# The Dementias

Diploma Course Lecture
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# Classification of Dementias

## Irreversible dementias

### *Neurodegenerative*

- Alzheimer's disease
- Diffuse Lewy body disease
- Pick's disease
- Parkinson's disease
- Huntingdon disease
- Progressive supranuclear palsy
- Amyotrophic lateral sclerosis with dementia
- Olivopontocerebellar degeneration

### *Vascular dementia*

- Cardiac disorders
- Vasculitis of central nervous system
- Delayed effects of irradiation
- Hemorrhage (subdural hematoma, subarachnoid hemorrhage, cerebral hematoma, vascular malformations)
- Hypoperfusion (cardiac arrest, profound hypotension, watershed ischemia)
- Multiple infarcts (amyloid angiopathy, large complete infarcts, lacunae of the basal ganglia & pons, frontal white matter lacunae)
- Strategic single infarct (thalamic, posterior cerebral artery, bilateral carotid occlusion, parietal infarct)
- Senile leukoencephalopathy (related to amyloid encephalopathy)

### *Mixed—vascular and alzheimer's*

## Reversible dementias

(Arnold & Kumar 1993)

### *Secondary dementias*

Specific diseases which can cause neurologically based cognitive impairment

**Normal pressure hydrocephalus**

**Mass lesions**

**Infectious diseases:** bacterial meningitis (chronic or partially treated), fungal, parasitic; AIDS-related dementia; neurosyphilis; Whipple disease; Lyme neuroborreliosis; Creutzfeldt-Jacob disease

**Collagen-vascular diseases:** systemic lupus erythematosus; temporal arteritis; other collagen-vascular diseases which may cause dementia

**Endocrine disorders**

**Nutritional dementias:** vitamin B12 deficiency; folate deficiency; pellagra; thiamine deficiency; chronic alcoholism

**Miscellaneous:** obstructive sleep apnea; chronic obstructive pulmonary disease; limbic encephalitis; radiation-induced dementia; dialysis encephalopathy

### *Medical conditions usually resulting in chronic delirium*

**Medication toxicity**

**Other causes of transient reversible disturbances of cognition**

- Disturbances in fluid and electrolytes, esp sodium, calcium
- Hepatic failure
- Renal failure
- Pulmonary failure
- Infection, eg urinary tract infection, pneumonia, septicemia
- Cardiovascular disorders, eg congestive heart failure, hypertensive encephalopathy, myocardial infarction
- Postoperative status

### *Psychiatric pseudodementias*

- Depression
- Other causes

# Epidemiology of Dementia

## Prevalence

In canada, 8% of those over 65, and 35% of those over 85, have some type of dementia. As the population ages, the number of dementia cases is expected to triple by the year 2031 (Flint 1995).

There are at least 250,000 Canadians with dementia, with more than 25,000 new cases annually (Clarfield et al 1991).

Less than 0.5% at ages 65 to 70.

Increases exponentially with age.

58% of those over 95.

MMSE scores of less than 24 were found in 84% of nursing home residents > 65 yrs; 84% of residents in a home for the aged; and 96% of pts > 65 in a psychiatric hospital (Teitelbaum et al 1991).

## Incidence

Dementia develops in approximately 1% of the elderly each year.

## Prevention

### *NSAIDs*

2651 participants in a hypertension study had their cognitive function monitored over 54 months. NSAID users showed less decline in the Paired Associate Learning Test than nonusers, with younger subjects seeming to benefit more than older (Prince et al 1998).

More than 21 independent studies, including the Canadian Study of Health and Aging, have reported a decreased prevalence of AD among patients taking anti-inflammatory agents on a long-term basis (Munoz & Feldman 2000).

### *Estrogen*

Meta-analysis of 10 observational studies of postmenopausal estrogen use suggests a 29% decreased risk of developing dementia among estrogen users (Yaffe et al 1998).

A review of 16 placebo-controlled prospective studies concluded that estrogen specifically maintains verbal memory in women; may prevent deterioration in short- and long-term memory that occurs with normal aging; decreases incidence of AD or retards its onset or both (Sherwin 1999).

Mechanism of action unknown (Dubal et al 1999).

### *Antihypertensives*

A study of 1238 pts with isolated systolic hypertension treated with medication compared to 1180 receiving placebo, showed that antihypertensive treatment was associated with a halving of the incidence of dementia (from 7.7 to 3.8 cases per 1000 patient-years). If 1000 hypertensive pts were treated for 5 yrs, 19 cases of dementia might be prevented (Forette et al 1998).

Since a previous study did not show any benefit from simply lowering blood pressure, it may be that calcium channel blockade has an effect on preventing Alzheimer's.

# Severity of Dementia

(Clarfield 1989)

| | |
|---|---|
| mild | although work and social activities are significantly impaired, the capacity for independent living remains, with adequate personal hygiene and relatively intact judgment |
| moderate | independent living is hazardous, and some degree of supervision is necessary |
| severe | activities of daily living are so impaired that continual supervision is required (eg unable to maintain minimal personal hygiene, largely incoherent or mute |

# Types of Dementia

## Alzheimer's Disease

### *Prevalence*

accounts for more than 60% of cases of dementia

### *Diagnosis*

#### Diagnostic Criteria

NINDS-ADRDA: National Institute of Neurological Disorders and Stroke-Alzheimer's Disease and Related Disorders Association:

*Definite AD*

- Clinical criteria for probable AD;
- Histopathologic evidence from autopsy or biopsy.

*Probable AD*

- Dementia established by clinical examination, documented by mental status testing, and confirmed by neuropsychologic tests;
- Deficits in two or more areas of cognition;
- Progressive worsening of memory and other cognitive functions;
- Onset between ages 40 and 90 yrs;
- Absence of other disorders that could account for the dementia.

*Possible AD*

Dementia syndrome with:

- Variations in onset, presentation, or clinical course, or a second disorder capable of producing dementia, but not thought to be the cause of dementia;
- Gradually progressive deficit in a single area of cognition, without identifiable cause.

#### Accuracy of diagnosis

Seven autopsy studies (462 autopsies altogether) of patients either prospectively or retrospectively using NINDS criteria obtained accuracy rates between 62 and 92% (Klatka et al 1996).

#### Features which suggest other diagnoses

(Klatka et al 1996)

- Presence of certain parkinsonian signs, especially resting tremor and cogwheel rigidity;
- Absence of language impairment, especially in moderate to severe dementia;
- Absence of visuospatial impairment (eg spontaneous drawing and copying of complex designs, identification of incomplete pictures);
- Early, marked personality change (eg inappropriate spending, hoarding, hyperreligiosity, irritability, aggressiveness);
- Focal neurologic signs.

#### Indicators

Two different isoprostanes, which are chemically stable peroxidation products of arachidonic acid and have been recently identified as markers of tissue damage, were found in significantly higher concentrations in the frontal and temporal lobes of AD patients compared to controls. One of these was also higher in the AD patients' CSF (Pratico et al 1998).

Endoplasmic-reticulum-associated binding protein (ERAB) is present in high concentrations in the brains of patients with AD particularly near deposits of β-amyloid. ERAB forms a complex with β-amyloid in a way that could attract extracellular beta-amyloid to join the process of destroying the neuronal membrane. Moreover, ERAB appears to be involved in cholesterol biosynthesis, like apoE ε4. The neurotoxic effect of β-amyloid is prevented by blocking the action of ERAB, and enhanced when ERAB is produced in higher concentrations (Yan et al 1997).

### *Risk Factors*

(Rocca 1994)

#### Family history of dementia

Relative risk 3.5 for those with a 1° relative with dementia; risk ⇑ with increasing number of relatives affected.

#### Family history of down's syndrome

Relative risk 2.7 for those with a 1° relative with down's.

#### Family history of parkinson's disease

Relative risk 2.4 for those with a 1° relative with parkinson's.

#### Late maternal age

Relative risk 1.7 for maternal age 40 or higher; higher risk in sporadic cases and in women.

Early maternal age may also be a risk factor.

#### Advanced paternal age

Children of older fathers had a higher inherited risk of developing the disease than did those in the higher genetic risk group or healthy people (anonymous 1998).

**Head trauma**
Relative risk 1.8 for reported head trauma with loss of consciousness; higher risk in men.

Records-linkage study failed to confirm this association.

**Viral agents**
Even though neurofibrillary tangles are found in brain diseases with proven viral causes, no association was found between AD and a history of encephalitis, meningitis, or infection with a neurotropic virus.

**Aluminium and other toxic agents**
Conflicting findings for aluminium; no positive associations found for other toxic agents, including solvents, lead.

A recent case-control study found a significant correlation between having AD and consumption of foods containing high levels of aluminium: pancakes, waffles, biscuits, muffins, cornbread and/or corn tortillas (Rogers & Simon 1999).

**Depression**
Relative risk 1.8 for late-onset cases.

**Vitamin B12**
Serum B12 levels were significantly correlated with MMSE scores in AD pts, but not in pts with other dementias or with mild cognitive impairment (Levitt & Karlinsky 1992).

**Apolipoproteins**
(Gauthier et al 1996)

Lipid carrier molecules; regulate lipid metabolism following peripheral & central nervous system injury.

Encoded on long arm of chromosome 19.

Three major isoforms (alleles): apoE ε4, ε3, ε2.

Three homozygous phenotypes (ε4/4, ε3/3, ε2/2) and three heterozygous (ε4/3, ε3/2, ε4/2).

Both sporadic as well as late-onset familial AD have markedly ⇑ apoE ε4 allele frequency, ie ε4/4 ⇑ risk of developing AD by 30, while the relative risk is 3.7 for the heterozygous condition (Burns & Murphy 1996).

An association has been found between apoE ε4 and ⇓ parietal lobe metabolism on PET scan in relatives of AD patients who are clinically unaffected (Filley 1995).

Preliminary evidence suggests that the ε2 allele, which is only half as frequent as ε4, may be protective against AD (Anonymous 1995).

At present, apoE genotyping is not sufficiently sensitive or specific to be useful as a diagnostic test, and is not recommended as a predictive (Anonymous 1995).

**Smoking**
Most studies show a ⇓ risk of AD in smokers (relative risk 0.8). However, a large follow-up study (the Rotterdam study) found that smokers without the apoE ε4 allele had a RR of 4.6 for AD compared to never smokers; smoking had no effect in people with apoE ε4 (Ott et al 1998).

**Estrogen**
Cognitive function deteriorated in patients who had had a hystero-oophorectomy but not in those having had a hysterectomy alone (burns & murphy 1996).

**Atherosclerosis**
A recent study (hofman et al 1997) indicates a correlation between atherosclerosis and dementia. The report says that "...indicators of atherosclerosis are associated with the presence of dementia, and both of its main subtypes, Alzheimer's disease and vascular dementia, and that the association between atherosclerosis and dementia is particularly strong in those with the apolipoprotein-E e4 genotype."

**Social factors**
Quebec study of 122 AD patients and 279 controls matched for age and gender: poverty and poor education in childhood led to 5 to 11-fold increase in risk of having AD for people with a family history of AD. No effect for poverty or education in those without a family history.

**Infectious agents**
Chlamydia pneumoniae was found in the brains of 17/19 Alzheimer victims, but in only 1/19 patients who had died from other causes. Regions of the brain that had sustained damage typical of AD showed the most pronounced Chlamydial presence (Balin et al 1998).

