

# Differential Diagnosis of Dementia

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The diagnosis and the differential diagnosis of dementia, although sounding to be a straightforward issue in practice and in research is not necessarily so. It seems that the age of 60 is the cut off point for the elderly in the Middle East, but 65 is the age in Europe and U.S.A., 20% to 25% have a reversible dementia (Hecht). The early and accurate diagnosis of the cause of memory loss is vital, as many of these conditions are treatable. Some studies, wrongly consider the dementia as equivalent to Alzheimer's dementia, the tools of diagnosis clinically, and in research do not seem to be standardized yet, the involvement of a team of professionals in dementia and the cooperation of neurologists, psychiatrists, neuropsychologists, geriatricians and care work is lacking. The need to give more attention to elderly health, and to have more research in this field, and also more training and education. Life expectancy in the past was lower and the elderly were looked after by their family, and didn't cause a demand in health and social services, but the picture is changing and more demented people are expected to demand the services, hence we should be ready for that.

**T**he dementias pose a major and growing clinical and public health challenge as we enter the 21st century. Estimates suggest that as many as one in two who live to be 85 years old is likely to develop dementia. Although dementia is mainly a problem currently affecting the developed countries, improvements in public health and increasing longevity in parts of the developing world, will make the numbers of dementia sufferers increase more rapidly than anytime in history. Prompt recognition and appropriate treatment of causes of treatable dementia are of great importance, because delays in treatment may result in death or permanent disability. At least 10 to 20% of patients presenting dementia illnesses have conditions that are treatable or potentially reversible.

## What is Dementia?

The International Classification of Diseases (ICD 10) published by the World Health Organization (1992) offers the following definition:

*“Dementia is a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is a disturbance of multiple higher cortical functions, including memory, thinking orientation comprehension, calculation, learning capacity, language, and judgment. Consciousness is not clouded. Impairments of cognitive function are commonly accompanied, and occasionally preceded by deterioration in emotional control, social behavior or motivation”.*

The primary requirement for diagnosis is evidence of decline in both memory and thinking, which is sufficient to

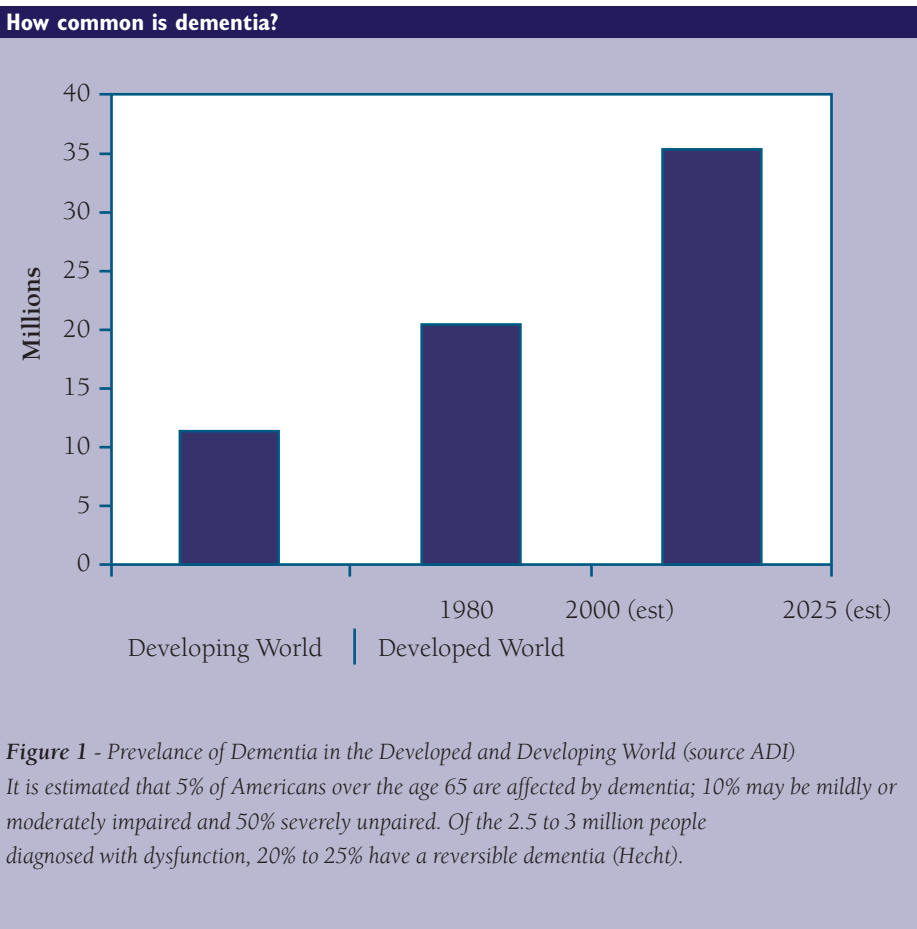
impair personal activities of daily living .... The above symptoms and impairments should have been evident for at least six months for a confident diagnosis of dementia to be made.

