Dementia: Overview and Latest Research

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About Me

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• Grant funding for research from the Alzheimer Society, Heart and Stroke Foundation of Canada and government agencies.
GOALS

• What is dementia? What is Alzheimer’s disease? How are they different?
• How common is dementia? What are the risk factors?
• What are the causes of dementia?
• How does a doctor evaluate someone with dementia?
• Research on causes and prevention.
DEMENTIA: impaired activities of living because of cognitive difficulties.

MILD COGNITIVE IMPAIRMENT: cognitive concerns with objective evidence of poor cognitive performance, but without the significantly impaired activities that characterize dementia.
SUBJECTIVE COGNITIVE DECLINE

• Memory and reasoning abilities decline with age, and this decline is detectable by at least age 45, and possibly sooner.

• “Crystalline” intelligence changes little, however.
CANADIANS ARE OLDER THAN EVER BEFORE
Stats Canada

- Population is aging
- Number of seniors will more than double by 2036, about 25% of the population
- First time in history there will be more seniors than children <15 years, and almost twice as many seniors by 2061
- By 2036 there will be a 260% increase in persons over 80, 400% increase in persons >100.
Projected prevalence: 
- 2008 – 480,618 people, or 1.5% of the Canadian population
- 2038 – 1,125,184 people, or 2.8% of the Canadian population

Prevalence of Dementia in Canada 2008 to 2038

LIFETIME RISK OF DEMENTIA
in Women is 1 in 5, and in Men is 1 in 10.

Lifetime risk of:
• Breast cancer in women: 1 in 8
• Prostate cancer in men: 1 in 6
• Parkinson’s disease: 1 in 15
• Epilepsy: 1 in 26
• Multiple sclerosis: 1 in 500
DEMENTIA IN CALGARY

Currently living with dementia: **11,700**

Newly diagnosed cases per year: **2,800**
DEMENTIA IN CALGARY

Seniors (≥65):
  – Prevalence: 11,700.
  – Incidence: 2,787 per year.

Early onset (<65):
  – Prevalence: 353.
  – Incidence: 92 per year.


BRAIN DISEASES THAT AFFECT MEMORY

Alzheimer’s Disease
- Senile Neuritic Plaques
- Neurofibrillary Tangles
- Risk: 50%

Cerebrovascular (Blood Vessel) Diseases
- Risk: 33%

Lewy Body Disease
- Risk: 7%
Alois Alzheimer, 1906

- 52 year old woman
- Progressive neurological decline
- Memory impairment
- Paranoia
- Immobility
- Death at 56 years
- Autopsy (plaques and tangles)
- Alzheimer disease
- Senile Dementia S.D.A.T
- Dementia - Probable Alzheimer disease

Auguste Deter 1850-1906
The Brain and Alzheimer Disease

A. Cerebral Cortex: Involved in conscious thought and language.

B. Basal forebrain: Has large numbers of neurons containing acetylcholine, a chemical important in memory and learning. Early in AD there is a decline in ACh.

C. Hippocampus: Essential to memory storage. The earliest signs of AD are found in the nearby entorhinal cortex (not shown).
Figure 1. Progression of AD

Natural history of Alzheimer's disease

- Early diagnosis
- Mild-Moderate
- Severe

MMSE SCORE (Measurement of Cognition)

- Symptoms
- Diagnosis
- Loss of functional independence
- Behavioural problems
- Nursing home placement
- Death

YEARS

Gauthier et al., 2001
Progressive Loss of Activities of Living

Each bar from left to right represents the range of MMSE scores over which 25–75% of Alzheimer’s patients in one study† showed loss of optimal (independent) ADL performance.
Vascular Dementia

• Some cases are due to effects of stroke.
• Some cases are due to the effects of silent strokes, recognized only when a brain scan is done.
• Risk factors (such as high blood pressure, diabetes, smoking, heart conditions) must be treated.
Fronto-temporal Degeneration (Dementia)—FTD, “Picks Disease”

- Behavioural variant:
  - Early signs: disinhibited behaviour, change in personality, apathy (Frontal Behavioural Inventory)
- Primary Progressive Aphasias
  1. Progressive non fluent aphasia variant
     - Early signs: effortful hesitant speech, word finding difficulties
  2. Semantic variant
     - Early signs: fluent grammatically correct speech, word finding difficulties
Lewy Body Disease (dementia)

1. Early visual hallucinations
2. Parkinsonism
3. Fluctuation in level of consciousness
   • Sensitivity to the typical and atypical antipsychotic drugs
Mixed Pathologies

AD

Vascular

Lewy Body

?
Increased Risk
- Age – If you plan to get old … you are at risk!
- High blood pressure
- High cholesterol
- Diabetes
- Smoking
- Atrial fibrillation (stroke)
- Head injury, concussion (i.e. hockey)
- Risk gene - APOE4 +ve (see next slide)
- Family History
- Low education level
- Down Syndrome

Reduced Risk
- Regular exercise
- Adherence to Mediterranean Diet
Mediterranean Style Diet
Genetics

• Most AD cases are sporadic, not inherited.
• Affected immediate family member increases risk by 50%.
• Rarely, can be caused by a single bad gene (<3% of cases) which causes early onset dementia (in 40s or 50s): presenilin or APP mutation.
• 19 other genes identified that modify risk, most prominent is APOE.
• APOE gene:
  – 3 isoforms E2, E3, E4.
  – Every person has 2 APoE genes – one from each parent.
  – APOE E4 is present in about 25% of the population, but 40% of AD cases.
WHAT CAN I DO TO LOWER MY RISK?

