# A DIAGNOSTIC STUDY OF DEMENTIA IN A LONDON ELECTORAL WARD



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**PREFACE**

The investigations which form the basis of this thesis were undertaken by the author between January 1987 and December 1989, during the period of her employment as a Research Fellow in the Department of Academic Psychiatry, Royal Free Hospital School of Medicine, London.

Professor Anthony Mann acted as advisor for the study. The subject for thesis was the responsibility of the author, who co-ordinated the entire study and conducted assessments personally. The screening interviews of the elderly population required the assistance of a team of interviewers. The author screened about half of the population herself. She carried out Phase II and III interviews, comprising G.M.S.(A), physical examination, biochemical screening and informant interviews personally. The psychometric testing was carried out by Ms Karen Sax, a Research Assistant. Computer analysis of data took place at the Royal Free Hospital by Mr Robert Blizard, in discussion with the author.

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## SUMMARY

Estimates of the prevalence rate of dementia in those aged over 65 and living in the community vary widely, from 0.5% to 6.3% for mild dementia, and from 1% to 7.4% for moderate or severe dementia. These figures have usually been obtained by screening and refer to non-specific dementia syndromes. Few studies have gone further to provide a detailed diagnostic breakdown on this cross-sectional detail, or followed patients up to obtain longditudinal data. Those that have provided further information have not provided full diagnostic profiles of unselected samples, leading to the likelihood of bias in the results.

Accurate results from community settings are crucial for the purposes of both services planning and to increase the knowledge of, and therefore improve management of the dementias. These studies by detecting and diagnosing early dementias, and following cases longditudinally will add to the knowledge of the natural history of dementia, leading to more accurate prognostic data. More accurate samples will also enable clearer evidence of genetic and environmental risk factors to be obtained. Prevention of dementia may ultimately be feasible when risk factors are known. Finally the best hope for effective pharmacological therapies lies in early dementia when there is less cell death.

This study concerns the elderly residents of an electoral ward, the Gospel Oak Ward, in the London Borough of Camden. A list was completed of the pensioners living in this area. The pensioners were then screened for dementia using two scales, a screening scale and a diagnostic scale, from a semi-structured instrument, the Short CARE, to determine the prevalence rate for dementia.

Subjects who scored above the cutpoint on either of the two scales were then assessed in detail. If re-interview was not possible, for example because of death, other sources of information were utilized. This further assessment was for the purpose of a diagnostic subclassification of the dementias. This enabled precise prevalence rates of the different dementias to be determined, reversible dementias to be detected, and finally assessments to be made of the use of the various instruments in clinical practice.

The final phase of the study was an eighteen month follow up. The outcome was investigated in terms of mortality and change in morbidity.

It was found that the way to obtain an accurate list of elderly residents was by visiting individual residences. This accurate sample differed from a list obtained from

service providers by 56%. 87% of the sample were interviewed. 56 (7.9%) crossed the cutpoint on the screening scale and 35 (4.7%) on the diagnostic scale (a total of 60). Prevalence of dementia on the diagnostic scale was 4.7% and rose with age.

48 (80%) of the study were assessed in detail, reinterviewed and 22 (46%) were diagnosed as having probable Alzheimer's Disease. One had multi-infarct dementia, five had mixed dementia, five had secondary dementia, ten had a dementia which could not be further classified and five were not demented. No subject had a reversible condition. The prevalence rate for clinical dementia was 6.1% and for Alzheimer disease 3.1%.

Eighteen months later 30 (79%) of those available were re-interviewed. 10 (23%) had died, those who had been screened positives but not diagnosed clinically as demented remained not demented. Of the other survivors, 14 (54%) had deteriorated, 4 (15%) of whom had been institutionalised; 6 (22%) were stable and 6 (22%) had improved. There was little difference in the outcomes on the different scales or different diagnoses, although those who were 'cases' on the dementia diagnostic scale were less likely to improve. Clinical diagnosis was a better predictor of deterioration than any of the instruments used.

This study confirms that dementia increases in prevalence in older age groups. The elderly suffering from dementia in the community were different in diagnostic composition to hospital samples which have been reported, therefore extrapolation from hospital samples can result in a distorted picture. There were excess deaths when compared to an age matched population. Many cases of dementia did not deteriorate over eighteen months. Therefore maximising patients' health in early dementia in the community, may be helpful in preventing deterioration.

# CHAPTER 1

# INTRODUCTION

## 1.1 THE AGEING POPULATION

"Methuselah lived a hundred eighty and seven years and begot Lamech. And Methuselah lived after he begot Lamech seven hundred eighty and two years, and begot sons and daughters. And all the days of Methuselah were nine hundred sixty and nine years, and he died" (Genesis).

Methuselah, and perhaps other individuals through the ages, had long lives; but for the majority as recently as the 18th century, life expectancy was 25 to 35 years of age and survival beyond 50 was infrequent (Midwinter, 1989). Even now in the late 20th century, life expectancy in some of the poorer nations is in a similar range.

This is illustrated in a world survey from the Centre for the Policy on Ageing, where the shortest life expectancy quoted (for those born in 1985), was in Sierra Leone, where men could expect to live till the age of 32.5 and women till 35.5 (Crosby et al. 1989). Similarly, in other nations (for example Gambia and Afghanistan) life expectancy is less than forty years. Some countries (like Taiwan, St Lucia and Grenada), are unable to quote any life expectancy figures, but have a similar or lower percentage of over 65s in their total population than Sierra Leone and Gambia. Therefore life expectancy in these countries is probably at least as low. However, even in these poorer nations the population is now ageing and

longevity is expected to increase by around 16 years for both men and women by 2025.

In contrast, in the richer nations, life expectancy has increased enormously in this century so that by 1985, the highest life expectancy for men was 74.3 years (in Japan), and for women 79.7 years (in both Japan and Switzerland). In the United Kingdom during this century, annual death rates have fallen from over 30 to 10 per 1,000 so that life expectancy for men has extended from 48.5 to 71.6 years and for women from 51.4 to 77.6 years (Warnes, 1989). This increased longevity, along with falling birth rates, has caused major changes in the age composition of the UK population. Further changes are now predicted in the numbers of very old people, that is those over 85 years of age. By 1996 they will number 1.9% of the population, a 50% increase in 10 years comprising approximately 400,000 people who will be mainly female, widowed and living alone. (OPCS 1987).

As the population comes to contain more very old people, the numbers of those suffering from dementia rises, because the prevalence of dementia increases with age, doubling with every 5.1 years increase in age after 65 years (Jorm et al. 1987). This problem resulting from our ageing population has been called the silent epidemic (Beck et al 1982), and has led to greatly increased research interest in dementia.

## 1.2 THE DEFINITION OF THE ELDERLY

The definition of elderly is inevitably arbitrary and may change as the expectation of lifespan and health change. The concept of elderly may be statistical, biological or social. In statistical terms, for example, the oldest 5% of the population may be regarded as elderly. On this basis, in some countries old age might therefore begin in the mid-forties, while in 1986 in England it would not begin till after 75 years old (OPCS 1987). In contrast, biological old age might be defined as when deteriorating health leads to a defined level of disability, in a person who was not congenitally handicapped. In these terms old age would not therefore be chronological, although it would be more common in older individuals. Finally, old age can also be regarded as a social phenomenon, that is, when a particular society defines old age. For example, in the UK, 65 is the current age of male retirement and the age at which the patient receives the label "geriatric" in the health services.

Any definitions of the elderly will be culturally determined and vary according to place and time. Nevertheless, whichever social definition is used,it is chronological age of people in the population that seems to affect the prevalence rate of dementia. Therefore, it is important to know what is meant when the word elderly

is used. In this thesis the word 'elderly' will refer to those of 65 and over, unless otherwise specified.

## 1.3 NEW INITIATIVES IN RESEARCH ON DEMENTIA

The consequences of dementia syndrome, are the disintegration of the intellect, personality, dignity and independence of the sufferer. This loss of independence means that the 'epidemic' affects the society as a whole, as help is required from both informal carers, and formal care, in the form of both medical and social services at home. As dementia usually follows a deteriorating course, in time it becomes impossible for informal carers to provide fully for the needs of the dementia sufferer and twenty-four hour care is needed in some form of residential care. Some two thirds of residents in social services facilities are demented (Mann et al 1984). Some become too difficult for these institutions, so that the health services, which up until that time has been in a supporting role are required to take over full care in a long stay facility. Therefore the implications of dementia for health and social policy is enormous.

As the numbers of people with dementia is increasing, and the disease has wide personal and socio-economic implications, it is essential to obtain accurate epidemiological data on the prevalence rate of dementia

and its distribution. Knowledge of the numbers of such cases provides useful data for management, and service needs. Dementia is a clinical diagnosis made on history and symptoms rather than upon underlying pathology or known aetiology. However, further diagnostic detail of the dementias is necessary, both for more accurate service planning and as a basis for further progress in investigating and managing this group of disorders.

To date most epidemiological research on the prevalence rate and diagnostic composition of the dementia syndrome has been carried out on unrepresentative samples. There is no report, in an unselected community sample, of a methodologically satisfactory study of the prevalence rate and complete diagnostic profile of those screened as suffering from dementia. The setting up of a register of all the elderly in a North London electoral area provided an opportunity to do this in three phases. In phase one, this sample has been screened to find population prevalence rates of dementia and depression, any other handicaps and of current service usage. Then a second phase investigation enabled a diagnostic profile of the dementias discovered in the sample, to be determined. Finally, in phase three an eighteen month follow-up of those subjects seen in phase two has been carried out, to determine the natural history of these dementias and to test the predictive value of the initial diagnostic subclassifications. The study is original and the author

the principal investigator and it forms the basis for this thesis.

# CHAPTER 2

# WHAT IS DEMENTIA?

## 2.1. THE EXPERIENCE OF DEMENTIA

"You have to begin to lose your memory, if only in bits and pieces to realise that memory is what makes our lives. Life without memory is no life at all..... Our memory is our coherence, our reason, our feeling, even our reaction. Without it we are nothing...(I can only wait for the final amnesia, the one that can erase an entire life as it did my mother's)"(Bunuel 1985).

This quote describes the experience of memory loss and its significance to the sufferer. In general most people with dementia lack this insight. This makes the mechanics of our task as doctors, to recognise and diagnose dementia, make services available and help advance knowledge of dementia; different from that in most illnesses, as the patient often does not recognise that there is a problem. The recognition of dementia and the difficulties in so doing are discussed in the rest of this chapter.

## 2.2. THE DEFINITION OF DEMENTIA

Dementia is a clinical term describing a symptom complex with many different aetiologies and pathologies. A consensus multidisciplinary conference in the United States of America defined dementia as :- "a clinical state

with many different causes, characterised by a decline from a previously attained intellectual level... Although long lasting some varieties of dementia may be arrested or reversed...Some criteria for dementia require deficits in one or more components of intellectual function other than memory. Some require that the deficit be global.

....Dementia is a very variable state . It may be progressive ,as in the degenerative diseases or static ,as in a post brain injury state.
....Dementia is distinguished from mental retardation. Many different disease states are capable of producing dementia.... They may be found in all the classic categories of disease : intoxicant, infectious, metabolic, nutritional, vascular, neoplastic, genetic and traumatic." (Office of the Medical Application of Research 1987). In addition, there is the category degenerative dementia, which includes Alzheimer's Disease, the most common cause of dementia.

Four commonly used criteria for dementia are:- 1) the Diagnostic and statistical Manual-III-R (DSM-III-R) 2) the International Classification of Disease 9 (ICD9) 3) pervasive dementia used in the semi-structured assessment instrument short CARE (cf chapter 6 section 5). and 4) the GMS/Agecat criteria (cf chapter 6 section 5).

1. D.S.M.IIIR

A) Demonstrable evidence of impairment in short and long term memory.

B) At least one of:

1) impairment in abstract thinking.

2) impaired judgement.

3) other disturbance of higher cortical function.

C) The disturbance of A and B significantly interferes with work or usual social activities or relationships with others.

D) Not occurring exclusively during the course of delirium.

E) Either:

1) evidence of a specific organic factor etiologicaly related to the disturbance.

or

2) disturbance cannot be accounted for by any nonorganic mental disorder eg major depression, accounting for cognitive impairment.

2. ICD 9 refers to the dementia syndrome as "organic psychotic conditions". They are "syndromes in which there is impairment of orientation, memory, comprehension,

calculation, learning capacity and judgement....of a chronic or progressive nature, which if untreated are usually irreversible and terminal".

3. Pervasive dementia is an operational diagnoses of cognitive impairment made from criteria comprised of ratings of the ShortCARE. They identify cases where there is a probable need for clinical investigation or intervention (Gurland et al 1984).

4. Finally the Agecat system defines a 'syndrome case' as a collection of symptoms which a psychiatrist would recognize as a characteristic and abnormal mental state for which intervention was appropriate, if available (Copeland et al 1986).

These definitions indicate the scope of the diagnoses of dementia, and attendant difficulties in reliable use of those diagnostic categories which will be discussed more fully in the next section.

## 2.3 PROBLEMS IN THE DIAGNOSIS OF DEMENTIA

The difficulties in the diagnosis of dementia fall into five main categories.

First the diagnosis is characterised by a decline from

previous intellectual levels. This means that some individuals suffering from early dementia could still be functioning at a higher level than others who have no cognitive impairment. Conversely others with congenital learning difficulties may be impaired but have not declined. Alternatively, decline may occur in those already impaired, as for example is common in Down's Syndrome, so that mental handicap and dementia may co-exist. In a clinical assessment, the history from an informant, together with a detailed psychometric tests, can usually overcome such diagnostic difficulties. However a community survey requires that large numbers of people be screened by an acceptable, economic and therefore rapid method. This can mean that some people will be wrongly classified.

Second, most dementia occurs in elderly people. With age there is a decrease in ability to learn new material and a slowing down in cognitive processes, which are countered by the use of stored knowledge and experience. It is therefore essential that testing for dementia does not emphasise the former abilities disproportionately or normal old people will be included, ie that testing is standardised for the appropriate age group . If this is not done then misclassification will occur, especially among the very elderly.

Third, other pathologies such as acute confusional state

or depression may mimic dementia, as well as making existing cognitive impairment more marked. A mental state, physical examination and history are therefore necessary for diagnostic accuracy, which is difficult in community samples. This is especially the case in very early dementia, where cognition is impaired but function is intact, and which are likely to be missed without longitudinal studies (Morris & Fulling, 1988).

Fourth, cultural differences mean that an instrument which is standardised for one population may be inappropriate in another, because of differences in education and experience.

Finally, there are many different criteria for identifying dementia. The four most common ones are discussed above. Use of different criteria may classify individuals into different categories. For example ICD-9 defines dementia as chronic, progressive and generally irreversible, none of which criteria are in DSM-III-R.

These difficulties are all brought together when the detection of early dementia in a community population is attempted - yet such detection is important.

## 2.4. THE NEED FOR ACCURATE ASCERTAINMENT OF EARLY DEMENTIA

There is general agreement that accurate ascertainment of early dementia is needed. The reasons for this requirement have been discussed by Mowry & Burvill (1988) and Henderson & Huppert (1984), who regard early detection as a compelling priority, as early accurate diagnosis of dementia is useful for both management and research purposes. The reasons for this are described in more detail below.

Currently, however the criteria for accurate early diagnosis of dementia have not been universally agreed. Jorm et al (1987) in their review of the literature of the prevalence rates of mild dementia, report results varying from 0.5% - 16.3% of those over 65 years. The corollary of a high rate of mild dementia, was a lower rate of moderate and severe dementia implying that some of the variance was due to different cut points in the spectrum of mild to severe. Mowry & Burvill (1988) report prevalence rates of between 3 and 64% of mild dementia, in a random sample of non-institutionalised people aged over 70. The rate depended on the instrument used. They therefore emphasise the importance of longitudinal studies, to validate the diagnosis of mild dementia.

In the area of management, early diagnosis may mean that

dementia can be arrested at an earlier stage, or increase the possibility of reversal, for example when an operable space occupying lesion is found. Alternatively, as in the diagnosis of depressive pseudodementia, treatment may shorten the course of the illness. In most dementias, at present, reversal and curative treatment are not available. Nonetheless, early detection of dementia can help in other fields. Firstly, in the clinical field, diagnosis should result in avoidance of inappropriate medication, such as benzodiazepines, which may lead to increased confusion. Risk factors may also be controlled. Although the diagnosis and prognosis may be very distressing to the family, the knowledge that a relative is ill and not just difficult or lazy, can be helpful both for their relationship, and in arranging practical assistance. When there is no family, a diagnosis enables the early alerting of services, and crises may be avoided, so that the patient can be maintained in the community longer.

Secondly, for research purposes the early detection of dementia will allow several benefits. Natural history studies to determine the subgroups of the different types of dementia, and the characteristics of these subgroups become feasible. This should lead to more accurate prognostic data. These subgroups of dementia will be discussed below in chapter 3. In addition a more representative sample which includes early cases, will

enable clearer evidence of risk factors for the dementias to be obtained. This applies to both genetic and environmental factors. Prevention of dementia, may ultimately be feasible when risk factors are known. Finally, pharmacological therapies require accurate diagnoses to enable accurate testing. The best hope for effective pharmacological treatment lies in early dementia, where there is less cell death.

## 2.5 CONCLUSIONS

1) Dementia is a symptom complex with different aetiologies.

2) The commonly used criteria for dementia differ from each other.

3) It is important to diagnose early dementia for the benefit of the patient and family and for future research progress.

# CHAPTER 3

# THE SUBCLASSIFICATION AND VALIDATION CRITERIA OF THE DEMENTIA SYNDROMES.

## 3.1 CLASSIFICATION SYSTEMS.

Traditionally dementia was classified by age into senile and presenile dementia, 65 being the age used as the cut off. However as more aetiological factors for dementias became known, dementia has been classified by category (such as degenerative or neoplastic), and into specific clinicopathological diseases such as Alzheimer's disease and multi-infarct dementia. These latter diagnoses require both the clinical features of dementia, and a diagnosis based upon pathological examination. They can therefore rarely be definitively made in life, except by brain biopsy. This unsatisfactory situation has led to many attempts to formulate clinical criteria that have predictive validity for a particular pathological picture, thus improving diagnostic accuracy during life. An alternative strategy of finding antemortem diagnostic markers is also being pursued.

Another system of classification of the dementias is into cortical and subcortical dementia (Albert et al 1972). Albert coined the term subcortical dementia to describe the changes of progressive supranuclear palsy and suggested that dementia could be divided into the subcortical and the cortical. The term subcortical dementias now include the dementias of Huntington's disease and Parkinson's disease. They are characterised by a slowness of thought and movement, forgetfulness, and

changes in personality, usually apathy and depression. The site of pathology is not in the cerebral cortex, but in the brainstem, red nucleus, thalamus and basal ganglia. This is in contrast to cortical dementias where pathology is in the cortex, and amnesia is an earlier and prominent symptom. In this latter category are Alzheimer's Disease, Pick's disease, Jacob-Creutzfeld disease and dementia associated with large vessel strokes.

This dichotomy, between cortical and subcortical dementia, has not been systematically validated and many dementias cross the lines between the pathologies (Chui, 1989). For example patients with Parkinson's disease may have Lewy bodies or plaques and tangles within the cortex and patients with Alzheimer's disease often show subcortical lesions. The individual neuropathological classifications are discussed in more detail in the rest of this chapter.

## 3.2. CLINICOPATHOLOGICAL CLASSIFICATIONS OF ALZHEIMERS DISEASE.

The diagnosis of definite Alzheimer's Disease (A.D.) remains based on a clinical picture and neuropathological features. The clinical features and neuropathology were first fully described by Alzheimer in a case report on a 51 year old woman. He described the symptoms progressing

from jealousy towards her husband. "Soon a rapidly increasing loss of memory could be noticed. She could not find her way around in her own apartment. She carried objects back and forth and hid them. At times she would think that someone wanted to kill her and would begin shrieking loudly ....

If one pointed to objects, she named most of them correctly ... When reading she went from one line into another, reading the letters or reading with a senseless emphasis. When writing she repeated individual syllables several times, left out others ... When talking, she frequently used perplexing phrases and some paraphasic expressions (milk-pourer instead of cup)...

The generalised dementia progressed however. After four and a half years of the disease, death occurred ...

The autopsy revealed remarkable changes in the neurofibrils. They merged into dense bundles. Finally the nucleus and the cell disintegrated...

Scattered through the entire cortex ... one found foci of deposition of a peculiar substance." (Alzheimer 1907).

For many years the term Alzheimer's disease was used to refer only to pre-senile dementias of the Alzheimer's type, as it was thought to be distinct from senile

dementia which was perhaps a part of normal ageing. As the neuropathology of the senile and pre-senile dementia does not differ, the term Alzheimer's disease is now used for both categories. The question of normal ageing is still current and is discussed in the next section.

## 3.3 ALZHEIMER'S DISEASE AND NORMAL AGEING.

Despite the recognition of Alzheimer's disease since the beginning of this century, and the warnings of an "epidemic" by the end of the century, there is still a debate about on the status of Alzheimer's disease as a discrete disease. Brayne & Calloway (1988a) reported a study of 70-79 year old women in rural Cambridgeshire. They found that that there are no discontinuities of score in this population, on a standardised dementia scale, between those with clinical dementia and those without. They concluded that Alzheimer's disease is at one end of the continuum of normal ageing, on the continuum with a "usual" group of the elderly having some of the characteristic neuropathological changes of Alzheimer's Disease, and a "successful" group, in terms of brain function having no such lesion. In a letter in reply Hoffman et al (1988) point out that the scale used (which measures cognition and behaviour) is a crude scale, which by its nature might blur any true bimodality of distribution in scores. This potential bimodality would

be further blurred by data which derived from a whole population, that is, including all dementing diseases, not just Alzheimer's disease. In addition, although Brayne & Calloway have shown a continuum in results on cognitive testing, this does not imply a neuropathological continuum. Hoffman et al end by suggesting that as atherosclerosis rises with age, the continuum model would imply that vascular dementia is also part of normal ageing, and challenge Brayne & Calloway to give a view on that question. Brayne & Calloway (1988b) continue the debate, by stating that removing all those subjects with brain pathologies other than Alzheimer's disease from the graph did not affect the unimodal distribution of the results, and that the neuropathological lesions of dementia are similarly unimodally distributed. They conclude by calling on Hoffman et al to prove that Alzheimer's disease is distinct from normal ageing.

This debate has little practical implications. Both sides agreed that whether or not Alzheimer's disease "exists" the clinical state which is described as Alzheimer's Disease has important consequences. The definition of this clinical state will be discussed in the next section. Both sides agree that aetiology may be multifactorial and that it is important to investigate genetic and environmental agents. While Hoffman et al think that the distribution of neuropathology and cognition between "normals" and those with Alzheimer's disease may

be bimodal, they do not insist that it is. The question which was not been addressed in this article or subsequent correspondence appears to be the meaning of the word normal. This is discussed further in Chapter 5.2.

