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*Occasional review*

# Recommended minimum data to be collected in research studies on Alzheimer's disease

SUMMARY In order to be able to compare the results of research work carried out in different centres on Alzheimer's disease and dementia, it is necessary for there to be standardised assessment methods. The Medical Research Council organised a workshop in order to see whether workers in Britain in the field of dementia research could agree on such standardised assessment methods. The workshop agreed guidelines for the minimum data which should be collected, in clinical and pathological studies, on patients with presumed Alzheimer's disease and dementia. These recommendations are compared with other approaches based on research diagnostic criteria.

Alzheimer's disease is the single major cause of dementia. The realisation of its importance has led to an increasing amount of research on the disease in recent years. If research carried out by different workers and in different centres is to be fruitfully compared, then it is necessary for there to be some standardisation of assessment methods.

In applications over recent years for research funding to the Medical Research Council (one of the major funding organisations, financed by Government, in the United Kingdom) a wide variety of basic assessment methods has been proposed. Such differences in basic assessment methods make the comparison of data collected in different research projects impossible.

The Medical Research Council (with financial support from the Grand Charity) therefore organised, through a *Steering Committee*, a two day workshop in order to see whether workers in Britain in the field of dementia research, could agree on guidelines for the minimum data which should be collected, in clinical and pathological studies on patients with presumed Alzheimer's disease (AD) and dementia.

A report from this workshop is available from the Medical Research Council.[1] The purpose of this article is to summarise this report and to compare it with other approaches.

There have been, broadly, two kinds of solution to the problem of standardisation for research comparison: the first is to use research diagnostic criteria; the second is to use a standardised assessment schedule. There are advantages and disadvantages to each of these solutions.

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*Research diagnostic criteria*

The use of research diagnostic criteria entails the specification of those criteria which must be fulfilled if the diagnosis of Alzheimer's disease is to be made. Research subjects can be divided, by means of these criteria, into those who have Alzheimer's disease and those who do not.

Some advantages of this approach are:

(i) A definition of the condition (Alzheimer's disease) is specified.
(ii) Research can be directly compared in that all subjects fulfil the criteria.
(iii) The applicability of any conclusions from the research is relatively clear-cut in the sense that the results pertain to a specific and defined population.

Two important examples of this approach are the report of the NINCDS-ADRDA Work Group[2]; and

DSM-IIIR.[3] The NINCDS-ADRDA Work Group was established to describe clinical criteria for the diagnosis of Alzheimer's disease of particular importance for research protocols and to describe the approaches which would be useful for assessing the natural history of the disease. The Group agreed clinical criteria for the diagnosis of possible, probable, and definite Alzheimer's disease as outlined in the appendix. The NINCDS-ADRDA Work Group criteria are compatible with the definitions given in DSM-III[4] which has been recently revised (DSM-IIIR). DSM-IIIR is a comprehensive classification of mental disorders for both clinical and research use. It provides diagnostic criteria for mild, moderate and severe dementia, and further criteria for specific causes, such as Alzheimer's disease and multi-infarct dementia (see Appendix).

Some disadvantages of research diagnostic criteria are:

(1) The use of criteria may introduce too much rigidity too early in the research. Diagnostic criteria can focus research on the "core" of the condition to the exclusion of the boundaries. If the criteria do not in fact correspond to basic biological categories then their use may well mask the underlying categories. If the underlying concept is dimensional rather than categorical[5] then the cut-offs which will have to be defined by the proposed criteria will be to some extent arbitrary, and may be unhelpful for some research aims.

(2) Conversely, there may be importantly different groups within any specified set of criteria, so that in comparing research it may be important to know more than that certain research criteria are fulfilled.

(3) Different workers within the field may not be able to agree on what criteria to adopt.

There is recognition of these difficulties in both DSM-IIIR and the report of the NINCDS-ADRDA Work Group. The Introduction to DSM-IIIR states: "for most of the categories the diagnostic criteria are based on clinical judgement, and have not been fully validated by data about such important correlates as clinical course, outcome, family history, and treatment response".

The report of the NINCDS-ADRDA Work Group states: "the criteria are not yet fully operational because of insufficient knowledge about the disease". To the extent that criteria are not fully operational it allows for less rigidity and more ready agreement between different workers within the field. But the cost of this is that there is more room for different workers to interpret the criteria differently.

