1 Shimpo S. Solitary plasmacytoma with polyneuritis and endocrine disturbances. *Nippon Rinsho* 1968;**26**:2444-54.
2 Takatsuki K, Yodoi J, Wakisaka K. Plasma cell dyscrasia with polyneuritis and an endocrine anomaly: endocrinological study of a new syndrome. *Nippon Naibunpi Gakkai Zasshi* 1974;**50**:567-75.
3 Saikawa S. On the etiology of "PEP syndrome (a peculiar progressive polyneuropathy associated with pigmentation, edema, plasma cell dyscrasia)." *Medical Journal of Kagoshima University* 1980;**32**:219-43.
4 Bardwick PA, Zvaifler NJ, Gill GN, Newman D, Greenway GD, Resnick DL. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes: the POEMS syndrome. *Medicine (Baltimore)* 1980;**59**:311-22.
5 Nakanishi T, Sobue I, Toyokura Y, *et al.* The Crow-Fukase syndrome: a study of 102 cases in Japan. *Neurology* 1984;**34**:712-20.
6 Crow RS. Peripheral neuritis in myelomatosis. *Br Med J* 1956;ii:802-4.
7 Meshkinpour H, Myung CG, Kramer LS. A unique multisystem syndrome of unknown origin. *Arch Intern Med* 1977;**137**:1719-21.
8 Saihan EM, Burton JL, Heaton KW. A new syndrome with pigmentation, scleroderma, gynaecomastia, Raynaud's phenomenon and peripheral neuropathy. *Br J Dermatol* 1978;**99**: 437-40.
9 Waldenström JG, Adner A, Gyndell K, Zettervall O. Osteosclerotic plasmacytoma with polyneuropathy, hypertrichosis and diabetes. *Acta Med Scand* 1978;**203**:297-301.
10 Liévre JA. Dyscrasie plasmocytaire avec polynéuropathie et troubles endocriniens. *Ann Med Interne (Paris)* 1977;**128**:561-3.
11 Moya-Mir MS, Barbadillo R, Martin-Jiminez T, *et al.* Plasma-cell dyscrasia with polyneuritis and dermato-endocrine alterations. Report of a new case outside Japan. *Postgrad Med J* 1980;**56**:427-30.
12 Driedger H, Pruzanski W. Plasma cell neoplasia with peripheral neuropathy. A study of 5 cases and a review of the literature. *Medicine (Baltimore)* 1980;**59**:301-10.
13 Kelly JJ, Kyle RA, Miles JM, Dyck PJ. Osteosclerotic myeloma and peripheral neuropathy. *Neurology* 1983;**33**:202-10.
14 Doi H, Itoyama Y, Yashinaga T, Sato Y, Onishi A. Endoneurial deposition of immunoglobulins in cases of plasma cell dyscrasia associated with polyneuropathy, edema and pigmentation. *Rinsho Shinkeigaku* 1982;**22**:237-43.
15 Besinger UA, Tyka KV, Anzil AP. Myeloma neuropathy: passive transfer from man to mouse. *Science* 1981;**213**:1027-30.
16 Matsumine H. Accelerated conversion of androgen to estrogen in plasma-cell dyscrasia associated with polyneuropathy, anasarca and skin pigmentation. *N Engl J Med* 1985;**313**:1025-6.

Regular Review

Differential diagnosis of dementia

G P MULLEY

Between 3% and 5% of people aged over 65 have severe impairment of memory, intellect, orientation, and personality and a similar proportion have milder dementia.[1 2] Dementia is no longer considered to be caused by "senility": though it is increasingly common with advancing age, 80% of people over the age of 80 are not demented. Nor can degenerative arterial disease always be incriminated[3]: 20-30% of demented patients have a vascular basis for their symptoms but most patients who become demented do not do so as a result of atherosclerosis.[4] Dementia is not a diagnosis but a syndrome whose aetiology must be ascertained in order to recognise the reversible or modifiable causes. Let us review those conditions which should be considered when a patient over 60 develops intellectual impairment and assess the usefulness of investigations.