## 3.4 THE CRITERIA FOR THE DIAGNOSIS OF ALZHEIMER'S DISEASE.

There have been several different criteria used for the diagnosis of Alzheimer's disease. Mayer-Gross et al (1969) in the Slater and Roth textbook characterise the presentation by a gradual, yet progressive, failure in the activities of daily life. Memory and intellectual failure dominate the early picture; dysphasia, dyspraxia and agnosia commonly evolve.

This clinical approach has been replicated by the criteria devised from the working group on the Diagnosis of Alzheimer's Disease, from the National Institute of Neurological and Communicative Disorder and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA). These criteria are comparable with the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) and the International Classification of Diseases (ICD). They are suggested for the purpose of making investigations in different studies comparable. The authors explained that the criteria are tentative and

subject to change, as they required confirmation by longitudinal studies and post mortem. These confirmatory methods will be discussed in 3.5 below.

According to the NINCDS/ADRDA criteria, Alzheimer's disease is defined as a progressive, dementing disorder of middle or late life. In this definition, dementia is the decline of memory and other cognitive functions in comparison with the patient's previous level of function, as determined by a history of decline of performance and by abnormalities noted from clinical examination and neuropsychological tests. A diagnosis of dementia cannot be made when consciousness is impaired by delirium, drowsiness, stupor or coma. It is a diagnosis based on behaviour and cannot be determined by laboratory instruments.

The diagnosis of Alzheimer's Disease using these criteria is divided into definite, probable and possible. The diagnosis is definite only in the presence of both a clinical diagnosis and histopathological evidence. The diagnosis is probable when dementia is established between the ages of 40 and 90 in clear consciousness, in the absence of other systemic disorders or brain diseases that could account for the progressive deficits in memory or cognition. Alzheimer's disease is possible when there is a second systemic or brain disorder sufficient to produce the dementia which is not considered to be the cause of

the dementia. (McKhann et al 1984).

## 3.5 VALIDATION OF CRITERIA FOR THE CLINICAL DIAGNOSIS OF ALZHEIMER'S DISEASE

Many attempts have been reported in the recent literature to validate clinical criteria by antemortem and postmortem neuropathology, by longitudinal studies and by cerebral blood flow studies.

### 3.5a NEUROPATHOLOGICAL VALIDATION CRITERIA FOR ALZHEIMER'S DISEASE

The first study to validate the diagnosis of dementia by neuropathological postmortem studies, tested clinical diagnoses made prior to the existence of specified criteria (Tomlinson et al 1970). More recent papers concerning the neuropathological validation have tested clinical criteria (Kokmen et al 1987), DSM-III (Forette 1989), the Mayer-Gross criteria (Wade et al, 1987) or most commonly the criteria laid down by the National Institute for Neurological and Communicative Disorders and Stroke with the Alzheimer's and Related Disorders Association (NINCDS/ADRDA criteria) (Martin et al 1987, Morris et al 1988, Tierney et al 1988, Boller et al 1989, Risse et al 1990).

The neuropathological criteria for the diagnosis of Alzheimer's Disease were first derived in the work of Tomlinson et al (1970). They compared the postmortem neuropathological findings of fifty patients with a diagnosis of dementia, who had died either in a mental hospital or in a geriatric unit, with the findings of twenty-eight non-demented old people. They considered the brain weight, the ventricular size, the volume of brain destroyed, the position of lesions, the number of senile plaques, the number of neurofibrillary tangles in the hippocampus and general cortex and the amount of granulo-vascular degeneration in the hippocampal pyramidal cells in both sets of brains. There was a bimodal distribution of neuropathological findings, with the controls and the demented group being clearly differentiated, both in cases of Alzheimer's Disease and of atherosclerotic dementia. The paper states that as the demented group were not representative, it is not appropriate to assume the bimodal distribution found will necessarily be replicated in all populations.

The important neuropathological findings to distinguish the groups were, 1) cerebral atrophy, 2) increased ventricular size. The neuropathological findings characteristic of senile dementia of the Alzheimer's type were:- heavy plaque formation, neurofibrillary change and granulo-vacuolar degeneration. The paper suggested criteria for Alzheimer's Disease which

were:-

1) More than 18 senile plaques per low power field in the cortex.

2) Neurofibrillary changes in both the neocortex and the hippocampus.

Since these standards were first formulated other neuropathological inclusion and exclusion criteria have been suggested. So the 'gold standard' of neuropathological validation, like the clinical criteria is varied. Clinicopathological agreement will therefore vary according to the neuropathological standards used. For example, a second pathological standard accepts tangles and plaques just in the hippocampus, without requiring changes in the cortex, as being diagnostic of Alzheimer's disease (Ball et al. 1985). Another definition states that plaques and tangles must be present only in the neocortex (Molsa et al, 1985), and a fourth that in those 66 or above, plaques without the requirement of tangles in the neocortex is diagnostic of Alzheimer's disease (Khachaturian, 1985).

Tierney et al (1988) reviews the clinicopathological agreement on the NINCDS/ADRDA standards using three different inclusion criteria for Alzheimer's disease, and three different criteria for exclusion of multi-infarct dementia. The sample consisted of 57 cases, 22 of which received a clinical diagnosis of Alzheimer's Disease.

They found that the pathological agreement on the clinical diagnosis of Alzheimer's Disease ranged from 64%-86%. The classifications which specified neocortical lesions only and that which specified both neocortical and hippocampal lesions produced identical groups and therefore proved to be equivalent.

Having considered both clinical and pathological criteria for Alzheimer's Disease, the next section summarizes studies which have correlated them.

### 3.5b. CLINICOPATHOLOGICAL STUDIES OF ALZHEIMER'S DISEASE

Clinicopathological studies of Alzheimer's Disease and the results are summarised in Table 1.

Table 1 CLINICOPATHOLOGICAL STUDIES OF ALZHEIMER'S DISEASE

| AUTHOR | CLINICAL CRITERIA USED | PM/BIOPSY | PATH CRITERIA | NO OF SUBJECTS WITH CLINICAL AD. | SENSITIVITY | SPECIFICITY |
|---|---|---|---|---|---|---|
| MARTIN et al 1987 | NINCDS/ ADRDA | biopsy | neocortical plaques + tangles as =<65yrs | 11 | n/a | n/a |
| WADE et al 1987 | Mayer-Gross Hachinski <4 | PM | hippocampal plaques and tangles | 39 | 87% | 78% |
| MORRIS and FULLING (1988) | NINCDS/ADRDA | PM | neocortical and hippocampal plaques and tangles. | 26 | n/a | 100% |
| JOACHIM et al 1988 | Clinical judgement | PM | neocortical plaques (+ tangles if =<65 yrs) | 150 | n/a | 87% |

| AUTHOR | CLINICAL CRITERIA USED | PM/BIOPSY | PATH CRITERIA | NO OF SUBJECTS WITH CLINICAL AD. | SENSITIVITY | SPECIFICITY |
|---|---|---|---|---|---|---|
| HOMER et al 1988 | Clinical judgement | PM | hippocampal plaques and tangles | 13 | 100% | 46% |
| TIERNEY et al 1988 | NINCDS/ ADRDA | PM | 1)hippocampal & tangles<br>2)neocortical plaques & tangles<br>3)hippocampal & neocortical plaques & tangles | 22 | 1)77-86%<br>2)64-77%<br>3)81-84% | 89-91%<br>89-91%<br>89-91% |
| BOLLER et al 1989 | NINCDS/ ADRDA -2 independent diagnoses | PM | neocortical plaques (+tangles if =<65yrs) | 1)29<br>2)21 | 1)85%<br>2)95% | 13%<br>33% |
| RISSE et al 1990 | NINCDS/ ADRDA, DSM III | PM | neocortical plaques (+tangles if =<65yrs) | 25 | n/a | 68% |

Morris and Fulling (1988) and Martin et al (1987) both find an impressive 100% correlation between their diagnosis of Alzheimer's disease using the NINCDS/ADRDA criteria and the neuropathological findings. Both groups used very rigorous inclusion and exclusion criteria in the diagnostic process. Morris and Fulling included only those with a gradual sustained deficit in at least three areas, including functioning, lasting at least six months and excluded all neurological, psychiatric and other medical disorders. Martin et al's criteria were similar in both inclusion and exclusion criteria. It therefore appears that using the NINCDS-ADRDA criteria and interpreting the criterion "absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition" narrowly, to mean the exclusion of patients with all other pathologies, is an effective method of diagnosing Alzheimer's Disease without false positives being included in the group. As no autopsy results are reported for those not so diagnosed, the number of false negatives are not known. This method is not useful as a way of estimating the prevalence or incidence of dementia, or of diagnosing most patients as sensitivity may be traded for specificity. This is because it is rare to find elderly people with dementia who are otherwise completely well. Applying findings from a small specialised group to other clinical populations can be misleading.

Boller et al (1989) who find a high sensitivity and a low specificity of clinical diagnosis, also used the NINCDS-ADRDA criteria. Two neurologists interpreted the criteria to diagnose probable Alzheimer's Disease in all those with clinical dementia, when another aetiology was not found on thorough investigation, even if there was another disease present. As the diagnoses were made on clinical records, the information available was sometimes incomplete. Unexpectedly, the accuracy of diagnosis was not significantly different in those cases in which relatively little was known, than in those subjects who had been documented and seen repeatedly and longitudinally in the Alzheimer's Disease Research Centre of the University of Pittsburgh. However there was a trend towards less extensive information resulting in less accurate diagnoses. Most discrepancies were accounted for by dementias which did not have the expected clinical features in life, for example, progressive supranuclear palsy occurred in one patient without any ocular signs.

Tierney et al (1988) also used the NINCDS-ADRDA criteria. Their results, using the different neuropathological criteria listed in table 1 suggest, that Boller's group employed the strictest neuropathological criteria available. Tierney's group diagnostic specificity is much higher than Boller's. This may be because Tierney's cases all had comprehensive information up until death; which was not the case in Boller's sample; as the dementia

progressed the clinical signs may have become clearer. Risse et al (1990) report a study of 25 male inpatients which is directly comparable with Martin et al (1987), Tierney et al (1988) and Boller et al (1989), as the same clinical and pathological criteria were used. Like Tierney et al (1988), comprehensive information was collected until death. There was a tendency, although numbers were too small, for the result to be significant, for diagnosis to be less accurate in the under 65s. In addition to these studies, Burns et al (1988) give a preliminary report in a letter, that 30 out of 30 post-mortem examinations confirmed the diagnosis of patients diagnosed as having Alzheimer's Disease on a narrow interpretation of the NINCDS/ADRDA criteria. No other recent studies have tried to validate the NINCDS/ADRDA criteria.

Studies such as Homer et al (1988) and Joachim et al (1988), do not state the clinical criteria used. Although these studies emphasise the inaccuracy of clinical criteria, the studies do not contribute greatly to the state of knowledge, as neither clinicians nor researchers can interpret the findings to improve diagnostic criteria.

Wade et al (1987) used the Mayer-Gross criteria to diagnose patients with Alzheimer's disease, with a good sensitivity and specificity, using less strict neuropathological criteria.

Crystal et al (1988) correlated a diagnosis made on results of psychometry with neuropathology in 28 longitudinally evaluated subjects aged 75-85. Six of the subjects who were not demented according to McKhann criteria, had numerous plaques in the cortex at post mortem. However five of these patients showed cognitive decline in the time from the first test, suggesting that very mild A.D. was present before it could be diagnosed by accepted criteria.

Overall, it appears that the criteria for clinical diagnosis of Alzheimer's Disease are evolving. However they are still vague enough to be open to different interpretation. While the pathological criteria are not vague, they differ. This can make a difference of 20% in results of clinicopathological correlations. In the few elderly people who have had no other physical illness and present with a typical insidious, progressive and unremitting Alzheimer's Disease, the diagnosis can now be made with confidence. Progress still remains to be made about the diagnosis in other patients. Improvements in clinical diagnosis may be either through the development of better clinical criteria or through antemortem diagnostic markers.

## 3.5c. ANTEMORTEM DIAGNOSTIC MARKERS FOR ALZHEIMER'S DISEASE

NINCDS-ADRDA Work Group on the diagnosis of Alzheimer's Disease referred to the absence of laboratory markers of the disease and mentioned regional cerebral blood flow (rCBF), electroencephalography (EEG), computerised tomography (CT), positron emission tomography (PET scan) and magnetic resonance imaging (MRI) as possibilities (McKhann et al 1984).

In a 1988 review of the literature, Cutler concludes that there is no definitive ante-mortem marker capable of replacing clinical examination in Alzheimer's Disease. He suggests that the search for a diagnostic marker should continue. The rest of this section will discuss work published since Cutler's review.

### MAGNETIC RESONANCE IMAGE SCANNING

Magnetic resonance imaging (MRI) provides both anatomical information similar to CT neuroscans and some biochemical information. The parameters associated with magnetic resonance phenomenon T1 and T2 correlate with tissue water content and cellular water binding, respectively.

Since Cutler's 1988 review, Christie et al (1988) have found by MRI techniques that tissue water content (T1), of the frontal lobes in patients with presenile Alzheimer's disease were similar to age matched controls. However the T1 values were raised in Korsakoff's psychosis and multi-infarct dementia, and they concluded that MRI of T1 values can assist in differentiating presenile A.D. from other causes of presenile dementia. In this study A.D. diagnosis was by criteria comparable with the NINCDS/ADRDA, and diagnosis of multi-infarct dementia, by a history of stepwise deterioration and a Hachinski score from 8-13. Another MRI study reports biochemical changes in the phospholipid membrane, which reflects the activity of metabolic pathways (Brain et al 1989). Seventeen patients with Alzheimer's Disease were compared with 10 patients diagnosed as suffering from multiple subcortical infarct dementia (MSID), and with seventeen non-demented controls. The diagnosis of Alzheimer's disease was made by using the NINCDS/ADRDA criteria. The MSID group were diagnosed by having more than one subcortical hypodensity on CT scan and a Hachinski score $\geq 7$. It is unclear that these criteria correctly diagnose subcortical infarct disease, as hypodensities are not the same as infarcts. The MSID group might therefore be more accurately described as vascular dementia. The vascular group and the Alzheimer group could be distinguished on MRI scan. The vascular group had elevation of the phosphocreatinine inorganic orthophosphate ratios (PCr/Pi) in both

temporperietal and frontal regions. In the A.D. group phosphomonoesters (PMe) were elevated in frontal regions, and Pi was elevated in temporparietal and frontal regions. Values of PCr/Pi accurately classified 100% of vascular dementia and 92% of A.D.

These are promising preliminary studies which suggest MRI scan may be helpful in the differential diagnosis of dementia. However, the clinical diagnosis is used in these studies as a "gold standard", without any neuropathological confirmation. In addition, as the dementia groups are not matched for levels of cognition, differences found in metabolic profiles, may reflect differences in stages of disease. Finally, it is often difficult to gain co-operation for scanning from people with dementia, and so MRI scanning may not be a practical method of diagnosis in many patients.

**SINGLE PHOTON EMISSION TOMOGRAPHY.**

Burns et al (1989) report a study using single photon emission tomography (SPET). They compare twenty patients with Alzheimer's Disease diagnosed by NINCDS/ADRDA criteria with six age matched controls. The A.D. patients showed cerebral blood flow deficits which correlated with psychometric testing and distinguished them from controls. They did not attempt at this stage to use SPET to

distinguish Alzheimer's dementia from other dementias.

**P300 AUDITORY EVENT-RELATED POTENTIAL**

Although event-related potentials have been found to be abnormal in dementia and there is a correlation between P300 latency and psychometric tests (Wright et al 1988), latency changes occur in both Alzheimer's disease and multi-infarct dementia and do not differentiate between them (Neshige et al 1988).

## 3.5d. LONGITUDINAL STUDIES OF THE DIAGNOSIS OF ALZHEIMER'S DISEASE

Blessed and Wilson (1982) published a validation study of the clinical diagnosis of Alzheimer's Disease. They did this by comparing the outcome of those diagnosed as suffering from arteriosclerotic and senile dementia, and measured outcome as either discharge, or death, or remaining an inpatient. In those terms, they found no difference in the outcome between the two categories. Thus there was no confirmation in the validity of this subclassification.

More recently, Huff et al (1987) used the cognitive deficits detected by neuropsychological tests to validate

the clinical diagnosis of probable Alzheimer's Disease using a narrow definition of NINCDS/ADRDA criteria. At a one year clinical follow up all those with a diagnosis of Alzheimer's disease had multiple deficits. They report that criteria had a sensitivity of 100% and a specificity of 89%. Similarly in France, Forette et al (1989) studied fifty five subjects who were diagnosed as suffering from a dementia, compatible with NINCDS/ADRDA criteria. One year later fifty-two subjects still had the same diagnosis indicating a reliability of 95%. However the reliability of the diagnoses over time does not prove the validity of the original diagnoses, this still requires neuropathological confirmation.

## 3.6. THE CRITERIA FOR THE DIAGNOSIS OF VASCULAR DEMENTIA

The phrases atherosclerotic dementia, vascular dementia and multi-infarct dementia tend to be used interchangeably. Tomlinson et al (1970) used the clinical diagnostic term "atherosclerotic dementia", for which they provided neuropathological validation by measuring the volume of infarcted tissue in the brain. However, Hachinski et al (1974) argued that this term had led to common medical misdiagnosis and over diagnosis of vascular dementia, as an image existed in many minds of atherosclerosis causing a relentless strangulation of the

brain's blood. They review the literature, concluding that atherosclerosis of the basal vessels of the brain does not by itself play any decisive role in the manifestation of dementia in old age. Instead, most vascular dementias are caused by cerebral infarcts secondary to emboli from extracranial arteries and the heart. Therefore they suggested the term "multi-infarct dementia", (MID) to define dementia caused by a series of infarcts. Hachinski believed this term would prevent over-diagnosis of atherosclerotic dementia because of a mistaken conceptual framework.

By 1988, however O'Brien was arguing that using the term multi-infarct dementia synonymously with the term vascular dementia, results in underdiagnosis of vascular dementia, as small vessel disease (Binswanger's disease or subcortical arteriosclerotic encephalopathy) is missed. In this thesis "multi-infarct dementia" will be used either as Hachinski defined it, or when quoting papers which use the term multi-infarct dementia. Vascular dementia will be used to include small vessel disease or again as it is used in published work. The evidence for underdiagnosis of small vessel disease will be discussed in the rest of this chapter.

## 3.6a. CLINICAL CRITERIA FOR THE DIAGNOSIS OF VASCULAR DEMENTIA

No comparable criteria to the NINCDS/ADRDA criteria for Alzheimer's disease have been developed for multi-infarct dementia. The DSM-III-R criteria for multi-infarct dementia are A. Dementia B. Stepwise deteriorating course with "patchy" distribution of deficits ( i.e. affecting some functions but not others) early in the course. C. Focal neurologic signs and symptoms. D. Evidence from history, physical examination, or laboratory tests of significant cerebrovascular disease that is judged to be aetiologically related to the disturbance. This last criteria is described by Brust (1988) as a combination of ischaemic score and gut response. "You may blame dementia on the stroke if you think the stroke caused the dementia".

Similarly ICD-9 defines arteriosclerotic dementia as dementia attributable, because of physical signs (on examination of the central nervous system) to degenerative arterial disease of the brain. Symptoms suggesting a focal lesion in the brain are common. There may be a fluctuating or patchy intellectual defect with insight, and an intermittent course is common.

More often the Hachinski Ischaemic Score (also known as the HIS, Ischaemic Score or the Hachinski Score) is used

as a diagnostic tool for multi-infarct dementia. This method of scoring was derived by Hachinski et al (1975) from the criteria outlined by Mayer-Gross et al, (1969) for multi-infarct dementia. It includes a list of thirteen features which are likely to occur in M.I.D., such as acute onset, stepwise deterioration and focal neurological signs. These items are scored positively so that the higher the score, the greater the probability of ischaemic dementia.

The paper describes a group of twenty-four demented patients. Patients with secondary dementia were excluded from this group by history, physical and laboratory examination, scan and EEG. The diagnosis of multi-infarct dementia was validated according to regional cerebral blood flow studies, using intracarotid 133 Xenon injection. The regional pattern of flow was deemed abnormal when it differed by 3.3 standard deviations from the value of the equivalent area in brains of controls, and abnormally low CBF was deemed to be diagnostic of multi-infarct dementia.

Application of the Ischaemic Score separated the patients clearly into two groups without any overlap. Patients scored seven or above were classified as having multi-infarct dementia, and patients scoring 4 or below who were not. No one scored between 4 and 7. The patients with a diagnosis of multi-infarct dementia showed a significant

decrease in cerebral blood flow per 100 gm brain per minute. An inverse relationship between C.B.F. and the degree of dementia was found to be present only in the multi-infarct group. No neuro-pathological confirmation was attempted. The place of cerebral blood flow in validating the clinical diagnosis of vascular diagnosis is discussed below.

### 3.6b CEREBRAL BLOOD FLOW AS VALIDATION OF THE DIAGNOSIS OF VASCULAR DEMENTIA

Hachinski used cerebral blood in 1975 to validate his Ischaemic Score. Since then controversy over the cerebral blood flow in dementia has continued. O'Brien (1986,1988) believes that cerebral blood flow (CBF) per unit mass falls only in early vascular disease. He argues that CBF/unit mass remain constant in Alzheimer's disease, although the total CBF would fall in parallel with the loss of tissue bulk, but in early vascular dementia, healthy neurones are impaired by inadequate blood supply, and eventually they die. In contrast to Hachinski, he argues that a state of "chronic ischaemia" exists which causes dementia. Cerebral cortex perfusion rates are therefore likely to be reduced early in the disease and out of proportion to the dementia. In late stages both A.D. and vascular dementia would show both a reduced flow, because of less metabolism and a reduced cell mass.

Rogers et al (1986) support O'Brien's viewpoint. They note reduced cerebral perfusion in high risk patients prior to the onset of dementia, and attribute it to "subclinical cerebral atherosclerosis". In contrast, when Deutsch & Tweedy (1987) studied cerebral blood flow in 15 patients with Research Diagnostic Criteria Alzheimer's Disease, 15 patients with M.I.D. (Hachinski score 7+) matched for the severity of cognitive symptoms, and 15 normal volunteers, they found a significantly lower C.B.F. in the AD disease patients than the M.I.D. group.

Brust (1988) argues that O'Brien is wrong about cerebral blood flow. If O'Brien's theory was correct, this would imply: 1) cerebral vasodilators or hyperbaric oxygen should offer therapeutic benefit to sufferers from vascular dementia. They do not. 2) that this 'misery perfusion' should lead to neurological symptoms triggered by any fall in blood pressure. This is not the case.

