

# Alzheimer Disease and Related Dementias

Alzheimer Society of Manitoba

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# What is Dementia?

- Dementia is a syndrome
- symptoms include loss of memory, judgment and reasoning, and changes in mood and behaviour.
- affect a person's functioning at work, in social relationships or in day-to-day activities.

# Dementia

- can be caused by conditions that may be treatable, such as depression, thyroid disease, infections or drug interactions.
- may be due to damage to the nerve cells in the brain. It is not a normal part of aging.
- each person is affected differently.

# Age and Dementia in Canada

Prevalence	Prevalence %	Age Range
1 in 50	2%	65-74 years
1 in 9	11%	75-84 years
1 in 3	33%	85-95 years
1 in 2	50%	95+ years

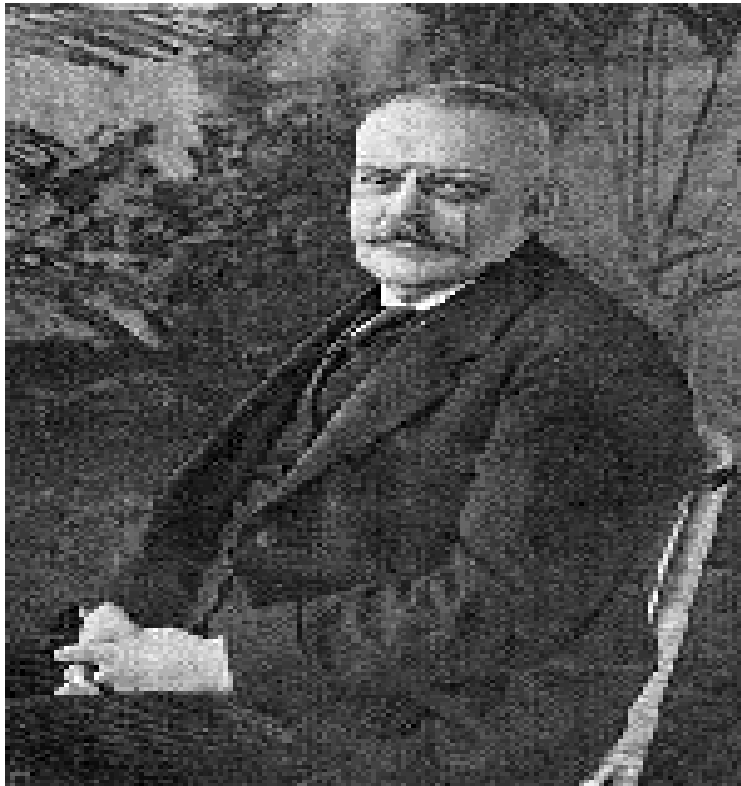
# Rising Tide: The Impact of Dementia on Canadian Society

- accounts for 64 per cent of all dementias.
- There were 480,000 Canadians diagnosed with dementia in 2008 (or 1/5% of the Canadian population)
- This number is expected to rise to 1,124,000 (or 2.8% of Canadian population) by 2038.
- The cumulative total economic burden attributed to dementia was almost \$15 Billion in 2008 and is projected to be almost \$873 Billion in 2038 (includes direct & indirect costs, informal caregiver opportunity & monetary economic burden costs).

# What is Alzheimer Disease?

- Alzheimer Disease is the most common form of dementia.
- accounts for 64 per cent of all dementias in Canada.
- gradual onset and continuing decline of memory, changes in judgment or reasoning, and inability to perform familiar tasks.

# Who was Alzheimer?



- Alois Alzheimer 1864-1915
- Professor of Psychology in Breslau
- In 1907 described case of a 57 year old and subsequent pathological findings

# Other dementias

- Other causes of dementia include:
  - Vascular Dementia
  - Lewy body Dementia
  - Pick's Disease(Fronto-Temporal dementia)
  - Creutzfeldt-Jakob Disease
  - Huntington Disease
  - and many other rare conditions



# Alzheimer Disease (AD)

- a progressive, degenerative, irreversible dementia.
  - the amount of damage done by the disease increases over time
  - the nerve cells in the brain degenerate or break down
  - damage done to the brain cells can't be repaired -- there is no known cure for this disease

# Alzheimer Disease

- no known cause or cure for the disease, but researchers around the world are working to find them.
- Two types:
  - sporadic AD can strike adults at any age, but usually occurs after age 65
  - familial autosomal dominant Alzheimer Disease (FAD), which runs in certain families

# Sporadic Alzheimer Disease

- makes up 90 to 95 percent of cases of the disease.
- People with this form may or may not have a family history of the disease.
- Children of someone with Sporadic Alzheimer Disease have a somewhat higher risk of developing AD, when compared to people with no family history of the disease.

