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The Diagnosis and Differential Diagnosis of Dementia and Pseudo-dementia in the Elderly

SUMMARY

Depression occurring in an elderly patient calls for evaluation. Though depressive illness may result in cognitive impairment and may occasionally mimic true dementia, that impairment more commonly occurs in the early stages of a dementing illness. If the patient is suffering from an organic brain disease, treatment of depressive pseudo-dementia rarely results in complete restoration of the patient's normal cognitive function. Nevertheless, antidepressant therapy is extremely valuable in improving the quality of the sufferer's life. Remediable factors contribute to, and sometimes are responsible for, the dementia syndrome. These factors are discussed, and suggestions are made for their investigation and management. (*Can Fam Physician* 1986; 32:2607–2610.)

SOMMAIRE

La dépression qui se manifeste chez une personne âgée nécessite une évaluation. Bien qu'une pseudo-démence dépressive puisse occasionnellement simuler une vraie démence et provoquer une altération des fonctions cognitives, cette altération se manifeste plus fréquemment pendant les stades précoces de la démence. Si le patient souffre d'un désordre cérébral organique, le traitement d'une pseudo-démence dépressive n'entraîne que rarement le rétablissement complet des fonctions cognitives normales. Néanmoins, les antidépresseurs sont extrêmement utiles pour améliorer la qualité de vie du patient. Certains facteurs corrigibles contribuent et sont même parfois responsables du syndrome de démence. L'article discute ces facteurs et suggère des modalités d'investigation et de traitement.

Key words: depression, depressive pseudo-dementia, anti-depressant therapy

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THE TERM 'DEMENTIA' can be used in a variety of ways. It is best used, however, to describe a syndrome of diffuse cognitive deficits which occur in the absence of an altered level of consciousness. The term, used in this way,[1] avoids any association with prognosis or reversibility and should, in my opinion, be used in the same sense as the terms 'chronic renal failure' or 'congestive heart failure'. Indeed, the term 'chronic brain failure' has been suggested as an alternative to 'dementia'. The adoption of the former term would assist the replacement of the traditional view of dementia as an irreversible, invariably progressive condition, with the concept of a syndrome which may have reversible features and specific causes that may lend themselves to successful treatment.

There are good reasons to dispense with the term 'dementia' in its traditional sense of an irreversibly progressive ailment. A number of studies from the medical and psychiatric literature have called into question the physician's ability to make a firm diagnosis of irreversible dementia, as many patients so diagnosed, when reviewed years later, have not progressed as expected, and the earlier diagnosis of dementia has had to be revised. Kendell[2] reviewed the diagnostic information on a sample of 2,000

patients first admitted to psychiatric beds in the United Kingdom in 1964, and readmitted on at least one further occasion before 1969. Of the 99 patients in this survey who were diagnosed as suffering from a dementing illness, only 75% had this diagnosis confirmed on follow-up. Of those whose diagnosis was revised, one-third were subsequently diagnosed as having depressive illness, and one-quarter as suffering from a confusional state (delirium). Nott and Fleminger[3] followed up 35 patients first diagnosed as having pre-senile dementia; after follow-up between one and 23 years later, only 15 (43%) had deteriorated in the manner expected with pre-senile dementia. Ron and her colleagues[4] followed up another sample of 51 patients with pre-senile dementia from five to 15 years after diagnosis, and were able to confirm the initial diagnosis in 69% only.

Two recent articles by Larson and his colleagues[5, 6] have specifically examined elderly patients presenting with dementia syndromes. These studies, which will be discussed later, question the current concept of reversibility pointing out that some patients whose dementia appears to have "reversible" causes (Table 1) did not improve, whereas others whose dementia showed no "reversible" features nevertheless did improve.

