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ALZHEIMER'S DISEASE DATA, LEVELS, AND CARING STRATEGIES

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1. Alzheimer's Disease

Alzheimer's disease (AD) is a form of dementia affecting the cerebral cortex. This neuro-degenerative cerebral disease leads to insidious and progressive brain destruction. The characteristic changes induced in the brain are: a marked reduction in the population of neurons, the appearance of neurofibrillary tangles, neurotic plaques, and granulovacuolar bodies; neurochemical changes also happen. A good description of the cortical destruction process involved in AD can be found for example in H. Braak and E. Braak (1997). Symptoms of AD include the decline of memory functions, personality changes, deterioration of language functions, impairment in visual and spatial tasks, and finally motor dysfunctions. In advanced cases, personality disintegrates and the person becomes totally dependent or bedbound. There is however a significant variability in the patterns of preserved and impaired cognitive abilities. Clinical diagnosis of AD is presently based on a series of standard methods of examination: medical history, neuropsychological testing, laboratory assessment, and various electrophysiologic methods such as Positron Emission Tomography (PET) or computerized tomography (Single Photon Emission Computerized Tomography or SPECT).

Present diagnostic protocols provide different levels of diagnostic certainty by classifying cases as definite AD, probable AD, or possible AD. In spite of all these methods of examination, in some cases the clinical features of AD are such that only a post-mortem examination can confirm the diagnosis. The etiology of AD is still largely unknown. As stated in ICD-10 (W.H.O., 1992, p. 312), "the disorder is usually insidious in onset and develops slowly but steadily over a period of several years". This period can be as short as 2 or 3 years, but it can also be considerably longer. Though the disease can occur in middle adult life or even earlier, in the case of AD with early onset, it appears mainly in later life after 65 years of age, usually in the late seventies or thereafter. In cases with early onset, there is a likelihood of a family history of the disease and a rapid deteriorating course marked by multiple disorders of the higher cortical functions. Finally, though some drugs such as Tacrin slows down cognitive decline, AD is still at present irreversible.

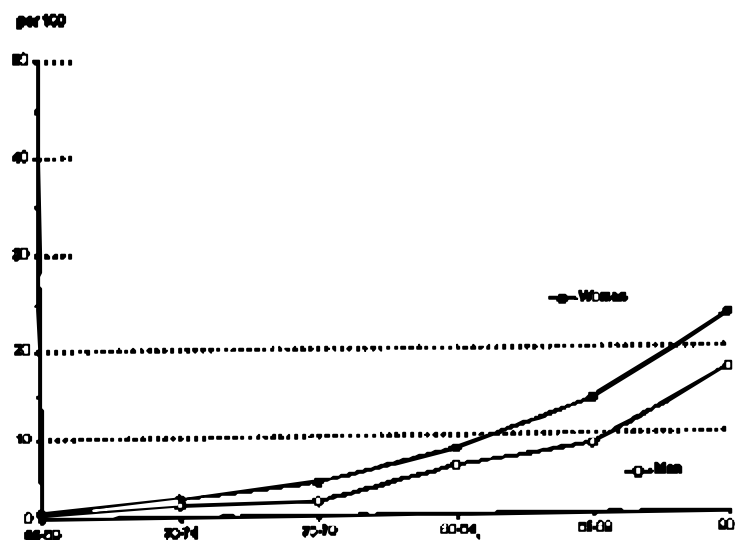
2. Prevalence and Incidence of the Disease

As AD is related more or less exponentially to age, one can expect a significant increase in the prevalence of the disease as the population grows older. This assumption is obviously based on the current situation and could change considerably if, for example, new drugs or other treatments could prevent or possibly reverse the disease. It has been estimated for example for the USA that if one projects age-specific prevalence rates based on the EURODEM surveys (see below) taking account of future US population change, the number of dementia cases (of which AD represents about 70 per cent) among persons aged 65 and over, would rise from 2.8 million in the year 2000 to 4.8 million in 2025 and to 9.2 million in 2050. Applying estimates available from the East Boston Survey, the number of persons with dementia would rise to 14 million in 2050¹ (Katzman and Fox, 1998). The incidence of new cases in 2050 would only be slightly less than cancer ! A similar projection made for Austria based also on data from EURODEM studies shows that the number of demented persons aged 65 or over would rise in this country from presently 80,000 to approximately 190,000 in 2050, meaning an increase by 140 per cent over the period (Haidinger et al., 1992). The increase in cost and care would be dramatic.

