

Current Status and Update of Dementia

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Dementia & Older People

- ❖ Risk of dementia doubles for every 5 years of age

- < 65 years	1%
- 65 years	2%
- 70 years	4%
- 75 years	8%
- 80 years	16%
- 85 years	32%

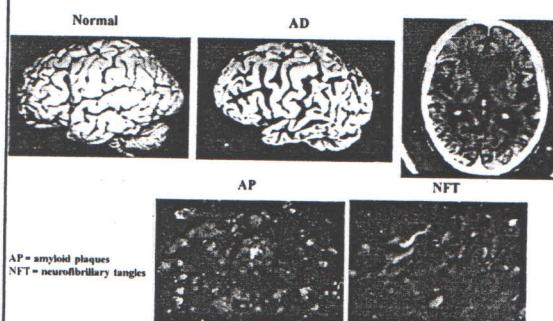
- ❖ Among 18,634 Thai older people : 22.2 % - mild to moderate poor cognitive ability.

Assantachai P, et al. Geriatr Gerontol Int. 2011;11:16-23.

Epidemiology of dementia

- ❖ Neuropsychiatric disorder : DALYs – first rank
- ❖ ผู้ป่วยสมองเสื่อมล่วงไประยะอุดม ให้มาต่อในประเทศไทย 60 ในปี 2544 → ร้อยละ 71 ในปี 2583
- ❖ ความขาดภาวะสมองเสื่อมในประเทศไทย 2 – 10 %
- ❖ ความขาด mild cognitive impairment 15%
- ❖ ผู้สูงอายุที่มี cognitive impairment-free life expectancy (CIFLE) สั้นกว่า ผู้สูงอายุรายอื่น
- ❖ ค่าใช้จ่ายในการดูแลผู้ป่วยสมองเสื่อมทั่วโลก ~ 1% ของผลิตภัณฑ์มวลรวมในประเทศ (gross domestic product - GDP)

Neuropathological changes of AD



Courtesy of George Grossberg, St Louis University, USA

Criteria for AD Diagnosis

- ❖ Old criteria 1984 by National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) + The Alzheimer's Disease and Related Disorders Association (ADRDA)
- ❖ New criteria 2011 by National Institute on Aging (NIA) + Alzheimer's Association

McKhan GM, et al. Alzheimer Dementia 2011; 7 : 263-9.

Comparing the 1984 and 2011 AD criteria

1984 criteria	2011 criteria
- Clinical diagnosis	- Clinical diagnosis + biomarkers
- Only 1 phase of AD dementia	- 3 phases : preclinical, mild cognitive impairment (pre-dementia, dementia phase)
- AD will have AD pathology	- Biomarkers (no need for biopsy)
- ไม่สามารถให้ specific neuropathologic changes	- Biomarkers บอกข้อมูลได้
- ไม่มีจำเป็นต้องมีพยาธิสภาพมาก่อน	- AD มีอาการมากตามไปด้วย แต่อารมณ์ชัดเจน ซึ่งแบ่งเป็น 3 ระยะๆ ทั้งนี้

5 biomarkers in 2011 AD criteria

category	biomarkers
- β-amyloid accumulation	Abnormal tracer retention – amyloid PET imaging ↓ CSF Aβ42
- Neuronal degeneration or injury	↑ CSF tau (total & phosphorylated tau) ↓ fluorodeoxyglucose (FDG) uptake on PET Atrophy on MRI

Mild Cognitive Impairment due to AD

Establish clinical and cognitive criteria

- Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)
 - Objective evidence of Impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)
 - Preservation of independence in functional abilities
 - Not demented
- Examine etiology of MCI consistent with AD pathophysiological process**
- Rule out vascular, traumatic, medical causes of cognitive decline, where possible
 - Provide evidence of longitudinal decline in cognition, when feasible
 - Report history consistent with AD genetic factors, where relevant

Dementia Criteria 2011

- ↓ ability to function at work, usual activity
- Functional decline from previous level
- Exclude delirium, major psychiatric disorder
- Cognitive impairment by Hx + objective cognitive assessment (MMSE / neuro.psychological test)
- ≥ 2 cognitive/behavioral impairment
 - Inability to acquire, remember new thing (amnesia)
 - Impaired executive function
 - Impaired visuospatial ability (agnosia, apraxia)
 - Impaired language function (aphasia)
 - Personality / behavioral changes

