from moderate numbers in the heart protection study), but responses among such patients would probably be similar. People with type 1 diabetes have substantial macrovascular risk, related to age and duration of diabetes. Statin therapy is indicated for those aged 40 and over, and also for adults under 40 who have microvascular complications, hypertension, sustained poor glycaemic control, metabolic syndrome, or an adverse family history.[3] Statins should be avoided, however, among women from the planning of conception to the end of breast feeding.

In statins we now have highly effective treatments to prevent cardiovascular disease in people with diabetes, and as clinicians we need to ensure that this treatment is widely used along with other effective strategies. Nevertheless, even with statin therapy, 70% of cardiovascular events still occur.

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Cerebral embolism and Alzheimer's disease

Early treatment of vascular risk factors may prevent or postpone dementia

Research p 1119

Until recently, advanced age and genes were the only well established risk factors for Alzheimer's disease; hence it has not been possible to develop preventive strategies. Now, evidence of modifiable risk factors for Alzheimer's disease is increasing. On p 1119, Purandare and colleagues report an association between spontaneous cerebral emboli and dementia.[1] This case-control study provides evidence for the longlasting debate on the causes of Alzheimer's disease versus those of vascular dementia.

Purandare and colleagues used transcranial Doppler to detect spontaneous cerebral emboli, monitoring patients with Alzheimer's disease, patients with vascular dementia, and age and sex matched controls for an hour. These emboli were detected significantly more frequently in patients with dementia, and the frequency was similar in Alzheimer's disease and vascular dementia. This study thus joins a series of articles that have pointed out a necessary shift from the concept of two sharply separated types of dementia to a dementia spectrum, with pure Alzheimer's disease and pure vascular dementia at the extremes and a mixture of the two in various degrees as the rule rather than the exception.

One of the main characteristics of research on dementia has been the tendency to separate neurodegenerative and vascular pathology. However, the complexity of the relation between the two main subtypes is now obvious, as more and more research data show considerable overlap in risk factors, neuropathology, and clinical features. Several epidemiological studies have suggested an association between Alzheimer's disease and vascular risk factors including hypertension, hypercholesterolemia, obesity, diabetes mellitus, dietary fat intake, and physical inactivity.[2 3] Moreover, carotid atherosclerosis[4] and atrial fibrillation,[5] two important sources of spontaneous cerebral emboli, have also been suggested as risk factors for dementia.

The coexistence of Alzheimer's-type changes and vascular neuropathological changes seems to be more common than would be expected by chance alone, and the two types of pathology have a synergistic effect, rather than simply additive effect, on the expression of dementia.[6] In addition, studies comparing neuropathological findings at autopsy with clinical diagnoses of dementia indicate important discrepancies between clinical labels and pathological reality.[7]

The typical clinical picture of Alzheimer's disease includes a long preclinical phase with an insidious onset of dementia, while the classical description of cognitive decline due to vascular causes comprises a stepwise onset and course. While there are cases that match this classical representation, in many situations identifying a date of onset proves impossible.[8] For example, large emboli may cause clinically visible strokes and lead to textbook cases of multi-infarct dementia, but small and clinically silent emboli occurring repeatedly over several months or years tend to cause slowly progressive brain damage and cognitive deficits.

The study by Purandare and colleagues is cross sectional and cannot draw a definite conclusion about cause and effect. The authors did not find any direct association between spontaneous cerebral emboli and cardiovascular risk factors (including carotid atherosclerosis and atrial fibrillation) in patients with dementia, implying that spontaneous cerebral emboli may be a universal phenomenon in dementia. But what mechanisms would lie behind an association between such emboli and dementia? It has to be kept in mind that factors such as blood pressure, serum cholesterol concentration, and body mass index often decline

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before dementia becomes obvious,[3] perhaps as a consequence of the disease, which may attenuate their effect in a cross sectional design. Indeed, Purandare and colleagues mention that body mass index was lower in both groups of patients with dementia than in the control group.

Even if this study leaves the question of mechanisms unanswered, it emphasises one very important issue related to preventing and treating dementia. The classical view of dementia has strongly influenced therapeutic approaches, making it difficult to tailor treatments to patients' various needs. If the diagnosis is vascular dementia, treatment aimed at cognitive impairment is sometimes overlooked, and if the diagnosis is Alzheimer's disease, vascular factors may be overlooked. Artificially labelling patients with one single diagnosis is less helpful than trying to identify and treat all possible aetiopathogenic factors. Early and effective treatment of vascular risk factors may have positive effects not only for cardiac health but may also help in preventing or postponing the onset of dementia.

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Kidneys for transplant

Radical changes should mean we get more of them, better allocated

See also p 1124

At the end of 2004, 5299 patients in the United Kingdom were waiting for kidneys from deceased donors, and during that year 1427 transplants from dead donors and 463 from living donors were performed.[1] The gap between supply and demand for kidney transplants continues to increase, but several important initiatives are under way to attempt to increase the total number of kidneys available and also to change the way donated organs are allocated.

Several centres are now retrieving organs from non-heart beating donors as well as conventional brain dead donors. These organs come from patients who have a cardiac arrest and cannot be resuscitated, whose kidneys are flushed with a cold preserving solution so that the kidneys can then be removed before irreversible damage occurs. With careful selection of donors and appropriate infrastructure these kidneys have been shown to perform as well as kidneys from brain dead donors.[2]

The drive to increase the number of kidney transplants from living donors has also been successful: the total number of living donor kidney transplants in the UK has increased by 33%, from 347 in 2000 to 463 in 2004.[3] However, many potential living donor transplants cannot proceed because of incompatible donor and recipient blood groups or preformed anti-HLA antibodies with donor specificity in the recipient. A change in the law may help ease this problem.

Later this year the new Human Tissue Act (www.opsi.gov.uk/acts/en2004/2004en30.htm) and the Human Tissue (Scotland) Act will allow the donor kidneys from two such immunologically incompatible potential living donor and recipient pairs to be interchanged to create two compatible pairs. The acts will also allow non-directed donations from so called altruistic donors—that is, a kidney donated by a healthy person without them being told who the recipient will be. UK Transplant, which coordinates the matching of donated organs and recipients, is exploring how best to facilitate these new types of donation, but experiences from other countries are encouraging.[4]

The shortage of organs has highlighted inequities in access to deceased donor kidneys, and after prolonged controversy the national kidney allocation scheme administered by UK Transplant has changed from this April. The main changes, hammered out by representatives of patients and professional groups, are radical but represent a fairer deal for patients in that they take more account of waiting time and less of tissue type matching. The scheme continues to take into account many factors relating to the donated kidney and potential recipients using complex computerised simulations designed to balance equity of access and utility of transplanted kidneys.

The background to the changes includes evidence of variation in access to kidneys and recent improvements in immunosuppression.[5] UK Transplant data reveal considerable variation in the proportion of dialysis patients put on waiting lists for transplantation in different parts of the country.[6] Time from starting dialysis to going on the waiting list also varies between centres.[7] Finally, the old UK Transplant allocation system, with its emphasis on tissue type matching, resulted in huge variations in waiting times for those patients listed, such that

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