¹ The East Boston Survey includes cases with very mild cognitive changes.

In Europe an important study (called EURODEM), conducted under the auspices of the European Commission DG V and coordinated by the Department of Epidemiology and Biostatistics of Erasmus University in Rotterdam, has brought together the results of ten population-based studies on dementia in older persons. Eight countries were involved in this project. EURODEM studies show that women at all ages have a higher prevalence of AD than men. There is a significant increase of the prevalence rate by age for both sexes leading to a rate of slightly over 20 per cent for women and slightly less for men in the age-group 90+. Figure 1 presents the prevalence rates by age-groups for the pooled data by sex drawn from the most recent EURODEM Report (1998). In the East Boston Study, prevalence rates for probable AD increased from 3.0 per cent in the 65 to 74 age-group, to 18.7 per cent for those aged 75 to 84, and to 47.2 per cent among those 85 years and over, with a 95 per cent confidence interval in this age-group of 37.0 per cent to 63.2 per cent (Evans et al., 1989). The difference between both studies is probably due to the fact that the American study includes more mildly affected persons. The EURODEM study shows rather similar patterns between European countries and it is doubtful that prevalence differs widely between countries and regions if one takes into account the same definition of the disease and the same case ascertainment procedure (Amaducci and Lippi, 1992). No differences have neither been found between races in a study using the same assessment criteria (Fillenbaum et al., 1998).

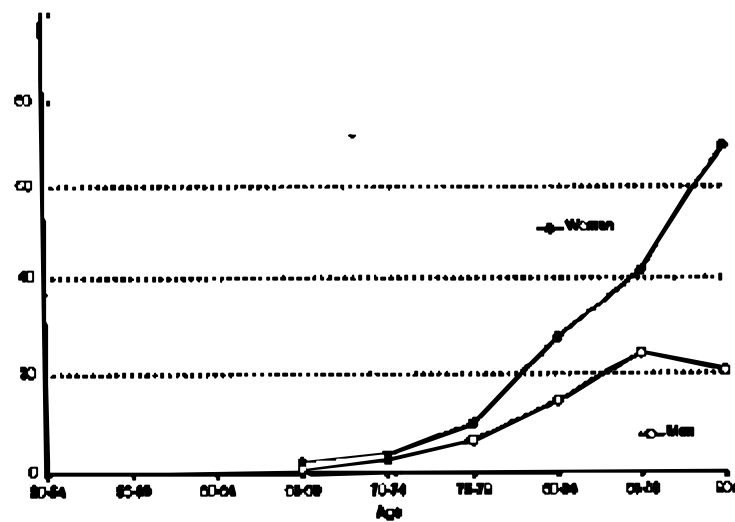
Figure 1. Prevalence of Alzheimer's disease by age and sex. Pooled analyses.



Source: EURODEM, 1998.

Incidence rates by age follow the same pattern as prevalence rates. Once again, the pooled data from the EURODEM studies show that rates for women are higher than for men, and furthermore that female rates increase more sharply by age than they increase for men (see Figure 2). Indeed the EURODEM data show even a slight fall in the incidence rate for the last age-group 90+. This could be due to the small number of cases involved or to a selection effect due to increases in other risks such as vascular dementia. It should be pointed out that this trend for older men is not necessarily observed elsewhere. For example, the Rochester study shows a continual increase in the rates with age for recent years (Kokmen et al., 1993).

Figure 2. Incidence of Alzheimer's disease by age and sex (per 1 000 person years).
Pooled analyses.



