Anticoagulant therapy: new hope for senile patients?

Until recently, the prognosis for patients with senile or presenile dementia, nearly 25% of all mental hospital first admissions, has almost always been considered “poor.” Elderly, often otherwise infirm, not brought to the hospital until rage, combative life, paranoia, depression, delirium, incontinence or impairment of memory and judgment have rendered them too difficult to manage at home. Most senile patients have had little to look forward to other than continued hospitalization, progressive deterioration and death within a few years.

In the past, attention has focused largely on special facilities and programs, counseling, group occupational and recreation therapies, tranquilizers, sedatives and other supportive measures—often very little. Now, however, a direct medical approach, the use of anticoagulants to facilitate circulation of blood to the brain, may make it possible for thousands of geriatric patients in psychiatric hospitals to return to their homes and communities and to the care of their family physicians. Although still in the initial stages of clinical study, “the potential of anticoagulant therapy is that patients can be started early enough, senile dementia may become a preventable disease,” Arthur C. Walsh, M.D., of Western Psychiatric Institute, Pittsburgh, told Roche Report.

Anticoagulant therapy for senile dementia is based on the hypothesis that the patient’s impairment is most often due to reduced circulation of blood to the brain because of thrombosis or blood sludging in stenosed intra or extracranial arteries, a disorder known to exist in varying degree in approximately 40% of the population over 50 years of age. “This hypothesis was borne out by the very first patient with progressive senile dementia to be treated with an anticoagulant,” Dr. Walsh reported at the 1968 meeting of the American Psychiatric Association. “In January of 1963, a 66-year-old lady was brought to see me by her daughter, who was a registered nurse and the wife of a surgeon and hence knowledgeable about medical matters. Her mother’s illness began in 1960 with very minor spells of confusion. Over the next few years the patient’s memory and reasoning power became gradually worse. When I first saw her, she was unable to use the bathroom, to dress herself or to light her own cigarette. A pneumoencephalogram had shown brain atrophy, and the neurological consultant predicted progressive deterioration. The daughter was starting to make arrangements to place her mother in an institution. In an attempt to avoid this, I suggested a trial of anticoagulant treatment to see if further deterioration could be prevented. Much to our surprise, Mrs. N. actually improved. In 2 months she was able not only to perform her own personal hygiene but also to once more do meticulous needlepoint work. The therapy was continued for the remaining 1½ years of her life, during which time she was able to live at her own home, by herself most of the time, even doing some of her own interior decorating. She died in August 1964 within 24 hours of the onset of a myocardial infarction.”

“A second patient, on whom we have autopsy proof of Alzheimer’s disease,” also responded to anticoagulant therapy,” Dr. Walsh continued. “He was a 56-year-old lawyer, engineer and successful executive whose first symptoms were his forgetting of his secretary’s name and an inability to sign checks without practicing his signature 10 times. After a period of several years, he deteriorated progressively until he became unmanageable and was admitted to our hospital. While on the drug, he was cooperative and able to go to the cafeteria, have no spells of confusion or collapsing and did not need a constant attendant. But on 4 occasions anticoagulant therapy was stopped, and each time his mind deteriorated noticeably: as soon as his prothrombin time returned to normal he became more confused, uncooperative and combative. Each time therapy was recommenced he improved. After it was discontinued for the last time, he soon became bedridden and died within 2 months.”

Prior to becoming a psychiatrist, Dr. Walsh had spent almost 20 years in general medical practice. His experience confirmed the “hopeless outlook” for patients with what was formerly called chronic brain syndrome associated with arteriosclerosis. “I had not only the opportunity but also the grim necessity of following the course of such patients from the onset of their initial symptoms to their reaching the eventful ‘vegetable’ state: incontinent, imbecile and bedridden,” he once wrote. “It was the repeated, hopeless, helpless watching of such patients that produced the present concept of treatment; at the same time, I had patients with transient ischemic attacks responding satisfactorily to anticoagulant therapy as proposed by C. H. Millikan, M.D. The thought was: Why could not the mental changes of the dementias be the psychic equivalent of the motor paralysis of the transient ischemic attacks? A bout of confusion could equal a weakened arm. In either situation, the

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Chromosome changes seen in senile dementia

Chromosome analysis of aging female patients (70 years or over) with senile dementia shows a greater loss of X chromosome material than in control patients. This increased loss of chromosome material may be “a basic part” of the etiology and pathogenesis of senile dementia, according to Johannes Nielsen, M.D., and associates at Aarhus State Hospital, Risskov, Denmark.

