### 알쯔하이머병 치료지침 개발에 부쳐

#### Introduction to Clinical Practice Guideline on Alzheimer's Disease

```
가
                                                            5
                                                                    20
                                                                                  8.1
                                         가
                                                                                       3
                                                 1
                                                                          가
                                                                                가
 가
                                                                                     2001
                                                     UN
                                                                                  65
                                                              7%
                                                                     )
                                                         2019
                      가
                                                     14%
                                                            )
                                     가
                                                        가
                                                가 가
                                                                         가
                                                                . 2003
                                                                                        30
                                                        가
                                                가
65
                  4
                         3
    65
                         8%, 70
                              가
15%, 85
                  30~40%
           85
                                                                                  8
                                47%가
```

가 가 '

· ,

(evidence -

based medicine)

\$200\$ . California "Guideline for Alzheimer  $\mbox{\ensuremath{\$}}$ 

disease management"(1),

"Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias of Late Life"(2)

"Practice parameter: Management of dementia(an evidence - based review)" (3), National Institute of Clinical Excellence(NICE) "Guidance on the use of Donepezil, Rivastigmine and Galantamine" (4)

가 가

# 근거에 입각한 알쯔하이머병의 약물치료 지침 -아세틸콜린분해효소 억제제-

Guideline of Alzheimer's Disease Drug Treatment by
Evidence - based Medicine
- Acetylcholinesterase Inhibitors -

50% 가 가 가 가 가 가 가 (M1)1907 Alois Alzheimer (nicotine) 가 가 가 가 가 가 가 가 25~40% (2). 가 가 (4, 5). 1993 FDA (tacrine) 1996 2

1.

Strategy	Donepezil	Rivastigmine	Galantamine
Dosing	once daily	twice daily	twice daily
Starting	F	2	0
dose (mg/day)	5	3	8
Lowest effective	_	,	
dose (mg/day)	5	6	16
Maximum			
dose (mg/day)	10	12	24
Dose increase	after 4~6 weeks	every after 2 weeks	every after 4 weeks

AchEls, acetylcholinesterase inhibitors

2.

Donepezil	NN	9 (8~14) for a 4 - point or more improvement in ADAS - Cog at 6 months
Donepezii	ININ	, , , , , , , , , , , , , , , , , , , ,
		8 (6~15) for any improvement on a clinical global scale at 6 months
	NNH	11 (7~15) for one withdrawal at 10 mg/day over 6 months
Rivastigmine	NNT	12 (8~20) for a 4 - point or more improvement in ADAS - Cog at 6 months
		15 (8~17) for any improvement on a clinical global scale at 6 months
	NNH	5 for one withdrawal at 6~12 mg/day
Galantamine	NNT	6 for a 1 - point or more improvement in ADAS - Cog at 6 months on 32 mg/day
		13~50 for any improvement on a clinical global scale on 32 mg/day at 6 months
	NNH	4~8 for one drop - out at 32 mg/day
Tacrine	NNT	30 for a 4 - point or more improvement in ADAS - Cog at 6 months
		10 for any improvement on a clinical global scale at 3 months
		40 for 'moderate' or 'marked' improvement on a clinical global scale at 3 months
	NNH	4 (withdrawal over 3 months)

<sup>\*</sup>NNH, number needed to harm NNT, number needed to treat

(donepezil)가 , 2000 1. Tacrine (Cognex)
(rivastigmine), 2001 (galantamine) Tacrine 1993 FDA
. 2

,

. 가 2~4 1 4

1, 2 (6~8),

•

2. Donepezil (	Aricept)								
199	6	FDA							
가 70									
1	5 mg		4~6	10				가	
mg									
J						FDA			
3. Rivastigmin	e (Exelon)					. 27.			
Rivastigmine		FDA							가
rtivastigiiiiile	2000	IDA			•				<b>7</b> 1
	Diversitions				,	,	,		
	. Rivastigm					•			
		(butyry	Icholineste	rase)					
			(9).			. 1~2	4		
6 n	ng	1 2	,						
9∼12 m	j .					6~8	12		
4. Galantamine	e(Reminyl)								
Galantamine		2001	FDA						
				(sy-					
napse)				( )	가				
(presynaptic)									
(ртсзупарис)	/ - II ( ' -		·> 71						
	(allosterio	modulat					•		
			8 mg			. 1			
1 2	,	16~	24 mg						

