Dementia
Backgrounder

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Introduction

In broad terms, ***dementia*** refers to cognitive and/or psychological deterioration associated with organic brain dysfunction. Dementia is more prevalent in the elderly, and the prevalence of dementia is increasing in the United States and the world as the population of individuals born after World War II (often referred to as the "baby-boomers") ages. This increase has far-reaching repercussions on health care and its delivery worldwide.

This backgrounder will define the types of dementia and will describe their impact on both the individuals who suffer from it and their caregivers. While the etiology of dementia remains to be clearly defined, prevailing theories of its pathophysiology will be related.

Recognition of dementia is not always straightforward; the disease is often insidious and differential diagnosis is complex. Current evaluative methods and diagnostic criteria will be described in accordance with current clinical standards of practice. Nonpharmacologic and pharmacologic treatment will be explained, along with the role of the caregiver in therapy.

Dementia Defined

Dementia refers to a broad clinical syndrome that involves deterioration of intellectual abilities due to impairment of the CNS.

Dementia refers to a broad clinical syndrome that involves deterioration of intellectual and cognitive abilities.[1] Pathogenesis is due to impairment of, or damage to, the central nervous system (the brain), but the exact dysfunction is not always easily defined.

Cognitive abilities are those that encompass the "knowledge" of events that continually occur during consciousness. When cognitive abilities are impaired there is diminished perception, recognition, idea or thought conception, judging, sensing, reasoning, and imagining. Memory of events, both recent and long-term, is impaired, and the ability to think abstractly and make appropriate judgments declines. Mental deterioration often is progressive, eventually leading to alterations in personality and diminished capacity to perform the most basic activities of daily living (ADL). Independent living may become unsafe for the patient, his or her environment, and caregivers. Depending on the individual patient's support system, institutionalization may be inevitable.

Primary dementias are those for which no other identifiable disease or condition can be found as the cause of the syndrome.

Etiology[1]

Dementia is characterized as an organic brain syndrome. *Organic brain syndrome* is a general term used to describe conditions of impaired mental function that are associated with diseases of the central nervous system. This contrasts with the majority of psychiatric syndromes which are called *functional* and have no physical basis. Dementias are classified into 2 types; secondary dementias occur as part of some other pathological process, and primary dementias are those dementias that the major abnormality is the dementia.[1]

Secondary dementias are those for which a pathological process has been found as the cause, eg, infections, trauma, toxic/metabolic disorders, circulatory disorders, brain tumors, or neurological diseases or conditions.

Table 1.
Classification of Dementias

Primary Dementias
Alzheimer's disease
Pre-senile dementia (before age 65)
Senile dementia (after age 65)
Pick's disease

Secondary Dementias
Infections
Chronic granulomatous meningitis (tuberculous, fungal)
Advanced syphilis
Creutzfeldt-Jakob disease (transmissible virus dementia)
Acquired immunodeficiency syndrome (AIDS)
Trauma, eg, subdural hematoma
Toxic and metabolic disorders
Pernicious anemia
Folic acid deficiency
Hypothyroidism
Bromide poisoning
"Alcohol" (withdrawal, Vitamin B1 deficiency)
Circulatory disorders
Multi-infarct dementia
Cerebral ischemia leading to brain anoxia
Brain tumors
Other neurological diseases
Huntington's chorea
Parkinson's disease
Parkinson-dementia complex
Progressive supranuclear palsy
Multiple sclerosis
Cerebellar degeneration
Normal pressure hydrocephalus

Seltzer B. Organic mental disorders. In: Nicholi AM, ed. *The New Harvard Guide to Psychiatry*. Cambridge, Mass: Belknap Press; 1988;358-383.

Prevalence

Alzheimer's disease represents 50% to 75% of dementia cases. Approximately 4 million Americans suffer from AD.

Vascular dementia is probably the next most common, but its prevalence is unknown.

While prevalence data for dementia vary depending on the definitions and criteria used, generally accepted data according to age are shown in Table 2.[2] Alzheimer's disease is the most common type of dementia; vascular dementia is probably the next most common, but its prevalence is unknown.[2]

Table 2.
Prevalence of Dementia

Age Group	Percent
Over 65 years	5% to 8%
Over 75 years	15% to 20%
Over 85 years	25%

American Psychiatric Association. Practice Guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. *Am J Psychiatry* 1997;154(suppl 5):1-39.

Alzheimer's Disease

Typical initial presentation of AD includes memory loss of recent events, and confusion and disorientation, eventually leading to deterioration in general health that greatly increases morbidity and mortality. Average survival is 8 to 10 years after diagnosis.

Alzheimer's disease (AD) is the most common of the dementias, accounting for 50% to 75% of all dementias.[2] Approximately 4 million people in the United States currently suffer from Alzheimer's disease.[3] AD can occur early, in the 40s and 50s, but typically presents after the age of 60.[2] AD also may be referred to as pre-senile or senile dementia, depending on whether it occurs before or after the age of 65.[1]

The course of AD is progressive.[2] Disease onset and course typically are gradual. Typical initial presentation includes memory loss of recent events, and confusion and disorientation, eventually leading to deterioration in general health that greatly increases morbidity and mortality. Average survival is 8 to 10 years after diagnosis.[4] Decline is progressive with occasional periods of stability that can last as long as a year or more.[2]

MID:
Multi-infarct dementia
Vascular dementia

Multi-infarct (Vascular) Dementia

Multi-infarct dementia (MID), also called vascular dementia, stems from one or more episodes of cerebral ischemia, which cause brain damage that leads to dementia. Risk factors for MID include advanced age plus those for general stroke and other cardiovascular disease (ie, cigarette smoking, high blood pressure). MID typically begins in the same ways as Alzheimer's disease, but MID can have an abrupt onset and a more fluctuating course.[4] MID accounts for approximately 10% to 20% of dementia cases.[4] AD and strokes often coexist.[2]

Risk Factors

The major risk factors for dementia include advanced age, family history, and presence of the apolipoprotein E gene.