Origins of "Pseudo-dementia"

One of the explanations for the lack of stability of the diagnosis of dementing illnesses is that some persons deemed to be demented were actually so depressed that cognitive deficits had occurred. As many cases of depression eventually resolve spontaneously, even in the absence of treatment, those who have undergone spontaneous recovery would appear to be less "demented" on subsequent examination. It was this observation that led to the introduction of the term 'pseudo-dementia' by Kiloh in 1961.[7] The concept of pseudo-dementia introduced a valuable principle: that the diagnosing physician should think of depression as an etiological factor in an individual presenting with a dementia syndrome. At no time was pseudo-dementia intended to be a diagnosis—a point emphasized by Wells in his classic article[8]—although it does seem to have evolved as a diagnostic rather than a descriptive term as originally intended. Since its introduction, various authors[9, 10] have appealed for its removal from medical terminology for two important reasons. The first reason is that in common with many other chronic diseases, dementing illnesses are often accompanied by depression, particularly early in their course.[11] The second reason for abandoning this term is that the lack of complete resolution of the cognitive abnormalities (e.g., memory loss, difficulty concentrating) in the depressed elderly is a consequence of the frequent co-existence of a dementing illness with depression and may lead to disappointment and unrealistic expectations on the part of the physician and relatives.

A contemporary view, therefore, is that dementing illnesses are frequently accompanied by depression. In one study of 88 patients with cognitive impairment, 23% met research diagnostic criteria for depression.[11] Moreover in a review of the available literature[9] Reifler suggested that most of the patients described as having pseudo-dementia actually had evidence of underlying organic brain disease. Researchers have concluded that it is rare for depression alone to be responsible for cognitive impairment sufficient to sustain a diagnosis of dementia. Such instances amounted to only 15% in one study.[11] The prevalence of depression in dementing illness appears to be greatest early in the course of the ailment, where there is a realization that cognitive function is failing. Later in the course of the dementia, depressive symptoms are apparently less prevalent,[11] presumably as the patient loses insight.

Table 1
Causes of "Reversible Dementia" Syndrome

1. All causes of subacute delirium (especially drugs, metabolic disturbance and infection)	4%
2. Chronic metabolic disturbances (e.g., hypothyroidism, B_{12} deficiency, hypercalcemia)	4%
3. Structural abnormalities (tumor, subdural hematoma, normal pressure hydrocephalus)	4%
4. Profound depression ("pseudo-dementia"—see text)	

Note: Percentages refer to prevalence of groups in study by Larson.[5]

Thus, dementing illnesses and depression commonly co-exist. Although treatment of depression may not cause complete resolution of the cognitive impairment, it is nonetheless important to treat depression of patients suffering from dementia in order to improve their quality of life. The mere presence of cognitive impairment should not dissuade the physician from prescribing an adequate course of antidepressant drugs, although certain precautions will be necessary. (These precautions are outlined in the section on management.)

Depression in the elderly is often atypical, lacking many of the usual vegetative features that one sees in younger depressed patients.[12] Depressed elderly persons may present with agitation or after a suicidal attempt, which is more often passive than ostentatious (e.g., discontinuing medications and not eating). Depression may appear in the form of chronic pain or other somatic symptoms, and feelings of self-reproach and paranoia are not infrequent. Change in behaviour (e.g., new onset of alcohol use, starting to swear) may occur. The suspicion of depression leading to cognitive impairment may be raised by a relatively sudden onset of symptoms, particularly following a loss or other life event. A personal or past family history of depression is often present. The type of complaint of memory loss is said to be typical: where a dementing illness is present, memory loss may be denied (anosognosia), whereas when memory loss is the result of depression, complaints are often exaggerated, and the patient "may almost parade them".[13] In answering questions, the depressed subject may reply with "Don't know", whereas those with dementing illnesses usually make an attempt, and a "near miss" answer is common.[8]

Reversible (or Partially Reversible) Dementias

By now most practitioners are familiar with the potentially remediable conditions which may cause a dementia syndrome. Although past studies have suggested that 15%–30% of patients presenting with dementia may have potentially reversible factors, many of these studies[14–16] were carried out on patients under 65 years of age, who were admitted to specific psychiatric or neurosurgical facilities. These results cannot be generalized to

include the elderly patient in primary care.