In summary, cerebral blood flow is not a clear cut way of making or validating the diagnosis of multi-infarct dementia or vascular dementia. Only one study of cerebral blood flow reinforces O'Brien's (1988) contention that vascular dementia is underdiagnosed because the chronic underperfusion due to cerebral atherosclerosis often exists, but is not considered. If those patients do exist, decreased cerebral blood flow prior to clinical dementia could still result from multiple emboli, or

infarctions rather than be the cause of vascular dementia.

### 3.6c. NEUROPATHOLOGICAL CRITERIA FOR VASCULAR DEMENTIA

Neuropathological examination has also been used to validate the diagnosis of vascular dementia. Tomlinson et al (1970), in their post-mortem comparison of the brains of patients with dementia, with the brains of those not suffering from dementia, found a pathological finding of 100 millilitres of brain destroyed, correlated in all cases with dementia. In most cases 50 mls of destroyed brain also correlated with this diagnosis. Multiple small diencephalic infarcts were seen as often in patients with or without dementia. In cases with the diagnosis of arteriosclerotic dementia, the small diencephalic infarcts were never the dominant lesion. Therefore these subcortical lesions were not regarded as important in the diagnosis of dementia. Since then, many studies have used the finding of 50 mls of infarcted brain tissue as the "gold standard" to confirm the diagnosis of multi-infarct dementia. More recently, a report has been published that in autopsies of thirty-two demented and sixty-eight non-demented patients over sixty, the frequency of cerebral infarcts was significantly higher among the non-demented patients (Kokmen et al, 1987). This finding has to be regarded sceptically, as it was based on a retrospective clinical diagnosis, made on case notes of

patients, not specifically investigated for dementia. Although the diagnosis of dementia is likely to be justified in the "cases" who were nearly all institutionalised, the other patients may have had a dementia which was not documented. This is borne out by the fact that 35% of the "non-demented" had plaques or tangles at autopsy.

However the position regarding neuropathological confirmation of vascular dementia is similar to Alzheimer's disease in that there are now varying pathological criteria in use to confirm the diagnosis of multi-infarct dementia. Tierney and colleagues (1988) cite three sets of pathological criteria currently in use to diagnose dementia. These are firstly, the Tomlinson et al (1970) criteria of ischaemic lesions totalling 50 mls or more of brain tissue in the neocortex. Secondly, any ischaemic lesion irrespective of size or site. Thirdly any ischaemic lesion in the neocortex, subcortical white matter and/or hippocampus. In a post-mortem these criteria can lead to varying clinico-pathological correlations, as described in more detail in the next section.

### 3.6d CLINICO-PATHOLOGICAL STUDIES OF MULTI-INFARCT DEMENTIA.

These studies are summarised in Table 2.

TABLE 2

CLINICOPATHOLOGICAL VALIDATION OF THE DIAGNOSIS OF MULTI-INFARCT DEMENTIA

| AUTHOR | CLINICAL CRITERIA USED | PATHOLOGICAL CRITERIA | NO OF SUBJECTS WITH CLINICAL MULTI-INFARCT DEMENTIA | SENSITIVITY | SPECIFICITY |
|---|---|---|---|---|---|
| MOLSA et al. 1985 | Dementia Hachinski score > 7 | any ischaemic lesion no neocortical tangles | 19 | 73% | 77% |
| WADE et al. 1987 | Dementia Hachinski score > 4 CT scan, history & exam suggested vascular cause. EEG, physical available. | not specified appears to be multiple infarcts | 4 | 17% | 25% |
| HOMER et al. 1988 | Dementia Hachinski score level not specified CT scan, physical blood tests available. | multiple infarcts of various sizes | 10 | 56% | 90% |

The few studies that exist vary in method, but overall the sensitivity and the specificity of the diagnosis of multi-infarct dementia does not appear to be as good as for Alzheimer's disease. Much of this can be accounted for by two factors: 1) the difficulty in differentiating multi-infarct dementia and mixed dementia, using the Hachinski score, and 2) the varying pathological and clinical criteria for multi-infarct dementia.

The pathological criteria used by Molsa et al (1985) did not include quantification of any ischaemic lesion, so that authors believe that "their significance for the mental deterioration may have been negligible". This seems likely, in view of Tomlinson et al (1970) finding that multiple diencephalic infarcts do not signify dementia. In Molsa et al's study the Hachinski score was 64% successful (29/45) in classifying patients into three groups, A.D.(Hachinski score 4 or less), mixed dementia (Hachinski score 5 or 6), and multi-infarct dementia (Hachinski score 7 or more). The multi-infarct dementia and combined groups were not properly distinguishable on the basis of the Hachinski score. The best result was obtained with a logistic regression model which identified correctly 82% of cases (37/45). The model included fluctuating course, nocturnal confusion and focal neurological symptoms as the best discriminating score variables. A similar finding in another study was that the Ischaemic Score did not differentiate between the

M.I.D. patients and those with mixed dementia, (Wade et al 1987). However 35 out of 38 cases of pure Alzheimer's disease had a Hachinski score of $\leq 4$. Homer et al (1988) also used the Hachinski score with the idiosyncratic interpretation of the item "relative preservation of personality" as meaning the presence of insight. All four patients who had a Hachinski score $\geq 7$ had multi-infarct dementia. However twelve other patients had multi-infarct dementia and their Hachinski scores varied from zero to six.

In summary, most patients with a Hachinski score of $\geq 7$ in these studies, had either multi-infarct dementia or mixed dementia, and most with H.I.S. $\leq 4$ did not. However the H.I.S. did not distinguish between multi-infarct dementia and mixed dementia. The results of computerised tomography neuroscans have been used in some of the studies in table 2 as aids to the diagnosis of vascular dementia. The next section discussed the use of CT Scans and other neuroimaging in this field.

## 3.6e VALIDATION OF VASCULAR DEMENTIA BY BRAIN IMAGING

### COMPUTERISED TOMOGRAPHIC NEUROSCANS

Discrete infarctions can sometimes be seen in CT scan and enable the diagnosis of multi-infarct dementia to be

confirmed, although the presence of infarcted tissue does not exclude any co-existing disease. These infarcts are seen as well demarcated wedge-shapes which follow specific vascular territory and usually extend to the cortex. There is enlargement of the upsilateral ventricle or sulcus. All these features contrast with deep white matter hypodensities commonly seen in CT and MRI scan (Steingart et al 1987).

Hachinski et al (1987), discuss the significance of these hypodensities in the first of a series of four papers. They believe that hypodensities do not signify Binswanger's Disease, of which there are fewer than 50 pathologically proven cases in the world literature. "We are witnessing the unfounded attribution of a specific pathologic cause to increasingly more sensitive images of the brain". They suggest the term Leuko-Araiosis (L.A.) from the Greek words leuko - meaning "white" and araio meaning "rarefied", or "of loose texture" should be used as a precise description of these hypodensities. If the term L.A. comes into use, the authors believe it will eventually lead to an aetiological subclassification of these CT lesion, so that the L.A. classification term becomes redundant.

The three papers immediately following the discussion paper, clarify the significance of L.A. in CT scans. Paper two presents a study of leuko-araiosis in 105

healthy volunteers aged 59-91. Subjects were excluded if they had evidence of dementia (DSM III criteria), or had had a stroke. The nine subjects (8.6%) with L.A. had significantly lower scores on psychometric testing, and were significantly more likely to have abnormal neurological signs, in the form of abnormal gait, limb power, planter response and primitive reflexes. These results suggested that leuko-araiosis might represent a marker for early dementia, before a DSM III diagnosis could be made (Steingart et al 1987).

The third paper reported the investigation of patients referred to the University of Ontario dementia study with suspected dementia. 113 patients with Hachinski ischaemic score $\leq 4$, had a CT scan. Clinical diagnosis was made on all 113 patients, but no criteria are specified. However the diagnosis was confirmed in twenty out of twenty-one patients who had had an autopsy. CT changes of L.A. were found in 35% patients with dementia. Leuko-araiosis was significantly associated with older age, hypertension, reduced limb power and extensor planter responses. 32% of patients with the diagnosis of Alzheimer's disease, 75% with mixed dementia and 30% of other dementia categories had L.A. Throughout the series of patients taken as a whole, the presence of L.A. did not predict a worse dementia. However in mild Alzheimer's Disease (classified by score on the psychometric test used, the extended scale for dementia) those with leuko-araiosis tended to have

more impairment (Steingart et al 1987).

In the last of this series Inzitari et al (1987) compare some of the patients in the two previous papers in a search for risk factors for leuko-araiosis and to clarify further the link between L.A., dementia, subclassifications of dementia and the Hachinski Ischemic Scale. Although in an univariate analysis leuko-araiosis was strongly associated with dementia, in logistic regression analysis, a history of stroke was the single most powerful predictor of leuko-araiosis. This history did not entirely explain the finding. The paper suggests that leuko-araiosis may be caused by "incomplete infarction", and note that this is consistent with the pathological observations by Tomlinson et al (1970) of a substantial proportion of cases with deep infarcts among patients with typical clinicopathological Alzheimer's disease. It is also consistent with reports that in some Alzheimer's patients at post-mortem subcortical vascular disease accounted for the subcortical lucencies (George et al 1986).

Independently of the Ontario group, Aharon-Peretz et al (1988) scanned 31 patients with a clinical diagnosis of M.I.D, diagnosed using DSM-III criteria and an ischaemic score $\geq 7$. They also scanned a group diagnosed as having probable Alzheimer's disease on NINCDS/ADRDA criteria. The two groups were comparable in age and severity of

dementia. CT scans were evaluated blindly for ventricular dilation and the presence and severity of L.A., and for the presence and location of infarctions. The severity of L.A. was also evaluated using a 4 point rating system. LA-0 no visible lucencies, LA-1, lucencies confined to anterior or posterior parts of the ventricles, LA-2 anterior or posterior perventricular lucencies, LA-3 continuous periventricular lucencies. 97% patients with M.I.D. and 56% of patient with Alzheimer's Disease had L.A. There was no correlation between severity of L.A. and severity of dementia. However infarction was significantly more likely in the M.I.D. group than the rest of the demented group, as 87% of the M.I.D. patients had infarction on their CT scan. In M.I.D. enlargement of the ventricles was associated with more severe dementia, but not in A.D.

This study is consistent with the earlier studies in that L.A. is found in A.D., but less commonly than in M.I.D. In summary L.A. appears to be associated with risk factors for vascular dementia rather than specifically diagnostic of subcortical vascular dementia. Therefore a focal infarction remains the main way of distinguishing M.I.D. and A.D. on CT scan.

These conclusions are supported by a report by Masdau et al (1989) of CT scans on 40 subjects in a nursing home; 20 of whom had episodes of falling, still unexplained

despite extensive investigation, and 20 controls. Controls were matched for age, sex, level of education and physical health. All subjects underwent physical examination, blood tests, E.C.G. and all were rated on the Blessed Dementia Scale. Diagnosis of dementia was made by neurologists according to DSM III and NINCDS/ADRDA criteria.

More fallers were demented than controls (66.7% vs 25%), and fallers had significantly more white matter hypodensity than controls. On univariate analysis white matter hypodensity did not correlate with tests of cognition, although it correlated with poor gait and balance. Logistic regression analysis confirmed these findings.

**MAGNETIC RESONANCE IMAGING**

Magnetic resonance imaging (MRI) visualises leuko-araiosis more sensitively than CT scan (Erkinjuntti et al. 1987). Similar patterns to CT scanning are found, in that 100% of patients with a diagnosis of vascular dementia have leuko-araiosis in MRI, but so do many with non-vascular dementia (Merskey et al. 1987, Harrell et al. 1987, Erkinjuntti et al. 1987).

## 3.7a. THE DIAGNOSIS OF MIXED DEMENTIA.

After considering the diagnoses of Alzheimer's Disease and of vascular dementia, the diagnoses of those diseases together, in the same person is discussed in this section.

Mixed dementia is usually taken to mean dementia which is due to both underlying Alzheimer's Disease and a vascular dementia. The diagnosis is therefore subject to the problems of diagnosing both Alzheimer's Disease and vascular dementia. The "gold standard" is again neuropathological confirmation. No DSM-III-R criteria are given for the diagnosis. Research groups use varying criteria for the clinical diagnosis.

These are:-

1) Primarily occurring progressive deterioration of memory and other cognitive functions and Hachinski score of 5 or 6 (Molsa et al. 1985).
2) Patients with progressive cortical dementia, plus a history of strokes or focal neurological signs on examination (Wade et al. 1987).
3) Unspecified clinical criteria (Homer et al. 1988, Tierney et al. 1988, Boller et al. 1989).

TABLE 3 CLINICOPATHOLOGICAL VALIDATION OF THE DIAGNOSIS OF MIXED DEMENTIA

| AUTHOR | CLINICAL CRITERIA | PATH CRITERIA | NO OF SUBJECTS WITH CLINICAL DIAGNOSIS OF MIXED DEMENTIA | SENSITIVITY | SPECIFICITY |
|---|---|---|---|---|---|
| Molsa et al, 1985 | Dementia + Hachinski score = 5 or 6 | Criteria for A.D. and any ischaemic lesions | 5 | 16.7% | 92.3% |
| Wade et al 1987 | Progressive cortical dementia & strokes/focal neurological signs | Not specified | 16 | 45% | 33% |
| Homer et al | Unspecified | Path features of either condition sufficient for dementia. A.D. = tangles & plaques in neocortex & hippocampus | 10 | 56% | 90% |

### 3.7b. NEUROPATHOLOGICAL VALIDATION CRITERIA FOR MIXED DEMENTIA

The three small validation studies for mixed dementia are summarised in Table 3. It is difficult to draw conclusions from the small numbers studied. The low sensitivity of the first study may be due to their pathological criterion being over-inclusive i.e. 'any vascular lesion'. (Molsa et al 1985). Many ischaemic lesions do not cause dementia (Tomlinson et al. 1970). As the final study does not specify the criteria they use their results are not helpful in improving the diagnosis of multi-infarct dementia (Homer et al 1988).

### 3.8. DEMENTIA AND PARKINSON'S DISEASE

There have been several recent reviews of dementia and Parkinson's Disease (Hulley and Mindham 1988, Gibb 1989, Baldwin & Byrne, 1989). James Parkinson's 1817 original description of 'shaking palsy' described "absence of any injury to the senses and to the intellect". However by 1923 Lewy's monography on Parkinson's disease (P.D.) recorded psychiatric complications in three-quarters of patients. The prevalence of dementia in P.D., when the age of onset is over 60 years old, is now estimated to be 10-20%. Alzheimer's disease may be coincident with P.D., in up to half of these cases. The clinical diagnosis of dementia in Parkinson's Disease is difficult, as motor impairment is characteristic of the disease. This makes results of neuropsychological tests such as the

performance scale on the Weschler Adult Intelligence Scale (W.A.I.S.) difficult to interpret. The neuropsychological tests most suitable for testing for dementia in patients with Parkinson's disease are visuospatial and orientation tasks. However clinical distinction between cortical Lewy body dementia and P.D. with Alzheimer's Disease is not possible, as both have the motor symptoms of Parkinson's Disease and a cortical dementia with a similar history of gradual decline.

Confirmation of the diagnosis of P.D. dementia is clinicopathological. Lewy bodies in the substantia nigra are the pathological hallmarks of P.D. dementia. In patients with P.D. dementia, there is significantly greater nucleus basalis cell loss than in the non-demented patients with P.D. (60% v 32%). In some P.D. patients with dementia, Lewy bodies are also present in the neocortex, so that the dementia of PD cannot be truly classified as subcortical. In others there is co-existent A.D.. The prevalence of A.D. neuropathological findings in P.D. appears to be no greater than would be found by chance. There are no neuropathological validation studies of a series of patients with a lifetime diagnosis of dementia of P.D. and therefore no agreed quantitative neuropathological criteria.

## 3.9 THE DIAGNOSIS OF OTHER DEMENTIAS.

Aside from the degenerative and vascular dementias, dementias can be due to all the classic categories of disease. Diagnosis is usually that of the aetiological factor and there are no specified criteria. For example, a metabolic dementia due to hypothyroidism require thyroid function tests for diagnosis. In the case where the primary disease was treatable, diagnostic validation would take place if the dementia was reversed. Similarly a dementia due to a neoplastic space occupying lesion, would be diagnosed by neuroimaging, or a nutritional vitamin B12 and folate deficiency, by full blood count and low serum B12 or folate.

Many secondary dementias may not be reversible. This would apply to some infectious dementias, like Acquired Immune Deficiency Syndrome Encephalopathy (AIDS), and sometimes to dementia secondary to alcohol or other intoxicant abuse.

## 3.10 CONCLUSIONS

1) Alzheimer's disease is a clinicopathological diagnosis. However currently clinical and pathological criteria vary between studies. Nevertheless it is now possible to diagnose

Alzheimer's Disease in people who are otherwise well, accurately, using a narrow definition of the NINCDS/ADRDA criteria. This diagnosis has a high specificity but there are still no operational diagnostic criteria, with both a high sensitivity and specificity in diagnosis.

2) Vascular dementia encompases both multi-infarct dementia and small vessel dementia. There are still widely varying clinical and neuropathological diagnostic criteria. Computerised tomography and magnetic resonance imaging have enabled leuko-araiosis to be visualised during life. It is found in a large proportion of patients with dementia. It correlates most strongly with a history of stroke. L.A. may be due to incomplete infarction. Some argue that this appearance on neuro-imaging is diagnostic of small vessel dementia but this claim has yet to be justified. The many uncertainties in the diagnosis of vascular dementia mean that estimates of the prevalence rates can range from rare to epidemic. Preliminary standardisation of diagnosis needs to be made explicit.

3. More research is required into the subclassification and validation criteria of dementia syndromes, especially the non-Alzheimer's dementias. The preliminary work on neuro-imaging reviewed above, appears promising.

# CHAPTER 4

# THE DIFFERENTIAL DIAGNOSIS OF PRESUMPTIVE DEMENTIA

## 4.1 THE DIFFERENTIAL DIAGNOSIS OF DEMENTIA - CROSS SECTIONAL EVALUATION

After comprehensive evaluation of patients with presumptive dementia, up to 17% have been found not to be demented (Clarfield 1988). Marsden and Harrison (1972) published the first study which recorded a more detailed diagnosis, in a series of patients referred to the hospital with a presumptive diagnosis of dementia. They judged fifteen per cent of the subjects not to be demented, but to be suffering from a functional psychiatric disorder or another organic syndrome. The most common diagnosis in this group was depression. Similarly in a meta-analysis of thirty-two clinical studies which investigated the diagnoses of a series of subjects with presumed dementia, there was an overall prevalence of 4.5% of subjects suffering from depression (Clarfield 1988). It was not clear whether some of those subjects had co-existing dementia, or whether depression mimicked dementia (pseudodementia). Overall the pattern replicated Marsden and Harrison's finding that depression was one of the two most common condition mistaken for dementia.

Despite this evidence of misdiagnosis, in some cases depression and dementia do co-exist (Reifler et al 1982).

It may be that sometimes the diagnosis of pseudodementia is

mistaken, for example, in one study, 57% of those diagnosed as suffering from depressive pseudodementia developed dementia over the next 3 years (Reding et al 1985). An overview of depression in Alzheimer's disease quotes thirty studies. Prevalence of affective symptoms ranged from 0% to 87% (median 41%) (Wragg and Jeste 1989). The lower prevalence tended to be found among non-hospitalised, and therefore perhaps more representative groups of patients. When 'depression' meant a specific disorder e.g. major depression, bipolar disorder, dysthymic disorder, and not an isolated mood disturbance, most prevalence figures lay between 10% and 20%. Similarly using more recent NINCDS/ADRDA and DMS-III-R criteria of depression, to make a diagnosis, a prevalence rate for major depression of 17% in a series of 144 outpatients with Alzheimer's disease was found. (Rovner et al 1989).

In addition a preliminary one year longitudinal study of matched patients, ten of whom had Alzheimer's Disease and met DSM-III-R criteria for major depression and ten with Alzheimer's Disease only, has taken place. Although the former group of patients satisfied both diagnostic criteria at outset, the diagnosis of major depression, which might suggest a pseudodementia did not affect the pattern of severity of neuropsychological deficits at one year, which was the same in both groups (Lopez et al 1990). The

longitudinal outcome of Alzheimer's Disease will be discussed further in Chapter 4.2.

It appears therefore that the decision to allocate a patient either a single diagnosis of dementia or of depression may be misleading. This finding is further illustrated by the discovery that a proportion of elderly patients with a clinical diagnosis of affective disorders have neuroradiological evidence of ventricular enlargement, more usually associated with degenerative brain disease, further blurring the boundaries between these conditions (Dolan et al 1985). Recently the predictive validity and concurrent validity of a forced choice category between dementia and depression in the very old (mean age 83) has been examined (Ames et al 1990). The two clinical diagnostic subgroups could not be distinguished by neuroradiological appearance on computerised tomography and there was no difference in outcome at one and two year follow up. This finding from a group of 34 institutionalised very elderly people, cannot be generalised to imply that there is no difference between depression and dementia in all old people, but it does illustrate that a categorical classification may not be appropriate in all circumstances.

Other final diagnoses in patients with presumptive dementia have been:

1) in the category of functional disorders: hypomania, hysteria (Marsden & Harrison 1972) and schizophrenia (Smith & Kiloh 1981).
2) in the category of other organic syndromes: drug toxicity, Korsakoff's psychosis, delirium, dysphasia, epilepsy and hepatic failure (Smith & Kiloh 1981).

## 4.2a. THE NATURAL HISTORY OF DEMENTIA

The diagnosis of dementia can be considered either cross sectionally as a differential diagnosis, or longitudinally in follow-up studies. The first follow-up study of patients with a diagnosis of dementia found that 35 of 50 patients discharged from hospital with a diagnosis of pre-senile dementia, could be traced 5-25 years later. (Nott and Fleminger 1975). 15 had deteriorated as expected and many had died but 2 remained unchanged and 18 had improved. The paper concluded that the original diagnosis had been wrong in more than half the patients. The patients wrongly diagnosed, consisted mainly of people with marked personality difficulties and severe neurotic or affective disorders, most of whom still showed chronic psychiatric disability on follow-up. Ron et al (1979) carried out a similar 5-15 year

follow-up on 51 patients discharged from the Maudsley Hospital with a diagnosis of presenile dementia. After follow-up examination, seven were suffering from a functional disorder, and nine had organic diagnoses which had not progressed, therefore there was a total of 16(31%) in which the authors rejected the original diagnoses. A previous history of affective disorder and the presence of overt depression at initial interview were the best predictors of a change in the diagnosis at follow-up.

