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gerontology research: drug therapy for senile dementia

At least half the clients of the TRIMS geriatric clinic who are 65 and older have some degree of late-life organic brain syndrome. They suffer from impaired memory functions, reduced intellectual skills and judgment, often in association with emotional and behavioral disturbances.

Clinicians attempt to identify the causes of these symptoms and to alleviate those that are treatable. Perhaps as many as 40 percent of late-life organic brain syndromes have one or more etiologies requiring specific therapeutic measures.¹ Examples are drug intoxication, alcoholism, thyroid and other metabolic disorders, pernicious anemia, benign intracranial neoplasia, syphilis or other infections. Although treatment aimed at the etiologic factors does not always restore the patient's intellectual functioning completely, therapeutic intervention often brings great improvement. A significant number of older patients who initially present with symptoms of organic brain syndrome may be primarily depressed. Treating the depression results in a dramatic improvement of the patient's cognitive status.

causes difficult to identify

Unfortunately, the majority of persons with true dementia in late life do not have clear-cut, easily identified causative factors. This group is of greatest interest to us in terms of trying to find treatment that might correct the symptoms or prevent the causes. Here the etiology is identified by a process of exclusion, that is, by medical identification and treatment of the more obvious ones mentioned above.

Persons in this large group have brain degeneration caused by either small cerebrovascular accidents (multi-infarct dementia) or a kind of cerebral neuronal degeneration nearly indistinguishable from Alzheimer's disease (presenile dementia). True senile dementia probably represents a later onset of the Alzheimer degenerative process. It is, in fact, morphologically and symptomatically indistinguishable from Alzheimer's presenile dementia, which was first identified in much younger persons.

Until recently it was assumed that senile dementia was caused by various kinds of cerebrovascular insufficiency with or without multiple small strokes. Current

data suggest, however, that the incidence of the cerebrovascular type of dementia in the elderly is exceeded by that of the Alzheimer type, or senile dementia, by at least three to one.

adjunctive drug therapy

For many years TRIMS researchers have been interested in identifying and developing drugs that, theoretically, might improve or at least alleviate cognitive decline secondary to aging and Alzheimer brain deterioration. No drugs have dramatic results. A few drugs on the horizon—for example, the ergot alkaloid Hydergine² and the choline precursor lecithin—give some hope of temporarily improving the condition of selected elderly persons who have organic symptomatology.

These *nootropic* drugs exert their effects on the metabolism and biochemistry of brain neurons and they may influence the transport of chemicals across the blood-brain barrier. Their mode of action differs from that of the so-called cerebral vasodilators which have now gone out of favor, even for vascular or multi-infarct dementia.

TRIMS studies

Gaitz, Overall, and I³ demonstrated in 1974 that Hydergine is significantly better than placebo in improving intellectual function when the drug is used for more than three months even by very old and debilitated persons with dementia. We did not attempt to differentiate vascular from Alzheimer dementia. In a 1979 TRIMS study, Gaitz and Hartford showed that doubling the dosage of Hydergine may be even more efficacious than the current recommended dosage, 3 mg per day. These data have not been published, although the results are promising. Hydergine may exert some of its effects by acting as a mild anti-depressant; another protocol is being developed at TRIMS that will attempt to demonstrate or rule out this possibility.

Other classes of drugs that may ameliorate dementia are being studied at TRIMS. Gaitz et al.⁴ are beginning to investigate praxiline (Nafrolyl). Drugs of similar structure are being given clinical trials in this country or are clinically available in Europe. Smith and his colleagues at TRIMS

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gerontology research. . . continued

are evaluating acetylcholine precursors and drugs that block the breakdown of acetylcholine in the brain.

If efficacious at all, these drugs may be expected to give only limited results by themselves. Clinicians must accept the concept of "alteration, modification, and improvement" rather than "cure" in treating the intellectual decline in the elderly, and to treat the total patient. We hope that cerebroactive drugs will be found that will make the curve of intellectual decline more gradual and that will also improve the overall well-being and emotional stability of persons as they grow older and are faced with cognitive decline.

—Roy V. Varner, M.D.

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