

Policy Forum

## Early Alzheimer's disease diagnostics: Wait! Wait! Don't tell me!

Meryl Comer

*President, Geoffrey Beene Foundation Alzheimer's Initiative*

News from this year's International Congress on Alzheimer's Disease (ICAD) meeting, attended by more than 5,000 scientists worldwide, offered many clear-minded reasons to hope for longer-term advances in the war against Alzheimer's disease (AD). Meanwhile here at ground zero, two developments combine to create an emotional and moral gridlock, a Catch-22 for our generation.

On the one hand, a new Mayo Clinic study tells us that a form of "mental decline" that is often a precursor to full AD is two to three times more common than previously thought, mostly in men [1].

*Is my youthful "senior moment" a multi-tasking lapse, or is it the slow creep of the same disease that stole my husband and mother away, now come to drag me down as well?*

On the other hand, dozens of very promising studies out of ICAD looked to a new era in early diagnostics as the most immediate conquest against AD. From many different clinical perspectives, we heard that early diagnosis biomarkers could revolutionize the search for therapies, especially preventive therapies; that the earlier diagnosis is made and therapy is initiated, the better the benefit to patients because there is presumably less brain damage at these early stages.

Thus we are face to face with the defining dilemma of our time: the disease is forecast to be an epidemic of the boomer generation worldwide; treatment breakthroughs, amidst the yet unproven hype about a few, are still yet to appear over the horizon; but we can now know with increasing certainty whether it has targeted us personally.

### 1. A defining dilemma: How do we respond?

*Early diagnostics for AD is the dark mirror of our own private future that the majority of us are not prepared to face. Those of us who have watched the indignity and painful distortions as a loved one's mind unravels are changed forever. Those of us who bear the burden of care—*

*spouses and family who wear the toll of its slow destructive force—vow that we will never let ourselves be its victim twice, or let our children bear the burden of our care.*

The week before ICAD 2008, early diagnostics was also the focus of one of the most widely accessed webinars in the history of the AlzForum [2]. During the Virtual Town Hall Meeting moderated by Dr Harold Varmus, representing the Alzheimer's Study Group, leading researchers presented updates on current or developing technologies in neuroimaging, biofluids assays, genomics, proteomics, metabolomics, and neuroimaging.

Such developments, we were told, would lead a new generation of people with presymptomatic AD to enlist in clinical trials, a prerequisite to any new therapy. There is no other path from bench to bedside, especially when effective disease-modifying therapies need to target AD earlier, perhaps years before the appearance of cognitive or functional symptoms.

But lingering in the question and answer session as an afterthought of all these promising forums on early diagnostics was the simple inevitable question: If genetic *risk* of possibly developing AD was *all* a test could tell someone, the Hippocratic oath to do no harm weighed in the direction of *don't ask, don't tell*—that is, why begin the AD discussion with a patient and his or her family until we know how to end it?

Today, genetic tests cover more than 1,500 conditions. Passage in May of this year, after a 13-year legislative saga, of the Genetic Information Nondiscrimination Act (GINA) promised us all limited protections against prejudicial treatments from insurers or employers based on what we might learn from such a test. Called the "first civil rights bill of the new century" by Senator Edward Kennedy (D-MA), who cosponsored GINA with Senator Olympia Snow (R-ME), it comes none too soon in an emerging era of personalized medicine and the need for early diagnostics and prevention.

Still, the "fear factor" keeps many from taking the tests. Not surprisingly, even among those people whose family history shows them to have a 50% chance of developing

E-mail address: [ADJ\\_SFEd@kra.net](mailto:ADJ_SFEd@kra.net)

Huntington's disease, few opt for a test that could either rule out their risk or confirm it as 100% [3]. The dilemma for the medical community across a range of diseases is "how to reduce the incidence of inherited disease without overloading the individual with unwelcome genetic information."

*Is a physician's decision not to recommend or not to educate a patient about a vastly inconclusive genetic test a matter of compassion or a sense of their own helplessness?*

*The benefits to the clinical war against AD aside, the question of whether to learn your risk for the disease while remaining unable to prevent it is a matter of personal conscience for individuals, not our doctors. But to their defense, physicians are not the only ones filled with ambivalence at the prospect. Our generation largely doesn't want to know.*

Such mixed feelings about early diagnostics might be understandable on many levels, but what is being lost in the current debate is the political consequence of this *Wait! Wait! Don't tell me!* attitude.