The conclusions of these two studies are based on the assumption that dementia must be progressive. However as the natural history of dementia is not known, this assumption is still being investigated. A review on the literature on the natural history of dementia revealed ten papers which reported original data on these conditions (Wilson et al 1987). Of these studies, only one study was based on an inception cohort "the most fundamental requirement for a natural history study" (Larson et al 1984). This study was also the only study performed on subjects who had not been inpatients in specialist centres, who are likely to be unrepresentative of all dementia sufferers. The study was a prospective analytic survey of 107 referrals to the internal medicine department, of patients over the age of 60 with cognitive impairment, mainly by the community old age psychiatry service, and as such was also subject to referral

bias (Larson et al 1984). Potentially reversible causes of dementia were identified in 15 of the original cohort. These were medication toxicity (6), hypothyroidism (4), subdural haematoma (2), transient ischaemic attacks (1), manic-depressive psychosis (1), and rheumatoid vasculitis (1). After treatment three patients regained normal cognition and eleven improved partially. On two year follow-up, eight of those diagnosed as suffering from a reversible dementia showed cognitive deterioration, four did not and two could not be found. Five patients from the remaining 92 had improved cognition but still remained demented at follow up. This was attributed to treating co-existing conditions. The authors of the study felt that a useful way of improving cognition in dementia, in general, was to treat co-existing conditions, rather than continue the search for reversible dementias.

### 4.2b THE NATURAL HISTORY OF ALZHEIMER'S DISEASE

Many papers consider the natural history of Alzheimer's Disease only, rather than the whole range of dementias. Since Wilson et al's review (1987), Heymen et al (1987) have published a prospective follow-up study of 92 white non-institutionalised patients with a diagnosis of pre-senile Alzheimer's disease compatible with NINCDS/ADRDA criteria.

Five year mortality rate was 24% compared with the expected rate of 9.5%. 63% were admitted to nursing homes, and those patients were also more likely to die. Death and institutionalisation were predicted by severity of dementia and younger age at diagnosis. All the patients remained demented, but it is not specified whether all deteriorated or not. Botwinick et al (1986) report a four year follow up study of 18 patients diagnosed as suffering from mild Alzheimer's dementia. Thirteen declined and five remained stable. The authors suggested that these five might represent a group of slow or non-progressive Alzheimer's disease. A third longitudinal study of Alzheimer's disease studied 16 patients aged 52-96 years with either possible or probable Alzheimer's disease according to NINCDS/ADRDA criteria (Katzman et al 1988). It found the mean annual rate of deterioration on the psychometric test used was similar whatever the initial error score, and was independent of the patient's sex, education or age. The group suggested that an average time period of 5.2 years could be specified from the onset of overt cognitive change to moderately severe dementia. Despite the constancy of mean rates there were wide individual variations in the rates of progression. Some patients had markedly rapid progression of more than three times the mean, while some improved or remained stable. Improved scores tended to be accounted for by improvement in orientation in time questions.

Similarly Teng et al (1987) found that the rate of decline on mini mental state examination was the same for early (age 53-64 years) and late onset (age 65-96 years) group of Alzheimer's Disease. However the early onset group performed more poorly than the late onset group on items that tested for language and visuoconstructive abilities. A later study found that in 86 patients with NINCDS/ADRDA diagnosed probably Alzheimer's disease age range 46-89, that age of onset did not significantly affect the rate of progression over one year (Becker et al 1988). However, if syntactical impairment of language was present in early Alzheimer's disease, this predicted a faster deterioration. Lexical and semantic impairment did not. Another study found that in 178 patients with NINCDS/ADRDA diagnosed Alzheimer's disease, cognitive deterioration over 12 months, was predicted by visual hallucinations but not by delusions (Burns et al 1990).

In summary, there are no reports in the literature of the natural history of an unselected community sample with dementia. The studies which have been reported confirm the clinical impression of a varying but usually slow decline and early death in dementia and stability of diagnosis, in patients diagnosed as outpatients. The questions either of different courses in pre-senile and senile dementia of the

Alzheimer's type or of factors predicting decline have not been resolved.

## 4.3. CONCLUSIONS

1) Present information on the diagnosis of dementia, suggest that a diagnosis of dementia indicates that the patients' cognitive state is unlikely to improve and will probably deteriorate over a period of years. It is not known what factors predict deterioration, although age, sex and severity of impairment are possible predictors. Improvement may be brought about by treating concurrent physical illnesses.

2) Screening studies are required in the community to obtain representative samples of subjects with dementia. These studies require a second phase to subclassify patients according to specified criteria. Using representative community samples, it will be possible to determine the relative prevalence of the dementias, and allow further studies of risk factors and natural history. This is probably the way that much progress will be made in the classification, aetiology, diagnosis and treatment of dementia, the epidemic of our time.

3) Longitudinal studies of the natural history of the dementias in unselected community samples are required. These will improve the subclassification of dementia by testing the validity of current diagnostic systems. They will also provide valuable prognostic data for patients, families and service planning.

# CHAPTER 5

# THE EPIDEMIOLOGICAL STUDY

## 5.1. HISTORY OF EPIDEMIOLOGY.

The previous chapters have considered the ageing population and the diagnosis of dementia. The next chapters combine these topics to consider epidemiology with respect to dementia.

The historical origins of epidemiological psychiatry have recently been reviewed by Bynum (1989). The word epidemiology probably dates from around 1850, when the London Epidemiological Society was formed to stimulate interest in epidemiology, which was defined by J P Parkan as being the study of "the remoter causes of epidemic diseases". The first paper in the society's transactions of any psychiatric relevance, did not appear until 1901-2 session when Frederick Mott published his study on 'Dysentery in Asylums'.

The study of epidemiological psychiatry was not at that time recognised. Despite this Daniel Hack Tuke's Dictionary of Psychological Medicine (1892) had articles on 'Epidemic Insanity', 'Statistics of Insanity' and on 'suicide' all of which contain epidemiological data. This data arose mainly from studies of asylums. Nevertheless Tuke discusses many problems which are relevant today. He recognised the concepts of prevalence and incidence, using the terms existing and occurring insanity; the problems of recognising

and defining a case; the existences of 'borderline cases' and the influence of sociodemographic status.

Currently, epidemiology may be defined as the study of the distribution of morbidity in time and place, and of the factors which influence this distribution (Kay & Bergman 1980). As this definition shows, the current use of the word epidemiology has been widened from the study of epidemics, to the study of all branches of medicine. It is concerned with the definition, classification, aetiology, prevalence, incidence and natural history of disease in a community. Since the Victorian era research using epidemiological method has been carried out in many areas of psychiatric illness including personality disorder, (eg. Mann et al 1981), the neuroses, (eg. Weissman & Myers 1978), psychosomatic disorders and the psychoses, (eg. Cooper & Sartorius 1977). It has also been used to study specific populations and their vulnerability to mental illness, for example women (eg. Murray et al 1981) and the elderly.

The first community survey of dementia was carried out in Sweden (Essen-Moller et al 1956). In the UK, the first reported community survey in the field of old age psychiatry came from a Scottish rural practice (Primrose 1962). Between 1945 and 1985, 47 epidemiological studies of the elderly in the community were published (Jorm et al 1987). These and

subsequent studies have used many different strategies for investigating prevalence rates and it is only by close scrutiny of these methods, that any broad conclusions can be drawn.

## 5.2. THE EPIDEMIOLOGICAL METHOD

### 5.2a. THE STUDY OF POPULATIONS

As epidemiology is the study of groups or populations rather than individual patients, it requires different methods of investigation from the traditional model of differential diagnostic taught in clinical medicine. Epidemiology requires some of the skills of clinical diagnoses together with the use of statistics.

In clinical practice, the decision making is usually dichotomous, patients either have or do not have a disorder, and either are or are not treated. In hospital practice this is often relatively easy, as borderline cases tend not to be referred to hospital. Thus the distribution of a rating scale for dementia in a psychiatric ward is likely to be bimodal, one mode corresponding to those admitted for dementia and one to those who were not.

However within the general population rating scales for mental illness shows a continuous unimodal distribution. Therefore within a community population the appropriate question may be not 'has he got it?' but 'how much of it has he got?'. If attention is confined to severe and therefore obvious cases, then epidemiology will be less likely to fulfil its potential to answer questions of causation. Epidemiology has the potential for understanding and therefore perhaps controlling, the mass determinants of population means, prevalence rates and incidence rates of illness and merges into social research and social policy (Rose 1989).

The epidemiologist does not investigate the patient who has presented with symptoms, but instead investigates a total population, most of whom may be well, and some who may have unrecognised pathology. As consultation is not patient initiated, epidemiologists must also be aware of, and concerned, about the purpose and ethics of investigations. These will be discussed further in section 5.3.

The most commonly used methods of epidemiological enquiry are the cross-sectional survey, which can be a one or two phase method; the case control study and the longitudinal study (see below). The epidemiological description of a disease is derived from relating the characteristics of a group of

cases, such as age and sex, to those of the population in which they belong. These characteristics of the population base are discussed in chapter 6, section 2.

### 5.2b. THE CROSS-SECTIONAL SURVEY.

The cross-sectional survey consists of examining a complete defined population for the conditions of interest. There are three aims of cross-sectional surveys,

(1) description of a disease in the community and its distribution

(2) study of the causes of disease

(3) screening for hitherto undiagnosed cases (Barker & Rose 1984).

The cross-sectional survey is an appropriate tool for chronic conditions such as schizophrenia or dementia, but as the probability of detecting a case of disease is related to the disease's mean duration, it is inappropriate for acute conditions such as infectious diseases. In the two phase cross-sectional method, the first phase is a case finding screen and the second phase defines and describes the cases in more detail.

## 5.2c. THE CASE CONTROL STUDY

The case control method matches cases to non-cases (controls). The method is reviewed by Lewis & Pelosi (1990). It is usually concerned with aetiological questions, and identifies differences in exposure between cases and non-cases. It is especially useful in rare conditions, when very few cases may be picked up by surveying whole populations. The difficulty with this method is selecting appropriate controls, who have to be matched for variables associated with the development of the disease, from the aetiological and social factors being studied. Statistical tests of significance estimate the probability of any association between exposure and disease being by chance. Reverse causality can occur when the disease may cause the exposure, for example in the debate about whether unemployment causes ill health, or ill health unemployment. Another mistake that can occur is when an independent risk factor (a confounding factor) is present in association with the exposure. This can lead to a spurious association, or can eliminate a real association.

## 5.2d. THE LONGITUDINAL STUDY.

Finally the longitudinal study can either follow a population

prospectively to determine risk factors and incidence, or follow early cases to determine natural history, and outcome, or compare the association between initial characteristics and the risk of future disease. One type of longitudinal study is a cohort study which is designed to test a specific aetiologically hypothesis. The difference between a case control and a longitudinal cohort study can be seen, for example, in the case of rubella and its association with congenital cataract. A case control study would compare people with a congenital cataract and a matched control group without, for example a history of maternal rubella, thus confirming the aetiological importance of rubella. A cohort study of rubella in pregnancy might follow up mothers who had developed rubella during pregnancy and the children born to them, and thus quantifying the risk associated with rubella.

## 5.3. SCREENING.

Once it is known how to recognise a particular disease before the patient may present spontaneously to doctors, the questions, whether to screen and who to screen for the disease throughout the at risk population arises. Sometimes only those at high risk are screened, this is known as targeting. Alternatively, opportunistic screening may take place when the screening procedure is part of a consultation

initiated for other reasons. These two procedures are cheaper than screening the whole population but cases may be missed.

Wilson & Jungner (1968) reviewed the ten principles of screening. These are: 1) that the disease should constitute an important public health problem 2) that there should be an accepted form of treatment for those persons having the disease once recognised 3) facilities for diagnosis and treatment should be available to the population in question 4) there should be general agreement among clinicians as regards the indication for treatment 5) the natural history of the condition should be adequately understood 6) there should be a recognisable latent or early symptomatic stage of the disease 7) a suitable test should be available 8) the screening method should be acceptable 9) the cost of case finding should not be excessive in relation to other existing health service priorities and 10) the screening programme should provide a basis for a continuing process of early detection.

They comment that these requirements now command broad acceptance in the field of preventative and social medicine. Using these principles in the United Kingdom, for example, cervical cancer screening is currently available to all women, and screening for anaemia, renal impairment and

syphilis is automatically carried out in antenatal care, because pregnant women are at high risk of anaemia and renal impairment and because, in the case of syphilis, the detection is easy and sensitive and congenital syphilis is a serious disease with effective and acceptable prophylaxis.

The debate over the purpose and ethics of screening the asymptomatic population has been intensified by the emergence of the autoimmune deficiency syndrome (AIDS) and the screening test now available for the human immunodeficiency virus (HIV). It is now generally agreed that HIV testing, unlike other screening procedures, requires both written informed consent and counselling prior to testing. In contrast in pregnancy, consent for testing is assumed. In HIV, the ethical dilemma lies in informing people who may be asymptomatic, that they had a virus which might lead to a fatal illness and for which until recently there was no treatment at either the asymptomatic or latent stage. This and the fact that the natural history of AIDS was not well understood went against the accepted principles of screening. However many people who felt that they might have been infected by HIV, wanted to know their status for the purposes of planning and controlling their lives. Counselling gives people the knowledge to enable them to make an informed choice as to whether to be tested or not. Recently, literature on the psychological costs of screening reports

high levels of anxiety in patients participating in screening programmes which are not always allayed by negative results. Conversely, others overgenerate a negative result, and this reinforces an unhealthy lifestyle. Increased knowledge of the reasons for screening the particular patient, the meaning of results and how the patient can reduce risks, all help allay anxiety (Marteau 1990).

The principles of screening have developed over the nineteen eighties. A new formulation might now be that if principles two to five are not applicable then counselling should be mandatory prior to screening.

## 5.4 RELIABILITY AND VALIDITY OF SCREENING INSTRUMENTS

Once a decision to screen has been made, any epidemiological studies require the use of screening procedures which must be reliable and valid. The concepts of reliability and validity are reviewed by Goldberg (1989) and Barker & Rose (1984) and are discussed in the remainder of this section. The practicalities of choosing a screening instrument are reviewed in chapter 6.5.

## 5.5 RELIABILITY

Reliability concerns the repeatability of a measurement. It is influenced by within-subject variability, and observer (measurement) variation. Intra-observer variation is random and occurs between observations of the one observer, made at different times. In contrast inter-observer variation can be decreased by training and is usually systematic, so that different raters can be trained to agree on how to classify a symptom or sign. This interrater reliability should be measured when survey instruments are developed, to ensure that the instrument is capable of being used consistently. In individual surveys, interrater reliability can be measured again, to ensure that raters are recording consistently.

Within subject variability is usually random and therefore on average cancel out in population studies and so will not be important. However inter temporal reliability, that is stability of categorization over time, is also related to what is being measured. For example a schedule rating short term illness would not be expected to show temporal stability.

## 5.6 VALIDITY

The ideal screening test would correctly classify all people

as either having or not having the condition in question. As the ideal measure does not usually exist and the question is often "how much" not "if", the validity of an instrument; the ability to measure what it is designed for, gives a numerical value to the accuracy of the instrument. Validity can be divided into four types. These are sensitivity, specificity, concurrent validity and predictive validity.

Sensitive tests correctly identify cases. The sensitivity of a test equals the true positives found expressed as a percentage of the number of true cases. Conversely a specific test will not misclassify normals as cases. The specificity of a test is the true negatives expressed as a percentage of the non-cases.

The concurrent validity measures the ability of a test to respond to the severity of the disorder rather than to classify it only as present or absent. It is usually measured by a rank-order correlation coefficient, between scores on the instrument and total severity scores on some standardised research interview.

The predictive validity is the ability of an instrument to classify as cases those who have an outcome on follow-up consistent with that expected of cases.

Three other measures of validity of a screening procedure are sometimes quoted. These are the positive predictive value (PPV), which is the probability that an individual case found on the instrument used will be found to be a case on future examination, the negative predictive value (NPV) which is the probability that a 'non-case' found on the instrument will be found to be a non-case on future examination, and the other overall misclassification rate (OMR) which refers to the percentage of misclassified cases. All are dependent on prevalence. Therefore when the prevalence rate of a condition is low the positive predictive value will decrease.

The concept of reliability and validity assume some absolute standard which can confirm the results of the screening instrument. As already discussed, most psychiatric diagnoses are not dichotomous but a question of spectrum diagnoses. Therefore it is important that validation is regarded as only confirming that an instrument can, to a specified degree, answer a specific question in a given population.

Having now discussed the theoretical issues related to screening for the dementias, the next two chapters will discuss the setting up of a community screening study for the dementias and published studies.

# CHAPTER 6

# SETTING UP A COMMUNITY SURVEY OF DEMENTIA IN THE ELDERLY

## 6.1 INTRODUCTION

Before a community survey can be undertaken a population must be defined and identified (a population register). Then appropriate tools must be employed to answer the questions posed.

Ideally a population register should contain every person within the population meeting the study criteria. Every person on this register should be interviewed by trained interviewers using a method of detection which identifies cases without error. The whole project should be acceptable and economic in the population studied. As these ideals are not achievable, many different methods have been tried to try to attain an ideal survey.

## 6.2. CHOOSING THE POPULATION BASE

The practical task of enumerating the population for study has been tackled in a number of different ways.

### a. General Practitioners' Lists

The most common source in the UK has been the general practitioners or Family Practitioner Committee list (Clarke et al 1986, Morgan et al 1987, Copeland et al 1987a, Copeland

et al 1987b, Brayne & Calloway 1989, O'Connor et al 1989). However populations are mobile so these lists become quickly out of date. For example recently nearly 25% of people in Liverpool lists were found to be dead or have moved away (Copeland et al. 1987), while in a London study, 35% of women did not receive letters posted to them because of inaccuracies in the Family Practitioner Committee's database (McEwan et al. 1989). Older people within the area studied may not be on any of the local General Practitioners' lists but may consult a General Practitioner some miles away, or be on the list of a private practice. Brayne & Calloway (1989) in rural Cambridgeshire state that they have surmounted difficulties in listing the population, by studying a highly stable group, which is served by one single health centre with virtually no cross boundary flow. However they do not cite any procedure used to validate the General Practitioners' lists they employed.

**b. Patients using services**

Alternative sources for obtaining a base population have been patients attending a health centre and any friend or relative accompanying them (Griffiths et al. 1987), or patients from the mental health services (ten Horn, 1985). However, as those in contact with health professions are always selected, elderly populations from these sources must be an inaccurate basis for a study.

### c. The electoral roll

The electoral roll has also been used as a basis for sampling (Kay et al. 1964, Cooper & Bickel, 1984, Mowry & Burvill, 1988, Lindesay et al 1989). In Britain the electoral roll is not fully satisfactory, as there is no compulsory registration and the voter's age is not recorded. British surveys using the electoral roll have therefore required to contact each individual regarding their age or date of birth, and follow up the non-responders (Kay et al 1985, Lindesay et al 1989). To support the use of the electoral roll, one study checked if those patients diagnosed as demented by the local psychiatric services were included in the electoral register (Lindesay et al 1989). They discovered 94% were on the register. However this validation exercise is still unsatisfactory as it is not known whether those referred to psychiatric services with dementia are the same as those who are not. It may be that the same people are neither known to psychiatric services, nor are on the electoral register.

### d. State Lists

Certain countries have a list of all elderly in a particular locality. These lists can be used as a sampling frame. For example in New York a list was used from the State Office for Ageing (Gurland et al. 1983). Similarly in China a list from the residents committee in Beijing is available (Li et al. 1989), as is the district register in South Africa (Elk et al. 1983). In Britain there is no such list available.

### e. Visiting every house

The only other method which remains is to visit every inhabited dwelling. This laborious method was undertaken in Mississippi for a whole county (Schoenberg, 1985).

## 6.3. DEMOGRAPHY OF THE POPULATION BASE

The variables to be defined in the target group can be divided into the personal, that is the age group, sex and race; and into the definition of the community, that is whether institutions should be included or not, and whether urban or rural areas should be surveyed.

### AGE OF THE POPULATION

The first UK community survey of dementia targeted exclusively those over 65 years of age (Kay et al. 1964); a decision which some later studies have followed (Morgan et al. 1987, Lindesay et al. 1989). Others have argued that as dementia is more prevalent in the more elderly, it makes more sense to restrict the study to an older age group and they have studied the over 70s (Kay et al. 1985, Mowry & Burvill, 1988), the over 75s (Clarke et al. 1986, O'Connor et al. 1989) or the 70-79 year age group (Brayne & Calloway, 1989). The younger elderly, the over 60s are the subjects in other surveys (Griffiths et al. 1987, Li et al. 1989). Finally some papers have described the prevalence of dementia throughout all age groups (Schoenberg et al. 1985, Folstein

et al. 1985). As the prevalence of dementia increases with age, the resulting overall prevalence rate will be greatly affected by the age groups which are surveyed.

**SEX OF THE POPULATION**

Most surveys have interviewed both men and women. Sayetta (1986) set a precedent by interviewing only men. Brayne & Calloway (1989) decided to interview only women, because a study "conducted on both sexes over an unlimited age range would have produced small numbers in some age groups and consequently little confidence in the distribution".

**RACE OF THE POPULATION**

Although usually the whole population is of interest, some studies have been specifically concerned with the differences between races (Schoenberg et al. 1985), or with one racial group, such as the coloured in Cape Town (Ben-Arie et al. 1983).

## 6.4. THE COMMUNITY.

The definition of the community is vague. According to the Shorter Oxford English Dictionary (1973), it is 'a body of

people organised into a political, municipal or social unity'. This has been taken by some workers to mean all those living in their own homes (Kay et al. 1985, Schoenberg et al. 1985, Morgan et al. 1987, Mowry & Burvill, 1988), while others have included hospital and social service institutions (Kay et al. 1964, Brayne & Calloway, 1989). As in Britain around 5% of the elderly, who are usually the most disabled elderly, live in institutions, prevalence figures will significantly change according to which definition is used.

Most recent studies have concentrated on urban environments, for example Liverpool and London, but the rural elderly have been studied in the UK (Griffiths et al. 1987, Brayne & Calloway, 1989), and in Japan (Shibayama et al. 1986). These surveys suggest that, for an unknown reason, prevalence figures for dementia may be lower in a rural, as opposed to urban environment but more data are still required.

## 6.5. CHOOSING THE METHOD OF ASSESSMENT (SCREENING)

A recent paper pointed out that cases are in fact concepts. "They exist only in the mind of the investigators and are not to be sought like precious stones, but should be defined as need dictates and then sorted according to these criteria". (Copeland, 1990). The remainder of this section is partially concerned with whether investigations have borne this in mind

when choosing assessment instruments.

As dementia is not usually accompanied by insight, self report has not been used as a method of assessment. Therefore methods of case ascertainment have been varied and seem to have been chosen according to composition of the survey group. They include:

(i) diagnosis by a psychiatrist.

(ii) a questionnaire - content not specified.

(iii) standardised brief screening tests for cognitive function.

(iv) semi-structured standard interview for the elderly.

(v) a combination of the above.