Dementia due to AD

Probable AD dementia

- Dementia by previous criteria
- Insidious onset (เรื้อรัง)
- Worsening of cognition by report/observation
- อาการเรื้อรังที่เด่นชัดที่สุด อาจเป็น 1 หรือมากกว่า
 - Amnestic + เสื่อมอิค : ล้าน
 - Nonamnestic
 - มีความจำเสื่อม + เก็บอั่ง ล้าน
 - Visuospatial + เสื่อมอิค : ล้าน
 - Executive dysfunction + เสื่อมอิค : ล้าน
- ต้องแยกไว้ตามองเพื่อมชนิดอื่นๆ ออกไปด้วย

Aphasia

Lesion in dominant hemisphere

- Alexia (inability to read) (39)
 - Agraphia (inability to write) (39)
“Word blindness”
 - Agrammatism (area 40)
 - Motor aphasia (area 44 & 45)
 - Sensory aphasia (area 22)
“Word deafness”
 - Global aphasia (area 44,45,22)
-

Apraxia

Impairment of skilled movement

Lesion in dominant hemisphere

- Motor apraxia (area 6)
 - Sensory apraxia (area 5,7)
-

Agnosia

Inability to recognize familiar objects or sound

➤ Lesion in dominant hemisphere

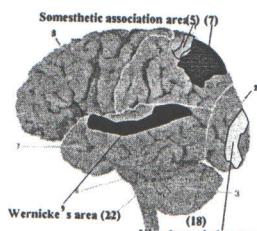
➤ Visual agnosia (area 18)

➤ Tactile agnosia (area 5,7)

- Astereognosis

- Agraphesthesia

➤ Auditory agnosia (area 22)



Behavioral changes

Lesion in Prefrontal cortex

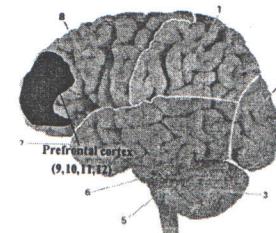
(area 9,10,11,12)

➤ Aggressive

➤ Dirty

➤ hyperactivity

➤ Apathy

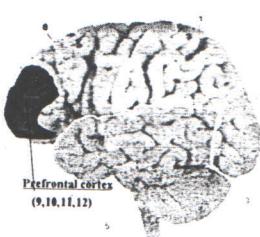


Executive function

Lesion in Prefrontal cortex

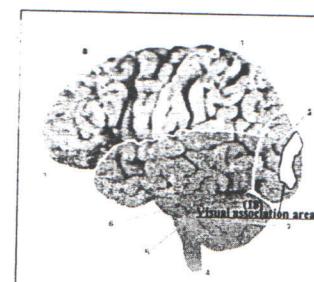
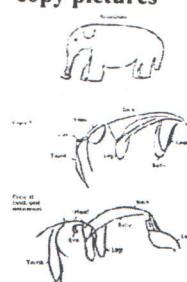
(area 9,10,11,12)

- Abstract thinking
- Judgement



Visuospatial function

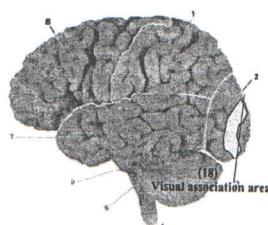
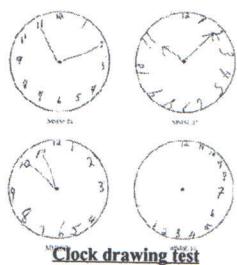
Lesion in dominant hemisphere : Inability to copy pictures



Visuospatial function

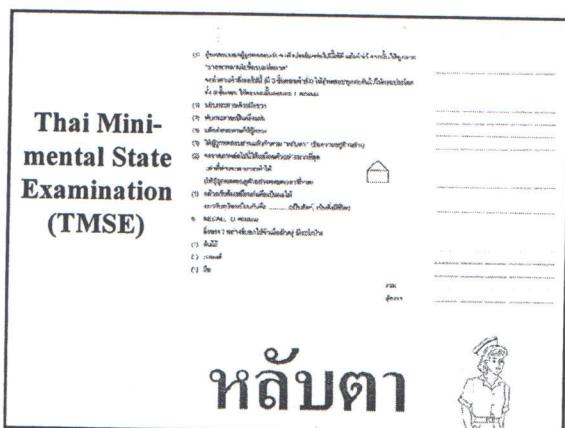
Lesion in dominant hemisphere

Inability to copy pictures



Thai Mini-Mental State Examination (TMSE)