# 항치매 약물의 투여 개시와 중단

### When to Start and When to Stop

Donepezil, Rivastigmine				
Galantamine		2~4	가	MMSE
	가		,	
		, ,	C	donepezil, rivas-
	tigmine	galantamine		,
	6	MMSE,		가
	MMSE	12		가
2001				
donepezil, rivastigmine galantamine		. NICE (	Guidance r	ivastigmine(13),
NICE Guidance가	memantine(14), donepezil(15), vitamin E selegi-			
(Mini - Mental State Examination : MMSE)(10~	line(16),	galantamine(1	7)	
12) 21 ~ 26 MMSE 26		2003		
donepezil, rivastigmine galantamine				
	NICE			가?
Donepezil, Rivastigmine	NICE (	Guidance		MMSE
Galantamine			NICE	
		MMSE	MMSE:	가 .
가		MMSE		•
가 . NICE guidanœ				
- MMSE 12	가	. MMSE		

가 가 65 60%가 가 MMSE NICE ( 가 MMSE 12 ) 7 (Global Deterioration Scale, GDS) donepezil, rivastigmine galanta-(18). mine MMSE 26 7 6 7 . ①

### 알쯔하이머병의 기타 약물치료

### Other Drug Treatment for Alzheimer's Disease

```
(basal forebrain)
                                                      (amyloid plaque),
                                                                                     (neurofibillary tan-
                                                    gle)
                                                                                           (reactive as-
                                   가
                                                    trocytosis)
                                                                         (microglial cell)
                                                                        (19).
                             가
                      가
(raphe nucleus)
    가
        가 가
                                                    1. Estrogen
                                                                                                   가
                                                      Estrogen
                                 가
                                                                                                    (es-
                                                                                     가
                                                    trous cycle)
(19).
                                                    (neurogenesis)
                                가
                                                                                          (20).
(deafferentation)
                                                           estrogen
                                                                                                (propa-
(limbic system),
                         (association cortex),
                                                    gation phase)
                                                                                    (initiation phase)
```

```
가
                            . Estrogen
                                         bcl - 2
                                                        (glutathione peroxidase)
                           (antiapoptotic protein)
                                                                       (peroxidation)
  gene - dependent upregulation
                                                                             (24). Selegiline
                      가
        estrogen
                                                       (oxidative free radical)
                                                                                (23).
                      upregulation
                                       가
                                                       1
                                                                 5~10 mg
          가
                    . Estrogen vitamin E
                                                                                     가
                                                             hypertensive crisis
                               (21).
                                                       tyramine
                                                                                          가
 Conjugated equine estrogen 1 0.625 ~ 1.25 mg
                                                                                            (22).
1
             71~81%
                               (vaginal bleeding)
                                                        (25)
                           86%
                                                     (psychomotor retardation)
                                                        (23).
 (thromboembolism),
                                                     3. Vitamin E
                           (22).
                                                       Vitamin E
2. Selegiline
                                                                                 (lipid peroxidation)
  В
                       (monoamine oxidase B:
MAO - B)
                                         (mono-
amine)
  В
                               가 가
                                                      1 2,000 IU 2
Selegiline
                       В
                                                             가
          가
                                           가
                                                      가
                             (arousal)
                                                                      (26).
                 (23).
                         (free radical)
                                                     4. Acetyl - L - carnitine
                                     (superoxide
                                                     Acetyl - L - carnitine
dismutase),
                      (catalase),
```

```
가
                                     (long chain
                                                                                 COX - 2
                                                       celecoxib rofecoxib
fatty acid)
             가
                                                     가
acetyl - L - carnitine acetyl coenzyme -
                 (cholinergic transmission)
                                                                 NSAID
                                    (membrane
                                                                       . Warfarin
stabilization)
                                                           COX - 2
                                                                   가
                                   (22).
                                                                                                 가
5. Non - steroidal anti - inflammatory drug(NSAID)
               가
                                  cyclo - oxyg-
nase(COX)가
                                         (parie-
                                                   6. Gingko Biloba
               .
                 COX - 1
tal cell)
       (metabolic signal)
                                        COX - 2
가
  NSAID
                                                   (ischemia)
  interleukin - 1 interleukin - 6
                                                           (22).
                                                                              (platelet activating fac-
                        (classical complement
                                                                              (long - term potentia-
                                                   tor)
cascade)
                                                   tion)
                                                                 (27).
        NSAID COX - 2
                                                                              240 mg
                                                                        . 1
                                                                                        가
                                    (23).
  Ibuprofen, naproxene
                          diclofenac
                                                                                      . 1 120 mg
                           NSAID
                                     COX - 1
                                                         33
                                                                      2
COX - 2
                                                                 가
                                                                       (28).
```