# Familial Autosomal Dominant Alzheimer Disease (FAD)

- FAD is rare and makes up only 5 to 10 % of all cases of Alzheimer Disease
- FAD is passed from generation to generation due to a dominant inheritance pattern
- If a parent has the mutated gene, each child has a 50 per cent chance of inheriting it

# Causes and Risk Factors

- The cause of Alzheimer disease remains unknown
- More is discovered through research each year
- Likely a combination of heredity, environmental factors and internal factors

# Causes of AD

- “ $\beta$ -amyloid” is a type of glycoprotein that is abnormally concentrated in the brains of people with AD
- deposited in clumps called “plaques”
- enzymes called *secretases* and *pre-senilins* are involved in producing  $\beta$ -amyloid
- other proteins called “Tau” make up “tangles”

# Amyloid hypothesis

- Not clear whether  $\beta$ -amyloid is a cause or a by-stander in AD
- May cause inflammation, oxidation or other cascades that damage brain cells
- Has to “aggregate” or clump together to be toxic

# Tau hypothesis

- Another protein called “Tau” is a normal part of cells
- Tau forms microtubules which transport nutrients within the cell
- In AD, “hyperphosphorylated Tau” makes up “neurofibrillary tangles” which damage cells



# Risk Factors

- Factors statistically related to the development of a disease
- May or may not be actual causes of the disease

# Risk Factors for AD

- Advancing age
- Family history of Alzheimer Disease
- Low education levels
- Head injury
- Down Syndrome
- Environmental factors.

# Vascular dementia

- Dementia caused by one or more strokes
- A stroke is the loss of blood supply to an area of the brain, leading to death of some brain cells
- Strokes are caused by atherosclerosis (hardening of the arteries), high blood pressure, diabetes, smoking and other factors

# Vascular dementia

- May have a “step-wise deterioration”, suddenly worse, then okay for a while, then suddenly worse again
- May have other symptoms of stroke:
  - localized weakness
  - localized numbness
  - double vision or loss of vision
  - difficulty speaking

# Vascular dementia

- May be combined with AD or another cause of dementia - “mixed dementia”
- Control of blood pressure, cholesterol and diabetes, quitting smoking, and treatment with aspirin or other “blood thinners” will prevent more strokes

# Lewy Body dementia

- Related to both AD and Parkinson disease, may be combined with either
- Dementia similar to AD except:
  - more day-to-day fluctuation
  - more hallucinations
  - Parkinson-type symptoms (muscle stiffness, slowness of movements, tremor, gait problems)

# Fronto-temporal dementia

- Also called Pick's disease
- Often starts with behavior change much more than memory loss
- Neglect of hygiene, lack of social awareness, loss of inhibitions, bizarre or inappropriate behavior

# How Alzheimer Disease Affects a Person

- Changes in mental abilities
- Changes in emotions and mood
- Changes in behaviour
- Changes in physical abilities



# Changes in mental abilities

- AD affects ability to understand, think, remember and communicate.
  - inability to learn new things and make decisions.
  - trouble remembering people's names, where he is, or what he was about to do.
  - misplace things, repeat questions or comments, forget appointments despite reminders

# Changes in mental abilities

- may continue to remember past events clearly.
- unable to do the simple tasks done for years.
- difficulty understanding what is being said and making self understood.

# Changes in Mental Abilities

- *Apraxia* - loss of ability to carry out a complex action, not due to weakness
- Early may affect ability to use appliances, devices
- Later may affect dressing, toileting, other functions
- *“Doesn’t know what to do next”*

# Changes in Mental Functions

- *Agnosia* - inability to recognise familiar faces or objects
- Early may not recognise less familiar surroundings (e.g. cottage, son's house)
- Later fail to recognise faces, even of family, or self in mirror
- *"The man who mistook his wife for a hat"*

# Changes in Mental Functions

- *Aphasia* - inability to communicate due to problems with language function
- Receptive aphasia - difficulty understanding what you hear
- Expressive aphasia - difficulty expressing what you think
- Also caused by strokes or other types of dementia

# Aphasia

- Often an early symptom of AD
- Word-finding difficulty increases
- Later, sentences become garbled or miss important words
- Later still, fewer and fewer meaningful words
- Eventually may progress to inability to speak or communicate

# Changes in emotions and mood

- usually less expression, less lively and more withdrawn than before - “apathy”
- may also lose the ability to control moods and emotions.
- may become sad, angry, laugh inappropriately, worry a great deal over small things or be suspicious of people close to her.
- whole personality may seem different.