At the same time our community demands an immediate and decisive response to AD from our lawmakers and drug regulators, we also set a poor example by our individual indecision about our AD status.

*None of us expects to know our futures with certainty, but each of us has a responsibility to be as well-informed as possible when it comes to planning that future, for ourselves and our families. To show the world a collective resistance to testing is a mixed message about how seriously we take the threat of this disease on the next generation—and our own.*

We could learn a lesson from other communities that have faced their own endangered futures with clearer vision. One of the reasons the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the nation's drug industry had no choice but to respond to the Acquired Immune Deficiency Syndrome (AIDS) crisis was because prominent members of that community pushed to learn their own personal status and their prognosis, with their own T-cell count as a metaphor for the ticking time bomb of the epidemic. From the depths of desperation and anger at an establishment that ignored their plight came a model for activism and advocacy.

This year, decades later, the Senate approved legislation that would triple funding authorized to fight AIDS and other diseases around the globe, rejecting efforts to pare down the bill's \$50 billion price tag. By contrast, this year the proposed NIH AD budget boosts funding for research to approximately \$662 million, far less than the \$125 million increase sought. In 2008-dollars the decline in NIH's AD funding is even more pronounced: \$736 million in 2005 to \$644 million in 2008 and possibly down to \$631 million by 2009, given a modest 2% increase in inflation, \$100 million dollars LESS for research in 5 years.

The lesson: ultimate power to rally a full-scale response to a disease might be proportionate to the level of personal commitment demonstrated by those fighting it.

But, it can be argued, we live in a very different time than

the AIDS Coalition to Unleash Power (ACT-UP) protests of the 1980s, or the breast cancer crusades of the 1990s, which similarly made that disease a matter of life or death. Today, the headlines and admonitions are everywhere. We are living in a period of large-scale *rescue* by executive order. The near collapse of the mortgage industry and a struggling global environment are among the more disconcerting examples of our national temperament—a preference for the machismo drama of a "first responder" *after* the catastrophe has already taken place, rather than a preemptive move to address the causes while they can still be managed.

What is most dazzling about the crises of our time is that many could have been anticipated and stopped by simple adjustments to existing systems. But politicians know that Americans as a whole love a great rescue.

*In some ways, we would be better off if Alzheimer's disease were a brand new emergency instead of a century-old threat, an exotic and deadly contagion that appeared from nowhere overnight, driving fear through every baby boomer about the slow and tortured death it brings, harboring the threat of a tsunami effect on the overburdened U.S. health care system. The media would signal daily casualty alerts with every "Prisoner of Alzheimer's" (POA) outbreak, already totaling more than half a million cases annually . . . a low estimate. Unlike the avian flu—a potential public health crisis—the devastation that will be visited on the baby boom generation by AD is a guaranteed pandemic.*

*Just consider the billions that have been spent globally to develop a whole new generation of avian flu vaccines, stockpiles of antiviral drugs purchased, and bureaucratic and organizational impediments leveled. What made all of this possible was the intense media focus on a perceived threat, the pandemic that could kill millions. In effect, everyone becomes a stakeholder; everyone is at risk.*

Could it be that the AD community too must demonstrate personal risk to get anything short of a rescue response after yet another generation is lost? This seems like a deeply insensitive question.

How could a community be asked to endure more than we have, as our loved ones are robbed of their identity and disappear before our eyes long before they pass away? If being at risk is what it takes to motivate systematic change in this country, then how could the AD community not have already won this war?

*I can only suggest from personal experience that endurance of unspeakable sadness and pain is not usually a politically active state. Endurance is private; the other creates noise. We are left too exhausted to protest; those who know their predisposition are empowered to demand a response on the public stage.*

## 2. Testing our resolve

This game of *Wait. Wait. Don't tell me!* when it comes to early AD diagnostics works to marginalize our cause yet

again. I do not mean to suggest that we should set aside our efforts with the drug industry, Congress, and the FDA, where headway is being made. What is missing from our generation's response is a clear sign to our leaders, without ambivalence or private reflection, that our own lives are on the line, and that we will face what risk and emotional discomfort we must to end the battle.