**Hypercortisolemia**
Cortisol secretion was measured annually for 5 yrs in 51 healthy elderly volunteers: in the group with with steadily increasing high cortisol levels, total hippocampal volume was reduced by 14% compared to the group with decreasing but moderate cortisol levels. Prolonged cortisol elevations were also associated with a decline in hippocampus-dependent memory tasks (Lupien 1998).

**Homocysteine & folate**
Homocysteine levels were much lower in 30 general practice AD patients compared to controls; folate levels were somewhat lower (McCaddon et al 1998).

A Canadian study of 1171 elderly in whom folate levels were compared to clinical presentation: those in the highest quartile for folate had significantly lower rates fo dementia and depression, and were less likely to be institutionalized (Ebly et al 1998).

In 43 patients with AD followed with CT scans, there was significant radiological evidence for disease progression in those with the middle and higher tertiles of homocysteine compared to the lower tertile (Clarke et al 1998).

## *Pathophysiology*

**Inflammatory mechanisms**
(aisen & davis 1994)

There is ample and growing evidence that alzheimer's disease fits the paradigm of the idiopathic rheumatic disorders:

- Acute phase proteins α1-antichymotrypsin and C-reactive protein are found in AD pts serum; α1-antichymotrypsin and α2-macroglobulin are components of the amyloid of senile plaques, the histopathological hallmark of AD
- Activated microglial cells that stain for inflammatory cytokines (interleukin-1 and -6) accumulate around senile plaques
- AD pts' serum contains elevated levels of tumor necrosis factor
- AD pts have components of the complement system in their brains; the pattern of complement fragments indicates activation of the complement cascade
- Microglia, which may originate as circulating macrophages, are found in markedly ⇑ numbers around senile plaques

If the hypothesis is true, then trials with anti-inflammatory drugs, such as corticosteroids, NSAIDs, antimalarial drugs, colchicine, methotrexate, or dapsone are indicated.

#### Correlates of psychotic phenomena

A study of 56 pts with AD confirmed at autopsy, showed hallucinations in 13 pts, paranoid delusions in 9 and delusional misidentification (eg Capgras-type and the "phantom boarder" symptoms) in 14. Misidentifications were associated with lower neuron counts in the hippocampus; delusions and hallucinations with fewer cells in the dorsal raphe nucleus, but less severe cell loss in the hippocampal gyrus (Forstl et al 1994).

### *Course*

(Filley 1995)

| Progression | Manifestations |
|---|---|
| Stage I<br>(1 to 3 years) | recent memory dysfunction<br>anomia<br>topographic disorientation<br>depression |
| Stage II<br>(2 to 10 years) | prominent amnesia<br>fluent aphasia<br>constructional impairment<br>acalculia<br>personality change |
| Stage III<br>(8 to 12 years) | severe dementia<br>nonsense speech or mutism<br>rigidity and flexion posture<br>incontinence |

#### Global Deterioration Scale (GDS)

| Stage | Cognitive Decline | |
|---|---|---|
| 1 | none | experiences no problems in daily living |
| 2 | very mild | forgets names and locations of objects<br>may have trouble finding words |
| 3 | mild | has difficulty travelling to new locations<br>has difficulty handling problems at work |
| 4 | moderate | has difficulty with complex tasks (finances, shopping, planning dinner for guests) |
| 5 | moderately severe | needs help to choose clothing<br>needs prompting to bathe |
| 6 | severe | needs help putting on clothing<br>requires assistance bathing; may have fear of bathing<br>has decreased ability to use the toilet, or is incontinent |
| 7 | very severe | vocabulary becomes limited, eventually declining to single words<br>loses ability to walk and sit<br>becomes unable to smile |

In mild dementia, a cognitive test battery may not be able to identify subjects who will deteriorate from those whose condition remains unchanged (O'Connor et al 1991).

### *Prevention*

A beta-amyloid vaccine has been shown effective in preventing the deposition of beta-amyloid in the brains of a transgenic mouse species which overexpresses a mutant form of beta-amyloid precursor. The vaccine thus prevents the development of degenerative lesions when given to young mice, and reduced disease progression when given to 11-month old mice in whom pathology was already established. The relevance of this to humans remains controversial, however (Blass 1999).

# Diffuse Lewy Body Disease

(Kalra et al 1996)

## *Lewy Bodies (LBs)*

Rounded, eosinophilic, intracytoplasmic neuronal inclusions, chiefly composed of altered neurofilaments; may also include ubiquitin (a small protein involved in the non-lysosomal breakdown of abnormal cellular proteins). Lewy bodies are thought to signify neuronal injury and fragmentation, as opposed to complete neuronal destruction, in which they do not occur (Anonymous 1989).

Classically associated with Parkinson's disease (PD), where they are found in some brainstem nuclei (substantia nigra, locus caeruleus, dorsal vagal nucleus), the nucleus basalis of Meynert, hypothalamus, and sympathetic ganglia.

Cortical Lewy bodies are difficult to identify (this may explain why diffuse Lewy body disease has in the past been considered rare) (Lennox et al 1989). Anti-ubiquitin immunochemistry is much more sensitive in identifying cortical Lewy bodies.

## *History*

First reported 1961

Term "diffuse Lewy body disease" (DLBD) was coined in 1983

The term "dementia with Lewy bodies" (DLB) is now preferred

## *Prevalence*

Ranks second to AD as cause of primary dementia

Prevalence in autopsy studies ranges from 15 to 27%; eg 23% in one series of 335 autopsies (LeBourdais 1999).

## *Pathology*

LBs found in same distribution as in PD, and also widely in cerebral cortex

Presence of ubiquitin-immunoreactive, tau protein-negative neuritic degeneration in the CA 2-3 region of the hippocampus is characteristic of DLBD, not found in AD

In 50%, accompanying abundant neuritic plaques and neurofibrillary tangles are found; thus, diagnose a concomitant AD

## *Clinical Features*

Male:female = 2:1

Most cases develop late in life; most present first with memory impairment, followed later by features of parkinsonism, esp. Rigidity

Can also have dementia, psychosis, overvalued and paranoid ideas, delusions, and visual > auditory hallucinations

Insidious onset

Progressive course

Parkinsonian features may include rigidity, bradykinesia, flexed posture, shuffling gait; tremor is uncommon

Fluctuating course may differentiate from other dementias: fluctuations in orientation, memory, behaviour, language; intermittent hallucinations, confusion, agitation, delusions, clouding of consciousness

Duration (from onset of symptoms to death) varies greatly; avg. 6.4 yrs

Most frequent cause of death: aspiration pneumonia

## *Diagnostic criteria*

(McKeith et al 1994)

a) Fluctuating cognitive impairment affecting both memory and higher cortical functions (such as language, visuospatial ability, praxis or reasoning skills). Fluctuation is marked with the occurrence of both episodic confusion and lucid intervals, as in delirium, and is evident either on cognitive testing or by variable performance in daily living skills.

b) At least one of the following:

- Visual and/or auditory hallucinations which are usually accompanied by secondary paranoid delusions
- Mild spontaneous extrapyramidal features or neuroleptic sensitivity syndrome, ie exaggerated adverse resonses to standard doses of neuroleptic medication
- Repeated unexplained falls and/or transient clouding or loss of consciousness

c) Despite the fluctuating pattern the clinical features persist over a long period of time (weeks or months) unlike delirium which rarely persists as long. The illness progresses, often rapidly, to an end stage of severe dementia.

d) Exclusion of any underlying physical illness adequate to account for the fluctuating cognitive state, by appropriate examination and investigation.

e) Exclusion of past history of confirmed stroke and/or evidence of cerebral ischaemic damage on physical examination or brain imaging.

Comparisons between Diffuse Lewy Body Disease, Parkinson's Disease, and Alzheimer's Disease:

| | DLBD | PD | AD |
|---|---|---|---|
| Brain stem and subcortical Lewy bodies | + | ++ | 0 |
| Cortical Lewy bodies | ++ | ± | 0 |
| Senile plaques | ± | ± | ++ |
| Neurofibrillary tangles | ± | ± | ++ |
| Neuropil threads | ± | 0 | + |
| Hippocampal degeneration in area CA 2-3 | ++ | ± | 0 |
| SN neuronal loss | variable | marked | variable |
| Dementia type | cortical | subcortical | cortical |
| Dementia features | onset before motor disturbance; fluctuating psychiatric features | minority | usually a "pure" dementing illness |
| Motor disturbance | parkinsonism, esp. marked rigidity; gait disturbance early, tremor uncommon | classic movement disorder: tremor, rigidity, akinesia, postural changes | gait disturbance, late |
| Abnormal EEG | early | ... | late |

## Frontotemporal Dementia

Possibly the third most common neurodegenerative dementia

### *Diagnosis*

#### Behavioural Disorder

- Insidious Onset & Slow Progression with either behavioural change or language impairment
- Early Loss of Social & Personal Awareness
- Early Disinhibition
- Mental Rigidity and Inflexibility
- Hyperorality
- Stereotyped and Perseverative Behaviour
- Utilisation Behaviour
- Early loss of insight

#### Affective Symptoms

#### Speech Disorder

#### Neurology

- Early primitive reflexes
- Early Incontinence
- +/- Bulbar Palsy, Fasciculation, Muscle Weakness
- Apraxia

Normal EEG

Focal Neuropsychological Deficits

Focal (+/- Asymmetrical) Atrophy

Variable Neuropathology: three types of histological change:

- Pick-type
- frontal lobe degeneration type
- motor neuron disease type

Significantly more euphoria, aberrant motor activity, and disinhibition, and significantly fewer delusions, compared to AD or DLB patients (Hirono et al 1999).

# Vascular Dementia

(Amar & Wilcock 1996)

## *History*

Cerebral atherosclerosis was thought to be the commonest cause of dementia at the turn of the century (Alzheimer's was considered rare, affecting only younger patients).

by 1950's, it was recognized that cerebral atherosclerosis was also found in normal elderly.

1970 Tomlinson et al used the label atherosclerotic dementia for the group in which autopsy showed areas of brain softening or infarction.

1974 Hachinski et al used the term multi-infarct dementia to reflect their understanding of the mechanism.

## *Epidemiology*

May be 2nd most common cause of dementia.

Sole cause in 9-33% of patients; contributes to dementia in a further 10-36% of cases (mixed dementia).

Averages for 5 autopsy studies combining 1529 cases: Alzheimer's alone 46%; vascular dementia alone 17%; combined 22%.

Some believe vascular dementia is underdiagnosed, as we are now recognizing that white matter ischemia may contribute; others believe it is overdiagnosed, eg when the pt has had a stroke.

## *Mechanisms*

### Multi-infarct dementia

Site of cerebral infarction is more important that volume of tissue lost.

Multiple cortical infarcts are commonly 2° thromboembolic disease, but can be 2° cerebral vasculitis.

Multiple lacunar infarcts result in subcortical dementia; often associated with white matter ischemia. Both conditions seen in hypertension.

### Single strategically placed infarcts

Angular gyrus syndrome: dementia following infarction of angular gyrus (inferior parietal lobule). Presents with acute onset of fluent dysphasia, visuospatial disorientation, agraphia, memory loss.

Thalamic dementia: esp paramedian thalamic infarction; presents with drowsiness, ocular palsies, apathy and slowness, memory loss.