**Psychiatrists' Assessment:**

1) In Newcastle, psychiatrists made a clinical diagnosis according to broad diagnostic criteria (Kay et al. 1964). This approach is an expensive one, requiring psychiatrists to make diagnoses on every survey subject. In the above study diagnostic criteria are not specified or standardised, so it has been difficult to compare with other studies.

**Questionnaire:**

2) Schoenberg et al (1985) in Mississippi, and Shibayama et al (1986) in Japan used questionnaires administered by trained interviewers. Although training of the

interviewers itself builds in some measure of reliability, no validation of the interview was reported.

**Brief assessment procedures:**

3) Brief assessment procedures for intellectual screening are more satisfactory. They are usually standardised, reliable and validated. However the standards that they are validated against are not designed to eliminate other illnesses which might mimic dementia, for example depression. In addition they may be validated against a standard which is not suitable for community surveys. For example the Clifton Assessment Schedule which was used in Melton Mowbray and Nottingham (Clarke et al. 1984, Morgan et al. 1987) was developed for use in institutions. It therefore has been found not to identify those with a mild dementia (Brayne & Calloway, 1989), suggesting that prevalence figures based on this test would be underestimated.

## THE MINI MENTAL STATE EXAMINATION

The Mini Mental State Examination (Folstein et al 1975) has been used for screening in Baltimore, Canberra, Cambridge, Beijing and London (Folstein et al. 1985, Kay et al. 1985, O'Connor et al 1989a, Li et al 1989, and Iliffe et al 1990), or as part of a semi-structured interview in Cambridge (Brayne & Calloway, 1989) and South Africa (Ben Arie et al. 1983). A particular

difficulty has arisen with the Mini Mental State (MMSE) which has different versions which are not all equivalent (Kay et al. 1985, Mowry & Burvill, 1988, Brayne & Calloway, 1989), as some surveys do not state which version is used. In addition, as the scores have been shown to vary with level of education of the respondent, different cut points are used in different populations eg in China $\leq$17 or in Baltimore $\leq$23. In South Africa the best cutoff point for the population is not known as the MMSE had not been standardised there. Thus all subjects 'screened' with the MMSE had to be re-examined by two independent psychiatrists.

Within the UK, Brayne & Calloway found that using a cut point of 21/22 on one version of the Mini Mental State, gave a sensitivity of 83% and a specificity of 87%. This sensitivity is too low if the purpose of screening is to find all causes of dementia either for research or service planning. O'Connor et al (1989), who used the MMSE as a screening instrument with the Camdex as validation, found that 13% of those who scored as high as 24 or 25 on the MMSE, regarded in some studies as in the normal range, had a diagnosis of dementia, but only 55% below the cutoff point were judged to have an organic disorder. Further there were 13 people in the area surveyed who were known by the services to be suffering from dementia but who had been missed altogether in the study. They concluded that the MMSE "cannot be used to

make even tentative psychiatric diagnoses" (O'Connor et al 1989b). It is therefore not established which cut point should be used even within the UK, when the Mini Mental State is used for screening, so that accurate figures for the prevalence of dementia can be attained.

(4) Semi-structured standard interviews for the elderly are tests which collect cognitive data in the setting of a more extensive mental state examination. The three interviews which are used are the Comprehensive Assessment and Referral Evaluation (CARE), the Geriatric Mental State (GMS) and the Cambridge Mental Disorders of the Elderly Examination (CAMDEX).

**THE CARE**

The CARE (Gurland et al 1984) has been used in the US/UK cross national study, in Canberra and London (Gurland et al. 1983, Kay et al. 1985 and Lindesay et al, 1989). The short-CARE was developed from the CARE, as the length of CARE is prohibitive for use as a screening procedure. While the CARE consisted of 1,500 items and 22 indicator scales, the short-CARE consists of 6 of the 22 indicator scales. With reference to the detection of dementia the short-CARE contains a screening scale, namely the organic brain syndrome scale (OBS) and a diagnostic scale, namely the dementia diagnostic scale (DDS). The OBS was designed as a

sensitive indicator scale for cognitive impairment, the DDS to detect probable cases of pervasive dementia which are severe enough for clinical intervention (Kay et al 1985). The OBS consists only of cognitive items, and the DDS of cognitive items linked with items indicating incapacity, from an activity of daily living scale. As with the MMSE, different cut points can be used for different studies. For example on the OBS scale the validated cut point is $\geq 4$. Lindesay et al (1989) study analyzed the data using two cut points of $\geq 3$ and $\geq 6$. These cut points were used to give a "broad" and "narrow" definition of cognitive impairment. Other studies use the DDS scale, which generates diagnosis of dementia as a basis for prevalence figures. The limitations with the short-CARE are firstly, the absence of a history incorporated in the short-CARE, so that the short-CARE is suitable only as a screening instrument identifying probable dementia, and not adequate to give a precise diagnosis, despite the scale called the Dementia Diagnostic Scale. Secondly, different cut points make comparison between studies difficult. One of the strengths of the CARE is that it allows the rater to score failure to answer as pathological. For example, for the question, "how old are you", the questionnaire allows either "states does not know or does not complete the answer" or "stated age different from the most accurate estimate" as pathological.

The CARE is a validated and reliable instrument. The inter-rater reliability of the dementia scale is .75 (Gurland et

al 1984) and a follow up study has been validated by a one year study which showed outcomes consistent with that expected of clinical dementia in all cases (Gurland et al 1984). However these advantages are lost when a non-standardised cut point is used, as happened recently in a London inner city population, similar to the population in which the CARE was first validated (Lindesay et al 1989).

**GERIATRIC MENTAL STATE**

The full CARE was developed from the Geriatric Mental State and is therefore similar (Copeland et al 1976). Algorithms have now been developed for a computerised diagnostic system for use in the community: GMS(A)/AGECAT (Geriatric Mental State (A)/Automated Geriatric Examination for Computer Assisted Taxonomy (Copeland et al 1986)). The GMS is a semi-structured clinical interview designed to record patients' current cognitive state and their mental state during the month prior to interview. Individual symptoms are rated in eight sections covering major syndromes (Gurland et al 1976). Although patients can score on all eight of the symptom clusters they are ultimately allowed only one diagnosis. The GMS (A) is a shortened version of the GMS which has been developed for use in the community, by analysis of data sets, to remove questions which are less relevant for a study population out of hospital (Copeland and Wilson 1989). The AGECAT programme ensures that patients with the same symptoms

are rated as having the same syndromes and given the same diagnosis on each occasion.

The strengths of the GMS are that it allows for a wide number of diagnoses, which should decrease the number of false positive diagnoses, and that its standardised programme means that different studies are directly comparable as investigators are not able to change diagnostic criteria. The GMS has been used in prevalence surveys without the AGECAT programme in Hobart, Australia and latterly with computerised diagnoses in Liverpool (Kay et al. 1985, Copeland et al. 1987). In published prevalence studies, the GMS did not have available an accompanying section collecting historical data. However now this is available and this measure can potentially be used for both screening and for diagnosis at the same interview.

The GMS has weaknesses, when used in prevalence studies. Firstly on the organic scale there is no assessment of activities of daily living, therefore the diagnosis generated by AGECAT cannot include the criterion of functional deterioration. Secondly, replies are only rated as pathological if they are wrong or the patient states that he does not know the answer. If the patient does not answer this does not score as pathological. However in the latest version GMSA (3) this scoring has been changed and as in the case of the short-CARE, irrelevant or incomplete replies to cognitive questions are also rated as pathological. Thirdly,

patients are only allowed one diagnosis despite the known occurrence of, for example dementia and depression together.

Copeland et al (1976) reported two studies of interrater reliability in rating the GMSA. In the first study agreement on principal diagnostic categories is 95%. The correlation coefficient for positive rating is 0.87. The second study which compared reliability on the GMS of raters from the USA, with each other, and raters from the UK with each other, resulted in a correlation coefficient of 0.72 in the UK and 0.71 in the USA.

After the introduction of AGECAT, the diagnostic validity was measured as the concordance rate between AGECAT and psychiatrists' diagnoses. The correlation coefficients were 0.84 in a psychiatric hospital setting, and 0.74 in a community setting (Copeland et al 1986).

**THE CAMDEX**

The semi-structured instrument, the CAMDEX (Roth et al 1986) consists of a neuropsychological battery (CAMCOG), a mental state examination, an informant interview, a physical examination and optional laboratory investigations.

Roth et al (1986) reported an interrater reliability study of the CAMDEX using inpatients and outpatients in Cambridge. Two psychiatrists interviewed patients using the CAMDEX as

an interview instrument, then made a diagnosis. There was complete agreement on cases diagnosed by the two psychiatrists as either normal or dementia. However the Kappa coefficient for diagnostic agreement was reduced to 0.63 when dementia was subdivided into Alzheimer's Disease, multi-infarct dementia, mixed dementia and secondary dementia. Sensitivity and specificity was measured using either the MMSE as a screening instrument or the Cambridge cognitive examination (CAMCOG) section of the CAMDEX. Sensitivity for the MMSE was 94% and specificity 85% using the optimal cutoff of 23/24. Sensitivity of the CAMCOG was 92% and specificity 96%.

The CAMDEX was used by Brayne & Calloway (1989) as a diagnostic instrument. All subjects were interviewed in depth without prior screening. The CAMDEX requires a doctor with specific training in its use to administer it, and takes on average nearly two hours per subject. This makes it a very expensive screening instrument. Nevertheless Brayne interviewed 365 elderly people using the Camdex. However as there are no other prevalence screening studies which have used the CAMDEX, it is not possible therefore to compare the prevalence rates published from the use of the CAMDEX directly with other studies.

This chapter has so far discussed the theory of setting up a community survey of dementia in the elderly. The next sections discuss the results of studies which have been

reported in the last four years; how the methods used have affected the findings and the ideal study.

## 6.6 RECENT RESULTS OF PREVALENCE SCREENING FOR DEMENTIA (PHASE I STUDIES)

The smallest overall prevalence of dementia in the over 65s (3.2%) comes from a survey using the CAPE, which is designed for use in hospital (Morgan et al 1987), and from a survey using the narrow diagnostic scale from the CARE, the DDS (2.3%) (Copeland et al 1987). Analysis of the same interviews using the GMS/Agecat increases the figures to 4.3%.

Studies published in the last four years are summarised in tables 4 and 5.

TABLE 4 PHASE I STUDIES: PREVALENCE OF DEMENTIA

| INVESTIGATORS | PLACE | SAMPLE SIZE | SEX | PREVALENCE IN WOMEN | CASE FINDING INSTRUMENT | AGES | PREVALENCES% |
|---|---|---|---|---|---|---|---|
| Morgan et al 1987 | Nottingham | 1042 | | Yes | CAPE | =>65,=>75s | 3.2% |
| Copeland et al 1987 | Liverpool | 1070 | | Yes | GMS/AGECAT diagnosis | =>65 | 5.2% |
| | | | | | GMS/AGECAT organic symptoms | =>65 | 10.1% |
| Lindesday et al 1989 | London | 890 | | Yes | CARE, OBS scale 3+ | =>65 | 4.6% |
| | | | | | OBS scale 6+ | | 1.1% |
| Copeland et al 1987 | London | 396 | | Yes | CARE/DDS pervasive dementia | =>65 | 2.3% |
| | | | | | GMS/AGECAT diagnosis | | 4.3% |
| | | | | | GMS/AGECAT organic symptoms | | 6.3% |
| | | | | | psychiatric diagnosis | | 4.3% |
| | | | | | DSM III | | 2.8% |
| Li et al 1989 | Bejing China | 1072 | | Yes | MMSE | =>60 | 3.9% |
| Shibayama et al 1989 | Nagoya | 3106 | | Yes of severe dementia | unspecified interview followed by psychiatric | =>65 | 5.8% |

TABLE 5 PHASE II STUDIES PREVALENCE OF DEMENTIAS

| INVESTIGATORS | PLACE | SAMPLE SIZE SCREENED AS DEMENTED | INCIDENCE IN WOMEN | AGE | CASE FINDING | PREVALENCE |
|---|---|---|---|---|---|---|
| Folstein et al | Eastern Baltimore | 36 | No | =>65 | MMSE in DIS psychiatric examination | dementia 6.1%<br>SDAT 2%<br>Multi-infarct 1% |
| O'Connor et al | Cambridge | 42 | No | =>75 | MMSE psychiatric records | dementia 10.5%<br>probable SDAT7.9%<br>vascular dementia 2%<br>other 0.2%<br>moderate & severe dementia 5.3%<br>mild dementia 5.2% |
| Brayne & Calloway | Cambridge-shire | 29 | N.A. | 70-74<br>75-79 | CAMDEX | dementia 4.3%<br>SDAT 1.6% 6.7%<br>MID 2.2% 2.8%<br>mixed0 0.6% 1.6% |
| Li et al | Beijing | 42 | Yes | 60+ | MMSE | dementia 1.3%<br>M.I.D. 0.83%<br>SDAT 0.37% |
| Shibayama et al | Nagoya | 382 | Yes | =>65 | | dementia 5.8%<br>SDAT 2.4%<br>MID 2.8%<br>other dementias 0.6% |

Phase I screening studies for dementia published between 1987 and 1990 show an increase prevalence of dementia with age and in females. This is not necessarily because of a true excess of dementia in women; the longer survival of women may lead to a higher prevalence of dementia in women.

This was first suggested by Tomlinson et al (1964) because of the excess of male deaths in their postmortem series. Later, Blessed & Wilson (1982) in their follow-up of patients with dementia noted longer survival of women with senile dementia. To date the data concerning the incidence of dementia has not been established so it is not known if the longer survival of women with dementia accounts for the excess of women.

The prevalence of dementia in the over 65 year old age group is somewhere between 2.3% and 10.1%. It is impossible to say whether these various figures reflect only methodological differences or true differences within populations.

## 6.7. RESPONSE RATES IN SCREENING SURVEYS.

Response rates in screening surveys vary enormously. Studies in the last 5 years have reported rates varying from 97% in Mississippi (Schoenberg et al. 1985) to 72% in Liverpool (Copeland et al. 1987). Schoenberg's study was the only study in which enumeration took place by door

knocking contact. Interviewing was carried out at the same time as enumeration, thus this appears to be the best method of gathering as complete a sample as possible. However the next most complete sample which achieved a 91% interview rate (Brayne & Calloway, 1989) had exactly the same methodology as in Liverpool. Letters were sent from the General Practitioner requesting interview, and non-respondents to these letters were visited personally at home. Cooper and Bickel (1983) had previously concluded from a literature review that the best way to gain a high response rate was for an invitation to come from the physician or other health professional whom the family already knew. It is unclear why there is this discrepancy in response rates using similar methods, but it may be that the higher inner city crime rates in the UK, make pensioners less willing to allow interviewers in their home than in rural Cambridgeshire. It may also be that an interviewer who is both a doctor and female is more likely to be allowed access than other interviewers.

It is important that those who do not respond to interview invitation are visited at home, as it may be that those who do not answer letters are different from those who do, particularly in terms of cognitive ability. This question has not been directly addressed, although Jorm et al. (1987) in his review of prevalence surveys concluded that differences in response rates did not materially affect prevalence rates.

## 6.8 CONCLUSIONS

### THE IDEAL STUDY

In conclusion the ideal study to determine the prevalence of the different types of the dementias has never been reported. This study would entail a community screening, from a population list compiled either by door knocking or by using General Practice lists either in an isolated area where there is no cross boundary drift or in areas where all general practice lists can be included. A screening instrument would be used which was known to be reliable and valid within the population studied. Both men and women would be screened as it is not known whether the prevalence is the same in both sexes. A high response rate would be achieved either by interviewing while enumerating, or by sending a letter from the general practitioner to request interview, followed by personal visits to non-responders.

There are at present no studies which completely fulfil these criteria. The best studies were those of Brayne and Calloway's (1989) which screens 91% of a total population, enumerated from general practitioner lists but interviews only women using an non-validated list; Schoenberg et al's (1985) study which screens 97% of a population enumerated by door knocking but does not use a validated instrument, and Gurland et al's (1983) US study which screens a

population from a list held by the State Office of Ageing using a semistructured instrument but achieves a response rate of only 71%.

# CHAPTER 7

# THE PHASE II STUDY - DIAGNOSTIC STAGE

## 7.1. CHOOSING THE METHOD OF ASSESSMENT (PHASE 2 STUDIES)

Five phase 2 studies in which the people who were identified as organic or dementia cases in a community sample are re-interviewed have been reported. The methods used for Phase II are either diagnosis by a doctor in accordance with published criteria (Folstein et al 1985, Li et al 1989, Shibayama et al 1986), or the use of the Camdex as a diagnostic instrument (Brayne and Calloway 1990, O'Connor et al 1990).

These studies were:-

1) The NIMH Diagnostic Interview Scale (DIS) in which the Mini Mental State Examination is incorporated as the organic screen. All subjects identified as having probable dementia and 17% of those without a diagnosis were then examined by a psychiatrist who made standardised clinical diagnoses according to the criteria of the Diagnostic and Statistical Manual, Third edition (DSM III). In a third phase all subjects diagnosed by a psychiatrist as having a definite or possible dementia syndrome were recruited for a clinical and laboratory workup, and medical records were reviewed (Folstein et al. 1985).

2) The Camdex was used in a combined two phase study in rural Cambridgeshire (Brayne & Calloway, 1989).

3) A phase I screening used the MMSE. Phase II interviewed all those who scored 23 or below on the MMSE, and one in three who scored 24 or 25. The Camdex was then used as a phase II instrument (O'Connor et al. 1989a). The two Camdex phase II results are not directly comparable as Brayne & Calloway included minimal dementia, which was excluded by O'Connor et al. and Brayne & Calloway unlike O'Connor et al performed laboratory tests.

4) In Beijing, initial screening of subjects was performed, using the Mini-Mental State (cut off ≤17). All suspected cases of dementia and 5.5% of all others were then seen for a full clinical examination. Subjects were diagnosed and classified according to DSM-III criteria (Li et al 1989).

5) In Nagoya, Japan, trained interviewers obtained details of health states, social and domestic data. People suspected of dementia by a psychiatrist on the basis of this interview were re-interviewed, and had a neurological examination. Diagnostic criteria and definitions were in accord with DSM-III with reference to ICD-9 and Hachinski's Ischaemic Score (Shibayama et al 1986).

## 7.2. RESPONSE RATES IN PHASE II STUDIES.

As might be expected the response rates in a phase II studies may also be less than 100%, resulting in a further loss of information. Folstein et al (1985) reported a 78% completion rate for phase I of his Eastern Baltimore service. 75% of those subjects who had a positive screening test completed phase II, 82% of whom agreed to the phase III procedure. However, a diagnosis could be made on the remaining 18%. O'Connor et al (1989) report a response rate in the first part of the study of 90%, with 82% of these agreeing to phase II of the study. In Beijing 82% took part in the first interview. All 42 patients who scored as cases were re-interviewed. Similarly Brayne and Calloway did not lose any subjects as their study combined phase I and II interviews. No information is given on response to phase I in Japan, 80% of the first phase cases were re-interviewed.

## 7.3. THE PREVALENCE OF THE SUBCLASSIFICATIONS OF DEMENTIA IN THE POPULATION (PHASE II STUDIES).

Marsden and Harrison (1972) in their study of the differential diagnosis of 106 patients under 65 referred to a neurological hospital with presumptive dementia found that 45% had presumed Alzheimer's Disease, 7.5% had arteriosclerotic dementia, 7.1% had a space occupying

lesion, 5.7% had an alcohol related cause. No other cause of dementia contributed more than 5% of cases. A total of 15% of their patients had a condition potentially amenable to treatment and 15% were judged not to be demented. This interesting finding led to a proliferation of studies, so that Clarfield (1988) found thirty-two studies, with a total of 2889 subjects in all, which investigated the prevalence of the different causes of dementia in clinical series of patients. In this overview, Alzheimer's Disease made up 56.8% of all dementias, multi-infarct dementia 13.3%, depression 4.5%, alcohol 4.2% and medications 1.5%. No single other cause contributed more than 1.6% of the cases. Potentially reversible causes made up 13% of all cases. The commonest reversible causes were medication (28%), depression (26%) and metabolic diseases (15.5%). Eleven studies provided follow-up data and in those 8% of the dementias had resolved partially and 3% fully. However there are certain biases in the studies that contribute to the review.

These are:-

1) A low mean age in the studies. Alzheimer's Disease manifests itself particularly in the over 75s, but the mean age of the patients in these studies was 72 years. Those studies which followed up patients with potentially reversible dementias had a mean age of 62. This age effect would imply that there would be less Alzheimer's Disease and more other causes of dementia

than in an older population.

2) Only four studies originated from the community. Selection for referral may mean that those with an atypical dementia are more likely to be seen by hospital doctors.

Clarfield compares this situation to that which occurred in hypertension. "Physicians thought they were faced with a high prevalence of a devastating condition, a significant proportion of which might be potentially reversible. It followed that there might be many potentially curable conditions obscured by the mass of essential hypertensive patients. Based on early figures from tertiary referral centres of 6% for 'surgically curable hypertension' a vigorous, costly and sometimes dangerous investigation was recommended and done on many patients, most of whom did not turn out to have a reversible disease. With time it became apparent that the true prevalence of reversible hypertension in the community was probably less than 1%". More accurate figures on the prevalence of the different dementias may be found by analyzing the community studies separately. Since Clarfield's review, 4 further studies have been published on the prevalence of the different dementias. The eight community studies are shown in Table 6. Only five of those incorporate a phase I screen of a community (see 7.1).

TABLE 6 PROPORTION OF THE DIFFERENT DEMENTIAS IN COMMUNITY STUDIES

| AUTHOR & PLACE | NO. SCREENED | AGE | NO. OF CASES OF DEMENTIA SUBCLASSIFIED | %ALZHEIMER'S | %MULTI INFARCT DEMENTIA | %MIXED | %0ther |
|---|---|---|---|---|---|---|---|
| Kokmen et al 1980 Minnesota USA | no screening procedure | 29+ | 102 | 33 | 18 | 12 | 27 |
| Folstein et al 1985 Baltimore USA | 564 | 65+ | 36 | 33 | 46 | 21 | - |
| Sayetta et al 1985 Baltimore USA | 519 | 60+ | 41 | 66 | 32 | - | - |
| Pfeffer et al 1987 California USA | 817 | 65- | 87<br>99 | not specified | ns 3% (24) | | - |
| Li et al 1989 China | 1090 | 60+ | 14 | 29 | 57 | 7% | 7 |
| O'Connor et al 1989 Cambridge | 2311 | 75+ | 81 | 75 | 21 | 2.5% | 2 |
| Brayne & Calloway 1989 Rural Cambridgeshire | 365 | 70-74 | 8 | 37.5 | 50 | 0 | 12 |
| | | 75-79 | 21 | 57 | 24 | 5% | 14 |
| Shibayama et al 1986 Japan | 3106 | 65+ | 382 | 42 | 48 | - | 10 |

The first community study of the patterns of the dementias was performed by a neurologist, retrospectively reviewing all medical records of Rochester residents (USA) (Kokmen et al 1980). Subjects had to have documented evidence of dementia presenting to medical attention. As many subjects with dementia are unknown to physicians this method does not ensure accurate numbers (Williamson et al 1964, O'Connor et al 1988). Folstein et al (1985) report differential diagnosis of cognitive impairment in the population of Eastern Baltimore using the MMSE. This study suffered from the limitations of the Mini Mental State as a screening interview, and from a fall out rate, at each of the three phases, of 20-25% of subjects. This meant that at the end a diagnosis was only made on 36 subjects. These diagnoses, made on DSM III criteria, were divided only into either Alzheimer's disease, multi-infarct dementia, mixed, or unspecified dementia. However Folstein comments that no reversible dementias were found.

