PAPERS AND ORIGINALS

Outcome of Investigation of Patients with Presenile Dementia

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Summary

Of 106 patients admitted for investigation to a neurological hospital with a presumptive diagnosis of dementia, 84 were confirmed to have intellectual impairment or loss of learning and memory function or both. A possible aetiology for the dementia was found in 36 of these 84 patients; the commonest causes discovered were intracranial mass lesions, arterial disease, and alcoholism. Fifteen of the 106 patients were found not to be demented but to have some other illness, most commonly depression. Of the whole series some 15% of the patients suffered from conditions that were amenable to treatment.

Introduction

Dementia is a clinical problem shared by general practitioners, psychiatrists, and neurologists. The presenting features of disordered memory, intellect, and personality often result in referral to a psychiatrist initially, but the extensive investigation required to exclude a treatable cause should lead to neurological consultation. Practitioners and relatives often wish to know the chances of discovering a remediable cause before submitting their charge to full investigation, but we have been unable to discover this information in the literature.

This paper describes the results of investigating 106 patients with presenile dementia who were referred to a neurological hospital.

Methods

Altogether 106 patients were admitted to the National Hospital, Queen Square, between January 1968 and December 1969 with a presumptive diagnosis of dementia. This diagnosis was made at outpatient consultation in most cases, but a few patients were admitted direct to hospital following a referral letter from psychiatrists elsewhere. Twenty of the patients were admitted from another hospital, the remainder from their homes. Thus all patients had been evaluated by a neurologist or a psychiatrist or both before admission. Patients were traced from the admission records so that the sample included those who were discharged with a different diagnosis after investigation. The sample could not include all cases of dementia but probably represented most patients admitted with this diagnosis during the two-year period under review.

Individual consultant neurologists at the hospital investigated dementia in a similar manner. The following investigations were carried out in most cases: psychometry; haemoglobin; erythrocyte sedimentation rate; electrolytes and urea; liver function; protein-bound iodine or triiodothyronine red cell uptake; vitamin B_{12} and folate levels; W.R.; C.S.F.; *x*-ray examination of skull and chest; electroencephalography; and lumbar air encephalography. In certain cases some investigations were omitted when the cause of dementia could be established by other means.

In 1970 the clinical records of each of the 106 patients were reviewed retrospectively by both of us to discover the results of investigation and to review the final diagnosis. The findings of investigations such as formal psychometry or air encephalography were taken from the report written by the psychologist or radiologist at the time the study was carried out.*

Results

Fifteen of the 106 patients admitted with the diagnosis of dementia were judged not to be demented after investigation. The psychologist reported that there was no evidence of intellectual impairment or loss of learning or memory function in these 15 patients. Their disabilities which prompted admission were felt to be due to the causes listed in Table I.

In the case of seven patients the psychologist was unable to come to a firm conclusion. One subsequently recovered spontaneously from a depressive illness with memory loss. Three of these patients were thought to have cerebral atrophy on air encephalography, and three had normal air encephalograms.

*Details of individual cases are available from the authors on request.

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In 84 of the 106 patients there was evidence of intellectual impairment and loss of learning and memory function, which was considered mild in 16, moderate in 29, and severe in 39 patients. The final diagnoses in these cases are listed in Table II.

TABLE I—*Conclusion Drawn after Investigation of 106 Patients admitted with Presumptive Diagnosis of Dementia*

Demented		84
Not demented		15
Psychiatric	Depression	8
	Hysteria	1
	Mania	1
Drug toxicity		2
Epilepsy		1
Unknown		2
Dementia uncertain		7

TABLE II—*Final Diagnosis in 84 Demented Patients*

Intracranial space-occupying mass	8
Arteriosclerotic dementia	8
Dementia in alcoholics	6
Possible normal pressure communicating hydrocephalus	5
Creutzfeldt-Jakob disease	3
Huntington's chorea	3
Posttraumatic cerebral atrophy	1
Postsubarachnoid haemorrhage	1
Limbic encephalitis	1
Cerebral atrophy of unknown cause	48

PATIENTS NOT DEMENTED

In 15 patients psychometry did not show any evidence of organic intellectual deterioration, and memory and learning were unimpaired.

Depression.—In eight cases the apparent dementia was attributed to a depressive illness. Depressive symptoms were prominent in six, but in two the disturbance of affect became obvious only during observation in the ward. In six of the eight patients disturbance of memory was a presenting symptom and had led to the suspicion of dementia.

