DEMENTIA: DIFFERENTIAL DIAGNOSIS

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CONTENTS

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Conceptual Development

The origin of the term "dementia" is in the Latin word demens, i.e., out of one's mind. It first appeared in the third book of De Re Medicina of Aurelius Cornelius Celsus, who used the term to describe the disorder which may follow fever-induced, transient delirium (Berrios, 1981). By recognizing that not all cases of delirium were followed by "insanity," but only those in which "a continuous dementia begins," Celsus - during the reign of Tiberius (AD 14-37) - set the stage for the development which culminated in the separation of chronic organic (neuropsychiatric) disorders from acute organic (psychotic) states.

The origin of current diagnostic concepts relevant to dementing illness is in the work of Bayle (1825). Stimulated by Morgani's (1761) attempt to correlate postmortem findings in the brain with clinical manifestations, Bayle (1822) recognized that chronic arachnoiditis (arachnitis) leads to dementia in the terminal stage of its development.

Bayle's (1822) recognition that chronic arachnoiditis leads to dementia triggered interest in the study of clinical neuropathologic correlations. It was in the course of this research that several dementing diseases with distinctive neuropathologic changes were identified. Included among them are

Huntington's chorea (discovered in 1872), Pick's disease (identified in 1892), Binswanger's disease (separated in 1894), Alzheimer's disease (described in 1907) and Creutzfeldt-Jakob's disease (recognized in 1920). The common characteristic of all these disorders is an irreversible-progressive course.

Simultaneously with this development, the dysmnesias -- disorders characterized by severe memory impairment with selective disorientation to time and place without global personality deterioration -- such as Kahlbaum's (1863) presbyophrenia (or paraphrenia senilis) and Korsakoff's (1887) amnestic psychosis (or amnestic syndrome) -- were separated from the dementias (Wernicke, 1900); the term "Vesanic dementia" was replaced by the term "pseudodementia" (Wernicke 1894); the diagnostic concept of pseudodementia, a reversible cognitive impairment in the absence of neuropathologic changes was differentiated from real (true) dementia; and the diagnostic concept of exogenous psychosis, displayed in delirium, was distinguished from the organic psychosis, displayed by dementia (Bonhoeffer, 1909). Considering that delirium is one of the two main conditions associated with pseudodementia, with the introduction of the diagnostic concept of exogenous psychosis, Celsus' original distinction between transient delirium and irreversible dementia has become of diagnostic significance.

It was in 1898 that Binswanger (1898) introduced the term "presenile dementia" for "degenerative disorders of the nervous system which give rise to dementia during middle age". The concept was adopted and further elaborated by Kraepelin (1909), who perceived presenile dementia as a malignant form of senile dementia, which begins at an earlier than senile age (Mayer-Gross, Slater and Roth, 1960). In spite of this and the rapidly increasing number of disorders with prevalent dementia identified, the diagnostic significance of the dementia syndrome had remained hidden in the classifications of Kraepelin (1883-1909). It was only in Eugen Bleuler's (1916) classification where the use of the term dementia was restricted for the first time to the "acquired psychoses with coarse brain disease" (Table 1).

At present, there are at least 10 different classes of disorders (Cummings, 1987) (Table 2), and more than 150 different illnesses (Koranyi, 1988) which lead to dementia in their terminal stage. Nevertheless, it is generally acknowledged that among all the dementias by far the most frequently encountered are the degenerative and the vascular dementias of old age (Table 3).

Dementing Illnesses

Senescent Forgetfulness

The origin of the diagnostic concept of "senescent forgetfulness" (SF) was in the work of Kral (1959) who was the

Table 1

Huntington's Chorea	**1872**
Pick's Disease	**1892**
Binswanger's Disease	**1898**
Alzheimer's Disease	**1907**
Creutzfeldt-Jakob's Disease	**1920**
Kahlbaum's Presbyophrenia	**1863**
Korsakoff's Amnestic Psychosis	**1887**
Wernicke's Pseudodementia	**1894**
Binswanger's Presenile Dementia	**1898**
Kraepelin's Senile Dementia	**1909**
Bonhoeffer's Exogenous Psychosis	**1909**
Bleuler's Acquired Psychoses with Coarse Brain Disease	**1916**

Development of concepts relevant to dementia and to the differentiation of the dementia syndrome from other syndromes.

