ADI

Global Perspective

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A Newsletter for Alzheimer's Disease International, (The International Federation of Alzheimer's & Related Disorders Societies, Inc.)

Cross-Cultural Studies Symposium Takes New Perspective on AD

Speakers from China, France, Italy, Nigeria and the U.S. (listed here with their topics) participated in the Cross Cultural Symposium during the 6th Conference

Robert Katzman, M.D., (U.S.) Chief, Neurosciences Dept., UCSD School of Medicine, *Risk Factors & Cross Cultural Studies;*

Jean-Francois Foncin, M.D., (France) Directeur d'Etudes a l'Ecole Pratique des Hautes Etudes Laboratoire Montyon La Salpetriere, *Genetic Factors in Alzheimer's disease;*

Pr. Luigi Amaducci, M.D., (Italy) SMID Center, *Prevalence of Alzheimer's Disease: European Studies & Proposed Cross Cultural Studies;*

Barry Gurland, M.D., (U.S.) Center for Geriatrics & Gerontology, U.S.A., *Methodological Issues & Findings in Cross Cultural Study; Upper Manhattan Study;*

Dennis Evans, M.D., (U.S.) Rush-Presbyterian-St. Lukes, Chicago, *East Boston Study;*

Benjamin O. Osuntunkon, M.D., (Nigeria) Department of Psychiatry, Indiana University Medical School, U.S., *Alzheimer's Disease in Nigeria;*

Mingyuan Zhang, M.D., (China) Shanghai Institute of Mental Health, *Dementia Survey in Shanghai.*

A number of people who were unable to attend wrote or called for information on the symposium. We wrote for abstracts of the presentations. However, because of busy schedules, and perhaps difficulties with the mails, we have not yet received all of them, (but have been assured they are on the way).

We have elected to go to press with the abstracts we have received from Drs. Katzman, Amaducci, and Foncin (pages 3, 4, & 6) and hope to include the rest in a future issue.

6th International Conference Hailed as Intensive Well-Planned Success!

ADI's 6th International Conference opened with a dynamic pre-conference on Sunday, September 22nd, where representatives from Latin-American countries, Spain, and Hispanics from the USA, discussed common goals and strategies for care of Alzheimer patients and their families. Participants' strong desire to continue the dialogue–and pledges of support–promise to help formalize development of the Spanish-speaking ADI Region.

More than 90 presentors filled the five-day Conference held in Mexico City, September 23-27, 1990. Participants lauded planners as the daily sessions covered the gamut of scientific, medical and social Alzheimer's concerns.

Conference Proceedings are being prepared under the direction of Dr. Luis Miguel Gutierrez. "A public announcement will advise when they are available," says 6th Conference Secretariat Lic. Lilia Mendoza.

Lilia Mendoza (center) Conference Secretariat, 6th International Conference & Pres., Mexican Alzheimer's Association, stands for photographs with (from left) Edward Truschke, ADI Secretary General; Michael Coote, Pres., Alzheimer Society of Ireland & Conference Secretariat, 5th International Conference, Ireland 1989; Jerome H. Stone, Chairman Emeritus, Alzheimer Association, U.S. & ADI Treasurer; and, Richard Gehring, Chairman, Alzheimer's Association, U.S .

In This Issue. . .

ADI Grows, Moves Forward in Public Policy, Education, MSAB Action Plan

Five new members were welcomed into ADI membership during the International Federation's Annual Meeting held in Mexico City, September, 1990. The addition of Argentina, South Africa, Spain, Switzerland and Venezuela, brings the total membership to 20 countries (distributed over five continents).

A major work of ADI has been the conduct of annual International Conferences on Alzheimer's disease. This has resulted in an increased exchange of scientific information and heightening of awareness worldwide about the impact of Alzheimer's on its victims and their families, a key to achieving ADI's goals.

ADI saw important advances in its own development during meetings in Mexico City. Notably, two Committees emerged, and an action plan for the ADI Medical and Scientific Advisory Board was given.

Ad Hoc Public Policy Committee Defines '91 Objectives

The Public Policy Ad Hoc Committee met to explore problems and opportunities in communicating with governments in members' countries, to gain awareness and support for the needs of persons with Alzheimer's disease and their families.