7. Hydergine Hydergine (22). 10. Propentofylline Propentofylline (glial cell) 가 8. Nimodipine (22). (homeostasis) (calcium channel blocker) dihydropiridine . Nimodipine 가 (open channel) Nimodipine 28% 9. Piracetam 가 (nootropic drug) Piracetam 가 ATP 가 (anti-. (3) thrombotic property)

### 치매의 행동. 심리 증상의 약물치료

### **Pharmacotherapy of BPSD**

가 가 **BPSD** 가 (Behavioral and Psychological Symptoms of Dementia, BPSD)" (29). BPSD 가 (30)가 . BPSD 가 가 (tardive dyskinesia) **BPSD** 가 **BPSD** risperidone haloperidol 가 (placebo) **BPSD** (31, 32)olanzapine 가 **BPSD** olanzapine **BPSD** BPSD가 (33, 34). Quetiapine (open label study)

가				
(35). cl	lozapine			
			1.	(Tricyclic Antidepressant, TCA)
	가		,	, ,
			. Amitriptyline	imipramine
	1 haloperidol	0.5 mg		nortriptyline, desipramine
가		halo-		
peridol 2 mg 가	<u>.</u>			
12 가				
4~8		가	2.	(Selective Seroto-
		가	nin Reuptake Ir	nhibitor, SSRI)
(36).				
	가			
				citalopram, sertraline,
			paroxetine	
			(41 ~ 44).	
1. Benzodiazepine			3.	
Benzodiazepine				-
	. Oxazepam	lora-		
zepam short - act	ting benzodiazepine		, mirtazapine	가
	(37). 4~6 be	enzodi-	(45). 가 가	moclobemide
azepine				가
(38, 39).			(4	16).
2. Buspirone				
Buspirone 5 - HT <sub>1</sub>				
			Lithium	
(40). BP	PSD		BPSD	. Carbamazepine
가			valproate	가

Special Issue •

Neuropsychiatric Inventory(NPI) valproate가 carbamazepine (48), Roster rivastigmine donepezil galantamine 가 (49). 가 ( - blocker) 1. . Zopiclone, zolpidem, lorazepam, temazepam - blocker가 가 가 (50, 51) BPSD . 가 - blocker 가 trazodone 2. Selegiline 가 가 В selegiline 가 BPSD, 가  $(52 \sim 55)$ . selegliline 가 (47). Palace donepezil . (3)

### 알쯔하이머병의 혈관성 인자

#### Vascular Factors in Alzheimer's Disease

가 가 가 (neurofibrilary tangle) (amyloid plaque) 가 가 2. 가 "Nun Study" 3 (58). (56, 57). 1997 가 가 678 (58). 161 1. (lacunar infarct) Alois Alzheimer가 1907 20.7 51

가

```
1.
                                                           )
                                                                     (marker)
                                        (thrombogenic factors)
                              ApoE4
                                              가
                                                                      1
                                       가
                가
                                                                            가
                                       (microvessel pathology)
                                                                                            가
          가
                                  가
                                         (59).
                                                                        60
                                                      (isolated systolic hypertension)
                                                                                             가
                                                                 50%
                                                    (60).
                                                                  가
                                                                         가
                                                                (small vessel disease)
가
                                     가
3.
                                                                                      1
                                                                           E(apolipoprotein E)가
                                              10
                                                                                    Ε
                                        가
                                                                                      가
                                                                         E4
                                                                  가
                                                                             가
```

(61~63).