Source: EURODEM, 1998.

3. Issues in Data Collection

Incidence and prevalence data on AD are based in the best cases on population-based random samples. These studies are necessarily costly and restricted in coverage. The sample size of the prevalence of dementia studies in Europe varies from a low 982 in Finland to a high 7,983 in the Netherlands. Confidence intervals for rates can therefore be high for some ages, as seen above. On the other hand, the advantages of these studies are a non-selected population and standardised criteria and methods of assessment. Other sources

are however available for studying the impact of AD, i.e. death certificates and hospital statistics.

3.1. Death certificates

Though not ideally suited for the study of AD and other dementias, vital statistics can nevertheless point out some useful facts if the death certificate contains both the underlying cause of death and the associated causes of death, meaning other significant conditions contributing to death but not resulting in the underlying cause. Information is even better if one knows if an autopsy was performed or not, and if the autopsy findings were available prior to completion of the information on cause of death on the death certificate. For example, the American CERAD data show that AD has been confirmed by autopsy in 88 per cent of patients with a clinical diagnosis of probable or possible AD (Mirra et al., 1997). Unfortunately, not many countries in the world incorporate all these questions on the death certificate even among the European countries. The US standard certificate of death contains however the information required. Furthermore, as we are dealing with a large population, the results obtained are less subject to randomness.

Offsetting these advantages, underreporting of dementias in death certificates is a severe handicap. It has been reported for example that neither AD nor other types of dementias are mentioned on a quarter to a third of death certificates for diagnosed persons (Hoyert, 1996). An American study in San Diego has shown for example that AD was reported in 62 per cent of cases in both clinically and pathologically diagnosed groups. Dementia was however reported in over 3/4 of the cases in each group (Olichney et al., 1995). These caveats notwithstanding, the following table gives the age-specific death rates for AD for the USA in 1990.

Table 1. Age-specific death rates for AD for decedents
65 years of age and over-United States — 1990

<i>Age groups</i>	<i>Age-specific death rate (per 100,000)</i>
65-74	10.2
75-84	58.6
85-94	176.5
95+	319.6

Source: Hoyert, 1996.

One sees that there is a quasi-exponential increase of the AD death rates according to age; the pattern is therefore rather similar to the incidence and prevalence rates given above. Though death rates certainly do not give the whole picture, it is worthwhile recommending the use on the death certificate of multiple causes of death and information on autopsies.

3.2. Hospital statistics

All European countries now have hospital statistics, the last countries to join the set are Luxemburg in 1997 and France which has data on public service hospitals since 1996. Prior to this date, the coverage was restricted for France to a few surveys of public hospitals of short- or medium-term hospitalization. Hospital statistics only concern cases which have required hospitalization and do not consider hospital out-patients. Furthermore, in most countries private hospitals are not included in the data base. Therefore hospital statistics do not identify all the cases, and most significantly will depend on the differences existing between the diagnostic means amongst different hospitals in a country and on the differences between the health systems of the countries (diagnostic means in public and private medicine, compulsory consultation of aGP or direct consultation of a specialist). Furthermore, the problem of the unknown reference population is always present though the problem is much less crucial at the national level, if the data base on hospitals is exhaustive.

The data that can be used for statistical aims are discharge diagnoses. To evaluate the incidence of hospitalization for a specific disease, it would be necessary to know if hospitalization for this disease is a new case or a recurrent case. This would give the true number of cases of hospitalization for this disease during a specific year, since repeated hospitalizations of the same patient will overestimate the frequency. Matching over several years would enable identification of the same cases reported several times for recurrent hospitalizations, but except in countries using personal identification numbers, linkage using individual characteristics such as name or address will often be difficult. It should be pointed that countries, such as Sweden, already match cases, but only on a yearly basis however. In addition, what are the coding practices when confronted with cases of co-morbidity (is the main disease clearly stated?) or uncertain cases such as possible AD? Finally, hospital statistics are sometimes published for a sample of hospitals only, or for all hospitals but for a sample of days of admission.

