The Complete Dementia Evaluation: Complications and Complexities

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Synopsis

In the last decade, there has been an increasing focus on the diagnosis of dementia for which an extensive test battery is recommended. However, numerous series of patients have been reported in which the battery was not complete and secondary diagnoses were not mentioned. The NINCDS-ADRDA Work Group suggested that Alzheimer's diagnosis be scaled by probability based on the presence of other conditions. Yet few authors have analyzed the complicating factors in this diagnosis, an especially important question in view of the search for peripheral medical problems associated with Alzheimer's disease.

In this study, first presented at the convention of the American Psychiatric Association in Washington, May, 1986, 60 patients were selected from admissions to the UCLA Geriatric Psychiatry Outpatient Clinic (a tertiary referral center) based on: 1) a complaint of memory dysfunction, and 2) evaluation completed at UCLA by a psychiatrist, neurologist, and neuropsychologist, with full laboratory testing including CT scan and EEG. Each patient's chart was reviewed independently by two board-certified psychiatrists; disagreements settled by a third. Data were assessed for DSM-III criteria for dementia and primary degenerative (PDD) and multi-infarct (MID) types. Neurologic, medical, and psychiatric conditions potentially contributing to memory dysfunction were tabulated.

Only 17 patients (28%) were diagnosed as uncomplicated PDD. However, an additional 25 patients (40%) were felt to have PDD complicated by MID (4), other diagnoses (12), or both (9). Thus, only 18 patients (30%) were judged with some confidence not to have Alzheimer's disease. Of these, 8 were felt to have clear MID. Depression was the sole factor identified in 2 patients. This series highlights the difficulties of making crisp diagnosis of memory dysfunction. More complete evaluation and less arbitrary selection may be an important research direction for Alzheimer's disease.

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Editors note: Readers of this article unfamiliar with medical terminology may wish to refer to the glossary at the back of the journal.

Introduction

Only in recent years has dementia come to be seen as a common illness generated by specific pathology of the nervous system distinct from the natural sequelae of the normal aging process. Dementia appears to be a relatively homogeneous syndrome with a variety of underlying causes.[1] Progress toward treatment and prevention is awaiting more distinct characterization of the etiologies of the dementia syndrome. Numerous authors have examined large series of clinical patient populations and presented their analyses of which illnesses lead to dementia (Figure 1). However, most studies of this nature are based largely on only that information which is available in each patient's chart and do not assure that evaluations are thorough or complete. Further, numerous discrepancies exist between these studies, which could be related to such selection factors as: geography, clinic population (e.g., high alcoholism rate in one veteran hospital study[2], or bias due to the specialization of the clinic.[3] Unfortunately, autopsy confirmation is rarely obtained and has not yet been applied to a representative sample population of demented subjects prospectively.

Another aspect of the complexity of the dementia picture is the presence of secondary diagnoses which may underlie or contribute to the neuropathological changes.[4] Recent attention has also been focused on peripheral metabolic changes which may accompany Alzheimer's disease,perhaps as part of some primary underlying diathesis.[5],[6] Although the time is approaching for a multi-center cooperative study on the evaluation and epidemiology of dementia, the efforts at this stage are still directed at establishing proper clinical evaluative procedures.

This study is based on a 20-month experience of diagnosing patients with memory complaints admitted to the UCLA Geriatric Psychiatry Outpatient Clinic. The results indicate considerable diagnostic diversity in this otherwise unscreened sample population.

Classifications of Dementia—8 Studies, 609 Patients†

		Range
Primary Degeneration	50%	(30-70)
Cerebrovascular	13%	(1-36)
Alcoholic	9%	(2-32)
Depression	6%	(0-24)
Huntington's	4%	(1- 7)
Hydrocephalus	3%	(0-12)
Tumor	3%	(0- 8)
Post-traumatic	2%	(0- 8)
Other (e.g., Creutzfeld-Jakob, Parkinson's, Post-infectious Encephalopathy, Toxicity)	10%	(7-26)