. (3)

가

# 기타 중추신경계 질환과 동반된 알쯔하이머병의 약물치료

Pharmacotherapy of Alzheimer's Disease with Other Factors

```
(parkinsonism)
                            (64)
          (resting tremor)
                                                                                      (66).
                                                                        가
                                    가
                  가
                                                          가
                              (65).
                                                                                                가
                                                                          가
                                                              가
                      가
                             (substantia nigra)
      가
                  (pseudoparkinsonism)
           (65, 66).
 가
                     (apraxia), paratonic rigidity
                                                                가
(gegenhalten),
```

			(dysthymi	a)		
(67, 68),						
(0., 00),	(69).			가	,	
가	가	-		가		,
,	가			(selective	e serotonin	reup-
			take inhibitors)			
,		가				
		가	(69).			
(depression	-induced cognitive imp	airment)(70),				
	(00)					
	(69).					
	,		(72). Dementia pugilist	ica		
			, ,		,	
	가					
60%	30		5~7		,	
가 (71).			apolipopro	otein E4		
					(73).	
			_,			
	•		가	•		
	,					가
					가	71
	•		,		71	가
		가	,			'
(	(69).					
	3					

	(Alcoho	ol - related					
	Dementia)					가	
				(76).			
(74).		Korsakoff	,		,		
	가	(75),				(th	niamine)
					가		
	•						
			가			가	
			. 1	ത			

## 요약 및 맺음말

		8	2.			,
						,
	•					
,		,		•		가
				1 halope	eridol 0.5 mg	가
1. 가					haloperidol 2	2 mg
donepezi	l, rivastigmine,	galantamine	가		12	2 4~6
		, ,			가	
,				가	•	
1	· ~2 4		3. Benzoo	diazepine		
				. 0	xazepam loraze	pam
6~8	12					
MMSE 26				. 4~6		
6						
				z	opiclone, zolpider	
,	7		temaze	pam		가
					가	
가				가	trazodone	
		,	4.			
		•				. Citalopram

#### Special Issue •

	rtraline, paroxetine 가			가 가	,	
	, ,	, '} .				
	nortriptyline, desipra	amine	8.			
5.	가			가	가	
	·		가		,	
		71				
6.	가	, 가		•	,	
		,		,	,	
7.	가					.`⊕

### 참고문헌

- California Workgroup on guidelines for Alzheimer's disease management. Guidelines of Alzheimer's disease management, 2002
- American Psychiatric Association. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. Am J Psychiatry 1997; 154: 1 - 39
- American Academy of Neurology. Practice parameter:
   Management of dementia (an evidence based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology, 2001
- National Institute of Clinical Excellence. Guidance on the use of Donepezil. Rivastigmine and Galantamine, 2001
- Qizilbash N, Schneider NS, Chui H, Tariot P, Brodaty M, Kaye J, et al. Evidence - based Dementia Practice. Malden: Blackwell Science Ltd, 2002
- Maj M, Sartorius N. Dementia, WPA Series Evidence and Experience in Psychiatry. Wiley, 2000
- 7. Richter RW, Richter BZ. Alzheimer's Disease. Mosby, 2002
- Doody RS, Stevens JC, Beck C, Dubinsky RM, Kaye HA, Guyther L, et al. Practice parameter: management of dementia (an evidence - based review). Neurology 2001; 56: 1154 - 66
- Francis PT, Palmer AM, Snape M, Wilcock GK. The cholinergic hypothesis of Alzheimer's disease: a review of progress. J Neurol Neurosurg Psychiatry 1999; 66: 137-47
- 10. Folstein MF, Folstein SE, McHugh PR. "Mini Mental State" : a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975 ; 12 : 189 98
- 11. Park JH, Kwon YC. Modification of the Mini Mental State

- Examination for use in the elderly in a non western society.