ITEM	DATE	DATE	DATE	DATE
1. COMPREHENSION TEST				
(1) Both hands above head for 30 seconds				
(2) Roll fingers				
(3) Stand straight				
(4) Turn different ways (left & right, front & back)				
(5) Close eyes				
(6) Walk in straight line (heel-to-toe)				
(7) Point to nose				
(8) Point to each finger				
(9) Point to each toe				
(10) Point to each ear				
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Dementia Prevention is better than cure

Risk factors of dementia

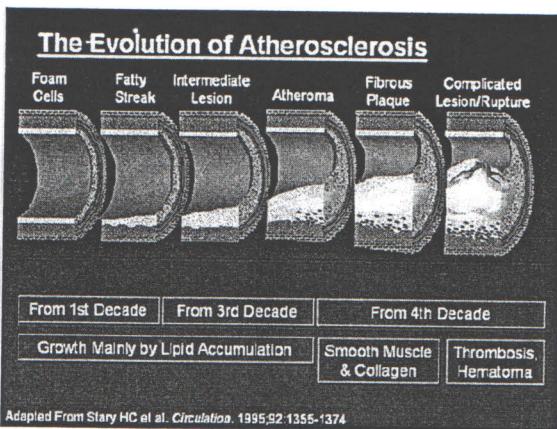
- Primary or Neurodegenerative dementia
 - ❖ Alzheimer's Disease (AD)
 - ❖ Pick's Disease
 - ❖ Diffuse Lewy's body Disease
 - ❖ Parkinson's Disease
 - ❖ Spinocerebellar Degeneration
 - ❖ Multiple system atrophy
- Secondary dementia
 - ❖ Vascular cognitive impairment (VCI)
 - ❖ Hydrocephalus
 - ❖ Brain tumor
 - ❖ etc.

VCI may be more common in some Asians
Two most common causes

Risk factors for AD

- Well-established :
 - ↑ age, genetic (family history of AD, Down's syndrome, Apo E - ε4, mutation)
- Likely :
 - head circumference, history of head injury,
 - vascular risk factors (hypertension, smoking, fatty diet)
- Less likely :
 - depression, ♀, ↑ homocysteine (↓ B₁₂ & folate), HRT (estrogen), sleep disorder, Aluminium toxicity

Woodward M, et al. Alzheimer's Australia. Paper 13, September 2007.



Risk factors for VCI

- Quite understudied, compared to AD
- Assumed that, the risk factors of VCI are the same as stroke.

1. Gorelick PB. Stroke. 2004; 35: 2620-2.
2. Evans GJ. Epidemiology and Ageing. An International Perspective. NY: Springer Publishing Co.; 1988: 36-53.

Risk factors for VCI

1. Demographic :
↑ age, ♂, ↓ education level
2. Atherosclerotic :
HT, cigarette smoking, DM, dyslipidemia, stroke, myocardial infarct, atrial fibrillation, ↑homocysteine.
3. Genetic :
apolipoprotein E - ε4, CADASIL
4. Neuroimaging :
volume loss, bilat.cerebral infarction, strategic infarction, white matter disease, ↑3rd ventricle size

-Woodward M, et al. Alzheimer's Australia. Paper 13, September 2007.
-Gorelick PB. Stroke. 1997; 28: 459-63.

Shared risk factors of dementia



Evidence-based Risk Factors from Observational Studies

HT: risk factors of dementia

Study	year	N	Findings
Honolulu Asia Aging Study	1995 2000	3735 3703	SP(midlife) ~ cognitive dysfunction ↑risk in HT (no Rx, poorly control)
Uppsala, Sweden	1998	999	↓ cognition in untreated HT men
NHLBI Twin study	1996	392	SP(midlife) ~ cognitive dysfunction ↑white matter, ↓brain volume
Longitudinal study in Goteborg	1995	382	SP & DP ~ dementia, small vv. disease, white matter lesions
Kuopio, East Finland	1993 vs.366	378	HT (esp.↑insulin) ~ cognitive dysfunction

Cigarette smoking : risk factors of dementia

Study	year	N	Findings
Rotterdam study	1998	6870	Current smokers ~ AD, esp. in those without Apo E - ε4
Honolulu Asia Aging Study	1997	3734	Midlife smoking ~ ↑AD (OR 2.18 – medium, OR 2.40 – heavy smoking)
Zutphen Elderly study	1996	489	X-sectional study: current smokers' cognitive tests ↓20% cf. to never smokers.

