Memories are made of this

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Physicians aiming to prevent vascular disease, either when managing an individual patient or when designing a clinical trial, usually think about reducing the risk of stroke or ischaemic heart disease, or their combination. And, yet, an explosion in numbers of another vascular-related condition is looming, namely in dementia. This first edition of *Heart & Brain* focuses on dementia in general, and vascular dementia more specifically.

Dementia

Dementia can be defined as a progressive dysfunction of brain function leading to cognitive decline. Classically, primary dementia was categorised into types such as Alzheimer's disease (AD), vascular dementia (VaD), Lewy body disease and frontotemporal dementia. Epidemiological studies have suggested that AD is commonest, explaining 37–58% of cases, while pure VaD is present in 3–20% of cases. It is now becoming clear that few patients have pure syndromes and these diagnoses often co-exist, such that mixed AD and VaD may be present in 15–60% of cases. Some of the variation in its prevalence reflects geographical differences; AD is more common than VaD in developed countries but is less common in developing regions. Furthermore, different subtypes exist within these broad groups, as discussed in this edition for VaD by Ballard (pages HB 4–HB 7).[1] Dementia may also be secondary to other conditions such as HIV/AIDS, syphilis, B_{12} or folate deficiency, and thyroid dysfunction.

Dementia is highly prevalent, affecting 2–5% of people over the age of 65, and doubling every four years to reach 30–50% of those over 80 years. As the numbers of older people increase, the absolute numbers of those with dementia will increase. Patients with dementia have a shortened life and suffer from a variety of neuropsychiatric disorders including memory impairment, affective disorders (e.g. depression, anxiety), behavioural difficulties (e.g. agitation, disinhibition, crying) and psychiatric disturbance (e.g. hallucinations, delusion). The diagnosis of dementia is often missed or delayed, partly because it can present in many ways to different physician groups, including general practitioners, geriatricians, psychiatrists, neurologists, and stroke physicians.

Diagnosis and prevention

The diagnosis of dementia, especially its likely type and cause, is complex, as discussed in this edition by Whalley and Murray (pages HB 8–HB 14).[2] History and examination need to focus on assessment of memory, language, orientation, agnosia, activities of daily living, apraxia, executive functioning, social interaction, and judgement. Deficiencies in memory alone do not allow a diagnosis of dementia to be made. Laboratory tests and neuroimaging are required so that secondary causes of dementia and other conditions can be identified. Neuroimaging may also help in differentiating types of dementia, for example VaD is often associated with white-matter lesions, and AD with temporal lobe atrophy.

The presence of vascular risk factors is necessary when diagnosing VaD but these are often present in other forms, especially in AD. Hence, preventing first or recurrent vascular events may also reduce the risk of subsequent dementia. It is now clear that reducing blood pressure (BP) lowers the risk of subsequent stroke, whether or not a patient has had a previous stroke. The role of lowering BP in reducing cognitive decline and dementia is far less clear, as Mangoni and Jackson remind us in this edition (pages HB 15–HB 19).[3] Several observational studies have found that the use of antihypertensive therapy is associated with a reduced risk for dementia. Positive evidence from randomised controlled trials exists from the Systolic hypertension – Europe (Syst-Eur) trial (involving nitrendipine) and the Perindopril Protection against Recurrent Stroke Study (PROGRESS) (involving perindopril and indapamide) trials,[4,5] but not in several other studies. The role

of lipid lowering is also unclear. Although meta-analyses of early trials suggested that statins might reduce the development of dementia, recent and larger trials – such as the Heart Protection Study (HPS) and the Prospective Study Of Pravastatin in the Elderly at Risk (PROSPER) – did not find any beneficial effect.[6,7] However, antihypertensive agents and statins have proven ability in preventing both coronary artery disease and stroke in high-risk individuals so they should be used whether or not they also reduce dementia. Interventions modulating other risk factors for dementia and cognitive decline are currently being studied, e.g. the use of triple vitamin therapy (B_{12}, folate and pyridoxine) which lowers plasma homocysteine levels in patients with prior stroke in the Vitamin Intervention for Stroke Prevention (VISP) and Vitamins to Prevent Stroke (VITATOPS) trials.[8,9]

Treatment

Where individuals already have overt cognitive decline or mild-to-moderate dementia, cholinesterase inhibitors have a role in delaying progression and even improving cognitive and functional performance.[1] These agents reduce the degradation of the neurotransmitter, acetylcholine. Much of the data for these agents related to patients with AD but the overlap between AD and VaD suggests that those with VaD may also benefit. Aspirin and other non-steroidal anti-inflammatory drugs may also prevent, improve or stabilise cognitive decline. The role of other cognitive modifying drugs, e.g. xanthine derivatives, such as pentoxifylline and propentofylline, needs to be defined but it is worrying that potential treatments such as these may have been 'lost' as patents run out in the presence of insufficient data, a situation that also exists for these agents in acute stroke.[10] It is also important to maximise vascular prevention strategies in patients with established dementia.

Bullock reminds us in this edition (pages HB 20–HB 23) it is easy to suppress some of the features of dementia, e.g. agitation and aggression in VaD, without addressing the underlying problem.[11] Psychosocial management is a key part of the management of patients with dementia, as is attention to their carers who themselves are at high risk of physical and mental disease.

A call for action must be made to better manage the impending explosion in dementia. Large randomised controlled trials are needed to define the role of modifying vascular risk factors, e.g. lowering BP and lipids, and of treating existing cognitive decline and dementia. Clinically, we need to identify how to detect cognitive decline and dementia in the population, how to diagnose its type and likely causes, and how to implement the findings of existing trials in vascular prevention and cognitive treatment. This edition of *Heart & Brain* explores some of these issues.

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References

1. Ballard CG. Treating the symptoms of vascular dementia. *Br J Cardiol (Heart Brain)* 2003;**10**:HB 4-HB 7.
2. Whalley LJ, Murray AD. Vascular dementia. *Br J Cardiol (Heart Brain)* 2003;**10**:HB 8-HB 14.
3. Mangoni AA, Jackson SHD. Antihypertensive treatment and the prevention of stroke and dementia in elderly patients. *Br J Cardiol (Heart Brain)* 2003;**10**:HB 15-HB 19.
4. Forette F, Seux ML, Staessen JA *et al*. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet* 1998;**352**:1347-51.
5. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001;**358**:1033-41.
6. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;**360**:7-22.
7. Shepherd J, Blauw GJ, Murphy MB *et al*. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002;**360**:1623-30.
8. Toole JF. Major ongoing stroke trials. Vitamin Intervention for Stroke Prevention (VISP). *Stroke* 2001;**32**:589-90 (abstract).
9. Baker R, Eikelboom J, Gelavis A *et al.* Major ongoing stroke trials. VITAmins TO Prevent Stroke (VITATOPS). *Stroke* 2001;**32**:590 (abstract).
10. Bath PMW, Bath FJ, Asplund K. Pentoxifylline, propentofylline and pentifylline in acute ischaemic stroke (Cochrane Review). *The Cochrane Library.* 4th edn. Oxford: Update Software, 1998.
11. Bullock R. Vascular dementia - a suitable case for treatment. *Br J Cardiol (Heart Brain*) 2003;**10**:HB 20-HB 23.