Table 2

1.	Degenerative	6.	Hydrocephalic
2.	Vascular	7.	Inflammatory
3.	Myelinoclastic	8.	Infectionrelated
4.	Traumatic	9.	Toxic
5.	Neoplastic	10.	Metabolic

Ten etiologically different classes of disorders which may lead to dementia in the terminal stage of their development. (Based on Cummings: Dementia Syndromes: Neurobehavioral and neuropsychiatric features. J. clin. Psychiatry 48 Supplement: 3-8, 1987)

Table 3

	Prevalence in General Population	Contribution to Dementia Syndrome
Alzheimer's disease	+ + +	+ + +
Pick's disease	+	+
Huntington's disease	+	+
Progressive Supranuclear palsy	+	+
Vascular		
- Postanoxic	+	+
- Multi-infarct	+ +	+ + +
- Arteritis	+	+
Parkinson's disease	+ +	+ +
Brain tumor	+	+
Head trauma	+ +	+
Normal pressure hydrocephalus	+	+
Drug toxicity	+ + +	+ +
Alcohol abuse	+ + +	+ +
Depression	+ + +	+ +
Sensory deprivation	+ + +	+
Metabolic disorders		
- Thyroid or	+ +	+
- Sodium or	+ + +	+
- Calcium or	+ +	+
- Glucose or	+ + +	+
- Hepatic failure	+ +	+
- Renal failure	+ +	+
- Adrenal or	+	+
- B_{12}	+	+
Nutritional		
- B_6	+	+
- Thiamine	+	+
- Folate	+	+
- Ascorbic Acid	+	+
Infections		
- HIV	+	+
- Neurosyphilis	+	+
- Other, e.g., (Whipples disease, Behcet disease, Creutzfeldt-Jakob disease)	+	+
Neurotoxic metals		
- Aluminum	+	+
- Heavy metals, e.g., (lead, tin, manganese, mercury)	+	+
Carcinoma (remote effects)	+ +	+
Miscellaneous conditions	+	+

[+ = low; + + = intermediate; + + + = high.]

Prevalence of different conditions which may cause dementia in the general population and their contribution to the development of the dementia syndrome. (Based on Canadian Consensus Conference on the Assessment of Dementia, 5-6 October, 1989)

first to demonstrate that SF consists of two distinctive diagnostic groups he referred to as "benign senescent forgetfulness" (BSF) and "malignant senescent forgetfulness" (MSF).

Within Kral's (1962) dichotomy, BSF represents an anomaly of recall with an effect on events in subjects remote memory; and is characterized by forgetfulness which remains restricted to relatively unimportant details, such as names and places, in subjects experience in the distant past which are not accessible for recollection at one time, but can be recalled at another time. Another important characteristic of BSF is that it does not extend to include the event of which the "unimportant details" are an integral part; and since registration and retention are preserved, it leaves the key experience accessible for recollection at any time. The third and final characteristic of BSF is that subjects are keenly aware and concerned about their forgetfulness.

MSF, in variance with BSF, represents an anomaly of recall with an effect on events in subjects recent memory; and is characterized by forgetfulness which does not remain restricted to relatively unimportant details, but extends to the event and/or experience of which the unimportant details are an integral part. Another important characteristic of MSF is disorientation, at first to time and place, but later on to personal data, with confabulations associated with a retrogressive loss of remote

memories. The third and final characteristic of MSF is that subjects are unaware of their deficit and, as a result, not concerned about their forgetfulness.