The two most important aspects of the clinical assessment of an apparently demented person are, firstly, the mode of onset and progression of the symptoms, and, secondly, the presence or absence of focal neurological symptoms and signs. Dementia is a chronic disorder developing over many months. "Acute dementia" resulting from profound cerebral anoxia is uncommon.

Confusion coming on abruptly may be the result of head injury—but apparent confusion of sudden onset may be caused by jargon dysphasia due to a stroke. If cognitive impairment develops over days or weeks and the patient's consciousness is clouded the diagnosis is of an acute or subacute confusional state (delirium); this has many causes including chest infection, adverse drug reactions, metabolic disturbances, or dehydration with constipation.[5]

Intellectual impairment which comes on insidiously and gradually worsens over months or years without any associated neurological features suggests several diagnostic possibilities.

Alzheimer's disease

The most common cause of dementia is Alzheimer's disease, in which initially there is loss of memory for recent events and impaired cognitive function. Together these symptoms impair the patient's ability to do everyday tasks. Often she (or he) has no insight into her decline. Only late in the course of the illness do neurological signs appear: the presence of fits or a disturbance of gait in the early stages makes the diagnosis unlikely.[6] Dysphasia and parietal lobe signs (agnosia and apraxia) also occur: Alzheimer's disease is therefore sometimes described as a "cortical" dementia. Those dementias in which cortical features are absent (for example, normal pressure hydrocephalus, Huntington's chorea, the dementia of Parkinsonism) have been labelled as "subcortical" dementias—but doubt has been cast on the validity of this distinction.[7 8]

Alzheimer's disease is a pathological diagnosis based on the presence of neurofibrillary tangles and plaques throughout the cerebral cortex. Unfortunately there is no laboratory test for Alzheimer's disease, and some patients in whom it has been diagnosed clinically prove to have other conditions at necropsy. The clinical diagnosis may be made only after other conditions have been excluded: the three disorders most important to exclude are benign forgetfulness, depression, and drug toxicity.

Benign forgetfulness, depression, and drugs

Occasional inability to recall names or relatively unimportant past events is a common experience which is more prevalent in men over 60.[9] The person with "benign senescent forgetfulness" may recall things on one occasion

but not on another; he is aware of this problem and may apologise for the lapses of memory.[10] There are no other cognitive defects, and he may be reassured that he is not becoming demented.

Depression is often mistaken for dementia[11,12] and must be considered in every patient who is thought to be demented.[13] Sadly it is often overlooked—even in patients on the psychiatric wards of teaching hospitals.[12,14] Perhaps this is not surprising: both depression and dementia are commoner as people age; they may coexist; and the time profile of the symptoms in the two conditions may be similar. The history is crucial.[15] In depressive pseudodementia there is often a personal or family history of depression. The patient readily complains of loss of memory (this complaint is rare in Alzheimer's disease) and yet does incongruously well on some memory tests.[16,17] The depressed patient will tend to say "I can't remember" when asked a direct question[18]; the demented patient may hazard a guess or make an excuse for not knowing the answer. Depressed patients do not try to conceal their disability, and they may communicate a sense of distress.

Drugs commonly cause intellectual impairment,[19] and this may be completely reversed when the medication is withdrawn.[20] Sedatives, tranquillisers, antiparkinsonian drugs, and antihypertensive agents are the main offenders.[19] A detailed drug history usually requires the help of a patient's relative or better still a domiciliary assessment. A search for empty bottles should also be made: abuse of alcohol may be incriminated in a sizeable minority of demented patients.[21]

Both Alzheimer's disease and these disorders which masquerade as dementia do not usually have neurological features, but other dementing conditions do, and clinical examination may show the Argyll Robertson pupil of neurosyphilis, the typical writhing movements of Huntington's chorea, the flapping tremor of hepatic encephalopathy, the myoclonus and rigidity of Creutzfeld-Jacob disease, and the tremor, rigidity, and bradykinesia of the Parkinsonism-dementia syndrome.[22] Two conditions deserve special mention: vasular dementia and normal pressure hydrocephalus.