In view of identifying available data on AD in the countries of the European Union, the present authors have sent a questionnaire to all the national institutes of statistics and ministries or national boards of health, taking account of possible regional institutions also. This study aims at obtaining information on the type of health institutions where AD patients are institutionalized, those which collect data on dementia in a systematic way, the procedures of codification and publication, and the possible collection of associated diagnoses. In particular we wish to know according to which ICD revision (9 or 10) the data were coded and if a three, four or five digit code was used (Table 2). Under ICD-9, the various types of AD were coded both under the chapter on diseases of the nervous system and the chapter on mental disorders. The latter concerns only dementia in AD. In ICD-9, code 331.0 (diseases of the nervous system) refers to AD without dementia, and code 290.1 (chapter on mental disorders) refers to presenile dementia including dementia in AD. Dementia in AD with an onset after 65 years can be coded under 290.0, 290.2, or 290.3. However, the term Alzheimer's Disease is never used as such.

Table 2. ICD-9 codes used for classification and publication of main diagnoses.
European Union — 1995

<i>Countries</i>	<i>ICD-9 codes (number of digits)</i>	
	<i>Classification</i>	<i>Publication</i>
<i>Austria</i>	4	3
<i>Belgium (for General Hospitals)</i>	5	following DRG*
<i>Denmark</i>	NA	NA
<i>England (ICD-10 since 1995)</i>		
<i>Finland</i>	NA	NA
<i>France (morbidity survey)</i>	4	specific list
<i>Germany</i>	4?	3
<i>Greece</i>	3	3
<i>Ireland Rep. (General Hospitals)</i>	5	4
<i>for psychiatric hospitals (ICD-10 since 1994)</i>		
<i>Italy (census survey)</i>	4	following DRG 4 (Psychiatric Depts)
<i>Netherlands</i>	4	specific list
<i>Northern Ireland (Mental Health Inpatient System)</i>	4	specific list
<i>Portugal</i>	5	following DRG
<i>Scotland</i>	4	specific list
<i>Spain (survey)</i>	3	3
<i>Sweden</i>	4(1)	4

DRG: Diagnosis Related Groups

NA: not available

Luxemburg began the collection of morbidity data only in 1997, and the ICD-10 is used.

(1) *The first three digits are from ICD-9, the fourth is specific to Sweden, but it is possible to identify an Alzheimer's disease.*

If the 3-digit code 290 is used, vascular dementias are also included under this grouping, but they have a different etiologic origin than AD. In the case of the 3-digit code 331, other degenerative diseases such as Pick or Creutzfeldt-Jacob are also subsumed. In ICD-10, AD is once again included in the chapters on Mental and Behavioural Disorders and Diseases of the Nervous System. AD can be identified with the help of three characters only (one letter and two digits), the 4-digit codes referring to early onset, late onset and atypical or mixed type. AD is now clearly identified as such, a fact which will most probably lead to more precise codification of this disease once ICD-10 will be in general use. Furthermore in ICD-10, the diagnostic criteria for AD are closer to those of DSM-IV (Diagnostic and Statistical Manual — fourth edition), the classification elaborated by the American Psychiatric Association, which is the standard reference for mental disorders (Henderson, 1995). ICD-10 has been adopted during the year 1995 in England and Wales, in 1996 in Scotland and Northern Ireland, in 1997 in France. Other standardized sets of diagnostic criteria could also be used, such as those of the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke / Alzheimer Disease and Related Disorders Association) in view of harmonizing clinical diagnostic procedures and reducing the margin of error of the diagnoses.

