• Dementia and our aging population.

• Dementia statistics.

• Causes of dementia.

• Diagnosis and management—physician perspective.

• Trends in research.
AGE OF CANADIANS

Statistics Canada
An Aging Population Requires An Increased Emphasis on Healthy Brain Aging
CANADIANS ARE LIVING LONGER THAN EVER BEFORE

- Current modal age of death 84; 88 in 2036; 91 in 2061
• 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
AGE AND MEMORY

• 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.
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.
LIFETIME RISK OF DEMENTIA
in Women is 1 in 4, and in Men is 1 in 6.

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
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

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
- 50%

Cerebrovascular (Blood Vessel) Diseases

Lewy Body Disease
- 33%
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

MCI

Early diagnosis

Mild-Moderate

Severe

Symptoms

Diagnosis

Loss of functional independence

Behavioural problems

Nursing home placement

Death

MMSE SCORE (Measurement of Cognition)

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.

Galasko et al., 1997
Figure 5. Interactions Between Vascular Dementia and Alzheimer’s Disease

80% of all Dementias
FTD Degeneration (Dementia) “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
   • Restless legs
Normal Cognition

Subjective Cognitive Decline: Memory symptoms but with deficits on cognitive testing.

Mild Cognitive Impairment: cognitive concerns with objective evidence of poor cognitive testing, but without the significantly impaired activities that characterize dementia.

Dementia: impaired activities of living because of cognitive difficulties.
Risk factors for Dementia

- **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): 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.
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
MRI or CT 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
Figure 4. Hypothetical Treatment Responses in AD

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<th>Early diagnosis</th>
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<th>Severe</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
“OUR government is ignoring what is likely to become the single greatest threat to the health of Americans: Alzheimer’s disease, an illness that is 100 percent incurable and 100 percent fatal…Experience has taught us that we cannot avoid Alzheimer’s disease by having regular medical checkups, by being involved in nourishing relationships or by going to the gym or filling in crossword puzzles…[U]nless unless we get to work now, any breakthrough will come too late to benefit the baby boomers. Whether the aging of America turns out to be a triumph or a tragedy will depend on our ability to fight this horrific disease and beat it before it beats us.”

SANDRA DAY O’CONNOR, STANLEY PRUSINER and KEN DYCHTWALD

New York Times Op-Ed, October 27, 2010
MOST EXCITING RECENT RESEARCH IN ALZHEIMER’S AND DEMENTIA

• AD may begin 20-30 years before symptoms.
• Dementia is preventable!
• Failure, so far, of anti-amyloid drugs and vaccines.
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.
Overall Dementia Prevalence 1.5% Lower Among >65 Yr Olds in 2008-2011 vs. 1989-1994
Large clinical trials of anti-beta amyloid (anti-plaque) vaccines and drugs (gamma secretase inhibitors) reported as failures in 2012 and 2013.

Next generation of trials:
- Testing anti-beta amyloid vaccines in cognitively healthy people with PET scan evidence of senile plaques (A4 trial).
- Testing anti-beta amyloid vaccines or drugs in pre-symptomatic disease mutation carriers.
- Testing beta secretase inhibitors.
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.
• There are opportunities to partly prevent or delay dementia, but no cure.
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.
HOW CAN I HELP?

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

www.ucalgary.ca/esmithresearch