Bob's LAST MARATHON

Living the Alzheimer's Journey

Second Edition

Planning in the Face of Uncertainty

PRACTICAL GUIDE TO DEMENTIA CAREGIVING

A PUBLICATION OF BOB'S LAST MARATHON FOUNDATION

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“A marvelous introduction to the series. It is invaluable for being informative AND easily digestible. Thank you!”

“Bob could not have had a better caregiver than you, Lena!”

“It was a gift to hear from Jennifer Fargo Lathrop, receiving her insights on hospice and palliative care and spiritual care. ‘Sheltering Walls,’ the John O’Donohue piece Jennifer read at the end, was deeply touching.”

Preface

The overwhelmingly positive feedback to *Bob's Last Marathon* podcasts since our launch in January 2021 is reason to believe that our program is serving a useful purpose for the many people—family, friends, caregivers—who are touched by the disease. Praise for the pragmatism, clarity, and relevance of our content is incentive to explore more ways to make our content more accessible and easier to use for day-to-day reference. Hence the development of this pilot e-book series.

This series of e-books follows the four categories of our podcasts—Planning, Living Well, Community, and Challenges—and includes links to our podcast library.

With gratitude to our Advisory Board, family, friends old and new, and especially our guest speakers, who so generously share their personal and professional experience in the care of people with Alzheimer's disease and dementia.

Five Key Elements of Dementia Care

🔈 Podcast Link

Lena Chow Kuhar

It was the fall of 2013, a year after Bob was diagnosed; I'd just started coming to terms with his illness. We had gotten a few things into motion—a support group and connecting with the Alzheimer's Association—and we were trying to figure out what lay ahead. A routine trip to visit my daughter led us to Dr. Arnold, at that time the director of the Penn Memory Center in Philadelphia.

What Dr. Arnold said to me that afternoon would inform every single decision I made for Bob, giving me the most valuable gift: a framework for caring for him. After listening to my barrage of questions, Dr. Arnold explained to me that there were five key elements of dementia care to keep in mind as I made choices to give Bob the best quality of life for the longest time possible. I don't know if I wrote them down, but from that point on, not a day went by without my thinking about them.

As Dr. Arnold explained it, the five key elements to keep in mind are medication, diet, exercise, social interaction, and cognitive therapy.

It seems so simple, but in a world that felt like it was crumbling beneath my feet, the five elements helped keep me grounded. Over time, I learned that they overlapped … managing one element often had a positive effect on others.

The mention of medication brought up something that I've learned in my years in health care communications, that following a drug regimen is critical; drugs don't work unless they're taken.

To ensure that happens, there usually comes a time when caregivers need to take over. In addition to two medications for Alzheimer's, Bob was taking medications for other health problems. So it was especially important that I take ownership of his medications, make sure they were taken as instructed, and that refills were ordered in time so there were no disruptions. Fortunately, it was early enough in the course of his disease that we could discuss it. And Bob was an easygoing person, so he happily allowed me to take over—which was kind of the dynamic of our relationship anyway.

As runners, Bob and I were fairly conscious about what we ate. So we wondered whether a diagnosis of Alzheimer's disease would call for a change in our diet. Dr. Arnold recommended the Mediterranean diet—which is well known for its heart-healthy benefits, but there's also some evidence it can help stave off Alzheimer's-related changes to the brain.

Bob and I were already big fans of fish and vegetables, so it wasn't a big leap to cook with fruits, vegetables, whole grains, and lean protein—the staples of the Mediterranean diet. One of our biggest challenges was cutting down on carbohydrates—pasta, bread, potatoes. So, yes, we cheated a little here and there. Life with Alzheimer's is tough enough without the occasional guilty pleasure, which for Bob was bread and cereal, and for me, ice cream.

Dr. Arnold didn't need to preach the benefits of exercise to Bob and me. Since we were runners, it was central to our routine. But when I learned it was important to the health of a person with dementia, I realized that I would need to consciously continue to make exercise a part of Bob's routines.

In Bob's case, vascular dementia contributed to a loss of coordination and fluidity in his movements … eventually his gait became awkward, and I could see in his eyes that walking took some determination. But we discovered different ways to make exercise work. We introduced a walker—I remember him stepping away from his walker momentarily to shoot hoops. To maintain muscle tone, Bob lifted weights and continued doing push-ups—but modified to do while standing up.

I also found that very often, exercise means interacting with other people—walking, dancing in a group, working out in a group—rather than isolation.

The day before he passed away, Bob was doing hand weights in his wheelchair—by that time he was no longer able to walk on his own. I found it comforting to feel his strong grip, and to see the inevitable smile, when he was up and about, exercising at the level that he could.

Next on the list of five key elements was social interaction, which benefits Alzheimer's patients by keeping the mind active. I remember other caregivers in support groups talking about needing to keep their loved ones at home full time for the best care. What they didn't realize was that they were depriving their loved one of social interactions—to say nothing of depriving themselves of a break, which is so important but often overlooked.

Knowing the importance of social interaction, both personally and for his disease, helped me make the decision to enroll Bob in a day care program, even when he was still largely independent. Sure enough, Bob became one of the best-liked members of his day care program. At first, he would hang around the coffeepot and chat. Later, I would find him clapping enthusiastically when someone told a story. Or, later still, he might wake up from his "snooze" as he called it when people started music or games.

The fifth key element, cognitive therapy, or cognitive training, was actually one issue on my mind before we saw Dr. Arnold. I first heard about it through the Alzheimer's Association and was considering in-home programs offered by a group in our neighborhood. We opted for in-home cognitive therapy, but as I learned, many adult day care programs include some form of cognitive therapy.

Twice a week, a trained cognitive interventionist would engage Bob in conversation, encourage him to tell stories, work on puzzles, solve math problems, and play games on an iPad. Often, as a warm-up, the interventionist would go for a walk with Bob. His monthly progress was tracked by his ability to engage and focus, as well as overall cognitive skills.

As Bob's Alzheimer's progressed, and solving math and picture puzzles became too difficult, therapy shifted toward art and music. Even the week before he passed away, when Bob was physically too weak to go to day care, he completed a painting with the supervision of his art therapist—a piece of art that graces the entry hall of my home now.

Medication. Diet. Exercise. Social interaction. Cognitive therapy. These five key elements were central to all my decisions for Bob's care. I used them as a checklist when I began to put together a care team, evaluate day care programs, interview home care staff, and decide between home care and long-term care facilities. Day to day, I used the five key elements as mental touchpoints as I planned out Bob's day, his meals, and his activities. Even today, as I look up from my desk, I have vivid memories of Bob walking with Miriam, one of two favorite regular caregivers, singing "You Are My Sunshine" as he started his day.

Lena Chow Kuhar

The Care Team

Podcast Link

Lena Chow Kuhar

Moments before Bob's memorial service, looking over the crowd of family and friends, I caught sight of my daughter, Andrea, with her two children and her husband, Steve, who was watching the door. Suddenly, Steve shot from his seat to greet a new arrival. It was Thomas, one of Bob's most beloved caregivers. As we had planned, Steve ushered Thomas to the empty seat in the front row, reserved for family.

Thomas is indeed family. Over the last six months of Bob's life, Thomas barely left Bob's side. He was one of several caring and knowledgeable members of the team who ran this last marathon with Bob and me. This care team, all professionals with specific areas of training, became Bob's lifeline—and mine.

I knew little about Alzheimer's care, but I did know this: I was facing a difficult and unmarked road, and I would need someone to help me navigate it. I didn't need to go far to find Stephne, a care manager familiar with the issues confronting aging adults with dementia. She was referred by Vicki, director at an age-in-place community literally around the corner from my house. Stephne was my go-to consultant and confidante, a trusted sounding board who guided me and talked me through decisions I made for Bob, large and small. Should he start day care? Which day care centers should I check out? When should I start looking for home care help? Stephne anguished with me over whether I should keep Bob at home, or whether a long-term care facility would be better for Bob—and for me.

And when Stephne did finally recommend home care, it was possibly as much for me as it was for Bob. At that point, Bob was still what professionals would call "high-functioning." He could still manage his day-to-day activities. He could still speak, read, and write. But we knew this would most certainly change. Before it did, Stephne knew it would help for me get used to the idea of someone else caring for Bob. So we started with home care twice a week for two or three hours.

Our first home care helper would mostly just chat with Bob and do some light housekeeping. Bob would say to me, jokingly, "So what time's my babysitter coming today?" As Bob's condition worsened, the home care visits became more regular. An aide would arrive when Bob came home from day care, and stay until I finished my work and was ready to make dinner. This schedule evolved into an early morning shift to help Bob get up, shower, and dress for the day—with the level of help increasing with Bob's needs.

Stephne shepherded me through these transitions, and helped me screen for the right people at each stage. Were they willing to engage in conversation and activities such as walking, singing, painting, or solving puzzles? Would they be respectful of my rules—for example, not allowing TV watching until after dinner? Were they genuinely interested in caring? Bob and I were fortunate to settle down, eventually, with a superb team of compassionate home caregivers who stayed with us for several years. Miriam, a blessed soul with smiling eyes whom I connected with right at our first meeting, took the morning shift. Thomas, her nephew, came in the afternoon. Later, when Bob's restricted mobility required someone to help lift him in and out of the wheelchair, Miriam had to relinquish her duties to Thomas.

Another central person on our team was Florence, the social worker and director at Rosener House, the wonderful day care center that Bob attended for five years. I so appreciated Florence's clear, direct but compassionate assessments of Bob, and the support group she led for caregivers. Kathy, at the front desk, always made me feel as though Bob and I were the most important people ever to walk into their facility. I learned the importance of cultivating trusting, positive relationships with key people at day care; their close, professional watch on Bob kept me in touch with the inevitable changes in his condition, giving me the information I needed to respond in a timely way.

When Bob first signed up at Rosener House, he was still driving occasionally. With Florence's wise guidance and gentle insistence, I found a driver to bring Bob, along with a few other attendees, to Rosener House. Jack drove a minivan and always wore a cowboy hat. He had a cheerful, upbeat personality, always starting Bob's day with, "How are you doing, Champ?"

Knowing that exercise is integral to dementia care, and because Bob enjoyed being athletic all his life, I decided to add personal training to the group exercise he was doing at Rosener House. At first, Bob trained at the gym with Brian. After a time, he trained at home with Andre, an old friend. Andre was creative with exercise—they shot hoops at a neighborhood court and worked out at our local park. Even when Bob was in a wheelchair, Andre kept Bob's exercise regimen going with arm weights.

Cognitive therapy was a part of Bob's routine for about three years. The cognitive interventionists were typically students—young and dedicated—who brightened Bob's day with their positive attitudes, engaging conversations, walks around the neighborhood, or strumming a guitar as the session began. Later, this would be replaced by art therapy. I will always remember Monique, the art therapist, who supervised Bob's last paintings at the Alzheimer's Association office in San Jose and later at our home, only five days before he passed away.

Alzheimer's disease can take an emotional toll on caregivers, and couples. Stephne referred us to Kathy, our psychotherapist. Trained as a nurse, Kathy was a licensed psychotherapist specializing in helping families of people with dementia. She worked at a local hospital, where she ran support groups, and maintained a busy schedule with her private clients. Bob and I met with her every month until Bob was no longer able to manage the stairs to her office. I continue to meet with Kathy to this day.

The summer before Bob's passing, his physical condition started to deteriorate. It began with his heart: valve disease that required surgery. Recalling his painful recovery after open-heart surgery 30 years before—when Bob was much younger and healthier—I decided against it. Then came a blister on his foot that turned into a wound infection that wouldn't go away. During his third hospitalization for it, the surgeon discussed the option of amputation. That was when I was offered a consult with the hospice group. Thus began the last 352 yards of our marathon, and the introduction of the final member of Bob's wonderful care team—a compassionate hospice nurse by the name of Elsa.

I was mentally prepared to make this difficult decision. From our past experiences with family, Bob and I were very clear about not wanting treatments just for the sake of extending life. Also, earlier that year, Bob's doctor had scheduled a call with me to, as he said, “talk about existential issues.”

So I felt confident about discontinuing treatments that would require hospitalization and add to Bob’s discomfort. And with guidance from the hospice team, including a physician and a chaplain, and knowing Bob’s preference to stay home, I found home hospice to be an easy decision. This meant that, while Bob would be cared for at home, Elsa would visit regularly to check his vitals and care for his wound. Elsa painstakingly trained me to change Bob’s dressing on her off days. Incidentally, Elsa’s experience in caring for Bob motivated her to become certified in wound care. She completed her course work right before Bob’s passing.

My experiences with our extended family of caregivers taught me so much, practically and personally. I learned to recruit people who met my criteria and to act quickly if they proved disappointing; to trust people and be committed to building a relationship of mutual respect. I learned to let other people do what I thought was only a wife’s job—from personal hygiene to picking out the day’s outfit. I learned to share my home and my “turf,” the kitchen. In turn, the support I received nourished me emotionally, and allowed me to continue building my career and to take care of myself—while making sure that Bob’s days were as healthy and full as they could be.

Lena Chow Kuhar

Daily Routine

🔊 **Podcast Link**

Lena Chow Kuhar

It is fair to say that few people know me better than my therapist, Kathy. Over the years, I've sat on the couch in her office, often with Bob, always with fresh flowers on the coffee table, and confided my fears and my hopes as a person, as a caregiver, and as a wife. Recently, as we were reminiscing about Bob, we laughed recalling how I used to pack his schedule with activities, as though to crowd out any chance for his decline. But then, in all seriousness, she said that it may have, in fact, worked. Keeping Bob active not only helped improve his quality of life, but possibly slowed some cognitive changes.

Looking back, I never planned to crowd Bob's schedule. It happened gradually, starting purely as a practical need to get organized so I could give Bob the care he needed while continuing my own work and activities. As Bob's level of function changed, his daily routine became more elaborate, and my role evolved into one of manager, working with home care and day care aides, and over time, coordinating activities through a network of services, support groups, and senior centers.

The routine changed over time, but his days were never without structure.

Bob's day started at 8 am, pretty much on the dot, and usually ended at 8 pm as he got ready for bed—though bedtime might vary to make room for a movie, concert, or gathering with friends, especially over the weekend.

Early on, I made a few rules for the home care team. One was that Bob could not lie down during the day. It was okay for him to nap sitting up in a chair—what he called a "snooze"—but the bed was for nighttime sleep only. I believe this routine helped ensure Bob would consistently get a good night's sleep, so important to his health. It wasn't until the last months before his passing that Bob's sleep got more erratic. He would wake up in the middle of the night and, quietly and inexplicably, start moving his legs.

Bob's morning routine was the same to the very end: toilet, shower, shaving, and getting dressed, which helped set his daily rhythm in motion. He was always ready for the day about 30 minutes after waking, well-groomed, in good spirits, and prepared for breakfast. I believe that even this simple goal helped Bob start his day with a sense of purpose and retain his sense of self. I still have beautiful memories of Bob smiling at me and saying, "Good morning, Lena" as he walked by my office on his way to the kitchen for breakfast.

Every day from Monday to Friday, Bob's core activity was day care. At 9:30, Jack, the driver, would bring Bob to Rosener House for his four to five hours of group activities—discussion of current events, exercise, art, music, plus lunch, coffee breaks, ice cream socials, and an occasional outing. Knowing that social interaction is a key element in dementia care, and knowing Bob's natural affinity for people, I viewed Rosener House as the most important activity of his day. From my conversations with fellow caregivers over the years, I've learned that some loved ones refuse day care. I always felt very sad for them, for what they were missing—the power of social interaction in slowing cognitive decline, and the respite for caregivers while their loved ones are safe and secure in a supportive environment.

Bob engaged in a variety of activities after day care. Workouts with his trainer, Andre, twice a week. Cognitive therapy twice a week. Time with his caregiver Miriam or Thomas for walks, reading the newspaper, listening to music, reminiscing. Bob loved talking about his days as an engineer working on the space shuttle. He also enjoyed sharing pictures and telling stories about his parents, proud immigrants from Slovakia, and his childhood in Yonkers, New York. Bob's days were richly active. Which brings me to the second rule I made for our home care team: no TV until after dinner. In my mind, watching TV is too passive, and it could not replace the activities that engaged Bob, and helped slow the decline in his verbal and other cognitive skills.

Bob liked sitting in the kitchen watching me make dinner. Afterward, we both enjoyed *Jeopardy* and then *Wheel of Fortune*. Bob would delight me with his observations about Alex Trebek, like "He doesn't have his mustache this week," or "He has new glasses." On occasion, he would solve a puzzle on *Wheel of Fortune* and look quite pleased with himself. I was ecstatic.

We both also loved going to our local bookstore, Kepler's, for events. One particularly memorable experience was meeting Elizabeth Strout after the release of her book *My Name Is Lucy Barton*. Likely noticing Bob in his wheelchair, Strout beckoned us to the front of the queue, greeting us warmly and signing Bob's copy of the book. By that time, Bob was no longer reading books on his own, but he liked being with me and the energy of the people in the room.