Almost 30 years after the introduction of the concept of BSF, Crook et al. (1986) proposed the introduction of a similar diagnostic concept, referred to as Age Associated Memory Impairment (AAMI); and developed criteria on the basis of which AAMI can be reliably diagnosed. An important impetus in the formulation of these diagnostic criteria were the findings that in variance with sensory, primary (short-term or immediate) and tertiary (remote) memories, which were little affected, secondary (recent or long-term) memory clearly showed substantial age-related deficits at early stages of the aging process, when the performance of old and young individuals were compared.

Senile Dementia of the Alzheimer's Type

Unitary Concept: AD

The origin of the diagnostic concept to become known as Alzheimer's disease (AD) was in the description of the clinical manifestations and the underlying neuropathologic changes in a 51-year-old female, admitted to the Psychiatric Clinic of the University of Frankfurt in November 1901. During her hospitalization, the patient displayed a "relentlessly progressive dementia" with aphasia, disorientation and paranoid thinking,

leading to death within a relatively short period of time. At the beginning, Alzheimer (1907) himself was hesitant to designate this rather dramatic clinical presentation as a nosologic entity. Therefore, it was only upon the insistence of Emil Kraepelin (1909-1915) that the early onset, rapidly progressing, deadly dementia with cerebral atrophy, ventricular enlargement associated with agnosia, aphasia and apraxia Alzheimer described (1907) became known as Alzheimer's disease (AD) (Koranyi, 1988).

Since Alzheimer (1907) identified the disease on the basis of specific histopathologic findings, to date, the hallmarks of the disease have remained the presence of argentophil (senile neuritic) plaques and neurofibrillary tangles.

Dichotomy: AD vs SDAT

In the eighth edition of his textbook, Kraepelin (1909) separated late onset senile dementia (SD) from the early onset presenile dementia of AD. Nevertheless, since apart from the arbitrary dividing line of 65 year of age, no qualitative difference between the two could be identified (Kidd, 1964), during the 1970's the early onset and late onset disease were pooled together under the diagnostic concept of senile dementia of the Alzheimer's type (SDAT) (Terry and Wisniewski, 1975).

In spite of all the similarities, however, Bondareff, Mountjoy and Roth (1982) focused attention on the biologic heterogeneity of

the population subsumed under SDAT. They contended that early onset presenile dementia (AD) differs from late onset senile dementia (SD) by its rampant course, greater parietal lobe involvement, more prominent ventricular enlargement and profound impairment of cholinergic functioning. Further support of the dichotomy was provided by Roth (1985), who separated a late onset, Type I (SD) and an early onset, Type II (AD) syndrome; and characterized the former by its continuity and the later by its contiguity with normal aging.

Trichotomy: AD vs SD vs SDAT

In their family genetic study, Heston and Mastri (1977) recognized that Down's syndrome and blood dyscrasias (e.g., leukemia and Hodgkin's disease) are encountered significantly more often among first degree relatives of AD patients (but not of SDAT patients) than in the general population. In view of this, and with consideration to postmortem neuropathologic findings which clearly indicate that there are late onset dementias without Alzheimer's lesions, Gottfries (1989) suggests that within the late onset dementias, the distinction between SD and SDAT should be retained, even if the two are clinically indistinguishable.

Multi-Infarct Dementia

Original Concept

The origin of the concept of multi-infarct dementia (MID) was

in the discovery of a positive relationship between the occurrence of dementia and of multiple cerebral infarcts - with a loss of more than 50-100 ml of cerebral volume - at autopsy (Tomlinson, Blessed and Roth, 1968, 1970). The term was coined by Hachinksi, Lassen and Marshall (1974) who characterized MID by abrupt onset, stepwise deterioration and fluctuating course.

For the diagnosis of MID, and for the separation of MID from SDAT, a simple assessment instrument, based on 13 variables relevant to the evaluation of cerebral ischemia, was developed by Hachinski et al. (1975) (Table 4). The original Hachinski scale, a highly reliable assessment instrument which had been validated in a series of autopsies, was modified by Rosen et al (1980). The modified scale, which consists of 8 of the original 13 variables, is a reliable and valid instrument for the separation of MID from the Alzheimer's type of dementia.

