An approach to the prevention of Alzheimer’s dementia – can we get there from here?

John C. S. Breitner, MD, MPH

Director, Centre for Studies on Prevention of Alzheimer’s Disease (StoP-AD)
Douglas Hospital Research Centre
Mcgill University Faculty of Medicine
Alzheimer’s 1st reported case

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. . .**

“Auguste D.” 1903 - 4
The rising pandemic of dementia

• Dementia is a syndrome that can have many causes

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

• Today the world has >35 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 > US $604 billion each year.
• Costs in Canada exceeded $5 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) -- more than the current US government debt!
Crushing costs of dementia (2)

• By 2050, annual costs for 115 million cases worldwide X $20,000 / case = $2.3 trillion

• By 2050, 24% of Chinese population will be > age 65. Some 40 million with dementia.

• All this is foreordained unless we can learn to prevent AD dementia
Can we get there from here?

Yes!! If we understand that . . .

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 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.
The “take home” messages (3)

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

Ctr for Studies on Prevention of AD (StoP-AD)

26 January 2015
We don’t know the cause. But 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.”
• As symptoms become more severe they may be recognized as Mild Cognitive Impairment
Evolution in the Development of AD

- **Latent** = No Cognitive Impairment
- **SCI** = Subjective Cognitive Impairment
- **MCI** = Mild Cognitive Impairment
- **AD** = Alzheimer’s dementia

**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**

Birth 10 20 30 40 50 60 70 80 90 100

Years
'MCI' – Is that where we should intervene?

• 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

• MCI/AD classification dependent of presence of 1 or more biomarkers typical of AD
However . . . .

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

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


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

J.A. Schneider, M.D., M.S.¹,²,³, Z. Arvanitakis, M.D., M.S.¹,², S.E. Leurgans, Ph.D.¹,², and D.A. Bennett, M.D.¹,²

¹Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL

²Department of Neurological Sciences, Rush University Medical Center, Chicago, IL

³Department of Pathology, Rush University Medical Center, Chicago, IL
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

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

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

Birth 10 20 30 40 50 60 70 80 90 100

Years

26 January 2015
Can we do that?
Can we ‘get there from here’?
If so, how?
Two broad approaches:

1. Find and replicate factors that predispose some people to delay or avoid onset of dementia (‘lifestyle interventions’)

2. Pharmacological interventions keyed toward interruption of the disease process (‘disease modification’)

26 January 2015
Several lifestyle intervention strategies appear to reduce risk of AD

- Regular exercise
- Reduce weight (Body Mass Index)
- Control blood pressure (in mid-life)
- Reduce insulin resistance and Type II (obesity-associated) diabetes
- Improved diet (“Mediterranean vs McDonald’s”)
What’s good for the heart is good for the brain!

26 January 2015
But . . . rates of heart disease and stroke have come down enormously in the last few decades. Shouldn’t that mean that rates of AD dementia would also be dropping?
They are!!

• **Age-specific** rates are actually declining – for first time ever observed

• But the rapid aging of populations will more than offset any improvement in age-specific rates

• Effects of aging most clearly evident in the developing world
We can be glad for now.

• There really are things we can do to reduce our risk of AD dementia . . .

• But we won’t win the battle against AD this way. Ultimately, we’ll need to deal with the biology of the disease.

• How?
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...
Development of Alzheimer’s disease

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

Birth

10

20

30

40

50

60

70

80

90

100

Years

LATENT = No Cognitive Impairment

SCI = Subjective Cognitive Impairment

MCI = Mild Cognitive Impairment

AD = Alzheimer’s dementia

26 January 2015
‘Biomarkers’ of AD precede symptoms

Abnormal

Normal

Pre-symptomatic

SCI

MCI

Dementia

Time

FDG-PET

MRI hippocampal volume

CSF AB42

Cognitive performance

Function (ADL)

CSF Tau

Can we use biomarkers to measure the effects of prevention strategies?
‘Biomarkers’ of AD as measures of pre-symptomatic disease progress?

N.B.

Biomarkers' of AD as measures of pre-symptomatic disease progress?
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
What are the study participation criteria?

- You must be 60 or older and in good health.
- You must have a parent, brother or sister who has - or had - Alzheimer’s disease.

Why should I participate?

- You will be evaluated regularly by health professionals who specialize in Alzheimer’s disease and age-related memory disorders.
- You will contribute to research that may lead to the discovery of ways to prevent Alzheimer’s disease.

Where will the study take place?

The Centre for Studies on Prevention of Alzheimer’s Disease [StoP-Alzheimer] is located on the campus of the Douglas Institute, where you will have access to the following services:

- Parking
- Clinics and laboratories
- Brain imaging facilities

How do I get more information?

Contact us at 1-855-888-4485 (toll free) or visit www.prevent-alzheimer.org.

Douglas Mental Health University Institute
Perry Pavilion – Suite E-2210
6875 LaSalle Boulevard
Montreal, Quebec H4H 1R3

Alzheimer’s and related dementias are caused by degenerative diseases of the brain. They slowly destroy memory and the ability to think, which leads to decreased independence and finally the loss of life. There is no cure.

With the aging of the population, about one in five baby boomers will suffer from Alzheimer’s disease in his or her life. What’s more, people with a family history of the disease have a two to three times higher risk.

The best hope for a cure is prevention.
www.prevenir-alzheimer.ca
www.prevent-alzheimer.ca
1-855-888-4485
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 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.
The “take home” messages (3)

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!
Merci beaucoup!

Ctr for Studies on Prevention of AD (StoP-AD)

26 January 2015