The following table (Table 3) presents *hospitalization rates* for Alzheimer's disease for three countries for which we have already obtained yearly data on hospital discharges for AD at the national level: England, Netherlands, and Sweden. The Swedish data concern only first hospitalizations during the year, while the other two include both first hospitalizations and rehospitalizations during the year. In order to reduce random fluctuations in the data, three-year averages of discharges by age group and gender were taken for the period 1994-1996 (mid-1992 to mid-1995 in England). These averages were then divided by the mid-period national population in each age and gender group, in order to obtain estimates of hospitalization rates for the three countries by five-year age groups over 45, and by gender. The last age group is 85+ for England and the Netherlands, and 90+ for Sweden.

Table 3. Hospitalization rates for Alzheimer's disease in England (1992-1995), Netherlands and Sweden (1994-1996) — (Discharges per 100,000)

A. Men

<i>Age groups</i>	<i>England</i>	<i>Netherlands</i>	<i>Age groups</i>	<i>Sweden</i>
45-49	3.9	0.7	45-49	1.1
50-54	5.8	2.6	50-54	3.8
55-59	20.3	3.9	55-59	18.0
60-64	41.0	6.6	60-64	35.8
65-69	105.4	13.3	65-69	78.1
70-74	223.9	34.2	70-74	218.3
75-79	561.8	72.1	75-79	464.1
80-84	971.3	163.6	80-84	778.4
85+	1525.3	212.2	85-89	1001.6
			90+	715.3

B. Women

<i>Age groups</i>	<i>England</i>	<i>Netherlands</i>	<i>Age groups</i>	<i>Sweden</i>
45-49	2.9	0.3	45-49	0.7
50-54	6.5	1.0	50-54	8.5
55-59	19.7	1.5	55-59	20.5
60-64	43.6	2.4	60-64	40.5
65-69	102.7	7.3	65-69	92.2
70-74	224.8	19.1	70-74	217.6
75-79	549.0	48.6	75-79	449.0
80-84	929.2	86.3	80-84	734.0
85+	1304.1	114.8	85-89	911.1
			90+	801.6

As expected, hospitalization rates for AD increase significantly with age in all three countries, though a decrease is observed for the last age group (90+) in Sweden, both for males and for females. There are significant differences in the levels of hospitalization between the three countries, England and Sweden having a much higher level of hospitalization for AD than the Netherlands. As Swedish data concern only first hospitalizations during the year, the inter-country difference is even more significant. The inclusion of associated diagnoses would significantly increase these rates, as a comparison of the totals with and without associated diagnoses for the Netherlands clearly shows (Wunsch and Gourbin, in print). The hospitalization rates for England and Sweden remain however much lower than the incidence rates for AD based on the pooled data by sex of the EURODEM studies presented in Figure 2 above. There is more or less a four-fold difference between the two sets of rates. Moreover, contrary to the incidence rates by sex which showed a much higher incidence for females than for males, the hospitalization rates are not very different between males and females. The latter even have a slightly

lower rate than the former at higher ages. In conclusion, as could be foreseen, incidence rates for AD are much higher than hospitalization rates, as most patients with AD are not hospitalized for their disease. From the health economics point of view, it is known that hospitalization is especially costly. However, as discussed below, patients with AD are mainly taken care of by their family or in nursing homes and old people's homes. Hospitalization rates therefore do not reflect the true cost of the disease (see Wimo et al. 1997).

4. Caring for AD patients

The crucial question concerning the use of hospital statistics for studying levels and trends in dementia is to what extent people suffering from these diseases are sent to an institution participating in the data collection procedure, public or private. Except in the later stages of the disease, many patients are never sent to a hospital or clinic and are therefore excluded from official statistics on this disease. Indeed, for mild or moderate symptoms the patient is probably examined, if at all, by a GP, who might or might not send his patient to a specialist. This situation will remain unknown from a statistical viewpoint. It was therefore decided in our study to conduct a second survey focused on the following problems: By whom has the disease been diagnosed? Who takes care of the patient? Are special benefits for AD patients provided by the social security system? The questionnaire was sent to the national and regional centers of the Alzheimer Associations or Societies as it seemed to us to be the easiest way to obtain relevant answers to our questions. Other solutions such as a survey of patients, of carers, or of physicians did not seem practical. Up to now we have received slightly less than four dozen replies, out of more or less 130 questionnaires which were sent out. Results presented here are therefore preliminary.

