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Normal pressure hydrocephalus

In 1965 Raymond Adams and his coworkers described a new clinical syndrome of dementia with psychomotor retardation, unsteadiness of gait, and urinary incontinence. It was of insidious onset and associated with a characteristic pneumoencephalographic appearance of ventricular enlargement with an absence of air over the cerebral cortex owing to subarachnoid obstruction but with normal pressure in the cerebrospinal fluid on lumbar puncture. Patients showed clinical improvement after cerebrospinal fluid shunt procedures.^{1,2}

From the beginning the aetiology and pathophysiology of the condition have been difficult to understand, and they are probably multifactorial. It has been described after head injury,^{2,5} subarachnoid haemorrhage,^{3,5-7} intracranial surgery,⁸ cerebrovascular disease,⁹⁻¹¹ meningo-encephalitis,^{1,3,4,9} and in association with a brainstem glioma,¹² third ventricular cyst,¹ cerebellar haemangioblastoma,¹³ aqueduct stenosis,⁵ and third ventricular compression from an ectatic basilar artery.^{14,15} In perhaps as many as half of all cases there is no obvious cause. The factor common to all of these conditions is impairment of outflow and resorption of cerebrospinal fluid; this leads to a rise of the intraventricular pressure, which diminishes as the ventricles distend.^{2,16,17} Neurological signs and symptoms are produced by a combination of mechanical stretching of periventricular fibre pathways,¹⁸ of parenchymal brain disturbance as a result of diminished cerebral blood flow and reduced metabolism,^{8,19-21} and of periventricular oedema from transependymal flow of cerebrospinal fluid.²⁰⁻²³ Cerebrospinal fluid diversion procedures, usually ventriculoatrial or ventriculoperitoneal shunts with valves which open at low pressures, have reversed these abnormalities and produced clinical improvement in some highly selected patients—as many as two thirds in some series.^{3,7,9,24-31}

It is, however, difficult on clinical grounds alone to select patients who will benefit from shunt procedures and to distinguish them from those with dementia due to irreversible causes such as Alzheimer's disease or multiple cerebral infarcts. Several investigations have been used. The first was pneumoencephalography with some specific diagnostic measures.^{1,2,32,33} Computed tomography is now the preferred imaging method,³⁴⁻³⁶ and it may be combined with metrizamide cisternography.³⁷⁻³⁹ Investigations which determine the absorption and flow characteristics of cerebrospinal fluid have included radionuclide encephalography and cisternography,^{5,40-42} estimation of blood radionuclide concentrations,⁴³ lumbar saline infusion tests, and monitoring of

intracranial pressure.^{7,17,31,44-46} Despite or because of this multiplicity of tests there has not been general agreement about which factors best predict a successful outcome from shunting, either singly or in combination, and their prognostic value has been questioned.^{3,7,23-25,27,28,30,31,47}

If surgery was free of risk it might be a reasonable proposition to carry out a cerebrospinal fluid diversionary procedure on any demented patient with ataxia and urinary incontinence and large ventricles on computed tomography. In practice, however, complications—shunt infection, subdural haematoma and effusion, epileptic seizures, and shunt malfunction—occur in about one third of patients (range 9%-44%),^{3,24,25,27,31,47} and such a policy would inevitably lead to operations being done on many patients with Alzheimer's disease and other irreversible brain degenerations and parenchymal damage who could not hope to improve. More recent studies of cerebral blood flow and metabolism have shown that the regional flow, volume, and metabolism are reduced in patients with normal pressure hydrocephalus, particularly in the frontal, temporal, and basal ganglia areas. If the ventricular pressure and size are reduced the clinical state improves and there has been an accompanying improvement in these factors in most but not all reports.^{20,21,48-53} These techniques are not, however, sufficiently sensitive yet to differentiate reliably between normal pressure hydrocephalus and Alzheimer's disease and other forms of dementia.

Changes in Alzheimer's disease are detectable by positron emission tomography⁵⁴—decreased cortical blood flow and regional metabolism for glucose and oxygen in frontal, temporal, and parietal regions. A recent report by Jagust *et al*, using positron emission tomography with labelled fluoro-deoxyglucose to map cerebral glucose metabolism, showed global cerebral hypometabolism in three patients with normal pressure hydrocephalus; this could be distinguished from the bilateral temporoparietal hypometabolism seen in Alzheimer's disease.⁵⁵ The apparent paradox of global metabolic disturbance in normal pressure hydrocephalus with positron emission tomography, whereas blood flow studies usually show focal reduction, has not been explained. Positron emission tomography is an expensive, technically complex, and time consuming technique, available in only a few centres world wide. Possibly metabolic analogues of positron emitters may be synthesised and labelled with γ emitters to allow single photon tomographic studies to be undertaken—and this should be possible in most departments of nuclear medicine. Preliminary results in Alzheimer's disease are encouraging.⁵⁶ Such studies are in a very early

stage, and the numbers are small, so no definite conclusions can be drawn, but these provide some optimism for the future.

Meanwhile, while waiting for new diagnostic techniques to become available, and faced with demented patients who may have normal pressure hydrocephalus, how should the clinician select those likely to benefit from shunt procedures? Other remediable causes of dementia should be excluded. Surgery seems to give best results in patients showing the full clinical syndrome of dementia, disturbance of gait, and urinary incontinence, in whom the history is short and progressive, and in whom a clear cut aetiology has been established. Computed tomography scanning should be performed to exclude tumours, substantial infarction, and considerable generalised atrophy. The ventricles must be enlarged, and favourable features are lack of cortical atrophy and the presence of frontal white matter periventricular lucency. Whether to proceed to complementary investigations of cerebrospinal fluid dynamics and absorption of cerebral blood flow and metabolism will depend on the availability of resources and the experience of the doctor.

It is now 21 years since the clinical syndrome of normal pressure hydrocephalus was first described, yet there is no general agreement on its strict definition or how to select cases for treatment—which carries a substantial risk. With such diverse aetiologies we are probably dealing with more than one condition, and I do not believe that we know their natural histories. Most published studies have been retrospective, without controls. With a rapidly increasing population of patients with dementia I believe that the time is ripe for a strictly defined prospective controlled study of a large number of patients to answer these questions.

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