Vascular dementia

Vascular or so called multi-infarct dementia is the second most common type of dementia. The course of the illness is of a step wise decline with sudden intellectual deterioration followed by a period of some improvement. Day to day fluctuation also occurs in these patients, who usually have a history of hypertension and will have had a number of strokes.[4,23] Focal neurological signs are usually present early in the disease.[24] The emotions are labile, the gait is abnormal with features of hemiparesis or petit pas. The different clinical features of multi-infarct dementia and Alzheimer's disease form an "ischaemic score"[25]; the validity of this diagnostic tool has been verified pathologically in a small study.[26]

Normal pressure hydrocephalus[27] is characterised by gait apraxia (the patient's feet seem glued to the floor[28]), incontinence of urine, and progressive dementia. In contrast with the pattern of Alzheimer's disease, in normal pressure hydrocephalus the gait disorder and psychomotor slowing are early features. Insertion of a shunt to reduce "normal" cerebrospinal fluid pressure to even lower levels may restore demented patients with normal pressure hydrocephalus to full mental function.[27] Age is not a bar to successful outcome, but those with severe prolonged dementia are less likely to be well.[29,30]

Most causes of dementia may be diagnosed by detailed history and examination. More than three quarters are due to Alzheimer's disease or multi-infarct dementia or a combination of the two.[31] In most cases laboratory tests are unhelpful. Thyroid function tests are abnormal in about 2% of demented patients, and the response to treatment is often disappointing.[19,32,33] The occasional demented patient with unsuspected hypothyroidism, however, does respond well.[20,21,34]

The large surveys of dementia have not reported a single case of vitamin B_{12} deficiency.[11,20,21,35] These studies were, however, retrospective analyses of patients referred to specialist centres; the incidence of B_{12} deficiency in an unselected group of demented patients is not known. Vitamin B_{12} deficiency may cause mental changes in the absence of haematological abnormalities,[36] and this type of dementia sometimes responds well to replacement treatment.[37] Unfortunately, even when low concentrations are reported the results may get scant attention by the clinician.[38]

Measurement of the serum concentration of folate is unhelpful, for deficiency is a common consequence of dementia. Red cell folate estimations should be limited to patients whose diet was grossly inadequate before the onset of cognitive impairment and who have megaloblastic anaemia. In these cases the response to treatment may be gratifying.[39] Simple haematological and biochemical tests may uncover coincidental medical illnesses.[19,40] Other blood tests—for example, serology[41] and measurement of serum concentrations of calcium and copper—should be limited to that tiny proportion of demented patients who have clinical features of the appropriate systemic disease. The electroencephalogram is not usually helpful in determining the cause of the illness, and lumbar puncture should not be performed in the routine evaluation of dementia.[42,43]

Scanning

Computed tomography is sometimes useful in the diagnosis of dementia, but again the pick up rate of reversible disorders is small. If the scan is normal a more diligent search for psychiatric or medical causes of cognitive impairment must be made. Cerebral atrophy on the scan occurs in intellectually normal people,[44] but ventricular dilatation is proportional to the degree of dementia, and appreciable dilatation suggests the possibility of normal pressure hydrocephalus.[45,46] CT scanning may support the diagnosis of vascular dementia.[35] Its main value, though, is in the detection of potentially treatable lesions; these are found in 10% of demented inpatients. A tumour is the most common lesion found, but in only about one in eight cases is surgery helpful—though some patients may get temporary symptomatic relief from steroids.

Clinical examination cannot identify those who should have a CT scan: in 30% of demented patients with cerebral tumour there are no localising signs. What of the other treatable conditions? In a survey of 500 patients with dementia, four had subdural haematoma (three of whom improved after operation) and six had normal pressure hydrocephalus.[47] Although about 40% of patients have sustained improvement with shunt operations for this condition,[29,30] one in three will develop shunt malfunctions

or other complications, and some are worse after the procedure.[18] The conclusion must be that, though many potentially treatable conditions are uncovered by CT scan, the number of patients in whom treatment significantly improves mental state in the longer term is small (about 2% of all demented patients).