The group, is functioning under the coleadership of Jeanne Bentley, Canada; Franceska Jordan, Australia; Nancy Lombardo, U.S. and Svante Svahnstrom, France. Meeting twice during the Mexico City Conference, the Committee looked at directions ADI might take in addressing the need to raise awareness and effectively advocate for more governmental funding for research and support provided to families.

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In the context of ADI goals and accomplishments and hopes for the future, they discussed ways to help move forward the public policy work of ADI.

They set three reasonable tasks to be accomplished by the Committee in 1991: (1) To create a glossary of terms used in the field of Alzheimer's disease and relating to care in the community. (2) To conduct a survey of members to obtain a profile of members' public policy programs and goals. (3) To undertake introduction of Home Care as a major public policy issue for ADI. Added was a fourth task of preparing the Committee for the next meeting.

In Amsterdam, September 1991, the Committee plans to meet twice. The first meeting will be a sharing session. For the second meeting, Committee members plan to discuss results of the survey and information gained through the sharing sessions to enable them to set new goals for the next year.

Trainer's Network Kicks Off Education Initiative

An Education initiative began during the Conference by way of a Trainer's Network. It comprises persons from eight countries, including: Argentina, Australia, Canada, Mexico, the Netherlands, New Zealand, Scotland, and the United States.

Jan Killeen, serving as facilitator, stated in a memo to Network members, "Hopefully there will be a number of benefits for members of the network: a). Sharing information on similar projects; b). Exchanging reports on methods and effectiveness of initiatives; c). Avoiding the duplication of effort where others have already produced materials which may be built on, translated or adapted; d). Highlight training policy/resource issues to inform the policy network."

MSAB Sets '91 Action Plan

The action plan for the ADI Medical & Scientific Advisory Board calls for the Board's Steering Committee to develop a document for discussion by the MSAB Executive Committee and, a full Medical & Scientific Advisory Board meeting during the Conference in Amsterdam.

Conference Overview

The following abstracts together with the Cross-cultural abstracts elsewhere in this issue of *Global Perspective*, provide an overview and insight into the broad range of topics covered during the 6th Conference.

➤ Finding a Cure and Easing the Burden: A Balanced Approach

Alzheimer's disease is a challenge of international scope that needs to be met by a balanced approach including basic research into finding the cure, and care reform, necessary to ease the burden of victims and their families. Tremendous advances in neuroscience are allowing us to understand the mechanism of cell death and develop therapeutic strategies designed to slow the progression of the disease. Short term treatments are focusing on replacing missing neurotransmitter elements such as acetylcholine; long term approaches depend on better understanding of neuronal viability such as the dependent on trophic factors. Advances in the understanding of the molecular biology of amyloid may lead to diagnostic tests based on either CSF studies or brain imaging. Despite those exciting advances, it is also important that we examine carefully the effectiveness of care systems that are present in different countries to care for victims of this disease. All countries will be facing an increasing burden from the elderly population. Major ethical issues concerning health care rationing, and balancing the priorities of youth and age, will need to be addressed. Alzheimer's disease is truly a lead issue both in the development of neuroscience and in the exploration of the quality of life for the elderly in different societies. **Peter J. Whitehouse, M. D., University Hospitals of Cleveland & Case Western Reserve University.**

➤ The Elderly Familial Policy for Intellectually Dependent People: An Example, the Gerontological Village in the City of Grenoble, France.

The Gerontological Village, an example of specialized domiciliary care, where staff training is provided (as well as information to family members) also offers day care,

—Continued on page 7

Risk Factors and Cross-Cultural Studies

A major challenge in regard to our understanding of Alzheimer's disease is to determine the causes or risk factors for this disorder. Cross-cultural studies offer a unique approach to determining risk factors since there may be very different "exposures" to a risk factor in differing countries. For example, in cardiovascular disease, the data in regard to a low incidence of heart attacks in countries such as Japan, where there is very little fat in the diet, has played a role in identifying the importance of diet in that disorder.

Several types of risk factors are now becoming apparent in Alzheimer's disease. There is general agreement that a history of Alzheimer's disease in a first-degree relative, that is, father, mother, brother or sister, increases the risk of the disorder. Another risk that has been found to be present rather consistently in different case control studies has been head trauma of sufficient degree to produce unconsciousness. Before a risk factor can be considered to be a cause of a disease, there must be biologic explanation as well as consistency and strength of association in epidemiological studies. In regard to these risk factors, it is possible that both produce excess production or abnormal degradation of the beta amyloid precursor protein in the form of diffuse plaques within the brain which then leads, in association with other factors, to the development of the Alzheimer process and ultimately progressive dementia.