Our Friday date night was sacrosanct. I would leave work mid-afternoon to meet Bob upon his return from day care, and we'd go straight to the movies—popcorn and diet soda for Bob, and a hot dog for me. Afterward, we would have dinner at a favorite restaurant. Over time, I settled in on two restaurants that were most accommodating of our needs—Bob was a bit of a sloppy eater and, later, bound to a wheelchair, which made navigating the tables difficult.

Bob and I always enjoyed cultural activities, and this continued over most of the course of his disease. We shared a special love for music, and attended concerts at the local venues, or in San Francisco at Davies Symphony Hall on a Sunday afternoon. We hosted recitals at our home periodically. I was a member of a local music group called Fortnightly Music, which held public concerts and private recitals at members' homes. Bob enjoyed listening to me on the piano and in duet with my flute-playing friend Deborah. He always applauded enthusiastically, and afterward took in the buzz of the room with a quiet smile while everyone shared a glass of wine.

We visited museums and went on art tours hosted by the Alzheimer's Association. When the Panama Canal celebrated its 50th anniversary, we saw the exhibit at the De Young Museum in San Francisco. I'll always remember the very last Memorial Day with Bob. Together with Thomas, his caregiver, we spent the day at the San Francisco Museum of Modern Art for the Magritte show.

Routines are meant to be broken—I felt it was important to be flexible. Often, I would ask for Bob to be excused from his day care programs to attend events I thought he'd enjoy, like a neighborhood storytelling hour or sing-alongs hosted by Avenidas, our local retirement-in-place community.

I did my best to keep our weekend routines very much like those of other older couples. Shopping in the mall, dim sum—Bob's favorite—or dinner with friends. Church on Sunday.

But we were always happy to make time for family. Bob's children—two sons, two daughters, and their families—would travel from as far as Kentucky to spend time with Bob, liven up his weekends, and show their love in their own unique ways.

His son Chris, who lives only about an hour away, would visit for the day with his partner, Werner, and their daughter, Tessa. They loved a trip to nearby Filoli Gardens, followed by dim sum. Bob's daughter Kim and her husband, Tom, would drive up in their truck from New Mexico on occasion. Bob and Kim shared a love for the outdoors, and he always enjoyed riding in the truck, getting updates about Kim's work as a forest ranger. Visits with his daughter Liz, from Kentucky, tended to have a more sentimental, nostalgic timbre. And when Mike came from Southern California, they talked about boats and we'd go for brunch at the beach.

These occasional detours from the normal routine helped break the monotony, and made returning to the regular schedule even more rewarding, and perhaps comforting. I'm still moved by Bob's deep relationship with his children, individually and as a group, and always admired how they stood by him—and each other—through difficult times.

Bob's activities might have changed as his function declined, but his days were never without structure. I believe the structure was not only important for practical reasons, but also helped fill an emotional need for stability while so much else was changing, replacing uncertainty with predictability—a much-needed constant in a constantly changing world.

Lena Chow Kuhar

Feeling at Home with Home Care

🔊 **Podcast Link**

Stephne Lencioni, LCSW, CMC

As a loved one's dementia progresses, there comes a time when most caregivers need help. The person with dementia may no longer be able to handle simple daily routines, such as meals and toileting. Or the caregiver may simply not have the physical strength to cope without risking their own well-being. In some cases, the caregiver may feel emotionally depleted, physically drained—or both.

There are many options available, but this discussion focuses on *in-home care*. By this I mean a caregiver who comes into your home to help with care, one on one. Their care may span a continuum from companionship and supervision to total hands-on help with activities of daily living such as bathing, dressing, and toileting. Caregivers can also help with laundry, housekeeping, meals, and errands. They can read with your loved one, do puzzles with them, or go for walks in the park. I had a client who had lived in France and loved everything French. Her husband hired a caregiver who, in addition to basic caregiving tasks, had conversations in French, and explored famous French sights, art, and music on an iPad.

Once you decide on the type of care you want, where do you find it? There are basically two sources for caregivers: You can hire a caregiver directly, known as private caregivers, or you can work with a reputable agency. I strongly recommend the latter. I have known many excellent private caregivers over the years. But when you hire privately, you become the employer and you assume all of the responsibilities and potential risks. You are liable if the caregiver gets injured on the job. You are responsible for managing payroll and taxes, and understanding the rules of overtime, among other things. If there's a performance problem, you need to deal with it. When the caregiver is sick or goes on vacation, replacement is up to you.

On the other hand, if you work with an agency, the caregiver is *their* employee, and the agency assumes the responsibilities of being an employer. Given the benefits, why would anyone *not* work with an agency? Usually it comes down to finances. Home care in general is expensive. And there's an impression that hiring directly is less expensive than going through an agency. But the tables can quickly turn if a caregiver breaks a leg on the job, or sues you for not paying overtime correctly. In fact, bottom line, some caregivers charge the same or even more than agencies. If you do choose to hire privately, at the very least check with your homeowner's insurance company about a rider to cover employees working in your home. It's also a good idea to draft a contract to formalize job expectations, salary, schedule, and time off.

Or you can hire a professional agency to handle all of this.

Once you decide you want to work with an agency, how do you find a reputable one? Start your search by asking friends who have hired in-house help, or your doctor's office. The resource person at your local senior center may be able to help. You might call the Alzheimer's Association, Family Caregiver Alliance, or your local Agency on Aging.

Once you have a few agency names, look at their websites to get a sense of their approach to caregiving and range of services, then start making some calls. I recommend starting a folder and taking notes.

In your initial call to each agency, you'll want to ask a lot of questions: How long have they been in business? What range of services do they provide and what is the fee structure? Do they have a minimum number of hours for service? Can they provide overnight and live-in care? Will they provide a consistent caregiver? What do they do if a caregiver calls in sick? Can you yourself interview a couple of different candidates for the job? Your particular situation will guide your questions, for example, if your loved one has mobility problems.

Once you've decided on the agency, be prepared to give as much information as you can to help them find the best caregiver for you.

They should be asking you a lot of questions about your specific situation and your loved one's care in order to clearly define and clarify the caregiver's duties. They might ask whether you think a male or female caregiver would be more successful. Should it be someone who is high-energy and engaging or quiet and unobtrusive? The "match" is everything. Having said this, I have experienced situations where the caregiver we thought would be the best fit turns out not to be—and the one we never thought would be accepted by the family turned out to be "the one." So the moral is: Keep an open mind.

The agency should allow interviews with candidates, and you should take advantage of them. Prepare a list of questions, and for the sake of comparison, ask each candidate the same questions. You'll want to know their experience working with people with dementia. How long have they worked with previous clients? What is their favorite part of being a caregiver? The most frustrating/stressful? You get the idea. You may have a difficult time choosing and if so, go with your gut. Although we hope that the first caregiver is the perfect match, in reality you may have to try a few before settling in with the right one. I should add here that flexibility is important when it comes to the caregiver's schedule as well. If the exact days or times are really not that important, go with what works best for the caregiver of your choice. A happy, respected caregiver will be much easier and more enjoyable to work with.

Now that you've selected the agency and the caregiver, and determined the schedule and tasks, what can you do in the beginning, on that first day, to set the stage for success?

- First, it helps to have a list of what you'd like done during their time with your loved one. Don't assume the caregiver knows exactly the tasks you have in mind, even if you've discussed them with the agency. You'll want to discuss your loved one's preferences and dislikes, as well as strategies you use to handle resistance. For example, turning on the heater in the bathroom and a little music make all the difference in getting your loved one in the shower. Maybe showers never happen in the morning, but work better after lunch. To succeed it's important to communicate with the caregiver.
- Second, give the caregiver a full tour of your house and where to find the necessities for care—gloves, wipes, Depends. What are your loved one's food preferences? If they go out for a walk, do they need a key to get back in the house?
- Third, where do you keep emergency information? (And if you haven't written this out, now is the time to do so, along with a copy of the current medication list.) If you aren't home, how can you be reached? If you can't be reached, who should be called?

- Again, flexibility is key: While you want to clearly communicate expectations and guidelines, you also don't want to be rigid. Give leeway on things that don't really matter. So there was an unwashed pot in the sink, but your loved one is smiling ear to ear from a walk in the park. While safety is not negotiable, almost everything else is. Don't sweat the small stuff. Flexibility!

Once you have successful home care help in place, you now have the opportunity to get out and do some *self-care*—whatever that means for you. Rest, relax, fill yourself up. While no amount of resources will change the fact that this is a difficult, exhausting, often gut-wrenching journey, having help in place to share the caregiving load can make all the difference in how you travel it.

Stephne Lencioni, LCSW, CMC

Geriatric Care Manager

Leaving Home

Podcast Link

Lorri Bernstein, MSW

Is it the right time to move your loved one with dementia to a care facility, or would they be better off living at home? This is one of the most difficult questions facing caregivers and their families—a question that usually doesn't arise until the caregiver reaches a critical point managing their loved one's care at home.

The question may be triggered by the emotional stress of handling behavioral issues, such as wandering or aggressive behavior. Or when physical limitations grow too difficult to handle within the home. For example, when loss of mobility requires a wheelchair, but the home isn't readily adapted for accessibility. Also, as your loved one's disease progresses and their needs become more complex and constant, the cost of home care will rise. When it reaches 24 hours a day, the costs can become overwhelming—another reason to consider community care.

These are just some of the challenges that drive caregivers to seek community care. No doubt, this decision can be fraught with great sadness and guilt. But I use the analogy of airplane oxygen masks. It might feel counterintuitive, but the reason we're told to put our own masks on first, before helping others, makes sense: We're no good to our loved ones if we collapse under the strain of their care.

So, how do we go about choosing the right facility or community for our loved ones? Where do we start? One way is word of mouth—from support groups, or the social worker working with your health care provider, to name a couple of possibilities. If you have a care manager, you can call on him or her to shepherd you through this process. There are also placement agencies that specialize in helping families navigate these decisions.

Fairly soon, if not immediately, you will need to start getting your affairs in order. All long-term care communities will require proof that an authority has been assigned to make medical and financial decisions on behalf of the person being placed. Terminology differs by state. The authority for medical decision-making can take the form of a health care proxy or an advance health directive. Financial decisions and the authority to release funds are assigned to a person with power of attorney. You can work on this while deciding the type of memory care facility you want.

A key factor to consider is the right level of care for your loved one. Some communities include both assisted living and secure memory care—an option for people with dementia and their aging spouse. Assisted living communities typically offer care services for people who are no longer able to live alone, but want to maintain a social, active lifestyle. They may feature group activities, outings, and restaurant dining, as well as help with laundry, housekeeping, and daily living, such as bathing, grooming, and medication management. Assisted living units usually make up the lion's share of these mixed-use residences.

Memory care communities are designed specifically for people with cognitive impairment and usually house between 50 and 60 residents. These communities typically offer both private and common areas, as well as outside areas for the residents to enjoy time away from group settings. The staff is usually trained to work with cognitively impaired people. Services vary but may include social hours, games, and activities to support motor and cognitive skills, as well as exercise.

A more intimate type of community, called care homes, is available in some parts of the country. As the name implies, these residences feature a home-like environment for 15 to 25 residents. Unlike most larger communities, care homes offer home-cooked meals, sometimes with customized menus, and the staff-to-client ratio tends to be higher. While not all care homes provide structured activities, residents may be able to bring in their own aides for specific services such as memory training and exercise.

Another consideration is the level of structure best suited for your loved one. For example, memory care communities typically offer scheduled programming from 8 am to 6 pm, whereas care home environments tend to be more relaxed, with the main goal being for residents to feel comfortable and at home.

Consider also the services the memory care community offers—such as physical therapy, occupational therapy, and transportation to appointments such as medical checkups. Many communities also include memory stimulation and cognitive therapy. How important are these to you and your loved one?

Finally, don't overlook the convenience factor. All other things being equal in terms of the quality of care, we suggest selecting the community that's easiest for you to visit.

After you've homed in on a community, you'll usually be given a chance to speak with the director or other coordinator, and observe how they interact with both residents and staff. This is important. This person will lead the team overseeing your loved one day in and day out, so you'll want to make sure you feel comfortable with their leadership and personal style.

It's also valuable to get the perspectives of the families of residents. Their opinions are just that, opinions, but you'll get an insider's view of life in the community, and whether it might suit your loved one. In terms of the actual accommodations in memory care communities, you should be able to visit the communal areas as well as the residents' rooms.

So you have chosen a community and negotiated the terms—and you're ready to make the move. As difficult as it may feel after spending so much time and energy caring for your loved one, it's vital that you allow for an adjustment period. Many memory care communities wisely suggest allowing the resident a week, or even two, to acclimate to their new surroundings and routines before visiting. If you have not already, this is an ideal time for you to join a support group—the community may even offer one.

To help with the details of moving, if finances allow, you can hire a transition specialist who works with seniors to sort through your loved one's belongings, and help you decide what to bring, and what to sell, donate, or dispose of. These specialists are often skilled at patiently and kindly understanding the emotional issues that come up during this sensitive time.

Once your loved one has settled in, we strongly recommend staying actively connected with the community, and becoming an advocate to make sure your expectations are being met. Do not feel reticent. A safe, well-managed, resident-centered community will welcome and encourage your involvement. They will want to foster your relationship and curiosity with compassion. They will want to assure you that they honor your loved one.

Deciding on home care versus community care—and finding the one that's right for you—can be a long and arduous process. The good news is there are many resources available to support you along the way. And in most cases, families who finally decide to place their loved ones in memory care often look back and wonder why they hadn't made the move sooner: Their loved ones are happier with their new home—and so are they. In other words, the hard work was worth it.

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Sheltering Walls: Palliative and Hospice Care

Podcast Link

Jennifer Fargo Lathrop, MDiv, BCC-PCHAC

The suggestion of palliative or hospice care for a loved one with dementia can be scary: It means their health has declined significantly. Although we know that change is a natural part of life, accepting it is a different story. Grief, anger, disbelief, and fear are just some of the emotions I've witnessed in patients, families, and friends. In the case of Alzheimer's disease and other forms of dementia, the caregiver often has the added burden of having to make these decisions on their loved one's behalf.

It might be hard to see it, but palliative or hospice care can be a source of comfort during a frightening time. A surprising fact is that people who are on hospice care live longer than those with similar types of illness who are not.

Why is that? I believe it is because of the care provided by hospice nurses and physicians 24/7. And I also believe it is because of the care that the entire team provides to the family by offering information about caregiver resources, documents such as advanced healthcare directives, and many other things—so that you do not have to figure out so much on your own.

As you witness the changes in your loved one and confront the decisions that need to be made in each phase of their decline, perhaps there will be comfort in the fact that you are providing this immensely challenging care in the expected final season of your loved one's life. And you are not alone. And I believe that's how we cope, together with the guidance of others—in this case, a team of professionals dedicated to bringing comfort during this unique time.

Hospice and palliative care have a long and rich history. Thanks to Dame Cicely Saunders, a nurse, physician, and social worker in Great Britain during World War II and the mother of hospice care, the phrase “total pain” entered our vocabulary. “Total pain” means that the pain of life-limiting illness is not just physical, but also has emotional, social, and spiritual dimensions. All of these are detrimental, and all require attention. Her second contribution was recognizing the need for a multidisciplinary team approach to address these diverse aspects of pain. Today, both hospice and palliative care offer patients and families a team that includes a physician, nurse, spiritual care provider, and social worker.

There’s often some confusion over what separates palliative care from hospice care. They’re similar in that they both address the care of people with serious, life-limiting disease. But there are important differences.

First, folks on palliative care have a more open-ended life expectancy than those on hospice.

Second, those on palliative care can receive both palliative treatment—that is, care to relieve symptoms and improve quality of life—and curative care. In contrast, those on hospice have a more limited life expectancy, and have moved from a treatment plan to a care plan that emphasizes comfort and quality of life.

Palliative care is also more accessible than hospice. The patient or family can ask for a referral to palliative care, or a physician can initiate the process. Palliative care services were initially found only in the hospital, but have started to appear in clinics to care for people who are not hospitalized.

The team members also make house calls.

Hospice care can also be requested at any time but can only be initiated after a physician certifies the patient's eligibility. A hospice referral happens when curative care options have been exhausted, and it's time to focus on the best quality of life where the patient lives—whether that is their family home or a care community.

Let me speak a bit about my particular role as a spiritual care provider. I use "spiritual" in a broad sense, focusing on more universal concerns that address the question, is there a way to find meaning in what is happening through the spiritual or values-based aspect of their lives? What drains the family emotionally, and what sustains them? What are their fears or concerns?

My goal is to meet my clients—whether patient or caregiver—where they are so that I can provide compassionate care consistent with their values. For some, my work is deep, attentive listening. For others I might offer sacred scriptures, poetry, or music. Some people feel more sustained by factual information and resources.

My approach to people with Alzheimer's disease is very specific. I take it slow. I move slowly, speak slowly, and allow silence. These intentional actions give the patient a sense of me as a non-threatening participant in their world.