Sayetta et al's (1985) study was a longitudinal study of male volunteers. This unrepresentative sample makes it difficult to interpret the results. Similarly Pfeffer et al (1987) study was of a middle class retirement community. This unusual community, together with a rate of cognitive screening of less than 60%, makes the representativeness of the results questionable. This impression is reinforced by the very high prevalence of dementia found (16.4%) for those aged over 65. This

figure is much higher than other American studies.

In China, Li et al (1989) only found 14 cases of dementia to classify. They do not specify the criteria for the eventual diagnoses. The other limitation of this study is the lack of validation of the screening instruments in the Chinese population.

The British studies (O'Connor et al 1989, Brayne & Calloway 1989) were of larger populations. O'Connor et al screened in Cambridge, using GP lists as a population register. No check of the accuracy of GP lists on which the sample was based was carried out. Surprisingly, the screening and diagnostic phase missed 13 patients known to the services and well documented as demented. These were added to the numbers thus perhaps skewing the results, and calling into question the sensitivity of the instruments used. No laboratory investigations were performed, thus cases of secondary dementia may have been missed. Nevertheless, this study was the first published attempt to carry out a full diagnostic study of dementia in the elderly by screening and follow up.

Brayne & Calloway's study is limited by the exclusion of men and the relatively small numbers. However, unlike O'Connor et al, they comment on the validity of their original sample, although they do not test their hypothesis, that people will not be lost to GP lists in a

country area such as theirs. They classify subjects only into four categories; SDAT, MID, SDAT plus MID and others.

The final study shown in Table 6 (Shibayama et al 1986) suffers from using a non-validated screening instrument.

Overall of the eight studies which have been carried out, three do not use a representative sample (Kokmen et al 1980, Sayetta et al 1985, Pfeffer et al 1987); none use a validated population register. One has a very low response rate (Pfeffer et al, 1987). One does not use a validated screening instrument (Shibayama et al, 1986), and one only examines women (Brayne & Calloway 1989) and one only men (Pfeffer et al) and one uses very small numbers (Li et al 1989). The final study (O'Connor et al), does not use a validated population list or make full investigations before diagnosis. Only two studies make full diagnoses of the dementias (Li et al 1989 and O'Connor et al 1989).

In summary, these studies find the commonest diagnostic subclassification is Alzheimer's Disease (5 studies) and multi-infarct dementia (3 studies). Those two diagnoses together accounted for between 51% and 96% of the dementias. As expected older populations had a higher proportion of subjects with Alzheimer's disease, and Alzheimer's Disease is the commonest diagnosis in the over 65s living in the community. Although the wide variations

in figure suggest that there may be a true difference in the prevalence of Alzheimer's Disease in different populations, it is impossible to be certain of this because of varying and flawed methodologies.

## 7.4 CONCLUSION

A satisfactory phase II diagnostic study requires a satisfactory phase I study, as if the sample obtained from screening is unrepresentative then the phase II findings may be misleading. In such a study all of those who might be suffering from dementia from the phase I are further investigated. Full investigation means that a mental state examination, physical examination, psychometric tests, an informant history and laboratory investigations would all be obtained. The most satisfactory diagnostic studies are those of Folstein et al (1985), O'Connor et al (1989), Brayne and Calloway (1989) and Shibayama et al (1986). These four studies all diagnose subjects found by screening a population in their own homes, by diagnostic criteria. However, as discussed above the studies are flawed, eg. high rates of subjects not interviewed (Folstein et al 1985); lack of validation of population lists (O'Connor et al 1989, Brayne and Calloway 1989); screening of women only (Brayne and Calloway 1989); and use of a non-validated screening instrument (Shibayama et al 1986). Many advances in knowledge regarding risk

factors, prognosis, prevention and therapy for the dementias, require the most accurate possible epidemiological data. Therefore the Gospel Oak study described in this thesis has been carried out and is reported in the following chapters.

# CHAPTER 8

# AIMS OF INVESTIGATIONS

The study reported in the thesis aimed to discover and describe the nature of dementia in a community population.

The specific aims are stated below. Those are:

Aim 1 To set up an accurate register of all pensioners (women of over 60, and men over 65) living in an inner city electoral ward in London.

Aim 2 To screen those people listed on the register using a valid and reliable semi-structured interview to detect dementia.

Aim 3 To determine prevalence rates of dementia within the population.

Aim 4 To determine prevalence rates of dementia within subgroups of the population. These subgroups are:

a. men and women

b. those residents known to general practitioners and other services, and those residents not known to general practitioners and other services.

c. the age groups 65-79
70-74
75-79
80 and above.

Aim 5 To determine the rate of the diagnosis of depression at screening in the group who are screened as suffering from dementia

and compare this rate with the whole study.

Aim 6 In a Phase II study to determine prevalence rates of Alzheimer's disease and other causes of dementia in this community.

Aim 7 To discover dementias which are reversible and how they may best be detected in clinical practice.

Aim 8 Using psychiatrists' diagnosis as a 'gold standard', to analyze the usefulness of the instruments used in the study.

Aim 9 To provide further information on the outcome of those screened or diagnosed by the different methods used for predicting dementia.

# CHAPTER 9

# METHODS OF INVESTIGATION

## 9.1. PHASE I - ESTABLISHING THE REGISTER

THE STUDY SITE.

The geographic area which was the basis for the sample in the study, was the Gospel Oak electoral ward. Gospel Oak is located within Hampstead Health Authority, an authority adjacent to central London. The ward has a population of 6136, in some 3000 households and has high rates of most indices of deprivation. For example in Gospel Oak there is twice as much overcrowding (defined as living at more than one person per room), 50% more unemployment and 50% greater infant mortality than nationally. Eleven per cent of the households are headed by a person in socioeconomic group II (in unskilled manual occupation) as opposed to 8.7% in the whole of England and Wales. There is also a higher proportion of one parent families, still births, perinatal, neonatal and infant mortality (Hampstead Health Authority, 1985).

### b. THE SAMPLE - PHASE I

The sample consisted of all women aged over 60 and men over 65 who were residents of the Gospel Oak ward. An original list was assembled of names provided by general practitioners,in and around the study area, community

psychiatric nurses, district nurses and social workers. Addresses were checked against the electoral roll to increase the accuracy of the list. A small validation exercise then took place; all households in one part of the ward were visited, and names of pensioners in each house were ascertained. By this means this first list was discovered to be too inaccurate to use as a sampling frame.

It was decided to compile a second list by visiting each household ('door knocking') in the whole ward. The police, general practitioners, the hospital and the community services were contacted before the door knocking exercise began. Then the ward was 'door knocked'. All houses were visited, and revisited, if no reply was received at first. Nevertheless some houses were empty at each visit. This resulted in a second list, which included all residents of appropriate age encountered by personal contact in their houses. There were also some provisional entries based either upon information obtained from neighbours eg. 'two pensioners live at 94', or names remaining from the original list, whose presence or absence was not established at 'door knocking'. This second list, although still containing some provisional entries, became the frame from which interviews were arranged. It included residents of the one local authority residential home which was situated in the ward.

## 9.2 PROCEDURE FOR INTERVIEW

At the time of 'door knocking' the Gospel Oak resident was asked to provide the name of his or her general practitioner. Although some residents were not available to give this information, they were often found on the lists originally derived from general practitioners. This meant that the names of most residents' general practitioner could be ascertained.

All general practitioners with more than three patients included in the sampling frame, were visited personally. The general practitioners were given a list of their elderly patient in the sampling frame and the study was explained. General practitioners agreed to check that their patients' addresses were still current, and that no-one had died since inclusion on the list, in order to avoid inadvertently sending letters to bereaved relatives. They also provided a supportive letter to be sent out with the letter from the research team requesting interview. If a general practitioner had less than three patients in our sampling frame, he or she was telephoned and permission was asked to contact their patients. They too provided letters. We were unable to trace some general practitioners who had been named, and thus a few residents were contacted without the general practitioner's permission. 96% of residents were

thus sent a General Practitioner letter and an explanatory letter from the hospital, together with a form to indicate a convenient time, and a stamped addressed envelope. If no reply was received, another letter was dispatched. If there was no response at this stage an interviewer visited on up to three occasions, to try to locate the person, or to firmly establish from neighbours whether he or she was living at the address.

## 9.3 THE INTERVIEW

### 9.3a THE SHORT CARE

All subjects were interviewed on the Short Comprehensive Assessment and Referral Evaluation (Gurland et al. 1984). This is a semi-structured interview, developed from the Core CARE (Golden et al. 1984). Its purpose in this study was to detect those subjects likely to be suffering from dementia, depression or to be impaired in daily activity. Six indicator scales make up this instrument assessing organic brain syndrome, depression, subjective memory impairment, sleep disorder, somatic symptoms and activity limitation. The indicator scales are best regarded as screening measures identifying problems in these areas for further assessment. Two scales, those for depression and dementia, have been

further refined to become depression and dementia diagnostic scales, which detect probable cases of pervasive dementia or pervasive depression. Pervasive dementia and pervasive depression are operational diagnoses which refer to syndromes of cognitive impairment and depressed mood, severe enough for further clinical intervention. These categories do not refer to specific conditions, disorders or subtypes but are meant to be useful in health services research and in health screening, because they identify cases where there is a probable need for clinical investigation or intervention. They are discussed in more detail below.

## THE DEMENTIA AND DEPRESSION SCALES

The inter-rater reliability of the depression and dementia scales are 0.94, 0.76 which are estimates of the average correlation between rater pairs (Gurland et al. 1984). They were gathered from data on a sample of 283 elderly community residents. The internal consistency coefficients for the depression and dementia scales are 0.75, 0.64. They are reliable whether used by a psychiatrist or non-psychiatrist. A correct prediction for an elderly subject can be made for 84% of the cases of pervasive depression and dementia and 91% of the non-cases. The dementia diagnostic scale was originally validated by a one year follow-up study of

subjects so identified, which showed outcomes consistent with that expected of clinical dementia in all cases. Both the depression diagnostic scale and the dementia diagnostic scales were validated against clinical judgement during a psychiatric investigation, which was part of a United States national study of hypertension in the elderly (Gurland et al. 1984).

The task of separating depression and dementia is attempted by using the depression and dementia diagnostic scales together. Allowance has to be made for the presence of cognitive impairment in those with severe depression. Lower levels of cognitive impairment together with higher levels of depression are classed as depression and conversely higher levels of cognitive impairment with lower levels of depression are classed as dementia.

**ACTIVITY LIMITATION SCALE**

The activity limitation scale is the third one of importance for this study. It too was developed from the Core CARE. It is scored by allocating one point to the respondent's report of limitation in activities of daily living such as going out, preparing meals, mobility and bathing. Activity limitation is considered present when a cut point $\geq 7$ was

reached.

### 9.3b ADDITIONAL INTERVIEW ITEMS

In addition to the Short CARE, questions were asked concerning the following:

1) demography - name, address, date of birth, sex, marital status, telephone number, general practitioner, previous or current occupation and whether the resident lived alone.

2) contacts in the last month with the general practitioner, the local hospital, the various arms of the social services and home nursing services. Details of visits to the home, attendances at local day centres or contact with local voluntary or church agencies were recorded.

3) details of current medication.

4) vision, hearing and mobility.

5) regular exercise and climbing stairs.

As this thesis is concerned with specific questions regarding dementia (see Chapter 8), only those relevant results will be reported here.

## 9.4 INTERVIEWERS

The 14 interviewers were trained in the Short CARE by studying and co-rating video-taped interviews. They were later supervised and co-rated during a live interview. Two psychiatrists conducted 61% of the interviews between them. The remaining 39% of interviews were conducted by other psychiatrists (35%) or psychiatric nurses (4%). All these interviewers were experienced in work with the elderly mentally ill. The field interviews took place during 1987.

Phase II

## 9.5 THE SAMPLE - PHASE II

All subjects living in their own home, who were cases on either the organic brain syndrome scale or the dementia diagnostic scale were reinterviewed during 1987 and 1988. Those who in screening were detected as suffering from depression, in addition to possible dementia, were still included in the study.

## 9.6 PROCEDURE FOR INTERVIEW - PHASE II

The subjects' General Practitioners were again asked to

agree to these assessments. They sent a letter to their patients to this effect, enclosed with the letter from the research team which requested permission to visit a second time. The General Practitioners also acted as informants on past medical history. Assessment of residents always began with a mental state. The order of the other investigations depended on the subject's preference and the availability of the informant. All the assessments reported here, apart from the CT scan, were carried out in the patients' home some months after first screening. Full assessment took between two and four visits.

## 9.7 PSYCHIATRIC ASSESSMENT FOR DIAGNOSIS

### a. CLINICAL EXAMINATION

The clinical examination consisted of 1) A mental state examination using the computerised diagnostic system GMS(A)/AGECAT (Geriatric Mental State (A), Automated Geriatric Examination for Computer Assisted Taxonomy) (Copeland et al. 1976, Copeland et al. 1986). 2) A physical examination and biochemical tests. A sample of blood was taken for levels of urea and electrolytes, for liver function tests, including gamma glutamyl transferase, for blood sugar, for full blood count, ESR, B12, folate, thyroid

function tests and syphilis serology. 3) Finally, subjects were asked to attend hospital for a CT Neuroscan.

### b. HISTORY

The history that was taken in this study was from informants whom the patient was asked to nominate. It consisted of the History and Aetiology Schedule (HAS) (Copeland et al. 1987), which was developed in Liverpool to be used in conjunction with the GMS. Second, a detailed family history was obtained, to enable family lifetime risk of dementia to be calculated. (Chase et al. 1983). All first degree relatives' age at death and the causes of death were recorded, in addition to any cases of dementia. Third, the informant was also asked about the subject's occupational contact with aluminium and use of vibrating tools, whether the subject had a family history of Down's syndrome, thyroid diseases or lymphomas, and whether the subject had had a previous head injury. These exposures are all thought to be possible risk factors for Alzheimer's disease (Henderson 1987, Edwardson 1988, Rocca et al. 1986). Finally, information concerning current medication and a medical history was obtained either from hospital notes or from the General Practitioner. Only the results from these enquiries which are relevant to the aims of this thesis will be reported.

## c. PSYCHIATRISTS' DIAGNOSTIC CRITERIA

Clinical diagnosis of Alzheimer's disease were made according to the NINCDS/ADRDA criteria (McKhann et al. 1984). This is a diagnosis based on a decrease in the patients' level of functioning. It defines "probable Alzheimer's Disease" as a dementing disorder with a typical insidious onset which progressively worsens over time. According to the NINCDS/ADRDA criteria, Alzheimer's Disease should only be diagnosed when there is no other systemic or brain disease that can account for the progressive memory loss and other cognitive deficits. (c.f.Chapter 3 section 4.) Definite Alzheimer's disease requires a histopathological confirmation.

The Hachinski score was calculated using informant history, medical history and physical examination. (Hachinski et al 1974.) In order for a diagnosis of multi-infarct dementia to be made in this study, one of the following criteria had to be fulfilled: 1) a Hachinski score of $\geq 4$, 2) evidence of infarcts on CT Scan or 3) a history of stepwise deterioration. Mixed dementia was diagnosed when, in the presence of either of the former two criteria, the subject had a history consistent with Alzheimer's disease.

In the present study, to ensure all cases of Alzheimer's

disease were identified, patients with other systemic disorders, such as diabetes or treated hypothyroidism, were not excluded from a diagnosis of probable Alzheimer's disease.

The data were collected by one psychiatrist (GL) and the clinical diagnosis checked with another (AM) so that a consensus was obtained.

All available information was used i.e history, GMS(A), physical examination, blood tests, CT scans and psychometric testing. However, the clinicians' diagnosis was made without knowledge of the results of the AGECAT classification.

## 9.8 PSYCHOLOGICAL ASSESSMENTS

The psychometric assessment included the following standard tests which will be reported here: 1) Mini Mental State Examination (MMSE), 2) National Adult Reading Test (NART), 3) Kendrick Object Learning Test (KOLT), and the 4) Word Generation Test or Fluency Test.

Prior to psychometric testing it was explained to carers and relatives that the subject required to be able to

concentrate. In most cases the tester (KS) was therefore left alone with the subject.

The MMSE (Folstein et al. 1975) was included because of its frequent usage in dementia studies. A community version was used (Folstein et al. 1985) in order to removed institutional references from the 'Orientation' questions. At least two versions of the attention and calculation section of the MMSE have previously been used (Folstein et al. 1975, Brayne and Calloway 1989), with either the 'serial sevens' item on its own, or this item with the option to spell 'World' backwards. To find out if these two test versions were equivalent, the results of both versions were analyzed. The repetition phrase, 'no ifs ands or buts', was changed to, 'no ifs or buts'. This change was made because the original item was not a recognised saying amongst our population. (Results will be given on the number of subjects who might have crossed the cut-off if the more difficult 'no ifs ands or buts' version had been used). Scores out of 30 were generated in the usual way.

The NART (Nelson 1982), a brief measure of current reading attainment, was selected because it has been shown to be a good guide to premorbid functioning in populations with dementia. It consists of irregularly spelled words which the subject reads aloud. These are scored for correctness

of pronunciation, up to a maximum 50 points.

The KOLT (Kendrick 1985) was chosen for inclusion in the study because it is a wide-ranging test of memory designed for use with the elderly. Set A stimuli were used throughout. The test was administered according to standard procedures yielding a maximum possible score of 70 points.

The Word Generation of Fluency test was based on a version of verbal fluency which has a long history in assessment of dementia and other organic conditions (Miller 1984). The procedure we adopted here was taken from data collected on elderly British samples shortly before this study started (Brotchie and Hart, written communication). In this study subjects were required to generate words from two categories - colours and animals - and a third category of words beginning with the letter M. One minute was allowed for each condition and the total number of words generated was used as the score.

## 9.9 RESIDENTS WHO COULD NOT BE ASSESSED

Some residents could not be assessed either because they had died in the period between interviews, or because they refused requests for reinterview. If a resident had died,

his or her notes were requested from the family practitioner committee. A death certificate was obtained from the coroner's office and any hospital notes were examined. None of those residents had had a neuropathological examination. If a resident refused reinterview the general practitioner and hospital notes were used to gather information. In some cases relatives were contacted, and they provided some information, in the course of ascertaining that the resident was not willing to be reinterviewed.

## 9.10 PHASE III EIGHTEEN MONTH FOLLOW UP

All residents were contacted again about eighteen months after first interview. They were asked to agree to reassessment, which consisted of Geriatric Mental State (A), ShortCARE, all the psychometric tests completed at first interview except the NART, and details of any illnesses since last seen. The same procedures were followed as in Phase II for those who were not available for interview. Psychiatric diagnosis was made using the information available. The categories improved, stable and deteriorated are clinical judgements made using all the raw data available.

## 9.11 STATISTICAL ANALYSIS

### a. PHASE I

The data were analyzed using the Statistical Package for the Social Sciences X (SPSSX) and Statistical Analysis System (SAS) by univariate and multivariate analysis. Univariate comparison used a chi-squared statistic and the relationships between the variables were further explored by logistic regression using a backward elimination method for variable selection. The data from the women pensioners aged 60-64 years were excluded from analysis of prevalence rates, so as to provide comparable data with other epidemiological studies.

The cut-off point for the dementia diagnostic scale was $\geq 7$ and for the organic brain syndrome scale $\geq 4$. For depression, the depression diagnostic scale became the basis of classification with a cut point of $\geq 6$. Activity limitation was considered present when a cut point of $\geq 7$ was reached.

A formal inter-rater reliability study was not carried out. However, to gain an estimate of interviewer variation, the prevalence rates of the three main conditions, depression, dementia and activity limitation were compared between the

two major interviewers who covered 61% of the interviews between them. The prevalence rates of dementia, depression and activity limitation for the remaining 39% of interviews, taken as a group, were then compared with each of the two major interviewers. Interviews were not allocated according to any set pattern and, therefore, there should be no reason for any one interviewer to discover higher or lower rates of the key conditions.

**b. PHASE II AND III**

A. All data, except the GMS, were analyzed using the statistical package for the social services (SPSSx) on the University of London computing Centre Amdahl mainframe. Associations between categorical variables were assessed using the Chi-squared test with Yates correction where appropriate. Associations between the continuous variables were assessed using the Spearman's Rank Correlation.

B. The GMS data were scored using the GMS/AGECAT package (Copeland et al. 1986) in Liverpool.

C. To determine interrater reliability on the GMS, eighteen subjects were assessed by the two raters (GL and KS). One rater observed while the other rater interviewed the

subject. The role of each rater was randomly allocated. The completed interview from each rater was collapsed into the syndrome clusters using the AGECAT computer programme. The reliability of the two raters on these clusters was obtained using the weighted kappa statistic (Cohen 1968).

## 9.12 WEAKNESSES AND STRENGTHS OF STUDY DESIGN

Weaknesses of the study are that 1) A three phase study inevitably means attrition of numbers for interview at each stage. This means that by the final stage a great deal of information will be lost. 2) In an elderly sample many respondents die. It would therefore be better to complete an immediate detailed assessment of screen positives, rather than await statistical analysis of the whole sample interviewed. This would allow Phase II interviews to be undertaken immediately rather than some months after Phase I.

3) A control group of age and sex matched subjects who had not scored as cases on either the dementia diagnostic scale or been screened as positive on the organic brain syndrome scale, could have been further investigated and followed up in the same way as those described in the study. This would have increased the information available, concerning the specificity and sensitivity of the screening scales used.

This was not done.

4) The design of the study means that the numbers studied in each phase are not be known in advance. This means statistical analysis may not prove possible if numbers are too small.

The practicalities of a dementia study in the community, such as the present study, means that without more financial and human resources, than was available to the author, so that very much larger populations and control groups could be studied, the above weaknesses are inevitable.

In contrast the strengths of this study design are:- 1) An accurate total population register was set up by 'door knocking' to use as a sample frame for the whole study. 2) Personal visits to those who did not reply to letters requesting interview, ensured a higher response rate and made the sample interviewed more likely to be representative. 3) The use of standardised, validated and reliable instruments in all phases of the study, meant that the results are interpretable and comparable with other studies.

