‘Early diagnosis’ of Alzheimer’s dementia – now and future

John C. S. Breitner, MD, MPH
“Auguste D.” 1903 - 4

First . . . jealous of her husband. Soon she developed a rapid loss of memory. . . . disoriented in her home, . . . carried things from one place to another and hid them, . . . thought somebody was trying to kill her . . . When reading . . . skips from line to line or reads by spelling words individually . . . In writing, she repeats syllables, omits others, . . . In speaking, she uses gap-fills and paraphrased expressions (“milk-pourer” instead of cup); She no longer remembers the use of some objects.
The rising pandemic of dementia

• Dementia is a syndrome that can have many causes

• Alzheimer’s disease (AD) is a neuro-degenerative disease of brain – causes 2/3 – 3/4 of all cases of dementia worldwide

• Today the world has 35.6 million cases of AD dementia. By 2050 this number will rise to 115 million cases - - - unless we learn to prevent AD dementia
The crushing costs of dementia

- In 2010, best estimates indicated worldwide costs of US$ 604 billion each year.
- Costs in Australia exceed $6.6 billion / yr.
- By 2050, cumulative costs of Alzheimer care in U.S. estimated at $10,000,000,000,000 – $20,000,000,000,000,000 ($10 to 20 trillion)
- By 2050, costs / yr for 115 million cases X $20,000 / case = $2.3 trillion worldwide
Crushing costs of dementia (2)

• By 2050, it is estimated that 981,000 Australians will be living with dementia, at a cost of more than A$ 50 billion a year.

• By 2050, 24% of Chinese population will be > age 65. => ~ 40 Million with dementia

• All this is foreordained unless we can learn to prevent AD dementia
The “take home” messages

1. Alzheimer’s disease is a chronic disease, similar to heart disease and cancer.
2. The disease has a biology that extends well into the decades before symptoms are seen.
3. As in heart disease and cancer, it is crucial to detect disease changes early.
4. As we learn more about the biology of the disease, we will learn how to prevent or control it.
The “take home” messages (2)

4. Improved methods of detection and early intervention will undoubtedly motivate physicians and other health professionals to seek and treat early signs of disease.

5. We are “on the verge” of an explosion in knowledge about the biology of Alzheimer’s disease and the prevention of its symptoms.
6. Prevention of Alzheimer’s dementia can be achieved without preventing the disease itself.

7. With research and resources similar to those dedicated to heart disease and cancer, we can achieve a similar measure of prevention – probably more!
Alzheimer’s disease

We know what it looks like . . .

Amyloid plaques  Neurofibrillary tangles

20 October 2011
But we don’t know the cause. We do know that . . .

- Alzheimer’s is a chronic disease . . .
- It begins in sometime in middle life
- Its earliest symptoms are barely noticeable and may be viewed as “normal for age.”
- Later symptoms become more severe and are seen as **Mild Cognitive Impairment**
Evolution in the Development of AD

- Aggregation and misfolding of Aβ followed by plaques and tangles
- Hypometabolism of AD vulnerable regions
- Medial temporal lobe atrophy
- Elevated CSF tau / Aβ ratio
- Dendritic & cell death

“Latent”
SCI
MCI
AD Dementia

Years
Birth 10 20 30 40 50 60 70 80 90 100

LATENT = No Cognitive Impairment
SCI = Subjective Cognitive Impairment
MCI = Mild Cognitive Impairment
AD = Alzheimer’s dementia

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‘MCI’ – What’s the story?

• Significant compromise in cognitive ability leading to some difficulty in function, but . . .
• NO dementia (can maintain independent activity)
• Divided into types: amnestic (memory loss is predominant) vs. non-amnestic
• Amnestic type is thought to be the typical first blush (*prodrome*) of AD symptoms
‘MCI’ – What’s the story?

- Diagnosis is difficult to establish at first, but...

- Once it’s clear MCI is there, ~ 80% of those who have it will develop dementia within 10 years.

- Helpful for optimum management (medical advice, planning for future events)
However . . . .

- Treatments for AD dementia have NOT been proven to be helpful for MCI, nor to delay the later onset of dementia.

Has the train left the station?
More than half of people with MCI have pathologic diagnosis of AD


The Neuropathology of Probable Alzheimer's Disease and Mild Cognitive Impairment

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Absolutely, we need to keep looking for better ways to care for and to treat people who already have symptoms,

but . . . . .

Ultimately, we must find ways to attack the disease in its pre-symptomatic stages and prevent the emergence of symptoms.
Development of Alzheimer’s disease

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Can we do that?

If so, how?
YES YOU MUST!
‘Biomarkers’ of AD precede symptoms

Biomarkers of AD may be useful for early diagnosis, before dementia is evident.

We may also be able to use biomarkers to measure the progress of AD in pre-symptomatic stage...
Can we use biomarkers to measure the effects of prevention strategies?
‘Biomarkers’ of AD as measures of pre-symptomatic disease progress?

Abnormal

Normal

Pre-symptomatic

SCI

MCI

Dementia

Time

FDG-PET

MRI hippocampal volume

Cognitive performance CSF AB42

Function (ADL)

CSF Tau
Association studies suggest several strategies may reduce risk of AD

- Regular exercise
- Reduce weight (Body Mass Index)
- Control blood pressure
- Reduce insulin resistance and Type II (obesity-associated) diabetes
- Improved diet (“Mediterranean vs McDonald’s”)
- Nonsteroidal Anti-inflammatory Drugs (NSAID)
Regular aerobic exercise improves tests of ‘frontal/executive’ function

L.D. Baker et al., Arch Neurol 2010;67:71-79
Mediterranean diet improves delayed visual memory

J.L. Bayer-Carter et al., Arch Neurol 2011;68:743-52
Mediterranean diet results in higher CSF concentrations of ApoE protein and reduced membrane oxidation

J.L. Bayer-Carter et al., Arch Neurol 2011;68:743-52
Intranasal insulin improves cognition and functional abilities

S. Craft et al., Published online Sept. 12, 2011
Intra-nasal insulin diminishes AD biomarkers in MCI and early AD

S. Craft et al., Published online Sept. 12, 2011
Naproxen may diminish incidence of AD and reduce AD biomarkers in non-demented elderly

J C. Breitner et al. for ADAPT Research Group
Alzheimers and Dementia, 2011;7:402-11
Ars longa, vita brevis

No time like the present . . .

Rome wasn’t built in a day!

Journey of 1000 miles begins with first steps

No sensible enterprise would commit less than 0.5% of its expenditures to R & D
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