The American psychiatric association DSM IV (1994) offers a slightly different definition, which does not require evidence of chronicity or progression. They have five separate elements:

- A Impairment in short and long-term memory.
- B At least one of:
  - I) Impairment in abstract thinking.
  - II) Impaired judgment.
  - III) Other disturbances of higher cortical functions.
  - IV) Personality change.
- C That the deficit in A and B significantly interferes with work or social activities.
- D That these deficits should not be caused by delirium.
- E Either there is evidence from a person's history or a physical examination to show that the deficits are not accounted for by any other condition.

On a clinical basis, some of the most common changes that may indicate that a person is suffering from a dementing illness include:

- ◆ A deteriorating memory, especially for recent events.
- ◆ Difficulty in learning new information.
- ◆ Difficulty in handling complex tasks.
- ◆ An impairment of the ability to reason and think in more abstract terms.
- ◆ Problems in using language to express themselves
- ◆ Changes in behavior, perhaps including wandering and restlessness, difficulty in holding a sensible conversation, being unusually rude, giving up previous interests and hobbies, and being uninterested in papers or TV.
- ◆ Emotional changes such as emotional blunting, self-neglect, and a general lack of initiative.
- ◆ Depression and paranoid attitude and even paranoid psychosis.



**Figure 1 - Prevalence of Dementia in the Developed and Developing World (source ADI)**  
 It is estimated that 5% of Americans over the age 65 are affected by dementia; 10% may be mildly or moderately impaired and 50% severely unpaired. Of the 2.5 to 3 million people diagnosed with dysfunction, 20% to 25% have a reversible dementia (Hecht).

**Table 1 prevalence of dementia (United Kingdom)**

Age Group	Male	Female	Overall
65-69	3.9%	0.5%	2.1%
70-74	4.1%	2.7%	3.3%
75-79	8.0%	7.9%	8.0%
80 plus	13.2%	20.9%	17.7%

Source - Kay and Bergmann (1980)

**Table 2 prevalence of dementia (Europe)**

Age Group	30-59	60-64	65-69	70-74	75-79	80-84	85-89	90+
Male	0.16	1.58	2.17	4.61	5.04	12.09	18.45	32.00
Female	0.09	0.47	1.10	3.86	6.70	13.50	22.76	32.82

Source - Gordon and Spiker (1997), p.43

- ◆ Illegal behavior, stealing, interfering sexually with children and females as well as exhibitionism. Estimates of the prevalence of dementia vary, but two of the most widely quoted studies suggest the rates shown in Tables "1" and "2".

As Tables "1" and "2" show, aging is the highest risk factor for developing a dementing illness, with the prevalence roughly doubling every 5 years between the ages of 65 and 85.

Figure "2" shows the prevalent dementia cases distributed in continents. It is evident that Alzheimer's disease (AD) reflects the most prevalent form of dementia followed by Vascular Dementia (VaD) and then other types. Prevalence studies in Arab Countries began in 1998 with Farrag et al. published in (Dement Geriat Cogn Disord) about the prevalence of Alzheimer's Disease and other Dementing Disorders. Assiut-Upper Egypt study, yielding a crude prevalence ratio of 4.5%, a diagnosis of subtypes of dementia 2.2 for AD, 0.95 for MID, 0.55 for mixed dementia's and 0.45 for secondary dementia's. Several other studies by Bowirrat et al. (in press) about the prevalence of Alzheimer's type dementia in elderly Arab population, in 3 Palestinian villages found DAT in 20.5% of the population which is a very high figure, difficult to comprehend or explain and needs further in depth scientific study.