I then evaluate the responsiveness of their sensory faculties—vision, hearing, smell, touch—and use them to guide my interventions. I carefully observe what folks are interested in. I will show photos of nature scenes and see if they look at them. I will sing a bit and see if they seem interested. If there is a flower in the room, I will bring it over to see if they respond to the fragrance. I will squeeze a shoulder or take a hand and see if they appear comfortable with touch.

This evaluation is ongoing. I've noticed that responses change and may require a different intervention over time. At the same time, I take into account that the patient is less likely to respond as their disease progresses, though I always assume they are still taking things in, which guides how I speak to them. So, unless unwelcome, I persist with the interventions they accepted earlier, such as music, prayers, poetry, and gentle touch.

With verbally responsive folks, I select topics of interest to them. I compliment their shirt or hair or talk about something concrete in our immediate view—a photo or memorabilia or the colors in their room. It doesn't matter if they don't reply. I orient them to the season and the weather, recent holiday celebrations.

I often sit beside my clients and settle into the peace of our shared space. If the space isn't peaceful, I join them in walking, or push them in their wheelchair, or try to understand and name their frustration.

Music can create a calming space. For patients with a faith tradition, I play music from that tradition. I play secular music from their youth. As an alternative to speaking, which can feel demanding, I often sing. I also find repetitive sounds and rhythms helpful in reaching my clients or creating a peaceful atmosphere. I may turn to chants, such as the Taizé chant "Dona Nobis Pacem," which means "Grant Us Peace." For non-verbal folks, I even go back to nursery rhymes.

My main goal is to simply be with the person I'm visiting—to enter their world and let their abilities guide my actions. I don't want to challenge them to do or remember things they cannot do or remember. I aim to find what they can do and what they enjoy, and provide these things as much as possible.

If you hear the recommendation for palliative care or hospice, I hope you won't feel afraid. You may feel brokenhearted. You may feel numb. You may feel shocked, sad, or even a little relieved. All of these feelings are part of this journey. But I hope your fear is quelled by the care offered by the professionals on your team. These words by John O'Donohue speak to the protective space created by palliative and hospice care:

"On our farm in the winter, we put the cattle out on the mountains into the winterage. ... Because the landscape is bleak, there is little shelter. Every so often out there, one notices semicircular walls. The cattle know them well. These are the 'sheltering walls' when winds and storms blow up."

May we be a sheltering wall for you at this time.

Jennifer Fargo Lathrop, MDiv, BCC-PCHAC

Spiritual Care Provider
Palo Alto Medical Foundation

Treating Alzheimer's Disease—Where We Stand

🔊 **Podcast Link**

Steven E. Arnold, MD

We are all looking for the magic pill that slows down or stops Alzheimer's in its tracks. We even have research that seeks to reverse some of the brain damage from Alzheimer's disease. Researchers are making good progress, but unfortunately, we aren't there yet.

Medical treatment for people with Alzheimer's disease and other degenerative dementias can be broken down into a few major categories: prescription medicines, prescription medicines for psychiatric symptoms that can occur in Alzheimer's, and over-the-counter and natural products.

In terms of current medicines, our ability to treat Alzheimer's disease is very limited. A few medicines in a category called *cholinesterase inhibitors* have been approved for the treatment of Alzheimer's dementia for about 25 years now. These medications have been shown to provide some very modest benefits for some people.

Aricept® is the most widely prescribed of these. Its generic name is donepezil. Other medicines in the same family as Aricept include Exelon® or rivastigmine, and Razadyne® or galantamine. The logic behind these medicines, and the reason we use them, is that some of the important brain cells that die in Alzheimer's disease produce the brain chemical acetylcholine—one of the many brain chemicals that enhance or sustain learning and memory. But acetylcholine has a limited lifespan. Cholinesterase inhibitor medicines like Aricept *inhibit* or decrease the turnover of acetylcholine in the brain, and so whatever acetylcholine is produced by the remaining brain cells lasts longer.

In addition to Alzheimer's disease, cholinesterase inhibitors also seem to provide some benefit in vascular or mixed dementias and in Lewy body dementia, related to Parkinson's disease.

The acetylcholine inhibitors are generally very well tolerated without many side effects. Some of the possible side effects, especially when someone just starts on the medicines, include stomach upset, nausea, loose bowels, or diarrhea. Some people get headaches or muscle cramps. Starting at a low dose and slowly building up usually avoids these side effects. A few people may develop very vivid and sometimes uncomfortable dreams, because acetylcholine also plays a role in dream sleep. Rarely, cholinesterase inhibitors can slow heart rate, which can be dangerous in people with certain heart conditions, leading to fainting or falls.

Another approved prescription medicine for Alzheimer's dementia is Namenda®, whose generic name is memantine. Memantine is in a different chemical class from the cholinesterase inhibitors. It works by blocking the activity of NMDA, a neurotransmitter in the brain that when unregulated, as can occur in Alzheimer's disease, can have negative effects on brain cell health.

Very recently, the FDA granted a special accelerated approval for a brand new medicine, aducanumab (brand name Aduhelm™). This is an immunotherapy that attacks amyloid in the brain. It is administered by a monthly intravenous infusion, and potential serious side effects have to be monitored carefully. Its approval has been very controversial. While the clinical research trials showed that aducanumab effectively lowered amyloid in the brain, they did not show that this provided any clinical benefits for the patients. Only additional studies will be able to tell.

Psychiatric medicines can play a very important role when behavioral or neuropsychiatric symptoms occur. While certainly not true for everyone, common symptoms include depression, anxiety, agitation, and sleep disturbances. Hallucinations or delusions are also not uncommon. These symptoms may emerge at different points over the course of the illness and in different ways. They may be mild and temporary, or severe and persistent. It's important to talk with a physician if these symptoms occur and to discuss whether medications could be helpful.

For the patient with a memory disorder, talk therapy or psychotherapy is often not that helpful because of the patient's inherent difficulty retaining information, such as insights or the counselor's suggestions. On the other hand, counseling for the caregiver or family members of the patient with Alzheimer's disease can be enormously helpful. Counseling can offer techniques for coping with mood and behavior problems, such as managing communications with their loved ones, or making adjustments in activities and their environment. In this way, very often we can avoid using psychiatric medicines. But if neuropsychiatric symptoms take on a life of their own in the patient, a dramatic benefit also can be achieved with various medicines, including antidepressants, mood stabilizers, antianxiety medicines, and antipsychotic medicines.

I often get asked about vitamins, nutritional supplements, or other herbal, natural, or alternative remedies for dementia. Understandably, this is a huge market as people seek solutions that scientific medicine doesn't yet provide.

I find it really difficult to give an opinion about any particular product. Some supplements make sense biologically and even show benefit in the lab in test tubes or animal models of Alzheimer's disease. But so few have been studied in well-designed clinical trials.

Vitamin E and ginkgo have undergone some study. Both generated a lot of interest based on their biological effects in cell culture and animal models, and both even showed a little bit of benefit in small pilot clinical trials in humans. But when they were put to a real test and compared with placebo in large national trials, neither showed any benefit. Nonetheless, these supplements, natural products, and some others warrant more serious investigation.

While we have no known cure for Alzheimer's disease, and only modestly effective treatments for its symptoms, we still have tremendous hope as research efforts increase to keep pace with the burgeoning population of people with mild cognitive impairment and dementia.

Today, Alzheimer's and related dementias are epidemic in scope, touching almost all of us personally. Its emotional and social tolls are huge. Economically, Alzheimer's has now superseded cancer and heart disease as the most costly health care problem in the U.S.

Recognizing the disease's sweeping effects, the U.S. Congress passed the National Alzheimer's Project Act, resulting in long-overdue increases in research funding from the National Institutes of Health as well as advocacy foundations like the Alzheimer's Association.

Thanks to research, we are making important headway. Today, we're much better at diagnosing Alzheimer's disease than we were even a few years ago. Research has also revealed many new insights into the cellular and molecular complexities of the aging brain that drive the emergence and progression of the disease. We recognize that Alzheimer's disease is more than the amyloid plaques or tau tangles. We see important contributions from inflammation, vascular injury, and fundamental cell biology processes like oxidative injury, mitochondrial and metabolic stress, protein misfolding, and synaptic plasticity.

While these mechanisms may seem daunting, all of these processes are potential clues, entry points for research into the vicious degenerative cycle of Alzheimer's disease.

We may even already have cures for Alzheimer's disease in hand with medicines developed for other conditions. We just don't know it yet. Some of the same fundamental drivers of conditions like rheumatoid arthritis, heart failure, diabetes, and certain cancers are also at play in the Alzheimer's disease brain. Could any of the medications that revolutionized treatment of these conditions also be helpful in Alzheimer's disease?

So I leave you with one thought: the importance of clinical research trials. We may already have a cure for the disease, but the only way to find out is for patients with Alzheimer's disease to partner with researchers to test treatments in well-designed clinical trials. Getting involved in a clinical trial is a way to actively fight back against this devastating disease that takes so much.

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The Diagnostic Process

🔊 **Podcast Link**

Steven E. Arnold, MD

When people with memory problems suspect they have Alzheimer’s disease, there are usually four main questions they have for me: Is there something wrong with me? What’s wrong with me? What’s going to happen to me? What can I do about it?

These questions can only be answered by first establishing a diagnosis. Not all memory problems and dementias are Alzheimer’s disease. There’s a long list of health conditions that can affect thinking, some of which are very treatable or even curable. Low thyroid hormone levels, low vitamin B12 levels, and liver or kidney disease can all have effects on the brain. A CT or MRI scan of the brain can reveal small strokes, fluid collections, or tumors that have been growing that are affecting memory and thinking areas of the brain, some of which may be very treatable.

When I meet with a patient for the first time, I follow a classical medical history and physical exam approach. I strongly recommend they bring someone who knows them well to the visit—a spouse or other family member or friend—in case the patient cannot remember important details.

I like to get background information about a person’s health history and life experiences. I want to know the signs or symptoms that made them believe their memory and thinking were off. I then look deeper: Have these symptoms gotten worse over time? How much do they affect day-to-day life? For example, is the patient independently taking care of their business affairs, housework, and self-care, or do they need help or prompting to get things done?

I ask questions to see if the difficulties are confined to memory or whether they affect other related functions, such as language, or organization and decision-making—what we call “executive functioning.” I ask about the patient’s visual or spatial abilities, like navigating space outside or inside the home. Changes in personality, as well as any new physical difficulties such as altered balance and walking, or loss of dexterity or ability to use utensils or tools, can also be indicators of thinking difficulties. I ask about changes in hearing, vision, or smell, which can be linked with cognitive difficulties.

Have they had any other neurological problems like strokes, seizures, or concussions? Have there been any changes in the person’s ability to control their bladder or bowels? Are there any painful conditions? You can imagine that this comprehensive evaluation takes time.

I then like to learn about personal and family health history, especially if their parents, siblings, aunts or uncles had neurological problems, like Alzheimer’s or Parkinson’s disease. It’s important to get a sense of someone’s personal background, whether their childhood was healthy or difficult, how far they went in school, what kinds of work they did, and their current and past habits—especially tobacco, alcohol, or drug use.

The patient’s environment can provide important diagnostic clues. Have there been any toxic exposures through work or hobbies? These factors may affect the risk for developing memory problems later on in life. It’s necessary to know about all medications or supplements, some of which can also affect memory and thinking.

A thorough physical exam is important to determine if the thyroid gland is enlarged, or if heart murmurs or heart rhythm irregularities are present, which might point to a risk for blood clots that cause strokes.

Neurological and cognitive testing are part of this exam. A neurological exam tests muscle strength, sensation, and coordination, all of which can indicate whether there are any focal problems in brain function, Parkinson's disease, or other neurological conditions that affect memory and thinking in ways similar to Alzheimer's but would require different treatments.

A formal cognitive screening exam can take as little as five minutes. It's important to note that people can often have significant memory and thinking difficulties but not be aware of it. The answers to specific questions in cognitive testing can help pinpoint problems in memory, visual-spatial abilities, language, and mental flexibility.

Say someone comes to me with a history of slowly worsening memory and thinking difficulties that at first were hard to distinguish from changes that normally happen in our 60s and 70s. Indeed it's not always easy to tell. All of us slow down some as we age. We find it harder to do two things at once. We might have more frequent, though generally benign short-term memory hiccups than in the past. You see someone familiar and can't quite place them, but then it comes back to you. It's common to have difficulty finding words—especially coming up with names of people or things that are just on the tip of the tongue.

With very rare exception, this is all a universal part of aging. Concerns arise when there's been a *noteworthy* decline from the person's previous ability to think and remember. As I just mentioned, a cognitive screening test might help isolate pathological problems from normal aging. Diagnostically, if we observe a significant change, but the patient's still getting by in their day-to-day life, albeit more slowly and with greater effort, we call it mild cognitive impairment. But if the impairment is bad enough to cause struggles managing day-to-day affairs, whether it be shopping or paying the bills independently, preparing meals and keeping house, or taking care of their personal hygiene—we call that dementia.

Cognitive impairment and dementia have many causes. We look especially closely for identifiable and treatable causes like other medical conditions, medication side effects, stroke, Parkinson's, or tumors. If we find no evidence, then the most likely cause is Alzheimer's disease.

But Alzheimer's is a hard disease to diagnose with certainty. The only way to be 100 percent sure of the diagnosis is by looking at someone's brain tissue under a microscope after they die, where we see, as Dr. Alois Alzheimer did over 100 years ago, amyloid plaques and tau tangles. These plaques and tangles are made of specific proteins that we all normally have, but in Alzheimer's disease, they get processed abnormally, crumple up in and between brain cells, and slowly accumulate over time. This accumulation is strongly associated with the death of brain cells. As these brain cells and the connections between them degenerate, memory and thinking decline.

While I say the only way we can be 100 percent certain of a diagnosis is by sampling brain tissue, it's important to note that over the past 10 to 15 years there has been tremendous progress in biomarker research. Biomarkers are laboratory or imaging tests that highly correlate with disease pathology in the brain. So, we now have MRI measures that can show patterns of brain degeneration, or PET scans that can reveal the amount of amyloid or tau in the brain. Spinal fluid samples allow us to measure levels of amyloid and tau proteins as well as many other proteins that reflect disease and degeneration in the brain.

With these biomarkers we can now predict with more than 95 percent certainty whether the cognitive difficulties are indeed caused by Alzheimer’s disease. Other very exciting research is now showing promise with ultrasensitive lab tests that detect amyloid and tau proteins that leak out into the bloodstream. These protein levels in blood are very low, but may be enough to determine if there is Alzheimer’s disease in the brain with a reasonable degree of confidence.

It’s important to recognize that more often than not, more than one disease process is at play in causing a person’s cognitive decline and dementia. In addition to Alzheimer’s disease plaques and tangles, it’s very common also to see brain changes such as atherosclerosis of the blood vessels as well as narrowing and stiffening of the small branching vessels feeding the deep parts of the brain.

Back in the old days, dementia used to be called hardening of the arteries in the brain. That’s because atherosclerosis in the brain’s blood vessels was so common. But that was before we were able to prevent atherosclerosis by diagnosing and treating its main causes: high blood pressure, diabetes, and high cholesterol. I think the term is still apt in some people who display vascular disease and mini-strokes. To a lesser degree, small vessel disease frequently contributes or adds to Alzheimer’s dementia in many if not most people. Some people also have Parkinson's disease pathology along with Alzheimer's and vascular pathologies. It's important to be aware that there is likely more than one thing going on. From a treatment standpoint, we need to tailor our approach to treat these other conditions if we think they are contributing to dementia.

When people ask me about my diagnostic approach to the "typical" patient with Alzheimer's disease, I say I'm still waiting to meet a typical patient. As we've seen, there are so many possible factors contributing to memory and thinking problems. For this reason, all of the steps in my evaluation I discussed today are critical to coming up with the diagnosis and recommendations that are right for any individual's treatment and care.

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The Stages of Alzheimer's Disease

🔊 **Podcast Link**

Felicia Greenfield, MSW, LCSW

As Executive Director of the Penn Memory Center, I am frequently asked by families living with Alzheimer's disease, "Which stage of the disease is my loved one in?"

I base my answers on what I've learned from the medical literature, confirmed by years of working with families living with the disease. I explain that Alzheimer's disease is generally broken down into three stages: early or mild, middle or moderate, and late or final. To define an individual stage, I take into consideration three factors: the person's cognition, their ability to function, and their behavior.

Cognition refers to memory, and the ability to speak and comprehend others, recognize friends and family, and exercise good judgment.

Function is the ability to perform day-to-day activities including personal care and social roles. These activities are usually divided into two groups: *basic* activities of daily living, which include feeding, dressing, grooming, toileting, and bathing; and what we call *instrumental* activities of daily living, such as using a phone, preparing a meal, maintaining a home, and managing money and medications.

Finally, behavior refers to how a person acts in social situations and at home.

