

## Diagnosis and management of Alzheimer's disease and other disorders associated with dementia. The role of neurologists in Europe

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In 1998 a task force to develop guidelines for diagnostic evaluation and treatment of dementia was initiated by the European Federation of Neurological Societies (EFNS) scientist panel on dementia. The aims of the task force were to provide evidence-based recommendations and to highlight the role of the neurologist in the management of patients with Alzheimer's disease and other disorders associated with dementia.

We based our recommendations on a review of available evidence-based guidelines supplemented with further literature reviews. The recommendations were derived from consensus meetings and relate to individual patient management, as there are inadequate data on the cost-effectiveness of different diagnostic evaluations and treatments for dementia. Their specific applications will depend upon available resources.

The particular contributions of the neurologist include: early identification and differential diagnosis of rare and common brain disorders causing cognitive and behavioural symptoms, referral for and interpretation of ancillary investigations, and identification and treatment of vascular and other concurrent diseases.

A review of the management of dementia in Europe revealed considerable variation. In some countries neurologists have taken the lead in the management of patients with dementia, while in other countries the neurologist is rarely involved.

We recommend that neurologists should have a clear role in the management of dementia in the whole of Europe. They should be involved in the diagnostic evaluation of dementia and facilitate the development of multidisciplinary teams for evaluation and management of patients with cognitive disturbances. The increasing role of neurology in the management of patients with dementia has important implications for training and education.

## Introduction

### Justification

Diagnostic evaluation of patients with dementia is a challenge for neurologists as well as for primary care physicians, geriatricians, psychiatrists and other health care professionals. Accurate diagnostic classification of patients with dementia is essential for the planning of appropriate medical and psychosocial treatment, for the identification of potentially reversible conditions

and relevant concomitant conditions, and for appropriate caregiver advice and intervention. With the advent of pharmaceutical treatment for Alzheimer's disease (AD), many more patients with memory problems or cognitive, emotional and behavioural symptoms will see physicians for diagnostic evaluation and treatment.

The diagnosis and management of dementia requires a multidisciplinary approach which includes the skills of the neurologist. For some patients the neurologist provides the specialist advice for the primary care physician, geriatrician or psychiatrist caring for the patient; for others the neurologist is the primary physician responsible for diagnosis and treatment. In general, neurologists see patients of younger age or those with a rapid progression, unusual clinical

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presentation, additional neurological features or abnormal brain imaging; some neurologists, however, may see a broader spectrum of patients of all ages.

The particular contributions of the neurologist comprise the early identification and differential diagnosis of rare and common brain disorders causing cognitive and behavioural symptoms, the referral for and interpretation of certain ancillary investigations, and the management of concomitant neurological complications. With the advances in the early identification of AD by neuroimaging and clinical neuropsychology, more patients will be referred to neurologists for diagnostic evaluation and treatment.

Previous practice guidelines have either focused on diagnostic evaluation (American Academy of Neurology, 1994; Wallin *et al.*, 1994; Corey-Bloom *et al.*, 1995) or on treatment (American Psychiatric Association, 1997), or aimed at assisting primary care physicians in the management of dementia (Small *et al.*, 1997; Canadian Consensus Conference on the Assessment of Dementia Organizing Committee, 1991).

### **Aim**

The aim of the task force was to provide neurologists with recommendations (evidence-based when possible) for diagnostic evaluation and treatment, and to highlight their role in the management of patients with AD and other disorders associated with dementia.

### **Development process**

These guidelines were initiated and developed under the auspices of the European Federation of Neurological Societies (EFNS) Scientist Panel on Dementia. The task force comprised neurologists with clinical and research expertise in dementia, and a specialist in old age psychiatry was consulted for review of recommendations concerning the identification and care of psychiatric symptoms. Evidence was coded according to the classification system suggested by the North of England evidence-based guidelines development project (Eccles *et al.*, 1996): (I) evidence provided by well-designed randomized control studies, meta-analyses or systematic reviews; (II) evidence provided by well-designed case-control or cohort studies; (III) evidence provided by uncontrolled studies or consensus statements. The development process included: (1) a review of the present role of neurology in the management of dementia in Europe; (2) a review of other guidelines for diagnostic evaluation and treatment of dementia; (3) a literature review; (4) consensus meetings and drafting by the work group; (5) approval by the EFNS Scientist Panel on Dementia and the EFNS Scientific

Committee; and (6) planned revisions at 3–5 year intervals.