The major risk factors for dementia include advanced age, family history, and presence of the apolipoprotein E gene.[5]

Advanced Age

From the age of 65 to 85, the prevalence of AD doubles approximately every 5 years.[5]

Family History

Individuals with first-degree relatives who have suffered from AD have a four times greater risk than others in the general population at any age.[5]

Apolipoprotein E Gene

The presence of the apolipoprotein E (APOE) gene has been found to correlate with both the prevalence and age of onset of AD, but not its clinical outcome.[5] The APOE gene is not found in all patients with dementia and all patients with dementia do not have APOE; therefore, it is important to recognize that the presence of APOE is a risk factor and not a diagnostic test.[5]

Other Risk Factors

Other risk factors for dementia that have been suggested, but not proven, include: history of head trauma; episodic depression or personality disorder; and mutations on chromosomes 21 or 14.[5] Differences of opinion exist about socioeconomic variables as risk factors for dementia. It has been suggested in one study that gender (females), limited education, and unskilled occupations were at greater risk for vascular dementia, and to a lesser degree AD, but this is not conclusive.[5]

Diagnosis

There are no definitive clinical or laboratory tests to diagnose dementia, but with a careful clinical workup skilled clinicians can make an accurate diagnosis in 90% of cases.

There are no definitive clinical or laboratory tests that can be used to diagnose dementia, but with a careful clinical workup skilled clinicians can make an accurate diagnosis in 90% of cases.[3] A diagnosis of dementia is made by combining patient history, family and patient interviews, cognitive screening, and a neuropsychologic examination (Table 3). The clinical challenge is to correctly distinguish cognitive changes due to normal aging from those due to dementia or another disorder, such as depression (Table 4).[6,7,8]

Table 3.
Diagnostic Evaluation for Dementia

Assessment	Information Sought
History	
• Family history	History of Alzheimer's disease, Parkinson's disease
• Caregiver interview/evaluation of patient's previous and current cognitive abilities	**Aphasia** • Has difficulty finding correct word • Substitutes incorrect words • Breaks off in midsentence; loses train of thought • Stutters/repeats words over and over **Apraxia** • Difficulty in dressing or bathing alone • Difficulty in using a brush or comb • Difficulty in self-feeding **Agnosia** • Loses ability to recognize people, places, things **Executive dysfunction** • Difficulty in understanding activities around him/her • Difficulty in using familiar tools, such as appliances, eating utensils **Changes in behavior or personality** • Passivity, apathy • Aggression, agitation, disinhibition

Table 3 continues on the next page

Table 3. (continued)
Diagnostic Evaluation for Dementia

Assessment	Information Sought
History (continued)	
• Review of medications, substance abuse	Use of antidepressants, sedatives/hypnotics, anticonvulsants, anti-parkinsonian drugs, antihypertensive agents, antihistamines, narcotics, past and present alcohol use
• Physical	Onset of symptoms, progression of symptoms, duration of symptoms, other acute or chronic medical disease, known neurological and psychological disorders, substance abuse, exposure to environmental toxins
Laboratory panel • CBC, urinalysis, electrolytes, calcium, urea, creatinine, hepatic enzymes, thyroid hormones, B_{12}, serology for syphilis, HIV, metabolic profile	Detection of anemia, diabetes, renal disease, liver disease, thyroid disease, vitamin deficiency, syphilis, infection, AIDS, metabolic disorder, blood disorder, endocrine disease, etc.
• Genetic testing (apolipoprotein E [APOE]) (Not a diagnostic test)	Genetic predisposition
Neurological imaging and other tests • Computed tomography (CT) • Magnetic resonance imaging (MRI) • Lumbar puncture • Electroencephalogram (EEG) • Single-photon emission computed tomography (SPECT) • Positron emission tomography (PET)	Rule out brain tumors, brain abscess, stroke, hematomas, arteriovenous malformations, hydrocephalus
Neuropsychological testing • Attention and concentration • Orientation to time, person, place, situation, and general insight • Intellect • Learning and memory • Language • Visuospatial function • Executive functioning: abstract ideation, creativity, multitasking, and behavioral flexibility • Bilateral sensorimotor function • Mood and personality	Degree and types of impairment, if any

Steffens DC, Morgenlander JC. Initial evaluation of suspected dementia. *Postgrad Med* 1999;106(5):73-83.
Daly MP. Diagnosis and management of Alzheimer's disease. *J Am Board Fam Pract* 1999;12(5):375-385.

Table 4.

Approximate Degree of Cognitive Impairment Associated with Aging, Alzheimer's Disease, and Depression

Cognitive Feature	Normal Aging	Early Alzheimer's Disease	Depression
Attention			
Selective	+	++	+++
Nonselective	++	+++	+++
Learning and Memory			
Learning	+	++	+++
Retrieval	++	++	+++
Immediate memory	N	N	+++
Recall	+	++++	+++
Recognition	N	++	N
Working memory	+	+++	+++
Intellect			
Nonverbal IQ	++	+++	+
Verbal IQ	N	N	N
Language			
Naming	N	+	N
Fluency	N	+	++
Comprehension	N	N	N
Calculation	N	++	N
Visuospatial ability			
Perception	+	+	N
Spatial judgment	N	++	N
Praxis	N	++	N

N = normal
+ = mild impairment
++ = moderate impairment
+++ = severe impairment
++++ = very severe impairment

Welsh-Bohner KA, Morgenlander JC. Determining the cause of memory loss in the elderly. *Postgrad Med* 1999;106(5):99-119.

Diagnosis

After history and physical examination, certain findings should raise suspicion that dementia is not caused by Alzheimer's disease (Table 5).