In a study in Shanghai that will be reported later in the symposium by Dr. Zhang, lack of education has been found to be a major risk factor for the development of dementia. Two-thirds of the cases were of the Alzheimer type. Lack of education in Shanghai is especially evident because over 26% of the elderly cohorts studied had had no formal education whatsoever and in these individuals there was an approximately 50% increase in the prevalence of dementia past age 75. Similar data has been found in other international studies. What could be the biological basis for such a finding? One possibility is that individuals who had no opportunity for formal education have lower brain reserve than individuals with education, so that when the biological process called Alzheimer's disease begins in the brain and begins to destroy nerve cells and their connections, that is, synapses, the individual without education has fewer total number of synapses and less redundancy or reserve and therefore begins to show symptoms three or four years earlier than individuals who have had education. This is an unproven hypothesis, but it is a testable one that needs to be explored in the future since it would have very important social implications.

It is likely that these beginning findings emerging from cross cultural studies will be added to, in future years, by new risk factors to be discovered by continuing this important approach to the understanding of Alzheimer's disease.

—Robert Katzman, M.D., Chief,
Department of Neurosciences,
University of California,
San Diego,
School of Medicine.

Strategies Sought to Raise Alzheimer Awareness. . .

New ADI members seek ways to raise the level of Alzheimer awareness in their countries. One strategy members use is the Focus Week (or Month), January is "Alzheimer Awareness Month" in Canada; a week in April is "Alzheimer's Action Week" in Australia. In the U. S., the Alzheimer's Association has "NADM—National Alzheimer's Disease Month" and Scotland conducts "Dementia Awareness" in 1991 from June 23-30.

In its newsletter to members Alzheimer's Scotland points out, "This will be our biggest and best chance in 1991 to let the public know about dementia and what we are doing to help both sufferers and carers. It is also an opportunity to fundraise on a national and local level."

In most countries, six months to a year in advance, special events for the designated period are devised to draw media attention. Often, it is hoped the events will also generate some funds. Special observances, educational opportunities and gala events are held by local groups and national associations. Press releases and informative Alzheimer's Awareness Kits sent to the news media help tell about AD and the Society. Public Service Announcements are distributed by Chapters and National.

A special event provides a "peg" on which to hang an Alzheimer story, together with information about AD (its impact on its victims and their families, its potential effect on the economy). This formula seems to provide a key to the success of awareness efforts worldwide.

And why all this aggressive public information and awareness activity? For a response, we quote the Alzheimer's Scotland newsletter, "Through a combination of national and local publicity and fundraising events we have the chance to "sell" the good work of Alzheimer's Scotland and all its supporters." And it should be noted that the funds raised help strengthen and expand the Society's service programs.

Public Policy Programs: *"A Fair Go For Dementia"*

Alzheimer's societies in Australia, Canada, New Zealand, and the U. S., all have dynamic advocacy programs to seek change in public policy and encourage earmarking of governmental funds for research to find the cause, treatment and cure of AD, and to provide support to afflicted persons, their families and carers.

Australia and New Zealand put out a publication *A Fair Go For Dementia* to help members in approaching legislators. The latest version of the U. S. publiction *National Program to Conquer Alzheimer's Disease*, was released in time for the Association's Third Public Policy Forum held in Washington D. C., April 20-24, 1991.

The Public Policy Forum offers Chapter members workshops on critical issues, techniques and strategies in addressing legislators on a one to one basis. Then, opportunities to meet their legislators are provided. Hearings and other special events are included during the Forum.

The WHO Program for Research on Aging, Age-Associated Dementia Project

This study is supported by the World Health Organization Program for Research on Aging; National Institute of Aging-National Institutes of Health (U.S.A.); and the Italian Multicenter Study on Dementia (S.M.I.D. Center). Participants include: A. Lippi, M.D.; P. Nencini, M.D.; M.P. Amato; M.D.; M. Baldereschi, M.D.; and L. Amaducci, M.D.