(Expanded from Wells, 1977)
†See references 2, 3, 17, 18, 19, 20, 21, 22

Figure 1

Methods

The UCLA Geriatric Psychiatry Outpatient Clinic is a division of the Adult Outpatient Department of the Neuropsychiatric Institute. In this clinic, 714 new outpatients were seen between March 1, 1982 and February 28, 1985. Patients over age 65 were specifically recruited, but the ages of clinic patients ranged from 51 to 101, with a mean age of 74 (Figure 2). The primary referral source was self or family member (about 35%), although many referrals came from local senior centers or private practitioners (Figure 3). Many of the patients were first-time evaluations, but some were tertiary referrals or "doctor-shopping" for a more palatable diagnosis. Organic brain syndrome diagnoses represented about 40% of the diagnoses (Figure 4).

Patients who presented with complaints of memory difficulty without prior complete evaluation were scheduled for a Primary Dementia Evaluation (PDE) by a psychiatrist and social worker or psychiatric nurse. The evaluation began with a complete psychosocial history and was usually followed by referral for complete neuropsychological testing. At this stage, patients who had clear dysfunction of cognition were referred for neurological examination and a complete battery of lab tests (CT scan, EEG, blood chemistries—LFTs,

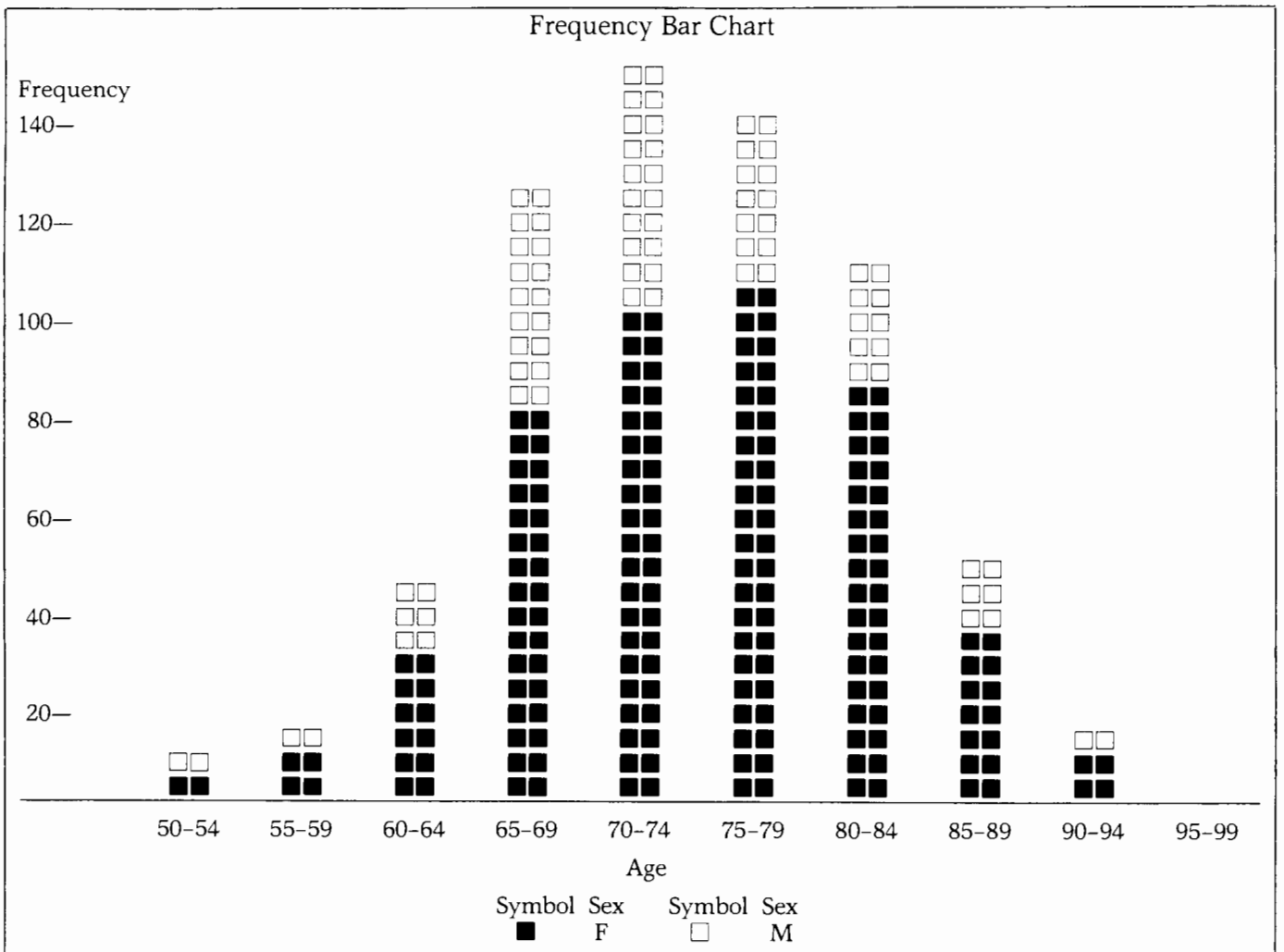

Figure 2

RFTs, electrolytes, Ca^{++} Mg^{++} etc., urinalysis, EKG, CXR).

Between July, 1982 and March, 1984, 60 patients were selected from this population for further study, based on their full evaluations having been completed at UCLA (a total of 431 patients were admitted during this time). The charts of the patients of this sample were evaluated independently by two board-certified psychiatrists. Records were evaluated first for the documentation of cognitive dysfunction and DSM-III criteria for dementia. An estimation was then made as to whether that dysfunction was clearly due to medical, neurological, and/or psychiatric disorders. Dysfunction thought due to neurological disorder was then evaluated for DSM-III criteria for primary degenerative dementia, multi-infarct dementia, both, or neither (e.g., another specific neurological disease). Discrepancies between the psychiatrists were usually related to the uncertainties inherent in this diagnosis, not questions related to the facts. Such disagreements were settled by a third independent psychiatric opinion; a few cases required additional discussion.

Results

In this sample of 60 patients (Figure 5), 56 met DSM-III criteria for dementia; 50 met criteria for primary