Four of these patients had lumbar air encephalography, and in two there was evidence of possible cerebral atrophy (some widened cortical sulci). One of these two patients improved on antidepressants. The other had not responded to medication or to a prolonged course of electric convulsion therapy. It remains possible that an atrophic process was the cause of depression in this patient at least.

Psychiatric Conditions other than Depression.—In two other patients a positive psychiatric diagnosis could be made. One had a history of disturbed behaviour due to recurrent mania, and the other complained of memory disturbance but was thought to have a hysterical "pseudodementia."

Drug Intoxication.—In two patients there was clear evidence of drug intoxication. Although there was a history in both of personality deterioration and memory loss or confusion suggesting possible dementia there were also symptoms suggestive of a toxic confusional state (agitation, restlessness, hallucinations). One was discovered to be a chronic barbiturate addict and the other had become intoxicated by therapeutic doses of anticholinergic drugs for Parkinson's disease.

Episodic Disturbances.—In three cases close inquiry disclosed that lapses of memory and concentration had in fact been short-lived. One patient was having frequent epileptic absences, and these were controlled by anticonvulsants. Another had a two-week illness with forgetfulness and disorientation from which she made a full recovery. The third had recurrent episodes of confusion with memory loss lasting between four minutes and 24 hours. Their nature was uncertain and they became infrequent without treatment.

DEMENTED PATIENTS

A clinical diagnosis of the cause of the dementia was reached in 36 of the 84 patients (43%) (Table II).

Space-occupying masses were found in eight patients referred with dementia. In seven the psychologist found evidence of intellectual impairment or loss of learning and memory function or both without focal psychological deficit. Three of these patients had no abnormal neurological signs, two showed a mild to moderate spastic quadriparesis, one had a hemiparesis, and one had isolated bilateral extensor plantar responses. Two had large temporal lobe gliomas in the dominant hemisphere. There was one case of glioma invading the corpus callosum, two cases with multiple metastases, one of meningioma growing from the clivus, and one with a mass in the region of the septum pellucidum (Table III). One patient (Case 8) was thought to be demented on clinical examination but the psychologist discovered a selective deficit of verbal function. The right plantar response was extensor but there were no other abnormalities on neurological examination; dysphasia was not detected. An arachnoid cyst was found overlying the Sylvian fissure of the dominant (left) hemisphere.

TABLE III—*Cerebral Mass Lesions in Patients Presenting with Dementia*

Case No.	Lesion	Site	Comment
1	Glioma	L. temporal lobe	
2	Glioma	L. temporal lobe	
3	Glioma	Corpus callosum	With hydrocephalus
4	Metastases	Multiple	
5	Metastases	Multiple	With hydrocephalus
6	Meningioma	Clivus	With hydrocephalus
7	Cyst	Septum pellucidum	With hydrocephalus
8*	Cyst	Sylvian fissure	

*Psychological testing showed a focal verbal deficit rather than global dementia.

Arteriosclerotic dementia was diagnosed when two of the following criteria were present: a history of acute episodes of neurological disability (strokes), significant hypertension (diastolic blood pressure $\geqslant$ 110 mm Hg), or neurological signs characteristic of cerebrovascular disease (pseudobulbar palsy, marche à petits pas). All eight patients had had strokes and seven were hypertensive. One had a pseudobulbar palsy and two showed marche à petits pas.

Dementia in alcoholics is not a clearly defined entity. For the purpose of this study it was diagnosed when there was a history of prolonged excessive consumption of alcohol associated with one of the following: peripheral neuropathy on clinical or electromyographic examination, typical cerebellar ataxia affecting gait out of proportion to the upper limbs, or cerebellar atrophy on air encephalography. There were six cases; three patients showed a peripheral neuropathy and four were ataxic. There was cerebellar atrophy on air studies in one case.

Hydrocephalus.—In four patients dementia was found to be associated with hydrocephalus due to cerebral tumour (see above). In another five lumbar air encephalography was reported to show possible communicating hydrocephalus with little or no air passing over the cerebral hemispheres. Adams, Fisher, Hakim, Ojemann, and Sweet (1965) drew attention to the existence of communicating hydrocephalus as a cause of dementia and showed that ventriculoatrial drainage of C.S.F. could bring dramatic benefit to some patients. Bannister, Gilford, and Kocen (1967) described the difficulties in diagnosing this condition—"Firstly, there is sometimes no obvious preceding cause such as a head injury or subarachnoid haemorrhage or meningitis that suggests the diagnosis. Secondly, the clinical features may be similar to dementia resulting from cerebral atrophy. Thirdly, contrary to common belief, the cerebrospinal fluid pressure is usually not raised." It is not known how common this condition is.