Other strategic areas: caudate & globus pallidus; basal forebrain; hippocampus.

### White matter ischemia

Binswanger's disease (1894)

CT showed that low attenuation (rarefaction) of white matter (termed leukoaraiosis by Hachinski) was much commoner than previously thought; MRI even more sensitive—shows that it occurs in almost 100% of subjects at age 85 (in normal subjects, it may be associated with slower mental processing & impaired concentration).

Commonest causes of leukoaraiosis: age and ischemia to white matter; other causes include head injury, cerebral irradiation.

Vulnerable because white matter is supplied by long penetrating end arterioles with little anastomosis, from the surface and base of the brain.

Associated with hypertension, heart disease, diabetes.

White matter lesions seen in 70-90% of vascular dementia pts, 10-20% of early onset AD, 70-80% of late onset AD.

## *Risk factors*

Age, history of stroke (relative risk 9); low education; hypertension; white matter lesions; history of MI; diabetes; cerebral atrophy; cortical infarcts; left hemisphere stroke; early urinary incontinence; falls.

## *Diagnosis*

**Hachinski Ischemia Scale:**

| Item | Score Value |
|---|---|
| abrupt onset | 2 |
| stepwise course | 1 |
| fluctuating course | 2 |
| preservation of personality | 1 |
| nocturnal confusion | 1 |
| depression | 1 |
| somatic complaints | 1 |
| emotional incontinence | 1 |
| history of hypertension | 1 |
| evidence of associated atherosclerosis | 1 |
| history of stroke | 2 |
| focal neurological symptoms | 2 |
| focal neurological signs | 2 |

score of 7 or higher ⇒ Dx vascular dementia

has low interrater reliability

**ICD-10 Diagnostic Criteria for Vascular Dementia**

| | |
|---|---|
| G1 | Evidence of dementia of specified level of severity |
| G2 | Unequal distribution of deficits in higher cognitive functions, with some affected and others relatively spared. Thus, memory may be profoundly affected, whereas thinking, reasoning, and information processing may show only mild decline |
| G3 | Focal brain damage is evident, manifest as at least one of the following: unilateral spastic weakness of the limbs, unilateral ⇑ tendon reflexes, an extensor plantar response, pseudobulbar palsy |
| G4 | The history, examination, or tests disclose severe cerebrovascular disease, which may reasonably be judged to be etiologically related to the dementia (history of stroke, evidence of cerebral infarction) |

## Reversible dementias

(Arnold & Kumar 1993)

### *Secondary dementias*

Specific diseases which can cause neurologically based cognitive impairment.

#### Normal pressure hydrocephalus

<2% of all cases of dementia.

Clinical triad of dementia, gait apraxia (slow, shuffling, sticky, wide-based gait), and urinary incontinence in association with ventricular enlargement.

Symptoms may be caused by pressure against frontal lobes and by stretching the most medial axons from the motor cortex which control leg and sphincter functions.

Frequent ventricular pressure elevations (B-waves) indicate better surgical prognosis, as do onset of gait disturbance prior to dementia, & lack of significant cortical atrophy on CT or MRI.

CSF shunting may improve symptoms, sometimes over several years.

#### Mass lesions

Tumours of frontal & temporal lobes, eg meningiomas.

Tumours are the cause of dementia in 1-4% of all dementia cases.

Chronic subdural hematomas may present weeks or months after a trivial head injury, or even spontaneously; may be bilateral.

Although focal findings are typical, some pts present with only cognitive or personality changes.

#### Infectious diseases

*Bacterial meningitis (chronic or partially treated), fungal, parasitic*

Infection with tuberculosis, fungal (cryptococcosis, coccidioidomycosis, histoplasmosis, candidiasis) or parasitic (toxoplasmosis, cisticercosis) organisms can cause an indolent CNS infection without signs of illness in other systems.

Immunocompromise due to AIDS, chronic illness, or immunosuppressive or steroid therapies predispose.

*AIDS-related dementia*

HIV directly invades CNS and can cause a variety of neurologic and neuropsychiatric disorders including dementia, which occurs in >50% of newly diagnosed AIDS pts.

Zidovudine can help prevent AIDS dementia; may partially reverse cognitive impairments.

*Neurosyphilis*

Tertiary syphilis produces a wide variety of neurologic syndromes, dementia (general paresis, dementia paralytica) being most common.

Personality changes (apathy, impaired judgment, irritability) may present first.

Argyll-Robertson pupils: irregular pupils that react to accommodation but not to light.

Penicillin arrests progression, may reverse some symptoms.

Up to 4% in neurologically asymptomatic HIV positive pts.

*Whipple disease*

Usually see weight loss, abdominal pain, diarrhea, malabsorption, & arthralgias, caused by a bacilliform bacterium.

CNS may be affected even without evidence of infection elsewhere.

Dx difficult without GI symptoms.

CSF may show pleocytosis, ⇑ protein.

Head CT may show focal lesions.

Definite Dx by brain biopsy.

Trimethoprim-sulfamethoxazole may reverse cognitive deterioration.

*Lyme neuroborreliosis*

Encephalopathy is the most common CNS dysfunction in late Lyme borreliosis; there may be no associated focal neurologic deficits.

*Creutzfeldt-Jacob disease*

#### Collagen-vascular diseases

*Systemic lupus erythematosus*

Cognitive dysfunction is the most common CNS manifestation of SLE, occurring in up to 80% of cases.

Irreversible if due to occlusive vascular disease, otherwise may resolve with immunosuppressive Rx.

*Temporal arteritis*
The most common rheumatologic disease in the elderly.

May cause dementia even without headache or visual changes.

Steroid Rx resolves dementia.

*Other collagen-vascular diseases which may cause dementia*
Rheumatoid vasculitis; Behçet's disease; thrombotic thrombocytopenic purpura; sarcoidosis; granulomatous angiitis of the nervous system.

**Endocrine disorders**
Hypothyroidism; hyperthyroidism; hypoparathyroidism; hyperparathyroidism; Cushing's disease; steroid therapy; Addison's disease; recurrent hypoglycemia; panhypopituitarism.

**Nutritional dementias**
Neuropsychiatric changes other than dementia are more common, eg delirium, psychomotor agitation, depression, apathy, mental dullness, & paranoid psychosis.

Usually associated with other neurologic or systemic findings.

*Vitamin B12 deficiency*
B12 deficiency has been associated with delirium, dementia, depression, mania, anxiety, and psychosis.

Some question its importance as a cause of reversible dementia; however, it can cause mental status changes which may be confused with dementia and which reverse with Rx.

*Folate deficiency*
Rarely seen in isolation; usually occurs in alcoholism, psychiatric illness, or in pts on anticonvulsants.

*Pellagra*
Very rare in US & Canada, but still found in 3rd world countries, & in pts with alcoholism & malnutrition.

Caused by niacin & tryptophan deficiency.

Three D's: dermatitis, dementia, diarrhea.

*Thiamine deficiency*
Acute:

Wernicke encephalopathy (delirium, abnormal eye movements (nystagmus, paralysis of lateral gaze), gait ataxia).

Lab: ⇓ blood transketolase.

Can be fatal if untreated.

Chronic:

Korsakoff syndrome (amnestic syndrome, impaired insight, aspontaneity).

*Chronic alcoholism*
Can produce dementia, even without nutritional compromise.

**Miscellaneous**

*Obstructive sleep apnea*
Frequent or chronic hypoxemia ⇒ progressive cognitive impairments which mimic dementia.

Look for: daytime hypersomnolence, nocturnal snoring & restlessness, obesity or nasopharyngeal deformity.

Confirm with polysomnography.

Rx: Continuous Positive Airway Pressure (CPAP), surgery, tracheostomy.

*Chronic obstructive pulmonary disease*
Can also produce a dementia-like picture due to hypoxemia.

*Limbic encephalitis*
Paraneoplastic syndrome, ie a remote effect of small cell lung Ca, ovarian Ca, or Hodgkin disease.

Present with dementia & weight loss.

Dementia is reversible with Rx of 1° tumour; possibly with plasmapheresis.

*Radiation-induced dementia*
Both with focused & with whole brain radioRx.

Can occur from 5 months to several years after Rx.

Corticosteroids, anticoagulation, pentoxifylline, ventricular shunting may improve Sx.

*Dialysis encephalopathy*
Thought to be 2° high aluminum levels.

Rare (0.2%) but often fatal.

Desferoxamine chelation Rx helps but has significant SE.

## *Medical conditions usually resulting in chronic delirium*

**Medication toxicity**
5-10% of pts seen in geriatric clinics for mental impairment have a potentially reversible drug-induced dementia.

Elderly at high risk:

- Receive more prescriptions, more polypharmacy;
- Liver blood flow, ⇓ hepatic enzymes ⇒ ⇓ metabolism of TCAs, some BDZ;
- Fat/lean body ratio ⇒ ⇑ volume of distribution ⇒ ⇑ half-life of elimination;
- Renal clearance of some drugs;
- Polypharmacy, illness may ⇒ altered drug absorption, protein binding, and renal clearance.

Drugs which can cause cognitive impairment:

- Tricyclic antidepressants (anticholinergic, sedating);

- Neuroleptics (anticholinergic, sedating;
- Benzodiazepines; lithium; psychostimulants; bromides;
- Barbiturates; non-barbiturate sedatives (eg glutethimide; meprobamate);
- Anticholinergic agents;
- Antihypertensive agents (eg methyldopa; propranolol; clonidine); diuretics;
- Anticonvulsants (barbiturates; phenytoin; ethosuximide);
- Antihistamines; narcotic analgesics; antiparkinsonian agents (l-dopa; bromocriptine; pergolide);
- Cardiovascular agents (digitalis; quinidine; procainamide);
- Others: corticosteroids; cimetidine; metoclopramide; antibiotics; antineoplastic agents; disulfiram; oral contraceptives; ergot.

**Other causes of transient reversible disturbances of cognition:**

- Disturbances in fluid and electrolytes, esp sodium, calcium;
- Hepatic failure;
- Renal failure;
- Pulmonary failure;
- Infection, eg urinary tract infection, pneumonia, septicemia;
- Cardiovascular disorders, eg congestive heart failure, hypertensive encephalopathy, myocardial infarction;
- Postoperative status.

### *Psychiatric pseudodementias*

- Definition of pseudodementia: "an intellectual impairment in patients with a primary psychiatric disorder, in which the features of intellectual abnormality resemble, at least in part, those of a neuropathologically induced cognitive deficit".
- Depression is the most common cause of pseudodementia.
- Other causes: late-onset schizophrenia; mania; delusional disorders of late life; anxiety states; atypical psychosis; Ganser's syndrome (hysterical pseudodementia); post-traumatic stress disorder; somatization disorder; personality disorder.