Generally speaking, we teach caregivers that in the early or mild stages of Alzheimer's, a person has less ability to function independently and perform complex tasks, but can still perform basic activities of daily living (feeding, bathing, dressing, grooming, toileting). Cognitively, the person with mild dementia may have trouble learning new things or finding words, and might have minor blips in judgment. We expect to see minor personality changes, such as being less socially engaged.

It's important to recognize that early-stage Alzheimer's looks different in every person. Consider the changes in these three people. John could still get around on public transportation by himself, and was still working out, but he couldn't tell me his address. He was mild-mannered and as friendly as ever, though much more reserved. Maggie, in her 40s with young children, was my youngest patient. She had significant problems finding words, cried frequently, and was angry. Then there was Sally, an artist who seemed oblivious to her illness; she was happy and delightful to be around, but this former artist refused to paint, and lost her short-term memory.

Caregivers often bear a double burden, coping not only with changes in their loved one's behavior but their own feelings, and changes in their own lives. I heard from a woman just yesterday who said that if this was the early stage, she didn't know how she'd make it to the later stages. The title of this podcast, *Bob's Last Marathon,* reminds us that the Alzheimer's journey truly is a marathon, not a sprint. And caregivers should know this from the start, to arm themselves with resources and build their inner strength to endure the long road ahead.

In the middle or moderate stage of Alzheimer's, function remains mostly intact, but the person with dementia may need some reminders or help with basic and instrumental activities of daily living. Cognitively, we notice significant memory loss and disorientation. Conversations are often disorganized, judgment is impaired, and attention span becomes shorter. In this stage, behaviors can become challenging. We sometimes see psychosis in the form of hallucinations or delusions. Some people wander, and often they appear more angry or agitated. Some sleep more during the day or have sleep problems at night.

This stage can be confusing for caregivers because the person living with dementia still looks like themselves, and they're able to function well in many ways. Caregiving becomes more difficult due to challenging behaviors. In an earlier episode, Occupational Therapist Rachel Wiley talked about becoming a behavioral detective to get at the root of the problem, and changing the environment to eliminate triggers. For example, Madeline's husband, who was weight-conscious, wouldn't eat because he felt she gave him too much food. Her ingenious solution was to use larger plates to make the meals look smaller. When adapting the environment doesn't work, medications may be needed to help calm or relax the person with dementia.

At the moderate stage, caregivers may benefit from counseling to manage the continual changes in this progressive disease—which may call for more support in the form of either added in-home care or care outside the home. As one caregiver told me, just as she got a handle on one set of challenges, she had to adjust to another "new normal." A family I worked with moved their loved one to a care facility when he began to wander out of the house alone, sometimes driving and getting lost in the middle of the night. Patricia felt her husband needed more care than she could provide when he became more agitated and started urinating all over their house. When Colleen's husband, Sam, got expelled from an adult day center for violent behavior, she felt she couldn't continue caring for him at home alone. But it wasn't long before she brought him back and hired full-time in-home care. Through her laughter, she said, "I didn't know I had this much patience inside of me!"

As trying as it can be to care for someone with Alzheimer's disease, new and beautiful relationships can emerge. Suzanne, an artist, created sculptures out of the copper wires her husband pulled from old television sets. She framed them, and they even showed their work together in galleries.

As Alzheimer's progresses to the late stage, the person with dementia can no longer function independently. Cognitively, only fragments of memory remain, language is significantly impaired, and they may no longer recognize friends or family. The individual can become restless and unable to focus, and be difficult to console or redirect. Their appearance can change, and they typically are unable to attend functions. In my experience, this stage comes on faster for people residing in care facilities.

Many caregivers request a hospice assessment in the final stage. I'm now working with three caregivers with spouses in home-based hospice who are sharing moments of joy and sadness, together until the end.

Through all three stages, Alzheimer's changes the lives of the entire family. As the disease progresses, so do the strains on the caregiver, which can put their health at risk. Self-care is so important: People are of little use to others without their own physical and emotional health intact. If you asked the people I've supported, I think they'd confirm that the reason they are strong, resilient, and compassionate is that they've figured out how to care for themselves. They've educated themselves in the course of this illness. They've found time to exercise and meditate. They've joined support groups and stayed connected to others, and kept up with their own health needs. They didn't ask for this situation, but they've worked hard on acceptance, and with the help of others, they've been able to endure the long journey of dementia caregiving.

The stories of people I support share themes of resilience and newfound sources of purpose and meaning. Finding meaning in the face of loss can propel you forward, sustain you, and provide a sense of hope, even in the darkest times.

Felicia Greenfield, MSW, LCSW

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Financial Concerns

🔊 **Podcast Link**

Nancy Galgoci, CPA

Ten years ago, my sister's 61-year-old husband was diagnosed with Alzheimer's disease, which began a new chapter in all aspects of Sue and Paul's life together, including their financial affairs. This was marked by Paul's retirement from his job as an accountant, and placement on Social Security disability. During most of the period of his diagnosis, Sue was employed as a hospital-based nurse. Paul found part-time work in a local grocery store, where he relished the social interactions. Over time, as his disease progressed, this job become too stressful and he left.

Paul was still functioning fairly well, so Sue was able to continue working and manage his care with the aid of a well-organized network of volunteers that included family, friends, neighbors, and members of their church. Sue created a schedule of support. Her volunteers would stop by regularly to visit, check up on him, chat with him, and drive him to activities and appointments. Thanks to this dedicated team, Paul was able to enjoy an active, rich life, much like any retiree—attending group activities like bingo, reading his favorite fast-paced thrillers, playing the saxophone, drawing, and spending time with Sue at night.

My role was helping Sue in financial planning and budgeting. Living with an accountant, my sister was not much involved in the family's finances. Documents were hard to locate, and sorting through financial paperwork and online documents took longer than expected. Even the most seemingly trivial task of changing their phone plan was daunting. This added to the stress and worry of providing comfort and care.

A turning point came in early 2016 when Sue broke her wrist. No longer able to drive or work, she too obtained Social Security disability—a painstaking process. As her wrist healed and her disability time was ending, Sue realized that Paul needed full-time care. She retired from nursing to care for Paul full time. As Paul's Alzheimer's symptoms worsened, Sue needed more help from her volunteer network, who along with friends and family ramped up their support, providing transportation, meals, help with household chores, and visits with Paul. By midyear, it was clear to Sue that even this vast support network was not enough. She needed to consider finding outside help.

This is when finances and insurance become tricky. Those like Sue and Paul who do not have the funds to hire outside help must rely on some form of insurance. Unfortunately, Medicare does not cover the costs of custodial care—that is, help with day-to-day activities like eating, bathing, and hygiene. Long-term private insurance options are difficult to obtain for several reasons. First, there are fewer and fewer available as many insurance companies decide to exit the market. Second, it is expensive. And finally, it is not available once a person has been diagnosed with dementia.

This leaves Medicaid or Medicaid waiver programs for custodial home care services. But as most people know, Medicaid is only available when income and assets are below a certain level. Eligibility thresholds vary from state to state, as do legal requirements and procedures. The caregiver spouse will also need to separate and protect their individual assets—for example, by setting up a trust, so that in the long term, the spouse will not be depleted of assets for his or her own needs.

Applying for Medicaid is a complex and time-consuming endeavor. I highly recommend hiring an elder care attorney who specializes in Medicaid eligibility for your state. When possible, a trust is set up to separate the spouses' assets in order to qualify one spouse for Medicaid and to provide for the spousal caregiver's own needs, immediately and in the future. Sue found her attorney through a neighbor, but the local bar association would also be a good referral source.

In Sue's case, the elder care attorney also recommended a geriatric social worker. The social worker coordinated the practical details of applying for Medicaid. Additionally, the social worker helped Sue select an appropriate organization for Paul's home care through the waiver program. Sue's social worker was a member of the National Association of Professional Geriatric Care Managers, an organization that helps navigate legal, financial, and entitlement issues. Local Area Agencies on Aging and Alzheimer's Association chapters can also be good sources of advice.

Do not expect overnight results. It took Sue time and patience to find the right people and work with local and federal agencies. It involved multiple conversations—sometimes repetitive ones with different people in the same organization—to keep the ball rolling. It involved getting records in order and digging for documents, some dating back seven years. Luckily, their perseverance paid off. By the end of summer, the New York State Department of Health granted Paul Medicaid status.

With Medicaid, Paul was able to be enrolled in a Medicaid waiver program, which allowed Sue to bring in home caregivers for much of the day and night. While they helped with Paul's day-to-day needs, most were not trained to handle his increasingly frequent psychotic episodes. In late October, one of these episodes resulted in a hospital admission. When he was discharged, he entered a Medicaid-certified nursing home. Sue visited daily, staying for a good part of the day to keep him company, entertain him, and make sure he had adequate care. The children visited when they could. Paul passed away a little more than a year later.

Throughout the Alzheimer's journey, especially in the face of financial constraints and worries, Sue's network of trusted, supportive family, friends, neighbors, and generous volunteers all proved invaluable. Knowing we are not alone on the journey can give us strength to endure, to value our time with our loved ones, and to find a level of peace within ourselves.

Nancy Galgoci, CPA (retired)

Let’s Support Family Caregivers

🔈 **Podcast Link**

Venus Wong, PhD BCBA

If you’re one of the 53 million caregivers in the United States, you may know instinctively, from hands-on experience, just how important your care can be to the quality of your loved one’s life—from feeding and hygiene to helping with medications and transportation.

But what you might not know is that the difference you make is measurable: Research shows that people who have caregivers are demonstrably healthier. And that has a ripple effect, resulting in fewer doctor’s visits, hospitalizations, and institutionalizations—which all translates to lower health care costs.

For example, a recent analysis showed that Medicaid patients with some family involved in home care spent $1600 less on health care over nine months than those without a caregiver. The authors considered a possible link between the lower cost and better health: These individuals had lower rates of infection, bedsores, and shortness of breath, among other measures, and as a result, used health care resources less often.

A different six-month study looked at whether the emotional health of the spousal caregiver—the husband or wife—had an effect on health care costs; specifically, they looked at the caregivers’ sadness on the depression scale. What they found is that the higher costs were significantly associated with caregiver sadness; sad caregivers spent over $1300 more on health care.

The importance of caregivers is even more evident for people with dementia, whose cognitive decline may make communications even harder. Of course it makes perfect sense that having a caregiver nearby would help by making sure that critical needs are met.

And yet, as essential as family caregivers are, health care plans and systems often neglect their needs—support is spotty at best. For example, only 1.5 percent of Medicare Advantage Plans offer coverage for caregiver-focused support and programs. Part of the problem lies in the misconception that caregiver support is just too expensive or irrelevant for health care systems. But as we've just seen, supporting caregivers may not only be good for the health of their patients, but also a good investment for health care systems. If family caregiving is healthier for patients and more economical, why isn't it better supported? Imagine what could happen if caregivers got support.

Fortunately, things are changing.

There are many ways that health plans and systems can support caregivers—and some do. They can make caregiver support groups part of their plans, giving enrollees the chance to share and learn important skills. They can acknowledge the central role of caregivers by making support part of the patient's health plan. They can use technology to make care easier. For example, they may leverage automated, customized phone check-ins and share timely care tips. These are just a few strategies identified by me and my colleagues through our research as being not only effective, but cost-effective.

A good model is the Resources for Enhancing Alzheimer's Caregivers Health (REACH VA) from the Veterans Administration. REACH VA combines caregiver education, support, and skills building. The program was not only shown to improve health-related outcomes for patients, such as less depression and better medication management, but by reducing outpatient visits, hospitalization, and medication uses, it reduced costs for the VA by more than a third. Programs similar to REACH VA can be found through local nonprofits, Area Agencies on Aging, and the Alzheimer's Association. What a win-win-win for patients, caregivers, and the health care system!

Health care policy is also starting to broaden its focus to include the support of caregivers. For example, about 40 states have signed the Caregiver Advise, Record, Enable (CARE) Act into law. The CARE Act sets standards of care for the support of family caregivers whose loved ones are hospitalized. It requires hospitals to identify caregivers, ensure that caregiver information is part of the patient's medical record, and put programs into place to make caregivers part of the plan for patients after discharge. Even though this is a hospital-specific program, it is really good news!

Also, about two years ago, the Centers for Medicare & Medicaid Services authorized Medicare Advantage Plans to cover direct support for family caregivers using supplemental benefits. What this means is that Medicare Advantage health plans now have more flexibility to design benefits that support their enrollees' caregivers. This is a huge improvement as it gives health plans more autonomy to directly develop or purchase services that support caregivers.

However, Medicare Advantage Plans have been slow to integrate the policies. We still have more work to do to make these recent advances a reality. Our efforts need to extend beyond private and public health plans, and even beyond state policy, to make high-quality support available to caregivers on a large-scale basis. We need to build caregiver support into our health care infrastructure, its very groundwork—and that demands national attention.

The Recognize, Assist, Include, Support, and Engage (RAISE) Family Caregivers Act, which became law in 2018, is a very promising step. It directs the Secretary of Health and Human Services to identify actionable steps for local communities, care providers, government, and other public agencies.

The aims of the RAISE Family Caregivers Act are wide-ranging. It is looking to support the health and independence of patients and caregivers across all health care and long-term settings through programs to improve access to housing, safe living spaces, food, and transportation, and also to reduce social isolation. It's examining ways that health care providers can create more meaningful and culturally relevant information, services, and support for family caregivers. The RAISE Family Caregivers Act is exploring respite care, as well as workplace policies that would include flex time or home office options for caregiver employees.

There's much left to do, but there is also help available to caregivers now.

Contact your health plan and ask them about care options for you and your loved one, such as support groups and respite care. If they do not have these offerings, simply asking may register as a gentle nudge that there is a need they should be considering!

Your local Area Agency on Aging (AAA) is also a good source, and may also provide respite care along with other valuable support services. Free insurance counseling is sometimes available, or they may direct you to other agencies.

If you want to take a more active role in effecting change, your AAA may be a great place to start. AAAs along with other national advocacy agencies such as the Alzheimer’s Association often invite public participation on local or national levels. Follow their social media and voice your opinions!

There’s no quick fix for this complex societal issue. But I’m optimistic that there will be more organizational and policy improvements to better support caregivers.

Venus Wong, PhD BCBA

Founder
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Looking Ahead

🔈 Podcast Link

Lena Chow Kuhar

One night, while Bob was on a trip in the remote deserts of New Mexico with his daughter Kim and son-in-law Tom, I received a call from Kim reporting that Bob's speech was sounding a little slurred, like someone who'd just been to the dentist. I immediately called our other son-in-law, Steve, a physician who, hearing Bob's speech, advised that he go to the emergency room. The doctors diagnosed Bob with a transient ischemic attack, or TIA, which, as the name suggests, is a temporary condition—but still a warning sign of stroke and a precursor of brain injury. Bob got home safely to California, but the incident triggered my thoughts about mortality. Something told me this might be a cue to get things in order.

Like most people, we had neglected updating our wills, or making decisions about health directives and life support in the event of a health crisis. But Bob's TIA was a wake-up call, prompting steps I'm not sure when we would have otherwise taken. Bob also took part in these next steps, since at this point he still had good cognitive skills—he was yet to be diagnosed with Alzheimer's.

We began by looking up our wills, which were first drawn up more than 20 years before when we were newly married, but our lives had changed significantly: Our children were grown and independent, we had several grandchildren and even a great-granddaughter, and one of Bob's sons had passed away, leaving behind three children.

We found an estate attorney to update our wills and set up a trust. Bob and I did everything together—found the attorney, gathered the necessary forms and information, and made decisions—as equal partners.

Our estate attorney also advised us to prepare our advance health directives. He explained that an advance health directive is a legal document that allows an individual to designate someone, usually a family member, to make health decisions for them when they can no longer make such decisions due to physical and/or mental conditions. Bob and I knew it was common for a husband and wife to name each other as the designated decision-maker. But since we have two physicians in our immediate family, I proposed that we each name our daughter, Andrea, and her husband, Steve, as a backup. Knowing how well Andrea and Steve work together, I felt secure that, if called upon, they would carefully study the facts and respect our individual wishes. Years later, when we were facing the prospect of transitioning Bob to hospice, I was especially grateful that Andrea could share in the decision and take the lead by signing the necessary documents.

Fast forward to the next year, on a different trip, this time aboard a cruise ship in the Galapagos, where Bob, in a confused state, began opening cabin doors looking for his car. Very concerned, I made it a priority to visit our physician upon our return. A series of doctor visits led to a diagnosis of mixed dementia—a combination of vascular dementia and Alzheimer's disease.

The year that followed was filled with confusion, anguish, and denial. But I finally came to terms with Bob's diagnosis and began putting together the support system we needed, which included enrolling Bob in a day care program. In the process, we met with Kate, a nurse and case manager in our health care system. Based on Kate's advice, we completed a document called POLST, P-O-L-S-T, or physician's order for life support.

Bob and I had heard about POLST from a guest speaker at an Alzheimer's support group. In a medical emergency, POLST gives specific directions for first responders about the level of medical intervention we would want to keep on living.