Table 5.
Findings that Exclude Diagnosis of Alzheimer's Disease

Findings Obtained by History-Taking	Possible Explanation
Sudden onset	Systemic disease, drug adverse effects, cerebrovascular disease, infection, tumor
No memory deficit	Psychiatric disorder, cerebrovascular disease, early frontal lobe dementia
Lack of progressive decline	Stroke, amnesic syndrome
Depression	Pseudodementia secondary to dementia
Personality change with minor memory deficits	Frontal lobe dementia
Seizures	Stroke, cerebral lesions (seizures are uncommon in the early stages of Alzheimer's)
Findings Obtained by Physical Examination	**Possible Explanation**
Hemiparesis (inability to move on one side of the body)	Cerebrovascular disease, lesion
Sensory impairment	Cerebrovascular disease or peripheral vascular disease
Memory loss without other deficits	Cerebrovascular disease, Wernicke's encephalopathy
Abnormal motor movements	Huntington's disease, Creutzfeldt-Jakob disease, Parkinson's disease
Early gait disturbance	Parkinsonian disease or normal pressure hydrocephalus (especially if incontinence also present)
Cerebral abnormalities	Spinocerebellar degeneration (usually genetic)

Burke JR, Morgenlander JC. Update on Alzheimer's disease. *Postgrad Med* 1999;106(5):86-96.

Memory impairment and other symptoms of dementia also can be symptomatic of psychiatric diseases.

Furthermore, since memory impairment and other symptoms of dementia can also be symptomatic of other psychiatric diseases, such as delirium, amnesic disorders, mental retardation, schizophrenia, and major depressive disorder, the diagnosis of dementia must meet specific DSM-IV criteria (Table 6).

Table 6.
DSM-IV Diagnostic Criteria for Alzheimer's and Vascular Dementia

Alzheimer's Dementia

To be given a diagnosis of ***Alzheimer's Dementia***, the patient must have:

A. Multiple cognitive deficits, as follows:
   1. Memory impairment
      – Impaired ability to learn new information or to recall previously learned information
   2. One (or more) of the following cognitive disturbances:
      a. Aphasia (language disturbance)
      b. Apraxia (impaired ability to perform motor activities despite intact motor function)
      c. Agnosia (failure to recognize or identify objects despite intact sensory function)
      d. Disturbance in executive functioning (ie, planning, organizing, sequencing, abstracting)

B. The cognitive deficits must each cause severe impairment in social or occupational functioning and represent a major decline from a previous level of functioning.

C. Onset of the disease must have been gradual, with progressively worsening cognitive decline.

D. The cognitive deficits in criteria A1 and A2 must not be due to any of the following:
   1. Other central nervous system conditions that cause progressive deficits in memory and cognition (for example, cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor).
   2. Systemic conditions known to cause dementia (for example, hypothyroidism, vitamin B_{12} and folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV [human immunodeficiency virus] infection).

E. The deficits do not occur exclusively during the course of a delirium.

The disturbance is not better accounted for by another axis I disorder (eg, major depressive disorder, schizophrenia).

Vascular Dementia

To be given a diagnosis of ***Vascular Dementia***, the patient must have fulfilled Criteria A & B and E above ***and*** there must be evidence of:

- Focal neurological signs and symptoms (eg, exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity), or
- Laboratory evidence indicative of cerebrovascular disease that is judged to be etiologically related to the disturbance (eg, multiple infarctions involving cortex and underlying white matter).

AD or vascular dementia may be subtyped according to prominent associated symptoms:

- With Delirium
- With Delusions
- With Depressed Mood
- Uncomplicated
- With Behavioral Disturbance

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: (DSM-IV)*, Washington DC; American Psychiatric Press, 1994:(4)142-146

Interdisciplinary and Multidisciplinary Team

Because of the insidious nature of dementia, the primary care physician (PCP) is often the first clinician to perform the differential diagnosis for dementia. When patients or family members describe problems of cognitive impairment, the PCP must consider dementia as a possibility and begin clinical assessment, usually with initial interviews with the patient and his or her family, and using some type of diagnostic screening tool and/or cognitive rating scale (Table 7). As evaluations reveal positive findings for dementia, and/or cognitive deterioration accelerates, the PCP will eventually refer the patient to a neurologist or psychiatrist for a thorough neuropsychologic evaluation (Figure 1) and involve other professionals in the treatment of the patient (Table 8).

Evaluation is meant not only to determine if the dementia is primary or secondary, but also to determine the level of cognitive impairment.