# Cortical vs Subcortical Dementia

Kalra et al (Kalra et al 1996) classify dementing illness into two broad categories depending on the clinical presentation. This classification gives direction towards a differential diagnosis, anatomic localization, and management plan.

| | **Cortical** | **Subcortical** (includes basal ganglia, thalamus, brain stem, and the frontal lobe projections of these regions) |
|---|---|---|
| Memory | learning deficit | retrieval deficit (aided by clues), forgetfulness |
| Cognition | cortical deficit: apraxia, acalculia, agnosia, impaired judgment and abstraction | "bradyphrenia" (slowed thought); inability to manipulate acquired knowledge |
| Visual Impairment | prominent | rare |
| Affect | unconcerned and disinhibited | apathy, depression |
| Motor | normal until late stages | extrapyramidal symptoms (tremor, rigidity, chorea) |
| Speech | aphasia | dysarthria, hypophonia |
| Differential Diagnosis | Alzheimer's disease, Pick's disease, diffuse Lewy body disease | Parkinson's disease, Huntingdon's disease, progressive supranuclear palsy, normal pressure hydrocephalus, multiple sclerosis, AIDS dementia complex, vascular disorders: Lacunar state, Binswanger's disease, multi-infarct dementia |

# Neuroimaging in Dementia

(Davis et al 1994)

## Imaging techniques

### *CT*

Relatively inexpensive.

Widely available.

Rapid; thus diminished sensitivity to movement.

Suffers from artifacts, limited imaging planes, and lack of sharply defined gray-white matter and CSF-bone interfaces.

Discriminant analysis using multiple CT measures could predict group membership (AD patients vs controls) in 81% of cases (Burns et al 1991).

### *MRI*

Compared to CT:

- Age-related changes are better visualized. For example, a study of healthy elderly over 65 showed that there is minimal brain volume loss observed over time (Mueller et al 1998);
- More sensitive in detecting changes related to dementia, such as vascular disease (lacunar infarcts, white matter lesions), and temporal lobe volume loss.

### *SPECT, PET, MR spectroscopy*

Provide information related to metabolism, for understanding pathogenesis, improving specificity, and possibly monitoring disease progression and therapeutic response.

SPECT can differentiate AD patients from normals with 86% sensitivity, 96% specificity, and 98% diagnostic confidence (Dewan & Gupta 1992).

A recent study showed that SPECT could distinguish four groups: normal controls; subjects with "questionable" AD at both baseline and followup; subjects with questionable AD at baseline who converted to AD at followup; subjects with AD at baseline (Johnson et al 1998).

## Normal aging

MR shows ⇓ volumes of the cerebral hemisphere, frontal lobe, temporal lobe, and amygdala-hippocampus complex; ⇑ ventricular volumes.

Focal hyperintense white matter lesions are seen; when extensive or confluent, are associated with memory loss and dementia.

## Alzheimer's disease

Frontal, temporal, & parietal cortex atrophy.

Enlargement of lateral & third ventricles is frequently observed, with disproportionate enlargement of the temporal horn of the lateral ventricle.

Atrophy of parahippocampal cortex, amygdala, and hippocampus.

MR volumetric techniques: atrophy of entorhinal cortex (parahippocampal gyrus) & temporal neocortex; greater CSF volume, smaller brain volume, widespread loss of subcortical volume without reduction in white matter volume, and preferential thalamic atrophy.

PET shows cortical regional hypometabolism before cortical atrophy can be seen by CT or MR.

Abnormal SPECT blood flow patterns and memory loss together give a probability of 82% of AD.

## Vascular dementia

MR or CT demonstration of vascular lesions is considered supportive of a vascular dementia Dx; absence of vascular lesions on MR or CT rules out vascular dementia.

Dementia is related to the extent of cerebral infarction; however, some investigators have found that the volume of white lesions correlates with age and chronic vascular disease, but not with decline in cognitive function.

PET shows focal asymmetric and variable regions of diminished metabolism; PET or SPECT defects often are larger than those seen on CT or MR.

The total volume of metabolically impaired tissue was directly related to dementia severity.

## Parkinson's disease

MR not helpful.

PET shows ⇑ glucose metabolism in basal ganglia early in the disease; also reduced striatal uptake of L-dopa labeled with fluorine-18.

## Pick's disease

MR & CT show atrophy of frontal or temporal lobes.

PET shows ⇓ fluorodeoxyglucose metabolic activity in frontal lobes; PET & SPECT show diminished frontal lobe blood flow.

# Evaluation of Dementia

(Arnold & Kumar 1993; Fleming et al 1995)

## Diagnostic Criteria

### *ICD-10 Diagnostic Criteria for Dementia (any cause)*

| | |
|---|---|
| G1.1 | A decline in memory, which is most evident in the learning of new information; in more severe cases, recall of previously learned information may also be affected. The impairment applies to both verbal and nonverbal material |
| G1.2 | A decline in other cognitive abilities characterized by deterioration in judgment and thinking, such as planning and organizing, and general processing of information. Deterioration from a previous level of performance should be established |
| G2 | Preserved awareness of the environment (that is, the absence of clouding of consciousness) during a period long enough to enable the unequivocal demonstration of G1. When episodes of delirium are superimposed, the diagnosis of dementia should be deferred |
| G3 | A decline in emotional control or motivation, or a change in social behaviour, manifested as at least one of the following: emotional lability ,irritability, apathy, coarsening of social behaviour |
| G4 | For a confident clinical diagnosis, criterion G1 should have been clearly present for at least 6 mo; if the period since the manifest onset is shorter, the diagnosis can only be tentative |

### *DSM-IV Diagnostic Criteria for Dementia*

Memory impairment, plus one or more of:

- Aphasia (impaired comprehension, naming, reading, writing);
- Apraxia (inability to perform certain movements on command or imitation);
- Agnosia (inability to recognize familiar objects);
- Disturbance in executive functioning (impaired planning, organization, abstraction and attention).

The criteria listed above cause:

- Impairment in occupational or social functioning;
- Decline from previous level of functioning.

## Examination

Pay special attention to history, use of medications, mental status.

### *History and mental status*

**Mini-Mental State Examination (MMSE) scoring**
Maximum score is 30.

Usual scoring method is single cutoff, with values <24 considered abnormal.

*Using a range increases clinical utility:*
<21 ⇑ odds of dementia;

>25 ⇓ odds of dementia.

*Using different cutoffs of educational level:*
<21 abnormal for 8th grade education;

<23 abnormal for high school education;

<24 abnormal for college graduates.

*Severity:*
24-30 no cognitive impairment;

18-23 mild cognitive impairment;

0-17 severe cognitive impairment.

### *Clock drawing*

Useful for assessing visuospatial and construction deficits.

Identifies older persons at high risk of cognitive decline and supplements the MMSE regarding prognosis (Ferrucci et al 1996).

Abnormal: counterclockwise rotation, inappropriate numbering (especially perseveration), irrelevant patterns.

A simplified test and objective scoring system based only on the number of digits placed in the fourth quadrant of a predrawn circle was shown to be effective in screening for dementia (Watson et al 1993).

The Shulman scoring method performed best in a comparison of 3 scoring methods, and outperformed the MMSE in correctly identifying mild or moderate AD cases (Brodaty & Moore 1997). In the modified Shulman method, subjects are asked to add the numbers of a clock face to a predrawn circle and to mark in the hands at 10 after 11. Scores:

1. a perfect clock
2. mild visuospatial errors
3. errors in denoting the specified time
4. moderate visuospatial disorganisation
5. severe visuospatial disorganisation
6. no reasonable representation of a clock

1 or 2 is normal, 3 or greater is cognitively impaired.

### *Cognitive Assessment Screening Test (CAST)*

This self-administered paper-and-pencil cognitive test designed to screen elderly people for possible dementia in GPs' offices, takes about 15 minutes and requires little expertise or staff time. It has been shown to have sensitivity and specificity equal to or better than the MMSE or the Blessed Dementia Scale cognitive portion (BDS-cog) (Drachman et al 1996).

### *Physical exam*

Primitive reflexes (glabellar, grasp, snout) may be present even in early AD.

Hearing loss from central auditory dysfunction is more common than cochlear hearing loss in mild AD.

Vascular dementia: may have focal findings, transient neurologic symptoms, gait abnormalities, incontinence. In advanced cases, may have pseudobulbar palsy (involuntary laughing or crying).

Tremor, abnormalities in muscle tone suggest basal ganglia disorder.

Sensory findings (eg peripheral neuropathy) may implicate a metabolic or toxic condition.

Gait abnormalities, impaired vibration or position sense, spasticity, paresthesias suggest B12 deficiency.

Ataxia, nystagmus, lateral gaze palsy may be alcohol-related dementia.

Normal-pressure hydrocephalus has the triad of cognitive impairment, gait disturbance, urinary incontinence.

Generalized myoclonus (with a prominent startle response), motor disorders, an rapidly progressive dementia suggest Creutzfeldt-Jacob disease.

## Routine laboratory investigations

- Complete blood count
- Electrolyte and metabolic screen
- Thyroid panel
- Vitamin B12 and folate levels
- Syphilis serology
- Urinalysis
- Chest radiograph
- Electrocardiogram
- Head CT scan

However, the probability of a treatable intracranial lesion is only 3.5%; thus routine imaging studies may not be indicated.

## Activities of Daily Living (ADL) Assessment

The Kitchen Task Assessment (KTA) (Baum & Edwards 1993) is a functional measure that records the level of cognitive support required by a person with dementia to complete a cooking task successfully. The results allow clinicians to help caregivers understand the level of support the impaired person needs to perform daily living tasks.

## Additional investigations (when justified by the clinical setting)

(Geldmacher & Whitehouse 1996)

### *Laboratory tests*

- HIV testing
- Drug screening
- Ceruloplasmin

- Urinary porphyrins
- Collagen vascular profile
- Urinalysis for heavy metals

### *Magnetic resonance imaging*

If motor dysfunction (eg rigidity, reflex asymmetry, or abnormal reflexes, MRI may help to detect strokes or ischemic changes that CT doesn't pick up.

### *Electroencephalography*

May help identify toxic or metabolic disorders, subclinical partial complex seizures, or Creutzfeldt-Jacob disease.

### *Cerebrospinal fluid examination*

- For atypical cases (eg young pts with a subacute course; pts with signs of systemic illness);
- Also for pts with evidence of hydrocephalus, immunosuppression, demyelinating disease, or vasculitis;
- Tests for tau protein and soluble β-amyloid in CSF are commercially available, but not recommended for routine testing.

### *Cerebral blood flow and metabolism measures*

### *Positron-emission tomography (PET)*

Demonstrate ⇓ glucose metabolism and blood flow in the temporoparietal region in early AD.

### *Single photon emission computed tomography (SPECT)*

As for PET.

### *Brain biopsy*

# Behavioural Disturbances in Dementia

(Loebel & Leibovici 1994)

## Description

The most frequently reported behavioural problem is agitation, including: pacing, aimless wandering, inappropriate dressing or disrobing, spitting, hitting/kicking, throwing objects, making strange noises or screaming, biting, self-destructive acts, cursing or verbal aggression, constant unwarranted complaints/requests/statements, and general restlessness.

Agitation can be broken down into 3 categories: aggressive (eg kicking); repetitious (eg wandering, repetition of words, unintelligible sounds); and socially objectionable (sexual disinhibition, undressing, screaming).

Other behavioural disturbances: kleptomania, myoclonus and seizures, personality changes, sexual problems, sleep disturbances, sundowning.

## Prevalence

Up to 90% of dementia pts exhibit behavioural disturbances. Eg, disinhibition (including aggression, wandering) 35%; apathy-indifference 31%; catastrophic reaction 32%, sundowning 62%; denial 37%.

Low prevalence behaviours: sexual disinhibition 3%; self-destructive behaviours 3%.