### Reversible and Progressive Dementia Syndromes

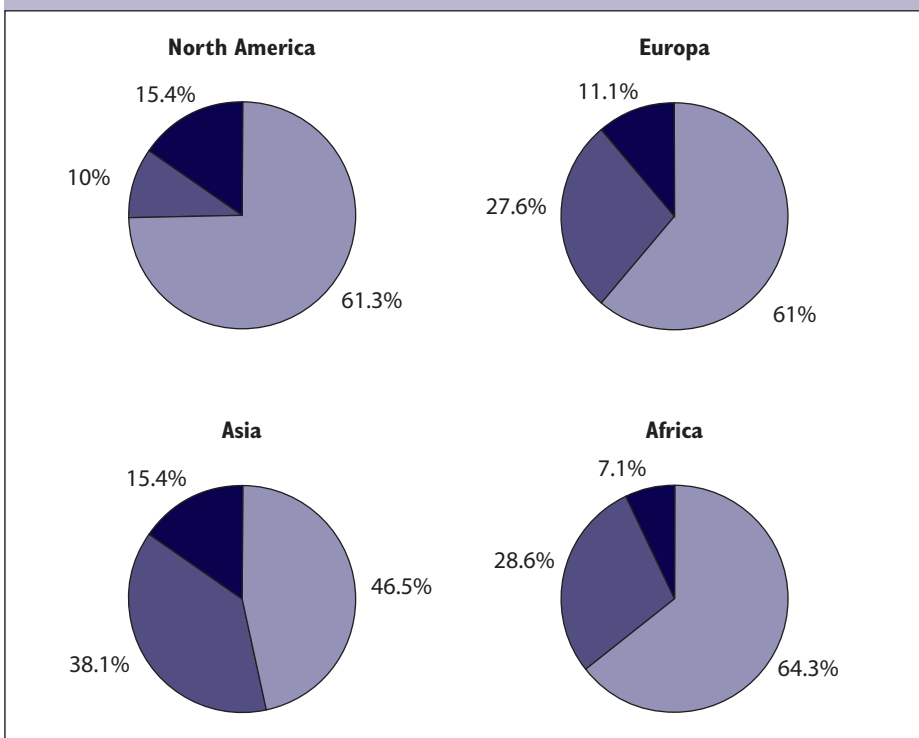
#### Reversible dementia syndromes

- ◆ Toxic encephalopathy
- ◆ medication induced
- ◆ substance abuse (alcohol and others)
- ◆ Metabolic encephalopathy
- ◆ electrolyte, hepatic and renal disorders
- ◆ thyroid insufficiency, B-12 deficiency
- ◆ hyperparathyroidism or pseudohyperparathyroidism
- ◆ Chronic subdural hematoma
- ◆ Normal pressure hydrocephalus
- ◆ Chronic meningitis
- ◆ Paraneoplastic disorder

#### Progressive dementia syndromes

- ◆ Alzheimer disease
- ◆ Vascular dementia
- ◆ AD and VaD

**Figure 2 Prevalent Dementia cases: Proportion of different dementing disorders in different continents**



- ◆ Diffuse Lewy body disease
- ◆ Pronto-temporal Dementia
- ◆ Parkinson disease
- ◆ Creutzfeldt-Jakob disease
- ◆ Genetic: Huntington's Chorea
- ◆ Paraneoplastic limbic encephalitis

### Conditions which can be mistaken for dementia

#### Drugs

Amongst the most common and reversible illnesses that can be mistaken for dementia are adverse drug reactions, depression and delirium.

The effects of drugs are the most common cause of reversible dementia. The overall incidence of adverse drug reactions and interaction in older patients is 2 to 3 times that found in young adults. Older patients have many characteristics that make them more sensitive to the negative effects of drugs on the CNS, such as poor compliance, polypharmacy, increase disease severity, reduced cardiac output, diminished renal clearance and liver function. Older patients are particularly sensitive

to cognitive impairment produced by psychoactive and other drugs with anticholinergic effects.