*Standardised assessment schedules*

The use of assessment schedules entails the specification of the information which should be collected, and the method by which this should be done. The advantages of this approach are:

(1) It does not impose a definition of the condition. This allows for flexibility amongst research workers as to which subjects are included in a study.

(2) Despite this flexibility, research workers can compare subjects because the same data has been collected in the same way.

(3) Sub-groups of subjects can be identified and compared post-hoc as long as the sub-groups can be defined with reference to the standardised assessment procedure.

(4) Research workers are more likely to agree on the information which should be collected than on precise diagnostic criteria.

The main disadvantage of this approach is that no definition of the condition is provided.

Two important examples of standardised assessment schedules relevant to Alzheimer's disease are the Geriatric Mental State (GMS)[6] and CAMDEX.[7]

*The MRC Workshop*

The Steering Committee first identified those who would be asked to participate in the workshop. The range of disciplines represented by the participants was very wide and included psychiatrists, geriatricians, neurologists, neuropathologists, biochemists, psychologists, molecular biologists and immunologists. The Committee asked each of these potential participants to answer those of the following questions which were within their area of competence:

(1) To specify the clinical information required in order to: (*a*) decide whether a person is suffering from dementia; (*b*) categorise the degree of dementia; and (*c*) decide on a clinical diagnosis of the cause of the dementia.

(2) To specify the pathological information required in order to be able to make a diagnosis of Alzheimer's disease and multi-infarct dementia.

It was clear from these replies that it would not be possible for participants to agree precise diagnostic criteria at either the clinical or pathological level. The Committee therefore decided that the aim of the workshop should be to provide guidelines for the minimum data which should be collected in clinical and pathological studies on patients with presumed Alzheimer's disease and dementia. On the basis of the answers to the above questions, the Committee drew up a proposal as to what these minimum data should be. In drawing this up there were two guiding principles. Firstly, the proposals should be as brief as possible so as not to burden research workers with an excess of data to be collected; and, secondly that the data to be collected should be specified as precisely as possible, so as to maximise the comparability between different research workers.

The Steering Committee's proposal was sent to all participants prior to the workshop. The workshop provided the opportunity for all participants to criticise and suggest alterations to the Steering Committee's proposal. Each session was devoted to one section of the proposal. The points made by participants were incorporated into a revised version and this revised version was reconsidered by the workshop. Further alterations were made until participants agreed to a final version. The workshop reached agreement on guidelines for the minimum data which should be collected in clinical and pathological studies of dementia and on the ways in which these guidelines should be applied in the collection of data. These guidelines cover both clinical and neuropathological data.

The workshop's recommendations are considered to constitute the minimum data which should normally be collected. Detailed well validated schedules (for example GMS; CAMDEX) are to be preferred, but it is recognised that these may be too time consuming to be used in all studies.

*The guidelines*

The guidelines specify the information which should be obtained, and the methods and sources which should be used to obtain it. They include a history from an informant, and cognitive, psychiatric and physical examination of the subject. The recommendations endorse the mini-mental state examination[8] and include further cognitive items from CAMDEX. In addition, neuropathological information which should be collected (where appropriate) is specified. The guidelines are listed in the Appendix below.

In contrast to the NINCDS-ADRDA Work Group report, these guidelines are not diagnostic criteria but recommendations as to what data should be collected. However, despite this major difference of approach there is considerable agreement about what information should be collected in research studies involving subjects with Alzheimer's disease. Indeed, the information to be gathered under these guidelines should be helpful in the application of diagnostic schemes such as DSM-IIIR, and the NINCDS-ADRDA Work Group.

*Review*

It is anticipated that the guidelines will be revised in 1989. The MRC would welcome comments and feedback which may help such revision.

We acknowledge the help of all those who replied to the Steering Committee's questions and all the participants. The specific questions proposed originate from a number of sources. Of particular help have been: CAMDEX,[7] Geriatric Mental State[6] and Mini Mental State Examination.[8]

*Appendix*

*(a) Criteria for clinical diagnosis of Alzheimer's disease from the report of the NINCDS-ADRDA Work Group.*[2]

I. The criteria for the clinical diagnosis of PROBABLE Alzheimer's disease include:
dementia established by clinical examination and documented by the Mini-Mental Test, Blessed Dementia Scale, or some similar examination, and confirmed by neuropsychological tests;
deficits in two or more areas of cognition;
progressive worsening of memory and other cognitive functions;
no disturbance of consciousness;
onset between ages 40 and 90, most often after age 65; and
absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition.