### **Scope**

The guidelines are for neurologists and apply to patients with memory problems or cognitive, emotional and behavioural symptoms suggestive of a dementia disorder. They cover aspects of diagnostic evaluation, as well as treatment, with particular emphasis on the type of patient often referred to neurologists. While focusing on AD, many of the recommendations regarding management apply to dementia disorders in general. These guidelines may not be appropriate in all circumstances, and decisions to apply the recommendations must be made in the light of the clinical presentation of the patient and of available resources. While the neurologist should consider all recommendations in these guidelines, the management of any patient should not necessarily be limited to the suggestions given here.

### **Management of dementia in Europe: the current role of neurologists**

The neurologist's role varies considerably across Europe both in general and specifically in relation to dementia. The relative involvement of psychiatrists, geriatricians and neurologists and the emphasis on primary care or direct self-referral to specialists has a major influence. A review of current practice by the EFNS Panel suggests that in all instances neurologists are involved in the diagnosis of dementia, and usually in the ongoing care, but only a minority in long-term and residential care. Clearly the number of patients per year seen by neurologists varies with the specific interests of the individual and the number of neurologists in the country. The latter varies considerably from 1 in 15 000 to 1 in 200 000. Most countries do have some specialized clinics and if these exist they are usually in a multidisciplinary setting. Only a minority of countries reported specific training in dementia and where it is offered it is usually optional.

### **Clinical differential diagnosis: the role of the neurologist**

A wide array of neurological diseases may present with cognitive impairment or dementia. In the diagnostic work up of dementia the role of the neurologist should be an active one. The large majority of dementias are a result of vascular dementia (VaD) and degenerative brain diseases of which AD, frontotemporal degeneration (FTD) and dementia with Lewy bodies (DLB) are

the most prevalent. The identification of more rare symptomatic causes of dementia, e.g. inflammatory diseases, intracranial tumour or normal pressure hydrocephalus (NPH), also relies on the neurologist. There is a general consensus that the management of dementia should be handled by a multidisciplinary team of which the neurologist should be a member (III).

What could be the specific role of the neurologist in the diagnostic evaluation of dementia?

- 1 General history taking, with special reference to previous neurological (vascular) events, of the patient and a close informant.
- 2 The neurological examination, with emphasis on focal signs, disturbances of eye movements, extrapyramidal signs and gait disturbances.
- 3 Referral for and interpretation of specific ancillary investigations, such as neuropsychological tests, neuroimaging, lumbar puncture, electroencephalography (EEG), electromyography (EMG) and brain biopsy.
- 4 The identification and treatment of vascular factors in dementia.
- 5 Diagnosis and treatment of seizures and extrapyramidal disturbances.
- 6 Advice to referring physician, patient and caregivers on neurological aspects of diagnosis and treatment.

#### *Recommendation*

- The neurologist should be involved in the diagnostic evaluation of patients with dementia.

### **Clinical diagnosis**

In the absence of neuropathological confirmation, the aetiological diagnosis of dementia can only be proposed in terms of probability (I). For instance, errors of diagnosis may occur in almost 25% of patients with AD (Boller *et al.*, 1989). The more systematic use of criteria for dementia, ICD-10 (WHO, 1992), and for AD, DSM-IV (American Psychiatric Association (APA) 1993) and NINCDS-ADRDA (McKhann *et al.*, 1984), constitutes real progress in terms of diagnosis (II).

### **Cognitive evaluation**

Dementia is classically defined by the existence of deficits in episodic memory and in other cognitive domains: language, visuospatial and visuo-perceptual function, praxis or executive functions. As neurologists increasingly see patients at early stages of the disease, it is possible to suspect a degenerative disorder on the basis of an isolated progressive amnesia or a deficit in a single cognitive domain: e.g. non-fluent progressive aphasia, progressive apraxia, progressive visuospatial

dysfunction, semantic dementia, FTD. Thus, cognitive assessment – from bedside to quantified testing – is useful for detecting cognitive change, at least in non-severely demented patients, and should investigate the following domains:

*Global cognitive function* is usually assessed by global scales such as the Mini-Mental State Examination (MMSE) of Folstein (Folstein *et al.*, 1975), the Mattis Dementia Rating Scale (Mattis, 1976) – more appropriate for FTD and subcortico-frontal dementias – or the Wechsler Adult Intelligence Scale (R-WAIS) (Wechsler, 1955).

*Temporospatial orientation* is impaired at early stages of AD, while it may be relatively preserved in other diseases with dementia.