The World Health Organization (WHO) on the basis of the resolution 40.29 of the World Health Assembly (May 1987), promoted a Program for Research on Aging (PRA); and, the WHO Advisory Committee on Health Research identified four priority areas (1):

- Dementia of healthy aging;
- Age-Associated Dementias;
- Nutritional changes associated with aging, with special emphasis on osteoporosis;
- Age-related changes in immune function.

The Age-Associated Dementias project is a cross-national, multicenter, epidemiological research. Its principal research goals are: the standardization and validation of research instruments for cross-national diagnosis of dementia and dementia subtypes; the estimates and the comparison across study centers of the prevalence and incident rates of dementia; and the study of risk factors for dementia.

Participating Countries

The study is coordinated by the Italian Multicenter on Dementia (S.M.I.D. Centre), located in Florence, Italy, under the supervision of a Steering Committee composed by an international panel of experts.

Canada, Chile, Malta, Nigeria, Spain, and the United States of America, are the participating countries. In each, at least one urban and one rural area have been identified as field areas. In each country, the population study is represented by the aging population over 65. The proposed sample size for each field area is 2,500. The field areas and sample-sizes for each participating country are shown in table 1.

In Canada, the study is carried out jointly by the Canadian National Study of Dementia in which five provinces are involved. Three areas located in Quebec Province, British Columbia and Atlantic Provinces, also participate in the WHO study.

Table No. 1
WHO-PRA AGE-ASSOCIATED DEMENTIAS
FIELD AREAS

COUNTRY	FIELD AREA	>65 YEARS	SAMPLE SIZE
CANADA	Quebec Province	650,666	2,500
	British Columbia	349,490	2,500
	Atlantic Provinces	249,610	2,500
CHILE	Concepcion	17,283	2,500
	Quillon	1,142	
	Florida	919	2,500
	Santa Juana	901	
MALTA	La Vailetta	1,680	1,680
	Gozo	3,120	3,120
NIGERIA	Idikan District (Ibadan)	500	500
	Igboora	1,800	1,800
SPAIN	Margaritas District (Getafe)	2,032	2,032
	Arevalo County	3,840	2,500
USA (Indiana)	Marion County	9,192	2,500

In Chile, the study is conducted on the white population resident in the city of Concepcion, and in 3 little villages: Quillon, Florida and Santa Juana.

In Malta, the sample is the whole population over the age of 65 (n=4,800) resident in the capital La Valletta and in the Gozo island.

In Nigeria, the study population, that is the subjects over the age of 65, resident in the Ibikan District of Ibadan (n=2,500) and in the rural area of Igboora (n=-2,500) will be identified by the means of a private census.

In Spain, a district of the city of Getafe, a metropolitan area of Madrid, and a rural area, Arevalo County, 100 Km from Madrid have been selected.

Finally, the black population of Marion County, near Indianapolis, Indiana, U.S.A., will be studied in comparison with Nigerian population.

Study Design

The first step in the study is the standardization of the diagnosis of dementia across the centers. Then, the pilot and the field study will follow in each participating country. The standardization of the diagnosis of dementia is a major issue of the cross-national study and one of the main goals.

The evaluation of the inter-observer agreement on the diagnosis of dementia is based on the sharing across centers of records filled in for actual patients, the blind re-assessment of the records and, agreement analysis by means of the kappa index (2). Iteration of this process might be necessary to reach the desired level of agreement.

Pilot and Field Studies

The pilot study will be carried out in each participating country. In the pilot study the screening instrument to be used in the field study will be validated on a sample of the study population and or clinical series of demented and non-demented patients in order to reach a suitable number of dementia cases. The proposed screening instruments to be validated in the pilot study are the Information-Memory Concentration Test (3) and the Mini Mental Status Examination (4). Both the tests will be validated, using the final clinical diagnosis as the gold standard.

Only one test will be selected for the field study. The cut-off score will be established on the basis of the best balance between sensitivity and specifically for each possible score. In the selection of the cut-off score the subject's educational level will be taken into account and different cut-off scores will be selected for different levels of education.

In the pilot study the cut-off score of the neuropsychological examination to be used in the diagnostic process will be validated by using the same procedure.

The field study is a prospective one and it is arranged in a cross-sectional and in a longitudinal survey. The cross-sectional survey allows us to identify the prevalent cases of dementia and to collect data on exposures to risk factors in non-demented subjects. The same population sample will be reassessed two years later, to identify

the incidence cases and to estimate the relative risk.