Modified Concept

In variance with the original unitary concept, today MID is perceived as a disease category which consists of four distinctive types (Alexander and Geschwind, 1984). It includes (1) bilateral hemispheric infarcts, the result of hypertensive disease; (2) water-shed infarcts, the result of low cerebral perfusion; (3) progressive infarction of subcortical white matter; and (4) multiple infarcts due to inflammatory arteritides (Gottfries,

Table 4

Feature	Unmodified Hachinski	Modified Hachinski
Abrupt onset	2	2
Stepwise deterioration	1	1
Fluctuating course	2	-
Nocturnal confusion	1	-
Relative perseveration of personality	1	-
Depression	1	1
Somatic complaints	1	-
Emotional incontinence	1	1
History of presence of hypertension	1	1
History of stroke	2	2
Evidence of associated atherosclerosis	1	-
Focal neurological symptoms	2	2
Focal neurological signs	2	2
Maximum score	18	12
Maximum score for MID	7	6
Maximum score for SDAT	4	3

Comparison of Original and Modified Hachinski Ischemic Score. Numbers indicate points value assigned to each feature in the original score proposed by Hachinski et al. (1975) and in the modified version proposed by Rosen et al. (1980). Minimum unmodified score for MID (multi-infarct dementia) and maximum unmodified score for SDAT (senile demential of the Alzheimer type) are those proposed by Hachinski. Modified score guidelines for the diagnosis of MID and SDAT are based on the experience of Blass and Barclay (1985).

1989). Among them, the most frequently encountered is progressive infarction of subcortical white matter, referred to as leukoaraiosis (Hachinski, Potter and Merskey, 1987), because it produces "white matter lucency" detectable by CT scan and/or MRI. Considering that leukoaraiosis is present in as many as one-third of the patients with dementia (Hachinski, 1990; Steingart et al., 1987), it should not be surprising that the high prevalence of MID in the general population has not changed, in spite of the steady decrease during the past three decades in the incidence of strokes (Brust, 1983; Whisnant, 1984) and in the incidence of widespread lacunar infarctions due to uncontrolled hypertension (Fisher, 1982; Roman, 1987a).

While it remains questionable whether it would be justified to lump all "white matter lucency" under Binswanger's disease or subcortical arteriosclerotic leukoencephalopathy (Roman, 1987b), by now it is generally acknowledged that leukoaraiosis is intimately linked with amyloid angiopathy, one of the causes of spontaneous intracerebral hemorrhage, a disorder which shows an increase in incidence with advancing age (Hachinski, 1990; Tomonaga, 1981).

Classification of Dementing Illness

During recent years, numerous classifications of dementing illness have been proposed. Although some of these

classifications, such as, for example, the classification of Gottfries (1989), which provides some insight into etiology, severity and course, may offer some advantages for the practicing physician, the generally accepted classification of dementing illness has remained the traditional dichotomy which separates the primary from the secondary dementias.

Primary Dementias

It is estimated that, with the inclusion of the vascular dementias, 80-90 percent of the dementias in elderly patients are primary dementias, in which the etiology of the dementia is a primary degeneration or dysfunction of the brain. Among the primary dementias, by far the most frequently encountered are senile dementia of the Alzheimer's type (or primary neuronal degeneration), multi-infarct dementia (including Binswanger's disease) and mixed (SDAT and MID) dementia. Considerably less common are Parkinson's disease (in which dementia may occur in up to 40% of patients), Pick's disease, progressive supranuclear palsy, Creutzfeldt-Jakob's disease and Huntington's chorea (Guterman and Eisdorfer, 1989).