Diagnosis

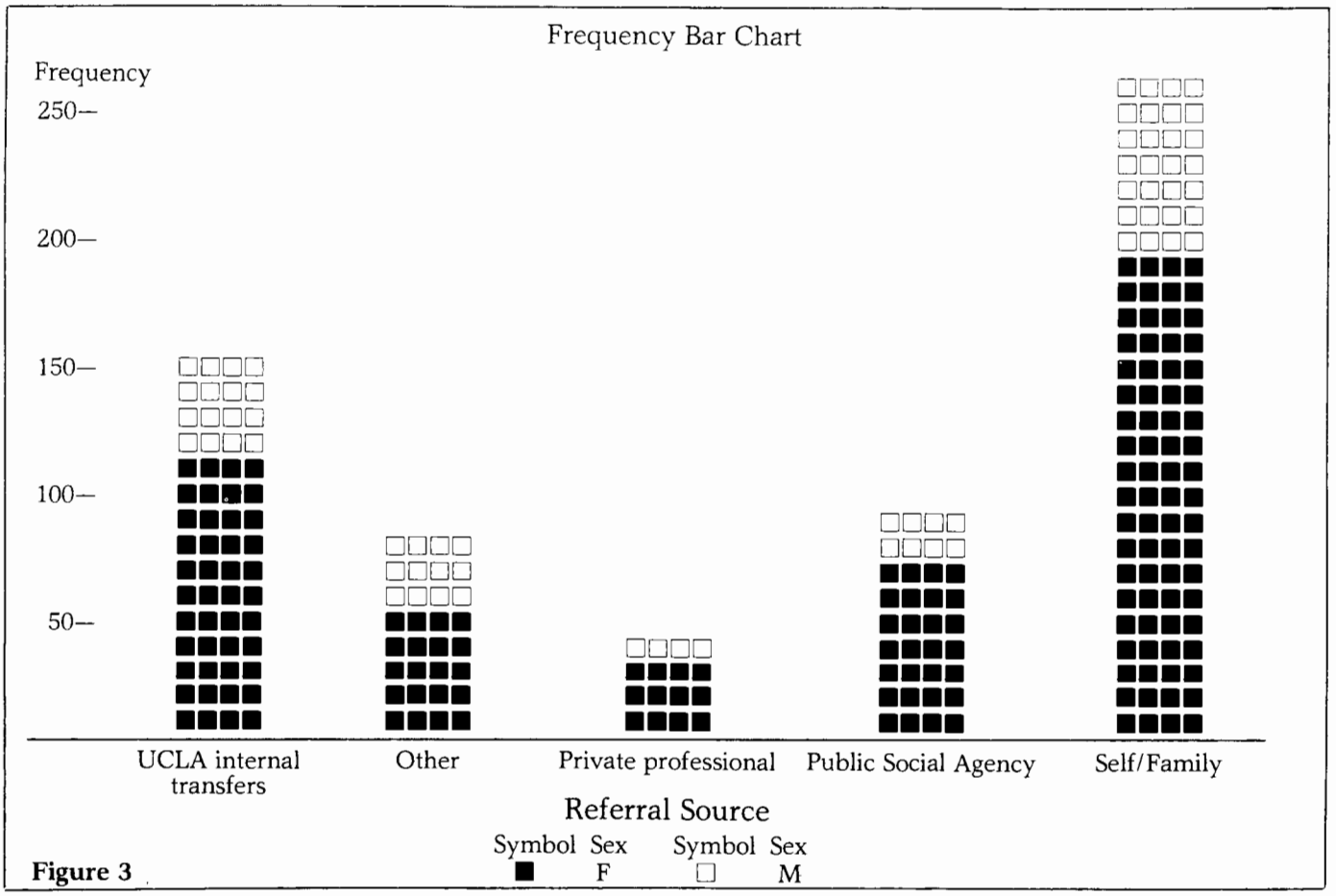

Figure 3

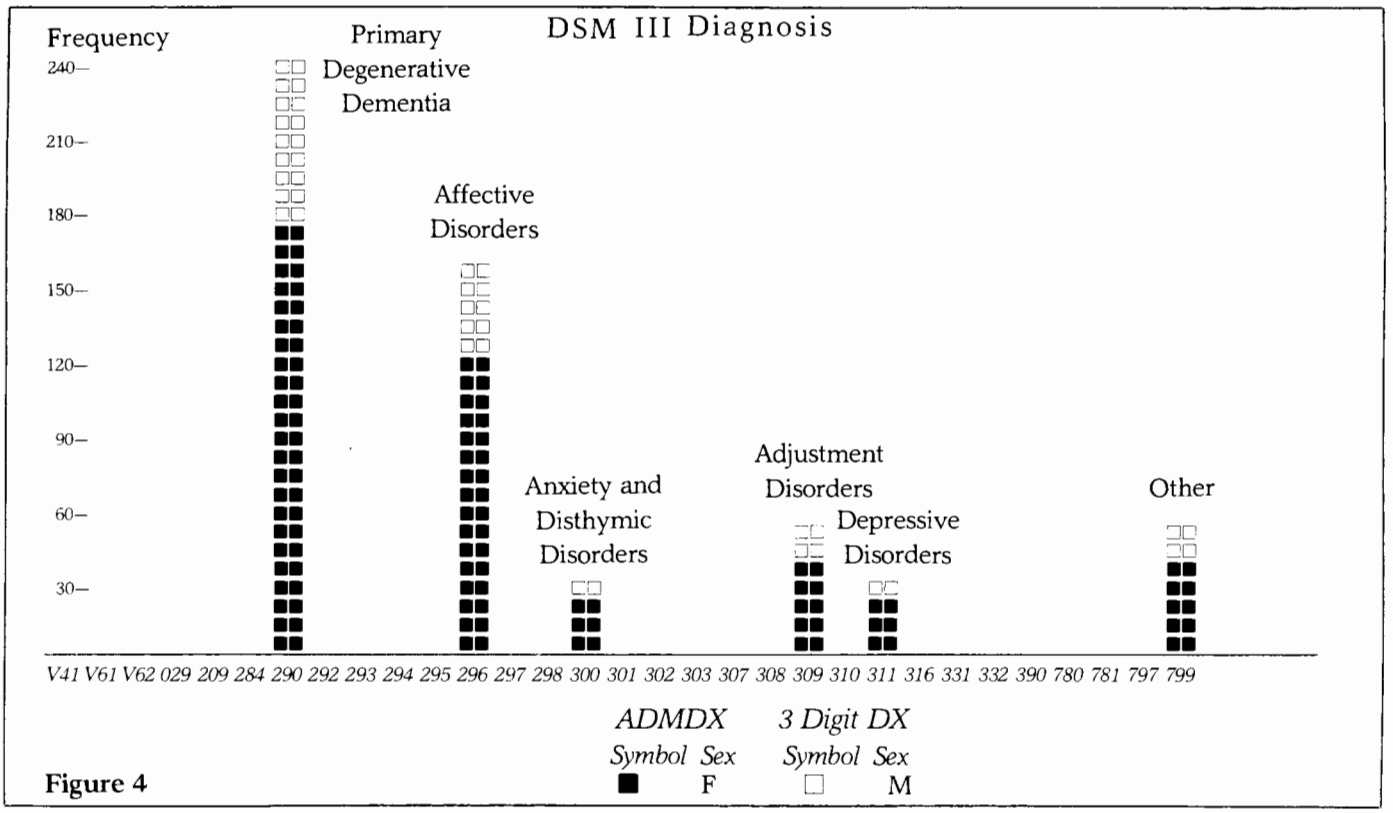

Figure 4

	Uncomplicated Diagnosis	Complicating Diagnosis				Total
		Specific Neurologic	Medical	Psychiatric	Combination of Other Conditions	
Primary Degenerative Dementia (PDD)	17(28%)	2	5	1	4	29(48%)
Multi-Infarct Dementia (MID)	4(7%)		3	1		8(13%)
Combination of PDD and MID	4(7%)	1	6		2	13(22%)
Demented: Neither PDD nor MID	X	2	1	1	2	6(10%)
Not Demented	X	1		1	2	4(7%)
Total	25 (42%)	6 (10%)	15 (25%)	4 (7%)	10 (16%)	60 (100%)

Figure 5

degenerative type (PDD) and /or multi-infarct type (MID) (84% of the whole sample). Only 17 (28%) met clear criteria for PDD uncomplicated by other factors. These patients would also have met criteria for "probable aiz- eimer s disease".[7] A further 25 patients (42%) were felt to have additional neurological, medical, and/or psychiatric conditions accompanying a primary degenerative process. Of this group 13 also met criteria for multi-infarct dementia (MID), but only four of these patients did not have still other diagnoses. Only 18 patients were considered with some certainty not to have a PDD-type presentation. Of these non-PDD patients, eight met criteria for multi-infarct dementia. Three of these MID patients also had additional medical problems, and one had additional psychiatric problems. Thus, 25 patients with PDD and/or MID as primary diagnoses also had secondary diagnoses (50% of the group) which are not generally recognized as directly causing these primary diagnoses, but could possibly be part of or contribute indirectly to these primary processes. These secondary diagnoses included 10 cases of depression, eight cases of hypertension, four cases of definite or probable head trauma, two cases of atrial fibrillation, two cases of hypothyroidism, and individual cases of hyperthroidism, low B-12 and folate, diabetes, and a mitral valve replacement. In none of these cases could a causal relationship between the dementia and the secondary diagnosis be established.

Of the remaining 10 cases, six patients met criteria for dementia. There were three patients with Parkinsonism, one viewed not to be demented in spite of initial memory complaints. These complaints improved considerably with L-dopa treatment. Of two patients with only depression diagnoses, one was felt not to be demented, but was having difficulties coping with depression. The other was thought to have cognitive impairment secondary to the depression. Among the other three demented patients, one had a probably alcoholic dementia, one had alcoholism and depression, and the etiology was uncertain in the other. The other two non-demented patients also had cognitive dysfunction, one due to head trauma and the other possibly secondary to cerebrovascular difficulty.

