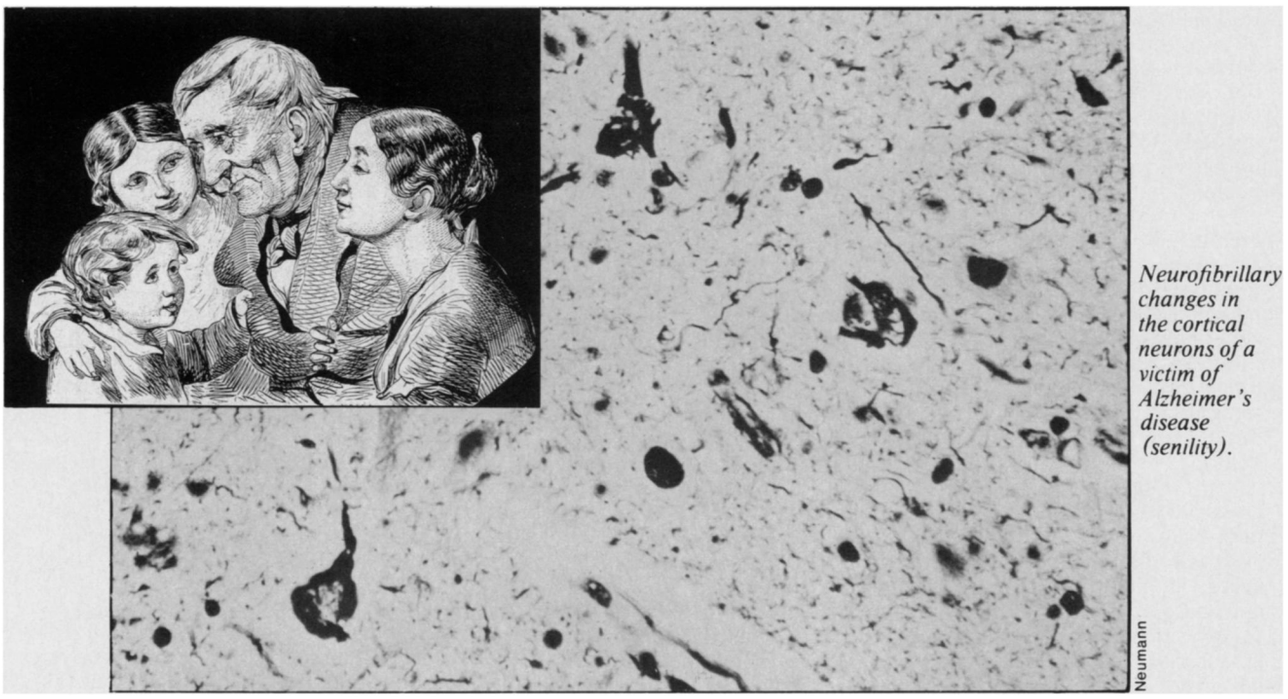
Senility: More Than Growing Old



Neurofibrillary changes in the cortical neurons of a victim of Alzheimer's disease (senility).

Neumann

Although progress is being made in diagnosing and explaining the pathology and causes of senility, much more will have to be learned before it can be effectively treated or prevented

BY JOAN AREHART—TREICHEL

In 1902, 51-year-old Alice K. began having trouble thinking, remembering and speaking. She became pathologically jealous of her husband, hid objects around the house and greeted her physician like a visitor. Her gait became impaired and her mental and physical state deteriorated rapidly. Four-and-a-half years later she died.

This woman suffered from senility (alias Alzheimer's disease) and, almost 70 years later, medical scientists have come to realize that this condition is a public health problem of major magnitude. As many as one million Americans may be victims of senility. Now, with increased interest in senility, researchers are beginning to make progress in diagnosing it, in understanding its pathology and in getting at its cause or causes, as revealed at a recent international conference on senility at the National Institutes of Health.