Instruments

A multi-phase procedure will be used for case identification and diagnosis. The procedure includes the screening (Phase One), the diagnosis of dementia (Phase Two), and of dementia subtypes (Phase Three).

❒ Phase One:

In Phase one, the screening test for cognitive impairment will be administered by lay personnel to the sampled subjects. The screening test will be administered in the local language and the items will be harmonized to specific cultures.

Subjects identified as potential cases by the screening test will also undergo the subsequent phases of the diagnostic procedure. A representative sub-sample (about 10%) of subjects above the cut-off level will undergo the clinical evaluation as a check on false negatives.

Together with the screening test the lay personnel will administer a risk factor interview to all the sampled subjects. The data collection on exposure to different risk factors in non-cases allows us to estimate the relative risk after the identification of the incident cases. The interview includes putative risk factors for Alzheimer's disease (dementia or Down's syndrome in the relatives, parental age at subject's birth, head trauma) questions on demographic factors (age, race, ethnicity, marital status, residence, living in institutions, education and occupation), and risk factors relevant to vascular and other dementias (smoking, alcohol consumption, hypertension, diabetes).

❒ Phase Two:

The subjects scoring under the cut-off level at the screening test will undergo the second phase of the diagnostic procedure. First of all, the degree of the cognitive impairment will be evaluated by means of the neuropsychological examination from CAMDEX (5). This neuropsychological examination will identify false positives at the screening test. A sample of this population (about 10%) will also undergo the subsequent diagnostic procedure as check.

The evaluation of the functional impairment will be based on an interview with a surrogate informant on the patient's present difficulty in the activities of daily living. This interview is based on CAMDEX (5) and on the Pfeiffer Functional Scale (6).

The clinical evaluation will also include a medical history and the physical and neurological examination according to CERAD. (7). Patients affected by depressive pseudodementia will be identified by means of a structured version of the Hamilton Depression Scale (8) and the DSM-III-R criteria for major depression (9). The diagnosis of dementia will be done according to both the DSM-III-R (10) and the ICD-10 (11) criteria.

❒ Phase Three:

Demented subjects will be classified into different diagnostic categories. The differential diagnosis will also be supported by laboratory tests and neuroimaging, when possible. The diagnostic criteria will be the NINCDS-ADRDA (12) for Alzheimer's disease and the ICD-10 for vascular and secondary dementias (11).

Follow-up:

Dementia cases will be followed, after one year in order to collect information on the natural history of the disease. Depressed patients, bordering or doubtful cases, will be rechecked after a six-month interval in order to confirm the diagnosis.

—Prof. Luigi Amaducci, M.D.; Italian Multicenter Study on Dementia (S.M.I.D. Center), and the Dept. of Neurologic & Psychiatric Sciences, University of Florence, Italy.

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Why Do They Call it Respite Care???

The term *Respite Care* was coined to refer to any form of care that would provide relief of the burden of care for the caregiver. Most often this involved day care, in-home care and short-term institutional care. As programs developed, it was recognized that a great service can also be provided Alzheimer patients, often improving their quality of life. The name and programs may vary, but the need does not.

Genetic Factors in Alzheimer's Disease

I am going to present the case for a genetic theory of AD. Genetics, as a part of biology, may be subdivided into formal or Mendelian genetics, population genetics, and molecular genetics. Formal genetics and population genetics are a necessary step towards any molecular genetics study.

Epidemiology Studies

Epidemiology studies show that the presence of a case of AD in the near family of a person significantly augments the risk for AD for that person. Apart from the increased risk with age, this finding is the only undisputed clue causal epidemiology has to offer concerning AD etiology. A large number of small pedigrees, drawn from interrogation of relatives of an AD index case, show AD "running in a family" over two or three generations,. Neither epidemiology studies nor small pedigrees do offer a proof of genetic transmission of AD: vertical transmission of an agent, or environmental factors common to a family, could give similar results.

Pedigrees are Studied

A few pedigrees of families with AD have been studied more extensively, drawing on written records to study transmission over more than three generations in a large number of individuals. These pedigrees carry early onset AD, which has often been construed as indicating the existence of two distinct forms of AD, one, mostly early onset, Mendelian dominant, the other, mostly late onset ("senile dementia of the Alzheimer type", SDAT), sporadic.

