An introduction to dementia

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21st Century is century of neurodegenerative disease

- 19th C – infectious disease
- 20th C – heart disease, cancer
- 21st C - neurodegenerative diseases
  - Alzheimer’s and other dementias
  - Cerebrovascular disease/ stroke
  - Parkinson’s disease
  - Macular degeneration
  - Balance and gait disorders, falls
Our brains ...

• ≈1.3 Kg of 12% fat, 8% protein, 78% water
• Consume 20% of body’s O₂ & almost 20% of blood flow
• Contain about 100 billion neurons, each with 1000 to 10,000 synapses and each neuron is supported by 10-50 support (glial) cells
• Most mysterious of body’s organs but now...
• .. more accessible through revolutions in neuroimaging, IT, genomics, other -omics
Translating dementia research into practice
Age Structure of Australia
1971 - 2050

1980
Total (mil.): 14.7

Aged 65
Born 1914-1915
Males: 54014
Females: 59940
Sex Ratio: 90.1
(males per 100 females)

Animate
play
pause
speed

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Translating dementia research into practice
Age Structure of Australia
1971 - 2050

1990
Total (mil.): 17.1

- Aged 65
  - Born 1924-1925
  - Males: 66937
  - Females: 71442
  - Sex Ratio: 93.7 (males per 100 females)

Highlight surplus of males or females

Animate
- play
- pause
- speed
Translating dementia research into practice
Australian Bureau of Statistics
An agency of the Australian Government

Age Structure of Australia 1971-2050

Age

Population (thousands)

Males

Females

2030

Total (mil.): 24.8

*Projected Data

Aged 65
Born: 1964-1965
Males: 144827
Females: 149668
Sex Ratio: 96.8 (males per 100 females)

Highlight surplus of males or females

Animate

play
pause
speed

End: 2050

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Translating dementia research into practice
Australia’s ageing population

• By 2050 the population aged ...
  – 65 yo+ will double: 3m → 7.5m (13% → 25%)
  – 85yo + will quadruple: 415,000 → 1.6m
• By 2025: more 65+ yo’s than > children 0-14 yo
• 30th June 2011, 4252 people 100 years or older

¹ Dementia in Australia, AIHW, 2012
Australia: Population projections

Population (approx):
• 2014: 23.5 million
• 2030: 29.0 million
• 2050: 35.3 million

In 2030, Australia’s population will be approx 28.48 million

Approx 1 in 5 will be 65 years or older
There will be almost 3 times as many centenarians as there are today.

2013: 6,364 centenarians  2030: 18,923 centenarians
Costs

- Cost of health in Australia is \( \approx \leq 10\% \) of GDP or about $130b and rising above inflation
- Drivers – costs, demand, > expensive investigations, medicines and procedures
- Dementia costs 0.8% GDP or \( \approx $6b \) pa.
- By 2050, dementia costs >1.8% GDP
Prevalence of dementia

- > 6% of population ≥ 65 years old
- 20% of persons ≥ 80 years
- 30% of ≥ 90 years old
- Prevalence doubles every five years after 60
Dementia Doubles in Frequency Every 5 Years After Age 60

% Affected

Age

60 65 70 75 80 85+

Global Cost of Dementia

- Total estimated cost worldwide US$604 billion in 2010
- If dementia were...
  - a country, it would have the world’s 18th largest economy
  - a company, it would be the world’s largest by annual revenue

World Alzheimer Report, ADI, 2010
Dementia in Australia

- 330,000 people with dementia in 2013
- 74% aged 75+ *but* ≈8% < 65 yrs
- 70% live in community
- Projections: 400,000 by 2020; 900,000 by 2050
- 3rd leading cause of death
- 4th leading cause of disease burden
- 3rd leading cause of disability burden; (1st in 65+)

* Dementia in Australia, AIHW, 2012
People with dementia and their CGs

- PWD all over the world have
  - Cognitive decline
  - Functional decline
  - Behavioural disturbances

- CGs all over the world face
  - Stress, depression, burden
  - Financial and social hardship
  - Stigma, ignorance
Dementia in Australia

- Aboriginal and Torres Strait Islanders have higher rate
- 200,000 family carers
  - >80% provide >40 hrs pw
- Direct health and aged care costs = $4.9bn
- If add unpaid costs of carers > $6bn pa
- 0.8% GDP → 1% GDP by 2030 → 1.8% by 2050

Bill’s story

- 70 y.o. architect
- Married, 3 children + GC
- Mistakes at work
- Admits to anxiety 2 yrs
- Referred for assessment
- Alzheimer’s diagnosed
Bill’s story

- Diagnosis = relief!
- Wife grateful
- Changes work duties
- Starts anti-Alzheimer Rx
- Monitors driving
Bill’s story

- Diet, exercise, mental stimulation
- Life priority decisions
  - more family time
  - plans holiday abroad
Remember this shopping list

- Milk
- Sausages
- Peas
- Flour
- Oranges
- Steak
- Cheese
- Apple
- Yoghurt
- Sugar
Dementia definition