One of the most common drug effects is that related to Benzodiazepines. Benzodiazepines may impair memory function in two distinct ways. **Firstly**, it may cause acute amnesia for a period of time following a high dose. **Secondly**, it may cause a chronic impairment of recall that persists throughout long-term Benzodiazepine administration. (American Psychiatric Association). Other less typical medications associated with memory dysfunction include anticholinergics, antidepressants, antiepileptic, antihistamines, antiparkinsonian drugs, antipsychotics, antihypertensive drugs, immunosuppressive and others.

#### Depression

The second most common treatable cause of dementia is depression, which is a common illness among older age groups and may be present with cognitive impairment. Depression in elderly patients may be masked and may go unrecognized by the patient as well as

their family. The presence of appetite changes, weight loss, disturbance of sleep patterns, mood disturbance and a history of depressive illness may assist in the recognition of dementia with depression. In addition, depressed patients with cognitive impairment more often are quite vocal in their complaints concerning the deficit that distinguishes them from patients with AD. A skilled bedside mental status examination or detailed neuropsychological assessment is necessary to differentiate memory impairment due to depression as opposed to dementia. The progress of the disease is helpful in the differentiation between AD and depression. In depression the progression is rapid whereas in AD it is slow. Finally the response to Anti Depressants might be helpful in the differentiation between the two conditions.

Depression is probably thought to be the most frequent cause of misdiagnoses of dementia.

When a person suffers from a depression rather than a dementia there tends to be a history of depression either in their own life or within their family, and more often than none an external cause (a life event such as bereavement or other loss). People who are depressed are more likely to experience a range of what doctors call somatic problems such as waking early, to be more depressed in the morning than later on and to move

medication and see if they improve.

The relationship between depression and dementia is a complex one, however. For instance, a person may well have both dementia and depression, thus making diagnosis very difficult.

### **Delirium (Acute Organic Brain Syndrome)**

*Possible reasons for delirium:*

- 1 Acute confusional states. These can be caused by infections (especially urinary tract infections and chest infections), congestive heart failure, hypothyroidism, diabetes, and B12 deficiency, concussion and some drugs.
- 2 Chronic confusional states. These can occur in terminal cancer, kidney and liver failure as toxic matter builds up in the body.
- 3 Anxiety.
- 4 Speech difficulties.
- 5 Resentment and anger.
- 6 Grief.
- 7 Depression.

Delirium is a reversible state of disorientation, behavioral disturbance with visual hallucinations and clouding fluctuation of consciousness. That is definitely the main differing point from dementia, which by definition should be in clear consciousness. Delirium usually has sudden onset within hours and in some cases takes a slower rate of a few days, it results from infections, tumors, organ failure, metabolic causes, drugs and withdrawal of alcohol or Benzodiazepines and Opiates.

A common clinical problem, is the presentation of Delirium on top of the dementing process, once delirium is diagnosed and treated, dementia will emerge. This picture is usually encountered when mildly demented patients have a small stroke or infection or are subjected to polypharmacy.

### **Age-Associated Memory Impairments (Benign forgetfulness):**

Deterioration of memory functions with aging is well known, which could

resemble mild dementia. People with fear of dementia because of family history or hypochondriacal tendency could seek professional help to be assured that they are not dementing. Such a question is not heard from those who are really dementing. But assessment of cognitive functions and some investigations are necessary in order to make a clear differentiation.

### **The Ganser Syndrome (Prison Psychosis):**

This is a rare condition in which the patient answers past the points and gives approximate responses, which is rather different from dementia.

### **Hysterical pseudodementia and Simulated dementia:**

Criminals referred for assessment usually present these in forensic psychiatry. A good psychiatric interview and proper mental state evaluation is usually sufficient to rule out dementia, as in these conditions people present the picture of dementia which is different from its clinical picture, relying on the public image of insanity.