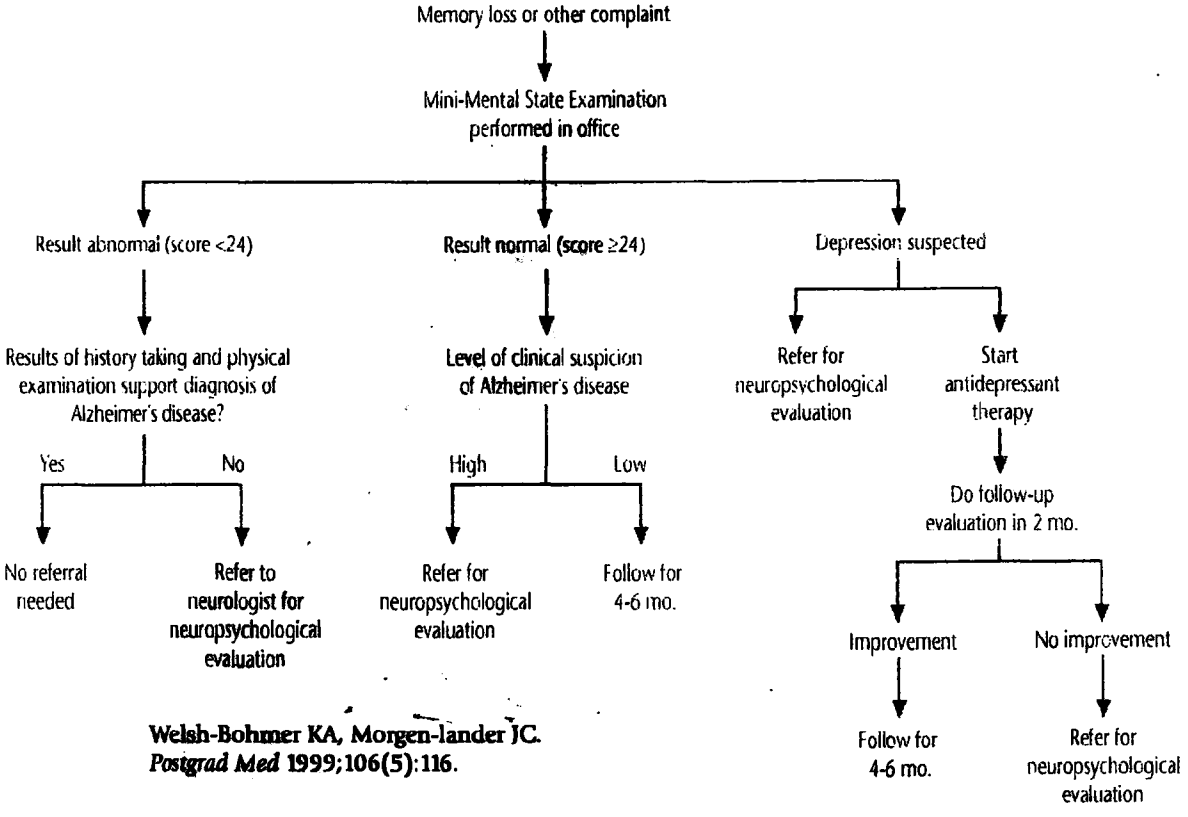
Table 7.
Diagnostic Tools for Dementia [5,6]

- DSM-IV criteria
- NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association) criteria
- World Health Organization Diagnostic Criteria for Vascular Dementia (International Classification of Diseases, 10th edition)
- Mini Mental State Examination (MMSE)
- Geriatric Depression Scale

Table 8.
Interdisciplinary and Multidisciplinary Team

Primary care physician
Geriatrician
Neurologist
Neuropsychologist or psychiatrist
Nurse
Social worker
Physical or occupational therapist

A thorough evaluation as delineated in Table 3 is important, not only to determine if the dementia is primary or secondary to another treatment or disease that may be correctable, but also to determine the level of cognitive impairment.



Welsh-Bohmer KA, Morgen-lander JC.
***Postgrad Med* 1999;106(5):116.**

Figure 1.
Decision Tree for Dementia Evaluation and Referral

Staging of Dementia

Questionable
Mild
Moderate
Severe
Profound
Terminal

Staging of Dementia[2]

Dementia is typically categorized in stages according to the level of functional impairment, ie, the ability to perform certain functions compared to the patient's previous level of functioning.

The following categories may be used to describe the level of functional impairment, and the same categories may be used to describe the degree of severity of any dementia.

Questionable

- No definite functional impairment
- Dementia is not diagnosed
  - May or may not progress to dementia
- Re-evaluation at appropriate intervals

Mild

- Definite but mild impairment, eg, difficulties with balancing checkbook, following complicated recipes, or medication regimens

Moderate

- Impairment causes difficulties with functional tasks, eg, simple meal preparation, household cleanup, raking leaves and other yard work, may require assistance with self-care (reminding to use bathroom, shaving, fastening clothing).

Severe

- Impairment necessitates help with many aspects of self-care and activities of daily living (ADL), eg, eating, grooming, bathing, and using the toilet.

Profound

- Patients may become oblivious to their surroundings and are almost totally dependent on caregivers.

Terminal

- Impairment necessitates continual care. Patients are generally bed bound, may be susceptible to accidents and infectious diseases, which often prove fatal.

Presentation of Specific Dementias[2]

While the various dementias have major commonalities, there are some differences in the patterns of presentation.

Specific Dementia Presentations

Alzheimer's dementia
Vascular dementia
Dementia due to
Parkinson's disease
Dementia due to
Lewy Body disease
Dementia due to
frontal lobe dementia
(Pick's disease)
Other progressive dementias
Dementia due to other causes

Alzheimer's Dementia

- Gradual onset and progression
- Usually begins with impairment of recent memory. Impairment in the following areas follows over several years:
  - Aphasia (impaired language/speaking)
    - In normal conversation, does the patient: have difficulty finding the right word to use; substitute an incorrect word, eg, calling a table a chair; break off in midsentence and lose his or her train of thought; stutter or repeat the same word over and over?[8]
  - Apraxia (impaired movement despite intact motor function)
    - Does the patient have any difficulty with dressing or bathing, or using a brush or comb, or using feeding utensils?[8]
  - Agnosia (impaired recognition/identification of objects despite intact sensory function)
    - Does the patient have difficulty recognizing familiar people or places, objects or personal items?[8]
- Impaired "executive" functioning also present in early phases, eg, inability to plan, organize, sequence, think abstractly
- Personality changes or increased irritability may occur in early stages
- Psychotic behavior is common in middle and late stages
- Incontinence, and gait and motor impairment typically lead to patient becoming totally bedridden

- Seizures and myoclonus may occur in advanced stages
- May be subtyped by predominant features: with delirium, with delusions, with depressed mood, or uncomplicated[16]

Vascular Dementia

- Caused by one or more episodes of cerebral ischemia or stroke
- Abrupt onset may occur at any age, but less common after age 75
- *Stepwise course as opposed to gradual progressive decline of AD*
- Cognitive deficits depend on what area of the brain was damaged due to ischemia
- Imaging studies may find multiple vascular lesions in the cerebral cortex and subcortical structures
- As with AD, may be subtyped as With Delirium, With Delusions, With Depressed Mood, Uncomplicated, and With Behavioral Disturbance[16]

Dementia Due to Parkinson's Disease

- Parkinson's disease
  - Progressive neurological disease typified by tremor, rigidity, bradykinesia (slow movement), postural instability
  - Onset middle to late in life
- 20% to 60% of Parkinson's disease cases will be accompanied by dementia
- Dementia usually occurs late in the course of Parkinson's disease

Dementia Due to Lewy Body Disease

- Clinically similar to Alzheimer's disease
  - Visual hallucinations and parkinsonian features occur earlier and are more prominent than in AD
- More rapid evolution than AD
- Biopsy of cerebral cortex demonstrates Lewy inclusion bodies
- May account for 7% to 26% of dementia cases
- Patients are very sensitive to the ***extrapyramidal*** (pronounced extra-pyr-RAM-ih-dahl) ***effects*** of antipsychotic medications.