Fatty diet: risk factors of dementia

Study	year	N	Findings
10/66 Dementia Research Group	2009	14960	Dose-dependent inverse association between fish consumption and dementia with PR: 0.81 (0.72- 0.91)
Italian Longitudinal Study on Aging	1999	5632	Mono-unsaturated fat ≠ cognitive decline
Rotterdam study	1997	5386	Dementia risk ~ total fat intake, saturated fat, total cholesterol ± fish intake
Zutphen Study	1997	1266	Linoleic acid ~ cognitive impair. Fish intake ± cognitive impair.

Dyslipidemia : risk factors of dementia

Study	year	N	Findings
Hisayama Study	2011	147	Dyslipidemia ~ neuritic plaques
Reitz C, et al. Arch Neurol;67	2010	1130	HDL >55mg/dl. ~ ↓ AD risk
InChianti study	2010	1051	↓HDL ~ dementia (OR 0.96 : 0.93-0.99)
Washington Heights, Northern Manhattan	1999	1111	↑LDL ~ ↑ risk of dementia with stroke (but not AD)

Homocysteinemia: risk factors of dementia

Study	year	N	Findings
Framingham study Seshadri S, et al.	2002	1092	↑ plasma homocysteine ~ strong, independent risk factor of dementia/AD
Sacramento Area Latino Study on Aging	2007	1779	Homocysteine – an independent risk factor for dementia/CIND
Ravaglia G, et al.	2005	816	↑ plasma homocysteine & ↓ serum folate – independent predictor of dementia/AD

Risk factors of folate deficiency in older people

- Prevalence of erythrocyte folate def. 38.8% vs. 3.3% in NZ or hardly found in Europe.

Risk	Adj. OR	95% CI
Male	1.59	1.22 – 2.08
Heart disease	1.96	1.22 – 3.14
Low HDL	0.986	0.977 – 0.999

Assantachai P, et al. Pub Health Nutr 2007;10:65-70.

Homocysteine

- homocysteine เป็นปัจจัยเสี่ยงอิสระต่อการเกิด atherosclerosis
- homocysteine $\geq 10 \text{ }\mu\text{mol/L}$ ความเสี่ยงต่อโรคในระบบหัวใจและหลอดเลือด จะเพิ่มขึ้นเป็นแบบเส้นตรง (linear dose-response relationship)
- hyperhomocysteinemia จะมีส่วนที่ให้เกิดโรคในระบบหัวใจประมวลร้อยละ 10 ของความเสี่ยงทั้งหมด
- folate deficiency เป็นสาเหตุที่บ่นอยู่ที่สุดใน hyperhomocysteinemia แนะนำให้รับโฟเลต $\geq 400 \text{ }\mu\text{g/day}$ หรือรับวิตามินบี9 400 ไมโครกรัมต่อวัน
- ผลกระทบของภาวะขาดวิตามินบี9 ผู้ที่มีภาวะขาดด้อยดีแลในเด็กภาวะ folate deficiency จะมีอัตราการเกิด atherosclerosis เข้มข้น การมีประวัติโรคหัวใจ ผู้ที่มีภาวะขาดด้อยดีแลในเด็กต่อ

Assantachai P, et al. Public Health Nutrition 2007;10: 65-70.

DM: risk factors of dementia

Study	year	N	Findings
Hisayama study	2011	1017	DM: a significant risk factor for all-cause dementia
Hassing et al.	2002	702	Aged ≥ 80 DM: RR 2.54 (1.35-4.78) for VaD but not AD
Honolulu-Asia Aging study	2002	2574	Type 2 DM: risk factor for AD /VsD. The association between DM and AD is particularly strong among carriers of APOE ε4.
Rotterdam study	1996	6330	Dementia ~ DM esp. with insulin Rx for both VCI & AD

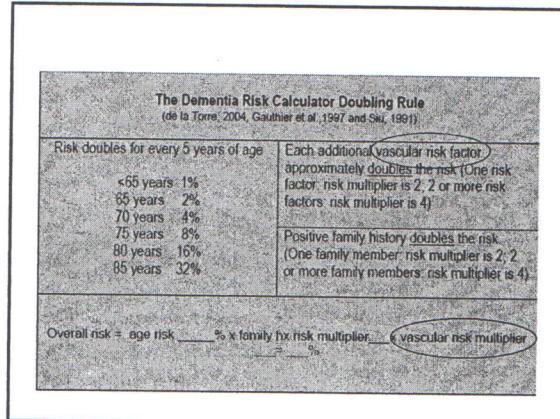
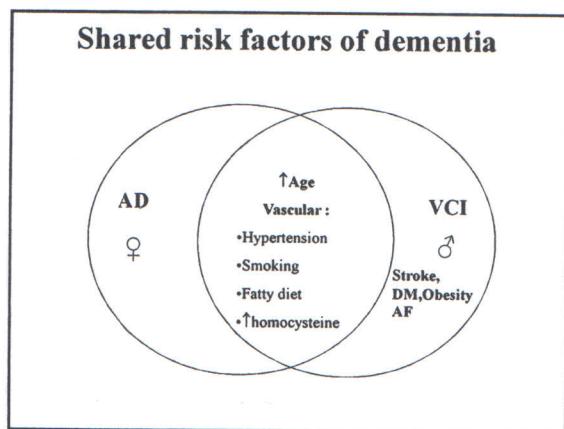
Obesity: risk factors of dementia