*Memory impairment* is classically required to fulfil the criteria for the diagnosis of dementia. However, the term memory encompasses more than one process. Episodic memory is affected early in AD. By contrast, impairment of semantic memory or procedural memory may be prominent in some non-AD dementias.

*Language and literacy skills, praxis, visuospatial and visuo-perceptual function* can all be affected in dementia disorders (I). These cognitive domains, often referred to as instrumental functions, are specifically impaired in diseases with a prominent cortical involvement such as AD and DLB.

*Executive functions* are mainly impaired in FTD (Neary *et al.*, 1988; Miller *et al.*, 1991) and subcortico-frontal dementias (Cummings, 1986; Pillon *et al.*, 1996) (I). These deficits may be apparent in spontaneous speech (echolalia or quasi-mutism) or in spontaneous behaviour (apathy and general slowing).

#### *Recommendations*

- Cognitive assessment is central to diagnosis and management of dementias.
- Quantitative neuropsychology exploring individual cognitive domains with validated tests of graded difficulty is a very powerful test. However, it is not routinely available throughout Europe. Neurologists should perform bedside cognitive testing. More extensive neuropsychological testing should be primarily dedicated for mild to moderate forms of the disease and is ideally performed by a neuropsychologist.
- For neurologists, a short cognitive assessment should include a global measure, such as the MMSE, and in addition more detailed testing of the main cognitive domains. These should include: (1) word list recall; (2)

temporospatial orientation; (3) naming; (4) drawing (the plan of the room, a cube or a clock); (5) uni- and bimanual postures execution; (6) similarities and verbal fluency.

### Behavioural assessment

Behavioural disorders may be observed in all dementias (Cummings *et al.*, 1994) (II). They are primary manifestations of the disease process, but environmental factors and concomitant disorders may contribute. Behavioural disorders may require specific therapeutic intervention and represent the main cause of institutionalization, given their burden on caregivers. Their presence may contribute to the differential diagnosis. For example, cognitive deficits predominate in AD, but lack of personal concern and disinhibition are the main characteristics of FTD (Neary and Snowden, 1996) (II), and delusions and hallucinations are early symptoms of DLB (McKeith *et al.*, 1996) (II).

*Apathy and inertia*, independently of depressive mood, are the most common behavioural changes in patients with dementia (Cummings *et al.*, 1994) (I). *Unawareness and anosognosia* are frequent in AD even at early stages. These patients, however, may show signs of anxiety and agitation when confronted with tasks or unfamiliar situations. In contrast a lack of concern and indifference are characteristic of FTD (Neary and Snowden, 1996) (II). *Dysphoria* must be assessed independently of weight loss, appetite changes, sleep disturbances and retardation that occur in dementia even in the absence of depressed mood. Evaluation must assess the core psychological manifestations of depression: tearfulness, sadness, thoughts of worthlessness and hopelessness, and statements about death and suicide. *Agitation and aggression* are one of the main causes of institutionalization. Purposeless activities such as pacing and rummaging are characteristic of AD (Reisberg *et al.*, 1987) (II), while compulsions and repetitive stereotyped behaviours are more common in FTD (Brun *et al.*, 1994) (II). Efforts to understand the possible meaning of agitation or aggression in patients with impaired communication, and to modify environmental and care guidelines accordingly, may be useful in managing these behaviours. *Disinhibition and euphoria* are characteristic of patients with frontotemporal dementias who may exhibit familiarity with strangers, jocularity, impulsivity, hyperorality, lack of social restraints, psychopathic behaviours and emotional lability (Neary and Snowden, 1996). *Delusions, hallucinations and misidentifications of persons or places* are frequently observed in patients with dementia. They are one of the earliest symptoms of DLB (McKeith *et al.*, 1996) (II). Delusions are often persecutory and frequently involve

convictions of theft (Morris *et al.*, 1990). Hallucinations are most commonly visual and occur in up to 30% of patients with dementia (Swearer, 1994).

### Recommendations

- Assessment of behavioural disorders is essential for the diagnosis and management of dementia.
- The assessment should be based on caregiver interview or questionnaire using measures that investigate several behavioural domains such as the Behave-AD (Reisberg *et al.*, 1987), the Neuropsychiatric Inventory (Cummings *et al.*, 1994) or, for FTD, the Lund and Manchester criteria (Neary *et al.*, 1998).