II. The diagnosis of PROBABLE Alzheimer's disease is supported by:
progressive deterioration of specific cognitive functions such as language (aphasia), motor skills (apraxia), and perception (agnosia);
impaired activities of daily living and altered patterns of behaviour;
family history of similar disorders, particularly if confirmed neuropathologically; and
laboratory results of:
normal lumbar puncture as evaluated by standard techniques,
normal pattern or nonspecific changes in EEG, such as increased slow-wave activity, and
evidence of cerebral atrophy on CT with progression documented by serial observation.

III. Other clinical features consistent with the diagnosis of PROBABLE Alzheimer's disease, after exclusion of causes of dementia other than Alzheimer's disease, include:
plateaus in the course of progression of the illness;
associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations, catastrophic verbal, emotional, or physical outbursts, sexual disorders, and weight loss;
other neurologic abnormalities in some patients, especially with more advanced disease and including motor signs such as increased muscle tone, myoclonus, or gait disorder;
seizures in advanced disease; and
CT normal for age.

IV. Features that make the diagnosis of PROBABLE Alzheimer's disease uncertain or unlikely include:
sudden, apoplectic onset;
focal neurologic findings such as hemiparesis, sensory loss, visual field deficits, and incoordination early in the course of the illness; and
seizures or gait disturbances at the onset or very early in the course of the illness.

V. Clinical diagnosis of POSSIBLE Alzheimer's disease:
may be made on the basis of the dementia syndrome, in the absence of other neurologic, psychiatric, or systemic disorders sufficient to cause dementia, and in the presence of variations in the onset, in the presentation, or in the clinical course;
may be made in the presence of a second systemic or brain disorder sufficient to produce dementia, which is not considered to be *the* cause of the dementia; and
should be used in research studies when a single, gradually progressive severe cognitive deficit is identified in the absence of other identifiable cause.

VI. Criteria for diagnosis of DEFINITE Alzheimer's disease are:
the clinical criteria for probable Alzheimer's disease and histopathological evidence obtained from a biopsy or autopsy.

VII. Classification of Alzheimer's disease for research purposes should specify features that may differentiate subtypes of the disorder, such as:

familial occurrence;
onset before age of 65;
presence of trisomy-21; and
coexistence of other relevant conditions such as Parkinson's disease.

*(b) Diagnostic criteria for dementia from DSM-IIIR.*[3]

**Diagnostic criteria for Dementia**

A. Demonstrable evidence of impairment in short- and long-term memory. Impairment in short-term memory (inability to learn new information) may be indicated by inability to remember three objects after five minutes. Long-term memory impairment (inability to remember information that was known in the past) may be indicated by inability to remember past personal information (e.g., what happened yesterday, birthplace, occupation) or facts of common knowledge (e.g., past Presidents, well-known dates).

B. At least one of the following:
(1) impairment in abstract thinking, as indicated by inability to find similarities and differences between related words, difficulty in defining words and concepts, and other similar tasks
(2) impaired judgement, as indicated by inability to make reasonable plans to deal with interpersonal, family, and job-related problems and issues
(3) other disturbances of higher cortical function, such as aphasia (disorder of language), apraxia (inability to carry out motor activities despite intact comprehension and motor function), agnosia (failure to recognise or identify objects despite intact sensory function), and "constructional difficulty" (e.g., inability to copy three-dimensional figures, assemble blocks, or arrange sticks in specific designs)
(4) personality change, i.e., alteration or accentuation of premorbid traits

C. The disturbance in 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) or (2):
(1) there is evidence from the history, physical examination, or laboratory tests of a specific organic factor (or factors) judged to be etiologically related to the disturbance
(2) in the absence of such evidence, an etiologic organic factor can be presumed if the disturbance cannot be accounted for by any nonorganic mental disorder, e.g., Major Depression accounting for cognitive impairment.

**Criteria for severity of Dementia:**
**Mild** Although work or social activities are significantly impaired, the capacity for independent living remains, with adequate personal hygiene and relatively intact judgement.
**Moderate** Independent living is hazardous, and some degree of supervision is necessary.
**Severe** Activities of daily living are so impaired that continual supervision is required, e.g., unable to maintain minimal personal hygiene; largely incoherent or mute.