  Part I. Development of Korean version of Mini Mental State

  Examination. Int J Geriatr Psychiatry 1990; 5: 381 87
- 12. Park JH, Park YN, Ko HJ. Modification of the Mini Mental State Examination for use in the elderly in a non - western society. Part II. Cutoff points and their diagnostic validities. Int J Geriatr Psychiatry 1991; 6:875-82
- 13. Giacobini E. Selective inhibitors of butyrylcholinesterase : a valid alternative for therapy of Alzheimer's disease? Drugs Aging 2001; 18:891-8
- Schmitt FA, Cragar D, Ashford JW, Reisberg B, Ferris S, Mobius HJ, et al. Measuring cognition in advanced Alzheimer's disease for clinical trials. J Neural Transm 2002(Suppl); 135 -48
- 15. Feldman H, Gauthier S, Hecker J, Vellas B, Subbiah P, Whalen E. A 24 week, randomized, double blind study of donepezil in moderate to severe Alzheimer's disease. Neurology 2001; 57:613-20
- Peskind ER. Pharmacologic approaches to cognitive deficits in Alzheimer's disease. J Clin Psychiatry 1998; 59(S)9: 22 - 7
- 17. Wilkinson DG, Hock C, Farlow M, van Baelen B, Schwalen S. Galantamine provides broad benefits in patients with 'advanced moderate' Alzheimer's disease (MMSE < or = 12) for up to six months. Int J Clin Pract 2002; 56: 509 14</p>
- Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry 1982; 139: 1136 - 9
- 19. Terry RD, Katzman R, Bick KL, Sisodia SS, eds. Alzheimer's

- disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 1999: 245 6
- 20. Mulnard RA, Cotman CW, Kawas C, van Dyck CH, Sano M, Doody R, et al. Estrogen replacement therapy for treatment of mild to moderate Alzheimer's disease. JAMA 2000; 283: 1007 - 15
- Pike CJ. Estrogen modulates bcl xL expression and beta amyloid induced apoptosis. J Neurochem 1999; 72: 1552 63
- 22. Qizilbash N, Schneider LS, Chui H, Tariot P, Brodaty H, Kaye J, et al. Evidence based dementia practice. Oxford: Blackwell, 2002
- 23. Freedman M, Rewilak D, Xerri T, Cohen S, Gordon AS, Shandling M, et al. L - deprenyl in Alzheimer's disease : cognitive and behavioral effects. Neurology 1998 ; 50 : 660 - 8
- 24. Watts RL, Koller WC. Movement disorders. McGraw Hill, 1997: 168 9
- 25. Agnoli A, Martucci N, Fabbirini G, Buckley A, Fioravanti M. Monoamine oxidase and dementia: treatment with an inhibitor of MAO B activity. Demetia 1990: 109 14
- 26. Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, Grundman M, et al. A controlled trial of selegiline, alpha - tocopherol, or both as treatment for Alzheimer's disease. N Engl J of Med 1997; 24: 1216 - 22
- 27. Wieraszko A, Li G, Kornecki E, Hogan MV, Ehrlich YH. Long term potentiation in hippocampus induced by platelet - activating factor. Neuron 1993; 10: 553 - 7
- Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic Gingko biloba ingestion. Neurology 1996; 46: 1775 - 6
- 29. Finkel SI, Costa e Silva J, Cohen G, Miller S, Sartorius N. Behavioral and psychological signs and symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment. Int Psychogeriatr 1996; 8(S)3: 497-500

- 30. Rabins PV, Mace NL, Lucas MJ. The impact of dementia on the family. JAMA 1982; 248(3): 333 5
- 31. Katz IR, Jeste DV, Mintzer JE, Clyde C, Napolitano J, Brecher M. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double blind trial. Risperidone Study Group. J Clin Psychiatry 1999; 60(2): 107 15
- 32. De Deyn PP, Rabheru K, Rasmussen A, Bocksberger JP, Dautzenberg PL, Eriksson S, et al. A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. Neurology 1999; 53(5): 946 - 55
- 33. Street JS, Clark WS, Gannon KS, Cummings JL, Bymaster FP, Tamura RN, et al. Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double - blind, randomized, placebo controlled trial. The HGEU Study Group. Arch Gen Psychiatry 2000; 57(10): 968 - 76
- 34. Street JS, Clark WS, Kadam DL, Miltan SJ, Juliar BE, Feldman PD, et al. Long term efficacy of olanzapine in the control of psychotic and behavioral symptoms in nursing home patients with Alzheimer dementia. Int J Geriatr Psychiatry 2001; 16(S)1: S62 70
- 35. Scharre DW, Chang SI. Cognitive and behavioral effects of quetiapine in Alzheimer's disease patients. Alzheimer Dis Assoc Disord 2002; 16(2): 128 - 30
- 36. Ballard CG, O'Brien J, James I, Swann A. Dementia: management of behavioural and psychological symptoms. Nord J Psychiatry 2003; 57(2): 159 60
- 37. Cummings JL, Frank JC, Cherry D, Kohatsu ND, Kemp B, Hewett L, et al. Guidelines for managing Alzheimer's disease: Part II. Treatment. Am Fam Physician 2002; 65(12): 2525 - 34
- 38. Qizilbash N, Schneider LS. Evidence based dementia practice. Oxford: Blackwell, 2002: 680
- American Psychiatric Association. Practice guidelines for the treatment of psychiatric disorders. Washington DC: 2000.