### Assessment of activities of daily living

A loss of functional autonomy is a feature of dementia. Therefore, the assessment of function in daily life is part of the diagnostic process and allows clinicians to evaluate the need for personal and institutional care. This evaluation can rely on generic scales [e.g. instrumental activities of daily living (IADL): Lawton and Brody, 1969] or on dementia-specific scales (e.g. the Blessed Dementia Rating Scale: Blessed *et al.*, 1968).

### Recommendation

- Assessment of activities of daily living should be included in the diagnostic evaluation and management of dementia.

### Neuroimaging

In the diagnostic work up of a patient with dementia neuroimaging may serve to rule out specific diseases, such as a space-occupying lesion, and to reveal abnormalities that may aid in diagnosing specific underlying causes (I–II). If structural imaging, X-ray computerized tomography (CT) or magnetic resonance imaging (MRI) is performed to rule out focal brain diseases that may cause dementia, the yield is generally low when there is no clinical suspicion (Engel and Gelber, 1992). However, in one study 6% of patients had unexpected findings on neuroimaging (Chui and Zhang, 1997) (II), and potentially life-threatening conditions such as a brain tumour or subdural haematoma may be identified as may ischaemic lesions that are potentially amenable to treatment and may alter the course of dementia even in AD (Pasquier *et al.*, 1998) (II).

In the ideal situation structural neuroimaging should be performed in every patient with suspected dementia. If exclusion of treatable causes and gross vascular abnormalities only is indicated, a non-contrast CT will suffice. When available, MRI should be performed. Functional brain imaging [single photon emission

computed tomography (SPECT), positron emission tomography (PET) and functional MRI] can show patterns of hypometabolism which may supplement structural imaging (II). The specific neuroimaging findings of some of the dementias are discussed below.

### **Alzheimer's disease (AD)**

In the early stage of AD atrophy of the medial temporal lobe occurs. This is clearly visualized with MRI and correlates well with loss of cognitive functions (Laakso *et al.*, 1995) (II). MRI is best used to visualize medial temporal lobe atrophy (Laakso *et al.*, 1995; Scheltens *et al.*, 1997; Laakso *et al.*, 1998) (II), although CT has been found to be useful in some studies (Jobst *et al.*, 1997) (II). In AD patients CT, and especially MRI, may show abnormalities of the white matter or basal ganglia that may add extra information regarding the coexistence of vascular damage which may alter the disease course (Wahlund *et al.*, 1994; Lopez *et al.*, 1995) (II). Temporoparietal hypoperfusion demonstrated by SPECT may support the clinical diagnosis of AD (AAN, 1996) (II) and hypoperfusion in the medial temporal lobe may be the earliest sign of AD (Johnson *et al.*, 1998) (II). The value of SPECT to differentiate AD patients from patients with VaD is limited (Mielke *et al.*, 1994) (III).

### **Dementia with Lewy bodies (DLB)**

There is no specific imaging characteristic of DLB. Recent MRI findings from a population-based study in Newcastle (Harvey *et al.*, 1999) suggest that the absence of medial temporal lobe atrophy has a high specificity for the distinction between DLB and AD (II). Medial temporal lobe atrophy on MRI is exceptional in DLB and suggests concomitant AD (Barber *et al.*, 1999).

### **Vascular Dementia (VaD)**

According to most criteria, a diagnosis of VaD cannot be made without neuroimaging evidence of cerebrovascular disease. The NINDS-AIREN criteria (Roman *et al.*, 1993) specifically mention multiple large vessel infarcts, one single strategic infarct, multiple lacunes in the basal ganglia and/or white matter or extensive white matter changes only. Changes in the white matter on CT are mostly vascular while on MRI this is less certain. SPECT has no added value in the diagnosis of VaD (III).

### **Focal atrophy syndromes**

In FTD CT and MRI may show focal atrophy in the

frontal and/or temporal regions, but may be normal in the early phase (Neary *et al.*, 1998). Focal atrophy may also be seen in cases of progressive non-fluent aphasia, semantic dementia, corticobasal degeneration and posterior cortical atrophy. In addition, specific cerebrovascular lesions may cause clinical syndromes mimicking FTD. SPECT may show focal hypoperfusion in the absence of clear atrophy and may be of diagnostic help in focal atrophy syndromes (Neary *et al.*, 1998) (II).

### **Creutzfeldt-Jakob disease (CJD)**

This rare condition usually shows cortical atrophy on CT and MRI. At some stage of the disease an unusually high signal is seen on T2-weighted MRI in the putamen or globus pallidus (Milton *et al.*, 1991), which may be specific (II).