Study	year	N	Findings
Cardiovascular Health study	2009	2798	-Midlife obesity (BMI >30) ~ increased risk of dementia -Risk estimates were reversed in assessments of late-life BMI
Kaiser Permanente Northern California Medical Group	2005	10276	Obesity in middle age - ↑ risk of future dementia, independent of comorbid conditions.
Gustafson D, et al.	2003	392	For women, every 1.0 increase in BMI at age 70 years, AD risk ↑ 36%

Shared risk factors of dementia

- Risk factors of one type of dementia may also relate to other dementia.
- High blood pressure in middle age → AD & VCI
- Stroke may unmask or potentiate AD (mixed dementia)
- Vascular risk factors & Atherosclerosis – AD

Gorelick et al. Alz Dis Assoc Dis 1999; 13(Suppl 3):S131-9.



Preventive strategies of dementia

Study	year	N	Findings
Mielke MM, et al.	2007	135	In AD, systolic HT ~ ↑ rapid decline of mental score
Solomon A, et al.	2006	1449	↑ Total cholesterol midlife ~ dementia AD ↓ TC after midlife ~ dementia AD
Honolulu-Asia Aging Study	2007	1027	↓ TC over 26-year change ~ dementia/AD

Preventive strategies of dementia

Diabetes mellitus

- Drug interventional trials addressing the prevention of cognitive decline through action on the metabolic syndrome are disappointing - albeit scarce at this time.
- Lifestyle interventions in middle-aged or younger-elderly subjects should also be implemented in the general population.

Bourdel-Marchasson I et al. Diabetes Metab 2010; 36: 173-81.

Preventive strategies of dementia - a long way to go

- Even if there are consistent findings from large observational studies regarding preventive or risk factors for dementia
- Few randomized controlled trials have been designed specifically to prove the protective effects of interventions based on such factors on dementia incidence.
- Due to the multifactorial origin, multidomain interventions could be a suitable candidate for preventive interventions, but designing such trials remains very challenging for researchers.

อาหารต้านสมองเสื่อม

- อาหารที่เพิ่มความเสี่ยงต่อภาวะหลอดเลือดแดงแข็งกระด้าง หลีกเลี่ยงอาหารที่เพิ่มความเสี่ยงต่อโรคเบาหวาน ความดันเลือดสูง ไขมันไม่อิծสูง
- อาหารที่มีไขมันอิ่มตัวและโกรกเลสเตอรอลสูงจะเพิ่มความเสี่ยงต่อภาวะสมองเสื่อม
- ปลาทะเล เนื้อปork ไก่ นมแพะ omega-3 fatty acid
- สารต้านออกซิเดชัน สารต้านอนุมูลอิสระ เช่นวิตามินบี ซี บี 6 ไนัก็อกโนไซด์ เช่น
- สาร homocysteinemia กับวิตามินเสริม folate B12 และB6
- โปรตีน
- ใบเปี๊ยะ Ginkgo biloba ??

สรุปการป้องกันภาวะสมองเสื่อม

- ❖ มีกิจกรรมที่กระตุนการใช้สมอง มีการเรียนรู้ก่อศรีวิชา
- ❖ ออกกำลังกายอย่างบ่อยๆ
- ❖ การพบปะดูแล / ช่วยเหลือดูแล (spiritual activity)
- ❖ มีกิจกรรมสันสนานกากา
- ❖ อาหาร : ↓ homocysteine, cholesterol, glucose
↑ อาหารที่มีประโยชน์ เช่น ผัก ผลไม้ omega-3 fatty acid
- ❖ นอนให้เพียงพอ
- ❖ หยุดบุหรี่
- ❖ ควบคุมปัจจัยเสี่ยงไข้高กอเด็จ เช่น HT, DM, DLP, obesity
- ❖ ดื่มน้ำอย่างมากๆ กินอาหารเชิงมีน้ำ หรืออื่นๆ ท่องรักษาให้ดี