Of the five patients in this series who appeared to have communicating hydrocephalus on air encephalography none had had a previous severe head injury, subarachnoid haemorrhage, or meningitis. Isotope cisternography confirmed the communicating hydrocephalus in one of these patients by showing persistence of isotope in the ventricles after 48 hours without isotope activity in the cortical subarachnoid spaces (Bannister *et al.*, 1967). Ventriculoatrial drainage did not appear to benefit this patient nor three of the other four patients in whom there

was evidence of partial communicating hydrocephalus on isotope cisternography. The results of isotope cisternography in relation to the diagnosis of partial communicating hydrocephalus in these patients have been reported previously and are still under review (Bannister, 1970).

Creutzfeldt-Jakob disease was diagnosed when rapidly progressive dementia was accompanied by myoclonus and E.E.G. changes of subacute spongiform encephalopathy (Nevin, McMenemey, Behrman, and Jones, 1960) or by clinical or electromyographic evidence of widespread muscle denervation. There were three cases; all ended in death after a total history of between four and 13 months. In two the diagnosis was confirmed at necropsy. In the third progressive dementia was accompanied by extrapyramidal features and repetitive E.E.G. complexes though no myoclonus was seen.

Huntington's chorea was diagnosed when there was a family history of the disease or when the typical involuntary movements were present. There were three cases; each patient had involuntary movements and two had a family history.

One patient with an eight-year history of progressive dementia and cerebellar ataxia after a severe head injury was diagnosed as suffering from *posttraumatic cerebral atrophy*.

A further patient's intellectual deterioration dated back to a *subarachnoid haemorrhage* and surgery for an anterior communicating aneurysm. Investigations showed that this was not due to the communicating hydrocephalus that may occur after subarachnoid haemorrhage (Kibler, Couch, and Crompton, 1961). The mental picture was that described by Logue, Durward, Pratt, Piercy, and Nixon (1968) in patients surviving after rupture of anterior communicating aneurysms.

In one patient dementia and drowsiness were associated with striking dilatation of the temporal horns on air encephalography. At the onset of the illness a raised C.S.F. protein (100 mg/100 ml) and paretic Lange curve were found. A diagnosis of *chronic limbic encephalitis* was suggested and confirmed at necropsy after an illness of two years' duration.

Dementia of Unknown Cause.—In 48 of the 84 demented patients (57%) no firm diagnosis could be achieved. Forty-one were thought to have cerebral atrophy on lumbar air encephalography, and in these the final diagnosis was "dementia due to cerebral atrophy of unknown cause." Two patients though definitely demented had normal air encephalograms. Five did not have air studies.

In some of these patients the clinical features suggested a possible aetiology—for example, vascular—but none fulfilled the criteria set out earlier. Many of these patients were presumed to have Alzheimer's disease or Pick's disease, but in the absence of histological confirmation we did not feel justified in making the distinction. Cerebral biopsies were not carried out.

This group is of special interest and will be the subject of further study.

Discussion

Patients suspected of losing their intellectual faculties prematurely require admission to hospital, not only to carry out investigations into the cause of the dementia but also to make sure that they really are demented. No fewer than 14% of the patients in this study, who were all admitted to a neurological hospital with a presumptive diagnosis of dementia, were found not to be demented. It required careful and prolonged observation in the ward and expert psychological testing to establish intact intellectual function.

Depression was the commonest cause of such apparent dementia, a fact well known to psychiatrists (see Kiloh, 1961). The poverty of thought and memory and the flattening of personality that characterize the retarded depressive can be very difficult to distinguish from the effects of dementia. A trial of antidepressant treatment may relieve symptoms but a therapeutic response is not conclusive, for some 25% of patients with dementia are depressed. The results of air encephalography are likewise not diagnostic, for on occasion obvious dementia may be associated with a normal air encephalogram (Gosling, 1955), as was the case in two patients in this study. Conversely, two depressed patients with no psychometric evidence of dementia had mild cortical atrophy on air studies. The difficulties of diagnosis can be illustrated by the problem of a 60-year-old man who presented in 1965 complaining of memory loss over the previous year. At that time psychometry showed a verbal I.Q. of 107 and a performance I.Q. of 92. It was not clear that he was demented and an air encephalogram was normal. Three years later his verbal I.Q. was 103, his performance I.Q. had fallen to 58, and a repeat air study showed severe cerebral atrophy. In general, when there is doubt about the diagnosis of dementia the matter is usually resolved by the passage of time, which allows obvious evidence of a true dementing illness to become apparent.