A FAD gene (McKussick's AD1) was mapped to chromosome 21 by St. George Hyslop, e.a., in 1987, and recently confirmed: In some instances (early onset forms) a linkage can be demonstrated between AD phenotype and markers on chromosome 21. The locus thus defined is situated between the centromere and the polymorphic marker S16, not very close to that marker (non-negligible recombination fraction), meaning that no molecular genetic diagnosis of (even familial) AD is available, and that direct access to the gene may be far away.

Formal Genetic Studies

These might bring some light to controversial issues in AD nosology, and indeed might lead to an unifying theory. The data to be discussed come from an ongoing study I originated in 1972. This study has lately been continued largely through the SMID-SUD facilities in southern Italy, notable by Drs. Amalia Bruni and Maria-Paola Montesi. Dr. D. Salmon (Paris) took an important part in the mathematical genetics study.

The object of study is an extended kindred (family "N") with early onset AD (mean age at onset 42 years), originating in Calabria (Italy) The methods we largely developed for this study stress the use of objective sources (municipal and hospital records, parish registers), and "blanket" study, with the purpose of minimizing bias in data collection. The pedigree now comprises about 6,000 subjects linked to the proband through the transitive (ascent, descent, marriage) set of relationships. Sixty-one of them are known to be or have been affected by early onset AD and thirteen are obligate transmitters under Mendelian dominant transmission, phenotype unknown. All known affected members of the kindred are descendents of a woman born in 1715 who died aged 45. Transmission is compatible with Mendelian autosomal dominant with "complete penetrance."

Glossary:

Allele: In genetics, one of a series of hereditary characters alternative to each other.

Epidemiology: The branch of medicine that deals with epidemic diseases, (breaking out suddenly and more or less unpredictably in a particular area in such a way as to affect many individuals).

Genotype: The genetic constitution of an organism

Pedigree: A line of ancestors, a list or table of descent and relationship.

Phenotype: The aggregate of genetic characteristics visibly manifested by an organism.

A striking feature of AD in family "N" is its phenotype variability as determined by the variability of the age of expression, whereas age at onset has often been deemed characteristic of separate forms of AD. Age at death of demented victims of AD in family "N", which we took as index of age of expression, has a mean of 50 years, with extremes 38 and 65 years, standard deviation six years: it takes twenty-four years to encompass 95% of the patients.

A description would be given by a theoretical age-specific mortality curve fitted with observed data. Weibull and Kaplan-Meier survival models, which suppose constant or adjusted risk, usually provide a good fit for cancer survival studies, but is very poor with our AD data. Best fit is given by a log-normal distribution, reflecting a (random) stochastic process with a zero lower bound of the variable.

In test, the environment hypothesis as an explanation for the variations in ag of expression, we compared patients having lived respectively in the nineteenth and the twentieth centuries, or in Europe and in America: a cross-cultural study. There is absolutely no difference in the phenotype of AD, as defined by mean and standard deviation of the age of expression, between any of the groups: a nineteenth century illiterate farm laborer in Southern Italy and a twentieth century business executive in north-eastern America share the same destiny. So much for the influence of aluminium pots and pans or the protective role of instruction on the expression of AD.

The Role of Expression Genes

We then have to study the possible role of expression genes in the variety of expression of AD. We chose to study the pairwise correlation between age at death of the affected parent and that of an affected child. If there is an expression gene linked with the FAD gene, this correlation will tend to 1, depending on the pene trance of the expression gene. If there is an unlinked dominant fully penetrant major expression gene, correlation will be 0.5. In other situations with an unlinked expres-

sion gene, a less strong but positive correlation is expected. Environmental factors shared by parent and child, if playing a role in gene expression, would also result in a positive correlation. In family "N", pairwise correlation between age at death of a demented parent and a demented child is 0.001, that is, zero: neither environmental (see above) nor expression genes play any role in the expression of AD in family "N". In that family, AD transmission is Mendelian autosomic dominant, monogenic, independent of environment; the large variability in expression age is purely stochastic.

We Then Apply These Results

...to a theoretical kindred identical to family "N," except the age of expression is 38 years later, bringing uncorrected mean age at onset to age 80. Combining age specific AD mortality with the survival curve of a control population show that most carriers of late onset AD will die before expression of the disease; only one over five genotype carriers will express the disease phenotype; apparent mean age at onset is lower than the theoretical one, since a larger portion of carriers "scheduled to express the phenotype" after age 80, is going to die before expression of disease.