Secondary Dementias

In variance with the primary dementias, in which etiology is a primary degeneration of the brain, in the secondary dementias etiology is a known somatic disorder in time relationship with the

clinical manifestations. Nevertheless, since the same somatic disorder with similar severity induces only in some, and not in all patients manifestations which are perceived as dementia, some believe that secondary dementia can be triggered only in those with a predisposition to dementia who can be expected to develop a dementing illness. An alternative possibility raised is that what is referred to as secondary dementia is not dementia at all, but a subacute confusional state or amentia, with incoherence of thinking and corresponding motor behavior. In keeping with this later contention is that vitamin B_{12} deficiency (i.e., serum B_{12} values below 130 pmol/l) was present in as high as 50 percent of the patients with confusional states, whereas B_{12} deficiency was present in only 23 percent of patients with SD, in 9 percent of patients with MID and 6 percent with AD (Regland et al., 1988).

In a study of elderly patients with dementia, Popkin and MacKenzie (1984) found that 15 percent of their cases were potentially reversible secondary dementias; and that seven special medical disorders accounted for 90 percent of these reversible dementias. Among the seven medical disorders the most frequently encountered were normal pressure hydrocephalus (31%), followed by mass lesions (30%), drug toxicity (12%), thyroid dysfunction, alcoholism, general paresis and psychiatric illness (Guterman and Eisdorfer, 1989).

Real vs Pseudodementia

Among the different psychiatric disorders which might lead to a clinical picture which closely mimics dementia, the most frequent is depression. Because of this, among the secondary dementias the so called pseudodementia of depression (Wells, 1979) has received special attention in the psychiatric literature and given special consideration in differential diagnostic decisions.

The concept of pseudodementia, however, is not restricted to the pseudodementia of depression, but includes a wide variety of other conditions. In fact, the term, introduced by Wernicke (1894), was originally used exclusively in reference to "chronic hysterical states mimicking mental weakness"; and it was more than 50 years later that Madden et al., (1952) adopted it for reversible cognitive impairment in subjects suffering from involutional (primarily melancholic) psychoses. More recently, the term has also been employed in reference to certain acute disorders of consciousness.

With consideration of the historical development of the concept, Bulbena and Berrios, (1986) contend that "pseudodementia represents a collection of clinical states rather than a process, a convergence point for pathological conditions of different etiology where (the) common denominator is an ability to impair cognition or to disable the mechanisms by which cognition is

experienced." By employing this broad frame of reference, they analyzed a "collective sample" comprised of 61 cases of pseudodementia from the literature and found that there are two important subtypes of pseudodementia, one which is associated with depressive illness and another which is associated with delirium, a disturbed state of consciousness.

Because of their frequent occurrence, the separation of delirium and depression from dementia is of great practical importance. Although there are no generally accepted scales for differentiating between the two, delirium can be separated from dementia on the basis of 13 key features identified by Kane, Ouslander and Abrass (1989) (Table 5). Included among these features are onset, awareness and thinking, which in case of delirium are acute, reduced and disorganized, whereas in the case of dementia are insidious, clear and impoverished. Similar to delirium, depression can be separated from dementia on the basis of 27 features identified by Winstead and Milke (1984) (Table 6). A more simple method, based on neurologic findings, memory and affect, was proposed by Vinogradov (1991) (Table 7).

Diagnosis of Dementing Illness

In recent years, numerous test batteries and clinical procedures have been implemented for the early detection and differential diagnosis of dementing illness. Although it is

Table 5

Features	Delirium	Dementia
Onset	Acute, often at night	Insidious
Course	Fluctuating, with lucid intervals during day; worse at night	Generally stable over course of day
Duration	Hours to weeks	Months or years
Awareness	Reduced	Clear
Alertness	Abnormally high or low	Usually normal
Attention	Hypoalert or hyperalert; distractible fluctuates over course of day	Usually normal
Orientation	Usually impaired for time; tendency to mistake unfamiliar for familiar place and persons	Often impaired
Memory	Immediate and recent impaired	Recent and remote impaired
Thinking	Disorganized	Impoverished
Perception	Illusions and hallucinations (usually visual) relatively common	Usually normal
Speech	Incoherent, hesitant, slow or rapid	Difficulty in finding words
Sleep-wake	Always disrupted	Often fragmented sleep cycle
Physical illness or drug toxicity	Either or both present	Often absent, especially in Alzheimer's disease