Discussion

This sample of patients represents a cross section of patients presenting to the UCLA Geriatric Psychiatry Outpatient Clinic because of memory difficulties. However, several potential biases inherent in the sample must be considered. Men are under-represented, many being seen at the nearby Brentwood Veterans Administration Hospital. UCLA is

situated in a high socioeconomic region and attracts patients from the local population. Although the geriatric clinic tends to be a tertiary referral source, about 35% of the sample was self-referred. (Efforts were also made not to repeat already completed evaluations, and several such cases were not included in the sample.) Early-stage dementia patients without recognized memory deficits may have been evaluated initially in other settings. However, as of this time, no clear demographic predispositions to dementia have been recognized.[8] Thus, the diagnostic complications encountered in this sample may be representative of those occurring in the general population.

The major finding of this study, which goes beyond that of many others, is the apparent complexity that is found in the detailed diagnostic evaluation of the dementia patient. The incidence of PDD diagnoses (48%) is consistent with other studies as is the incidence of MID (13%). On the other hand, in several cases (22%) the differentiation between PDD and MID was either not possible clinically, or both conditions may have coexisted.

Further, half of the diagnoses were complicated by other factors. It is not yet clear whether these other factors may predispose to PDD or MID (e.g. hypertension, head trauma), were caused by the dementia (e.g., depression), were incidental (e.g., hypothyroidism, atrial fibrillation), or were related to some underlying metabolic diathesis (e.g., diabetes).

These findings suggest two possibilities. The first is that patients who contract dementia have some underlying predisposition to the disease (beyond that of their age-matched cohort). This has been suggested by the increased incidence of Down's syndrome and leukemia in relatives of Alzheimer's patients[5] and the demonstration of peripheral metabolic abnormalities in Alzheimer patients.[6] Further, risk factors for other diseases could overlap with risk factors for dementia (such as heart disease and MID[9]); or peripheral disease could cause brain disease by some unknown mechanism (HTN contributes to MID).

The second possibility is that concomitant diseases (more likely to occur in the elderly) may be working together to cause brain dysfunction. These perspectives call into question the approach of finding the "pure culture" dementing disease and studying it to the exclusion of all else. The coexistence of PDD and MID also questions the utility of the Hachinski Embolic Index[10], which assumes no overlap of these two diseases.

A question that is not answered in the literature is why so many different types of pathology can lead to a syndrome which is so homogeneous in its clinical presentation. One approach tried to distinguish subtypes of dementia that can be recognized neuropsychologically.[11] However, such studies highlight the major similarities between dementias of different etiological types. It has been widely considered that the hippocampus, specifically Sommer's sector, may be selectively vulnerable to a wide variety of conditions associated with dementia, including hypoglycemic (perhaps the final insult of alcoholism), hypoxemic, vascular, and Alzheimer type changes.[12,13,14,15] If this region of the brain has such a selective vulnerability, it might also account for why diverse diagnoses can team together synergistically, impairing hippocampal and thus memory function. In terms of multi-infarct dementia, it could be pathologically verified whether damage to this region is disproportionately correlated with the clinically documented cognitive dysfunction.

It is still far from certain that the hippocampus is the anatomically vulnerable structure whose disruption leads to dementia. Alzheimer's disease, which has been most widely studied histologically, causes destruction of many cell groups throughout the brain. The underlying physiological process of synaptic plasticity may be the vulnerable mechanism at risk in this disease, thus accounting for the relationship between cytoskeletal disruption and memory dysfunction.[16] The vulnerability of this process could explain the disproportionate pathology found in Sommer's sector, probably the most plastic structure of the brain. Further, the plasticity process may also prove to be vulnerable to other types of dementing pathology. Clearly, there is a great need in this field for a more uniform approach to the thoroughly clinical evaluation, followed by more regular and complete post-mortem brain study.

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