The two recent studies by Larson and his colleagues[5,6] do, however, provide valuable information on the primary-care setting. The patients in these studies were either self-referred or referred by their families to a geriatrics and family-services program in Seattle for evaluation of possible dementia. The mean age of the study population was 75.8 years. Extensive investigations led to the conclusion that between 60%–70% had Alzheimer's disease, and that other forms of dementing illness (alcohol-related dementia, multi-infarct dementia, and other irreversible dementias) accounted for another 10%–13%.

Of the 16 patients who experienced improvement in cognitive function, 11 had been diagnosed as having potentially reversible causes for their dementia; in five, however, the dementia had originally been classified as irreversible. Cognitive improvement was transient in about half of those who improved.

A particularly revealing feature of this study was the very high prevalence of diseases which were discovered during the diagnostic work-up. Among the 107 patients who participated in the initial study, a total of 88 new, previously unrecognized but treatable disorders were discovered in 48 patients. Twenty-nine of these disorders were forms of depression. Significantly, although the majority of these patients responded well to antidepressant therapy, treatment brought about little overall change in their cognitive state. Neurological abnormalities of prognostic or management significance, discovered on CT scan, were virtually all found on patients who had a history of acute or sudden deterioration within 12 months, or who had mild cognitive impairment (Folstein mini-mental state[17] greater than 20). Although the finding of a chronic metabolic disturbance such as hypothyroidism or Vitamin B-12 deficiency may produce exuberance on the part of a physician who believes that the dementia may be remediable, all too frequently, correction of these deficits may fail to produce a return to normality. Nonetheless, no physician should be dissuaded from seeking or treating such deficiencies, as the secondary prevention of myxedema or pernicious anaemia justifies replacement therapy.

Diagnostic Work-Up for Dementia Syndrome

Unquestionably, the most valuable investigation is a carefully taken history that emphasizes the evolution of the cognitive impairment, seeking particularly features such as a recent onset or any symptoms of depression. Associated symptoms that may point to coexistent physical disease should be noted. A meticulous review of all drugs, both prescribed and purchased over-the-counter, must be made by direct inspection and not by history alone. As memory loss is likely to be present in someone suspected of having dementia, corroborative history should be taken from a relative or some other observer. Physical examination should be thorough and should search for any sign of physical disease; a neurological examination should also be made, in a search for localized abnormalities and primitive reflexes (grasp reflex, palmar-mental, snout). The patient's level of consciousness should be carefully assessed and may be manifest by only a fluctuation in orientation or lack of attention during the interview. Cognitive assessment should include evaluation of memory, language, behaviour and judgement. A short instrument such as the Folstein mini-mental state[17] is a valuable asset for establishing a score which can be compared on subsequent occasions. Symptoms of depression should be carefully sought, including changes in appetite, sleep disturbance, any feelings of self-reproach or guilt, suicidal intent, crying or withdrawal. A variety of depression scales are available, but there is, unfortunately, no ideal scale for the measurement of depression in the elderly.[18]

The basic laboratory work-up should include a complete blood count, measurement of electrolytes, renal and liver function, and measurements of thyroid function, serum B-12 and serum calcium. These investigations are intended to exclude potentially reversible abnormalities. An EEG is frequently unhelpful, although the finding of an entirely normal EEG in someone who appears demented may strengthen the case that the cognitive impairment is solely the result of depression. A CT scan is recommended if there is a short or atypical history, or where focal neurological symptoms or signs are present.