# CHAPTER 10

# RESULTS OF PHASE I & II

## 10.1 THE SAMPLE - PHASE I

The first list from those in service contact with this population consisted of 1,231 names. The second list obtained after door knocking, differed from the first by 56%, 385 names were removed because these people were known to be dead or had moved, and 305 additional elderly people were located. The total number in the second frame was 1,151, but this still included some provisional entries. The accurate frame was eventually established after further contacts with residents during the approach for interviews. Another 32 names were added, either from hearing of new arrivals in the neighbourhood, or discovery of someone missed by door knocking. Against this, 109 subjects were now discovered to have died, 115 had moved, 21 were too young and 6 had been included twice. The final accurate sample for interview consisted of 932 people, (women over 60, men over 65), who represented 15.2% of the ward population.

## 10.2 RESPONSE RATE

813 (87.2% of the sample) people were interviewed. 90 (9.7%) refused to be interviewed, 17 (1.8%) although known to be resident, were not found after three visits to their home, 8 (0.85%) spoke no English and had no translator and 4

(0.42%) were impossible to interview because they were too demented. These last 4 all lived in Part III accommodation.

## 10.3 THE SAMPLE INTERVIEWED

779 interviews were conducted in the residents' own homes, 34 in the local Part III home. The 813 interviews were made up of three sub sections a) 681 living in their own homes who had replied to one of the two letters b) 98 also living at home who had not replied but agreed to an interview after a personal visit c) 34 residents of the Part III home. These three groups differed in the proportion scoring above cut points on the organic brain syndrome and depression diagnostic scales. 6.3% of responders of group (a) scored above the cut point on the organic brain syndrome scales (as opposed to the dementia diagnostic scale), whereas the rate was 13.3% among group (b), who had not responded to letters and 58.8% among group (c), the Part III home residents. This was in contrast to the depression scale where 19.7% who answered the letters scored above the cut point on the depression diagnostic compared to 9.2% of those requiring home visits and 35.2% in Part III.

## 10.4 RELIABILITY DATA

There was no statistically significant difference in prevalence rate of diagnoses of depression, dementia, or disability among the subjects interviewed by the two major interviewers or those interviewed by all other interviewers.

## 10.5 DEMOGRAPHIC DATA

a. AGE The age range of the population studied was between 60 and 98 years old with a mean age of 73.8. The 60-64 year old group of women pensioners consisted of 9.1% (74) of the sample interviewed. Their data have been excluded from other figures presented in this paper. The remaining sample consisted of 739 people, 34 of whom lived in Part III homes.

The age of the remainder 27% were between 65 and 69, 50% between 70 and 79 and 23% more than 80.

b. SEX 63% of the population was female and 37% male.

c. MARITAL STATUS 41% were married, 39% widowed, 5% divorced, 13% single and 2% separated.

d. SOCIAL CLASS Conventional classifications of social class were not informative when applied to these study subjects, as most were retired. Forty-two per cent of women in the survey had worked mainly in paid domestic work, 23% had always been housewives, 19% had done clerical work, 9% had served in shops and only 7% had had professional or skilled work. 8% of men had previously been employed in professional or skilled work, 52% in semi-skilled and 40% in unskilled occupations.

e. LIVING ARRANGEMENTS 80% of the survey population living in their own homes lived in local authority housing and 20% were owner occupiers or rented from private landlords. 45% of pensioners in Gospel Oak lived alone.

f. RELIGION Most elderly in Gospel Oak were of a Christian denomination - either Church of England (45%), Roman Catholic (17%), Greek Orthodox (1%) or other Christian denomination (8%). 23% did not state a religion. Of the other 5% less than 1% belonged to any other single religious group.

## 10.6 RESULTS OF SCREENING FOR DEMENTIA

### a. PREVALENCE RATES

Of the 705 respondents living in their own homes, 7.9% (56) were screened positively on the organic brain syndrome scale. 5.0% (35) scored above the cut point on the dementia diagnostic scale and were classed, therefore, as probably suffering from pervasive dementia.

### b. DEPRESSION & DEMENTIA

12/35 (34%) of these subjects scoring as cases on the D.D.S. also scored above the cut point on the depression diagnostic scale. This compares to 102/670 (15%) who score as depressed but are not so classified (Chi-squared) 8.92 $p<.003$ Using the formula to discriminate between diagnoses, 10 of these 12 were then classed as suffering primarily from dementia. Removal of two subjects, reduced the prevalence rate to 4.7%. The prevalence rate, however, increased to 7% of the sample if the residents of the local authority home were included.

### c. AGE AND SEX EFFECTS ON PREVALENCE

The variations in prevalence rate amongst the age and sex groups of the study population is shown in Table 7.

TABLE 7

Prevalence rates amongst the age groups for males and females identified as cases by the dementia diagnostic scale.

| Females (n=447) | | | | Males (n=258) | | | |
|---|---|---|---|---|---|---|---|
| | | n | % dementia diagnostic scale | | | n | % dementia diagnostic scale |
| Age | 65-69 | 126 | 0.8% | Age | 65-69 | 66 | 0. % |
| | 70-74 | 75 | 4.1% | | 70-74 | 97 | 1.3% |
| | 75-79 | 121 | 5.0% | | 75-79 | 62 | 0. % |
| | 80+ | 55 | 12.7% | | 80+ | 103 | 12.7% |

The increase in prevalence rate in both sexes with age is clearly demonstrated. However there appears to be a marked difference between the sexes in the prevalence of dementia in the younger age bands. Standardisation of this population for the age distribution of the over 65's in England and Wales as a whole, allows an estimate of the prevalence rate to be 4.1%.

Table 8 demonstrates the distribution of the diagnosis of pervasive dementia throughout the age groups, i.e. all those subjects scoring above the cut point on the dementia diagnostic scale.

TABLE 8

The distribution of the diagnosis of pervasive dementia by age

| | Dementia cases | Non cases |
|---|---|---|
| Numbers | 35 | 670 |
| Age 65-69 | 3% | 29% |
| 70-79 | 31% | 51% |
| 80+ | 66% | 20% |

Univariate comparisons show this diagnosis of dementia was closely associated with age ($p < 0.001$) but not sex or marital status.

**d. THE DISTRIBUTION OF PERVASIVE DEMENTIA ACCORDING TO POPULATION LIST**

6/35 (17%) of those over 60 living in their own homes, were classified as cases on the dementia diagnostic scale but were not on the first list of those in contact with the services. This compares with 299/744 (40%) of those not

classified as cases who were not on the original list (chi squared 7.45 $p < 0.006$). Similarly, 9/56 (16%) of those classified as a case on the organic brain syndrome scale were not on the original list. But 296/723 (41%) of those not so classified were on the original list (chi squared 13.49 $p < 0.0002$).

10/60 (17%) of all those who crossed the cut points on either the OBS or the DDS were not registered on the electoral roll.

### e. PREVALENCE OF ORGANICITY ACCORDING TO RESPONSE TO LETTERS

6.3% of responders scored above the cut-point on the organic brain syndrome scales, whereas the rate was 13.3% among the group who had not replied to letters.

## 10.7 THE POPULATION DETECTED BY OBS AND DDS SCALES - PHASE II

35 subjects had been identified as cases on the DDS scale and 56 on the OBS scale. 31 were cases on both scales. 48 (80%) of the 60 people initially identified by screening agreed to further assessment. As for the remaining 12 subjects, 7 (12%) had died by the time of follow-up, 4 (7%)

refused interview, and 1 (1%) was lost to follow up.
37 (77%) of those interviewed were female and 11 (23%) male, with a mean age of 80 (range 65-93). 23% were married, 17% single, 58% widowed and 2% separated. 59% lived alone. 12% had never worked outside the home, 55% had unskilled occupations, 28% had worked in semi-skilled or skilled occupations and 5% were professionals.

44 (92%) lived in council houses. 34 (71%) left school at 14. Only 2 (4%) people in the sample had 10 or more years of education.

## 10.8 PSYCHIATRIC DIAGNOSIS OF THE DEMENTIAS

Of the 48 people interviewed, twenty-two subjects (46%) were diagnosed as having probable Alzheimer's dementia according to the NINCDS/ADRDA criteria. Five (10%) were diagnosed as a mixed dementia, one (2%) as multi-infarct dementia, five (10%) as secondary dementia. Five (10%) were not suffering from dementia. In ten subjects (21%) dementia was not classified because of insufficient information. Three of these latter subjects provided no-one as an informant apart from their general practitioner. Seven others had informants who were unable to give any history as the development of memory loss. Table 9 shows the diagnoses of

the groups detected by the DDS or the OBS scales of Short-CARE.

Table 9: Psychiatrists Diagnoses of Subjects Detected by the OBS and DDS Scales of the short-CARE

| | OBS Scale n = 56 | | DDS Scale n = 35 | | Total overall n = 60 | |
|---|---|---|---|---|---|---|
| | no | (%) | no | (%) | no | (%) |
| Interviewed | 47 | (84) | 23 | (66) | 48 | (80) |
| No. of deaths | 4 | (7) | 7 | (20) | 7 | (12) |
| Refused or lost to follow up | 5 | (9) | 5 | (14) | 5 | (8) |
| | no | (%) | no | (%) | no | (%) |
| McKhann Probable | 21 | (45) | 12 | (52) | 22 | (46) |
| Multi-Infarct | 1 | (2) | 1 | (4) | 1 | (2) |
| Mixed Dementia | 5 | (11) | 4 | (17) | 5 | (10) |
| Secondary Dementia | 5 | (11) | 2 | (9) | 5 | (10) |
| Unclassified dementia | 10 | (21) | 4 | (17) | 10 | (21) |
| Not Demented | 5 | (11) | 0 | -- | 5 | (10) |
| Total | 47 | (10) | 23 | ( 99*) | 48 | (99*) |

* figures were rounded to the nearest whole number, the total is not 100%.

Of twelve people not interviewed, four were reported, by either their family or their General Practitioner, to be suffering from dementia. Of the remaining eight people, seven were dead and neither hospital notes nor death certificates mentioned dementia. General practitioner's notes were requested from the Family Practitioner Committee. Four were located and two of these had recorded the diagnosis of dementia. The final subject had no general practitioner or other informant.

## 10.9 PREVALENCE RATES OF THE DEMENTIAS

From the psychiatrists' diagnoses, the prevalence rate of Alzheimer's disease for the whole Gospel Oak population was calculated as 3.1% (22/705), of multi-infarct dementia .01% (1/705), of mixed dementia .7% (5/705) and of secondary dementia .7% (5/705). Therefore the overall prevalence rate for dementia of any type was 6.1% (43/705). If the four subjects reported by informants to be demented, but who were not assessed are included, then the total prevalence rate for dementia rises to 6.7% (47/705).

Table 10 shows the prevalence by age and diagnoses for each sex.

Table 10: Prevalence of different causes of dementia by age & sex

| | Alzheimer's Disease | | | Other dementias | | | Definite Dementia (unclassified) | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | case no | pop at risk | prev % | case no | pop at risk | prev % | case no | pop at risk | prev % | case no | pop at risk | prev % |
| males | | | | | | | | | | | | |
| 65 - 79 | 1 | 203 | 0.5 | 0 | 203 | - | 3 | 203 | 1.5 | 4 | 203 | 2.0 |
| 80+ | 4 | 55 | 7.3 | 1 | 55 | 1.8 | 0 | 55 | - | 5 | 55 | 9.0 |
| | 5 | 258 | 1.9 | 1 | 258 | .4 | 3 | 258 | 1.2 | 9 | 258 | 3.5 |
| females | | | | | | | | | | | | |
| 65 - 79 | 6 | 344 | 1.7 | 5 | 344 | 1.5 | 4 | 344 | 1.2 | 15 | 344 | 4.4 |
| 80+ | 11 | 103 | 10.7 | 5 | 103 | 4.9 | 3 | 103 | 2.9 | 19 | 103 | 18.4 |
| TOTAL | 17 | 447 | 3.3 | 10 | 447 | 2.2 | 7 | 447 | 1.6 | 34 | 447 | 7.6 |

## 10.10 REVERSIBLE DEMENTIA

No dementia was found to be reversible. The diagnoses of the five subjects with secondary dementia were: Parkinson's disease (2), Korsakoff's psychosis (1), previous subarachnoid haemorrhages (1), and an inoperable glioma (1).

## 10.11 DIAGNOSTIC CRITERIA

a. GMS/AGECAT Diagnosis

The GMS(A)/AGECAT diagnosis in this study did not include the HAS, as a computer diagnosis incorporating history was not then available. The GMS(A)/AGECAT diagnosed 28 out of 48 subjects as being organic cases, and 4 subjects as being subcases. An additional eight subjects had another principal diagnosis, but according to AGECAT, also had an organic syndrome. Eight subjects were rated as not suffering from an organic syndrome. Thus by the GMS diagnoses, the prevalence rate of organic caseness was 4% (28/705). If the 12 subjects, who did not reach organic caseness are included, then the prevalence rate of organicity was 5.7%.

GMS diagnoses and psychiatrists' diagnoses were highly significantly related ($p < 0.003$). Six of the patients, who

were diagnosed by the psychiatrists as suffering from dementia, were not given an organic rating by the GMS/AGECAT system, while three other subjects who were not given a clinical diagnosis of dementia were classified by the GMS as organic subcases (Table 11).

GMS/AGECAT was more likely to diagnose as 'organic' those subjects whom the psychiatrists diagnosed as having Alzheimer's diseases ($p < 0.04$).

TABLE 11: Discrepancies Between Clinicians' Diagnosis and GMS/AGECAT Results

| Psychiatrists' Diagnoses | Reasons for Psychiatrists Diagnoses | GMS/AGECAT |
|---|---|---|
| 1. Secondary Cognitive Deficit | 2 subarachnoid haemorrhages confirmed by CT scan & history MMSEI = 20 | Phobic Subcase |
| 2. Mixed Alzheimer's & Multi-Infarct Dementia | confirmed by CT scan MMSEI = 19, Kendrick = 16 | Psychotic Depression |
| 3. Dementia (unclassifiable due to no history) | MMSEI = 22 | Neurotic Depression |
| 4. Secondary Dementia (Parkinson's disease) | confirmed by history Kendrick = 20 | Depression Subcase |
| 5. Mixed Dementia | confirmed by history MMSEI = 18 Kendrick = 18 | Anxiety Neurosis Subcase |
| 6. Alzheimer's Disease | confirmed by history, MMSEI = 20 | Anxiety Neurosis Subcase |
| 7. No psychiatric diagnosis diagnosis | grieving, MMSEI = 26 Kendrick = 27 | Organic, Phobic & Depressed Subcase |
| 8. Personality Disorder history of depression | Previously long term hospital patient Wanted to be looked after by doctors MMSEI = 26 Kendrick = 27 | Organic Subcase Neurotic Depression |
| 9. Depression | Very depressed man. Unable to pay attention MMSEI = 15 | Organic Subcase |

### b. RELIABILITY

Inter-rater reliability for GMS/AGECAT showed a highly significant agreement between the two raters on the syndrome cluster variables. Specifically for the organic variable the observed agreement was 94.4% Kappa 0.84 ($p \leq 0.0001$). For depression the observed agreement was also 94.4% Kappa 0.88 ($p \leq 0.0001$).

## 10.12 PSYCHOMETRY

Of the 48 people who were interviewed using the GMS(A), 43 (90%) agreed to complete the MMSE. However, only 32 (67%) subjects completed all the psychometric tests reported here.

NART: Results on these tests were approximately normally distributed, with an absence of floor and ceiling effects except on the National Adult Reading Test. On this latter test three subjects scored zero and nine scored three or below. The mean reading attainment of this group - 11 words out of 50 - is considerably lower than that for the UK population as a whole (Nelson 1982).

MMSE: Including the alternative item - spell WORLD backwards -in the Attention and Calculation section of the MMSE

increased the mean group score by one and a half points (from 17.7-19.1). This shift meant that twice as many subjects were classified as 'non-demented' using a cut-off of 23, when the alternative was included (6 v. 3 subjects). A further two of those latter three subjects scored 24 on the MMSE I version, but arguably might have scored 23 if the phrase 'no ifs and or buts' had been used instead of 'no ifs or buts'.

KOLT: The conventional cut off point for the KOLT ($\leq$ 22) classified 23 (59%) of the sample as impaired.

WORD GENERATION: classified 27 (71%) below the cut off of $\leq$ 22.

The relationships of the various psychometric instruments were measured using Spearman's Rank Correlation. 34 people completed both the NART and the MMSE. The NART scores correlated with the scores from both versions of the MMSE (MMSEI .32, MMSE .42, both $p < .01$). There was a significant positive correlation between MMSE scores and KOLT (MMSEI .53, $p < .01$) and Word Fluency (MMSEI and fluency .4, fluency and KOLT .45, both $p < .01$).

The scores of patients diagnosed as probable Alzheimer's disease were compared to those from patients suffering from other types of dementia. Although differences between the

two groups failed to reach statistical significance, the Alzheimer's patients obtained lower scores on all the tests.

## 10.13 PHYSICAL EXAMINATIONS AND BIOCHEMICAL SCREENING ABNORMALITIES

Two subjects had abnormal biochemical results which might have indicated the cause of their dementia. One subject was hypothyroid, despite thyroid replacement, and another subject suffered from B12 and folate deficiency. However, neither subject showed improvement, when these abnormalities were corrected.

## 10.14 HACHINSKI SCORES

Enough information was gathered for a Hachinski score to be calculated for 37 subjects. 32 subjects scored < 4, and five scored five or six. No subject scored more than six.

## 10.15 COMPUTERISED TOMOGRAPHIC NEUROSCANS

Eighteen (38%) subjects had CT Scans. CT Scan appearances are grouped according to diagnosis as shown in Table 12.

TABLE 12: A Comparison of Clinician's Diagnoses & CT Scan Results

| Diagnosis | No | CT Scan Results |
|---|---|---|
| Alzheimer's Disease | 7 | 6 with cerebral atrophy only<br>1 cerebral atrophy & leuko-araiosis |
| Mixed Dementia | 2 | 2 cerebral atrophy & leuko-araiosis |
| Not Clinically Demented | 3 | 1 normal, 1 leuko-araiosis<br>1 cerebral atrophy & leuko-araiosis |
| Secondary Dementia | 3 | 1 glioma, 1 aneurysm, 1 cerebral atrophy & leuko-araiosis |
| Multi-Infarct Dementia | 1 | 1 cerebral atrophy & leuko-araiosis |
| Unclassified Dementia | 2 | 1 cerebral atrophy only<br>1 cerebral atrophy & leuko-araiosis |

# CHAPTER 11

# PHASE III EIGHTEEN MONTH FOLLOW UP

## 11.1 THE ASSESSED POPULATION

48 people were interviewed in Phase II, the diagnostic phase of this study (see Chapter 10). Eighteen months later 31 (82%) of those available for interview, agreed to another interview and seven (18%) refused re-interview. The remaining ten had died.

Of those interviewed, 26 (84%) were female and 5 (16%) male. The mean age was 80 (range 66-95). At phase II, 13 (42%) had been classified as having Alzheimer's disease, 4 (13%) as mixed dementia, 4 (13%) as not demented, 3 (10%) as secondary dementia and 1 (3%) multi-infarct dementia. 6 (19%) had a dementia which was not classified because of lack of information.

The Short CARE was completed in 30 of the 31 people who were interviewed. GMS (A) -AGECAT was completed in 22 and psychometric testing in 20.

## 11.2 THE POPULATION - DEATHS AND REFUSALS

By follow up ten elderly people from the original 48 had died. Of those ten, 6 (60%) were female and 4 (40%) male. There is a trend towards the males being more likely to die

than the females, but chi-squared analysis showed this not to be significant at the $p < .05$ level. The mean age at death was 84 (range 75-92).

At the diagnostic stage those ten individuals had been classified as follows - six (60%) probable Alzheimer's disease, two (20%) secondary dementia, one unclassified dementia and one was not demented. Death certificates recorded the major causes of death as bronchopneumonia (3), malignancy (3), cerebrovascular accident (1), septicaemia (1), peripheral vascular disease (1) and chronic obstructive airways disease (1).

The only reported cause of death that matched the diagnosis of dementia applied in Phase II, was that of a woman with a glioma. The patient who had died of a cerebrovascular accident had been diagnosed as suffering from Alzheimer's disease at Phase II.

Seven people refused reassessment. 5 (71%) were female, 2 (29%) male. The mean age of this group was 80 years (range 67-88). In phase II, 4 (57%) had been diagnosed as probable Alzheimer's disease, 2 (29%) as unclassified dementia and 1 (14%) had mixed dementia.

Conclusion: 10/48 (21%) of those who were assessed in Phase

II had died. This is twice the expected death rate in this age distribution (Warnes 1989). 7/48 (15%) refused reassessment. Neither group differed significantly from the total group seen in Phase II.

## 11.3 PSYCHIATRIST'S DIAGNOSES

At follow up, 31 subjects were seen of whom 30 completed as least the Short CARE. The outcome of those classified as demented in Phase II is shown in Table 13. Those 7 subjects whose outcome is unknown have been excluded.

The numbers of subjects in each category, are too small to permit statistical analysis as to the significance of any differences regarding the outcome of each subclassifications of dementia. There was no difference between the outcome of Alzheimer's Disease and non-Alzheimer's Disease. Overall, at follow up of dementia 10 (23%) seen in Phase II were dead. Of the remainder 4/30 remained not demented. 14/26 (54%) of those originally classified as demented had deteriorated, of whom 4 had been institutionalised. 6 (22%) were stable and 6 (22%) had improved. Of the 6 who had improved, 5 still showed evidence of cognitive deterioration but were no longer cases, one was no longer intellectually impaired.

TABLE 13

| | Deterior-ation | Stable | Improvement | Dead | Total |
|---|---|---|---|---|---|
| Probable Alzheimer's Disease | 9 (69%) | 3 (23%) | 1 ( 8%) | 6 | 13 |
| Mixed dementia | 1 (25%) | 2 (50%) | 1 (25%) | 2 | 4 |
| Unclassified dementia | 3 (60%) | - | 2 (40%) | 1 | 5 |
| Secondary dementia | 1 (33%) | - | 2 (66%) | - | 3 |
| Multi-infarct | - | 1 | - | - | 1 |
| Total | 14 (45%) | 6 (23%) | 6 (23%) | 9 | 35 (100%) |

Outcome at Phase III according to psychiatric diagnosis at Phase II

Table 14 shows the clinical outcome of those who were crossed the cut point on the various instruments used in Phase II.