If there is one thing that senility investigators have come to realize during the past few years, it is that senility is not the same thing as the minor memory loss or increased forgetfulness that sometimes comes with old age. Researchers have dubbed the latter "benign senescence." Senility, in contrast, is a disease. It usually strikes persons past the age of 65, but may affect some younger ones as well, such as Alice K., cited above. As Robert Butler, director of the National Institute on Aging, puts it, "This devastating, dehumanizing disease is often associated with aging in the public mind. But senility is separate from normal aging."

The major symptoms of senility are increasing failure in problem solving, remembering and speaking, and a progressive disorganization of personality until the victims no longer recognize loved ones, familiar places or even themselves. For instance, one patient showed a deterioration in writing and in adding numbers early in the course of his disease, but he could still draw human figures. Four years later he could not even do the latter, drawing one human figure with no arms and drawing only a head for another. A good example of senile failure to recognize people and objects comes from an anecdote told at the senility conference. A physician showed a photograph of a voluptuous redheaded woman in a bikini to a senile man and asked him who or what it was. The man replied, "I know it isn't a tractor. But could it be a house?"

Still another major difference between senility and benign senescence is that victims of senility die sooner than would be predicted were they not senile. A number of investigators are also beginning to concur that senility and Alzheimer's disease are one and the same. Until recently, clinicians usually reserved the former description for senility after the age of 65, and the latter for younger victims.

Autopsies on the brains of senile patients are helping uncover the biology of the disease. There are striking, puzzling similarities between the senile brain and the normal, aged brain. If one weighs senile brains and compares them with age-matched control brains, they weigh the same. "This was a big surprise to us," admits Robert Terry of Albert Einstein College of Medicine in the Bronx. The relatively new technique of computerized axial tomography (SN: 3/13/76, p. 171) shows that the senile brain has the same sized ventricles (spaces) as that of a normal aged brain. There is no difference in the number of neurons found in many areas of the normal, aged brain and of the senile brain. That, too, is unexpected, says Terry.

Even with these and other similarities between the senile and normal, aged brain, however, pathology peculiar to the senile brain stands out.

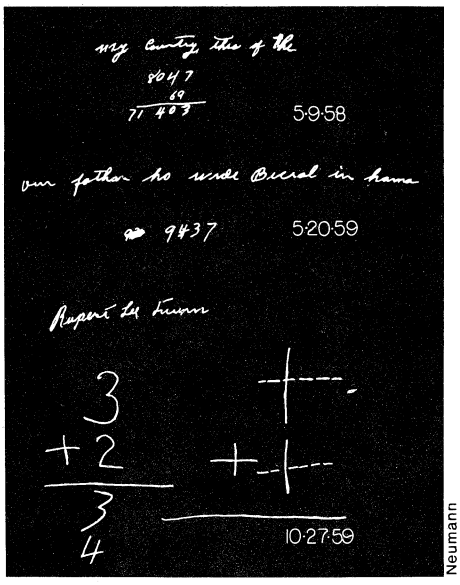
For one thing, the senile brain contains numerous plaques and tangles, whereas the normal, aged brain contains only a few. Plaques, interspersed among neurons, consist of cores of an abnormal protein called amyloid that are surrounded by paired helical filaments. Tangles, located in the cytoplasm of the neuron body, consist of twisted fibers. Whether the tangles are related to microtubules normally present in neurons, "we are not yet certain," says Terry. The plaques and tangles are common in the frontal and temporal lobes of the cerebral cortex —especially in the hippocampus, which is in the temporal lobe. Interestingly, the hippocampus is known to be involved in memory storage, an area in which senile victims show especially striking deficits. "Few other brain areas have shown such a clear psychological-physiological relationship," explains David Drachman of Northwestern University Medical School.

A greatly reduced number of neurons can also be found in the senile hippocampus compared to the normal aged hippocampus, reports J.A.N. Corsellis of Runwell Hospital in Wickford, Essex, Great Britain. There is also a dramatically reduced blood flow to the cerebral cortex, especially to the hippocampus of the Alzheimer patient, asserts David H. Ingvar of the University Hospital of Lund, in Sweden.