35% of a nonclinical community –living sample of AD patients had sleep disturbances, the most common being increased sleep time and early morning awakening, although these were the least disturbing to caregivers. The most disturbing behaviour for caregivers was being awakened at night by patients (McCurry et al 1999).

Negative symptoms (lack of interest in self-care, work and household tasks, social and family activities, and emotional needs of others) are prominent in AD patients even in the absence of depressive Sx (Reichman et al 1996).

Some studies found no relationship between degree of cognitive impairment and behavioural disturbance.

## Consequences of disruptive behaviours in nursing homes

(Beck & Shue 1994)

- Stress experienced by both residents and staff;
- ⇓ quality of resident care from use of physical or pharmacologic restraints;
- Economic consequences, including injuries, property damage, staff burnout, absenteeism, and turnover;
- Emotional costs to the disruptive resident through social isolation;
- ⇑ incidence of falls.

Consequences of extreme or recurrent aggressive behaviour:

- Alienation—avoidance by staff;
- Negative reputation—labeling the resident as a problem;
- Cycle of self-fulfilling prophecy—resident acts out perceptions of others and continues problem behaviours;
- Heightened risk of retaliation from other residents and staff;
- Restrictions in everyday living—avoidance leads to ⇓ participation in activities.

## Neurobiology

CT scans of Alzheimer pts showed that aggression was associated with temporal lobe atrophy; wandering with ⇑ size of the sylvian fissure; and hyperorality with ⇑ size of the 3rd ventricle and frontal, parietal, and occipital atrophy.

In agitated Alzheimer pts, platelet binding of tritiated imipramine is higher than in nonagitated pts, as is monoamine oxidase activity.

## Risk factors

Physical aggression correlates highly with male gender, sever cognitive loss, previous history of aggression, and tendency to fall.

Verbal aggression is associated with female gender, more physical problems, less cognitive deficit.

## Relationship with circadian rhythm disorders

Behavioural disorders such as delirium, agitation, or wandering in dementia pts may be related to disrupted biological rhythms of sleep-waking and body temperature (Okawa et al 1991).

# Psychosis in dementia

(Loebel & Leibovici 1994)

Hallucinations, delusions, misidentification syndromes, persecutory ideas.

Often associated with emotional incontinence, agitation, and insomnia.

Prevalence in Alzheimer's: delusions 11-35%; hallucinations 14-34%. Visual hallucinations are more frequent than auditory.

Visual hallucinations may be the first symptom of dementia, occurring even before cognitive impairment (Haddad & Benbow 1992).

Neuropsychological testing indicated frontal/temporal dysfunction in delusional Alzheimer pts.

Extrapyramidal symptoms are more prevalent (perhaps due to presence of Lewy bodies) and cognition may decline more rapidly in pts with psychosis (Cantillon et al 1998).

Delusions are inversely related to cortical atrophy, suggesting that intact cortical functions are necessary for delusions to be experienced; however, patients with delusions have lower MMSE scores and are more impaired on other cognitive tests (Jeste et al 1992).

Treatment is with antipsychotic medication. However, benefits are only modestly greater than placebo; other behaviours do not usually improve; some patients get worse; side effects are common.

# Management of Dementia

## Pharmacologic and other biological therapies

(Fleming & Evans 1995)

### *For cognitive impairment*

#### Cholinergic agents

In AD, cortical acetylcholinetransferase activity ⇓ and acetylcholine (ACh) neurotransmission is impaired.

Lecithin, choline: supply ACh; physostigmine, oxotremorine: inhibit ACh degradation—unsuccessful 2° medication intolerance or lack of therapeutic effect.

Opiate receptor antagonists (eg naloxone, naltrexone): stimulate ACh release through endorphin inhibition—limited cognitive improvement.

IV nicotine—modest memory improvements (smoking protects against AD development).

*Tacrine (tetrahydroaminoacridine)*
Centrally acting reversible acetylcholinesterase inhibitor: ameliorates cognitive Sx in some pts (up to one-third) with mild/moderate AD. Adverse effects limit usefulness: serum transaminase ⇑ (50%); serum alanine transferase ⇑ (25%); nausea, vomiting, diarrhea, dyspepsia, myalgias, anorexia are dose-related; improvement may reverse rapidly when drug stopped; must monitor liver function frequently for 24 wks, and when dose ⇑.

Never approved in Canada (limited efficacy vs liver toxicity).

*Donepezil (Aricept)*
AChE (acetylcholinesterase) inhibitor.

Available in Canada since Sep 1997.

A multinational placebo-controlled study (double-blinded for 24 weeks, with a 6-week single-blinded placebo washout at the end): 10 mg/day improved cognitive and functional measures more than 5 mg/day, using ADAS-cog and CIBIC-plus (Clinician's Interview-Based Impression of Change with caregiver input) scores (Rogers et al 1998).

Transient nausea and diarrhea were reported; no evidence for liver toxicity.

An open-label study demonstrated no loss of treatment benefit over 98 weeks (Rogers & Friedhoff 1998).

Start at 5 mg/day; if no significant side effects at 4 wks, increase to 10 mg/day.

Bedtime administration may cause nightmares (Ross & Shua-Haim 1998); if so, give qam.

*Metrifonate*
AChE inhibitor.

Used for schistosomiasis Rx for > 30 yrs.

Not metabolized by cytochrome P450 system.

Only mild GI side effects (diarrhea, nausea).

Study of 480 patients with probable AD (MMSE scores 10 – 26) for 12 weeks: significant improvement, apparent after 2 wks, in high-dose group (30 to 60 mg) in cognitive function and clinician ratings; placebo group declined.

Another study of 408 patients with mild to moderate AD: loading dose (100-180 mg) for 2 wks, then maintenance dose (30-60 mg) for 24 wks. Significant improvement in cognitive function, and behavioural symptoms, particularly hallucinations.

*Rivastigmine (Exelon)*
AChE inhibitor.

Side effects: nausea, vomiting, dyspepsia, anorexia, asthenia; generally transient, and mild to moderate severity.

Study of nearly 700 patients on 6 to 12 mg for 26 wks: 56% of patients showed improvement of stabilisation of cognitive function; pts also maintained or improved in activities of daily living.

Also found effective in improving behaviour and cognition in patients with dementia with Lewy bodies (DLB) compared to placebo (LeBourdais 1999). Apathy, anxiety, hallucinations and delusions improved, but agitation, restlessness, pacing, wandering, and irritability did not.

#### Ginkgo Biloba Extract

52-wk, randomized double-blind placebo-controlled study of 309 patients. 27% of treated pts improved by 4 points or more on the ADAS-cog, cf 14% taking placebo (Le Bars et al 1997).

#### Ergoloid mesylates

eg, Hydergine, may ⇑ cholinergic activity through an effect on receptors.

Recent studies show no substantial improvement.

#### Psychostimulants

eg methylphenidate: ⇑ alertness and attention in pts with depression; ⇑ mental status and behaviour in withdrawn, apathetic pts; several studies concluded that psychostimulants do not improve cognitive functioning in dementia, but one study (Galynker et al 1997) found modest cognitive improvement in vascular dementia with methylphenidate.

#### Aspirin

Since risk factors for multi-infarct dementia (MID) are the same as for stroke, it's reasonable to utilize similar preventive interventions.

A small trial of aspirin in MID pts demonstrated maintenance or improvement in certain cognitive tests, cf controls.

AD pts often have vascular risk factors: active treatment with indomethacin in AD pts resulted in less cognitive decline cf placebo.

**Miscellaneous therapies**

*Chelation therapy*
EDTA (ethylenediaminetetraacetic acid) to remove high concentrations of aluminum in the brain: not efficacious in AD; serious SE.

*Vitamins, neurotransmitter precursors*
Studies of thiamine, tryptophan, tyrosine have had inconsistent results.

*Hormonal therapies*
TRH, ACTH, vasopressin treatments have shown no convincing evidence for cognitive improvement.

Estrogen ⇓ risk of developing AD, or delays its development. Effects on cognition after AD diagnosis are controversial.

*Anticoagulants*
Warfarin was shown in a pilot study (reported by (Walsh 1993) to prevent deterioration in a group of nursing home dementia patients.

**Investigational agents**
Studies of cholinesterase inhibitors, muscarinic agonists, antidepressants, calcium channel blockers, nicotinic agonists, selegiline, angiotensin-converting enzyme inhibitors, estrogen, anti-inflammatory drugs, and hemorheologic agents (eg pentoxifylline) are under way.

## *Psychiatric and behavioural disorders*

(Sky & Grossberg 1994)

**General principles for medication treatment of dementia-related behavioural disorders**
It should be noted that placebo response averages 37.5% in studies of medication for the treatment of these disorders (Lantz & Marin 1996).

Although there have been hundreds of reports on the use of psychoactive meds on agitated behaviours in dementia pts, only 13 studies were found which address the issue of sundowning by examining both sleep and behaviour by time of day (McGaffigan & Bliwise 1997).

Establish an accurate diagnosis of a dementing illness (consider lifelong personality disorder or chronic psychiatric disorders).

1. Document the specific behaviours:
   - description (specific);
   - frequency, timing, location;
   - personnel involved; how they responded;
   - potential antecedents or triggers;
   - immediate consequences of the behaviour;
   - what has worked, what has failed.
2. Assess for causative or contributing factors:
   - anxiety, depression;
   - medications;
   - physical limitations, functional disabilities;
   - medical illness, delirium (infection, drug effect, cardiac disease);
   - pain or discomfort (fatigue, distended bladder, constipation, bedsores);
   - hearing impairment, visual loss;
   - boredom, isolation, loneliness;
   - environmental sources (staff interaction, hospitalization, under- or overstimulation).
3. Determine whether intervention is necessary:
   - patient safety vs staff convenience;
   - distress to pt (eg some hallucinations or delusions are not bothersome or frightening);
   - interference with activities of daily living (ADL) or socialization;
   - impact on placement (institutionalization) options;
   - are the behaviours symptoms of depression?
4. Attempt individualized nonpharmacologic approaches.
5. Psychoactive medications:
   - schedule (avoid prn);
   - monotherapy if possible;
   - plan duration of trial (not open-ended);
   - "start low, go slow" but avoid underdosing;
   - continue nonpharmacological approaches;
   - choose target symptoms and desired or reasonable endpoints;
   - document outcomes;
   - monitor for and document adverse effects;
   - taper to lowest effective dose;
   - attempt periodic drug removal. A double-blind, crossover study of 58 nursing home residents receiving either haloperidol, thioridazine, or lorazepam: half were tapered from psychotropic meds to placebo, kept on placebo for 6 weeks, then tapered back to their previous regimen, while the other half were tapered to placebo. There was no impact of drug therapy discontinuation on their behaviour (Cohen-Mansfield et al 1999);
   - consider longer-term medication for recurrent or relapsing disorders and for chronic psychiatric illness.

**Antipsychotic agents**
Behaviours which may respond include anxiety, hostility, hallucinations, excitement, and emotional lability.

A meta-analysis showed 18% of pts benefited from neuroleptics beyond that with placebo, esp for agitation, uncooperativeness, and hallucinations.

Sedation is common, may account for some of the "improvement".

Anti-ACh effects can accelerate cognitive decline, impair memory, result in confusional states.

*Risperidone (Risperdal)*
May be useful because of minimal extrapyramidal symptoms and low incidence of cardiovascular effects (Lantz & Marin 1996). Case reports document efficacy in reducing persistent vocalizations (Kopala & Honer 1997).