This representation of AD epidemiology is strikingly similar to that proposed in 1988 by Breitner, e.a., starting from a large sample of (mostly late onset) AD cases. The minor differences between the Breitner representation and our model may be due to the implicitly monoallelic nature of our model. The dispersion of the age of manifestation of "real" AD would be attributed, according to our theory, to a combination of allelic multiplicity and stochastic variation inside one allelic species.

A Unifying Theory

We present an unifying theory or frame of reference for the interpretation of the many data steadily accumulating about AD; Alzheimer's disease is Mendelian monogenic polyallelic, possible multilocal, disease on the model of the thalassomies, which used to be known under the syncretic eponym "Cooley's" disease," until genetics and molecular biology allowed mapping of the involved genes to two different chromosomes. The various clinical forms (early onset, late onset...) could then be attributed to various mutations in the alpha of (more frequently) the beta chain globine genes.

Empirical formal genetics of late onset AD is a nearly hopeless endeavor, with so many missing links (carriers dying before expression age) breaking the chain of transmission. Moreover, AD genes are very frequent in the general populations (0.20 in our simplified monoallelic late onset model). As a consequence, linkage studies of late onset FAD are at best very difficult, due in particular to false recombinations. This may account for discrepancies between the results of linkage studies using respectively early onset and late onset familial AD.

The so-called "normal aged" with plaques and tangles really are AD genotype carriers who died before clinical phenotype expression. This conception entails that a very large proportion of humans are carriers of various alleles of the AD gene(s), but does not invalidate the disease paradigm for Alzheimer's disease, as distinct from an aging paradigm: measles used to affect almost all children before vaccination, and yet is a disease.

Proposed diagnostic procedures must distinguish between Alzheimer genotype and Alzheimer phenotype. Peripheral markers might only be indicative of genotype, which, if not coupled with an indication relating to the allele involved (early or late onset), would be almost useless as a predictor of clinical course.

Any apparent difference between populations regarding AD epidemiology may be due to ascertainment bias, and/or to demographic factors, and/or to founder effect, but not to environment. Systemic cross-cultural, or cross-population, studies of founder effect and rare alleles are a promising way for the understanding of the natural history of Alzheimer's disease.

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Laboratoire Montyon LaSalpétriére;
Paris France

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assessment, group or collective residences, psychogerontological units and coordination between geriatricians and psychiatrists. **Professor Robert Hugonot, Faculty of Medicine, University of Grenoble, France.**

➤ Institutional Response to the Sexuality of the Elderly with Dementia

Health care professionals and society in general are slow to accept the critical importance of sexual expression in the later years of the human cycle. The Hebrew Home for the Aged at Riverdale has analyzed its practices on this subject, as well as reports by similar facilities; redefined its written policies on sexual expression by its residents; and instituted an education program for residents, families, professional staff, and personnel. Lectures, case studies, and follow-up evaluations are components of a three hour training program to modify cultural barriers regarding sexuality in a predominantly Jewish resident population. Evaluations reflect positive responses to needs for intimacy, and more freedom of expression in a broad range of attitudes and behaviors. This paper will report on this education and self-study process with an emphasis on the special needs of patients with dementia. Specifically, the impact of "problem sexual behaviors" will be addressed in the context of family and staff responses. Issues of continuity of sexuality through personal intimacy with one's partner, masturbation, gender continuity, and related activities including dance and touch will be explored. **Jacob Reingold, Hebrew Home for the Aged, Riverdale, New York City**

➤ Resilience in the Face of Dementia

Caring for a family member with dementia is psychologically stressful. There is now a body of research to indicate which carers

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Alzheimer Europe to Raise Awareness with EC

Alzheimer Europe (AE) began in September 1990 when representatives of six European national Alzheimer's societies met with Dr. Franz Baro and Dr. Henk ter Haar and Michael Coote, in Louvain, Belgium, to discuss formation of a European presence to establish Alzheimer awareness with the European Council, Commission, Parliament and other national and supra-national organizations to gain support for the Alzheimer cause.