Ingvar and his colleagues made this discovery on autopsied brains using a special technique they have developed during the past 20 years and which is available in Scandanavia. Radioactive Xenon 133 is injected into the internal carotid artery of a subject. As the material moves up into the blood vessels of the subject's brain, it can be used to chart blood flow to various regions of the brain. The flow to diverse regions changes as the patient's brain activities and behavior change. The flow pattern is analyzed by a computer and displayed visually in color on an oscilloscope screen. The afflicted patient's brain, in contrast to a normal aged brain, shows drastically reduced blood flow in the cerebral cortex, and the decrease is proportional to the patient's psychological deficits. This technique, Ingvar concludes, "represents a new means of diagnosing cerebral defects in the living patient."

There are also some provocative leads on the possible cause or causes of senility. For instance, there is some evidence for a genetic basis for senility. Senility, along with Down's syndrome (mongolism) and leukemia, has been found to cluster in certain families (SN: 4/23/77, p. 263). One study of senile patients and their relatives showed a 60 percent risk of senility among identical twins, a 40 percent risk among fraternal twins, a 6 percent risk among siblings and a 3 percent risk for parents of victims of senility. Still another investigation of senile patients demonstrated a 10 percent risk of senility for parents and a 4 percent risk for siblings, compared with a 1 percent risk for the general population. As F. C. Stam of Vrije University in Amsterdam reports, three blood proteins are especially prevalent in senility victims. The proteins, called haptoglobins, are coded by three different genes that are all on chromosome number 16. Persons with those proteins are also more at risk for leukemia, a finding that dovetails with the study cited above linking senility and leukemia genetically.

Still other evidence suggests that impaired cholinergic neurons, especially in the hippocampus region of the brain, underlie senility. Cholinergic neurons are nerve cells that use acetylcholine as their neurotransmitter. Drachman and his coworkers studied both young and old subjects and found that cholinergic neurons play a significant role in memory. Another study showed that the cerebral cortex, especially the hippocampus, is rich in cholinergic neurons. Peter Davies



Neumann

Samples of the deteriorating arithmetic and writing performance of a senile patient.

of the Thomas Clouston Clinic in Edinburgh, Scotland, reports that there is a massive reduction in the senile brain, particularly in the hippocampus, of some of the enzymes used by cholinergic neurons.

Might senility be a disease of the immune system? There is some evidence for this hypothesis. George C. Glenner of the National Institute of Arthritis, Metabolism and Digestive Diseases has found a striking amino acid similarity between the terminal region of the light chains of antibodies and the amyloid cores of senile plaques. Therefore, protein material destined to be incorporated into antibodies may end up becoming plaques in the senile brain. Perhaps senility results from antibodies reacting by mistake against neurons in the brain. Kalidas Nandy of the Veterans Administration Hospital in Bedford, Mass., and his colleagues studied 24 pre- and post-65-year-old senile patients and 24 control patients 30 to 100 years old. They found that antibodies that attack neurons in the brain are especially prevalent among senile patients. The scientists are now trying to see whether the level of such antibodies in the senile brain can be correlated with the degree of mental impairment.

As if the roles of genes, cholinergic neurons and the immune system in senility were not confounding enough, there is evidence for still another possible cause of senility—slow viruses. As Henryk Wisniewski of New York State Institute for Basic Research in Mental Retardation in Staten Island points out, a slow virus may be responsible for the neurotangles of senility, because slow viruses like to reproduce in the microtubules of cells and, thus, change the configuration of the microtubules. Plaques have also been found in the brains of victims of some slow virus diseases, reports Clarence Gibbs of the National Institute of Neurological and Communicative Disorders and Stroke. But the strongest evidence that a slow virus may indeed trigger senility comes from Gibbs and his colleagues. When they injected brain material from senility victims into the brains of three monkeys, all displayed senile behavior.