Table 4. Patients dealing with the national or regional Alzheimer Associations - European Union - 1998.

Countries and Regions	A. Age Structure (per cent)			B. Source of diagnosis (per cent)			
	<65	65-80	>80	GP	Neurologist	Psychiatrist	Geriatrician
<i>Austria</i>		NA				NA	
<i>Belgium (1)</i>	20	50	20	30	65	5	
<i>Denmark Nat.</i>	15	60	25	/	50	50	
<i>Tollose</i>	10	70	20	2	80	18	
<i>England</i>	8	56	36	20	55	25	
<i>Finland Nat.</i>	5	85	10	10	85	5	
<i>Pyhäsalmi</i>	5	50	45	60	30	10	
<i>Ylihärmä</i>	2	65	33	25	55+10 neu- ropsychologists	10	
<i>Helsinki</i>	30	50	10	5	80	5	10
<i>France</i>							
<i>Franche-Comté</i>	10	60	30	15	85		
<i>Hautes Pyrénées</i>	15	60	25	10	55	10	25
<i>Loire</i>	20	70	10	10	90		
<i>Nord</i>	20	60	20	5	95		
<i>Puy de Dôme</i>	10	80	10	15	60	25	
<i>Tarn et Garonne</i>	2	65	33		100		
<i>Vaucluse</i>	20	65	13	10	80	10	
<i>Germany</i>	5	80	15	15	35	50	
<i>Greece (2)</i>							
<i>(Thessalonike)</i>	20	65	15	2	90	8	
<i>Ireland Rep.</i>	5	90	5	15	35	10	40 psycho- geriatricians
<i>Italy</i>							
<i>Crema</i>	10	40	50	<5	10	5	80
<i>Firenze</i>	/	90	10	5	20		75
<i>Roma</i>	5	75	20		20		80
<i>Varese</i>	30	45	25	5	80	10	5
<i>Luxemburg</i>	8	58	34	30	50	15	5
<i>Netherlands</i>		NA				NA	
<i>Portugal</i>		NA				NA	
<i>Scotland Nat.</i>	8	35	56	40	15	45	
<i>Glasgow</i>	10	80	10	35	5	60	
<i>Aberdeen</i>	5	80	15	70	5	25	
<i>Barrhead</i>		60	40	35		65	
<i>Kilmarnock</i>	28	28	44	50		50	
<i>Spain</i>	30	60	10		80	17	3
<i>Sweden</i>		NA				NA	

NA: Not available.

(1) French and German Community only.

(2) For Greece, only the local branch of Thessalonike, whose head is a neurologist, has sent us data. Other answers from Greek Islands have underlined the fact that diagnoses are mainly made by GPs.

In general, when the patient is at home, the main carers of the patients are the spouse and children; in the latter case the carer is usually the patient's daughter(s) or daughter(s)-in-law. According to the results of our survey of the population having recourse to Alzheimer Associations and Societies, AD patients are usually cared for at home in most countries. The percentage of patients at home varies from a low 55 per cent in Scotland (with significant regional differences) to a high 90 per cent in Italy and the Republic of Ireland. Outside from home, AD patients are cared for in nursing homes, old peoples homes and to a much lesser extent in long-care wards in hospitals. Recently specially supervised accomodation for group living have been developed e.g. in Netherlands, Sweden, Luxemburg, Belgium. Good examples are the "cantous" in France and the BESTA flats (smart house installations) in Norway. The advantage of this solution is that it maintains the patient in a socially stimulating but not medically oriented environment under well-trained carers. The disadvantage is at present the cost.

Though most patients with AD stay at home, the burden for the family may be quite heavy. Therefore most countries have now developed day-care centers, where the patient may stay several times a week. Usually these centers deal with a dozen patients at a time, with the help of professional staff. Their number is however still insufficient at present, and their cost remains high. In Scotland however, the major part of the cost is supported by public and private funds, the patient himself paying only a slight contribution for his meal. At the later stages of the disease, it becomes difficult to care for the patient at home and the person is often institutionalized in old people's homes or in geriatric and psychiatric wards.