Dementia Due to Frontal Lobe Dementias (eg, Pick's Disease)

- Difficult to diagnose and differentiate from atypical AD
- Brain imaging shows atrophy of frontal and/or temporal lobes
- Diagnosis is confirmed at autopsy by finding characteristic Pick inclusion bodies in the brain
- Onset usually between age 50 and 60, but can occur in older population
- Progressive course that is more rapid than AD
- Early stages
  - Personality changes
  - Executive function impairment
  - Deterioration of social skills
  - Emotional blunting
  - Lack of behavioral inhibition
  - Language abnormalities
- Follow later in the course:
  - Memory deficits, apraxia, and other symptoms of dementia
  - Primitive reflexes (eg, snout, suck, grasp)
  - Either apathy or extreme agitation

Other Progressive Dementias

- Huntington's disease
  - Hereditary neurological disease that causes motor, behavioral, and cognitive deterioration
- Creutzfeldt-Jakob disease
  - Rapidly progressive disease of the brain caused by a slow virus or prior infection

Dementia Due to Other Causes

- Structural lesions
  - Brain tumor or subdural hematoma, normal pressure hydrocephalus (NPH)
- Head trauma
- Endocrine disorders
  - Hypothyroidism, hypercalcemia, hypoglycemia
- Nutritional deficiencies
  - Thiamin, niacin, vitamin B_{12}
- Infectious diseases
  - HIV, neurosyphilis, *Cryptococcal meningitis*
- Effects of medication
  - Benzodiazepines, beta-blockers, diphenhydramine (anti-allergy medication)
- Toxic effects due to long-term substance abuse, especially alcohol
- Derangements of renal and hepatic function
- Neurological conditions
  - Multiple sclerosis

Options to Facilitate Care

Once the diagnosis of dementia is made, treatment must begin as soon as possible. Treatment decisions are made in accordance with the stage of the dementia, symptoms present, and any other comorbid medical or psychiatric diseases and conditions. The goals of treatment[7] are interrelated and are to:

1) enhance the current functioning level;

2) maintain quality of life as long as possible; and

3) preserve independence as long as possible.

The medical, psychological, and social needs of the patient and caregivers must be part of the short-term and long-term treatment plan. A multidisciplinary team is necessary to delay and/or prevent the onset of comorbid medical conditions in the patient, to help caregivers and family members cope with the disease and its repercussions, and to help in short-term and long-term treatment planning.

Care Environment

The success of treatment, the presenting symptoms, and the stage of the illness determine whether the patient can be managed in a home setting or whether institutionalization is necessary. In addition, the presence of a caregiver and his or her ability to manage the patient must be considered.

Home Management

Home management requires a caregiver. In very early stages, part-time care and surveillance may be sufficient if steps are taken to simplify the home environment and make it safer. Several regional or national support organizations are now available to assist caregivers in their care of patients with dementia: Alzheimer's Association; Alzheimer's

Disease Education and Referral Center; Administration on Aging; and Children of Aging Parents.[7]

Safety-proofing the Home

In the early stages, patients may remain in the home, if:

- certain precautions are taken to ensure that the patient cannot accidentally harm him or herself or others;
- a spouse who does not have dementia is in the home; or
- a caregiver makes scheduled visits to check on the patient. A move to a small, one-story home will simplify the environment and eliminate stair hazards. The entire contents of the home must be examined, and potentially harmful utensils, tools, cleaning supplies, and furniture must be eliminated or locked away from the patient's access.

Adult Day Care[2]

Adult day care is similar to child day care in that patients may be dropped off at a facility for a certain period of time. Adult day-care facilities provide social stimulation and meals to patients with dementia in a safe, therapeutic environment.

Long-term Care Facilities[2]

Eventually, as dementia progresses, patients will require treatment in a long-term care facility either periodically or permanently, usually due to the progression of the illness, behavioral problems, or because the caregivers are unable to continue to care for the patient. Combativeness and physical violence tend to occur more often in the later stages of disease, often in response to frustration, misinterpretation, delusions, or hallucinations. If this behavior cannot be brought under control at

home, nursing home or hospital placement is necessary.

Table 9 lists the factors that have been shown to predict hospitalization.[5]

Table 9.
Factors that Predict Institutionalization in Patients with Dementia

Cognitive/behavioral problems, especially aggressive behavior, delusions, incontinence
Not married
Caregiver is son or daughter (especially if employed)
Large number of caregivers
High level of stress in caregiver
Poor health in caregiver
Increased use of health care or home help services
Increased functional impairments (by ADL scales)
Lower cognitive status at baseline
Death of spouse
Hospitalization
Prior institutionalization

Fleming KC, Adams AC, Petersen RC. Dementia: diagnosis and evaluation. *Mayo Clin Proc* 1995;70:1093-1107.

Group Living

Several types of long-term care facilities exist under a variety of names: group living (GL); residential care; group homes; and collective living. Group living was developed in Sweden in the 1980s[15] as a housing alternative in the management of dementia. GL units house six to nine patients, who are supervised by round-the-clock staff. GL units may be part of a nursing home or may be specially built facilities.