For example, if we were unconscious and had no pulse or stopped breathing, would we elect CPR, or would we want to allow a natural death, also known as DNR, or "do not resuscitate"? If we were alive, but couldn't make decisions about treatments for our condition, would we prefer comfort measures only—for example, using medication only to relieve pain and suffering—or limited treatments such as IV fluids or antibiotics? Would we want to be intubated, or not? Or, at the highest level of intervention, would we choose full treatment—everything medicine can offer?

The signed POLST documents, one for each of us, became a part of our health record. A copy was kept in a place where first responders would know to look on an emergency call. In the case of our community, that place is one of the shelves on the inside of our refrigerator door. I also made sure each and every home care person and member of our family was aware that we had a POLST document, and knew where to find it.

By completing the advance health directives and POLST forms ahead of time, we had the benefit of clear thinking and thoughtful analysis of our options, which might be very difficult during a health emergency. We also relieved our loved ones, as educated as they might be, of the burden of making these difficult decisions with little knowledge about our wishes.

Bob's diagnosis triggered yet another action. On the advice of our care manager, I had a candid talk with Bob while he was still high-functioning, clinically speaking. Together, we saw the estate attorney again, this time to update our trust and to name me as the sole trustee—the one who would make all decisions related to our wills and our assets. This was an emotional moment. I felt pangs of sadness watching Bob relinquish his power and sign away all of his possessions. At the same time, I was deeply touched by the strength of our marriage and Bob's unconditional trust in me to make the right decisions for him, for me, and for our heirs.

Looking back, I am grateful we had the forethought to complete the wills, the advance health directives, and POLST. Having them in place makes me feel more secure, and I also see them as important tools. Going through the process of completing them helped us take the time to face realities and look ahead. They helped us reflect on our priorities. They gave us a sense of power to make key decisions, during a time when our lives were overtaken by a disease we couldn't control. Today, in the hands of the next generation, they are road maps to help navigate the inevitable changes to come.

Lena Chow Kuhar

Beyond Plaques and Tangles

Understanding Alzheimer’s Disease

🔈 Podcast Link

Steven E. Arnold, MD
Stephen M. Strittmatter, MD

Dr. Arnold: Before we dig into specifics about the treatment landscape in Alzheimer’s disease, I’d like to just refresh people on some of the terms and concepts we use in the field. So for all of us, memory and thinking slow down as we get older. We have more senior moments, it’s harder to multitask, and it takes longer to get things done. But while it takes more effort, we still manage our lives independently.

Dementia is the term we use when we have more than mild cognitive difficulties where it affects our day-to-day independent functioning and we require assistance. And this will affect a third to a half of us as we commonly live into our 80s or 90s or even beyond now. Dementia is not normal aging. It indicates that there’s a disease affecting the brain. Alzheimer’s disease is by far the most common disease causing dementia, but other diseases like vascular dementia from strokes and mini-strokes, Parkinson’s disease–related problems, different frontal lobe dementias, and a long list of other rarer diseases can cause dementia.

If you examine brain tissue under the microscope after someone dies, each of these diseases has its own signature lesions in the brain that you can see. For Alzheimer’s disease, the signature lesions are the so-called senile plaques made out of amyloid protein and the neurofibrillary tangles that are made out of tau protein. In vascular dementia, it’s atherosclerosis in the large blood vessels feeding the brain or narrowing of the small vessels deep inside the brain. For

Parkinson's-related diseases, it's the Lewy bodies made out of a protein called alpha-synuclein. And other diseases have their own pathological lesions that define them.

But these lesions that we see in the microscope aren't the whole story. They may be just tips of the icebergs. We know that there are many complicated cellular abnormalities going on that we can't really see under the microscope, problems in cell metabolism, abnormal functioning of genes, inflammation, oxidative stress and more. And to varying degrees, all of these exist in vicious cycles with the amyloid, tau, and synuclein or other protein abnormalities that define the different types of dementia.

In Alzheimer's disease and all of these diseases, the final common pathway from all these different factors to memory loss is malfunction and degeneration of synapses. Synapses are the connections between brain cells. Vast networks of brain cells need to fire in concert for us to think, to learn and remember. If the connections between brain cells aren't working or are lost, brain cells won't activate together and cognitive activity fails, and Dr. Strittmatter will be telling us more on this.

In trying to discover and develop new treatments to prevent, to slow down or cure Alzheimer's disease, most of the attention over the last 20 years has focused on the amyloid plaques that define the disorder. Some of the approaches try to prevent the production of amyloid protein itself in the brain, others have tried to prevent amyloid from misfolding or clumping up in the brain, and of greatest interest in the news recently have been the immunotherapies. With these immunotherapies, you administer monoclonal antibodies by vein once a month or so, and these antibodies are designed to attack bad amyloid in the brain and clear it out.

One leading immunotherapy, aducanumab or Aduhelm by Biogen, recently received accelerated approval from the FDA. Other major drug companies are right behind. And these immunotherapies do effectively clear the brain of its amyloid and we can see this with a PET scan. But aducanumab's approval has been very controversial. Two large Phase III clinical trials showed that it can successfully clear amyloid in the brain even back to normal, but people's dementia, their clinical symptoms of memory loss and their problems with daily functioning, still got worse. And it's still not clear from the data whether the rate at which their symptoms worsened slowed down at all. But overall, people still got worse despite removing the amyloid. So what does this mean? To me, it says that in people who already have cognitive impairment due to Alzheimer's disease, removing amyloid alone is not enough to stop the disease. Maybe it's necessary to do that, but it's not sufficient. And more likely, we'll need to get rid of amyloid in combination with therapies for the other factors contributing to progressive decline. We're still learning about this.

Now, tau tangles are the other signature lesions of Alzheimer's disease. And the amounts of tau tangles in the brain actually correlate a lot better with the severity of dementia than amyloid does. So perhaps if we can reduce tau tangles in the brain, that will stop the dementia from getting worse. Tau has been a harder target to develop drugs against than amyloid. It's a more complicated protein in a lot of ways. But there are now tau trials that are in clinical development. We're still waiting for the results to come in. It's still too early to tell how well they'll work.

But whether we are targeting amyloid, tau, inflammation or anything else, our ultimate goal is to save our synapses. If we can protect or even regrow the connections between brain cells, we can preserve our cognitive functioning and stop dementia. There's really no one better to help us understand this than Dr. Strittmatter, who has done such seminal work in both the laboratory and clinic on the growth and maintenance and regeneration of synapses.

Dr. Strittmatter: Thanks very much, Dr Arnold. Billions of neurons in the human brain create a complex electrical network that underlies cognition. In a sense, you could say a biological supercomputer, but even more than that. The electrical impulses in one neuron are transmitted over long distances via nerve fibers called axons. However, when the signal gets to the end of one cell, it can't get into the second cell. The cells are insulated from one another, and it's these synapses which are the specialized contacts between neurons that allow an electrical impulse in the first cell to be converted to a chemical signal which diffuses to the second cell and then triggers an electrical impulse in that cell, all of this through neuronal biochemistry. And we call that chemical that goes from one cell to the other a neurotransmitter.

What's important in Alzheimer's is that these synapses are highly vulnerable to the neurodegenerative process. And as Dr. Arnold mentioned, if you lose synapses, you no longer have a neural network and then you have cognitive symptoms. So this is really at the crux of Alzheimer's disease. Importantly, synapses are not damaged by one thing in Alzheimer's. They're really damaged by a collection of factors: of course, aggregated beta amyloid, but also aggregated tau, inflammation, in particular in the microglial cells of the brain, and metabolic changes, the poor use of glucose, the accumulation of reactive oxygen species. And it's really all these factors together which synergistically damage the synapse. And once we don't have synapses in the brain, then we don't have cognitive function and we have mild cognitive impairment and the progression of dementia.

Here, timing is critical. Amyloid builds up very early. It's actually one of the first things we can detect clinically in the entire Alzheimer's process. But synapses and cognition may actually be okay for 5, 10 or even more years while this amyloid builds up. Eventually though, there's inflammation, tau starts to accumulate, and it's in this phase that synapses are lost because of the coalescence of these multiple factors, and people develop mild cognitive impairment we see the first time they come to the clinic with complaints. We know a lot about this from new brain imaging studies and the pathology of individuals who come to autopsy very early in the disease.

Later in the disease, in the moderate and severe phases of Alzheimer's when even basic functions are lost, there's actually a death of the neurons themselves. So it starts with accumulation of proteins, inflammation, loss of synapses, and then eventually the neurons start dying and there's widespread shrinking or atrophy of the brain. So all of this points to synapse loss really being at the crux of the initial symptoms of cognitive dysfunction. And not only is it the thing that causes neural network failure, it's the location where these multiple factors—amyloid, tau, inflammation, metabolism—come together, and in a synergistic way, produce the symptoms. That's what, in part, makes Alzheimer's a complex disease, a hard target to solve completely with any one approach.

What can we do with this knowledge about synapses? Can we leverage this, discover new therapies? I would say the answer is yes. Laboratory experiments can delve into the idea that synapses are lost and try to understand, at a molecular level, why these synapses are lost in response to these multiple factors. Once we can nail down the mechanisms, then we can try to intervene. If we can intervene to preserve synapses in the brain, even if there's still amyloid and tau and inflammation, we'll have synapses, we'll have a neural network and cognitive performance will be adequate.

As an example, in my own lab here at Yale, we've studied how amyloid, misfolded amyloid beta, triggers synaptic damage, and we've uncovered a pathway that involves a protein called metabotropic glutamate receptor 5 or mGluR5. But the point is that that target is required for synapse loss and memory deficits in laboratory models of Alzheimer's, animal models. And armed with that knowledge, we've developed some compounds that can restore synapses and recover memory function, again in laboratory models, and there's a startup company that's now advancing one of those into early clinical trials.

One way to use knowledge about synapses is to develop new approaches to therapy for Alzheimer's. But equally important, I think, is that this gets us biomarkers for the disease. *Biomarkers* means many different things. Of course, we've probably heard about amyloid beta and tau as biomarkers. They can be measured by PET scans, by CSF, that is cerebrospinal fluid or plasma measures. And these are diagnostic markers in the sense that when they're detected, one can be certain to some degree that Alzheimer's is present as opposed to the other causes of dementia. But biomarkers can also reflect the disease itself and be therapeutic biomarkers.

What about for synapses? I just told you they're tightly correlated with memory and cognition. Can we actually measure synaptic density in the clinic as the disease progresses? There's one method that's been around for quite a while that's based on the brain's utilization of glucose. The brain uses a lot of energy. The brain uses a lot of glucose to drive synapses and cognition. And so by labeling glucose, injecting it and then scanning the brain, one can tell whether different regions of the brain are using glucose at the rate that they should. And in Alzheimer's disease, certain regions of the brain stop using glucose as effectively and that can be detected on a PET scan and it's tightly correlated with the progression of mild cognitive impairment and mild Alzheimer's disease, a so-called surrogate endpoint.

The advantage of this is that that measurement is actually detecting synapses as opposed to measuring memory and cognition. These are highly variable day-to-day. Memory performance can change a lot, but if we want to actually track synapses, we can do it indirectly with this well-known PET measure. However, there's actually been a further development. Recently, another group at Yale developed a way to use the derivative of an anti-epileptic drug to directly measure the synapse structures in the brain. So this is based on a drug called levetiracetam. When it's been labeled and injected, it will bind to the synapses in the brain, and the signal in the brain is a direct measure of how many synapses are present.

This has been used already in Alzheimer's studies and there's a tight correlation with the progression of the downhill course in mild and early Alzheimer's disease. So this allows one to really have a way to track this synapse loss. No matter what drug one may want to develop to make a difference in the progression of Alzheimer's disease, by having these tools, we have a much better way to accelerate the drug development process.

So overall, I'm going to say there is recognition that we've gone beyond amyloid and tau. We recognize the role of inflammation, metabolic changes, and the fact that synapse loss is at the nexus of all these factors really takes us much farther in understanding Alzheimer's, and I think it gives us a lot of optimism and hope that rather than testing amyloid lowering over and over again, there are many more shots on goals that we can take that we can test in the clinic and get meaningful answers and really get to something which, either alone or with combination therapy, makes a difference in Alzheimer's disease.

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Beyond Plaques and Tangles

Looking Ahead

🔈 Podcast Link

Steven E. Arnold, MD
Stephen M. Strittmatter, MD

Dr. Arnold: Alzheimer's disease and other neurodegenerative disease dementias are complicated with a lot of other factors driving the loss of synapses and the death of brain cells. We're rapidly learning how other factors contribute to dementia, and there are many already available and safe drugs that target these factors in other diseases. Could they be helpful in Alzheimer's disease? Will drugs that attack inflammation in diseases like rheumatoid arthritis or psoriasis also reduce brain inflammation in Alzheimer's disease? Will drugs that are used to improve blood flow in people with heart failure help people with Alzheimer's disease? How about drugs we use to improve cell metabolism in diabetes? This is called drug repurposing, taking a medicine that has been shown to be safe and effective for one condition and trying it in another where the biology of the disease suggests that it may respond. We may already have better treatments for Alzheimer's disease in hand, but we don't know it because they haven't been tested in clinical trials yet to see.

Overall, there's been an increase in the number of investigational drugs in registered late-phase clinical trials for Alzheimer's disease over the last five years. Back in 2016, there were 70 different drugs in research trials and now there are over 100. For the medicines designed to modify Alzheimer's disease, over half were focused on amyloid in 2016, and now two thirds of them focus on other factors. There's also a significant pickup in the number of trials of repurposed drugs, and this is a big interest of ours at my institution, Mass General.

One of the biggest challenges in research is, how do we know whether a drug is actually working? Do we really have to wait a few years to see whether the disease progresses or can we get an indication early on? And so the development of biomarkers that can tell us whether synapses are changing, whether they're being preserved or not, is really important.

Timing is really critical because different things that happen in Alzheimer's disease may have different effects at different times during the disease. And this is really important and speaks to the importance of having good biomarker tests to know what is happening in the brain in a given person at any given time.

We need to be able to treat the right person with the right drug at the right time. Yale has been a real leader in PET imaging, especially PET scanning of synapses and many types of synaptic receptors. At Mass General at Harvard a big interest of ours has been in the fluid biomarkers, measuring levels of different proteins in spinal fluid and blood. And I think the huge advances in biomarkers, whether with neuroimaging or with bio fluids, is another reason for optimism. In one sample of spinal fluid or blood, we can measure thousands of different protein molecules involved in inflammation and metabolism, cell stress, along with amyloid, tau, and more recently, synaptic proteins.

With these biomarkers, we're seeing that people also can vary a lot in how much amyloid or tau or synaptic degeneration they have, how much blood vessel disease or inflammation they may have. One of the things that we're recognizing is that Alzheimer's is heterogeneous. Your Alzheimer's disease isn't necessarily the same as my Alzheimer's disease. We should be able to use this information to select the right drug or possibly the right combination of drugs and then be able to measure how effective those drugs are with these biomarkers.

I'd love to hear some of your thoughts about that approach in terms of profiling folks and trying to personalize treatment.

Dr. Strittmatter: There are several very positive aspects. One is Alzheimer's may really be composed of multiple diseases. And if we want to get the right treatments for the right people, we need detailed biomarker profiling of individuals because some drugs may work better for one group than another group, one point. Another is that we provide much more learning data from any one trial if we have biomarker evidence of what's really going on.

One of the things that you touched on earlier was about drug repurposing, and I wanted to say a few words about that. I think that has great potential because developing a completely new drug from scratch is a very slow process. Whereas a drug that's used for some other indication shortens the process and lets us get to meaningful trials much more quickly with drugs that we know at least are safe in some situation.

We've had some experience with that, and the NIH has recognized that this is really a very promising way to speed drug development. The sub-institute within the NIH called NCATS has an entire program where they collected drugs that were on the shelves of various pharmaceutical companies, negotiated terms, and made them available to academic investigators to test new indications. And through that program, we were able to identify a cancer drug which didn't work so well for cancer, but was safe, and we were able to move it into Alzheimer's trials very quickly.

There are some challenges in drug repurposing. Many drugs aren't developed to get into the brain. If we're going to have an effective Alzheimer's drug, we need to know that the drug actually gets into the brain. So there usually is some work to be done to prove that a drug is actually entering the brain if it's been used for some other purpose.

Secondly, Alzheimer's is a slow process. So many drugs are used for other indications, say for cancer, for a month or two at a time, not for years and decades on end the way an effective Alzheimer's drug would be used. So knowing that the drug is safe in the chronic situation is key.

But still, we moved from identifying a drug, testing it in animals, to testing it in humans in a process of two or three years instead of the 8 to 10 to 20 years that it takes for a completely new chemical entity. So I think this holds huge promise to accelerate the process in combination with really robust biomarker profiling. So I think there's again another reason for optimism in the field.