The survey also gathered data on the age structure of the AD patients with whom the Alzheimer Associations are dealing with. Table 4 presents this age structure by broad age groups at the national and regional level.

It can be seen that there are very great differences in the age-structure of the patients. In Spain, for example, 30 per cent of the patients covered by the Association are younger than 65 years of age, while in Finland only 5 per cent of the patients are in this age-group. The high percentage of AD patients at younger ages is explained by the fact that the diagnosis is better at relatively young ages and because at these ages both patients and family seek maximum information and help. This explains why the age-structure of AD patients in Alzheimer Associations does not correspond to the age schedule of the prevalence rate of the disease as presented in Fig. 1.

The source of the diagnosis varies among countries and within countries, and also according to the age of the patient. For example, in

Germany or Denmark the diagnosis is mainly made by a psychiatrist. In countries such as Belgium, Spain or Finland, the majority of diagnoses are done by a neurologist. In Italy diagnoses are mainly made by geriatrists while in the Republic of Ireland, psychogeriatrists are mostly the source of the diagnosis. GPs are an important complementary source in Belgium, in England and in Scotland. Furthermore GPs are also the main source in the rural areas within the countries. For example, in the Kilmarnock region in Scotland the first diagnosis is always done by a GP and is confirmed in only 50 per cent of the cases by a specialist. The same situation can be found in the rural region of Pyhäsalmi in Finland, 80 per cent of the diagnoses are made by GP, and only one-fifth of these are confirmed by a specialist. Finally there is also an age effect; for example in Helsinki for people aged under 80, 95 per cent of the patients are seen by a specialist (mainly a neurologist), while if the patient is over 80 years of age, diagnosis is only done by the GP. Some respondents have told us that with the new drugs on the market, there could be a greater reliance on the diagnosis by a specialist in the framework of hospitals and clinics. The same is true if the patient lives near a memory clinic.

5. Heterogeneity in AD

In addition to age and gender which have been well documented, other factors have been shown to be associated with AD. Once again association is not causality, but taking account of the fact that associations are usually due to common causes or to causal relationships between the variables examined, associations can point out paths for future research. In some cases, some risk factors have even been pointed out. For example, there are specific genetic risk factors in the field of AD. It is now clear that carrying apolipoprotein E (APOE) is a relatively important genetic determinant for the onset of this disease. The risk of AD for carriers of one allele 4 of APOE (APOE* 4) is 1.7 times increased, while carriers of two APOE*4 alleles have a 6.2 increase in risk. The APOE*4 allele could explain up to 15 per cent of the incidence of the disease (Van Duijn, 1998).

Other factors are also associated with AD. For example, head injuries have been found to increase the risk of AD. There is also evidence for a link between vascular risk factors, vascular dementia, and AD. Estrogen use could possibly reduce a woman's risk of AD but not all results concur. Non-steroidal anti-inflammatory drugs could possibly prevent or treat AD, as inflammatory processes may contribute to neuronal dysfunction and degeneration. Other

factors such as aluminium intake, aspirin use, or age of the parents have also been examined but results are not always conclusive².

Several behavioural factors seem to be associated with AD. One such factor is smoking. Though the latter has not been pointed out in all studies, it now seems quite clear, thanks to the Rotterdam Study, that there is a significant increase in the risk of AD for smokers. However, the converse seems true for the carriers of the APOE*4 allele. The Rotterdam Study has found out that the increase in risk was particularly present for smokers without the APOE*4 allele (Ott et al., 1998; Altmann, 1998). The same Rotterdam Study has demonstrated that the intake of dietary saturated fat is also a risk factor for the incidence of dementia. In particular, fish consumption, which is a source of polyunsaturated fatty acids, is inversely related to the incidence of AD (Kalmijn et al., 1997). Furthermore, the PAQUID study conducted in France, in the Bordeaux region, has shown that moderate wine consumption is also associated with a lower risk of AD (Dartigues, 1998). We therefore recommend to the readers of this report to stop smoking, eat fish, and... drink wine! More seriously, it is interesting to note that the same three factors have been shown to have an impact on cardiovascular diseases (CVD). As the relationship between vascular disorders and AD has been pointed out above, it should not be surprising that some of the factors leading to CVD could also cause AD.