• See a family physician to have your blood pressure checked.

• Exercise!

• Healthy diet with fruits and vegetables.

• Stay mentally active.
Pathologies

- Alzheimer’s
- Cerebrovascular
- Other

Cognitive Reserve

+ Development
+ Education
+ Genetics
+ Physical Activity
Overall Dementia Prevalence 1.5% Lower Among >65 Yr Olds in 2008-2011 vs. 1989-1994
Alzheimer’s Begins 20 Years Before Symptom Onset in Mutation Carriers

Figure 2. Comparison of Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes as a Function of Estimated Years from Expected Symptom Onset.
MEDICAL WORK UP FOR COGNITIVE IMPAIRMENT
Blood test all patients

- CBC (anemia)
- TSH (thyroid ↑ or ↓)
- Electrolytes (Na+ or K+)
- Kidney Function (Bun creatinine)
- Calcium (↑ or ↓)
- Glucose (diabetes)
- Vitamin B12

No blood test for Alzheimer’s disease—yet!
MRI, CT or PET Scan

Recommended by guidelines for most but not all clinical scenarios:

• Short duration (less than 2 years)
• Younger age
• Suspicion of focal structural problem—e.g. based on physical exam findings, history of recent head trauma or active cancer, etc.
Current Treatment Options

Mild to Moderate Alzheimer Disease

- Acetylcholinesterase Inhibitors
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)

Moderate to Severe Alzheimer Disease

- Memantine (Ebixa) – not covered by AB Blue Cross
Hypothetical Treatment Responses in AD

- **Early diagnosis**
- **Mild-Moderate**
- **Severe**

<table>
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<th>Years</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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- **a)** ideal response - complete normalization
- **b)** partial improvement
- **c)** maintained improvement while on medication
- **d)** stabilization

Gauthier et al., 1996
TRIALS OF NEW DRUGS

- Symptomatic treatments
  - Act on brain receptors to help restore brain function.
- Disease modifying treatments
  - Prevent progression of disease: a “cure”.
  - Large clinical trials of anti-beta amyloid (anti-plaque) vaccines and drugs (gamma secretase inhibitors) reported as failures in 2012 and 2013.
Canada’s National Research Strategy for Dementia

Funded beginning September 2014

32.5 million dollar effort involving all of Canada’s major research universities
What CCNA Will Do

• Enroll participants with Alzheimer’s disease, vascular cognitive impairment, fronto-temporal dementia, and Lewy body disease.
  – To understand the prognosis and causes
  – To develop diagnostic tests.
  – New ideas for treatments.
• Laboratory research into causes and new drug approaches.
• Impact of dementia on quality of life and caregiving.
1. Recruitment Into CCNA

2. Informed Consent Signed

3. History, Physical, Cognitive Evaluation

- Shared consent procedures
  - iPAD/tablet clinical data (upload)
  - Web-based computerized intake
  - Assess inclusion/exclusion criteria
  - Demographics, medical/surgical history
  - Physical/Neurological examination

4. Questionnaires

5. Psychometric Testing

6. Biosamples

   6a. Blood
   6b. Saliva
   6c. CSF

7. Sample Processing

8. Sample Shipping to Biobank

9. MRI Imaging Acquisition

10. MRI IT and Databasing

11. Brain Donation Program and Follow-up in Clinic

Note: Can be recruited into OBI, CIMA-Q as well

Mental health
Social
Psychiatric
National battery

Brain Donation Program and Follow-up in Clinic

C-Brain
LORIS
RESEARCH AT THE UNIVERSITY OF CALGARY

• CCNA study (to start in early 2016).
• Blood test for Alzheimer’s disease: blood test and lumbar puncture (spinal tap) (ongoing).
  • We also need controls without Alzheimer’s disease to have blood test and lumbar puncture.
• Clinical trials: mild cognitive impairment or mild Alzheimer’s disease, both symptomatic and disease-modifying treatments.

Please call 403-944-1594 if you are interested in learning more.
RESEARCH STUDIES

• Involve more visits and tests.
• Not all who are screened are eligible.
• No guarantee of direct benefit.
• Clinical trials: experimental drugs with potential side effects

Ask the researcher:

What does the research involve?
What are the risks?
Would anything else about my medical care change?

Please call 403-944-1594 if you are interested in learning more.
TAKE HOME MESSAGES

• Dementia means disabling cognitive impairment; it is caused by diseases of the brain.
• Medical work up consists of blood tests and, depending on the situation, a brain scan.
• There are medical treatment options but no cure.
• Healthier living may prevent dementia.
HOW CAN I HELP?

• Get medical help for friends and family if needed.
• Fight against stigma.
• Support research.
THANK YOU

www.ucalgary.ca/esmithresearch

Please call 403-944-1594 if you are interested in learning more about research on dementia.