**Diagnostic criteria for Primary Degenerative Dementia of the Alzheimer type**

A. Dementia (see above).
B. Insidious onset with a generally progressive deteriorating course.
C. Exclusion of all other specific causes of Dementia by history, physical examination, and laboratory tests.

**Diagnostic criteria for Multi infarct Dementia**

A. Dementia (see above).
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 (e.g., exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity, etc.).
D. Evidence from history, physical examination, or laboratory tests of significant cerebrovascular disease that is judged to be etiologically related to the disturbance.

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(c) *MRC Alzheimer's Disease Workshop Guidelines.*[1]

**1. Clinical information to be gathered from prospective studies**

IMPORTANT It is essential that the Introduction and Guidelines to this report are read before proceeding with the collection of data.

**A Basic demographic data about the subject**
Age
Last occupation
Place where living now
Education level attained: number of years of education and educational level attained
Handedness

**B History from informant**
Date and place of interview
(Note: the source(s) of information should be specified. If possible the major informant should be a relative or friend who has known the subject well from before the onset of dementia. If this is not possible, multiple informants would normally be necessary.)

**(i) Family history**
How many brothers and sisters does he/she have?
(This information is best collected in the form of a family tree giving ages at death and presence of dementia.)
How many of his/her first degree relatives have been affected by dementia?

**(ii) Past medical history**
Including, specifically a past history of:
epilepsy
meningitis
mental handicap
head injury with either a period of unconsciousness, or hospital admission
boxing at any time in adult life
stroke, including subarachnoid haemorrhage
transient lateral weakness
hypertension needing treatment

**(ii) Past psychiatric history**
Including specifically:
treatment by a psychiatrist
treatment for depressive illness or chronic schizophrenia

**(iv) Evidence for cognitive impairment**
Does he/she have difficulty remembering short lists of items, e.g., shopping?
(no difficulty/slight difficulty/great difficulty)
Does he/she have difficulty remembering when he/she last saw you?
(no difficulty/slight difficulty/great difficulty)

Does he/she have difficulty remembering what happened the day before?
(no difficulty/slight difficulty/great difficulty)
Does he/she have difficulty knowing where he/she is?
(no difficulty/slight difficulty/great difficulty)
Does he/she have difficulty discriminating between different types of people, such as doctors, visitors, relatives?
(no difficulty/slight difficulty/great difficulty)
Does he/she have difficulty finding the way about the home (or ward) e.g., finding the toilet?
(no difficulty/slight difficulty/great difficulty)
Does he/she have difficulty finding the way around the neighbourhood e.g., to the shops or post office near home?
(no difficulty/slight difficulty/great difficulty)
*General mental functioning*
When speaking, does he/she have difficulty finding the right word or use wrong words?
Does he/she seem to find it more difficult to make decisions lately?
Is there a loss of any special skill or hobby he/she could manage before?
(no/yes/unrateable because of physical disability)
Does his/her thinking seem muddled?
Does he/she continually repeat him/herself?
Is he/she aware at times that he/she is ill?
*Everyday activities* (Comparisons to be made with premorbid functioning where appropriate.)
Does he/she have any difficulty performing common household chores, e.g., can he/she make a cup of tea?
(no difficulty/slight difficulty/great difficulty/unrateable because of physical disability)
Does he/she have difficulty managing small amounts of money?
(no difficulty/slight difficulty/great difficulty/unrateable because of physical disability)
Does he/she have difficulty dressing?
(no difficulty/needs help with buttons/wrong sequence, often forgets items/unable to dress self/unrateable because of physical disability)
Does he/she wet or soil him/herself?
(no/wets occasionally/wets often/doubly incontinent)
Has wandering been a problem with him/her?

**(v) Personality**
Have you noticed any changes in the way he/she behaves socially?
Type of change should be noted.
Does he/she show less concern for others?
Does he/she get excessively suspicious or mistrusting of others?

**(vi) Delusions**
The interviewer should ascertain from the informant whether or not the subject has experienced delusions, and should specify any.

**(vii) Onset**
(Establish and specify the earliest symptom/s).
Did the first changes happen suddenly or come on slowly? Over hours, days or weeks?