In their study, 10 women with senile dementia were compared with 10 controls of the same age group and 10 controls below age 40. Patients with dementia, aged 70 years or more, showed a “statistically significant higher percentage of hypodiploid cells” compared with the similar control group. The percentage of hypodiploid cells was also found to be statistically significantly higher in the aged control group compared with the control group below the age of 40. Such chromosome losses apparently interfere with metabolic functions and lead to rapidly increasing dementia, rapidly increasing aging processes and death, the investigators said.

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attack could and often did leave a major and permanent disability. Why not test this theory by a therapeutic trial?"

Fifteen other patients, with mixed diagnoses but all having motor deficits, psychologic deficits or both, were given a course of anticoagulant therapy, bringing the total to 17. "Most stayed the same, some improved but none deteriorated while under therapy," Dr. Walsh said in his initial report, early in 1967. The results seemed to warrant a more formal pilot study, only of patients firmly diagnosed as having presenile or senile dementia. Such a study subsequently began at Woodville State Hospital, Carnegie, Pa., during the summer of 1967.

Omitting those with any contraindications to anticoagulant therapy (e.g., bleeding ulcers), 13 rapidly deteriorating patients were chosen from the geriatric wards. During the 2½-month clinical trial, no patient died or deteriorated while under therapy and there were no bleeding problems. Prothrombin time tests were conducted by the hospital's lab, so that anticoagulant dosage could be controlled and adjusted for each patient. Of the 13 patients, 11 improved with anticoagulant medication (bishydroxycoumarin) and 2 "improved dramatically." Three of the 4 patients originally incapable of feeding themselves were able to do so during treatment; one of the 5, originally incontinent, became continent. As 9 of the patients became less confused, less disoriented and more cooperative, the amount of major tranquilizer given them was reduced. After anticoagulant therapy stopped, 8 of the 13 patients continued to deteriorate as before and 3 subsequently died. A more extensive trial, with controls, is anticipated.

At the A.P.A. meeting in Boston, Dr. Walsh suggested that in senile dementia, the site of the brain damage may be more important than the extent and that the changes in brain cells may often be functional rather than morphologic. This reduction in function would account for the discrepancy between the degree of dementia observed clinically and the amount of brain atrophy found at autopsy. Further, the patient's emotional reaction to his brain dysfunction—such as severe anxiety, depression or paranoia—may overshadow other symptoms.

Presenile dementia, on the other hand, appears to depend on a "chance combination" of thrombosis, stenoses of the vertebral and/or internal carotid arteries, common in people over 50 years of age, and reduced collateral circulation beyond the stenosis.

Patients who improve with anticoagulant therapy rather than remain stable may do so because they also have blood sludging that is relieved by the treatment, Dr. Walsh said. "The arterial lumen at the site of the stenosis may be only a few millimeters in diameter, and beyond this point the blood flow is sluggish and turbulent, with a tendency for its cellular elements to aggregate into clumps. This thickened blood cannot flow freely through the distal capillaries, with the result that some of the brain cells are prevented from functioning normally due to inadequate blood supply. This is the probable cause of delirium, which may be considered to be a temporary interruption of association pathways. Anticoagulants have been shown to break up this sludging so it is reasonable to expect these drugs to improve circulation and hence brain function, which should show clinically with relief of the delirium."

"The selection of patients for anticoagulant therapy and their subsequent supervision should be done very carefully. The dangers of treatment will have to be weighed against the prognosis without treatment," Dr. Walsh suggested. However, since the prognosis for senile dementia without treatment is "usually very poor" and "even worse" in Alzheimer's disease, since the incidence of hemorrhagic complications in patients on long-term anticoagulant therapy has been reported at only 3% per year, physicians "should not perhaps be overly fearful of giving a patient a trial of therapy."