- APA: 108
- Holzer JC, Gitelman DR, Price BH. Efficacy of buspirone in the treatment of dementia with aggression. Am J Psychiatry 1995; 152(5): 812
- 41. Gottfries CG, Nyth AL. Effect of citalopram, a selective 5 HT reuptake blocker, in emotionally disturbed patients with dementia. Ann N Y Acad Sc 1991: 640: 276 9
- 42. Nyth AL, Gottfries CG, Lyby K, Smedegaard Andersen L, Gylding Sabroe J, Kristensen M, et al. A controlled multicenter clinical study of citalopram and placebo in elderly depressed patients with and without concomitant dementia. Acta Psychiatr Scand 1992; 86(2): 138 45
- 43. Lyketsos CG, Sheppard JM, Steele CD, Kopunek S, Steinberg M, Baker AS, et al. Randomized, placebo controlled, double blind clinical trial of sertraline in the treatment of depression complicating Alzheimer's disease: initial results from the Depression in Alzheimer's Disease study. Am J Psychiatry 2000; 157(10): 1686 9
- 44. Katona CL, Hunter BN, Bray J. A double blind comparison of the efficacy and safely of paroxetine and imipramine in the treatment of depression with dementia. Int J Geriatr Psychiatry 1998; 13(2): 100 - 8
- 45. Raji MA, Brady SR. Mirtazapine for treatment of depression and comorbidities in Alzheimer disease. Ann Pharmacother 2001; 35(9): 1024 7
- 46. Roth M, Mountjoy CQ, Amrein R. Moclobemide in elderly patients with cognitive decline and depression: an international double blind, placebo controlled trial. Br J Psychiatry 1996; 168(2): 149 57
- 47. Kaufer DI, Cummings JL, Christine D. Effect of tacrine on behavioral symptoms in Alzheimer's disease: an open - label study. J Geriatr Psychiatry Neurol 1996; 9(1): 1 - 6
- 48. Paleacu D, Mazeh D, Mirecki I, Even M, Barak Y. Donepezil for the treatment of behavioral symptoms in patients with Alzheimer's disease. Clin Neuropharmacol 2002; 25(6): 313 - 7

- 49. Rosler M. The efficacy of cholinesterase inhibitors in treating the behavioural symptoms of dementia. Int J Clin Pract 2002; 127(Suppl): 20 - 36
- 50. Petrie WM, Ban TA. Propranolol in organic agitation. Lancet 1981; 1:324
- 51. Weiler PG, Mungas D, Bernick C. Propranolol for the control of disruptive behaviour in senile dementia, J Geriatr Psychiatry Neurol 1986: 1:226 - 30
- 52. Goad DL, Davis CM, Liem P, Fuselier CC, McDormack JR, Olsen KM. The use of selegeline in Alzheimer's patients with behavior problems. J Clinical Psychiatry 1991; 52: 342-5
- 53. Schneider LS, Pollock VE, Zemansky MF, Gleason RP, Palmer R, Sloane RB. A pilot study of low dose L deprenyl in Alzheimer's disease. J Geriatr Psychiatry Neurol 1991; 4(3): 143-8
- 54. Lawlor BA, Aisen PS, Green C, Fine E, Schmeidler J. Selegiline in the treatment of behavioural disturbance in Alzheimer's disease. Int J Geriatr Psychiatry 1997; 12(3): 319 22
- 55. Burke WJ, Roccaforte WH, Wengel SP, Bayer BL, Ranno AE, Willcockson NK. L deprenyl in the treatment of mild dementia of the Alzheimer type: results of a 15 month trial. J Am Geriatr Soc 1993; 41(11): 1219 25
- 56. O'Brien MD. How does cerebrovascular disease cause dementia? Dementia 1994; 5:133-6
- 57. Gearing M, Mirra SS, Hedreen JC, Sumi SM, Hansen LA, Heyman A. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) part X: neuropathology confirmation of the clinical diagnosis of Alzheimer's disease. Neurology 1995; 45: 461-6
- 58. Snowdon DA, Greiner LH, Mortimer JA, Riley KP, Greiner PA, Markesbery WR. Brain infarction and the clinical expression of Alzheimer's disease. The Nun Study. JAMA 1997; 277: 813-7
- 59. Nagy Z, Esiri MM, Jobst KA, Morris JH, King EM, McDonald B, et al. The effects of additional pathology on the cognitive deficit in Alzheimer's disease. J Neuropath & Exp Neurol 1997; 56:

