

The Leon Thal Symposium (LTS) 2009 on the Prevention of Dementia was held October 27th - 28th in Las Vegas. This annual commemorative think tank celebrates the efforts of the late Dr. Leon Thal, a leading investigator into the cause, prevention and treatment of Alzheimer's disease (AD). The LTS assembles leaders in the field who have been inspired by his efforts and encourages further development of strategies to move AD prevention forward.

At the time of Dr. Thal's death in 2007, he was poised to shift his focus from treating to preventing AD. He and other leaders in the field realized that by the time symptoms are recognizable, the disease has progressed much too far to be reversed or even slowed appreciably.

In 2008, the LTS formulated a plan that was incorporated in large part into the Alzheimer's Study Group's National Alzheimer's Strategic Plan. This plan was presented to

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the 11th Congress and the Obama administration in March, 2009. The recommendations were incorporated into the Alzheimer's Breakthrough Act of 2009 (S. 1492 and H.R. 3286), legislation that by fiscal year 2010 would double the funds allocated for Alzheimer's research by the National Institutes of Health. The bill also calls for a National Summit on Alzheimer's, which would bring together scientists, policymakers, and public health professionals to move the enterprise forward.

Actionable recommendations of the LTS 2009:

1. Establish a national registry

The 2009 symposium was charged with planning a national initiative to establish a database registry that would help characterize the natural history of AD and other dementia-related diseases throughout a person's lifespan—particularly in the years prior to the development of symptoms. Such a registry would facilitate the validation of assessment tools that are urgently needed to anticipate preventive and

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therapeutic trials. The lack of these tools has been the limiting issue for advancing the concept of prevention.

The goal of establishing a 'National Registry' of asymptomatic volunteers at risk for dementia will be to recruit large numbers of healthy people willing to undergo a minimal set of assessments to establish a baseline dataset. From this group, subgroups could be selected for additional studies to evaluate different methods of identifying the earliest predictors of disease. Such tools and knowledge are needed to select at-risk individuals appropriate for preventive and therapeutic trials, and to demonstrate whether a therapeutic agent is having a positive effect so that future preventive and therapeutic trials can be accomplished in a reasonable time frame.

2. Compare screens to determine which are best

Consensus was also reached on the probability that multiple screening approaches will be required in order to identify individuals who are at high risk for developing AD. A workgroup will be formed to further evaluate the screening approaches discussed above and to formulate a plan to evaluate which combination of screens would be needed at baseline, and then which assessments might be added for smaller subgroups of subjects. A National Registry and Clinical "Test Bed" might enroll 10,000 households across the United States to participate in non-invasive home monitoring techniques; provide saliva samples for whole genome sequencing; participate in home assessments of diet, lifestyle, and family, medical, and social histories; and collect water, soil, and air samples in the home. These households could then be divided (either randomly or by some pre-determined criteria) into subgroups to undergo: a) wet biomarker studies and structural imaging, b) cognitive testing, c) functional imaging, and d) other tests.

3. Address public misunderstandings about AD

Despite the huge public health implications of the growing AD problem, there is a high level of public misunderstanding about AD and healthy brain aging. For example, "brain games" have been successfully marketed as effective in slowing dementia despite a lack of scientific evidence, while the effectiveness of exercise, which has been documented, is less widely accepted. Because a person's level of understanding correlates with his or her willingness to participate in clinical trials and because recruitment for trials is so important, the need to address public understanding of the issues is critical.

4. Go global - Extending the registry beyond the United States

While the current effort is to establish a registry in the United States, the problem of AD is a global one, and will require worldwide cooperative efforts if it is to be addressed effectively. Among the participants at the workshop were those who represented studies underway around the world. A European Union / North American collaboration was initiated in Barcelona last year. A global initiative is also underway in Canada, which has so far developed a partnership with France and is now in discussions with other European countries and the United States. Studies in Canada and some other countries will benefit from the presence of national health systems that ensure care and treatment for all citizens. In France, President Nicolas Sarkozy unveiled a five-year plan in 2008 to invest \$2.4 billion in a foundation for AD research. A prevention trial of omega 3 fatty acids plus physical and cognitive treatments targeting patients at risk for dementia is also underway in France.

Conclusion

The longevity revolution in combination with the baby boom generation has created the conditions for a tsunami of individuals developing AD in the coming decades. With this in mind, AD researchers around the world have recognized the urgency of identifying preventative strategies as soon as possible. We are now at the point of needing specific recommendations and a plan for implementing those recommendations in the next few years. If Leon Thal were here, he would be leading this effort. In his memory, the Cleveland Clinic Lou Ruvo Center for Brain Health has brought together collaborators from across the nation and beyond, with a singular focus on preventing AD. This symposium represents another step forward on the path to prevention, but will require the sustained effort of all stakeholders to ensure continued progress.

Donna Thal presents the Leon Thal Prize to Virginia Lee, PhD, and John Trojanowski, MD, PhD, of the University of Pennsylvania.