• Loss of at least one cognitive function
  – memory
  – Language
  – Executive abilities - planning, organisation, abstract thinking, conceptual shift
  – Visuo-spatial abilities
• Represents a decline
• Impairs daily function - occupational or social
Dementia - concepts

• Dementia is an umbrella term to describe a syndrome
• Alzheimer’s disease is most common
• Some causes reversible - but rare

• Mild Cognitive Impairment
  – intermediate between normal and dementia
AETIOLOGY OF DEMENTIA

• Over 100 causes
• Alzheimer’s disease (AD) up to 50%
  – includes other degenerative dementias
• Vascular (VaD) or multi-infarct dementia (MID) about 15-20%
• Mixed AD and VD about 15%
• Lewy body disease (up to 20%)
• Fronto-temporal dementias
• Alcohol
• Head injury
Potentially reversible or able to be halted causes of dementia

- B12 or folate deficiency
- Thyroid deficiency
- Calcium excess
- Tumours
- Normal pressure hydrocephalus
- Infection eg HIV, syphilis
MRI: profound atrophy
MRI scan of brain showing ischaemic changes
PiB-PET Scans: AD vs MCI vs control

From the online newspaper of Prof Yasser Metwally
Early Dementia -Vs- Ageing

Suspect early dementia if:

• Progressively worse
• Difficulty learning even with effort
• Events, not just details, forgotten
• Interferes with normal function e.g. hobbies, social life, shopping
• Other cognitive difficulties
  - hard to understand a story/follow movie
  - difficulty finding words
  - can’t do calculations
  - more disorganised
Alzheimer’s disease

- Memory loss
- Language disturbances
- Visuospatial deficits
- “Dysexecutive”: Impaired judgment, motivation
- Neuropsychiatric symptoms: depression, anxiety, sleep disturbance, psychosis

Alzheimer’s original patient: Auguste Deter
Symptom Progression in AD

- **Mild AD**
  - Forgetfulness
  - Short-term memory loss
  - Repetitive questions

- **Moderate AD**
  - Progression of cognitive deficits
  - Aphasia
  - Dysexecutive syndrome

- **Severe AD**
  - Agitation
  - Altered sleep patterns
  - TOTAL dependence: dressing, feeding, bathing, toilet

- **MCI**
  - Mild subjective memory loss
  - Objective memory loss
  - Normal ADL function

- **MMSE**

BADL=basic activities of daily living.

Pathology of AD

• *Macroscopic*: atrophy, mostly temporo-parietal and frontal

• *Microscopic*
  - loss of neurones and synapses
  - neurofibrillary tangles (NFTs)
  - amyloid plaques
  - degeneration
Pathology of AD

• **Chemistry**
  - Build up of abnormal proteins aggregates
    - Aβ
    - Tau (τ) protein - phosphorylated
  - Loss of neurotransmitters
    - especially acetylcholine (ACh)
AD: a progressive CNS disorder with a characteristic pathology

Katzman, 1986; Cummings and Khachaturian, 1996
Causes of AD unknown, possible factors

Genetic

- Early onset - Familial AD (FAD), auto dominant
  - age of onset 40s & 50s, rare
  - mutations on C14, C21, C1

- Late onset sporadic AD
  - associated with ApoE4 (gene on C19)

Environmental
Strong risk factors for AD

- Age
- Down’s syndrome
- Family history
- Certain genes associated with increased risk but do not cause AD eg ApoE4
Risk factors for A.D.: 1

Age

Prevalence rate %

- Baseline rates
- Campbell et al (1983)
Risk factors for AD: Down’s syndrome
Less strong risk factors for AD

- High blood pressure in mid-life
- High cholesterol in midlife
- Diabetes (Type II)
- Obesity in mid-life
- Current smoking
- Family history of Down’s
- Head injury
- ? Depression
- Low education, little cognitive stimulation
- Others – (prob. not Aluminium exposure)
Vascular dementia

- earlier onset than AD and M>F
- sudden onset, stepwise deterioration
- history of hypertension
- history of strokes
- evidence associated atherosclerosis
- focal neurological symptoms
- focal neurological signs
- focal pathology on brain imaging
Lewy Body Dementia

- Dementia
- Lewy bodies diffuse in cortex
- REM Sleep disorder
- Fluctuating cog. impairment ++
- Visual &/or auditory hallucinations
- Paranoid delusions
- Falls
- Extrapyramidal features
- Neuroleptic sensitivity
- Visuo-spatial deficits
Frontotemporal Dementia

FTD

Behavioural form

Language form
(Primary progressive aphasia)

Progressive Nonfluent aphasia (PNFA)

semantic dementia

MND

Slide from John Hodges
Clinical

- Onset usually 40-60y.o. (20-80 y. range)
- Up to half cases of pts <65yo
- Usually sporadic but 20% of cases familial with autosomal dominant inheritance
- Death occurs sooner than AD
  - esp if with Motor Neuron Disease

Fronto-temporal Dementias
(Pick Syndrome)
Fronto-temporal dementias

On examination

- preservation of memory until late
- early, prominent personality changes
- apathy
- irritability
- jocularity and euphoria
- loss of tact and concern
- impaired judgement and insight
Can Alzheimer’s disease be prevented?
What was that shopping list?