Dr. Arnold: I think there are two types of repurposing. There are huge numbers of medicines that were designed and tested and didn't, for whatever reason, quite make it out of the drug companies. The other aspect of drug repurposing is drugs that are already approved for other conditions. There are medicines that are used chronically in asthma that may have some benefit for brain disorders including Alzheimer's disease. We're in the middle of a clinical trial with an anti-tuberculosis vaccine that seems to have some really remarkable properties in terms of improving the immune system and perhaps decreasing the hyperinflammation that we see in Alzheimer's disease. Even the most common diabetes drugs. There's a big clinical trial based in New York that's going on, testing Metformin.

Dr. Strittmatter: Since you brought up Metformin, you might comment on one of these questions in the Q&A.

Dr. Arnold: We've been doing work in this area for a long time. And it taps into what I was saying before about the metabolic activity of cells. Some people started noticing that there were higher rates of Alzheimer's-type dementia in people with long-standing diabetes. And so we wanted to know, what is the main feature of type 2 diabetes? It's insulin resistance. Our cells are resistant to the hormone insulin, which helps absorb glucose and enhance the metabolic activity of cells. And so we started looking for evidence of insulin resistance in brain cells in people with Alzheimer's disease. And we saw a lot of features in brain cells that look like the cells are resistant to the insulin. But the thing is that we saw it not only in diabetics who had Alzheimer's disease, but also people with Alzheimer's disease who didn't have a history of diabetes. So this made us think, "Okay, the brain is different than the rest of the body in this regard." And we know that insulin does other things in the brain than it does in the body. It acts more as a growth factor. It even enhances synaptic growth and maintenance of synapses. So if there were ways to use drugs that can enhance insulin sensitivity and if they get into the brain, do they have beneficial effects on brain cells? Can we see this? So that's a very, very lively area of research now. There are a number of clinical trials.

Lena: There are several questions related to diet and supplements. Would you like to answer some of these, Dr. Strittmatter?

Dr. Strittmatter: I'll just say a general statement about supplements is, they may be beneficial, but there is not proof that they're beneficial that's risen to the level that's accepted in the medical community. There's not the kind of standard of proof that we accept in medical practice that these are beneficial.

Dr. Arnold: Many of them do work in mice with Alzheimer's disease. They work in cell cultures that kind of mimic Alzheimer's disease. And some of us like to say now, "It's a great time to have Alzheimer's disease if you're a mouse," because we can prevent it or even cure your Alzheimer's disease if you're a mouse. But how many of them actually work in humans?

And the big frustration is that it's hard to move these things into bona fide rigorous clinical trials. A lot of that is financially based. Some of them do look as good as some of the most promising new chemical entities that we create to drive amyloid down, improve inflammation, enhance metabolism, improve blood flow to the brain and the like.

Lena: Dr. Strittmatter, what are the most encouraging biomarkers now being studied that you think might correlate with Alzheimer's disease and progression?

Dr. Strittmatter: The type of assay that's attracted the most attention recently is using plasma samples to look at specific species of tau. This has been shown in research studies to be highly correlated with the presence of Alzheimer's disease as proven by PET scans. It also correlates with progression and it requires a simple plasma test. These aren't widely available in clinical practice. It's still a research tool at this point, but I think that's going to really make it much easier to diagnose the disease and also track the progression of disease. At least so far, some of these plasma phospho tau biomarkers have the best data around them in terms of changing the way we run clinical trials.

Lena: So then, Dr. Strittmatter, what's your best guess of when a new class of therapeutics might be available to the patient?

Dr. Strittmatter: Realistically, because Alzheimer's is a slow disease, anything that's going to be newly registered as part of standard practice is going to require these large Phase III trials that monitor people over 12 to 18 months. To get to that endpoint is a several-year process. But I guess it would be hard to say that something's going to be there in the next two years, but two to five years is plausible and 2 to 10 years is a safer number to say.

Lena: There's a very interesting question about the rates of Alzheimer's disease crossing different countries and cultures. Have you observed any of these cultural differences?

Dr. Arnold: This does tap into one of the things I talked about before with heterogeneity, that there are a lot of different risk factors that can affect the onset and the course of Alzheimer's disease. Certainly genetics is one thing that affects it. The occurrence of cardiovascular disease or metabolic diseases, high blood pressure, diabetes, high cholesterol, heart disease, these are all things that can increase the rates of occurrence and perhaps the progression of Alzheimer's disease. Depression, stress, environmental stresses, these are also factors that can affect the occurrence of Alzheimer's disease and dementia. Each of these different risk factors may translate into its own biological changes and biomarker changes that we can see in the brain—heterogeneity we actually use to better personalize a treatment program for people.

Dr. Strittmatter: This is something I think that the research community and the NIH in particular has very much recognized, that differences are likely to exist. There's now a lot of research going on about differences across cultures, across lifestyles, and really trying to nail down, what are the important factors and how big are they? Different aspects of culture, lifestyles and socioeconomic status, race, etc.

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Reflections: AAIC 2022

Podcast Link

Katie Brandt

AAIC 2022, the Alzheimer's Association International Conference, drew more than 9,000 scientists and featured more than 4,000 presentations in person in San Diego, CA, and online around the world. As Director of Caregiver Support Services for the Massachusetts General Hospital Frontotemporal Disorders Unit, I was attending as a professional in the field. This lens made me feel energized as I scanned the program and saw so many opportunities to connect with leaders around the world. And as I walked into the opening plenary with thousands of attendees, I felt a wave of gratitude wash over me. I am a former caregiver to my late husband, who lived with frontotemporal dementia, and a current caregiver to my father, who has been living with Alzheimer's disease for 13 years. The rush of grateful emotion was for those who do what I can't. They are the scientists who have dedicated their professional lives to uncovering the mysteries of dementia. Many speakers at that first plenary, and throughout the five days of conference activities, shared their own lived experiences as caregivers. They talked about loving and losing people in their own lives. They spoke through deep grief lifted with tenacity and determination. Their fierceness gave me hope that we won't stop until a cure is realized.

My role as a presenter at AAIC was to shine a light on one of the most complex aspects of care and support, advanced care planning. *Courage in Care Planning: Advanced Care Planning Readiness in the Context of COVID-19 for Caregivers of*

Individuals Living with Dementia was both a scientific poster and an oral presentation. Through a grant funded by the National Institute on Aging, our team in the MGH FTD Unit is conducting a study about the utility of video decision aids for advanced care planning, and the work we presented at the AAIC highlighted a sub-study with caregivers of individuals living with dementia during some of the hardest days of the pandemic, when many communities were in lockdown and the vaccine was not yet available. Forty-six caregivers completed online surveys, watched educational videos about COVID-19 and advanced care planning, and participated in study sessions one day, one week, and one month after viewing the videos.

Participants completed the Advanced Care Planning (ACP) Engagement Survey before and after the intervention—which included watching videos and participating in the study sessions. After the intervention, about one third of total (N=46) participants increased their scores about ACP knowledge, thoughts, plans, and readiness to be a substitute decision-maker or to make decisions for their loved one if they became very sick.

I was humbled by the bravery with which caregivers answered one question in particular: “How ready are you to discuss with your loved one’s doctor whether or not there are certain health situations that would make your loved one’s life not worth living?” Seventy-four percent of participants increased their engagement score immediately after the intervention, showing that educational materials about the topic could help them feel more prepared to face this situation. Overall, 57 percent reported that they engaged in ACP conversations after the intervention.

Why does this matter?

Today, we don't have a treatment to slow or stop the progression of Alzheimer's disease. Dementia cannot yet be undone. High-quality care is about dignity and personhood at every stage. It honors cultural values and wishes for goals of care at the end of life. By talking about these difficult topics ahead of time, caregivers are more likely to feel as though they have done what their loved ones would have wanted at a time when they will likely be unable to speak for themselves. Empowerment can happen through education. Our team is continuing to study how and when caregivers and families would benefit most from this education.

There was a heightened focus on the social determinants of health and their potential impact to increase or reduce the risk of dementia. In a pre-conference workshop, *Addressing Dementia Risk Through Social Determinants of Health,* Craig Thomas, CDC Director, Division of Population Health Centers, highlighted loneliness as a public health threat and social connectedness as the strategy to fight against it. He said that loneliness is a health risk that rivals smoking, obesity, and physical inactivity, and it is a serious public health issue. Human beings are social by nature, and high-quality social relationships are vital for health and well-being. As a professional in the field, and a caregiver myself, this got my attention.

We know that loneliness is something that many caregivers and people living with a diagnosis of dementia struggle with. Dementia presents challenges to communication, it changes the dynamics of relationships, and it makes the logistics of travel, being out in public, and navigating everyday experiences like grocery shopping or eating in a restaurant difficult. These challenges may promote loneliness for individuals living in the greater dementia community.

We also know that there are strategies to combat loneliness and protect your health and your future. Today we do not yet have a cure for dementia, but we do have care for those living life with a diagnosis and their caregivers. For me, the way to turn inspiration into action is through connection. I think that is why it is so critical that we continue to come together. Whether we are caregivers attending a support group or scientists in a lab, the power of connection is undeniable.

No one person on his or her own can care for an individual living with dementia. In the same way, the cure for Alzheimer's disease will not be discovered by one scientist or even one organization. This makes it even more critical that everyone in our community be connected. During a workshop on research engagement, we were reminded that you can't manage what you don't measure. Our research community is called to a commitment for inclusion, to make sure that studies are accessible and culturally appropriate for all racial, ethnic, geographic, and socioeconomic groups. This will allow for a full understanding about our risk of developing dementia and meaningful strategies to provide treatment, care, and support.

Our scientific community knows that the world is waiting for a cure. AAIC showcases the dedication of the worldwide efforts to move us in the right direction for risk reduction, more accurate diagnosis, treatment, and a cure. If you are a person living with a diagnosis or a caregiver who is interested in learning more, go to www.ALZ.org/aaic to read about this year's conference. Consider attending the 2023 conference in person or online July 16–20, 2023. Complex solutions require the inclusion of all voices. Be a part of the chorus, the rallying cry, that we must move faster toward the care that families need today and the cure that we demand for tomorrow.

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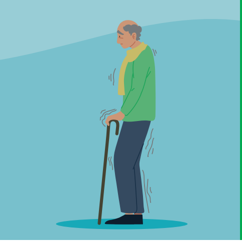

The Lewy Body Dementias

🔈 **Podcast Link**

Stephen Gomperts, MD, PhD

The Lewy body dementias are the second most common neurodegenerative dementia after Alzheimer's, affecting some 1.4 million Americans, yet few of us have heard of them. Two clinically distinct but related diseases comprise the Lewy body dementias: dementia with Lewy bodies, also known as DLB, and Parkinson's dementia. The hallmark neuropathology of these diseases is the Lewy body, a protein aggregate that accumulates in specific brain cells. We'll first focus on dementia with Lewy bodies, DLB, and then turn to Parkinson's dementia.

In DLB, cognitive impairment develops together with other, characteristic problems. The first of these is motor changes suggestive of parkinsonism. Movements slow and grow more effortful. Gait slows and starts to shuffle. Posture degrades, and balance may deteriorate. A tremor can develop. Facial expression and speech volume may diminish, too. These changes can lead to a misdiagnosis of Parkinson's or related diseases.

Visual hallucinations are the second clinical feature. These often arise early in the course of disease, and are usually nonthreatening. Most often, people see hallucinations of people or animals, which are not accompanied by sound.

The third characteristic feature of DLB is REM sleep behavioral disorder, a phenomenon in which people can act out their dreams. REM sleep is a dream-rich state in which our bodies are normally paralyzed while our eyes are free to move. In REM sleep behavioral disorder, the normal paralysis of REM sleep is diminished. As a result, patients may punch, kick, or even fall out of bed, potentially injuring themselves or their bed partner.

The fourth clinical feature of DLB is fluctuating cognition, with profound variation in clarity of thought or level of alertness. People can stare off into space at times or be intermittently tangential in conversation. Marked but episodic daytime sleepiness can develop, despite a good night's sleep.

Together with progressive dementia, these characteristic features comprise the core clinical presentation of DLB. While they tend to co-occur, not all patients with DLB will have all four.

In DLB, the thinking problems that develop can mimic Alzheimer's, with early and progressive short-term memory loss. More often, however, additional domains of thinking tend to be involved from the beginning. Many patients experience early problems with executive function, with resulting difficulties in planning and organization that can impact their ability to manage the household finances or use a smart phone, for example, and to multitask. Some patients develop early problems with visual-spatial function. As a result, sense of direction may degrade.

Interestingly, there is significant overlap in the clinical features of DLB and Parkinson's dementia. In Parkinson's, patients develop these same motor changes—but in the absence of significant cognitive impairment. As Parkinson's progresses, however, the risk of developing cognitive impairment accrues. As a result, dementia is common in Parkinson's, affecting some 30 to 80 percent of patients living with the disease.

DLB and Parkinson's dementia share other clinical features as well. In both, REM sleep behavioral disorder and visual hallucinations are common. In both, memory loss, executive dysfunction, and visuospatial impairments are frequent.

The key differentiating feature between DLB and Parkinson's dementia is the timing of dementia relative to motor problems. When cognitive problems start prior to or within one year of Parkinsonian motor changes, a diagnosis of DLB is made. Otherwise, a diagnosis of Parkinson's dementia is made. However, this one-year rule is arbitrary. Together with the shared hallmark neuropathology, the Lewy body, the clinical overlap between DLB and Parkinson's dementia supports the idea that these illnesses reflect a clinical spectrum of the same disease.

There is currently no cure for the Lewy body dementias. Even so, making the diagnosis matters: Several treatment strategies exist that can help Lewy body dementia patients, improving both function and quality of life; additionally, certain medication classes can be dangerous in the Lewy body dementias and must be avoided.

Given the need for clinical expertise, patients and their loved ones may want to access tertiary care centers for diagnosis and management of the Lewy body dementias. The diagnostic evaluation includes a careful history including a review of medication exposures, a neurological exam, blood testing (to identify reversible contributions to cognitive impairment), and brain imaging. There is as yet no FDA-approved test that can make the diagnosis. However, several studies can be helpful, such as dopamine transporter imaging or a sleep study.

Clinical expertise is also needed for the management of the Lewy body dementias. The clinical features of these diseases can respond both to pharmacologic and nonpharmacologic strategies, and it is important for physicians to work systematically to optimize treatment.

For example, cognitive impairment can respond to drugs known as an acetylcholinesterase inhibitors that increase brain acetylcholine levels. The brain cells that make acetylcholine play an important role in thinking and are universally impacted in the Lewy body dementias. These same drugs are used to treat Alzheimer's but tend to be more effective in the Lewy body dementias. Every patient deserves an optimized trial of this drug class.

Conversely, several medications can exacerbate thinking problems in these diseases. Thus, a careful review of medications is vital. This is also true for Parkinson's medications, as many can cause or exacerbate cognitive impairment or hallucinations. These can be substituted as needed.

Hallucinations often respond to nonpharmaceutical strategies, such as closing the blinds before dusk, keeping the home well lit, and verbal redirection. In addition, acetylcholinesterase inhibitors can help. If hallucinations grow pervasive or threatening, there are other medications to consider, including some antipsychotics, but these need to be selected and used with caution and expertise. While some can be effective, all antipsychotics come with risks. In fact, antipsychotics with strong activity against the dopamine D2 receptor—such as haloperidol—are extremely dangerous in the Lewy body dementias. They significantly increase the risk of death and need to be avoided.

With respect to treating the motor manifestations of parkinsonism, physical therapy plays an important role, as do medications that target the brain dopamine system. Such medications—like carbidopa/levodopa—can be very helpful in some patients, but they also require careful selection and dosing to avoid worsening cognitive impairment or hallucinations.

Exercise is another important treatment strategy. Exercise can help with both thinking and motor function and is an invaluable tool in the armamentarium.

In managing REM sleep behavioral disorder, one key step is to remove sharp objects such as nightstands from the sleep environment. Melatonin is helpful in some patients. Doctors can consider other classes of medicine as well.

Because the Lewy body dementias are complex diseases that affect cognitive, physical, and behavioral function, patients benefit from a care team. In addition to the treating neurologist, physical therapists help with motor function and fall prevention, occupational therapists optimize home safety and activities of daily living, speech therapists treat speech and swallowing, and social workers support patients and their caregivers, guiding discussions around optimizing home care and helping with possible transitions to long-term care facilities.

I'll leave you with one thought. The shared brain changes of DLB and Parkinson's dementia together with their overlapping clinical features not only support the concept of a clinical spectrum of disease: More than this, they raise the possibility that a cure for one of these Lewy body dementias will be a cure for both.

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Genetics and Alzheimer's Disease

🔊 **Podcast Link**

Sara Manning Peskin, MD, MS

A lot of us are concerned about our risk of developing Alzheimer's disease, particularly if we've watched parents or siblings die of the disease. If we've lost partners to Alzheimer's disease, we may wonder whether our children are destined for the same course. Researchers have found that we're more likely to worry about having dementia than to actually develop it, and this gap is even more pronounced in people who have had a family member with dementia. So if we've watched our relatives die from Alzheimer's disease, we tend to assume that we're destined for the same fate—even when we don't have any symptoms.