- 165 70
- 60. Forette F, Seux M L, Staessen JA, Thijs L, Birkenhager WH, Babarskiene MR, et al. Prevention of dementia in randomised double - blind placebo - controlled Systolic Hypertension in Europe (Syst - Eur) trial. Lancet 1998; 352: 1347 - 51
- 61. Moretti R, Torre P, Antonello RM, Cazzato G. Rivastigmine in subcortical vascular dementia: a comparison trial on efficacy and tolerability for 12 months follow - up. Eur J Neurol 2001; 8:361-2
- 62. Erkinjuntti T, Kurtz A, Gauthier S, Bullock R, Lillenfield S, Damaraju CV. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. Lancet 2002; 359: 1283-90
- 63. Pratt R, Perdomo CA. The Donepezil Study Group. Results of clinical studies with donepezil in vascular dementia. Am J Geriatr Psychiatry 2002; 10(S)1:88-9
- 64. Brown RG, Marsden CD. How common is dementia in Parkinson's disease? Lancet 1984; 2:1262-5
- 65. Korczyn AD. Dementia in Parkinson's disease. J Neurol 2001 ; 248(S)3:1-4
- 66. Kurlan R, Richard IH, Papka M, Marchall F. Movement disorders in Alzheimer's disease: More rigidity of definitions is needed. Mov Disord 2000(15); 1: 24-9
- 67. Wrgaa RE, Jeste DV. Overview of depression andpsychosis in Alzheimer's disease. Am J Psychiatry 1989; 146: 577 87
- 68. Burns A. Psychosis in dementia of the Alzheimer type. In

- Katona C and Levy R, eds. Delusions and Hallucinations in Old age. Royal college of psychiatrists, London: Gaskell, 228 242
- Devanand DP. Depression in dementia. In Gauthier S, Cummings JL, eds. Alzheimer's disease and related disorders annual 2001. London: Martin Dunitz, 97 - 123
- McAllister TW. Overview: pseudodementia. Am J Psychiatry
   1983; 140: 528 33
- 71. Reding MJ, Haycox J, Wigforss K, Brush D, Blass JP. Follow up of patients referred to a dementia service. J Am Geriatr Soc 1984; 32: 265 8
- 72. Mortimer JA, van Duijn CM, Chandra V, Fratiglioni L, Graves AB, Heyman A, et al. Head trauma as a risk factor for Alzheimer's disease: a collaborative re analysis of case control studies. Int J Epidemiol 1991; 20: S28 35
- 73. Mayeux R, Ottman R, Maestre G, Ngai T, Tang MX, Ginsberg H, et al. Synergistic effects of traumatic head injury and apolipoprotein epsilon 4 in patients with Alzheimer's disease. Neurology 1995; 45: 555 - 7
- 74. Joyce E. Dementia associated with alcoholism. In: O'Brien J, Ames D, Burns A, ed. Dementia. 2nd ed. London: Arnold, 2000: 799 - 811
- 75. Victor M, Adams RD. The alcoholic dementias. In: Vinken PJ, Bruyn GW, Klawans HL, eds. Handbook of clinical neurology, Vol 2. Amsterdam: Elsevier Science Publishers, 335 - 52
- 76. Sachdev P, Trollor J, Looi JCL. Alcohol related dementia. In:

  Qizilbash N, Schneider LS, Chui H, et al, Evidence based dementia practice. Malden: Blackwell Science Ltd, 620 1