hereditary factors until 2004, when Brian and Doug began to struggle at their jobs in the North Dakota oil fields where they had worked all their lives.

Unbeknownst to any of them, Galen had carried an extremely rare genetic mutation that guaranteed he would develop Alzheimer's in his 40s and die in his 50s. Worse yet, five of his six children – everyone except Karla – had inherited the gene. Those who had it bore a 50 percent chance of passing it on to their own children, and all had established families by the time they knew. Brian, the oldest sibling and Kassie's father, was already in a nursing home.

What astonished me was their approach to what was happening to them. Instead of dwelling on the devastation of their predicament, they had made a collective choice: they would fight back. So they agreed to become test subjects – first at the National Institutes of Health, then later at the ADRC – to give science an unprecedented opportunity to watch Alzheimer's disease unfold in real time in their brains.

Thanks to Pittsburgh Compound B (PiB), the radiotracer developed by Klunk and Pitt's Chester Mathis, researchers were able to watch the development and proliferation of amyloid plaques, one of the signature proteins of Alzheimer's disease, in living patients. Prior to the development of PiB, which took several years of trial and error, doctors had to look at amyloid under a microscope during autopsy.

Now, with the DeMoes, they could see amyloid growth in its earliest stages, years before any symptoms were apparent. In time, they would also be able to watch the growth of tau, another signature protein, as well as other brain changes related to the disease, and line those up against a person's cognitive tests to parse out what stages were associated with diminished brain function. By better understanding the disease's biological progression, science is more precisely able to develop treatments that focus on halting Alzheimer's in its earliest stages, which is thought – as with many complex diseases – to be the point at which an intervention is most likely to succeed.

By the time I walked out of that hotel room, hours had passed, but I felt as though I had only scratched the surface

The DeMoes – August 2013

Niki and Dean DeMoe – Tioga, July 2012

of the DeMoes' story. I walked to the parking garage in a stupor, and when I went to unlock my car door, I realized I was shaking. All I kept thinking was: *The world needs to know what these people are doing.*

In that moment, I had a thought that was both exhilarating and terrifying: *I should write a book about them.* Only I didn't really have any experience in the publishing world, which is different from the news business, where I had worked all my life. I had no contacts. I had no agent. What I had were two young children, and bills to pay, and a job that required a lot of hustle. I put the idea on the back burner, where it simmered for another year and a half.

And then Brian DeMoe, a man I never had the chance to meet, forced my hand. He died in December 2010. The realization smacked me in the face: if I was serious about telling this story, I was going to have to do it soon, when the people it was about still had the ability to talk to me. I called Karla.

Surprisingly, she remembered me. She agreed to take my proposal to the rest of her family. I outlined it up front: I would not be fictionalizing anything. I would be using their real names. I would be asking them hard questions. This was the only way I knew how to do it.

A few days later, Karla reported back to me with their answer. They were all in.

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After that, everything seemed to fall into place. A former work colleague had written a book and walked me through the process, then offered to introduce me to his agent, who loved the idea and signed me. We pitched it to Simon & Schuster; they bought it. And then I began writing the book that would become *The Inheritance*.

Five years passed before the book would finally become a reality, and not everyone who started that journey lived to see its end. I will never fully wrap my head around the trust the DeMoe family placed in me as I wrote their story. They became my family. We even coined a name for our relationship: I was their "author-in-law."

At first, I tried to keep them at arm's length, as I'd been trained to do. I didn't tell them much about my personal life. I let them in on only the superficial details.

But in time, that kind of distance became impossible. "They're disarming," Dr. Klunk would later say to me, and he was right.

When I began writing the first draft, in December 2012, Gail DeMoe wrote me a letter of encouragement. "We are so very lucky to have you in our lives," she wrote. "God knew what he was doing!!" I tacked it up on the bulletin board over my desk. Every day, I strove to be worthy of her faith in me.

Six months later, the woman I had come to know as Grandma Gail died from a heart attack. In the years that followed, as I poured over draft after draft, trying to find the right words, I would look at that note and think of her. I felt a sometimes overwhelming sense of responsibility.

I danced at weddings. I held babies. I sat quietly with my notebook as younger family members learned their fate. I crisscrossed the country learning everything I could about Alzheimer's, about genetic mutations, about drug development and clinical trials and government funding. I watched researchers design their attack using the history of how other seemingly intractable diseases were solved.

In March 2016, I stood before a congregation in the church down the street from the DeMoe family home and gave a eulogy for Lori, who fought Alzheimer's with everything she had until the day she died: *You know you're going down eventually*. In April 2017, I stood in the same spot, in the same church, and gave a eulogy for Doug, who had wrapped me in a bear hug the day I left the William Penn hotel.

"Imagine her," Lori said then, in that hotel suite. "How would you like to be her?"

I remembered what Lori said, the first time I met her, about her sister Karla: that it was harder to be the sibling who didn't have the mutation, because you had to watch the others die.

"Imagine her," Lori said then, in that hotel suite. "How would you like to be her?"

Eight years later, I am beginning to understand the answer to that question.