*Clozapine (Clozaril)*
Has been successfully used in pts with dementia and severe parkinsonian syndromes who were refractory or intolerant to other neuroleptics (Lantz & Marin 1996).

*Olanzapine (Zyprexa)*
Atypical antipsychotic.

Study of 206 nursing home patients with moderate to severe AD for 6 wks; randomized, double-blind, placebo-controlled; olanzapine significantly reduced agitation, delusions, and hallucinations; response rate with 5 mg was almost double that for placebo.

*Quetiapine (Seroqeul)*
Effective antipsychotic in both Parkinson's and AD without EPS; may improve cognition in psychotic patients (Cantillon et al 1998).

**Anxiolytic agents**
BDZ may be useful in anxiety, fearfulness, or insomnia.

Efficacy in management of agitation in dementia pts has not been adequately demonstrated.

SE include cognitive impairment, confusion, dysarthria, unsteady gait, incoordination, amnesia, sedation, disinhibition with paradoxic agitation, falling, and physical dependence.

Repeated doses can cause accumulation⇒prolonged sedation, habituation.

Withdrawal Sx on treatment cessation.

Short-acting agents without active metabolites (eg lorazepam, oxazepam) may be helpful for recurrent behaviour disruptions associated with predictable situations.

Buspirone, a 5HT1a agonist, may help control aggression at doses of 5 - 15 mg tid. Onset of action may take up to 2 months.

**Antidepressants**
Improvement can occur even when criteria for a mood disorder are not met.

SSRIs are generally safest; however, may worsen baseline agitation.

Trazodone (50-400 mg/day), with or without tryptophan, may be useful for anxiety, sleep disruptions, agitation, and other behavioural problems, including aggression, according to a number of case reports.

**Anticonvulsants**

*Carbamazepine (Tegretol)*
effective in decreasing impulsivity & aggression in wide variety of psychiatric pts.

Limbic antikindling effect, ⇑ locus coeruleus firing rates, ⇑ serum tryptophan levels, possible enhancement of presynaptic dopamine release.

Carbamazepine (200-1000 mg/day) ⇑ cooperation and ⇓ tension, hostility, agitation in 5/9 neuroleptic-refractory pts.

In placebo-controlled studies of nursing home patients with dementia, carbamazepine led to improvement in agitation and aggression in 77% of patients, compared to 21% for placebo. More ataxia and disorientation was noted in the carbamazepine group (Tariot et al 1998).

Doses should be from 200 to 600 mg per day, divided, aiming for serum levels between 17 and 38 $\mu$mol/L; response should be noted in 2-4 wks.

SE include leukopenia, hepatotoxicity, thyroid abnormalities, ataxia, dizziness, cardiac problems, skin rashes, and fatal agranulocytosis or Stevens-Johnson syndrome.

May take up to 7 weeks to demonstrate improvement.

Case report of dramatic response to carbamazepine of visual hallucinations in a woman with probable diffuse Lewy body disease (Stewart & Yelton 1995).

*Valproic acid (Epival)*
A GABA-enhancing anticonvulsant: note that AD brains have GABA deficits.

16 pts treated with divalproex sodium between 750 and 2500 mg daily, divided; serum levels were 184 to 742 $\mu$mol/L. Average scores on the Cohen-Mansfield Agitation Inventory and Behave-AD declined significantly. Side effects included sedation, ataxia, and GI disturbances (Herrmann 1998).

**β-blockers**
β-blockers control aggressive behaviours 2° traumatic brain injury; usefulness in dementia is anecdotal; propranolol (40-520 mg/day in divided doses) or pindolol (60-100 mg/day).

Response time varies from days to several months.

Cardiac failure, COPD, diabetes, asthma, hyperthyroidism are relative contraindications.

Propranolol may cause confusion and depression in elderly; pindolol produces less hypotension and bradycardia (Jenike 1996).

**Other medications**
**Lithium** may control agitation when Sx are manic in character (sleeplessness, hyperactivity, pressured

speech). May control hyperaggressivity and hypersexuality (Jenike 1996).

Conjugated **estrogens** may control aggressive behaviours in elderly men with dementia (Kyomen et al 1999).

#### ECT

Several cases are reported of improvement in uncontrollable screaming or severe verbal disruption with ECT (Lantz & Marin 1996).

## Nonpharmacologic therapies

### *For cognitive impairment*

#### 3R Mental Stimulation Programme

A programme incorporating Reminiscence, Reality orientation, and Remotivation (testing and stimulation of the individual's intellectual and cognitive characteristics through discussion, thought, and deduction) in a small group therapy format with 15 dementia pts attending day care over 8 weeks had improvements in their Mental Status Score (MSS) from 4.4 to 7.3, while a control group showed deterioration (4.1 down to 3.4) (Koh et al 1994).

### *For Behavioural Problems*

A randomised controlled trial of individualised care plans to treat problem behaviours so as to

1. reduce the frequency and/or duration of specified behaviours;
2. reduce caregiver exposure to the behaviour;
3. improve the caregiver's ability to cope with the behaviour;

showed that immediate intervention of 16 weeks duration was effective, whereas delayed intervention was not (Hinchliffe et al 1995).

**Nonpharmacologic management** (Carlson et al 1995)

| Behaviour | Potential Causes or Antecedents | Management Strategies |
|---|---|---|
| Wandering | stress—noise, clutter, crowding | reduce excessive stimulation |
| | lost—looking for someone or something familiar | provide familiar objects, signs, pictures; offer to help find objects or place; reassure |
| | restless, bored—no stimuli | provide meaningful activity |
| | medication side effect | monitor, reduce, or discontinue medication |
| | lifelong pattern of being active or usual coping style | respond to underlying mood or motivation; provide safe area to move about (eg, secured circular path) |
| | needing to use the toilet | institute toileting schedule (such as every 2 hr); place signs or pictures on bathroom door |
| | environmental stimuli—exit signs, people leaving | remove or camouflage environmental stimuli; provide identification or alarm bracelets |
| Difficulty with personal care tasks | task too difficult or overwhelming | divide task into small, successive steps |
| | caregiver impatience, rushing | be patient, allow ample time, or try again later |
| | cannot remember task | demonstrate action or task; allow subject to perform parts of the task that still can be accomplished |
| | pain involved with movement | treat underlying condition; consider pain medication or physiotherapy; modify or assist the movement needed |
| | cannot understand or follow caregiver instructions | repeat request simply; state instructions one step at a time |
| | fear of task—cannot understand need for task or instructions | reassure, comfort, distract from task with music or conversation; ask patient to help perform the task |
| | inertia, apraxia; difficulty initiating and completing a task | set up task sequence by arranging materials (such as clothing) in the order to be used; help begin the task |
| Suspiciousness, paranoia | forgot where objects were placed | offer to help find; have more than one of same object available; have a list where objects should be placed; learn favourite hiding places |
| | misinterpreting actions or words | do not argue or try to reason; do not take personally; distract |
| | misinterpreting who people are; suspicious of their intentions | introduce self and role routinely; draw on old memory, connections; do not argue |
| | change in environment or routine | reassure, familiarize, set routine |
| | misinterpreting environment | assess vision, hearing; modify environment as needed; explain misinterpretation simply; distract |
| | physical illness | evaluate medically |
| | social isolation | encourage and provided familiar social opportunities |
| | someone is actually taking something from patient | verify the situation |
| Agitation (also: "sundowning", catastrophic reactions) | discomfort, pain | assess and manage sources of pain, constipation, infection or full bladder; check clothing for comfort |
| | physical illness (such as urinary tract infection) | evaluate medically; eliminate caffeine and alcohol |
| | fatigue | schedule adequate rest; monitor activity |
| | overstimulation—noise, overhead paging, people, radio, television, activities | reduce noise, stress; remove from situation; use television sparingly; limit crowding (for example, dining hallways just before meals) |
| | mirroring of caregiver's affect | control affect; model calm with low tone and slow rate; use support system and groups for outlet |
| | overextending capabilities (resulting in failure); caregiver expectations too high | do not put in failure-oriented situations or tasks; understand losses and reduce expectations accordingly |
| | patient is being "quizzed" (multiple questions that exceed abilities) | avoid persistent testing of memory; pose one question at a time; eliminate questions that require abstract thought, insight or reasoning |
| | medication side effect | assess, monitor, and reduce medication if possible; monitor health concerns |

| | | |
|---|---|---|
| Agitation (also: "sundowning", catastrophic reactions) (continued) | patient is thwarted from desired activity (for example, attempting to escape) | redirect energy to similar activity; ask patient to help with meaningful activity; have diversionary tactics for outbursts; choose battles—assess whether behavior is merely irritating, rather than compromising patient safety or obstructing care |
| | lowered stress threshold | simplify tasks, create calm; lower expectations and demands; avoid arguments and reprimands |
| | unfamiliar people or environment; change in schedule or routine | be consistent; avoid changes, surprises; make change gradually |
| | restless | plan calming music, massage, or meaningful activities; assign tasks that provide exercise |
| Incontinence | infection, prostate problem, chronic illness, medication side effect, stress or urge incontinence | evaluate medically |
| | difficulty in finding bathroom | place signs, picture on door; ensure adequate lighting |
| | lack of privacy | provide for privacy |
| | difficulty undressing | simplify clothing, use elastic waistbands |
| | difficulty in seeing toilet | use contrasting colors on toilet and floor |
| | impaired mobility | evaluate medically, treat associated pain (include physiotherapy); provide a commode, reduce diuretics when possible |
| | dependence created by socialized reinforcement | provide ⇑ attention for continence rather than incontinence; allow independence whenever possible, even if time-consuming |
| | cannot express need | schedule toileting (such as every 2 h while awake); reduce diuretics and bedtime liquids when possible |
| | task overwhelming | simplify; establish step-by-step routine |
| Sleep disturbance | illness, pain, medication effect (for example, causing daytime sleep or nocturnal awakening) | evaluate medically |
| | depression | prescribe antidepressant (consider bedtime sedative such as trazodone) |
| | less need for sleep | schedule later bedtime; allow activities or tasks safely done at night; plan more daytime exercise |
| | too hot, too cold | adjust temperature |
| | disorientation from darkness | use night-lights |
| | caffeine or alcohol effect | reduce or eliminate alcohol; limit caffeine after noon |
| | hunger | provide nighttime snack |
| | urge to void | ensure clear, well-lit pathway to bathroom |
| | normal age- and disease-related fragmentation of sleep (like that of an infant or toddler) | accept; plan for safety |
| | daytime sleeping | eliminate or limit naps; provide activity and exercise instead; for naps, use recliner rather than bed |
| | fear of darkness | provide soft music, massage, night-light |
| | restless | |
| Inappropriate or impulsive sexual behavior | dementia-related ⇓ judgment and social awareness | do not overreact or confront; respond calmly and firmly; distract and redirect |
| | misinterpreting caregiver's interaction | do not give mixed sexual message (double entendres and innuendoes—even in jest); avoid nonverbal messages; distract while performing personal care, bathing |
| | uncomfortable—too warm, clothing too tight; need to void; genital irritation | check room temperature; assist with comfortable weather-appropriate clothing; ensure that elimination needs are met; examine for groin rash, perineal skin problems, stool impaction |
| | need for attention, affection, intimacy | increase or meet basic need for touch and warmth; model appropriate touch; offer soothing objects (such as stuffed animals); provide hand or back massage |
| | self-stimulating, reacting to what feels good | offer privacy; remove from inappropriate place |

**Behaviour modification**
(Gugel 1994)

Behavioural approaches involving the application of operant conditioning are effective with demented elderly for a variety of problems in a variety of settings.

