The present programme deals specifically with destitute male hostel residents, for reasons identified elsewhere (Fernandez, 1985). It currently has the following components: a 16 bed admission unit and a day centre which caters for up to 70 attenders each day, both situated in the grounds of St Brendan's Hospital. In addition, programme facilities include the following community-based components: a rehabilitation programme which caters for 22 residents and ten day attenders, a supervised high-support hostel which caters for ten residents and six day attenders, and a supervised group-house which caters for five residents (Fernandez, 1989). A recent review of the foregoing programme (Kelleher, 1990) concluded with recommendations that "comparable facilities be established by other Health Boards in areas where the needs of the homeless mentally-ill are currently not being met" (p. 25) and that similar specialist facilities be established in the Eastern Health Board area for homeless females.

Many of the programmes implemented since 1986 were of necessity done on a slim budget which precluded a significant research component of a medical audit nature. This, however, has been rectified and several research projects are in being to evaluate and audit the new services. The lack of SR positions and of a properly organised higher training scheme is being attended to. As of January 1991 five general adult SR posts have been filled and an Eastern Regional Higher Training Scheme is being set up.

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Expert opinion

The molecular biology of Alzheimer's disease

For some years, the pace of progress in clinical neuroscience has progressively quickened but none more so than with molecular biological techniques. Clinical psychiatrists have been promised (some say forewarned) that the systematic application of these techniques will swiftly cut through the multifactorial aetiologies of many mental illnesses and revolutionise diagnosis, treatment and, possibly prevention. Not surprisingly, given the fact that Down's syndrome and Alzheimer's neuropathological changes (senile plaques and neurofibrillary tangles) are so tightly linked, understanding of Alzheimer's disease (AD) was the first mental illness to benefit from these new methods. Once the amyloid β protein component of the senile plaque had been isolated and its 39–43 constituent amino acids sequenced, then it became almost a routine matter to locate the gene and describe comprehensively the much larger (approximately 710 amino acids) amyloid β protein precursor (APP). Almost simultaneously, the gene responsible

for familial pre-senile Alzheimer's disease (FAD) was located, like the APP gene, on chromosome 21 (Tanzi *et al*, 1989). Soon, a claim was made that these (FAD and APP) were the same gene, and, in a manner akin to the presumed causal gene dosage effects in Down's syndrome, Alzheimer's disease was attributed to excess production of amyloid (by way of APP). However, this was quickly refuted and data to support a gene dosage effect in AD were not confirmed. The trail then seemed to go cold. Several studies indicated that FAD was genetically heterogeneous and distinct from senile AD (St George-Hyslop *et al*, 1990), and the problems of prion disease in animals and man secured more attention (Westaway *et al*, 1989).

Recently, two separate strands of research on the molecular biology of AD have emerged as potentially very informative indeed. Firstly, Yankner and colleagues in Harvard reported on the neurotrophic effects of amyloid β protein on hippocampal neurones early in culture and neurotoxic effects later on (Yankner *et al*, 1990). Similarities between parts of the amyloid sequence and the tachykinins (a family of neuropeptides containing Substance P) prompted Yankner to show that pretreatment with tachykinin antagonists could prevent the neurotoxic effect. The argument that amyloid β protein is an important cause of neuronal degeneration in AD was thus importantly strengthened. Previously, others had cautioned that amyloid need not be causal and could be a consequence of neuronal death, even of extra-cerebral origin.

A second recent study has again underlined the likely importance of amyloid β protein. Alison Goate and her colleagues at St Mary's (1991) have carefully examined the APP gene in 2 FAD kindreds (English and Dutch) and identified a single mutation in the transmembrane domain that was not found in 100 control subjects or in 14 cases from nine families with familial late-onset AD. Her finding raises a number of possibilities. Potentially, FAD is caused by mutations in APP, not necessarily identical between families, but sufficient to impair regulation of synthesis and biodegradation of APP. Accumulation of amyloid β protein would lead to neurotoxicity and the formation of extraneuronal plaques or, perhaps in a manner hypothesized by Chalfie & Wolinsky (1990), lead to vacuolation and neuronal death. A second and very challenging prospect is that there are other selective mutations in the APP gene that lead to other familial dementias, perhaps in a manner akin to prion disease (Hsiao *et al*, 1990). Clinicians could then be faced by an array of dementias and hold precise information about genetic causes but lack the clinical diagnostic methods to distinguish between them.

Obviously, all expect psychiatrists to be well-prepared to respond to the clinical implications of molecular biological research on AD. It is our commonest mental illness and the major public health challenge of the next century. In part, that response will be more effective the sooner (and better) collaborative research links are established with the laboratory teams. The success of the St Mary's group has placed UK Alzheimer's research once more at the forefront of the enormous international effort to understand AD. In context, it is one of our very few recent successes in a field where British research once held centre stage. To capitalise on this success, early replication of the findings is urgently required and this can only be achieved if clinicians caring for patients with FAD seek to contribute with the research effort.

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