There is still a fifth candidate cause for senility—the trace metal aluminum. Donald R. Crapper of the University of Toronto and his colleagues studied brain samples from 8 healthy persons and from 16 senile ones. Four times as much aluminum was found in the nuclei of neurons in the senile brains as in the nuclei of healthy brains, and the aluminum was especially prevalent in areas of the brains with lots of neurotangles. When the researchers gave animals toxic levels of aluminum, the metal produced senile behavior.

Finally, a sixth possible cause of senility is physical trauma to the brain: One man who was knocked unconscious in an automobile accident became senile; so did another who was hit on the head with a golf ball. Do these instances represent a cause-and-effect relationship? Possibly. Unfortunately, not enough case histories of this nature have been reported to represent conclusive findings. Corsellis and his colleagues studied 15 boxers, and a definite pattern of brain damage emerged. Curiously, masses of nerve cells had developed the fibrillary change associated with senility, but the other signs of severe senility were absent. Only the 15th boxer had experienced advanced senility before death and, thus, showed a senile brain on autopsy.

These various findings, however titillating, raise more questions than they answer about senility. Are all, some or none of the above factors causes of senility? Does it take multiple factors,

Continued on page 221

. . . Senility

working together, in order to produce senility? For instance, might senility be due to some inherited inability to metabolize aluminum properly? Intriguingly, Down's syndrome might be the result of a similar interaction because it too has been reported to have a genetic basis and because it too is characterized by abnormally high levels of aluminum in the brain.

Another challenge facing researchers is the task of coming up with some easy and accurate diagnostic test for senility. At present none exists, even with the sophisticated new computerized axial tomography. The problem is that the psychiatric and behavioral symptoms of senility, which are all doctors have to go on until death occurs, mimic those of numerous other diseases. For instance, silent depressives, like senile patients, suffer a defective memory and a high death rate. Victims of stroke, delirium, manic-depression and alcoholic dementia, like senility victims, can suffer impaired learning and memory. Normal pressure hydrocephalus, caused by tumor or head injury, can lead to a senile-like dementia.

Still another pressing question is why senile victims die prematurely. Is the cause of senility the same as the cause of premature death among the senile or is it separate—perhaps, pneumonia, weight loss or reduced resistance to infection that comes with self-neglect? Arthur Peck of the Jewish Home and Hospital for the Aged in New York City suggests a disturbing possibility—that the senile are woefully aware of their deteriorating mental and physical states and, not being able to do anything about them, experience a death wish. Martin Roth of the University of Newcastle upon Tyne in England agrees. "It looks like death from boredom."

Finally, do certain factors earlier in life (such as family history, occupational exposure, seasons and climate, life trauma, or personality differences) predispose one to senility later? No studies to answer these questions have been conducted to date, but one is getting underway—the Framingham study. Actually, the Framingham study was started in 1950, focusing on a population of 4,000 people in Framingham, Mass., and it has answered a number of questions about lifestyle and disease predisposition already, one of the most notable being the link between cigarette smoking and lung cancer. Now researchers will determine whether any of the Framingham population has succumbed to senility since the study started and, if so, whether certain factors in their lives might have predisposed them to this disease. If any links emerge, they will represent a step toward the prevention of senility.

Other valuable insights into senility should also emerge in the near future as NIH increases funding for senility research around the United States and as the NIA sets up a senility registry. □

. . . Voyager

these bases for deciphering our message had been established, then we could proceed to the list as given in SN, while we continued to use the translation-bridge-building method of 'read-hear-see.'"

She also raises another interesting possibility: "I wonder," she writes, "if any experts were consulted from the fields of deciphering dead languages, linguistic and communicative studies, communication with the mentally impaired, autistic, blind or deaf?" The answer is no, according to Cornell astronomer Frank Drake, who helped with the project. But, he says, such ideas would certainly be worth pursuing in the case of a more comprehensive message.