Behaviours are manifested because they fulfill a need; to change a behaviour, either the need has to be satisfied with a different behaviour, or the behaviour has to have a different consequence.

Problem behaviours occur when the physical environment or caregivers inadvertently reinforce and thus maintain maladaptive behaviours.

Steps:

- Identify the behaviour to be changed;
- Identify an appropriate & acceptable alternative behaviour;
- Complete a behavioural analysis: documentation of the behaviour's occurrence;
- Identify the antecedents/precursors to the problem behaviour;
- Identify the reinforcer(s) of the problem behaviour; eg an Alzheimer's patient who screams when the caregiver is not in the room. Each time the screaming behaviour occurs, the caregiver returns and the screaming stops. Here, the return of the caregiver reinforces future screaming behaviour whenever the patient is left alone;
- Identify reinforcer(s) which will reduce or eliminate the problematic behaviours, eg the caregiver needs to come into the room when the alzheimer patient is not screaming and leave or not enter the room when the pt is screaming;
- Finally, develop a strategy to facilitate the occurrence of an alternative/acceptable behaviour and its reinforcement. This behaviour may need to be cued or prompted.

Dementia patients respond well to praise and poorly to negative reinforcers or punishment.

The reinforcer must be presented immediately on occurrence of the desired behaviour.

Given the cognitive impairment, reinforcement may have to be continued indefinitely.

**Other interventions for disruptive behaviours**
A review by Beck & Shue (Beck & Shue 1994) describes and gives references for the following therapeutic interventions:

- Validation therapy: aims to maintain the dignity and well-being of disoriented elderly people;
- Multimodal approaches, eg the Progressively Lowered Stress Threshold (PLST) model and plan of care;
- Group programs, such as Self-Esteem, Relaxation, Vitality, and Exercise (SERVE): listening to music, exercising, and relaxing for 1 hr, 3x/week;
- Low lighting (or avoidance of fluorescent lights) and music during mealtimes, ⇓ noise level, feeding time, and ⇑ food consumption;
- Nature sounds, soothing music, or white noise to ⇓ screaming;
- Touch, eg stroking across the back, to ⇓ agitation;
- Massage and therapeutic touch to induce relaxation;
- Pet therapy;
- Stimulus items, such as busy boxes, entertain patients, hold their attention, and may ⇓ agitation & combativeness;
- Education for nursing assistants in nonverbal communication techniques and other aspects of working with dementia pts;

*Bright light therapy*
Two hrs of bright light between 9h and 11h daily for 4 wks markedly improved sleep and behaviour disorders in 12 dementia inpatients. Nocturnal sleep increased, while daytime sleep decreased (Mishima et al 1994). However, in another study, sleep length improved but there was no improvement in agitated behaviours (Lyketsos et al 1999).

8/10 pts with late afternoon/early evening confusion leading to agitation and irritability (sundowning syndrome) improved with 2 hrs of bright light therapy each evening.

*Sleep restriction*
Restricting the amount of time in bed to 6 or 7 hrs nightly will improve sleep quality (Reynolds et al 1987).

*Physical activity*
Walking for 30 minutes, 3 times a week for 10 weeks, significantly improved communication performance in a randomized controlled study of 30 nursing home residents with probable AD (Friedman & Tappen 1991).

14-wk program of exercise resulted in decreased agitation, less time in bed during the day, and higher percentage of time asleep at night as measured by wrist actigraphy (Alessi et al 1999) compared to controls.

## Care environments

(Abraham et al 1994b)

### *Risk factors for institutional placement*

- Decline in functional status
- Recent hospitalization
- Self-reported health status
- Poverty
- Living alone
- Being white
- Female
- Among men: insomnia

### *Living at home (Independently or with a caregiver)*

Assessment of the home environment is important, both because of the intrinsic therapeutic value of the home and because of the frequency and severity of injuries sustained at home.

Living at home presumes that community-based health care, food, transportation, and related services are available & accessible; if eligibility requirements are too stringent, pts may be institutionalized prematurely.

### *Continuing Care Retirement Communities (CCRCs)*

Many older adults actively seek relocation into CCRCs because they want:

- Accessible specialized services (including medical, social, and nursing home services);
- Safety;
- Financial security (structured long-term care expenditures and protection of family estate);
- Relief from home ownership responsibilities;
- Social contacts and recreational activities;
- Selected ADL support (eg meals, shopping, transportation);
- Relief from the fear of being a burden to family members.

### *Group living*

Foster homes provide a home-like environment; a wide range of care options can be provided.

Home sharing, in which 2 or more unrelated individuals share a single-family dwelling owned by one of the individuals; each participant makes a material or personal contribution for everyone's benefit.

"granny flats" are small mobile units which can be grouped, or attached to larger houses, and provide independent living near to people who provide a support network.

### *Community resources*

Home care services include: companionship services; homemakers; personal care; home health care; home nursing.

Critical to the success of such services is the relationship between the formal and the informal (usually family) caregivers. This relationship should be clearly spelled out.

### *Respite care*

For various durations of time: several hours; one to several days; weeks to months.

In various care settings: in the pt's home; in day care centres; in foster homes, nursing homes, or hospitals; cooperative agreements.

Caregivers prefer in-home respite care for short periods.

Studies show respite care improves caregivers' morale, lower subjective but not objective caregiver burden levels.

### *Adult day care*

Commonly available services include:

- Nursing observation and supervision;
- Case management;
- Health assessment;
- Nutritional education;
- Therapeutic diets;
- Counseling;
- Therapeutic services.

### *Other community services*

- Transportation services for elderly persons;
- Home-delivered meals;
- Social health maintenance organizations;
- Support and advocacy groups for Alzheimer's families;
- Telephone "help-lines";
- Support groups for the dependent elderly person and the caregiver;
- Senior centres.

### *Alzheimer's Special Care Units*

Characterized by (Maas et al 1994):

- Admission of residents with cognitive impairment;
- Special staff specification, selection, and training;
- Activity programming for the cognitively impaired;
- Family programming and involvement;
- Segregated and modified physical and social environment.

#### Models of care

*Person-environment fit model*
Derived from systems theory.

Modify the environment to reduce demand on the ad pt's cognitive abilities.

*Person-environment interaction model*
Based on the notion that AD pts need ⇑ environmental stimuli to correct cognitive and functional deficits.

Most have not been successful; some evidence that AD pts attempt to reduce environmental stimuli.

*Medical model*
Emphasis on pathology, illness, and physical aspects of care, rather than function, daily living, and quality of life.

Use of medications to control behaviour and other symptoms.

Because of concern for legal liability, pts' autonomy and freedom may be compromised to provide safety and prevent risk (eg physical and chemical restraints used to prevent falls and elopement).

*Rehabilitation model*
Strategies include ⇑ sensory input; reality orientation therapy; skills remediation; pet, art, music, and exercise therapy; remotivation groups; reeducation in adls; individual or group therapies.

Results have been small or mixed.

*Psychosocial model*
Focuses on maximizing functional abilities so that individuals can continue to enjoy as much independence and social activities as possible.

Associated risks are considered necessary for individuals to maintain optimal function and quality of life.

#### Segregation vs integration

Integration of demented & non-demented residents has been proposed with the idea that regular exposure to nondemented residents provides role models and more normal stimulation, such as lucid conversation, for the demented.

Others suggest that segregation gives the demented more opportunities for maximum function and dignified living.

It has also been argued that integrating confused and nonconfused residents is a violation of the rights of each.

## Safety issues for patients living at home

(Marchello et al 1995)

Home safety hazards for demented pts can be reduced by the following:

- Alarm devices to warn caregivers about wandering out-of-doors;
- Electrical safety devices such as outlet covers, light motion detectors, and "off" switches that can be installed to deactivate dangerous appliances;
- Childproof cabinet and drawer stops to deter access, with locked drawers from sharp utensils and valuables;
- Providing a secure, safe wandering area;
- Indirect lighting to reduce glare;
- Furnishing the home with comfortable chairs, pastel colour schemes, and nonskid floors or carpeting.

## Telling the patient and family

(Jutagir 1994)

While some feel that telling a patient about an illness for which there is no cure and which has a progressive downhill course would be cruel, or would exacerbate symptoms, others believe that disclosing the diagnosis promotes self-determination and enables the patient to help develop plans for advance direc-

tives, financial matters, and other personal affairs while still able.

Telling a patient that the problem is due to normal aging may be perceived as lack of understanding by the physician of the extent of the patient's problems, or lack of competence.

Someone who has developed a relationship with the patient (usually the physician) presents test results in the presence of family members, reviewing all components of the evaluation and all hypotheses that were entertained and ruled out.

The patient can be told he or she has a loss of cognitive ability, and the pattern is characteristic of dementia. The term should be defined and a distinction made between "demented" and "crazy".

If patients continue to deny symptoms, the family can be called upon to confirm that there is a problem.

For emotionally fragile patients, avoid using "Alzheimer's" or "dementia"; instead, tell that patient that he or she has a memory disorder or a significant memory loss.

### Treatment of Pseudodementia

#### *ECT*

One study showed that the cognitive improvement which accompanied remission of depression by ECT in elderly pseudodementia pts was maintained over 4 yrs of followup (Stoudemire et al 1995).

## Interventions with Family Caregivers

(Collins et al 1994)

### Caregiver burden

#### *Factors contributing to caregiver burden*

(Chenier 1997)

- Continuous supervision or worry about the care receiver;
- Interrupted sleep;
- Lack of time for self or social and leisure activities;
- Greater impairment in ADLs/IADLs;
- Older caregivers.

#### *Psychosocial problems reported by family caregivers*

- Feelings of guilt & inadequacy;
- Concerns over the caregiver-recipient relationship.

#### *Chronic stress*

A case-control study of family caregivers of AD victims found greater distress and loneliness in caregivers associated with more impairment in the AD patient; caregivers also had worse immunologic status (Kiecolt-Glaser et al 1987).

#### *Needs expressed by caregivers*

- Responding to issues in the extended family;
- Improvement of coping skills;
- Strategies to deal with the elderly person's care needs (emotional and behavioural, physical safety, and legal and financial issues);
- Long-term planning issues.

### Categories of interventions

- Psychosocial interventions that provide emotional support, problem-solving assistance, and education;
- Service interventions that provide help with direct care of the person with dementia.

#### *Education*

Teaching of in-home caregivers, with the objective of improving the family's competence in managing problematic behavioural symptoms in order to decrease caregiver stress, delay institutionalization, and reduce the costs of direct care, is facilitated using a nursing care plan based on a model of modifying environmental demands to accommodate declining cognitive and functional abilities (Hall et al 1995).

### *Family support groups*

Provide emotional support, enhancement of coping skills, and general information;

May be professionally or peer led;

Studies so far show inconsistent results.

### *Psychoeducational and counseling interventions*

Individual or group interventions; professionally led; time limited.

Teach specific psychologic and behavioural skills to caregivers.