**(viii) Duration**
How long ago did these earliest symptoms first occur?
(Rate number of months).

**(ix) Course**
Since the onset of (the problems) have there been any occasions when the symptoms have suddenly worsened over three days or less and have stayed worse? On how many occasions has this happened?
(never/on one occasion/on more than one occasion)
Is there marked fluctuation in the subject's condition either from one day to another, or within a day?
(Specify)

**(x) Depression**
Since the onset of the problems has he/she appeared to be unusually low in his/her mood? In what way? (Do not rate brief episodes of tearfulness.)
When did this start (in relation to the onset of the memory problems)?
Since the onset of the problems has he/she said things which suggest that he/she is weary of life or feels that he/she is better off dead?
Since the onset of the problems has he/she said things which suggest that he/she is a failure or that he/she feels guilty or deserves to be punished or that he/she feels that he/she is a bad person?

**(xi) Alcohol**
Did you ever think he/she was a heavy drinker?

**(xii) Drugs**
List of medication taken over the last week.

## C Examination of subject

**(Note date, time of day and place of examinations and any factor which may affect the results of this examination independently of the dementia, e.g., has never been fluent in English.**

**(i) Cognitive assessment**
(The letters MM beside an item indicate that it is taken from the Mini-Mental State Examination.[8])

**(a) Orientation**

*Time*

| | | |
|---|---|---|
| | What is the time of day? | Incorrect ..... |
| | | Correct..... |

**(Rate as correct if within an hour of the correct time.)**

| | | |
|---|---|---|
| MM | What day of the week is it? | Incorrect ..... |
| | | Correct..... |
| | What is the date to-day? | |
| MM | Day | Incorrect ..... |
| | | Correct..... |
| MM | Month | Incorrect ..... |
| | | Correct..... |
| MM | Year | Incorrect ..... |
| | | Correct..... |
| MM | What is the season? | Incorrect ..... |
| | | Correct..... |

**(Allow flexibility when season changes, i.e: March = winter/spring; June = spring/summer; September = summer/autumn; December = autumn/winter.)**

*Place*

| | | |
|---|---|---|
| | Can you tell me where we are now? | |
| MM | For instance, what county are we in? | Incorrect ..... |
| | | Correct..... |
| MM | What is the name of this town? | Incorrect ..... |
| | | Correct..... |
| MM | What are two main streets nearby (or | Incorrect ..... |
| | near your home)? | Correct..... |
| MM | What floor of the building are we on? | Incorrect ..... |
| | | Correct..... |
| MM | What is the name of this place? (Or what | Incorrect ..... |
| | is this address—if person tested at | Correct..... |
| | home?) | |

**(b) Language**

*Comprehension*

| | | |
|---|---|---|
| | Please nod your head. | Incorrect ..... |
| | | Correct..... |
| | Point to the window and then to the | Incorrect ..... |
| | door. | Correct..... |

**(Should the patient not complete the full sequence then the whole instruction may be repeated to ensure that it has been heard and understood. Prompting and coaching stage by stage is not allowed.)**
**(Read full statement and *then* hand over the paper).**

| | | |
|---|---|---|
| MM | I am going to give you a piece of paper. When I do, take the paper in your right hand. | Right hand .... |
| | | Folds ..... |
| | Fold the paper in half with both hands and put the paper down on your lap. | On lap ..... |

*Repetition*
**(Only one presentation is allowed so it is essential that you read the phrase clearly and slowly, enunciating all the 'S's.)**

I am going to say something and I would like you to repeat it after me.

| | | |
|---|---|---|
| MM | No ifs ands or buts | Incorrect ..... |
| | | Correct..... |

*Naming*

| | | |
|---|---|---|
| MM | **Show pencil.** What is this called? | Pencil ..... |
| MM | **Show wristwatch.** What is this called? | Wristwatch .... |
| | What is the name for this? (*Indicate your elbow.*) | Incorrect ..... |
| | | Correct..... |
| | What is the name for this? (*Indicate your shoulder*) | Incorrect ..... |
| | | Correct..... |

*Fluency*
Tell me as many different animals as you can think of. Number correct

**(Only if subject asks for clarification, explain that animals include birds, insects, humans, etc. If subject gets stuck, encourage him/her with "Can you think of any more?" Record number correct in 60 seconds. Do not count repetitions.)**

*Reading*
Please read what is written here and do what it says.

| | | |
|---|---|---|
| MM | Close your eyes | Incorrect ..... |
| | | Correct..... |
| | Cough hard | Incorrect ..... |
| | | Correct..... |

**(It is not necessary for respondent to read aloud. Score as correct only if action is carried out correctly. If respondent reads instruction but fails to carry out action, say "Now do what it says".)**