Delirium vs dementia: differential features. (Based on Kane, Ouslander and Abrass: Essentials of Clinical Geriatrics, 2nd. ed. McGraw Hill, New York, 1989. Adopted from Canadian Consensus Conference on the Assessment of Dementia, 5-6 October, 1989.)

Table 6

Primary depression	Primary dementia
General	
Family usually aware of illness	Family unaware of illness
Onset dated and more accurate	Insidious onset, broadly and vaguely dated
Symptoms of short duration	
Rapid progression	Slow progression
Family history of affective disorder	Possible family history of Alzheimer's disease
Personal History	
Patient with history of depression	No history of depression
Patient complains of cognitive deficits and seeks help	No complaints of cognitive deficits
Patient complains in detail	Complaints are vague
Patient's complaints of cognitive deficits are emphasized	Deficit is concealed
Patient highlights his/her failures	Patients delights in his/her accomplishments
Patient does not try to keep up	Patient struggles with tasks
	Patient relies on notes, calendars and the like
Patient is in distress	Patient unconcerned
Affective symptoms pervasive	Affect is labile and shallow
Behavior incongruent with cognitive dysfunction	Behavior compatible with cognitive dysfunction
Examination	
No sun-downing	Sun-downs
Attention and concentration preserved	Faulty attention and concentration
"I don't know" answers are typical	Frequent "near miss" answers
"Don't know" answers on orientation	Orientation tests poor
Recent and remote memory loss are similar	Recent memory loss greater than remote memory loss
Distressed memory for specific periods is common	No gaps in memory
No glabella or snout reflexes	Glabella and snout reflexes present
Psychological Testing	
Variable performance	Consistently poor performance
Wechsler shows no typical pattern	Great discrepancy between oral and performance scores
Examination of mental status	
No apraxia or agnosia	Has apraxia or agnosia
Will correct and word intrusions	Demonstrates word intrusions
Neurologic Testing	
CT scan normal	Possible abnormal CT with increased ventricular size and cortical atrophy
DST* 60% nonsuppressed	DST may or may not suppress

*DST - Dexamethasone Suppression Test

Primary depression vs primary dementia: differential features. (Based on Kane, Ouslander and Abrass: Essentials of Clinical Geriatrics, 2nd ed. McGraw Hill, New York, 1989. Adopted from Canadian Consensus Conference on the Assessment of Dementia, 5-6 October, 1989.)

Table 7

	Pseudodementia	Dementia
Neurologic Findings	• None	• Dysphasia • Apraxia • Agnosia • Frontal lobe release signs • Other neurologic findings
Memory Tests	• ↓ attention • ↓ concentration • "forgetfulness" • mild confusion about orientation	• short-term memory • patient covers up deficits • disorientation
Affect	• depressed • anxious • irritable • not influenced by suggestions	• mobile affect • patient is redirectable, easily influenced

Differentiation of the pseudodementia of depression from real dementia. (Adopted from Vinogradov: Depressive subtypes differentiated fro pseudodementia in the elderly. The Psychiatric Times. Medicine & Behavior, April, 1991).

increasingly recognized that cognitive changes are not the earliest signs of dementing illness, some believe that testing of memory, language, perception, praxis, problem solving, attention and functional status might still be useful for "planning treatment and management programs for the patient, as well as in determining the rate of deterioration in patients followed over a period of time and the effect of any treatment" (Guterman and Eisdorfer, 1989).