Symptoms

Estimates are that behavioral problems will occur in up to 90% of patients with dementia.[10] Psychiatric symptoms exhibited with dementia, especially in Alzheimer's disease, include: depression; suicidal ideation and behavior; hallucinations; delusions; anxiety; psychosis; agitation/aggression; disinhibition; sleep disturbances; and apathy/vegetation.

Agitation is broadly described as inappropriate verbal or motor activity that is not explained by apparent needs or confusion.[11] As shown in Table 10, as many as 50% of patients with dementia are likely to exhibit agitated behaviors during the course of their disease, and 25% to 33% may demonstrate aggressive behaviors.[10]

Table 10.
Behavioral Problems in Dementia Based on Worldwide Review of Literature

Behavior	Patients Affected % (Median)
Disturbed affect/mood	0-86 (19)
Disturbed ideation	10-73 (34)
Altered perception	
Hallucinations	10-90 (44)
Misperceptions	0-50 (18)
Agitation	
Global	21-49 (28)
Wandering	1-49 (23)
Aggression	
Verbal	11-51 (24)
Physical	0-46 (14)
Resistive/uncooperative	27-65 (14)
Anxiety	0-50 (32)
Withdrawn/passive behavior	21-88 (61)
Vegetative behaviors	
Sleep	0-47 (27)
Diet/appetite	12-77 (34)

Tairot PN. Treatment of agitation in dementia. *J Clin Psychiatry* 1999;60(suppl 0):11-20.

Neuropsychiatric Presentation of Agitation in Dementia[12]

The presence of agitation in a patient with dementia is serious and can be life-threatening. Since some types of agitation can be caused by medical conditions, attention to and treatment of any comorbid medical problems must be given, along with treatment of the agitation. (Treatment of agitation will be discussed later in the treatment section of this backgrounder.) Agitation associated with dementia can include one or more of several behavioral states.

Delirium

Delirium is a change in the patient's baseline mental status caused by a general medical condition. There is an impairment in the level of consciousness and cognition, which can fluctuate rapidly over minutes or hours. Delirium indicates the presence of a medical emergency requiring urgent identification and treatment..

Psychosis

A psychosis is said to occur when the inability of the patient to recognize reality causes severe confusion and the patient is unable to relate to and communicate with others in a normal way. Patients often believe they have had items stolen from them (because they have forgotten where they placed them), or that their spouse is having an affair (because the spouse was away on a trip). Hallucinations, altered perceptions of reality, may occur, and may be visual or auditory.

Depression

Depression in dementia patients may be mistaken because the symptoms resemble the symptoms of a general medical illness (e.g., weight loss, sleep disturbance, fatigue) or dementia (e.g., flat affect, loss of interest, poverty of speech).

Anxiety

Patients with generalized anxiety exhibit symptoms of anxiety through facial expressions, nervousness, fear, or physical complaints, such as palpitations or stomach disorders. Patients often express obsessive concern about heart or stomach pain, the safety of their belongings, or the whereabouts of their loved ones.

Insomnia

Insomnia is a common source of distress in the elderly who often sleep less and have reduced sleep efficiency as part of the aging process. Insomnia may be due to an identifiable cause, such as arthritic pain, and should be treated appropriately.

Sundowning

The clustering of agitation, confusion, and disorientation beginning in the late afternoon and becoming more severe at night is referred to as sundowning. Patients may wander, climb over bed rails, or behave in other ways that are unsafe.

Aggression or Anger Not Due to Other Causes

Anger that does not include physical aggression is considered mild. Anger that is accompanied by physical aggression, such as pushing, slapping, scratching, and extremely loud and extended yelling, is considered severe.

Treatment

There is no cure for dementia. Treatment goals are to maintain the independence and quality of life of the patient and the caregivers, as safely as possible, for as long as possible.

There is no cure for dementia. As stated previously, treatment goals are aimed at maintaining the independence and quality of life of the patient and the caregivers, as safely as possible, for as long as possible.

Nonpharmacologic Treatment

Nonpharmacologic treatment strategies can be used to enhance the patient's orientation and help him or her to avoid confusing situations, but they can only provide limited assistance in the daily care of the patient. This is why a multidisciplinary approach is necessary for the treatment and support of both the patient and caregiver. Nonpharmacologic treatments are listed in Table 11.

Table 11.
Nonpharmacologic Strategies for Management of Dementia [7,10,12]

Target	Activity
Family and caregivers	• Education program about dementia, short- and long-term management, course, and prognosis
	• Support groups
Physical and psychosocial environment	• Make patient's daily regimen routine and predictable
	• Minimize noise and disruptions in immediate environment
	• Control accessibility to certain rooms that are deemed unsafe, as well as doors to outside
	• Use a nightlight in the bedroom during sleep
	• Provide stimuli that increase patient awareness of time and place, eg, clocks, calendars, family pictures
	• Provide good daytime and evening lighting
Behavior management	• Reduce isolation
	• Identify activities or people who increase patient's agitation and minimize exposure
	• Provide continual verbal assurances
	• Provide a safe place for patient to pace
	• Encourage pleasant, calming activities, such as recreation, pets, arts

Pharmacologic Treatment[2]

Because most patients with dementia are of an advanced age, there are certain pharmacokinetic and pharmacodynamic factors that may affect medications that are prescribed. Some of these factors will make patients more susceptible to adverse events and/or drug interactions.

Special Considerations in the Elderly

The elderly population typically has decreased renal clearance and slowed hepatic metabolism. Therefore, lower starting doses, smaller increases in dose, and longer intervals between dosage increments should be used. This population can have multiple medical problems requiring multiple medication and attention should be paid to potential drug interactions and side effects. In some demented patients, medications can lead to worsening of cognitive impairment. Sedative effects of many medications can leave patients more prone to falls, and patients with AD or Parkinson's are especially susceptible to extrapyramidal side effects. For Depakote information, please see the WARNINGS section of the package insert.