Conclusions: There was a trend for a worse outcome in Alzheimer's Disease than in other dementias, but this is not statistically significant. The clinical improvement seen in people who had both crossed the cut point in the screening instruments, and been diagnosed as demented clinically was unexpected. It may be explained by a number of factors. Firstly, dementia may fluctuate according to physical, psychological or social factors, causing people to cross or re-cross the border of caseness. Secondly, the practice effect of completing many cognitive tests over a short period of time, will also enable some people to improve their performances. Finally, improvement may be due to misclassification of acute confusional state as dementia. This last explanation seems least likely as subjects ewre impaired on both screening and further investigations some months apart. In addition there were no investigation results suggesting a secondary dementia, on physical and biochemical screening. The clinical diagnosis of "not demented" predicted failure to deteriorate. The outcomes of non-cases or screen negatives in the DDS, and AGECAT are discussed in the rest of this chapter.

TABLE 14

Phase III: Clinical outcome at eighteen months of those who crossed the cut point in Phase II "cases" on OBS, DDS or Agecat organicity.

| | OBS | DDS | GMS(A) AGECAT organicity |
|---|---|---|---|
| Numbers positive on instrument at Phase II (1) | 47 | 23 | 40 |
| Numbers of (1) reinterviewed | 30 (64%) | 16 (70%) | 18 (45%) |
| Dead | 10 (21%) | 4 (17%) | 9 (22.5%) |
| Refused/Incomplete | 7 (15%) | 3 (13%) | 13 (32.5%) |
| Clinical Outcome (excluding death) | | | |
| Deteriorated | 14 (47%) | 7 (44%) | 9 (50%) |
| Stable (including never clinically demented) | 10 (33%) | 7 (44%) | 6 (33%) |
| Improved | 6 (20%) | 2 (12%) | 3 (17%) |

## 11.4 DEMENTIA DIAGNOSTIC SCALE

17/23 (74%) of those who had been cases on the dementia diagnostic scale at first screening were reinterviewed. One did not complete the interview, the other 16 remained cases on this scale. Four (17%) people who had been cases on the DDS had died. Two refused re-interview. Three of the 13 (23%) who had been cases on the organic brain syndrome scale and not on the dementia diagnostic scale in phase II became cases on the DDS.

Conclusion: In this study the DDS predicted either continuing DDS caseness or death. However around half the cases did not deteriorate or improved. This contrasts with earlier reports (Gurland et al 1984).

## 11.5 ORGANIC BRAIN SYNDROME SCALE (OBS)

31 (66%) of the 47 who had crossed the cutpoint on the organic brain syndrome scale at the diagnostic phase were re-interviewed, ten (21%) had died and 6 (13%) refused re-interview.

Of the 30 who completed the interview, eight (27%) no longer crossed the cutpoint. Of these eight who were non-cases,

three had been diagnosed clinically as not demented but five were thought to be demented in the Phase II diagnostic study.

Conclusion: The OBS screening scale outcome appeared to be similar to the other measures, despite the fact that a larger group crossed the cut point. This apparent similarity may be due to a type II error, that is a false negative because the small numbers interviewed in Phase III mean that there is a low probability of detecting a true difference.

### 11.6 GMS (A)/AGECAT

GMS (A) was completed for 22 subjects. Seventeen of these were classified by the AGECAT programme as organic. The remaining five were not classified as organic.

There had been nine discrepancies between GMS/AGECAT and clinical diagnoses at phase II (see Table 11). The first eight subjects were alive and had a follow up interview. The ninth subject had died. Eighteen months later, four of the six subjects AGECAT who had classified as non-organic were now classified as organic, the other two had no change in classification. The two subjects who had been classified as organic, while clinical diagnosis had been non-organic were still classified as organic. One of those subjects also

remained a case on the OBS scale of the Short CARE. The other was no longer a case.

Conclusion: The outcome of GMS organicity is similar to other measures. In this study the GMS and the DDS are less specific than the clinical diagnosis, as four of the GMS non-organic and three of the DDS non-cases changed status at follow up. This is in contrast to clinical diagnosis as all those who were clinically non-demented at Phase II remained so as Phase III.

# CHAPTER 12

# DISCUSSION AND CONCLUSIONS

## 12.1 MAJOR FINDINGS OF THE INVESTIGATIONS

The main findings of this three phase study of dementia in the community are:

**PHASE I**

1. Neither the electoral register nor General Practitioner and service contact lists provided an accurate total population register of the elderly in an inner city area.
2. The elderly population who did not respond to letters were more likely to be suffering from cognitive impairment than those who did respond; therefore prevalence surveys which do not include follow up of non-responders may provide misleading results.

**PHASE II & III**

3. The elderly suffering from dementia in the community were different in diagnostic composition to hospital samples which have been reported, therefore generalisation as to the nature of dementia from hospital studies of dementia will be unwise.
4. No dementias were diagnosed as being potentially reversible in this population in phase II. Despite this in Phase III six cases had improved .
5. Many cases of dementia did not deteriorate over 18

months and seven subjects improved.

6. The diagnosis of dementia predicted death in 21% and deterioration in 54% of the survivors whose outcome is known at 18 months.

7. Almost 50% of the survivors did not deteriorate.

## 12.2 RESULTS OF SCREENING FOR DEMENTIA IN THE COMMUNITY (PHASE I) METHODOLOGICAL LIMITATIONS

Despite both written and personal contact, 13% of residents did not take part in the interviews. Some were not interested because they felt they were too well to be considered in a survey of pensioners. Others were protected by their families who said that their relative was too old to be troubled. The response rate would probably have been increased, if interviewing had taken place at the same time as 'door knocking' and assembling the register. This procedure in a previous screening survey resulted in the highest response rate reported in the literature of 97% (Schoenberg et al 1985).

## 12.3 THE PREVALENCE RATE OF DEMENTIA

The prevalence figures were produced by an analysis of responses to the Short CARE. However, although the population interviewed was representative in terms of sex,

of the general UK population, it was slightly older (OPCS 1985). In the UK generally 32% of the elderly are 65-69, 50% 70-79 and 18% over 80. Standardization of the age of the Gospel Oak population reduces the dementia prevalence rate of the dementia diagnostic scale from 5% to 4.1%.

Many factors have influenced the reported prevalence rate of dementia. The use of a frame established by 'door knocking', instead of using the electoral register, or a list provided of service users, affected the numbers of dementia cases. If the list provided of service users had not been modified, then a higher prevalence rate of dementia would have been found. This contrasts with the use of the electoral roll as a frame which might result in a lower prevalence rate, as 17% of those crossing the cut point at screening were not on the electoral roll (cf Chapter 10.6). This may account in part for the lower rate of dementia found in one study, which used the electoral role as the screening frame (Lindesay et al 1989).

In addition the importance of the decision as to whether or not to include the local authority home for the elderly is emphasised. The decision alters the prevalence figures, reducing the dementia diagnostic scale by more than 2% (cf Chapter 6.3).

Thirdly there was a marked effect of the age distribution on prevalence rate. Age correction in this sample reduced the prevalence rate of dementia by nearly 1%.

The prevalence rate of dementia using the dementia diagnostic scale was 4.7% of the over 65s, similar to some recent surveys (Copeland et al 1987 a,b). The importance of the assessment instrument used is reconfirmed by lower prevalence rate found using the Clifton Assessment Schedule (Morgan et al 1987). The CAPE is an instrument which is designed for hospital populations not for use in the community (cf Chapter 6.5). However the figures differ from another recent London inner city survey which used the Short CARE. In it a lower rate (4.6%) of dementia on the organic brain scale was found, despite using a lower cut point of 2/3 (Lindesay et al 1989). This contrasts with the Gospel Oak Study's finding of a rate of dementia on the OBS of 8%, using the higher cut point of 3.4. The populations were of similar size and both were drawn from inner city areas of London. The lower rates found in Lewisham may be partially explained by the fact that the Lewisham sample was of a similar age group to the general population of England and Wales. In addition the use of the electoral register would be expected to yield a lower prevalence of dementia, possibly in the region of 20% lower (cf Chapter 10.6). Finally, in Lewisham forty-seven elderly residents were 'not contacted'. No reason is given for this,

and they are not included in the 14% who were not interviewed. It is possible that those were people who did not answer letters sent to confirm their age and address and may therefore have been more likely to be cognitively impaired (cf Chapter 10.3). In summary the prevalence rate of dementia is so influenced by the survey design, as to render comparisons between surveys using different methodology almost impossible.

## 12.4 SEX DIFFERENCES IN RATES OF DEMENTIA

Dementia was uncommon among the younger males in the sample. This sex difference reflects the similar unexplained patterns in many other studies (c.f. Table 4). As discussed before, this effect may be because men with dementia survive less long than women with dementia. The trends in the follow-up data from this study, lends some support to the explanation that men with dementia survive less long than women with dementia, as 40% of deaths were male, compared with 23% at outset in this sample.

It is also possible that the gender difference is an artefact created by the properties of the screening instruments. As the number of years of higher educations is inversely related to caseness, in at least some screening instruments for

dementia (Brayne & Calloway 1990, O'Connor et al 1989), the lesser education of women as a group when compared to men as a group, may account for this phenomenon. For example in the Gospel Oak Sample, 40% of men as compared to 74% of women had worked in unskilled occupations.

## 12.5 PHASE II DIAGNOSTIC COMPOSITION OF DEMENTIA IN THE COMMUNITY

This study demonstrates several diagnostic differences between the elderly with dementia, reported here and those that have been studied in hospitals. In the present study, 46% were diagnosed as Alzheimer's disease, 10% a mixed dementia, 2% a multi-infarct dementia, 10% secondary dementia and 21% suffered from a dementia which was unclassifiable because of lack of information. This contrasts with the samples used in studies summarised by Clarfield (1988) (see Chapter 7.2). In this paper the overall rates for the common diagnoses were calculated; 57% of cases were due to Alzheimer's Disease, 13% to multi-infarct dementia, 4.5% to depression and 4% to alcohol abuse. Four community studies were quoted by Clarfield. In only one study was the sample found by screening (Folstein et al 1985). Folstein et al reported only the rates of Alzheimer's disease and multi-infarct dementia. Recently, further studies of the

diagnostic composition of dementia in the community have been published (see Table 5) (Shibayama et al 1986, Brayne & Calloway 1989, O'Connor et al 1989). However none of these studies report a full diagnostic profile of subjects detected as suffering from dementia by a validated screening instrument, and then examined in a Phase II study. Therefore the present study is the first to report a full diagnostic profile of an unselected community sample and has no complete data for comparison. In the present study the 21% of dementias, which were unable to be classified might change the diagnostic profile reported here considerably. However there is no cause to believe that those unclassified dementias should be of a different diagnostic composition to the remainder of the sample, as dementia was usually unclassified only because of lack of informant history. They may be predominantly suffering from Alzheimer's Disease, as the outcomes were most similar.

In this study it was striking that no subject fulfilled the Hachinski criteria for multi-infarct dementia (score $\geq 7$). As there is no reason for subjects with cerebrovascular disease to be particularly rare in this population, this may reflect the fact that subjects with multi-infarct or mixed dementia may have neurological symptoms and signs, associated with physical disability, together with a more rapidly deteriorating mental state and behavioural problems and thus

be more likely to be institutionalised or die. A prediction which follows from this is that the proportion of vascular dementia in comparison with Alzheimer's disease in incidence rates will be higher than that in the prevalence rate.

## 12.6 PHASE III EIGHTEEN MONTH FOLLOW-UP

Forty-three subjects had been clinically diagnosed at Phase II as having dementia. Eighteen months later 9 (21%) of those had died. Of the remainder, 54% had deteriorated, 23% were stable and 23% had improved.

The clinical diagnosis of dementia, even in this community sample, with relatively early dementia was associated in the main, with an poor outcome. The death rate was twice that which is expected for the age composition of the samples studied (Warnes 1989), and in addition half of the survivors deteriorated. However this means that in contrast, nearly half of the survivors did not deteriorate. This may be because of practice effect as the same tests were administered several times. This has been documented in other studies (Teng et al 1987). Dementia may also show fluctuations in its course, and these may be of physical, social or psychological aetiology. For example physical illness, depression, nutrition and the receipt of formal or

informal services may all affect the severity of impairment. It is possible that the present study, which was designed to be observational, may have influenced its own findings by alerting medical and other services when appropriate, and by administering cognitive tests many times to the same people. Finally subjects may have suffered from an acute confusional state on both screening and at Phase II interview.

The present study gives added weight to the conclusions of a previous longitudinal study, that the most useful way of improving cognition in dementia is to maximise the patient's health in all spheres, rather than continue the search for reversible dementias (Larsen et al 1984).

## 12.7 PREVALENCE RATES OF THE DEMENTIAS

The total prevalence rate of dementia as diagnosed by the psychiatrists was 6.1%, between the initial screening study prevalence rate of 4.7% according to the DDS and 8% according to the OBS. The DDS scale is probably too restrictive to detect all forms of the dementia syndrome. In this study, according to the clinical diagnoses, the prevalence rate of Alzheimer's disease was 3.1%. The only other comparable data in the over 65 age group were from Baltimore and from Nagoya, where the overall prevalence rate for dementia was similarly

6.1%. (Folstein et al 1985, Shibayama et al 1986). More recent British studies have used different age groups thereby making comparisons more difficult (cf Tables 5 & 6). However it appears that the Cambridgeshire study finds a lower rate of the dementias, particularly Alzheimer's disease, than other studies, although only women are screened (Brayne & Calloway 1989). This may be because there is a lower prevalence of dementia in rural areas as had been previously suggested (cf Chapter 6.3). The explanation for this phenomenon is unknown, but possibilities include either different environmental exposure to risk factors, or drift into more urban areas of those with disease. A final possibility is that the isolation which occurs in large cities is a social phenomenon which may increase the likelihood of those who are cognitively impaired becoming "cases".

It is not surprising that a higher rate of dementia was found in the present study, than in some other contemporary UK studies. Firstly, personal visits to non-responders in the initial screening study increased the number of cases found at screening. Secondly, Gospel Oak contains more very old people than the UK elderly population in general.

The low numbers studied meant that no statistical analysis could be made as to the significance of differences in

outcomes in each of the different subclassifications. There appears to be a trend for a worse outcome in Alzheimer's Disease, but this cannot be confirmed by this study. Any difference might be explained by the trend for those with Alzheimer's Disease to have a more severe dementia at outset.

## 12.8 REVERSIBLE DEMENTIA

In Phase II five subjects had a secondary dementia and two had a biochemical abnormality on blood screening, but none of these dementias proved reversible in practice. The total numbers of potentially reversible dementias seems small, so a case for population screening and investigation of the elderly in order to detect reversible dementias cannot be made from the data. This study again emphasises the differences between hospital and community. The review of studies by Clarfield indicated that there were 13.2% potentially reversible dementias, among all dementias. Yet, the only other study based upon a representative sample in the community and reporting the rates of reversible dementias, like the present study, did not report any reversible dementias (Folstein et al, 1985).

In contrast, in Phase III six subjects had improved cognitively, although five were still impaired. Despite no

cause of secondary dementia being found in screening they proved to have a dementia which was reversible. As those subjects were impaired on both screening and on further investigation, it is unlikely that they had acute confusional state. A more probable explanation is the fluctuation of mild dementia according to physical, psychological or social factors.

## 12.9 THE DIAGNOSTIC CRITERIA

### a. CLINICAL

The variation in rates of subclassifications of the dementias compared to other studies have been discussed in terms of sample bias. However, this variation may also reflect the use of current standard diagnostic criteria which were developed from work on specific clinic subjects rather than on a community sample. The NINCDS/ADRDA criteria, have been validated by post mortem examination either in samples where the diagnosis was made late in the illness, prior to death (Tierney et al. 1988), or in samples where the subjects were selected to have no concurrent physical illness (Morris 1988, Martin 1987) (cf Chapter 3.6). Community samples are likely to contain less advanced cases and subjects who often have physical illnesses. In the case of vascular dementia,

studies reporting post-mortem validation of the Hachinski score found it less accurate in diagnosing multi-infarct dementia than other criteria (Homer et al 1988, Molsa 1985) (cf Chapter 3.6). Finally, on practical grounds, the criteria were limited in this study, for it was impossible to make a differential diagnosis in ten subjects because of insufficient information, indicating again how different hospital based samples are.

Clinical diagnosis of dementia was as sensitive and more specific than the standardised measures. It therefore appears that from this data using clinical diagnosis as a 'gold standard' for validation of ante-mortem diagnosis is still appropriate.

**b. AGECAT DIAGNOSIS**

It is a new observation that AGECAT criteria for organicity appear to be more concordant with a clinical diagnosis of Alzheimer's dementia, than the secondary dementias. This may be because the pattern of deficit is atypical in secondary dementia, or because the trend was for the Alzheimer's Disease patients to have a more severe illness. However, the AGECAT diagnosis was then imperfect in that it neither took into account history, eg. low intelligence; nor did it allow for the interviewer's inability to code pathology when no

answer is given. For example, the question in the GMS (A) is not used in conjunction with other instruments. These problems of diagnosis are likely to be remedied as the History and Aetiology Schedule (HAS) can now be incorporated into the AGECAT diagnosis.

Other discrepancies between the GMS/AGECAT diagnoses and the psychiatrists' diagnoses may reflect the continuing difficulties in differentiating depression from early dementia. The 18 month follow up results suggest that, while psychiatric diagnosis was by no means a perfect predictor, the AGECAT criteria were no better than other criteria at predicting death or deterioration, and were less good than clinical diagnosis at distinguishing false and true negatives.

### c. PSYCHOMETRY

There have been criticisms of the Mini-Mental State Exam (MMSE). Different versions have been created for different populations with differing cut-off points, so that it was not immediately apparent which version would be preferable for this study. This was investigated by scoring the MMSE in two ways. The results showed that inclusion of the option to spell 'WORLD' backwards simplified the test. Therefore, fewer subjects fell below the conventional cut-off of 23 on

the easier, rather than the harder version (37 as opposed to 40 respectively). The clustering of the community sample around the cut off point, suggests that it may be useful to use a modified MMSE, with an expanded scoring range in order to make finer differentiations between demented and non-demented patients, as was done by Teng et al (1987). Another factor which may have influenced outcomes on the MMSE test scores was that the subjects were interviewed at home, and it is possible that this improved their scores in orientation questions.

Even so, the power of the MMSE to differentiate demented subjects was greater in this study than that of the two other cognitive tests used, KOLT and Word Generation. This may partly have been because the former is a multi-component test, combining information from language, attention, memory, literacy and drawing ability. Alternatively, the cut-offs on these latter tests may have been set too high. This idea receives support from a similar findings in a study of 164 community residents aged over 65, which found that the Kendrick battery failed to detect one third of those diagnosed as suffering from dementia by a neurologist (Fillenbaum et al 1990). Despite this, the MMSE was found to correlate significantly with premorbid intelligence as measured by the NART, while KOLT and Word Generation did not. The latter tests may therefore be free of educational bias.

An alternative explanation of this finding is that the NART is strongly related to current levels of cognitive function in the community dwelling elderly (Brayne & Beardsall 1990), this may be another indication of the usefulness of the MMSE.

### d. PHYSICAL EXAMINATION AND BIOCHEMICAL TESTS

The physical examinations were of little help in the subclassification of dementia. This is confirmed by another study of patients with NINCDS/ADRDA diagnosed mild to moderate Alzheimer's disease, which found that although there were neurological abnormalities in Alzheimer's disease, they are too infrequent early in the course to serve as diagnostic markers (Palasko et al 1990). Although necessary for the Hachinski scores and relevant in the diagnosis of multi-infarct dementia, this diagnosis was rare in this sample. Both the blood testing and the physical examination did uncover some abnormalities, but neither helped in diagnosis, nor led to any action that reversed the impairment. Nevertheless, subjects and their relatives were very pleased to have a full physical examination and investigations and a subjective impression was gained that these increased co-operation with the interviewer. However the study's results would not justify a recommendation that every community patient with dementia requires physical examination and

biochemical screens.

### e. CT SCANS

Neuroimaging was the only part of this diagnostic procedure that took place in hospital. The co-operation of the subjects was markedly less either because of inconvenience, or fear of hospital, or because it seemed too difficult to come to the hospital because of physical disabilities.
The results of the CT Scans were available to be used as part of the diagnostic process by the psychiatrists. However only three diagnoses were influenced by the CT Scan results, namely those of the subject with a glioma and two cases where there was evidence of multi-infarctions, but the history was consistent with Alzheimer's disease. Among the remainder of the scans, both leuko-araiosos (white matter changes) (Hachinski et al 1987) and cerebral atrophy were found among subjects of all diagnostic categories, including those subjects who did not suffer from clinical dementia. These results indicate that while neuroimaging can be a useful diagnostic tool in a few subjects with an atypical history of dementia, in general it does not clarify diagnoses. The major disadvantage of its use is the distress caused to this population at the prospect of coming to hospital.

## 12.10 SCREENING TESTS

The two scales of the Short CARE behaved differently. The DDS detected 35 subjects, all of those interviewed were deemed later to be suffering from dementia. However this scale missed 19 subjects with clinical dementia. The OBS scale detected a larger group which contained five subjects without dementia. Four of the DDS cases did not appear in the OBS group; three of these had died by the time of further assessment, suggesting that their loss of function could be associated with concurrent physical illness. Terminal illness is perhaps picked up by the activity of daily living items in the DDS which are not in the OBS scale. Thus, at the diagnostic stage the OBS scale appeared a more useful screen whereas the DDS predicted dementia or early death.

## 12.11 IMPLICATIONS FOR FURTHER RESEARCH

Despite the small numbers in this study some conclusions can be drawn concerning the most appropriate setting for and the format of assessments, which should be used with the community dwelling elderly suffering from dementia.

First, it is important to see people immediately after they

have been screened. In this study seven people had died and were thus lost to follow up by the time contact was initiated some months after the first screening. Second, it is important to assess people at home, since many elderly people will be reluctant to come to hospital unless they are acutely ill. Third, the most important factor affecting the acceptability of the psychometric testing appeared not to be the tests themselves but the length of testing time. Though there was no strict testing order, the MMSE was always conducted first; the response rate for this test was 90%. The tests that were left until later were less likely to be completed. It seems that the shorter the testing time the more likely it is that more complete data will be collected. The diagnostic differences demonstrated between this study of community dwelling elderly people and studies which are conducted with subjects from hospitals show that it is no longer satisfactory to extrapolate from hospital studies in order to draw conclusions concerning the elderly demented people living in the community. As it has been almost exclusively the data from hospital studies, which has led to diagnostic criteria and subclassification of patients with dementia syndrome, further studies need to be conducted in the community, with the special needs of this population in mind.

Finally, because of the small proportion of those suffering from dementia in the over 65s age group, and the large number of deaths in those suffering from dementia 17 (28%) of those originally screened as demented) future studies should employ larger and possibly older community population samples. This would increase the numbers of subjects, so that any differences which exist in outcome between the diagnostic subclassifications of dementia, could be found.

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