Let early diagnosis be our sign—a personal decision elevated to political commitment. While we must demand genetic tests that are safe and clinically valid, let the entire AD community—the millions of people working in various ways to fight the disease—all pledge to do everything we can to manage our own lives under the shadow of AD, starting with learning all we can about our own risk status. Also, let the millions of other Americans not yet affected by the disease break the pattern of denial and become a part of preventing the catastrophe ahead, starting by knowing their risk status too.

Life planning against a disease predisposition would become an act of defiance, as well as the only sensible approach to living in a world where AD is still left unchecked. We would enlist for clinical trials and population registries en masse and become pioneers in the largest generational Framingham-type study [4] in history. We would up the rhetoric of our memory walks into a protest march for more NIH funding and FDA reform. The legions of a generation of “worried well” would thrust the AD community out of the haze of private suffering and into the spotlight of volatile political action.

What we need is this kind of unconflicted message to send our new President during his first 100 days. Ironically, the best we can hope for now is that France's President Nicolas Sarkozy will carry his pledge to make AD a national priority and top health agenda issue, during his turn at the rotating European Union presidency, to a White House state visit in early 2009. France already spends four times more than the U.S. for its citizens with AD. The fact that neither major U.S. presidential candidate has even mentioned AD at this writing also further demonstrates the wait-until-rescue approach of our system here at home. What has happened to our national pride?

But we have the opportunity to send a message: *the emergency is now, with us, in us. Presymptomatic AD testing is not fail-proof, but doing nothing is sure to fail. As a generation, we must refuse to forget who we are.*

That means daring to know our future. Are we ready?

## References

- [1] AP wire story. Study: ‘pre-dementia’ is rising, especially in men. Marilyn Marchione, July 28; filed 10:29 PM EDT.
- [2] Alzforum Live Discussion. Early detection of Alzheimer disease: a virtual town hall Meeting, sponsored by the Geoffrey Beene Foundation Alzheimer's Initiative. Moderated by Harold Varmus, Nobel laureate, former director of the National Institutes of Health, president and CEO of Memorial Sloan-Kettering Cancer Center, and member of the Alzheimer's Study Group (ASG). Presenters included Welcoming comments by June Kinoshita, Executive Editor, Alzheimer Research Forum; About the Alzheimer's Study Group, presented by Rob Egge, Center for Health Transformation; The strategic importance and challenges of early detection of AD, presented by Sid Gilman, MD, Director, Michigan Alzheimer's Disease Research Center; Early-stage and preclinical AD, presented by John Morris, MD, Director, Alzheimer's Disease Research Center, Washington University St Louis; Imaging biomarkers for early detection of AD, presented by Michael W. Weiner, MD, principal investigator, Alzheimer's Disease Neuroimaging Initiative Director, Center for Imaging of Neurodegenerative Disease, VA Medical Center, San Francisco; Early detection of AD: fluid biomarkers, presented by Anne Fagan, PhD, Research Associate Professor of Neurology, Washington University, St Louis; Translating early detection to the clinic, presented by Doug Galasko, MD, Interim Director of UCSD Shiley-Marcos Alzheimer's Disease Research Center; The role of clinical and research Centers of Excellence in early diagnosis, presented by Rachelle Smith Doody, MD, PhD, Effie Marie Cain Chair in Alzheimer's Disease Research, Baylor College of Medicine; What pharma has/what pharma needs, presented by Richard Mohs, PhD, leader, Alzheimer's Disease Team, Eli Lilly and Company; Early detection of AD: the patient's and caregiver's perspective, presented by Bill Bridgwater, patient advocate, National Board of Alzheimer's Association; and Early detection and drug development: a brief overview, presented by Paul Aisen, MD, University of California, San Diego (UCSD) School of Medicine's Department of Neurosciences, Director of the Alzheimer's Disease Cooperative Study (ADCS). A recording of the webinar is accessible at [alzforum.org](http://alzforum.org).
- [3] Cookson C. Decoding the past. *Financial Times*. July 26/27, 2008; Life and Arts section:13.
- [4] Generational model: the Nevada Vital Aging Initiative.