Management Suggestions

1. Be alert to any atypical features in the history of an elder presenting with dementia. Some atypical features are outlined in Table 3. Such features may prompt a more extensive neurological examination, or may signal the suspi-

Table 2
Causes of Delirium[a] (mnemonic "dementias")

D–DRUGS:	including withdrawal (alcohol, barbiturates)
E–ENDOCRINE:	hypothyroidism, hyper- or hypoglycemia, hyperparathyroidism, Cushing's
M–METABOLIC:	hypoxemia, fluid, electrolyte disorders (especially dehydration and hyponatremia) severe liver and renal disease
E–EPILEPSY:	postictal confusion (may last for days)
N–NEOPLASM and STRUCTURAL:	intracranial tumour, NPH. remote effects of malignancy (e.g., lung)
T–TRAUMA:	fracture, postsurgery, concussion, subdural hematoma
I–INFECTION:	extracranial (e.g., lung, UTI, abdominal) intracranial (e.g., meningitis, encephalitis)
A–"APOPLEXY":	i.e., vascular event (e.g., stroke, MI, pulmonary embolism, peripheral embolism)
S–SOCIAL:	especially relocation, usually in combination with above.

a. Causes often multiple; sometimes known as "the bits" (a bit of heart failure, a bit too much digoxin, a bit of UTI, etc.)
Note: For comprehensive review of delirium see: Lipowski ZJ. *Am J Psychiatr* 1983; 140:1426–36.

cion of a co-existing or causative depression.

2. Drug withdrawal and attention to metabolic or other physical illnesses should take place before the physician considers specific antidepressant therapy.

3. It is important not to raise false hopes in either the patient or the family. Needless anxiety may be engendered by focusing attention on "potentially reversible" causes for the dementia, with a resulting anticlimax if none is found. A realistic picture should be projected, with emphasis on management, including psycho-social and other types of support, which become increasingly important when the flurry of diagnostic enthusiasm subsides.

4. In the presence of depressive symptoms, a trial of tricyclic or other antidepressant drugs is recommended.[19] Drugs with a low potential for anticholinergic side-effects should be chosen, such as desipramine or nortriptyline. Alternatively, the physician can prescribe trazodone, a newer drug with a serotoninergic profile similar to amitriptyline, but one which is virtually devoid of anticholinergic effects. Undoubtedly there will be other newer antidepressant drugs with fewer and fewer anticholinergic side-effects available. It is recommended that low starting doses be used (e.g., desipramine 25 mg, nortriptyline 10 mg, trazodone 50 mg) with cautious increase in dose and monitoring of drug levels to ensure that a therapeutic level is present for four to six weeks at least before the abandonment of that particular drug for lack of effect. Common side-effects of these drugs include the development of confusion (anticholinergic delirium), urinary retention, constipation, dry mouth and blurred vision. Cardiac side-effects include postural hypotension, increased heart rate and, occasionally, more serious effects such as arrhythmias and cardiac failure. Tricyclic drugs have a quinidine-like effect; they are safe, as a general rule, provided that serious conduction defects, arrhythmias, unstable angina and congestive heart failure are absent. If doubt is present, referral to an internist is recommended.

5. Do not feel obliged to make a firm diagnosis of dementing illness immediately. After serious or potentially reversible disease has been ruled out, it may be necessary for the physician to observe the patient over a few months to determine whether progressive cognitive deterioration is occurring before a firm diagnosis of dementing illness is appropriate. ◉

Table 3
Atypical Features in Dementia Syndrome: Pointers for Alternative or Specific Diagnosis

Feature	Diagnosis to Consider
Abrupt, recent or rapid onset	Stroke, depression, delirium, Tumour, Jakob-Creutzfeldt
Early neurological symptoms:	
• Shuffling	Parkinson's, multi-infarct, Normal pressure hydrocephalus Progressive supranuclear palsy
• Headache	Tumour, subdural,
• Onset after trauma	Concussion, subdural
Multiple drug use	Delirium
FINDINGS	
• Physical disease (severe organ failure)	Delirium
• Neurological signs	Specific neurological disease
• Personal or family history of depression	Depression
• Prominent complaints of memory loss	Depression
• Feelings of distress	Depression
• Recent and long-term memory equally affected	Depression
• Complete absence of language disturbance	Depression

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