### **Normal pressure hydrocephalus (NPH)**

This diagnosis is made clinically, but on CT or MRI the characteristic ventricular enlargement is visualized. Vanneste *et al.* (1992) formulated CT criteria for a positive response to shunting, of which the absence of white matter lesions and cortical atrophy are the most important (II).

### *Recommendations*

- Neuroimaging should be performed once in all cases of dementia referred to a neurologist. Non-contrast CT will suffice, but if available MRI is preferred and may be used to show specific abnormalities.
- Functional imaging should not be used routinely, but may be of help where there is clinical suspicion of degenerative disorders and structural imaging is normal.

## **Other investigations**

### **Laboratory investigations**

The aim of blood tests is rarely to identify the cause of dementia, but rather (1) to identify comorbidity and/or complications; (2) to reveal potential risk factors; and (3) to explore the background of frequently associated confusional states. Laboratory screening is recognized as an important integral part of the general screening of a patient presenting with cognitive disturbances. However, in a patient presenting with a typical phenotype of AD the diagnostic yield of laboratory tests is low unless there is comorbidity. The neurologist is often dealing with patients with confusional states, rapid progression,

mild cognitive disturbance or atypical presentations, in whom blood tests may be of diagnostic value (II).

#### *Recommendations*

- Laboratory screening should be included as a part of the general screening of a patient presenting with cognitive disturbances.
- The following blood tests are generally proposed for all patients: blood sedimentation rate; complete blood cell count; electrolytes; glucose; renal and liver function tests; thyroid-stimulating hormone. Serological tests for the detection of *Borrelia*, syphilis and HIV, serum lipids and vitamin B12 are optional. More extensive tests will often be required in individual cases.
- Electrocardiography (ECG) is recommended in all patients aged above 50 years for screening purposes, in patients with cardiac symptoms or cerebrovascular lesions, and for monitoring possible side-effects in patients receiving drug therapy (e.g. acetylcholinesterase-inhibitors). X-ray of the chest is indicated if relevant to the symptoms.

#### **Cerebrospinal fluid (CSF)**

Examination of CSF may be useful in cases of CJD (Hsich *et al.*, 1996), central nervous system inflammatory disease or vasculitis, demyelinating diseases and in atypical cases (young onset, rapid progression, marked fluctuation, extensive white matter changes on CT or MRI) (I–II). Tests for biological markers of AD in spinal fluid, such as tau protein and soluble  $\beta$ -amyloid are available (Hulstaert *et al.*, 1999) (II), but their diagnostic value is not yet established.

#### *Recommendation*

- CSF analysis (with routine cell count, protein, glucose and protein electrophoresis) is optional and recommended in patients with a clinical suspicion of certain diseases and in patients with atypical clinical presentations.

#### **Electroencephalography (EEG)**

EEG has no added value in the diagnosis of AD and VaD. EEG may be diagnostic in some unusual causes of cognitive disturbances: CJD and epilepsy. EEG is often normal in frontotemporal dementia (Neary *et al.*, 1998)

#### *Recommendation*

- Electrophysiological examination is not recommended as a routine study.

#### **Brain biopsy**

Brain biopsy is indicated only in cases where the suspected disease can be causally and/or symptomati-

cally treated and where brain biopsy is the only method of achieving specific confirmation of the underlying disease (e.g. primary cerebral lymphoma, vasculitis). Other tissue biopsies (lymphoid system, skin, muscle, liver or bone marrow) for diagnostic evaluation of certain disorders require the involvement of experts working in specialized neurological centres.

#### *Recommendation*

- Brain biopsy is recommended in very carefully selected cases only.

#### **Genetic testing**

The majority of degenerative dementias can occur as autosomal dominant disorders with similar phenotypes to sporadic disease. The frequency of familial occurrence varies from being a rarity (e.g. in DLB) to frequent, as with some of the frontal lobe degenerations. Many familial disorders may be associated with cognitive impairment which is overshadowed by other clinical features and many metabolic disorders with recessive inheritance, which may present to neurologists (Coker, 1991), are not discussed further here. A number of pathogenic mutations associated with familial degenerative dementias have now been identified, providing opportunities for specific diagnoses in affected patients and pre-symptomatic testing in at-risk individuals. Mutations associated with degenerative dementias have been identified in pre-senilin and amyloid precursor protein genes (AD), in the tau gene (chromosome 17 linked dementias), in the prion protein gene (prion disorders) and in the Notch 3 gene (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy: CADASIL). Mutations in the synuclein, superoxide dismutase, Huntington, ubiquitin hydrolase and ataxin genes have been reported in familial neurological disorders in which cognitive disturbance may also occur. In addition, an expanding list of genetic risk factors have been identified for dementia of which the apolipoprotein E4 allele as a risk factor for AD is the best established.