Treatment for Cognitive and Functional Loss Due to Dementia

Goals

As stated earlier, there is no cure for dementia, but within the past ten years, several medications have become available that can be used to prevent further reduction in and/or restore cognitive and functional abilities to patients diagnosed with dementia.

Many medications are used in the treatment of dementia; however, it is important to note that some of the medications listed here do not have labeled indications for this use.

Cholinesterase inhibitors (tacrine, donepezil, and others)

Acetylcholine is a neurotransmitter that transmits impulses between the forebrain and the parts of the brain responsible for memory and information

processing.[3] The rationale for use of cholinesterase inhibitors in the treatment of dementia and specifically Alzheimer's disease is based on several known facts about acetylcholine and AD.

AD is accompanied by a loss of cholinergic neurons. The level of enzymes responsible for the synthesis of acetylcholine is reduced by 58% to 90% in selected areas of the brain. By inhibiting the enzyme *acetylcholinesterase (AChE)*, which hydrolyzes acetylcholine at the neuron, the concentration of acetylcholine at the nerve endings is increased; in some patients this can lead to improved cholinergic functioning and improved cognitive processing. The two cholinesterase inhibitors currently approved for AD in the United States are tacrine and donepezil.

Other drugs currently being investigated for their affect on cognitive functioning in the dementia patient include metrifonate, rivastigmine, and physostigmine.[7]

Side Effects of Cholinesterase Inhibitors

Cholinergic Excess

The most commonly experienced side effects with cholinesterase inhibitors are those associated with "cholinergic excess" (increased levels of acetylcholine).

- Mild to moderate nausea and vomiting occur in 10% to 20% of patients.
- Bradycardia (slow heart rate) may also occur, which can be dangerous for patients with cardiac conduction problems.
- Stomach acid may increase, which is a particular problem for those who already have a history of ulcer or who are taking NSAIDs.

Hepatotoxicity

Tacrine is associated with a direct medication-induced hepatocellular injury. Approximately 30% of patients develop significant (three times the upper limit of normal) but reversible and

asymptomatic liver enzyme elevations. Marked elevations (10 times the upper limit of normal) occur in 5% to 10% of patients requiring discontinuation of the medication. However, perhaps 80% of patients who initially develop elevations can be successfully rechallenged with more gradual increases in dose. Alanine aminotransferase (ALT) should be monitored prior to treatment initiation and after each dose increase. Donepezil has not been associated with this adverse event, but experience with the agent is limited.

Vitamin E

One theory of aging is that free radicals cause oxidative damage, which causes neuronal death characteristic of many diseases, including AD. Vitamin E, also known as α-tocopherol, initially was tried for treatment of AD because of its antioxidant properties, and because in animal models it was shown to slow damage and death of neurons. One study evaluated Vitamin E, selegiline alone, both or placebo and found single therapy with Vitamin E or selegiline alone decreased the rate of functional decline equivalent to approximately 7 months. It should be noted that there was no improvement in function compared to baseline and all groups showed similar rates of cognitive decline during the 2 year study period. Vitamin E (200-3000 IU/day) has been shown to be safe and well-tolerated in many studies. At high doses it has been found to worsen blood coagulation defects in patients with vitamin K deficiency.

Selegiline

In the United States, selegiline (also known as l-deprenyl) is used for Parkinson's disease, and in Europe it is approved for dementia. While its mode of action is not fully known, it has been suggested that selegiline may act as an antioxidant or neuroprotective agent and slow the progression of AD, although, because of its effects on catecholamine metabolism, it could also act in a variety of other ways. The main side effect of selegiline is orthostatic hypotension (low blood pressure on standing, causing dizziness or fainting),

which may be more common in patients with Parkinson's disease than those with dementia. Selegiline has been reported to be activating which is helpful for some patients, but may lead to anxiety and/or irritability in others. Drug interactions have included changes in mental status, seizures, and even death have been observed with meperidine, SSRIs, and tricyclic antidepressants, although there have been reports of patients tolerating these combinations.

Ergoloid Mesylates

Ergoloid mesylates have been on the market for a number of years. A recent meta-analysis suggested that there might be improvements in neuropsychological and behavioral measures, but the overall benefits were not statistically significant. Ergoloid mesylates may cause mild nausea or gastrointestinal distress.

Other Agents Proposed for the Treatment of Dementia

Based on epidemiologic data or pilot studies, other agents have been proposed for the treatment of dementia; however, at this time their use is not recommended.

- Estrogen – Preliminary data show that estrogen replacement therapy can delay onset and/or decrease risk of cognitive loss. A clinical trial is in progress in postmenopausal women with AD.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) – Based on epidemiologic data, it has been suggested that these agents protect against the development of the disease. In addition, since one theory of the development of AD involves inflammation, NSAIDs may have a role in the treatment or prevention of dementia.
- Melatonin, Ginkgo biloba – Interest has been shown in both of these over-the-counter products. It should be advised that these agents are marketed with limited quality control and have not been subject to safety and efficacy evaluations.

- Desferrioxamine – a chelating agent theorized to have a place in AD treatment because of the hypothesis that heavy metals have a role in the pathogenesis of AD. However, efficacy data are sparse. Because of the toxicity of chelating agents, they are not recommended for treatment of dementia.

Managing Common Behavioral Problems in Dementia[13]

Disruptive behavior related to dementia is the chief factor leading to institutionalization. Common behavioral symptoms include: aggression and psychotic features, depression, and sleep disturbances.

Treatment for Psychosis and Depression[13]

Psychosis and agitation are common in demented patients and often coexist.[2] Usually a pharmacologic agent is the treatment of choice, but which drug is best for an individual case requires careful consideration.

It should be noted that the psychotic symptoms associated with dementia are not considered schizophrenia even though the terminology used to describe behaviors may be shared between definitions. Furthermore, there currently is no treatment approved for the agitation, aggression, psychosis, and depression due to dementia. The antipsychotic drugs used to treat psychotic behaviors in dementia are typically those found effective in treating psychotic behaviors due to schizophrenia, but antipsychotic drugs are approved only for schizophrenia.

