

Expert opinion

Drugs for Alzheimer's disease

ANDREW W. PROCTER, Senior Lecturer in Psychiatry, United Medical and Dental Schools, Guy's Hospital Campus, London SE1 9RT

The view (Anon, 1990) that "drugs for Alzheimer's Disease (AD) are generally ineffective" is a reasonable conclusion to draw from the results of treatment studies to date. However in recent years there has been a rapid expansion of knowledge of both basic neurobiology and the pathology of AD. Future advances may be expected to arise from this, so when the authors of *Drugs and Therapeutics Bulletin* next review this subject they may well be able to draw a more optimistic conclusion.

When considering treatments for AD, it is important to remember that this is a progressive neurodegenerative condition with a characteristic pathology, from which patients die slowly distressing both to themselves and their carers. In this respect it differs from 'Age-Associated Memory Impairment' (McEntee & Crook, 1990) and similar conditions, the basis of which remains to be established. The results of studies in this latter group of conditions may have little relevance to AD, because the underlying neurochemical pathology is likely to differ.

There are many theories regarding the aetiology of AD but none are proven, so it seems appropriate to try to treat the condition symptomatically with drugs targeted at neurotransmitter dysfunction (see Whalley, 1989). Most studies hitherto have evaluated cognitive function, yet the mood and behavioural symptoms may be of considerable social, economic, and neurobiological importance (Fairburn & Hope, 1988), determining the care patients need, and maybe reflecting abnormal serotonergic systems (Palmer *et al*, 1989). Drugs with actions on this neurotransmitter may offer hope for more specific treatments of behavioural disorders. The reversal of cognitive symptoms may be more difficult as by the time the disease is clinically apparent, substantial cell loss has probably occurred. The importance of the pyramidal cells of the cerebral cortex (Bowen, 1990) and their likely neurotransmitter, glutamic acid (Greenamyre & Young, 1989) has been emphasised recently, perhaps because of this substance's putative role in memory function and some forms of neurode-

generation. In terms of the neurotransmitter dysfunction in AD, it could be considered that a glutamatergic theory is now threatening the pre-eminence of the cholinergic theory, in part perhaps because of the disappointing results of cholinomimetic therapies. Enhancing glutamatergic function directly may cause excitotoxic brain damage, so indirectly acting modulatory compounds have been proposed as therapy (Bowen, 1990). However the efficacy of this remains to be investigated.

In the day to day management of demented patients, the neurobiological research of AD may appear to have produced relatively esoteric information, but further advances are most likely to follow from the close collaboration of clinical and pre-clinical scientists. The clinician would be better advised, not that drugs are ineffective, but instead to keep an open mind, to test systematically drugs which basic research indicates may be of value, and to publicise the results.

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