Screening for mutations involves management of the family as well as the individual, with adequate counselling and explanation of risk. This should only be performed in association with clinical geneticists or in specialist centres with appropriate expertise. Mutation screening in individuals without a family history is rarely indicated unless there is a characteristic phenotype and inadequate pedigree history. Where there is a clear family history of autosomal dominant inheritance, appropriate gene screening can be guided by the clinical phenotype. Where the family history is less clear, the

consent becomes more important, and the likelihood of identifying mutations reduced.

### Recommendations

#### Affected individuals

- It is essential to obtain consent from the patient and/or family carer and to provide counselling, as identification of the mutation has clear implications for other family members.
- Post-mortem diagnosis of the cause of a familial degenerative dementia is critically important in future counselling for the family and should be discussed.
- At present there is no clear benefit in apolipoprotein E genotyping to assist with diagnosis (American College of Medical Genetics/American Society of Human Genetics Working Group on ApoE and Alzheimer disease, 1995; McKeith and Morris, 1996; National Institute on Ageing/Alzheimer's Association Working Group, 1996).

#### Pre-symptomatic testing

- Pre-symptomatic testing is available where there is a clear family history and where there is a known mutation in an affected individual to ensure that a negative result is clinically significant. It is recommended that the Huntington's disease protocol (Harper *et al.*, 1990) is followed.
- Apolipoprotein E genotyping for risk assessment is not recommended (American College of Medical Genetics/American Society of Human Genetics Working Group on ApoE and Alzheimer disease, 1995; McKeith and Morris, 1996; National Institute on Ageing/Alzheimer's Association Working Group, 1996).

## Treatment of dementia

### General management principles

The physician in charge of the treatment and care of the patient should schedule regular follow-up visits (American Psychiatric Association, 1997) (II). The purposes of planning systematic follow-up include: (1) to ensure identification and appropriate treatment of concomitant conditions and of complications of the primary dementia disorder; (2) to assess cognitive, emotional and behavioural symptoms; (3) to evaluate treatment indications and to monitor pharmacological and non-pharmacological treatment effects; (4) to assess caregiver burden and needs; (5) to assess sources of care and support; (6) to provide continuous advice and guidance to patient and caregiver on health and psychological issues, safety measures, driving, legal and financial matters; and (7) to administer appropriate caregiver interventions. Support groups for mildly affected

patients with AD may facilitate advice and education for patients (III).

### Treatment of cognitive symptoms in dementia

Recent attempts at treatment of cognitive symptoms in dementia have largely been aimed at AD and to some extent VaD. Among various strategies developed acetylcholinesterase inhibitors (AChE-I) have emerged as the only treatment approach with demonstrable efficacy in large-scale trials. The efficacy of tacrine (Davis *et al.*, 1992), donepezil (Rogers *et al.*, 1998) and rivastigmine (Corey-Bloom *et al.*, 1998) has been shown in placebo controlled, prospective, randomized clinical trials in patients with mild to moderate AD (I), and these drugs are registered in most of Europe. Statistically significant effects were shown on cognitive functions, activities of daily living and overall functioning; some beneficial behavioural effects were also observed. Currently AChE-I represent the only drugs registered for the symptomatic treatment of AD.

In addition to symptomatic treatment strategies there have been attempts to modify disease progression. Meta-analysis of retrospective, cross-sectional epidemiological data suggest that long-term use of non-steroid anti-inflammatory drugs (NSAIDs) (McGeer *et al.*, 1996) (II) and use of oestrogens in post-menopausal women (Yaffe *et al.*, 1998) (II) may have prophylactic effects, although the results are not consistent for the latter. High-dose vitamin E and selegiline were found in a post hoc analysis to slightly improve functional outcome in patients with moderately advanced AD after two years of treatment (Sano *et al.*, 1997) (I). None of these drugs is, however, yet registered for the treatment of AD, and their routine use cannot be recommended at this time.

Aspirin was found to improve or stabilize decline in cerebral perfusion and cognitive performance of patients with multi-infarct dementia in a small study (Meyer *et al.*, 1989) (II). In a pilot study the AChE-I donepezil was found to have beneficial effects in patients with DLB, mostly on hallucinations, less so on cognition and overall function (Shea *et al.*, 1998) (III). A more extensive evidence-based review of pharmacological treatment is found elsewhere (Emre and Hamadasy, 2000).