Most surveys of investigations for dementia have been on inpatients; only a few such patients have been aged over 75. Yet most demented patients are very old and are not in hospital. One study of 92 outpatients over 60 (mean age of 76) with mild to moderate dementia found that CT scanning identified only one patient whose mental state improved after surgical treatment.[19]

Without further large scale prospective surveys of dementia in the elderly firm recommendations on the usefulness of investigations cannot be made. The cost of missing a reversible or modifiable cause of mental impairment is, however, enormous in human and financial terms. Even though less than 1% of demented patients may respond to thyroxine or vitamin B_{12}, the cost of doing the necessary tests is probably justifiable. CT scanning should be performed only after a thorough medical and psychiatric assessment of the patient; the proportion of positive cases would be higher if we limited scanning to patients with mild to moderate dementia of less than two years' duration who are not too frail for neurosurgical intervention. To deny demented patients comprehensive assessment is neglect; to subject them all to detailed investigation is unnecessary.

G P MULLEY

Consultant Physician,
Department of Medicine (Elderly),
St James's University Hospital,
Leeds LS9 7TF

1 Nielsen J. Geronto-psychiatric period-prevalence investigation in a geographically delimited population. *Acta Psychiatra Scand* 1963;**38**:307-30.
2 Kay DWK, Beamish P, Roth M. Old age mental disorders in Newcastle-upon-Tyne. Part I. *Br J Psychiatry* 1964;**10**:146-58.
3 Anonymous. Vascular disease, senility and dementia [Editorial]. *Lancet* 1984;ii:1310-2.
4 Hachinski VC, Lassen NA, Marshall J. Multi-infarct dementia. A cause of mental deterioration in the elderly. *Lancet* 1974;ii:207-10.
5 Seymour DG, Henschke PJ, Cape RDT, Campbell AJ. Acute confusional states and dementia in the elderly: the role of dehydration volume depletion, physical illness and age. *Age Aging* 1980;**93**:137-46.
6 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan CM. Clinical diagnosis of Alzheimer's disease. *Neurology* 1984;**34**:939-44.
7 Whitehouse PJ. The concept of subcortical and cortical dementia: another look. *Ann Neurol* 1986;**19**:1-6.
8 Foster JB. Subcortical dementia. *Br Med J* 1986;**292**:1035-6.
9 Fisher CM. Vascular disease, senility and dementia. *Lancet* 1985;i:173.
10 Kral VA. Senescent forgetfulness: benign and malignant. *Can Med Assoc J* 1962;**86**:257-60.
11 Marsden CD, Harrison MJG. Outcome of investigation of patients with pre-senile dementia. *Br Med J* 1972;ii:249-52.
12 Ron MA, Toone BE, Garralda ME, Lishman WA. Diagnostic accuracy in pre-senile dementia. *Br J Psychiatry* 1979;**134**:161-8.
13 Kiloh LG. Pseudo-dementia. *Acta Psychiatra Scand* 1961;**37**:336-51.
14 Nott PN, Fleminger JJ. Pre-senile dementia: the difficulties of early diagnosis. *Acta Psychiatra Scand* 1975;**51**:210-7.
15 Pitt B. Management problems in psychogeriatrics. *Br J Hosp Med* 1980;**24**:39-46.
16 Kahn RL, Zarit SJ, Hilbert NM, Niederehe G. Memory complaint and impairment in the aged. *Arch Gen Psychiatry* 1975;**32**:1569-73.
17 Roth M, Myers DH. The diagnosis of dementia. *Br J Psychiatry* 1975;(special publication):87-99.
18 Wells CE. Pseudodementia. *Am J Psychiatry* 1979;**136**:895-900.
19 Larson EB, Reifler BV, Featherstone HJ, English DR. Dementia in elderly out-patients: a prospective study. *Ann Intern Med* 1984;**100**:417-23.
20 Freeman FR. Evaluation of patients with progressive intellectual deterioration. *Arch Neurol* 1976;**33**:658-9.
21 Smith JS, Kiloh LG. The investigation of dementia: results in 200 consecutive admissions. *Lancet* 1984;i:824-7.