- **Dairy**
  - Milk
  - Yoghurt
  - Cheese

- **Staples**
  - Sugar
  - Flour

- **Butcher**
  - Steak
  - Sausages

- **Greengrocer**
  - Apple
  - Oranges
  - Peas
Prevention: Eliminate v Postpone

• Disease elimination
  – eg smallpox vaccination
  – best prospect is AD vaccine

• Disease postponement (Brookmeyer R, 1998)
  – delay AD onset by
    – 2 yrs $\rightarrow$ ↓ prevalence by 20%
    – 5 yrs $\rightarrow$ ↓ prevalence by 50%
Can AD be prevented? May be delayed....

- Look after your heart
- Be physically active
- Mentally challenge your brain
- Follow a healthy diet
- Enjoy social activity

yourbrainmatters.org.au

www.cheba.unsw.edu.au
www.dementiaresearch.org.au
BrainyApp - your brain health tracker
Download BrainyApp today.... And join over 200,000 others looking after their brain health, because Your Brain Matters.

FIND OUT MORE
Mind your diet
- Mediterranean diet
- Antioxidants
- Tumeric/curcumin?
- Fish? Vegetables?
Mind your Body

- Regular physical exercise
The power of physical activity

Erickson et al., 2011
Exercise benefits

- Heart disease, blood pressure
- Obesity, Diabetes
- Sarcopenia, Osteoporosis
- Lower levels of biomarkers - CSF and PET PIB in cognitively normal adults\(^1\)
- For PWD – behaviour\(\sqrt{\ }\); cognition?

\(^1\)Liang et al, Annals Neurology 2010
Mental Activity & Dementia

• Meta-analysis of 22 studies, 29,000 individuals
• ↑ complex mental activity in late life = ↓ risk of dementia by half; OR = 0.54 (0.49-0.59) ¹
• Dose - response relationship evident¹
• Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence¹
• Results held when covariates in source studies were controlled for²

Cognitive training

- Systematic review of RCTs with longitudinal follow-up (>3mths) in healthy elderly\(^1\)
  - 7 RCTs met inclusion criteria, low quality
  - Strong effect size for cognitive exercise intervention vs wait-and-see controls
  - Longer FU duration (>2yrs) $\rightarrow$ ES no lower
- Review of cog. training or rehab in dementia\(^2\)
  - 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)
The “second patient”

**Effects on carers**

- High levels of stress
- Physical health suffers
- Social isolation
- Financial hardship

‘Unfortunately as Alzheimer’s disease progresses, the family often bear a heavy burden. I only wish there was some way I could spare Nancy from this painful experience. When the time comes, I am confident that with your help she will face it with faith and courage.’

These were the words of Ronald Reagan, former President of the United States, in a letter to the American people on November 5 1994, announcing that he had been diagnosed with Alzheimer’s disease.
Alzheimer’s Australia

- Support -1 800 100 500 (helpline)
- Counselling, training programs
- Information, brochures, videos
- [www.alzheimers.org.au](http://www.alzheimers.org.au/)
- Advocacy; Research funding
- *Living with memory loss program*
  - 980 50 100 or 1-800-100-500
- Dementia Alliance International
  - [www.dementiallianceinternational.org](http://www.dementiallianceinternational.org/)
Drugs for AD

Four drugs approved
- all symptomatic, non curative:

*Cholinesterase inhibitors*
- Aricept (donepezil)
- Exelon (rivastigmine)
- Reminyl (galantamine)

*NMDA receptor antagonist*
- Ebixa (memantine)

Souvenaid – Nutriceutical/ Medical food
The cutting edge

• Drugs to prevent AD
• Drugs to cure AD
  – >200 trials recruiting
  – Vaccines, block build up of $\beta$ amyloid protein
  – $\gamma$ and $\beta$ Secretase prevent $\beta$ amyloid protein forming
• Better ways to help families and people with dementia
• Better long term care
• Treatment of behavioural and psychological symptoms of dementia
Conclusions 1

- Dementia is common
- One in five of people over 80
- Main cause is Alzheimer’s
- For most people cause of AD is unknown
- Major public health and economic issue
- Planning for future is a priority
Conclusions 2

• Management is complex & continuing
  – Patient
  – Family
  – Medication
  – Legal and financial advice
  – Practical advice

• Pace of research is exciting
Dementia Collaborative Research Centres
www.dementiaresearch.org.au

Centre for Healthy Brain Ageing
www.cheba.unsw.edu.au

Alz Australia: www.fightdementia.org.au
www.yourbrainmatters.org.au

ADI : www.alz.co.uk