### Recommendations

- A therapeutic trial with an AChE-I may be considered in patients with mild to moderate AD (MMSE 10–26).
- If a trial is given, there should be a caregiver who can assist in administering the treatment. Treatment effects and side-effects should be monitored periodically and

discontinuation of treatment be considered when there are no signs of benefit.

- Data are still being gathered on long-term benefits, activities of daily living and health economics. Until these data are available, decisions on a trial to treat should be on an individual physician basis.

#### **Pharmacological treatment of non-cognitive symptoms**

Dementia can be associated with a variety of non-cognitive problems (agitation, aggression, irritability, restlessness, hallucinations, delusions, anxiety, depression, insomnia). These symptoms are usually dealt with by psychiatrists, but at times neurologists may have to treat them as well. Before considering pharmacological treatment for non-cognitive problems all potential exogenous factors should be sought and if possible eliminated. Should the non-cognitive problem still persist it should first be decided if the problem is severe and significant enough to necessitate pharmacological intervention. As a rule the treatment should be started at low doses and increased only slowly if no response is elicited. Monotherapy should be the target, introducing one drug at a time and optimizing the first drug before changing or adding new drugs. In general, drugs with fewer anticholinergic adverse effects should be considered. After successful treatment the need for continued treatment should be assessed by lowering the dose and eventually an attempt should be made to discontinue the medication. An evidence-based review of the extensive literature on the treatment of non-cognitive symptoms of dementia can be found elsewhere (American Psychiatric Association, 1997; Emre and Hamdasy, 2000).

#### *Recommendation*

- Neurologists should be aware of non-cognitive symptoms in patients with dementia. Assessment and treatment of non-cognitive symptoms is best undertaken by multidisciplinary teams.

#### **Non-pharmacological treatment**

Non-pharmacological treatment, or psychosocial interventions, should be considered in the treatment of cognitive, as well as emotional and behavioural, disturbances and other functional manifestations of the disease. The term is often used to comprise a number of specific therapeutic intervention principles for patients, as well as caregiver intervention programs.

Psychosocial interventions may be classified into cognition-orientated, behaviour-orientated, emotion-orientated and stimulation-orientated treatments. The treatment programs differ in goal and content, but are all non-specific in that they apply to patients with dementia of any type. The treatment principles and

scientific evidence were recently reviewed by the American Psychiatric Association (1997), and the Cochrane library holds recently updated systematic reviews on the effects of reality orientation therapy (Spector *et al.*, 1999a) and reminiscence therapy (Spector *et al.*, 1999b). In general, there is limited evidence for treatment effects from randomized clinical control trials. Thus, most of the treatments are supported by other research findings, clinical practice or common sense. Patients with emotional symptoms, sleep disturbances and problem behaviours may benefit from behaviour-orientated therapy (Landreville *et al.*, 1999) (II–III). Psychosocial interventions, and particularly cognition-orientated treatment, may precipitate or worsen anxiety, depression or frustration. Therefore, any psychosocial treatment program must be designed in the light of the cognitive capacity and level of tolerance of the patient and possible adverse effects of the treatment must be monitored.

#### *Recommendation*

- In a patient with dementia and problem behaviours or emotional symptoms it is important to consider non-pharmacological interventions as an adjunct – or substitute – to pharmaceutical treatment.

#### **Intervention for caregivers**

Most AD patients are cared for at home by a family caregiver, most often a spouse, and caregivers play an essential role in the care of patients, even when formal care programs and support services are also available. Numerous studies have documented the burdens and stress and the psychological and physical morbidity associated with the role of caregiver to a patient with AD (Haley, 1997; Dunkin and Anderson-Hanley, 1998). Caregiver stress may affect the course of the dementia and is a significant predictor of institutionalization. Caregivers may benefit from education and information about AD, support groups, respite care and individualized intervention (Flint, 1995; Haley *et al.*, 1987; Brodaty *et al.*, 1993; Knight *et al.*, 1993; Haley, 1997; Dunkin and Anderson-Hanley, 1998). Some centres have set up formal and structured caregiver intervention programs, often combining education, support groups (for caregivers displaying minimal distress), respite care, family therapy (for selected families) and individual psychological intervention (for caregivers with moderate to severe distress or psychopathology). Combined intervention programs have been shown in a large randomized controlled trial to reduce psychological morbidity in caregivers (Mittelman *et al.*, 1995) (I) and to delay institutionalization and death of patients (Brodaty *et al.*, 1993; Mittelman *et al.*, 1993, 1996) (I), although other studies have failed

to show any effect. Respite care has been shown in controlled studies to delay nursing home placement, but effects on caregiver burden or depression could not be demonstrated (Dunkin and Anderson-Hanley, 1998).