22 Brown RG, Marsden CD. How common is dementia in parkinson's disease? *Lancet* 1984;ii: 1262-5.
23 Harrison MJG, Thomas DJ, DuBoulay GH, Marshall J. Multi-infarct dementia. *J Neurol Sci* 1979;**40**:97-103.
24 Bucht G, Adolfsson R, Winblad B. Dementia of the Alzheimer type and multi-infarct dementia: a clinical description and diagnostic problems. *J Am Geriatr Soc* 1984;**32**:491-8.
25 Hachinski V. Cerebral blood flow: differentiation of Alzheimer's disease and multi-infarct dementia. In: Katzman R, Terry RD, Bick KL, eds. *Alzheimer's disease. Senile dementia and related disorders*. New York: Raven Press, 1978:97-103.
26 Rosen WG, Terry RD, Fuld PA, Katzman R, Peck A. Pathological verification of ischemic score in differentiation of dementias. *Ann Neurol* 1980;7:486-8.
27 Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH. Symptomatic occult hydrocephalus with "normal" cerebrospinal fluid pressure. A treatable syndrome. *N Engl J Med* 1965;**273**: 117-26.
28 Knuttson E, Lying-Tunnell U. Gait apraxia in normal-pressure hydrocephalus: patterns of movement and muscle activation. *Neurology* 1985;**35**:155-60.
29 Greenberg JO, Shenkin HA, Adam R. Idiopathic normal-pressure hydrocephalus—a report of 73 patients. *J Neurol Neurosurg Psychiatry* 1977;**40**:336-41.
30 Gustafson L, Hagberg B. Recovery in hydrocephalic dementia after shunt operation. *J Neurol Neurosurg Psychiatry* 1978;**41**:940-7.
31 Task Force sponsored by National Institute on Aging. Senility reconsidered: treatment possibilities for mental impairment in the elderly. *JAMA* 1980;**244**:259-63.
32 Henschke PJ, Pain RW. Thyroid disease in a psychogeriatric population. *Age Ageing* 1977;**6**: 151-5.
33 Bahemuka M, Hodkinson HM. Screening for hypothyroidism in elderly in-patients. *Br Med J* 1975;ii:601-3.
34 Olivarius B de F, Röder E. Reversible psychosis and dementia in myxoedema. *Acta Psychiatr Scand* 1970;**46**:1-13.
35 Delaney P. Dementia: the search for treatable causes. *South Med J* 1982;**75**:707-9.
36 Strachan RW, Henderson JG. Psychiatric syndromes due to avitaminosis B12 with normal blood and marrow. *Q J Med* 1965;**34**:303-17.
37 Fox JJ, Topel JL, Huckman MS. Use of computerised tomography in senile dementia. *J Neurol Neurosurg Psychiatry* 1975;**38**:948-53.
38 Rose M. Why assess vitamin B12 status in patients with known neuropsychiatric disorder? *Lancet* 1976;ii:1191.
39 Strachen RW, Henderson JG. Dementia and folate deficiency. *Q J Med* 1967;**36**:189-204.
40 Anonymous. Uncovering physical illness in elderly patients with dementia [Editorial]. *Br Med J* 1977;ii:1499-500.
41 Ropper AH. A rational approach to dementia. *Can Med Ass J* 1979;**121**:1175-90.
42 Becker PM, Feussner JR, Mulrow CD, Williams BC, Vokaty KA. The role of lumbar puncture in the evaluation of dementia: the Durham Veterans Administration/Duke University Study. *J Am Geriatr Soc* 1985;**33**:392-6.
43 Hammerstrom DC, Zimmer B. The role of lumbar puncture in the evaluation of dementia: the University of Pittsburgh Study. *J Am Geriatr Soc* 1985;**33**:397-400.
44 Fox JH, Kaszniak AW, Huckman M. Computerised tomographic scanning not very helpful in dementia. *N Engl J Med* 1979;**300**:437.
45 Roberts MA, Caird FI. Computerised tomography and intellectual impairment in the elderly. *J Neurol Neurosurg Psychiatry* 1976;**39**:986-9.
46 Cutler NR (Moderator). Brain imaging: aging and dementia. *Ann Intern Med* 1984;**101**:355-69.
47 Bradshaw JR, Thomson JLG, Campbell MJ. Computed tomography in the investigation of dementia. *Br Med J* 1983;**286**:277-80.
48 Peterson RC, Mokri B, Laws ER. Surgical treatment of idiopathic hydrocephalus in elderly patients. *Neurology* 1985;**35**:307-11.