The final factor which will be considered here is education. Most studies have indeed shown that there is an inverse relationship between the level or length of one's education and the probability of developing AD. Obviously when considering the impact of education on AD, one has to take account of the fact that better educated people could more easily pass the neuropsychological tests than those with a lesser education (Henderson, 1995). Education-free tests have however been developed and the role of education seems therefore to be real. This effect is furthermore not due to confounders such as CVD (Ott et al., 1995). In their study of the prevalence of AD in Shanghai (Zhang et al., 1990) invoked the possibility of a lower "brain reserve" for people with less education, allowing the symptoms of AD to appear at an earlier date during disease progression. Education would therefore not only provide a reserve compensating for neuropathological changes due to AD, but it would also delay the onset of its clinical manifestations (Stern et al., 1992).

² The PAQUID study in the South-West of France has recently pointed out once again, on the epidemiological level, the role of aluminium in the etiology of AD.

We suggest, following Katzmann (1993), that the inverse relationship between education and incidence of AD could be due to the positive relationship between education and plasticity of the brain. Education would increase synaptic density, leading to the delay of symptoms by several years. As AD leads to a degeneration of neurons and synapses, development of synaptic density would counterbalance to some extent the process. Other cognitive activities would lead to the same result. It has been shown, for example, that more cognitively demanding occupations are negatively related with the incidence of dementia (Stern et al., 1994). It is well known that cerebral plasticity at young ages is highly dependent upon the quantity and quality of the stimuli in the environment (Boisacq-Schepens and Crommelinck, 1996). Is this relationship only limited to very young ages or can we expect improving brain plasticity at higher ages still? Studies conducted during the past years on second language acquisition and violin playing, for example, have clearly shown that these activities lead to cortical reorganisation (Elbert et al., 1995; Kim et al., 1997). Plastic changes in the cortex are therefore not limited to childhood and can also be experienced at later ages. It is therefore conjectured that the process of AD could be delayed at a very early stage by developing the patient's brain plasticity, in addition to his adoption of other individual coping or re-educational strategies based on e.g. mental imagery (such as face-name), retrieval practice, or the use of memory note-books (for an overview, see Van der Linden 1995). On-going research at our University (Laboratory of Neurophysiology) and others is currently testing this assumption.

Conclusion

In this paper we have shown that the evaluation of the prevalence and incidence of AD requires population-based surveys such as those conducted in the framework of the EURODEM project. Death due to AD can possibly be measured if the death certificate contains both the underlying causes of death and the associated causes, and if the information is confirmed by an autopsy. Hospital statistics can also be collected, especially now that the ICD-10 deals specifically with AD. As many patients are not hospitalized, hospitalization rates for AD remain much lower than the incidence rates for this disease. However, the medicalisation of AD, especially if new drugs appear on the market, would require a battery of tests and exams which normally would be carried out in hospitals. In any case, it would be useful to obtain data on out-patients both for public and private hospitals, as these could significantly improve the statistics.

The survey among the Alzheimer Associations has shown that most patients are cared for at home by their family. The development of day-care centers at a reasonable cost can be recommended in this case. Most diagnoses are made by a specialist, especially in the urban areas and at relatively young ages. Finally, on the basis of the existing literature the heterogeneity of the disease has been stressed. In particular, education seems to be highly associated with AD, the reason probably being that it develops the plasticity of the brain. Stimulating environments could therefore possibly protect and delay the symptoms of AD.

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