Still, regardless of its specific contents, the Voyager message tempts one to try seeing ourselves as alien recipients might see us. The following example—an excerpt from a "Report On Artifact Found Free-flying in Space"—was sent by Louise Ireland-Frey of Cedaredge, Colo.:

. . . Finally, High-placed One, there is a rubrous-metal disc and an odd article with a sharp-pointed awl or spine, to be used together. Several meteorites have dented these but not enough to destroy them. They appear to have been created, together with the entire artifact and its contents, in the dim past ages by some aniplant on an orb somewhat like ours but with a vastly greater intensity of heat and light. We could not have survived there.

One side of this metal disc contains noise-vibrations of diverse types. The meaning, if indeed there is meaning, escapes us, though we assume there must be meaning of utmost importance, else why should this have been selected to be thrust out into space? We sorrow at the thought that a perishing alien species attempted to cry into the depths of the Cosmos for help and the assistance never came. It would have helped us if the creator-aniplant had included a type of "prime-reader" or some very rudimentary instructions instead of hoping that this whirl-storm of noise-vibrations might be understood by any off-orb creature. When we ourselves send out messages, we test them first on aniplants of our own orb to see if our orb-fellows of other species can understand them.

The noises, however, are all grouped strictly in the mid-ranges . . . . Therefore, we believe this species must have had sensory organs limited entirely to the range of sound-vibrations represented . . . . But perhaps these creatures had other compensatory mechanisms. . . .

On the other side of the metal disc we managed to decipher picture-images of articles and creatures we take to be those common on the alien orb. A few are recognizable (as images of planets, diagrams of systems, etc., especially). Many are of strange figures, apparently all drawn as if viewed horizontally on a level with the object, not (as with practiced space explorers) from a higher level looking down, with shadow-studies providing horizontal configurations. This is very interesting, revealing that this species must have begun space exploration only a short time before sending out this artifact . . . .

Our experts have studied the pictures carefully and with puzzlement. It is sad that these pictographs of the various aniplants do not show how much is carapace and how much is pile and soft matter, nor how much is reducible, how much elatable, etc. The [markings on the] earlier-discovered artifact [presumably one of the Pioneer plaques—J. E.], *showing what we thought to be pictographs of constellations—inasmuch as the diagram of a sunplanet system was clearly discernable below—now appear to have been vastly enlarged (relative to the planetary diagram) pictographs of two of the aniplants shown on the rubrous metal disc!*

We are of the opinion, after conferring together, that these are two rather similar species, both quite common on the orb, perhaps even like the creatures who made the disc and some of the other articles. Both have smooth carapaces and unfurred facial areas; both have pile on that aspect of the head-end that is apparently the end farthest from the planetary surface (if, as we assume, the figures are intended to be viewed as if from the horizontal). The pile must be equivalent of our fur-basins, but located on the upper aspect of the head-end, for the holding of the eggs or spores . . . . They show no signs of budding . . . .

If aliens can form their own opinions, how about earthlings? Many readers asked whether there is or will be a commercially available version of the entire message, pictures and all, and Columbia Records, which donated its production services to the original project, is working on it. The problems are considerable—the large number of recording companies that contributed music, for example—and Columbia says that it may be the beginning of 1978 before the product (probably two disks for the sounds and a booklet for the pictures and explanations) can be available. Interested readers may address comments—and they could help make a difference—to Rick Smith, Vice President of Business Development, Columbia Records, 51 W. 52nd St., N.Y. 10019. One suggestion, which Columbia is considering, is a proposal by Carl Sagan that all profits be donated to a proposed foundation for extraterrestrial research.

The interest of earthlings is important, of course, but it is still those hoped-for aliens that are the inspiration. Let Mrs. Robin G. Lee, a reader from Ocean, N.J., close this column:

Right now, today, the earth is the only home we have. Everything on earth is one, it is all part of the very stuff the stars and the rest of the universe are made of. We are all part of the universe, and it is part of us. I sincerely hope that some day, many hundreds of thousands of years from now, this message does reach some far away world. But will it really be that far away? They will be our relatives, for their world, too, will be part of the same universe that our world is a part of.

—Jonathan Eberhart