# Changes in behaviour

- kinds of behaviour change and the length of time they are present are different for each person.
- may be challenging for the caregivers or family to deal with
- may have meaning - may be a reaction to a situation, or an attempt to communicate or perform a function or activity



# Typical Behaviours

- pacing
- repetitive actions
- hiding things
- constant searching
- undressing
- disturbed sleep
- false beliefs
- physical outbursts
- restlessness, agitation
- swearing
- arguing, anger
- inappropriate sexual advances
- hallucinations

# Behaviours

- May exaggerate the person's tendencies or be completely new and foreign
- It is important to know that these changes in behaviour are not intentional -- they are caused by the disease.
- If you are a caregiver, there are things you can do to better understand and deal with these behaviours.

# Changes in physical abilities

- Decreased physical or functional ability:
  - at first difficulty with finances, driving or cooking
  - later have difficulty feeding, dressing or bathing
  - eventually lose bladder and bowel control
  - become less and less able to move about

# Finally

- The type of change and the speed at which Alzheimer Disease progresses is different for each person.
- The disease may progress quickly in some people, while others have many years during which they can live relatively normal lives.

# Eventually...

- Memory loss is severe and the past is forgotten.
- will lose ability to speak, walk and feed self
- will appear to have little or no reaction at all to people or her surroundings.
- will still be able to hear, respond to emotions and be aware of touch.

# Eventually...

- will lead to complete dependence and finally to death, often from another illness such as pneumonia.
- will need 24-hour-a-day care.
- this care may continue at home or the care may be given in a long-term care facility, depending on available resources

# Making the Diagnosis

- Need information from the person and from knowledgeable family members or friends - “collateral history”
- History of all medical, psychiatric illnesses, all medications
- Onset, duration, progression of symptoms
- Functional status, “activities of daily living”

# Making the Diagnosis

- Differentiate between dementia, depression, delirium
- Delirium is temporary confusion, Dementia is usually permanent and progressive
- Depression can easily look like dementia with memory loss, apathy and loss of function



# Making the Diagnosis

- Mental status test
  - Mini Mental Status Exam - MMSE
  - Tests memory, orientation, concentration, aspects of language, construction ability
- Physical Examination
- Focus on neurological system, evidence of stroke or other illnesses causing memory problem

# Medications which can worsen memory

- Over-the Counter:
  - All sleep aids, sedating antihistamines (for allergies, colds, nausea, sleep)
- Prescription
  - Anti-cholinergic medications (some antidepressants, antipsychotics, antihistamines, antiparkinson, overactive bladder meds, others)
  - Sedative drugs (anti-anxiety, narcotics, sleeping pills, antipsychotics, others)

# Laboratory tests

- Blood tests are usually done to test for anemia, diabetes, blood chemistry, thyroid or vitamin problems
- Scans such as CT (computerised tomography), MRI (magnetic resonance imaging) or SPECT (single photon emission computerised tomography) may be done, but are not always needed

# Treatment of Alzheimer Disease

- Alzheimer Disease and other dementias have always been treatable
- Treatment includes:
  - Identification and treatment of contributing factors
  - Assessment of function and meeting functional needs
  - Memory aids and coping strategies
  - Advance planning
  - Medications

# Function and Safety

- “Safety checklist”
- Driving, risk of fires, wandering, not eating, financial risk, medications, behaviour
- Mobilise family support
- Supplement with Home Care, hired care, other formal services

# Memory aids

- Limited evidence for formal “cognitive rehabilitation”
- Memory books, reminder systems (blister pack medications), automatic bill payment
- Routines are helpful
- “Use it or lose it” - growing evidence that mental stimulation may prevent or postpone decline in memory

# Caregiver Support

- Caregiver may be instrumental in maintaining the person's independence
- Caregiver burden and stress in common
- Caregivers have more health problems than non-caregivers
- Caregiver education, counselling and support shown to improve function and delay need for nursing home