### **Specific sub-diagnostic types of dementia**

Three main subtypes of dementia are distinguished:

- a) Dementia of the Alzheimer's type (DAT);
- b) Vascular dementia also known as multi-infarct dementia (MID); and Lewy-body dementia (DLB).

These illnesses are generally characterized as having the following characteristics:

### **Dementia of the Alzheimer's type (DAT)**

This form of dementia is perhaps the most common, with studies suggesting that up to two-thirds of all dementias fall within this category. DAT is thought to result from neurological changes

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and react more slowly. They also tend to make self-incrementing remarks and have a lower opinion of their own abilities than is actually the case. Often the best test of whether a person has depression rather than dementia is to start them on a course of anti-depressant

(Amyloid plaques and neurofibrillary tangles) within the brain.

It is a slow progressive dementia in which usually a memory disorder is the presenting symptom. Memory impairment is the cardinal feature in early stages of DAT and is characterized by difficulty in learning and retaining new information. With advancing disease, learning is further compromised and retrieval of even highly learned ("remote") memories is lost. Other cognitive deficits early in the disease process include impaired judgment, and executive abilities and temporal or spatial disorientation; rarely, "focal" deficits of language, praxis, or visuospatial function may appear early. The cognitive losses caused by DAT interfere with usual functions. Patients misplace important

items, forget appointments, become easily disoriented, have difficulty managing finances or medications, and have problems using appliances and performing complicated tasks (meal preparation; driving an automobile).

As the disease advances, problems with language, calculations, visuo-spatial functions, and praxis become increasingly apparent. Behavioral alterations such as depression, agitation, delusions, anxiety, and hallucinations may become evident at any time during the course of the illness. The frequency of seizures, usually of generalized onset, varies widely in DAT, but generally occurs in much less than 10% of patients, and rarely as the initial feature. Using the NINCDS-ADRDA or other criteria, with suitable laboratory and diag-

nostic studies, at least 80 to 90% accuracy in the clinical diagnosis of DAT can be achieved. DAT is distinguishable from vascular dementia (absence of focal neurological deficits and absence of step-wise deterioration), DLB (absence of prominent visual hallucinations and parkinsonism early in the course), and the tauopathies and FTD (absence of disturbed social conduct, nonfluent aphasia, and extrapyramidal dysfunction early in the course). Other dementing illnesses such as communicating hydrocephalus and Creutzfeldt-Jakob disease are distinguished from DAT by the absence of gait disturbances and incontinence early in the course in the former and by the absence of a rapidly progressive course in the latter.

#### **Vascular Dementia or Multi-Infarct Dementia**

In Vascular Dementia (VaD) symptoms generally appear when a certain volume of infarcted tissue is present or if small strokes are strategically placed. Features suggestive of vascular dementia such as the sudden onset of dysfunction in one or more cognitive domains with a multifocal distribution of deficits and a step-wise deteriorating course are suggestive of a vascular etiology. Changes in mood and psychiatric presentations along with gait disturbance and early incontinence are suggestive of vascular dementia. There are patterns of MRI findings that are suggestive of a vascular contribution to the dementing picture.

#### **NINCDS-AIREN criteria for vascular dementia**

**Possible Vascular Dementia:** Dementia in the absence of either neuroimaging evidence of infarction or in the absence of a clear temporal relationship between dementia and stroke.

**Probable Vascular Dementia:** dementia defined by cognitive decline from a previously higher level in 3 areas of function including memory; evidence of

cerebrovascular disease by neurologic exam and neuroimaging; and the onset of dementia either abruptly or within 3 months of a recognized stroke.

**Definite Vascular Dementia:** Clinical probable vascular dementia plus histopathological evidence of infarction in the absence of other histological markers of dementia (e.g. plaques, tangles. Pick bodies, etc)

**Alzheimer's disease with cerebrovascular disease:** reserved for patients with possible AD who have imaging evidence for infarction, or clinical history of stroke, both of which appear incidental by clinical judgment.

Emphasis that NINCDS-AIREN-Type criteria lead to diagnostic accuracy confirmed by autopsy in up to 80% of patients with dementia.