AE delegates plan to make personal contact with their members of the European Parliament, keep them informed of progress of Alzheimer Europe, and when appropriate, urge them to put forward and support proposals that will benefit Alzheimer patients and carers.

A second AE meeting was held in Amsterdam in January 1991. Members represented were: Belgium (Franz Baro), England (Nori Graham), Finland (Leila Mustanoja), France (Laurence d'Aramon), Germany (Eleanor von Rotenhan), Ireland (Michael Coote), The Netherlands (Henk ter Haar), Poland (Tadeusz Parnowski), Scotland (Evelyn McPake), and Spain (Micheline Selmes). Members unanimously endorsed the existing Executive Committee: Michael Coote, Chairman; Franz Baro, Honarary Secretary; and Henk ter Haar, Honorary Treasurer. Leila Mustanoja will serve as newsletter editor and Jacques Selmes, as public relations officer. Miet Wouters will serve as coordinating secretary.

AE premises and facilities are provided in Brussels through its membership in ECAS, (European Citizens Action Service). ECAS helps strengthen the position of voluntary sector non-governmental organizations in relation to the EC institutions.

Alzheimer Europe will also serve to fulfill the European Region role of ADI.

Finding Yet Another Way...

Alzheimer societies around the world are creative in the way they meet the service needs of patients and families. The following article tells of Yet Another Way an Alzheimer's association helps relieve the burden of caregivers and helps improve the quality of life of persons with Alzheimer's disease. This idea will appeal to ADI members who are seeking additional ways to expand their patient and family services programs on a limited budget.

Persons with Alzheimer's disease can enjoy daily walks. Unfortunately, Alzheimer's disease soon leaves some patients too confused to venture out alone. Confined, they become restless and frustrated. And, families–with conflicting outside business and social commitments–may not always be as free to help as they might like.

Now enters a new Canadian ADS Chapter-based program called *Walkabout.*

It began when the Family Support Committee of the Alzheimer Society of Cornwall and District heard about how the problem affected one patient and her family, they introduced her to one of their members, who is an avid walker. The two women went out together daily, often for up to five miles at each outing. As the walks continued, her family was delighted to see the patient's social skills improve. They also noted that she became less restless and slept through the night.

Based on this initial experience, the idea of volunteers walking with Alzheimer patients has grown into a full-fledged program. Begun in 1989, the Society's *Walkabout* has matched nineteen volunteers with Alzheimer patients.

The Chapter's Family Support Services Committee and staff members Linda McDevitt and Shelley Vaillancourt, developed the program. Linda explains that before a *Walkabout* match is made, volunteers take a 6-hour training course that involves case studies and role playing. Linda and Shelley monitor the program closely, keeping in regular telephone contact with volunteers and caregivers. *Walkabout* matches are assessed every six months, and volunteers meet at least three times a year to discuss their experiences.

"The hardest thing volunteers have to face is knowing that the time will come when their companions will no longer be well enough to continue the walks," Linda says. She works with volunteers, helping them through the adjustment.

Linda recommends the program to other Chapters since it is inexpensive to run and it provides much-needed relief for caregivers, as well as exercise and companionship for persons with Alzheimer's. She points out that it appears that even very confused patients have less tendency to wander when they are in the program.

The Society has developed a *Walkabout* Program Manual and is currently producing a training video. For information, write to Linda McDevitt, Alzheimer Society of Cornwall and District; Box 1852; Cornwall, Ontario, K6H 6N6; Canada. Tel: (613) 932-4914

ADI Membership Criteria Approved

A policy establishing criteria for membership in Alzheimer's Disease International (The Federation of Alzheimer's Disease and Related Disorders Societies, Inc.) was approved by the ADI Council during its annual meeting on September 22, 1990, Mexico City. The policy is as follows:

The following criteria shall be considered in determining eligibility for membership in ADI:

1. Organizational maturity
   a. A Board of Directors with adequate representation of Family Members affected by Alzheimer's disease or related disorders.
   b. National credibility and favorable image in their own country.
2. Programs and services such as:
   a. Helpline
   b. Support Groups
   c. Public information and education programs
   d. Development program to provide a network of Chapters, etc.
3. Financial ability to participate in ADI, such as:
   a. Membership dues
   b. Attendance at meetings
   c. Communications
4. In all the above, consideration must be given as to whether the applicant operates in the best interest of any person with Alzheimer's disease or related disorders and their families.