# Medications

- Cognitive enhancers
  - Aim to increase memory, function
  - Do not treat underlying disease
- Behaviour and mood changes
  - Treat complications



# Donepezil (Aricept)

- A cholinesterase inhibitor
- Increase the level of acetylcholine in the brain, a chemical messenger that helps the memory cells talk to each other
- Tested in patients with mild to moderate Alzheimer disease but otherwise healthy
- About 30% of people get stomach upset, vomiting, diarrhea or other side effects

# Donepezil

- Costs \$150 per month, covered by Pharmacare if meet criteria
- Benefits seen in memory tests - 1 point on MMSE and a global test of memory, behaviour and function
- Later studies show similar small benefit on tests of functioning and behaviour

# Donepezil

- Benefits are modest - most people do not improve but remain stable for 4-6 months instead of getting steadily worse
- A small group (about one in seven) get noticeably better
- Cost effectiveness controversial

# Reminyl and Exelon

- Exelon (rivastigmine) and Reminyl (Galantamine) are also cholinesterase inhibitors like donepezil
- They have similar benefits, side effects, and cost, but are both taken twice instead of once a day
- Studies in vascular dementia and Lewy Body showed similar benefit as in Alzheimer Disease

# Memantine (Ebixa)

- Licensed in Canada December 2004
- Partial activator of NMDA (N-methyl-D-aspartate) receptor, prevents overstimulation by glutamate, possibly other effects
- Studies in mild to severe Alzheimer, vascular or mixed dementia
- Few if any significant side effects

# Memantine

- Similar cost as donepezil etc.
- Studies show similar degree of benefit in moderate to severe Alzheimer disease (MMSE  $\leq 14$ ) as donepezil , either alone or added to donepezil
- Small benefits to memory, function, behavior
- Less convincing benefit in mild Alzheimer or in vascular or mixed dementia

# Memantine

- Coverage by Pharmacare not yet decided
- Coverage in nursing homes not yet decided

# Other cognitive enhancers

- An older cholinesterase inhibitor, Tacrine, was licensed in the U.S. but not Canada
- Many, many others have been tested



# Other Medications

- Ginkgo biloba, extract of the leaf of a tree
- Several studies showed benefits even more modest than with donepezil, other studies no benefit
- Few side effects, small risk of increased bleeding

# Other Medications

- Vitamin E, an antioxidant vitamin
- One study, using 2000 Units daily, suggested benefit in delaying need for nursing home
- Controversial whether study was valid
- Recent study – no benefit
- Concern recently about serious cardiovascular side effects

# Preventive Medications?

- Estrogen - observational studies suggest that women taking estrogen are less likely to develop Alzheimer disease
- So far, studies of treatment of AD with estrogen are negative, increasing concerns about toxicity and harm
- Similar story with anti-inflammatory medication (e.g. Voltaren or Vioxx)

# New theories in development

- Immunisation to prevent  $\beta$ -amyloid plaques from developing
- Drugs to stop *secretase* enzymes from creating abnormal  $\beta$ -amyloid
- Drugs to prevent  $\beta$ -amyloid from aggregating
- Drugs for Tau

# Medication for Mood and Behavior

- Depression is common in people with Alzheimer Disease
- If severe enough, anti-depressant medications can be safely used
- Some anti-depressants worsen memory and should be avoided

# Medication for Mood and Behavior

- Behaviour changes are common and may increase caregiver burden and decrease quality of life
- Often there is an underlying cause to the behaviour (pain, constipation, infection, drug side effect)
- Environmental changes or behavioural approaches may be effective

# Medication for Mood and Behaviour

- For uncontrollable agitation, aggression, hallucinations or delusions, anti-psychotic medication may be needed
- Haloperidol, chlorpromazine or newer, more expensive risperidone, olanzapine or quetiapine can be used
- All can cause serious side effects and need careful adjustment and monitoring

# Summary

- Dementia is a common age-related syndrome which affects memory and other areas of brain function
- Alzheimer disease and stroke are the most common causes of dementia
- Clinical assessment can rule out other conditions and help make the diagnosis



# Summary

- Treatment involves eliminating contributing problems, supporting the person and family to ensure safety, and can involve medication treatment for memory and other symptoms
- Intensive research is looking for the cause and ways to prevent and treat these diseases