Of the 84 demented patients studied a diagnosis of the cause was made in 31, and an additional five patients possibly had communicating hydrocephalus. The commonest causes were cerebrovascular disease, cerebral atrophy associated with alcoholism, and intracranial tumour. This series does not include many of the known but obviously rare causes of dementia. We found no examples of vitamin B_{12} deficiency (Strachan and Henderson, 1965), myxoedema (Olivarius and Röder, 1970), hypocalcaemia (Robinson, Kallberg, and Crowley, 1954), or even neurosyphilis. The patients included in this study, however, had already been screened for an obvious cause for their dementia in the outpatient clinics of the hospital or at other hospitals. The finding of Argyll Robertson pupils, for example, at the outpatient consultation would have led to the patient's admission with a diagnosis of neurosyphilis, and such a patient would not have been included in this survey.

No fewer than 10% of the demented patients were found to harbour an unsuspected tumour, which proved to be a benign lesion in three patients. To find that 1 in 10 patients with dementia had a cerebral tumour may reflect some bias in the demented patients sent to a neurological hospital, but the fact that 2 or 3% of such patients have benign, potentially curable intracranial tumours reinforces the necessity for neurological investigations. These cerebral tumours were unsuspected on clinical grounds and discovered only by investigation. Although isotope scanning of the brain can frequently detect a tumour (or subdural haematoma) it must be remembered that not all intracranial tumours or other masses accept isotopes, and small masses under 2 cm in diameter cannot be defined as yet by this means. Air encephalography is required to exclude such tumours and is also the method of detecting communicating hydrocephalus.

Our series does not include many other uncommon intracranial space-occupying lesions that may present with dementia —for example, supratentorial meningioma (Sachs, 1950; Hunter, Blackwood, and Bull, 1968), intraventricular tumours (Riddoch, 1936; Kelly, 1951), pituitary tumours (White and Cobb, 1955), craniopharyngiomas (Tiberin, Goldberg, and Schwartz, 1958), subdural haematomata (Selecki, 1965), and giant cerebral aneurysms (Bull, 1969). Once dementia has supervened in these cases it is often very difficult to detect the signs that indicate that focal disease is the cause. For instance, to demonstrate unilateral anosmia due to a subfrontal meningioma, or a bitemporal hemianopia due to a parapituitary lesion, may be quite impracticable in the demented patient. The responsible lesion will be discovered only by full clinical, metabolic, and neuroradiological investigation.

In conclusion, the results of this survey reaffirm the value and necessity for full psychiatric and neurological investigation of patients with dementia in the presenium, for some 15% of such patients have a condition amenable to treatment.

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References

Adams, R. D., Fisher, C. M., Hakim, S., Ojemann, R. G., and Sweet, W. H. (1965). *New England Journal of Medicine*, **273**, 117.
Bannister, R. (1970). *Proceedings of the Royal Society of Medicine*, **63**, 921.
Bannister, R., Gilford, E., and Kocen, R. (1967). *Lancet*, **2**, 1014.
Bull, J. (1969). *Brain*, **92**, 535.
Gosling, R. H. (1955). *Journal of Neurology, Neurosurgery and Psychiatry*, **18**, 129.
Hunter, R., Blackwood, W., and Bull, J. (1968). *British Medical Journal*, **3**, 9.
Kelly, R. (1951). *Brain*, **74**, 23.
Kibler, R. F., Couch, R. S. C., and Crompton, M. R. (1961). *Brain*, **84**, 45.
Kiloh, L. G. (1961). *Acta Psychiatrica Scandinavica*, **37**, 336.
Logue, V., Durward, M., Pratt, R. T. C., Piercy, M., and Nixon, W. L. B. (1968). *British Journal of Psychiatry*, **114**, 137.
Nevin, S., McMenemey, W. H., Behrman, S., and Jones, D. P. (1960). *Brain*, **83**, 519.
Olivarius, B. de F., and Roder, E. (1970). *Acta Psychiatrica Scandinavica*, **46**, 1.
Riddoch, G. (1936). *Brain*, **59**, 225.
Robinson, K. C., Kallberg, M. H., and Crowley, M. F. (1954). *British Medical Journal*, **2**, 1203.
Sachs, S. (1950). *Journal of Mental Science*, **96**, 998.
Selecki, B. R. (1965). *Medical Journal of Australia*, **1**, 383.
Strachan, R. W., and Henderson, J. G. (1965). *Quarterly Journal of Medicine*, **34**, 303.
Tiberin, P., Goldberg, G. M., and Schwartz, A. (1958). *Neurology (Minneapolis)*, **8**, 51.
White, J. C., and Cobb, S. (1955). *Archives of Neurology and Psychiatry*, **74**, 383.