Studies report on a wide variety of intervention types, but indicate ⇑ social support, ⇓ depression, ⇓ burden, and ⇑ knowledge about dementia care.

### *Community service interventions*

#### Information and referral services

#### Case management services

Tasks of case management:

- Case finding or screening;
- Comprehensive assessment to determine unmet needs;
- Care planning;
- Implementation of the plan of care;
- Monitoring the client's progress and adequacy of services;
- Formal reassessment at regular intervals to determine continuing need.

Provide services that temporarily relieve the caregiver.

#### Community-based services

Examples: adult day care, in-home companions, skilled nursing services, housekeeping assistance, temporary overnight care.

## Helping families decide when to place patients with dementia

During early and middle stages of Alzheimer's, home is the best place for most patients (Pfeiffer 1995):

- Less expensive;
- Familiar and pleasant environment;
- Possibility of continued social and emotional interaction with family;
- Virtually all needed services can be provided.

### *Triggers for institutional placement:*

- Bladder and bowel incontinence;
- Patient cannot help with care, eg unable to walk to bathroom, or get in and out of bed on their own;
- Unable to recognize caregiver or own home;
- Paid caregiver withdraws (eg quits, becomes ill);
- Primary caregiver's health is at risk;
- Primary caregiver feels unable to continue.

### *Triggers for early institutional placement*

- No family member able to be caregiver;
- Disruptive behaviour.

# Depression Coexisting with Dementia

(Jones & Reifler 1994)

Depression and dementia are the two most common clinical psychiatric problems in the elderly. Because symptoms can overlap and because treatment of depression can reduce disability in dementia pts, recognition of the two syndromes is important.

## Epidemiology

Prevalence of dementia increases with age.

Prevalence of depression in older adults in good health without substance abuse decreases with age.

Prevalence of depression in dementia pts varies from 23 to 50% in different studies.

For pts who are medically ill or who are referred for evaluation of memory problems, the prevalence of depression is estimated to be 20-30%.

## Risk factors for depression

Medical illness; CNS disease (eg Parkinson's); stroke.

Family history even in the absence of personal history of previous depression.

Alzheimer pts with depression have more damage to the locus coeruleus than Alzheimer's without depression.

Depression is less frequent in the severely demented.

## Association between dementia and depression

15% of pts referred for dementia evaluation in one study were found to be depressed, not demented; however, on 3-yr followup, 53% of these had developed progressive cognitive impairment. These pts were significantly older, but no different in terms of symptom duration of frequency of complaints of cognitive impairment. Most of those progressing to dementia had neurologic abnormalities: focal neurologic signs or symptoms, extrapyramidal signs, or evidence of spinocerebellar degeneration.

Studies show that in demented pts with a given level of cognitive impairment, those with coexisting depression have significantly greater impairments in activities of daily living (ADLs). Depressed demented pts are also at higher risk of dying early.

## Assessment

Recent studies show that cognitive impairment in dementia of depression is indistinguishable from the deficits of mild irreversible dementia.

Vegetative and psychological symptoms of depression are found much less frequently in nondepressed than in depressed demented pts.

Sleep deprivation was found to rapidly reverse cognitive impairment in a treatment-resistant elderly depressed patient, thus helping to distinguish pseudodementia from true dementia (Williams et al 1994).

***Differentiating AD from depressive dementia (pseudodementia) (Flint 1995)***

| Feature | Alzheimer's disease | depressive dementia |
|---|---|---|
| onset | insidious | subacute |
| progression of illness | slow | rapid |
| attitude towards illness | unconcerned; patient does not seek help | distressed; patient seeks help |
| memory complaints | none or minimal & vague | exaggerated & detailed |
| affect | shallow, labile | depressed, anxious |
| delusions (if present) | compensatory | mood congruent, nihilistic |
| hallucinations (if present) | variable | auditory (self-deprecatory) |
| **Cognitive Testing** | | |
| motivation | struggles with tasks | makes little effort |
| shortcomings | concealed | emphasized |
| accomplishments | valued | downgraded |
| performance on tasks | consistent | variable |
| answers to questions | confabulation; guesses; excuses | "I can't" responses |

# Ethical and Legal Issues

(Caralis 1994)

## Decision-making capacity

- A definitive test does not exist;
- The physician should first make sure that information presented is pertinent to the specific decision. Patients should understand the relevant information, manipulate it rationally, appreciate the situation and consequences, and communicate stable choices;
- A sliding-scale model has been proposed that applies increasing stringent standards to different medical decisions, depending on complexity.

## Termination of life-prolonging treatments and quality of life issues

- Important to recognize the influence of physicians' perception of the patient's quality of life; studies show that physicians use different measures to rate quality of life and undervalue it compared with their pts. They were less likely to resuscitate and would terminate life-prolonging treatment sooner than their pts desired.
- Artificial feeding is now considered a life-prolonging treatment. In the US, the courts permit incompetent pts the right to terminate artificial feeding through substituted consent-givers.

## Futile treatments, family conflict, and euthanasia

- Some would consider it unethical to admit a patient to a hospital or nursing home without consideration of the patient's CPR status.
- Patients should not be placed at risk of receiving highly invasive and perhaps inappropriate therapy.
- When no advance directive is available, and families are in conflict with the physician's medical judgments, pts would prefer that their families' wishes be honoured.

## US federal regulations regarding nursing homes

(Streim & Katz 1994)

- In response to concerns about the misuse of physical and chemical restraints in widely published reports of poor quality of care and even inhumane treatment in nursing homes, the US congress in 1987 passed the Nursing Home Reform Amendments of the Omnibus Budget Reconciliation Act of 1987 (OBRA 87), applying to nursing homes receiving federal funding.
- Regulations cover licensure, staff qualifications, record keeping, quality assurance; space, equipment, safety; infection control; specialized services such as nursing, dietary, dental, rehabilitation, pharmacy.

### Assessment

All residents must be comprehensively assessed: eg for pts with dementia, the Minimum Data Set (MDS) assessment instrument covers background information (including guardianship status and advance directives), cognitive patterns, communication/hearing patterns, vision patterns, physical functioning, continence, psychosocial wellbeing, mood and behaviour patterns (including expressions or signs of sad or anxious mood, wandering, verbal or physical abusiveness, socially inappropriate or disruptive behaviour, and resistance to care), activity pursuit patterns, comorbid disease diagnoses and health conditions. Responses on the MDS indicating specific deficits trigger the use of Resident Assessment Protocols (RAPs) which are more specific and comprehensive. For example, identification on the MDS of problems with memory, decision making, and comprehension and diagnoses of Alzheimer's disease or other dementias, mental retardation, Parkinson's disease, or aphasia are triggers to the cognitive loss/dementia RAP. This RAP identifies basic goals of nursing home care for these pts, including the identification and treatment of acute confusion and behaviour problems. It provides a comprehensive outline of factors that can cause or aggravate cognitive dysfunction and behavioural disturbances, such as concurrent medical problems, distressing symptoms, (eg pain, constipation), perceptual difficulties, impaired communication, mood disorders, and medication effects.

### Psychotropic drug use

Regulations state that the resident has the right to be free from any psychoactive drug administered for purposes of discipline or convenience and not required to treat the resident's medical symptoms. Specifically, antipsychotic drugs can be given only if necessary to treat a specific condition as diagnosed and

documented in the clinical record, and they must receive gradual dose reductions and behavioural interventions, unless clinically contraindicated, in an effort to discontinue these medications. Their use in dementia pts is justified only if the patient exhibits associated psychotic or agitated features. The nature and frequency of agitated features must be documented; it must be shown that there are no preventable causes of the psychosis or agitation; and they must be documented to cause danger to the patient or others; or continuous crying, screaming, yelling, or pacing; or resident distress or impairment in functional capacity. Some individual phenomena which by themselves cannot be used to justify antipsychotic drug use include impaired memory, wandering, restlessness, insomnia, uncooperativeness, or agitated behaviours without dangerousness.

#### Physical restraint use

Restraints may not be used unless there is documentation that efforts were made to identify and correct preventable or treatable factors that cause or contribute to the problem, that prior attempts to use less restrictive measures failed, and that the restraints enable the resident to achieve or maintain the highest practicable level of function. Physical or occupational therapists must be consulted if restraints are required to enhance body positioning or mobility. the resident or responsible family member or guardian must consent to the use of physical restraints.

#### Impact of OBRA 87

Simply educating medical directors, primary care physicians, and directors of nursing about OBRA regulations resulted over 6 months in a 36% reduction in the use of antipsychotic drugs.

## Consequences of apolipoprotein E testing

(Mayeux & Schupf 1995) It is now possible to enter genetic information contained in an individual's DNA into widely accessible computerized databases. This raises novel privacy issues, as this data provides information about future risks for the individual and also for other family members.

Employers might require apoE testing as a prerequisite of employment. This testing does not benefit the individual, as there are no known effective ways to reduce risk or treat AD. However, it might be used by employers to deny health care insurance; other insurers will then also deny insurance (Issa & Keyserlingk 1999). The information might also be used to deny employment or insurance coverage to the person's offspring.

## Consequences of screening for cognitive impairment

Potential benefits of early identification (Patterson 1991):

- Identify individuals who may benefit from existing treatments for cognitive impairment;
- Identify potential subjects for research;
- Identify those at high risk for delirium;
- Help predict further cognitive decline (eg to assign power of attorney before mental incompetence occurs);
- Give time for planning relocation to a more protective environment;
- Early involvement with support groups may assist the caregiver.

Potential harm of early identification:

- A dementia label may preclude life or health insurance;
- May influence attitudes of health care professionals;
- Stigmatizes the individual;
- Even mild cognitive impairment may be used as justification by family or others to restrict a person's managing their own affairs.

## Capacity to drive a vehicle

(O'Neill 1993) a hierarchical approach to decision-making, divides the driving task into 3 levels of risk taking: strategic, tactical, and operational. Each level can be assessed separately:

- Strategic performance: the driver's choice of level of risk, eg planning of choice of route, time of day, or even the decision not to drive and to take public transportation;
- Tactical decisions: those which take a risk, eg decisions on overtaking (passing), going through amber lights, or signalling in good time;
- Operational performance: the reaction to risk, eg the response to specific traffic situations, such as speed control, braking, & signalling.

Operational performance is the level most frequently assessed; however, it may have the least to do with actual risk of accident.

A computerized screening test, called the DriveABLE driving competence screen, is being used in Alberta, Quebec and B.C. To succeed, a driver just demonstrate memory, judgment, decision-making, attention and motor speed abilities and be able to shift or integrate these skills.

Although MMSE scores may not correlate well with car crashes or moving violations, MMSE scores do correlate well with both road tests and computer-based driving tests (Bédard et al 1997). Thus, in general, scores of 25 or more, when there are no problems with function or behaviour, suggest minimal impairment in driving ability. Scores or 14 or lower are reasonable grounds for the automatic revocation of driving privileges. Scores in the 15 to 24 range indicate impairment that warrants further testing, by a geriatric clinic or a specialized test centre.

In Québec, physician reporting of unfit drivers is not mandatory; however, physicians are explicitly protected from liability when reporting (Bédard et al 1997).

# Additional Reading

(Abraham et al 1994a)
(Ballard & Oyebode 1995)
(Colenda et al 1996)
(Emery & Oxman 1992)
(Stolley et al 1993)
(Vitiello et al 1992)
(Yeager et al 1995)

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