Routine Test Batteries

In recent years, there has been a steadily increasing number of "memory disorders clinics" established for the early detection of dementing illness (Knopman et al., 1985; Larson et al., 1984; Van der Cammen et al., 1987; Zemcov et al., 1984). The establishment of these clinics was triggered by the recognition that patients with a dementia syndrome may have a secondary or reversible dementia which should be detectable by employing a series of biochemical-laboratory tests, neuroradiologic screening and electrophysiologic examinations. However, by now it has been acknowledged that memory clinics employing these procedures have provided a low diagnostic yield (Brodaty, 1990). In keeping with this are the findings of Creasey (1989), who, on the basis of her own data and a review of the literature, concluded that an abnormal test was consistently found in only about 10 percent of cases

screened for dementia. Similarly, Larson et al. (1986), in a study of the diagnostic evaluation of 200 patients older than 60 years with suspected dementia, found that in only 11 cases were laboratory tests required for the diagnosis.

Considering all available information, first Barry and Moskowitz (1988), and later on Gordon and Freedman (1990) concluded that "the large battery of tests frequently ordered has proved to be inefficient and expensive for routine screening to identify total reversible dementia." Although Gordon and Freedman (1990) acknowledged that (in the majority of cases) in the absence of "reversible dementia," there is still a possibility that a considerable proportion of patients has "modifiable" dementia, (i.e., a multifactorial disorder in which certain aspects can be ameliorated), they also recognized that only 3-11 percent of cases, at best, can be improved. Because of this, they asserted that "the most important diagnostic procedure involves careful history-taking and physical examination, including assessment of the mental status, and not an extensive laboratory and neurologic investigation."

Special Procedures

EEG and Brain Imaging

There are only a few special procedures which may contribute to diagnostic decisions in dementing illness. In spite of this,

surface electroencephalography (EEG) and computerized tomography (CT) are routinely employed in the diagnostic evaluation of demented patients. Nevertheless, while EEG results have little to offer beyond the detection of the slowing of alpha rhythm and/or focal abnormalities, there are some indications that studying event related evoked potentials (ERP) may allow for discrimination between cortical and subcortical dementias (Canter, Hallett and Growdon, 1982) and within these categories between different types of dementia, e.g., between AD and SD (Duffy, Burchfield and Lombroso, 1984). Furthermore, some believe that topographic brain imaging by EEG may, in the future, become one of the most valuable tools for the clinical evaluation of dementia, both for initial diagnosis and longitudinal monitoring (Lehmann, 1989).

The same holds true for brain imaging, where routine CT scans have little to offer beyond revealing subdural hematomas and other space occupying lesions, such as cerebral tumor, as well as ventricular enlargement and cortical atrophy. On the other hand, there are some indications that regional cerebral blood flow (CBF) measurements, single photon emission computerized tomography (SPECT) and especially high resolution proton emission tomography (PET) can separate even mildly demented patients from normal subjects by their more severe metabolic abnormalities in the association areas of the neocortex than in the sensorimotor and

calcarine regions (Kumar et al., 1991). Furthermore, some believe that by employing magnetic resonance imaging (MRI), periventricular white matter lesions, i.e., leukoaraiosis, may be detected at a time when no other indicator of dementing illness is present (Hachinski, 1990).

However, in spite of the tremendous progress made in recent years in diagnostic techniques, Lehmann (1989) maintains that at the present time "none of the new sophisticated procedures can give specific and confident diagnostic information on dementias. There are many demented patients whose EEG and CT scans are not abnormal, particularly in the early states of the illness. There are even more patients with abnormal EEG and CT scan findings who are not demented."