Acute Asymmetrical Neuritis Associated with Rapid Ultrafiltration Dialysis

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Summary

Three patients with chronic renal failure treated by haemodialysis developed acute asymmetrical sensory and motor neuropathies when ultrafiltration was induced to treat oedema. The neuropathies were characteristic of acute mononeuritis multiplex rather than uraemic polyneuritis, and we give our reasons for believing that they were not caused by toxic uraemic metabolites but by an ischaemic process due to vasoconstriction resulting from ultrafiltration.

Introduction

Peripheral neuropathies in patients undergoing intermittent haemodialysis were first noted in 1961 and later described in detail (Hegstrom *et al.*, 1962). They usually lead to bilateral and symmetrical defects due to distal non-inflammatory destruction of myelinated fibres, and often affect debilitated patients in whom dialysis was started late. Infrequent dialyses together with restricted protein intake may also cause rapid nerve damage which regresses when the number and duration of dialyses are increased (Lange and Lonergan, 1969), and a progressive neuropathy during maintenance haemodialysis is usually considered a sign of "inadequate dialysis" (Jebsen *et al.*, 1967). The pathophysiology of the condition is poorly understood, and a neurotoxic dialysable metabolite (Tenckhoff *et al.*, 1967; Giovannetti *et al.*, 1969), a lack of some neurotrophic substance (Callaghan, 1966; Tyler, 1968), and an impairment of carbohydrate tolerance (Asbury *et al.*, 1963) have been suggested as causes.

We have seen a rapidly progressive neuropathy in three patients undergoing maintenance haemodialysis in which several of the features were those of a mononeuritis multiplex rather than of the polyneuritis usually seen in these cases. The rapid onset, distribution, asymmetry, and the triggering role of ultrafiltration suggested separate lesions of ischaemic origin affecting several distinct nerve stems or roots. These are characteristic of mononeuritis multiplex. In one case electron microscopy of nerve and muscle tissue showed vascular lesions which supported the diagnosis.

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Case 1

A man aged 31 had had chronic renal disease for more than 20 years. In May 1968 his blood urea nitrogen was 210 mg/100 ml and his blood pressure 180/110 mm Hg. There were no neurological abnormalities, except that the nerve conduction velocity in both peroneal nerves was 34 m/sec (normal, 40±5 m/sec). There was no impairment in other peripheral nerves.

Like the other two patients, this patient was dialysed twice weekly for eight hours via an arteriovenous fistula between the left radial artery and the nearest vein, using Travenol coil UF 145. Ultrafiltration was applied during the third dialysis on 29 May, and two hours after it began the patient suddenly complained of right otalgia which was followed by a right-sided Bell's palsy. There was a loss of tendon reflexes in the right upper and both lower limbs. The plantar responses were flexor. Systolic blood pressure had fallen to 60 mm Hg on ultrafiltration but rose with saline infusion. Three hours after the end of dialysis the right facial palsy subsided and the blood pressure was 150/90 mm Hg when the patient was lying down and 90/70 mm Hg when upright.

Before the fourth dialysis on 1 June there was loss of flexion and lateral movements of the third, fourth, and fifth fingers of the left-hand; loss of all tendon reflexes except those of the left biceps and triceps; sensory loss in the area of the median nerve; and a partial impairment of the right sixth cranial nerve. One hour after beginning haemodialysis there were observed successively a reappearance of the right Bell's palsy (after otalgia), sensory loss in the right ulnar nerve, and complete paralysis of the right sixth cranial nerve with diplopia. Three hours later there were distal paralysis and anaesthesia of both legs and sensory loss in the whole right hand. After the dialysis ended all the neurological signs subsided within a few hours except those which were present before dialysis and the right facial paralysis, which persisted. During dialysis the serum phosphorylated thiamine was 8 μg/100 ml (normal, 3·5 μg/100 ml), and the next day the serum pyruvate was 0·62 mg/100 ml (normal, 0·5±0·1 mg/100 ml).