As Bowler and Hachinsky pointed out in their editorial in the Sept 2000 issue of "Archives of Neurology", the most critical unresolved matter is in the identification of mixed dementia with elements of both VaD and DAT, which accounts for about 15 to 20% of cases of dementia. An absolute diagnosis of mixed dementia in such cases is almost impossible to ascertain clinically and can be made only on neuropathological grounds, although, clinically, improved mentation associated with treatment of any vascular risk factors supports a vascular component, while improved mentation associated with Cholinesterase inhibitors supports an Alzheimer's component. However, even in the field of neuropathology, considerable problems have arisen, so that it's not only difficult to define mixed dementia of VaD and DAT on clinical grounds, but even the final neuropathological diagnosis itself is associated with major difficulties.

#### **Dementia with Lewy-Body (DLB)**

Lewy-Body is an intracytoplasmic inclusion seen classically in Parkinson's Disease, mainly in the substantia nigra, Locus Cereleus and dorsal motor nucleus of the Vagus nerve. Cases desig-

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nated as Diffused Lewy-Body disease demonstrate wide spread cortical and subcortical Lewy-Body formation.

Clinically, DLB is often mild at the outset and can be extremely variable from day to day. Patients with DLB experience the early appearance of what is known as extrapyramidal symptoms (difficulty in initiating movements and physical rigidity) which do not respond to medication with dopamine (unlike most symptoms of this sort, for instance those due to Parkinson's disease). The person with DLB may also be extremely confused, experiencing delusions and hallucinations. In many ways the duration of the illness and the sort of cognitive impairments found in people with DLB are similar to those of people with Alzheimer's disease.

Dementia with Lewy-Bodies (DLB) is a recently recognized cause of dementia that overlaps clinically and pathologically with DAT and Parkinson's Disease.

### Differentiation between DLB and DAT

- ◆ DLB exhibits a more rapid course
- ◆ Age of onset is younger in patients with pure diffused DLB
- ◆ Marked variation in cognitive function with pronounced variation in attention and alertness in DLB
- ◆ Neuroleptic sensitivity in DLB
- ◆ Visual Hallucination present in 40 to 75% of patients with DLB as compared to 5 to 20% in DAT.
- ◆ Presence of Extrapyramidal symptoms

### Differentiation between DLB and PD

- ◆ Resting tremor is rare in DLB
- ◆ Bradykinesia and rigidity are present bilaterally and symmetrically in DLB
- ◆ Older age at onset in DLB
- ◆ Shorter disease duration in DLB
- ◆ Lower rate of clinical responsiveness to L-Dopa in DLB

### Consensus criteria for clinical diagnosis of probable and possible DLB

- 1 The central feature required for a diagnosis of DLB is progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in early stages but is usually evident with progression. Deficits in tests of attention and of frontal-subcortical skills and visuospatial ability may be especially prominent.
- 2 Two of the following core features are essential for a diagnosis of probable DLB, and one is essential for possible DLB:
  - a Fluctuating cognitive with pronounced variations in attention and alertness
  - b Recurrent visual hallucinations that are typically well formed and detailed
  - c Spontaneous motor features of parkinsonisms
- 3 Features supportive of the diagnosis are:
  - a Repeated falls
  - b Syncope
  - c Transient loss of consciousness
  - d Neuroleptic sensitivity
  - e Systematized delusions
  - f Hallucinations in other modalities

Levodopa or other dopaminergic therapy do run the risk of worsening the confusional syndrome in the dementing condition.

But if the therapy proves beneficial for motor symptoms, it can be considered, although the control of psychotic symptoms by neuroleptic could worsen the extrapyramidal features, although in past decades Clozapine as a typical Neuroleptic, has been used successfully because it is devoid of Extrapyramidal side effects.

### Conclusion

The diagnosis and the differential diagnosis of dementia, although sounding to

be a straightforward issue in practice and in research is not necessarily so. It seems that the age of 60 is the cut off point for the elderly in the Middle East, but 65 is the age in Europe and U.S.A., 20% to 25% have a reversible dementia (Hecht). The early and accurate diagnosis of the cause of memory loss is vital, as many of these conditions are treatable. Some studies, wrongly consider the dementia as equivalent to Alzheimer's dementia, the tools of diag-

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