When we think about our familial risk of Alzheimer's disease, we're in part considering whether there's something wrong with our DNA. We're asking whether the seeds of Alzheimer's disease were sown in our bodies years ago at the moment we were conceived—and whether we have any power to change our fate as adults.

We often think of genetics as a black-and-white indicator; if you have a mutation then you'll get a disease, but if your DNA is normal, you'll emerge scot-free. When it comes to Alzheimer's disease, the story turns out to be far more complicated. For the vast majority of people with Alzheimer's disease, we can't point to a single genetic mutation as the cause of the symptoms. Instead, Alzheimer's disease is usually the result of complex genetic and environmental factors, some of which we still don't even understand.

Most people with Alzheimer's disease carry mutations in some of the 70-odd "risk genes." This is a group of genes that are associated with an increased risk of developing Alzheimer's disease, but each of them alone isn't enough to cause disease 100 percent of the time. Environmental factors such as education, diet, and head trauma also contribute to the risk of getting Alzheimer's disease, so genetics alone don't account for everything by any means.

The most famous risk gene for Alzheimer's disease is called "ApoE." This was the first risk gene that scientists identified, and it's still the most strongly correlated with the disease. Each of us has two copies of the ApoE gene, and each copy comes in one of a few different versions, called ApoE2, ApoE3, and ApoE4. ApoE3 is the most common version of the gene. People who carry two copies of the ApoE2 version turn out to have a much lower risk of Alzheimer's disease, whereas those who carry one or two copies of ApoE4 have a much higher risk of Alzheimer's disease. Researchers estimate that about 50 percent of people with Alzheimer's disease are ApoE4 carriers. For people who report lots of family members having Alzheimer's disease that starts in their 60s, 70s, or 80s, we often wonder whether ApoE4 might be playing a role.

Patients often ask whether they should do genetic testing to find out if they are ApoE4 carriers. Some people even come to our clinic after finding out from 23andMe or another similar genetic testing company that they carry one or two copies of ApoE4. There are a couple of things to consider when it comes to finding out your ApoE status. First, knowing if you carry ApoE4 won't tell you whether or not you will get Alzheimer's disease. We've seen many people in our research center who have two copies of ApoE4 but do not have symptoms of

Alzheimer's disease, and likewise we know that half of people with Alzheimer's disease don't have any copies of ApoE4. In the end, knowing your ApoE status doesn't tell us much more about your genetic risk of Alzheimer's disease than what we can already glean from your family history. Second, it's important to keep in mind that we don't typically recommend any changes to family-building plans based on the result of ApoE4 testing. Even if you are an ApoE4 carrier, we don't recommend using reproductive technology to decrease the risk of passing it on. In short: Outside of research endeavors, it's not usually clinically useful to find out your ApoE status.

So, when should you do genetic testing for Alzheimer's disease? We tend to suggest this in patients who have symptoms before age 65 and also have a strong family history of Alzheimer's. These are the people at the highest risk of carrying a mutation in one of three genes that can single-handedly cause Alzheimer's disease. Less than 1 percent of people with Alzheimer's disease carry a mutation in one of these genes—so it's very uncommon, even in people where the disease starts before age 65—but identifying people with these mutations can help families make decisions about genetic testing and management.

If you're wondering if you're in this group, consider bringing it up with a neurologist and asking whether you should see a genetic counselor. Genetic counselors often work closely with neurologists to help decide which genes could be useful to evaluate and also to help patients and their families cope with the prospect of receiving genetic information.

While we don't have control over our genetic status, there are lifestyle changes that can significantly affect our risk of developing disease. A recent study found that 40 percent of the burden of Alzheimer's disease is attributable to modifiable risk factors like high blood pressure, diabetes, and obesity. Regardless of what's contained in your genes, one of the most effective things you can do to decrease your risk of Alzheimer's disease is exercise. The best outcomes come from doing at least 40 minutes of aerobic exercise, three to four days a week. Diet-wise, the Mediterranean diet has been associated with the lowest risk of Alzheimer's disease, but limiting alcohol and not smoking have also shown a huge benefit. Finally, social and intellectual engagement are critical for preserving cognitive function.

Sara Manning Peskin, MD, MS
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University of Pennsylvania

Public Policies to Help Us Live Well with Dementia

🔊 **Podcast Link**

Jason Karlawish, MD

My colleague, Steven Arnold, talked about how we've made and we will continue to make some path-breaking and even spectacular advances in developing better diagnostics and, especially, better therapeutics. Particularly the therapeutics that target the mechanisms of the diseases. And I can identify the patients who are most likely to respond to those therapeutics.

So, what does that mean? Well, we should expect that Alzheimer's disease is becoming a treatable disease—or, as pharma calls it, a "druggable" disease. But we shouldn't expect that every cause of disabling cognitive impairments will be treatable, certainly not curable. Not everyone is eligible for the drugs that have been developed, and the finding from research over the last 20 or 30 years has been heterogeneity. Namely, that the typical person with Alzheimer's has not just Alzheimer's pathology, but other pathologies.

So there's a real policymaking implication to that, which is that we're going to have to learn how to live with disabling cognitive impairments, or, in a word, how to learn to live with dementia, and disabling cognitive impairments. Treatments may slow, for some patients, the course of their disease—perhaps for some, completely arrest it—but we need to live with the fact that we will have to live with dementia.

So let's talk about that. How can we set up a society in America that allows us to live well with dementia? I think we can break this into two parts. First, how will persons living with dementia and their caregivers carry on with their lives—in particular, with benefits from the kinds of interventions and supports that Felicia Greenfield described?

Second, how will persons living with dementia die of it?

Let's first start with living with the disease. Felicia explained that we have the means to make these diseases livable. For both patients and for caregivers, we have what's known as long-term care services and supports. That's what she described. But those aren't routinely available. In America, we have a federally funded social insurance program for health care. It's called Medicare.

In the Medicare statute, signed into law in 1965 by President Johnson, there is an explicit list of items of interventions that Medicare does not cover. They include hearing aids, plastic surgery, and "custodial care." In 1965, that was the term used to describe the care that someone gave to another person who was disabled from an illness. Custodial care. Think about what that word suggests. It's as if the person is a building to be swept and mopped, etc., not a person who needs care. But that was the way we thought about it back then, was custodial care, and the statute explicitly prohibits it. So long-term care services and supports are not supported by Medicare. Medicare supports hospital-delivered services, and outpatient-delivered services. It supports the delivery of *medical* care.

For example, Dr. Arnold talked about some spectacular diagnostics and therapeutics that are coming out. Those may be covered by Medicare. There's been debate about that, but I expect that they will be. However, the kind of services that Felicia Greenfield talked about are *not* routinely provided. Indeed, at Penn Memory Center, access to people like Felicia and her colleagues is available, but it's made possible by a generous gift from a grateful patient's spouse. Without that donation, we couldn't provide the long-term care services and supports that are the standard of care after diagnosis.

Put another way, if we relied on Medicare billing to support our memory center, we would not be able to provide services and supports that are so essential. And again, I'm very encouraged about the prospects of treatments that will slow the progress of the disease, but that will only extend the period of time that people need long-term care services and supports. We're not going to drug our way out of the need to care, so we're going to have to face that as a society. Right now, access to social insurance for long-term care services and supports is made possible on a state-by-state basis through *Medicaid*. Not Medicare, but *Medicaid*. Medicaid is a means-tested program, though, where you have to qualify for certain poverty thresholds in order to receive the supports. It also varies from state to state how much support is available. And frankly, because of legal matters that are excepted, essentially long-term care services and supports through Medicaid are rationed when the funds run out in a state in any given year.

I think a lot of what we're witnessing in supports for caregiving in America reflects that term that was in that Medicare statute: custodial care. At the same time that America committed to paying for medical care, it was unable to even conceptualize what it means to provide care for someone who is disabled. Indeed, the word "caregiver" wasn't even in use in the English-language lexicon at that time. It was not until the 1980s that we began to use the word "caregiver" to describe that person who essentially supports the mind of another person whose mind is being transformed by a disease.

The concept of caregiving is as old as the Bible and the Book of Ruth. Naomi is cared for by her daughter-in-law Ruth. And yet nowhere in the Book of Ruth does it call Ruth a caregiver. She's just a good daughter-in-law, doing what good daughters-in-law do when their mother-in-law has no one else to care for them.

I thought that the pandemic would make us realize how important humans are to care for other humans, because as we all know, when humans were put into lockdown and taken away from access to visitors in long-term care residential facilities, or visitors in hospitals, that we would realize that not all visitors are visitors. They're essential mind support for a damaged mind. Much like lecanemab is a support for the mind that was damaged by beta-amyloid plaques.

I thought that after the pandemic we would realize that we needed to support America's caregivers. But that hasn't happened. In the language that was drafted after the pandemic, in the Inflation Reduction Act, there was clear support to expand the wages paid to providers of long-term care services and supports. But that was rapidly lined out in the negotiations. It was never part of the Inflation Reduction Act. And so we never made any progress in expanding long-term care services and supports. And this matters, because the hours spent caregiving are the argument for why this disease is such a problem. The triple-digit, billion-dollar cost of Alzheimer's in America, of dementia, is not the cost of providing medical care, it's taking the hours that a spouse, a daughter, and rarely, a son, spend caring—and putting a wage on it, and calculating wages spent by America's families caring for a disabled family member, disabled from dementia.

These wages are wages that are not available for other things a family needs, like paying for college tuition. These wages cause people to have to be out of the workforce, and therefore not paying into Social Security or advancing their jobs. So America is paying for long-term care services and supports, but it's the American family paying out of their strained pocket that's doing this.

What this will take is amending Medicare to expand its coverage for long-term care services and supports. This isn't a radical idea. In Japan, Germany, the Netherlands, long-term care services and supports are backed up by the government. Germany has had a system in place for over 25 years paid for by a payroll tax. It's solvent and it works. It keeps the German family from the fiscal threat that they would face when a family member is diagnosed with dementia. So we can do this, we just have to muster the political will.

We also have to recognize that for persons living with dementia, the theory of at-home-is-best has to be questioned. Increasingly, over the last decade or so, Medicaid has directed its funds towards what are known as home-based, community-based services and supports in the home. This means that they'll provide support for a family member to give care in the home. But sadly, as we know in this disease, there comes a time when "home" is no longer working. The person being at home is lonely, the person caring for them is overwhelmed, and a residential setting, with experts in how to care for people with damaged minds, is what's needed. But unfortunately, the trend in America is not to provide good-quality residential care. Indeed, the nursing home has become a dreaded place, and also an industry used by venture capital in order to simply make money. Not to deliver care. So we really need to rethink what it means to have residential long-term care.

Finally, we need to think about in the beginning of the disease, the laws that we've set up to support someone to exercise their autonomy. Right now, you're either competent and capable, or you're not competent and not capable. That's the way that we've all envisioned things. For the vast majority of people living with these diseases, they have marginal capacity. They're able to make decisions, but they need someone else to support them. That's oftentimes the caregiver. But we don't recognize the role of the caregiver in the law to help people make decisions. There's a concept known as supportive decision making, developed in the world of disability rights, that allows an adult to be designated as the supporter for another adult, to help them make decisions. This isn't a guardianship. It doesn't strip the right from that individual, but it recognizes, for financial matters, for medical matters, that this other person should be there and be part of the decision making process. This could go a long way to support the lives of persons with mild cognitive impairment (MCI) or mild-stage dementia.

Finally, I'll close with a somewhat dark topic: It's all very well to know when to *start* the treatments that Dr. Arnold talked about, but when should we stop them? And after we stop those treatments, how should we care for someone? Hospice benefits are limited to people who have six or fewer months of life left to live. Prognostication of dementia is extremely difficult, to know how long someone has to live. Many a time, when I've referred one of my patients to hospice, the family will say to me, "Gosh, I wish we had access to this earlier. Why not?" and I unfortunately have to say to them that they're lucky to have gotten it when they've gotten it, given controversies of access. So we need to rethink what palliative care is for this disease—when the mind oftentimes is more damaged than the body. When palliative care is needed. I thank you for this opportunity to talk about some of the policy initiatives that are needed: expanding access to long-term care services and supports, recognizing the role of supportive decision making, rethinking and revolutionizing residential long-term care. These are things that we can do. We know how to do them. We just have to muster the political will to do it.

Question: You talk about these very ambitious goals, and one of them is, how do we improve residential care? Where do we begin? How would you go about doing that?

Dr. Karlawish: Number one, we really need to rethink the financing that surrounds nursing homes. There are huge conflicts of interest in nursing home ownership, such that the owners of the nursing home also will own the businesses that supply the nursing home. In a sense, for many corporations, nursing homes have become just simply real estate ventures. That's what they're there for. So we really need to scrutinize the business models that surround nursing homes. More generally, also, the memory care units are often embedded in assisted living facilities. I have no fundamental problem with assisted living, except assisted living sort of operates on a state-by-state, ad hoc basis. There are some really good models out there for developing residential settings for individuals living with dementia. I think the Green House model is a good example of how architecture and staffing can be thoughtfully deployed to create a space that allows an individual's mind to be supported, but this just requires the recognition that the sort of hospital ward design that we have for residential long-term care just simply doesn't serve a mind that needs support. So those are all steps that we can do. Reforming the regulations, the financing structures, and embracing, frankly, the building of facilities that adhere to the kind of principles developed by programs like the Green House program.

Question: I'm not aware that a U.S. payroll tax to pay for LTS has ever been legislatively proposed. Is it realistic that it will be?

Dr. Karlawish: The last effort in the United States to create a system of long-term care services and supports was in the 1980s. The 1988 presidential election. Every single candidate lined up in support of creating an essentially Medicare-style benefit for long-term care services and supports paid for out of the payroll tax. Because you have to have a tax that essentially covers everyone who is going to tap into a widely spread risk. Hence the payroll tax is a good model. Long-term care '88 never became statute, because there was one candidate who just wouldn't come down in favor of it, and that was George Herbert Walker Bush, who of course would go on to win the election.

Since then, the political climate has been one that has never advanced any significant legislation to address this. The CLASS Act was buried in the Affordable Care Act (Obamacare), when it was widely recognized from the moment it was written that it was actuarily unsound, and essentially died even after passage. So let me give you sort of a bleak statement. One half of the American political system, if you look at it by the parties, has come down plainly saying that raising taxes is anathema to what we're doing. So as long as you have a political party simply saying that any tax increase or attempt to increase revenue is a non-starter, you pretty much have a non-starter for addressing the problem through taxation, which is disappointing.

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Updates on Diagnosis and Treatment of Alzheimer's Disease

🔊 **Podcast Link**

Steven E. Arnold, MD

We've made tremendous strides in our ability to diagnose Alzheimer's disease and other causes of cognitive decline, of dementia in older people. And in terms of treatment, we've had a major scientific advance this past year, with the news that amyloid-lowering immunotherapies can slow down the progression of Alzheimer's. I'll be coming back to the new amyloid treatments, lecanemab, or Leqembi, as it's called by its brand name. And aducanumab, or Aduhelm. But first, let me talk about where we are with diagnosis.

So, as we get older, we all experience changes in our memory and thinking. There are "senior moments" where you may have trouble remembering a name, or why you walked into a room. Or maybe it takes more effort to get organized and out the door in the morning. These experiences are almost universal as we age. But when it's more than a little trouble, when there's a significant difference in our memory and thinking from usual, and especially if it's interfering with our daily functioning, this is a signal that there may be a disease. There are lots of causes of cognitive impairment. Not everything is Alzheimer's disease. So it's important to get a proper diagnosis with an experienced health care provider. The first step is to determine if there truly is a problem. Aside from recognizing the symptoms of memory loss, there are a number of good screening tools, brief memory and thinking tests, that can help see if there is a problem or not. Sometimes, though, it takes more in-depth testing by a neuropsychologist to suss out if someone has a memory problem. In Boston, we sometimes get these physics professors coming in worried that they have Alzheimer's because they can only think 12 moves ahead in a chess game when they used to be able to think 18 moves ahead. And these folks may do fine on a cognitive screening test, but based on where they started from, they actually may have a serious problem emerging. And so a neuropsychology evaluation could help. Then it's important to have a good general medical checkup with lab tests. Thyroid disease, certain vitamin deficiencies, side effects from some medicines people use for sleep or bladder control, can cause memory problems. Depression is another condition we want to be on the lookout for. Most everyone has ups and downs, but if depression takes hold, everything in the brain can shut down. Thinking and memory get foggy, and it can look like dementia. We also recommend an MRI or CAT scan of the brain to make sure there are no tumors or fluid collections or silent strokes. Some of these conditions that we discover from time to time also are quite treatable. If there is a noteworthy cognitive decline, and a good medical and neurologic exam doesn't turn up any alternative explanations, then statistically, Alzheimer's is the most common cause in people over 60. But there are other causes that can look very similar. Vascular cognitive impairment is due to the long-term effects of high blood pressure, affecting small blood vessels feeding the brain. They used to call this hardening of the arteries.