#### *Recommendation*

- Assessment of caregivers' distress and needs and administration of intervention programs for caregivers should be an integral part of the management of patients with dementia.

### **Implications for driving**

Cognitive impairment is an important cause of road traffic accidents, and advice about driving is an essential part of the management of the patient with dementia (Johansson and Lundberg, 1997). There is however, considerable variability across Europe with respect to the national driving regulations for patients suffering from disorders associated with dementia and to the role of neurologists. Few countries have specific guidance although some (Sweden) give specific guidance and recommend the DSMIV (American Psychiatric Association, 1993) or ICD-10 (World Health Organisation, 1992) diagnostic criteria. By contrast, many countries use outdated terminology such as cerebral sclerosis or severe senescence. In some (Portugal) there is a designated role for neurologists in the decision to permit a license. Some countries draw a distinction between an ordinary driving license and one which permits the driving of large vehicles such as lorries or public service vehicles such as buses and trams. Confidentiality also varies. In some countries (UK, the Netherlands) confidentiality to the patient takes precedence, whereas in others (e.g. Denmark), the physician has an obligation to inform the health authority and/or police department if advice to stop driving is ignored.

#### *Recommendations*

- All patients and or caregiver should be asked about driving.
- An assessment of driving ability should be guided by current cognitive function and by a history of accidents or errors whilst driving. Particular attention should be paid to visuospatial, visuoperceptual, praxis and frontal lobe functions together with attention.
- Advice either to allow driving but to review after an interval, to cease driving, or to refer for retesting should be given. This decision must accord with the national regulations of which the neurologist must be aware.

### **Education and training of neurologists**

We recognize that these guidelines anticipate an increased work load for neurologists, and a commensurate focus on education and training of neurologists in this area. With the significant advances in neuroscience research, particularly in the field of behavioural neurology, and with the increasing prevalence of dementia, the need for appropriate and timely neurological involvement will increase. Hence, it is essential that diagnostic evaluation and management of dementia should be included in the training of all neurologists (Menken, 1998). The training should include individual patient based training under competent mentoring, as well as the teaching of up-dated information on basic science issues relevant to dementia, and on diagnostic evaluation and treatment of AD and other dementia disorders. The education of neurologists in the field of dementia should be guided by the 'Edinburgh Declaration' (World Federation for Medical Education, 1988) and the 'Doctors for Health' global strategy of the WHO (WHO, 1996) and provide the neurologist with a population-based perspective that encourages appropriate utilization of available specialized resources and personnel.

#### *Recommendation*

- Diagnostic evaluation and management of dementia should be included in the training of all neurologists in Europe.

### **Conclusion**

Neurologists should play an active role in the diagnostic evaluation of patients with cognitive disturbances and have a key role in the referral to and interpretation of certain ancillary investigations (lumbar puncture, neuropsychological testing, brain imaging, brain biopsy).

For some patients the neurologist is the primary physician in charge of the treatment and care. In these circumstances the neurologist should take part in the general management and in specific psychosocial treatments, and assure the organization of psychosocial interventions for patients as well as for caregivers in collaboration with the community facilities. For most patients the neurologist acts as a consultant, but should be aware of available psychosocial treatment principles and caregiver intervention programs and refer the patients to appropriate programs.

There are inadequate data on the cost-effectiveness of practice parameters for diagnostic evaluation and treatment of dementia. Therefore, the recommendations in this guideline are consensus recommendations based on individual patient management, and their

practice has to be implemented in the light of available resources.

There is a clear need to clarify the role of the neurologist. Our review of the management of dementia in European countries revealed considerable differences. In some countries neurologists have taken the lead in the management of patients with dementia, while in other countries the neurologist is rarely involved. We recommend that neurologists should have a clear role in the management of dementia in the whole of Europe. Neurologists should be involved in the diagnostic evaluation of dementia, and should facilitate the development of multidisciplinary teams for diagnostic evaluation of patients with cognitive disturbances and dementia. After the diagnostic evaluation the neurologist should ensure that the management of patients with dementia includes multidisciplinary multi-agency collaboration.

It is essential that diagnostic evaluation and management of dementia should be included in the training of all neurologists.

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