Biologic Markers

Neurochemical investigations of the brains of demented patients have shown that there are rather general disturbances present, such as reduced concentrations of choline acetyltransferase activity and reduced concentrations of hydroxytryptamine and 5-hydroxyindolacetic acid in cortical and subcortical areas (Gottfries, 1989). However, in studies by Parnetti et al. (1987) and Brane et al. (1988), the only consistent finding in the CSF was the significantly reduced homovanillic acid concentration in AD as compared to SD and normal controls; and in

the study by Navaratnam et al. (1991), an additional band of acetylcholine-esterase (AcHE-AD) in the CSF of patients with AD. It has also been noted that there is an increase in red cell choline in AD as compared to normal controls (Friedman et al., 1981; Barclay et al., 1982). Nevertheless, because this increase of choline in the red cells is neither unique to AD red cells, nor in variance with it, Blass and Barclay (1985) maintain that its usefulness in AD diagnosis remains dubious (Wood et al., 1983).

Based on an entirely different line of investigations, Wolozin et al. (1987), identified a monoclonal antibody, referred to as ALZ 50, which reacts against brain tissue homogenates of patients with AD (Wolozin and Davies, 1986). Recognition that ALZ 50 binds to a protein marker, referred to as A-68, which is highly selective of AD -- and can detect an early cytologic change that precedes the formation of neurofibrillary tangles and senile plaques -- led to the development of an enzyme immunoassay for the detection of AD associated proteins in postmortem human brain tissue (Ghanbari et al., 1990) Pursuing the same line of research, another group of investigators - based on the recognition that the paired helical filaments (PHF), one of the hallmarks of AD, belong to the tau species of proteins - is in the process of developing a diagnostic kit which, by ELISA testing, should be able to determine the presence of the PHF antigen in the cerebrospinal fluid and thereby

indicate the presence of AD (Iqbal, Grundke-Iqbal and Wisniewski, 1987; Lehmann, 1989; Sirkin, 1986).

Simultaneously with the development of this CSF-based diagnostic test, there is also a blood test in development for AD. It is based on the presence in the blood of a beta-amyloid protein (related to the specific amyloid found in senile plaques) which is similar to Glenner and Wong's (1984) beta-amyloid protein, present in the cerebral vessels of patients with AD and Down's syndrome.

Concluding Remarks

In variance with the commonly held belief that dementia begins with cognitive changes, there is increasing evidence that neurologic signs, transient consciousness disturbances, personality changes and psychopathologic symptoms are the earliest detectable manifestations of a dementing process. Because of this and other considerations a Canadian Task Force on the Periodic Health Examination (1991) concluded that in spite of the high incidence of dementing illness "there is insufficient evidence to include routine screening for cognitive impairment in or exclude it from the periodic examinations of people over 65 years". On the other hand, with consideration of their high prevelence rate and/or reversibility, in case of the slightest indications for their presence, checking for SDAT, MID, normal pressure hydrocephalus, drug toxicity, alcohol abuse, depression and certain metabolic disorders is of primary importance (Table 8).

Table 8

Condition	Reversibility: Spontaneous	Reversibility: Intervention dependent	Detection manoeuvre: Hx	Detection manoeuvre: Px	Detection manoeuvre: Lab
Alzheimer's disease	0	+	+ + +	+	0
Multi-infarct dementia	+	+	+ + +	+	++
Normal pressure hydrocephalus	+	+ +	+ + +	+ +	+ + +
Drug toxicity	+	+ + +	+ + +	+	+
Alcohol abuse	+	+ +	+ + +	+ +	+
Depression	+ +	+ + +	+ + +	+ +	0
Metabolic disorders					
- Thyroid ↑ or ↓	+	+ + +	+ +	+ +	+ + +
- Sodium ↑ or ↓	+	+ + +	+ +	0	+ + +
- Calcium ↑ or ↓	+	+ + +	+ +	+	+ + +
- Glucose ↑ or ↓	+	+ + +	+ +	+	+ + +
- Hepatic failure	+	+ +	+ +	+ +	+ + +
- Renal failure	+	+ +	+ +	+	+ + +

Conditions which may cause dementia; reversibility of dementia in the different conditions; priorities in terms of the "detection triad" in the different conditions; and assessment priorities within the Public Health System of the different conditions (Canadian Consensus Conference on the Assessment of Dementia, 5-6 October, 1989).

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