I have no doubt that one day, science will solve Alzheimer's disease. When that day comes, I hope the rest of us will remember the price that was paid for that singular achievement. And I hope I will be celebrating with the DeMoes. ■

Research Opportunities:

4 Repeat Tauopathy Neuroimaging Initiative – Cycle 2 (4RTNI-2)

- Purpose: To identify the most reliable methods of analysis for tracking CBD, PSP and o/vPSP over time. The results from this study may be used in the future to calculate statistical power for clinical drug trials. This study will also provide information about the relative value of novel imaging techniques for diagnosis, as well as the value of imaging techniques versus testing of blood, urine, and cerebrospinal fluid (CSF) biomarkers.
- Eligibility: Men and women ages 40 to 80, diagnosis of Progressive Supranuclear Palsy, Corticobasal Degeneration (CBD) or o/vPSP.
- Locations: USA - CA, MA, MN, PA; Canada
- Contact: PH: 415-476-9578 or 4RTNI2 webpage: http://memory.ucsf.edu/research/studies/4rtni2

Dominantly Inherited Alzheimer Network (DIAN)

- Purpose: To study brain changes in people who carry an Alzheimer's disease mutation in order to determine how the disease process develops before the onset of symptoms.
- Eligibility: Men and women ages 55 to 80 years, diagnosis of mild to moderate Alzheimer's disease, good general health and medically able to undergo neurosurgery.
- Locations: USA - CA, IN, MA, MO, NY, RI; United Kingdom; Australia
- Contact: PH: 314-286-2683 or DIAN webpage: http://www.dian-info.org

Advancing Research and Treatment for Frontotemporal Labor Degeneration (ARTFL)

- Purpose: "New therapies targeting some of the molecular causes of FTLD are rapidly becoming available for testing in human clinical trials. The ARTFL's goal is to prepare for clinical trials of these new therapies by evaluating people who might eventually be candidates for participation in clinical trials and by developing new diagnostic technologies to evaluate the effectiveness of new treatments for FTLD." *(Citation: https://www.rarediseasesnetwork.org/ARTFL/index.htm)*
- Locations: USA - AL, CA, FL, IL, MD, MA, MN, MI, NY, NC, OH, PA, TX, WA; Canada
- See this website for more information: https://www.rarediseasesnetwork.org/ARTFL/index.htm

Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS)

- Purpose: To model the rates of decline in clinical function of those suffering from Frontotemporal Lobar Degeneration (FTLD) and identify genetic and biofluid factors that modify these rates.
- Eligibility: Must be a member of a family with a known mutation, have a reliable informant who personally speaks with or sees that subject weekly, the subject and informant must be fluent in English, the subject must be willing to undergo yearly evaluations for a period of three years, and the subject must be willing to undergo neuropsychological testing and MRI imaging.
- Locations: USA – CA, FL, MA, MN, MI, NY, PA; Canada
- Contact:

  Mayo Clinic Rochester
  Alzheimer's Disease Research Center
  507-284-1324

NCRAD Welcomes Your Ideas and Suggestions

We hope that you and your family find the NCRAD newsletter informative. We would welcome suggestions on future topics for articles, questions you would like to ask the NCRAD doctors, or anything you would like shared with our readers about your family's experience with Alzheimer's Disease. Please send us your ideas by email or by phone.

Phone: 1-800-526-2839 **Email:** alzstudy@iu.edu **Website:** www.ncrad.org

Sources for Information and Support

Alzheimer's Association
http://www.alz.org
Trial Match
Tel: 312-335-8700 or 800-272-3900

Alzheimer's Disease Education and Referral Center (ADEAR)
http://www.nia.nih.gov/Alzheimers
Tel: 301-495-3311 or 800-438-4380
** ADEAR lists all 29 Alzheimer Disease Centers (ADCs) and their contact information.

Assisted Living Directory, Assisted Living Facilities Information & Senior Care
http://www.assisted-living-directory.com/

The Association for Frontotemporal Dementias (AFTD)
http://www.theaftd.org
Tel: 267-514-7221 or 866-507-7222

Family Caregiver Alliance
http://www.caregiver.org
Tel: 415-434-3388 or 800-445-8106

National Parkinson Foundation
http://www.parkinson.org/
Tel: 305-547-6666 or 800-327-4545

Parkinson's Disease Foundation (PDF)
www.pdf.org
Tel: 212-923-4700 or 800-457-6676

Society for Progressive Supranuclear Palsy
http://www.psp.org
Tel: 410-486-3330 or 800-457-4777

National Organization for Rare Disorders (NORD)
http://www.rarediseases.org
Tel: 203-746-6518 or 800-999-NORD (6673)

Center for Disease Control and Prevention (CDCP)
http://www.cdc.gov
Tel: 800-311-3435

Creutzfeldt- Jakob Foundation Inc. (CJD)
http://cjdfoundation.org
Tel: 954-704-0519 or 305-891-7579

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.
http://www.clinicaltrials.gov/

Research Match is a free service that pairs volunteers interested in participating in research opportunities from surveys to clinical trials with researchers. Open to all, including healthy volunteers.
http://www.researchmatch.org

National Society of Genetic Counselors
http://www.nsgc.org/
Tel: 312-321-6834

10 Signs of AD

1. Memory loss
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation to time and place
5. Poor or decreased judgment
6. Problems with abstract thinking
7. Misplacing things
8. Changes in personality
9. Changes in mood or behavior
10. Loss of initiative

For more information, call the Alzheimer's Association at (800) 272-3900

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