Lewy body disease is a cousin of Parkinson's disease that also causes symptoms that overlap with Alzheimer's disease. Frontotemporal dementia is another, and there's a very long list of other rare conditions that do so, too.

We used to say that the only way you could be 100 percent sure that a person has Alzheimer's was if you looked at brain tissue under a microscope after they'd died, and it showed the telltale amyloid plaques and tau tangles of Alzheimer's disease. Based on the clinical symptoms alone, even the most experienced Alzheimer's neurologist is correct with the diagnosis only 70 percent or maybe 80 percent of the time. And this may have been okay when we had no real treatment for Alzheimer's, but now it's not good enough, as we enter a new era with medications that specifically target Alzheimer's disease, amyloids, but also come with some possibly serious, even fatal, side effects. And we need to be very confident in our diagnosis if we're going to give someone one of these medicines. And diagnosis is where the Alzheimer's field has made huge progress. If the disease is defined by the amyloid plaques and tau tangles, then we have to be able to detect and measure them to make a certain diagnosis.

We now have a range of biomarker tests that can tell us if there are plaques and tangles in the brain with very high certainty—almost 100 percent. So the most widely available are spinal tap tests that measure amyloid and tau in spinal fluid. But there are also PET scans that use radio-label tracers to show brain amyloid on X-ray—and these amyloid PET scans are expensive and not widely available or used, but if positive, they are diagnostic of the disease. There are also PET scans to measure the amount of tau tangles in the brain with Alzheimer's. And these are still only used in research, where they're especially helpful in measuring how far the disease has spread through the brain. The newest, most exciting, and potentially transformative advances coming right now are diagnosis with blood tests. These are mostly used in research so far, but new ultrasensitive laboratory tests can measure the very low levels of tau proteins that leak out into the blood from the brain or spinal fluid. And if the tau levels are high, the accuracy for diagnosis, based on the blood test, compared to spinal fluid or PET scans, is around 90 percent. This is good enough for screening, but if you're about to commit someone to a new course of immunotherapy, you'll need to be even more certain with a spinal fluid test or PET scan.

So let me move on to treatment. There are medicines like donepezil, or Aricept; rivastigmine, or Exelon; galantamine, or Razadyne; memantine, or Namenda; and we've had these for the last 20 to 30 years. These are safe, and most people have no, or very mild, side effects with them. But they provide only very modest benefits for some vague number of people—keeping people stable in their daily functioning for a little longer than if they were not taking them. But the big news over the last year is the accelerated approval by the FDA for two anti-amyloid immunotherapies, and a third drug in this family that's likely to follow soon. Aducanumab and lecanemab are drugs that attack and clear out amyloid plaque proteins from the brain in Alzheimer's. The drugs are administered by an intravenous infusion once or twice a month, and what we've learned from the large clinical research trials with these drugs is that they're both very effective at clearing amyloid. Lecanemab reduces amyloid load in the brain an average of maybe 70 percent, and aducanumab even more, reducing amyloid maybe as much as 90 percent. And this reduction actually brings people's amyloid levels back down almost to normal, if not normal. And as a secondary effect, they also reduce tau levels. So that is what the biomarkers show with these new drugs.

What happens clinically to people? This is what we really care about. Over the course of the 18-month clinical trial for lecanemab, most everyone in the placebo and the active lecanemab groups still got worse in terms of memory and functioning. But the people receiving lecanemab declined more slowly—27 percent more slowly.

Statistically, this was a highly significant difference and benefit for the active drug. For aducanemab, there were two big trials. One of them showed no clinical benefit between the active drug and the placebo groups. And the other showed marginally slower decline in the active aducanemab group.

Now, I want to emphasize that these findings are a huge scientific advance. After 40 years and billions of dollars of research chasing amyloid, these studies do, for the first time, convincingly demonstrate that if you can clear amyloid in the brain in people with Alzheimer's, not just lab mice with Alzheimer's disease, but people, that clearing this can moderate the clinical course of the disease. But do you change it enough to make a meaningful difference in someone's day-to-day life? That's still a question that we have. And at what risk and cost? About 20 to 40 percent of people can have side effects, including brain swelling and micro-hemorrhages. Most of these are benign and just noticed incidentally on MRI scans. But they can be serious, causing headache, stroke, seizures, or even death. And the financial cost of the drugs would be high, between $25,000 and $30,000 per year, plus the cost of infusion services, MRI scans, and other laboratory tests to monitor for side effects and more. So while they are successful, in that clearing amyloid or reducing amyloid does *moderate* the course of Alzheimer's disease, it's not enough. One thing that is clear in the data from these amyloid immunotherapies is that Alzheimer's dementia is driven by more than just amyloid plaques or tau tangles. It's complicated. You know there are important roles for inflammation, vascular factors, metabolic factors, oxidative stress, neuroplasticity, and many other fundamental cell biology factors that go off in the disease, and any combination of these may be even more important than the amyloid or tau. And that's why continued research is so important into these contributors. But while the research moves forward, there are other things that we can all do now to optimize the brains we have, in whatever shape they are. Physical exercise, mental and social stimulation, a heart-healthy, brain-healthy diet, restful sleep and stress management. All of these are helpful. And for people in the throes of dementia, our most effective treatment is good care.

Question: Do we now accept amyloid and tau as causes of AD?

Dr. Arnold: So yes, but it's not sufficient. I think we define the disease by the presence of amyloid and tau, the plaques and tangles of Alzheimer's disease. And that's actually how we've defined it since 1900, when Alois Alzheimer first started discussing it, or showing it. But I think that we do recognize that the causes may be much more complicated. And whether amyloid and tau are cause or consequence, or both, of more fundamental brain neuronal changes or inflammatory changes in the brain, that is still a question. For some people, it is primary. There are some rarer forms of Alzheimer's disease that are genetically based. In other, more sporadic, and much more common, and heterogeneous, forms of Alzheimer's disease, amyloid and tau may be part of the complicated web of changes that occur with aging, so it gets a little tricky to say that it is the cause. We know, and I think we do feel confident, that it is a contributor, and may be a major contributor, and for some people it may be the first cause, but for other people it may just be in the mix of things.

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The Road to Diagnosis

Podcast Link

Lena Chow Kuhar

When friends struggle to encourage their family members to get tested for cognitive impairment, they sometimes ask how long it took me and Bob to talk to his doctor and start the process. It surprises my friends when I tell them that my best estimate is six years—six years after the first symptoms of cognitive impairment were noticed by me and by our family.

The first signs seemed innocuous enough. About six years before Bob was formally diagnosed, I began noticing oddities in his day-to-day activities. Once or twice, he mistakenly folded away used bed linen instead of putting it through the washer and dryer. When he came to the airport to pick me up after my business trips, it started to take him an unusually long time to find his car in the parking garage.

Three years before diagnosis, on what was to be our last trip to Paris, he had forgotten all the street names and metro stops that he used to know so well.

Two years before diagnosis, at the prompting of his daughter Kim, he went through neuropsychological testing, but the results were equivocal. At the time, we were told he tested "fine," and to come back in a year—a direction that we both promptly forgot and ignored.

Two years later came the drama. On a small cruise ship with 20 cabins in the Galapagos Islands, the captain instructed all passengers to keep our cabin doors always unlocked for safety reasons, in case of an emergency. While I slept soundly through the night, Bob was caught on camera wandering through the ship, opening cabin doors to look inside. Later he would explain that he was looking for his car, thinking we were at home and that the cabin doors opened to our garage. The ship captain confronted me with it, and I had a hard time convincing him that I did not bring my husband on the trip knowing that he was cognitively impaired. We spent the rest of the cruise with the ship doctor keeping Bob company in the daytime while I went on day tours. At night, I would block our cabin door with our luggage so Bob could not venture out. Once we came home to California, I scheduled the testing. This time, the diagnosis was clear. I remember that day, on a hot and sunny California afternoon, when Bob and I literally stumbled onto the streets after being told by a newly minted neuropsychologist that his mental skills were, in her words, “profoundly impaired.” All I could remember were the words “profoundly impaired,” repeated over and over again, like a judgment, a sentence for life.

Later, we would find our way to Bob’s primary care doctor, a referral to a neurologist, a diagnosis of mild cognitive impairment and, eventually, mixed dementia—a case of Alzheimer’s disease and vascular dementia.

In retrospect, that diagnosis, difficult as it was—both getting to the test and the lack of compassion in the delivery of the results—was a positive turning point in our journey with Alzheimer’s disease. The guessing, the suspicion, and the denial were over. Bob’s future, and mine as his caregiver, were now in our hands. Follow-up visits with his primary care doctor, his neurologist, the clinical social worker at our health system; consulting the leadership at our local senior community, contacting the local chapter of the Alzheimer’s Association, and reaching out to friends—all played a part in formulating a road map to live our journey to the best of our ability and, ultimately, to thrive despite the unfavorable prognosis. A key milestone was when Bob and I were parking our car at the garage as we walked to the Alzheimer's support program that was about to begin. I turned to Bob and said, "We are going to an Alzheimer's support program. The key word is 'Alzheimer's.' This is the diagnosis. This is what we both must accept and live with, from this point on." We took the first step—acceptance. And doors opened as we learned to find our way to the resources we needed—the doctors, social workers, day programs, therapists, home care—that ultimately helped Bob live well despite the many challenges that kept coming our way.

After Bob passed away, when I received his medical records from the health system, I learned that during the first visit to the neuropsychologist, two years before the definitive diagnosis, the neuropsychologist noted that Bob did not appear as intelligent as would be expected for his education level. Bob was a career engineer with a doctoral degree in clinical psychology. Although the neuropsychologist did not tell me, his written notes indicated that cognitive impairment *could not be ruled out* at the time. Somehow, the neuropsychologist was not able to tell that to me directly—because I did not stay in the waiting room and had left the premises when the testing was completed, and when the neuropsychologist came looking for me. Looking back, I now know why. I didn't want to know. And as I watch people around me put off their testing, I wish I knew how to tell them that there is so much more to gain than to lose. Knowledge *is* power, even when knowing hurts.

Lena Chow Kuhar

The Promise of Biomarkers

🔊 **Podcast Link**

Steven E. Arnold, MD

More and more, the term "biomarkers" is being used in the context of diagnosing and monitoring Alzheimer's disease and related disorders. But what does the term "biomarker" mean? In essence this is a biological feature of a disease that we can measure either through imaging, laboratory tests, or other kinds of recordings from the body. Let's use an example that most everyone can relate to. Say you go to the doctor complaining of shortness of breath and maybe a cough. Now, there are many illnesses that can cause these symptoms, and the treatment will vary accordingly. The causes might range from an upper respiratory viral infection to bacterial pneumonia to asthma, emphysema, heart failure, or cancer. The doctor can suspect some of these based on history or examination findings. But to be sure, she may order a variety of biomarker tests. These might include a chest X-ray, an electrocardiogram, a CT scan, or lab tests on blood or sputum and more. With these biomarker data, the physician can make an accurate diagnosis, recommend the right treatment, and follow whether a person is getting better or worse.

Now let's take the case of someone going to the doctor with memory decline. Based on symptoms of forgetfulness or word-finding difficulties, how long the symptoms have been present and the like, the doctor can suspect what might be causing the cognitive impairment. She might suspect Alzheimer's disease. However, she'll want to make sure other things that can cause cognitive decline aren't present, so she may order some common biomarker studies—a brain MRI scan or head CT scan to look for evidence of strokes, tumors, or fluid collections. She might order some blood tests to look for hypothyroidism or vitamin deficiencies. If all these tests come back negative, then her suspicion of Alzheimer's disease may be higher. These biomarkers rule out other causes of memory loss, but she still hasn't made a positive identification.

We used to say that the only way to be sure that Alzheimer's disease is the cause of someone's cognitive decline is if you look at someone's brain tissue under a microscope after they die and see the telltale amyloid plaques and tau tangles that define the disease. This would be a positive ID. What has transformed the field of Alzheimer's disease over the last two decades is the development of biomarkers using molecular neuroimaging, spinal fluid laboratory tests, and, most recently and importantly, blood tests that indicate the presence or absence of these brain amyloid plaques and tau tangles with a very high degree of certainty.

Let me briefly discuss the different types of biomarkers for Alzheimer's disease.

PET scans, or positron emission tomography, are a kind of brain imaging test that is now used to visualize the presence, absence, or amount of specific molecules in the brain. The most important kinds of PET scans used in Alzheimer's disease are glucose, amyloid, and tau PET scans. Glucose PET scans have been used for many years to look for patterns of metabolic activity in the brain. Amyloid PET scans are now approved for clinical use as well as research, although their cost is usually not covered by insurance. Tau PET scans are still for research use only.

The way PET scans work is that a radio-labeled tracer is injected into the bloodstream through a vein and then it circulates throughout the body. When the tracer reaches the brain, an amyloid tracer for example, it will bind temporarily to amyloid plaques if there are any. Tau tracers will bind to tau tangles. And glucose will be taken up by metabolically active brain cells. When the tracer sticks to its target, it emits positrons that are detected by the scanner before the tracer washes out. Radioactivity is always a health and safety concern, but the amount of radioactivity from a PET scan is relatively low, similar to what one gets from a chest X-ray.

Glucose is the major fuel for brain cells. In Alzheimer's disease, frontal lobe dementias, and possibly even Lewy body dementias, there are distinctive patterns of metabolic activity. These scans are approved and usually covered by insurance and can provide useful biomarker information for distinguishing different types of dementia whose symptoms can often look similar.

Amyloid PET scans are especially accurate for identifying the presence or absence of Alzheimer's disease in the brain. Beyond helping with clinical diagnosis, amyloid PET neuroimaging was extremely informative in the recent clinical trials for Alzheimer's disease treatment using anti-amyloid immunotherapy. In these trials, there was a dramatic lowering of amyloid in the brain, as measured by amyloid PET imaging, sometimes down to normal undetectable levels.

Tau PET imaging, while still pretty new and not yet approved for clinical use, may turn out to be even more informative than amyloid PET. The reason for this is that tau PET imaging allows us to see not only if the disease is present in the brain, but how far it has spread through the brain. This ability to stage the disease may be very important in selecting the right treatment for the right patient at the right time.

Spinal fluid tests are also extremely informative in the diagnosis of Alzheimer's disease and other types of dementia. A sample of the spinal fluid, which is safely collected in the lower part of the back in a simple procedure called a lumbar puncture, can be used to measure a host of brain proteins and other chemicals. Spinal fluid analysis provides an enormous amount of information about the health of brain cells. Not only can we measure levels of amyloid and tau, but we can measure many more and varied proteins for inflammation, degeneration of synapses and different types of brain cells, oxidative stress, injury to the blood vessels of the brain, and metabolism. Spinal fluid tests for amyloid and tau are approved for clinical diagnosis and usually are covered by health insurance, and they provide equivalent information or more compared with amyloid PET scans.

The most exciting and important progress in the dementia field over the last few years has been the development of blood tests for Alzheimer's disease. With new, highly sensitive and specific lab reagents and technologies, we can now detect the extremely low levels of tau, amyloid, and some other brain proteins that are produced in Alzheimer's disease and leak out into the bloodstream. While these tests are as yet not as accurate as PET scans or spinal fluid tests, they will be extremely useful for screening purposes and possibly for monitoring response to new treatments. They will help in establishing a positive diagnosis of Alzheimer's disease or other conditions affecting our cognitive abilities as we age. They are also essential in clinical research for new treatments for Alzheimer's disease as they allow us to measure whether a new drug or other treatment is working and give us insights into how the drug might be working—for example, by looking at changes in the levels of amyloid, tau, inflammation, or other features of neurodegeneration with use of the drug.

Biomarkers are an active area of research. As more biomarkers are discovered and as we better understand the information that each biomarker is giving us, how to measure them, and how to use them, the value of biomarkers in understanding, diagnosing, treating, and monitoring Alzheimer's disease will continue to increase.

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Bob's LAST MARATHON

Living the Alzheimer's Journey

Bob and Lena began their life together as long-distance runners. But they weren't prepared for the long, unmapped journey that began in 2012 with Bob's diagnosis of mixed dementia (vascular dementia and Alzheimer's disease). Even as a professional in health care communications, Lena was overwhelmed by the issues she faced. It took time to connect with caring professionals who helped her to map a path for giving Bob the best possible quality of life while caring for herself. Today, she wants others to benefit from her experience.

Like many of her fellow caregivers, Lena feels a calling to give back by helping others as they reach the common Alzheimer's milestones—the shock of diagnosis, transitioning from denial to acceptance, keeping pace with the relentless changes, and passing the final milestone. Lena has been there. While affirming our listeners' loss, confusion, and grief, *Bob's Last Marathon* will hopefully be a source of practical guidance, comfort, and encouragement in living the Alzheimer's journey.

"So much sound advice, wisdom about living life for anyone, and love—with an emphasis on love as a verb."

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