*Writing*

| | | |
|---|---|---|
| MM | Write a complete sentence on this sheet of paper. | Incorrect ..... |
| | | Correct..... |

**Ask patient what he/she has written and record.**
**(Spelling and grammar are not important. The sentence must have a subject (real or implied) and a verb and it must make sense. "Help!" "Go away" are acceptable.)**

**(c) Copying**

| | | |
|---|---|---|
| MM | Here is a drawing. Please copy the drawing on the same paper. (Drawing from MM is provided in MRC Working Party Report) | Incorrect ..... |
| | | Correct..... |

**Correct if the two five-sided figures intersect to form a four-sided figure and if all angles in the five-sided figures are preserved.**

**(d) Memory**
*New Learning 1*
I am going to name three objects. After I have finished saying all three, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes.
Name three objects taking one second to say each.

| | | |
|---|---|---|
| MM | Apple, Table, Penny | Apple ..... |
| | | Table ..... |
| | | Penny ..... |
| | | Total ..... |

**Score first try. Repeat objects until all are learned.**

**(e) Attention and calculation**

| | | *Subject's answer* |
|---|---|---|
| MM | Now I would like you to take seven away from 100. | 93..... |
| | Now take 7 away from the number you get. | 86..... |
| | Now keep subtracting 7 until I tell you to stop. | 79..... |
| | | 72..... |
| | | 65..... |
| | | Total ..... |

**(Record answers. Score one point each time the difference is seven even if a previous answer was incorrect—Maximum score—five points.)**

**(f) Memory**
*Recall 1*

| | | |
|---|---|---|
| MM | What were the three objects I asked you to repeat a little while ago? | Apple ..... |
| | | Table ..... |
| | | Penny ..... |
| | | Total ..... |

**(g) Memory**
*New learning 2**
**(Choose an address in an area in which the subject does not currently live, but which is near enough to be familiar to him/her. If the first attempt is not correct, repeat the whole name and address until the subject repeats it correctly—up to a maximum of five attempts.)**

| | |
|---|---|
| Please listen carefully to the following name and address and repeat it: e.g., John Brown, 42 West Street, Bedford. | Incorrect ..... |
| | Correct..... |

Please go on remembering this name and address and I will ask you about it later.
*It is important that the name and address is not asked until after the three objects have been recalled, in order to avoid interference between the two tests of new learning.

*Remote memory*
I am going to say the names of some people who were famous in the past and I would like you to tell me who they were.

| | |
|---|---|
| Neville Chamberlain | Chamberlain .. |
| Guy Burgess | Burgess ..... |

**(Tick each name answered correctly)**

*Recent memory*

| | |
|---|---|
| Who is the present Prime Minister? | Incorrect ..... |
| | Correct..... |
| Who is the current President of the United States? | Incorrect ..... |
| | Correct..... |

**(h) Praxis**
*Gesture*

| | |
|---|---|
| Show me how you wave goodbye. | Incorrect ..... |
| | Correct..... |
| Pretend to brush your teeth. | Incorrect ..... |
| | Finger as brush |
| | Correct mime .. |

**(If subject uses finger to represent brush, say "pretend you are holding a toothbrush". Tick intermediate category if subject makes brushing movement but not as though holding toothbrush.)**

**(i) Abstract thinking**
(This question assesses ability to think abstractly. Abstract answers score 2, concrete answers score 1. Examples are given beside each score.)

| | |
|---|---|
| In what way are an *apple* and a *banana* alike? | Incorrect ..... |
| | Food, grow, have peel ..... |
| | fruit ..... |

| | |
|---|---|
| In what way are a *boat* and a *car* alike? | Incorrect ..... |
| | Have seats .... |
| | Means of transport ..... |

**(j) Perception**

**(Photographs of a shoe, spectacles and pipe as provided in MRC Working Party Report.)**

| | |
|---|---|
| These are pictures of ordinary things taken from unusual angles. Can you tell me what they are? | Shoe ..... |
| | Spectacles ..... |
| | Pipe ..... |

**(Score as correct if object is recognised; it does not have to be named correctly.)**

**(k) Memory**

*Recall 2*

| | |
|---|---|
| What is the name and address I asked you to **remember a short while ago?** | John ..... |
| | Brown ..... |
| | 42 ..... |
| | West Street .... |
| | Bedford ..... |
| | Total ..... |

**(Tick each item answered correctly and enter number correct under Total.)**

**(i) Clinical observation**

| | |
|---|---|
| Was there evidence of perseveration on any of the tasks? | Yes ..... |
| | No ..... |
| Did the subject produce a string of words (five or more) which made sense, during the interview?) | Yes ..... |
| | No ..... |

**(ii) Psychiatric assessment of mental state**

*Questions to subject*

Have you been sad, depressed or low-spirited recently?
Do you feel guilty, or sinful, or bad about some of the things you did, or mistakes you made in the past?
How do you feel about the future; are there times when it seems bleak or hopeless?
Have you felt so low that you have thought of ending it all?
Do you feel that people are trying to harm you or do you believe that people are watching you or plotting against you?
Do you believe others are trying to rob you or get you out of your home?
Do you hear things other people do not hear?

*From observations of subject*

*Depression*—appearance of depression as judged by cues such as apparent sadness, or tearfulness, or slowing of speech and movement.
*Anxiety*—looks or sounds tense, worried or fearful.
*Clouding of consciousness*—is there any evidence of impaired consciousness, for example: drowsiness, perplexity, fluctuation in conscious level, inability to maintain attention?

**(iii) Physical examination**

Pulse rate and rhythm
Systolic blood pressure
Diastolic blood pressure
Does the subject have a hemiparesis with associated changes in reflexes?
Is the subject's gait abnormal? (In what way?)
Deafness—record if he/she can hear without examiner raising voice, or if unable to hear with voice raised.
(normal/needs aid/unable to hear)
Does the subject have significant visual handicap?
(no difficulties/sees with difficulty/cannot see)
Does the subject have hemianopia?
Does the subject have abnormal involuntary movements (including tremor)?
(Specify)
Does the subject have any rigidity (specify type).
Is the subject dysarthric?
Is there any physical disability interfering with motor ability (excluding dyspraxia)?
List any current medical diagnoses.

**(iv) Investigations**

The workshop concluded that a minimum set of investigations should not be recommended. Investigations should be chosen according to the study proposed.

## 2 Clinical information to be collected for pathological studies

Where brain tissue is being used for pathological, biochemical or other similar studies, the information specified above should normally have been collected.

It may not always be appropriate to collect all this information. In such cases the investigators must obtain sufficient information in order to decide whether their subjects were demented or not, and they must specify the information, and its source, on which this decision will be based.

### Controls

A clear reason should be given if control material is not assessed in the same way.

## 3 Neuropathological assessment for Alzheimer's disease

The purpose of collecting these data is to provide a pathological baseline for comparative purposes.

Sections should be prepared from paraffin-wax-embedded or frozen blocks of tissue from the following regions:

(i) temporal lobe containing the three temporal gyri, hippocampus, parahippocampal gyrus, etc, at the level of the lateral geniculate body;
(ii) frontal lobe representative section, e.g., superior frontal gyrus;
(iii) parietal lobe representative section, e.g., superior parietal lobule.

In projects in which neurochemical investigations will be carried out the methods of sampling should be clearly stated.

Quantification of neurofibrillary tangles (in the neocortex and/or the hippocampus) and assessment of senile (neuritic) plaques in the neocortex are recommended. These should be performed in a series of random fields from the above areas.

The thickness of the sections, from which the tangle count per unit area is derived, should be defined.

A histological stain for amyloid would be preferred. A good technique for neurofibrillary tangles (NFT) in paraffin sections is alkaline Congo Red (Puchtler H, Sweat F, Levine M; *Journal of Histochemistry and Cytochemistry* 1962;**10**:355) examined in polarised light. A suitable method for plaques is acid thioflavine T (Burns J, Pennock CA, Stoward PJ; *Journal of Pathology and Bacteriology* 1967;**94**:337) examined in ultraviolet light. Both plaques and NFT can be visualised with thioflavine S (Kelenyi G; *Acta Neuropath* 1967;**7**:336–48) also under ultraviolet light. Alternatively a silver technique already validated is acceptable. We envisage that in the next few years, more extensive use of validated immunocytochemical techniques will be made.

The neuropathological diagnosis should be made blind to clinical information when appropriate.

It is important that dementing conditions other than Alzheimer's Disease are excluded by standard neuropathological techniques, in

particular: the various forms of cerebral vascular disease, Pick's disease, Parkinson's disease, Creutzfeldt-Jakob disease, Huntington's disease and Wernicke's/Korsakoff's Syndrome.

In general the nature and extent of any vascular changes should be specified.

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