Drug selection is based on the relationship between the side effect profile and the characteristics of a given patient.[2]

Antipsychotics

Antipsychotics (neuroleptics): Haloperidol and thioridazine are often referred to as "high-potency" neuroleptics.[13]

Atypical antipsychotics: Clozapine, risperidone, olanzapine, and quetiapine are referred to as "atypical" antipsychotics and are associated with a lower frequency of extrapyramidal side effects than the typical antipsychotics.[13]

Antipsychotic agents are associated with serious complications that must be considered in the risk/benefit analysis for treatment of any psychosis, especially in the elderly with dementia.

Extrapyramidal symptoms (EPS) of antipsychotic medications include:[9]

- Dystonia (dis-TOE-nee-ah)[9]
  - Facial grimacing
  - Torticollis (tort-tih-KOLL-is) – spasm of neck muscle that turns head sideways and to one side
  - Oculogyric (ock-ku-low-JYE-ric) crisis – rotation of eyeballs
  - Opisthotonos (oh-pis-THOUGH-oh-nohs) – backward arching of head
- Parkinsonism[9]
  - Akinesia (ay-ki-NEE-shah) – involuntary movement
  - Masked facies
  - Rigidity
  - "Pin-rolling" hand tremor
- Akathisia (ay-kah-THIZ-ee-ah) –Continual nervousness and restlessness
- Tardive dyskinesia (TAR-div disk-in-NEE-shah)[9], with and without EPS, may also be seen as an adverse effect of antipsychotic medications.

- Involuntary movements of tongue, face, mouth, jaw, extremity muscles, eg, repeated lip-smacking, chewing, protruding of the tongue, jerky or writhing movements

The risk of tardive dyskinesia increases with increasing dose and duration of treatment, and is greater in women, the elderly, and those with dementia.[2] The risk of tardive dyskinesia with antipsychotics is as high as 30% in the elderly.[2]

Neuroleptic malignant syndrome (NMS) is also a risk of antipsychotic medication, and is potentially fatal.[2,9] NMS, which may occur at any time during antipsychotic therapy, includes the following: increased temperature; muscle rigidity; altered mental status; altered pulse and blood pressure; sweating; and irregular heartbeat.

Benzodiazepines[2]

Studies of benzodiazepines in the treatment of behavioral symptoms are limited by poorly specified diagnosis, a mixture of target symptoms, limited outcome measures, and in most cases, high doses of long-acting agents. Benzodiazepines have been shown to perform better than placebo, but not as well as antipsychotics in reducing behavioral problems. The most common side effects of benzodiazepines are dose-related and include sedation, ataxia, amnesia, confusion and delirium, and paradoxical anxiety. These side effects must be watched for, as they can lead to worsening of cognition and behavior problems and/or may be responsible for falls.

Anticonvulsants[13]

Divalproex sodium and carbamazepine have been shown to be effective in treating behavioral disturbances in preliminary clinical trials, but their efficacy has yet to be proven in placebo-controlled, double-blind clinical trials. They do not have the same potential for tardive dyskinesia and NMS as antipsychotics.

Some important side effects of divalproex sodium include: hepatic failure, pancreatitis, somnolence, nausea, and dizziness. Some important side effects

of carbamazepine include: aplastic anemia, agranulocytosis, dizziness, drowsiness, and nausea.

In psychiatry, divalproex sodium has a labeled indication for the treatment of mania associated with bipolar disorder.

Treatment for Depression

Depression occurs in up to 20% of patients with dementia.[13] Patients may experience depression as a result of their progressive neuronal loss, or, less frequently, as a reaction to the disease process.

Antidepressants

- **SSRIs (selective serotonin reuptake inhibitors):** Fluoxetine, paroxetine, and sertraline are first-line therapy for depression in patients with dementia. Psychotherapy is not at all useful in this population with impaired insight, and these agents generally are well-tolerated in patients with concomitant dementia and depression.
- **Tricyclic antidepressants:** Desipramine and nortriptyline have lower anticholinergic activity than amitriptyline, which is associated with an increased risk of worsening cognitive impairment.
- Phenethylamine antidepressant: venlafaxine is useful when marked apathy is present because it stimulates both the serotonergic and adrenergic neurotransmitter systems.[13]

Treatment for Sleep Disturbance

Hypnotics or benzodiazepines: Trazodone and zolpidem are useful in the short-term treatment of sleep disorders that lead to wandering and behavior disorders during normal sleep hours. Families often can cope with the agitation, delusions, and other behavior disorders when they occur during the daytime, but when sleep disorders cause them to continue into the night, institutionalization is often considered.[13]

Approach to Treatment of Agitation and Psychopathology of Dementia

Behavioral psychopathology due to dementia is a key factor in the overall management of dementia for three reasons:[10]

1) The distress caused by behavioral symptoms is significant and affects the well-being of both the patient and the caregiver.

2) Behavioral psychopathology, especially when physical hyperactivity and aggression are involved, can be dangerous for the patient and for the caregiver as well.

3) The practice of treating behavioral symptoms with antipsychotic medication can lead to serious adverse events that further affect the well-being of the patient and caregiver.

Prevalence and Impact of Caregiving[14]

Data from the 1996 National Survey on Family Caregiving was analyzed in order to provide a detailed description of the differences between dementia and nondementia caregivers.

This report showed when compared to other caregivers, dementia caregivers:

- spent more than 40 hours/week on caregiving;
- provided assistance for more activities of daily living;
- experienced employment complications, necessitating taking a less demanding job, taking early retirement, turning down a promotion, or having to give up work completely and losing job benefits;
- reported forfeiting pleasurable activities, having less time for other family, holding grudges against other family members for not doing their fair share, and experiencing a greater degree of family conflict;
- experienced greater emotional and physical strain; and
- experienced higher levels of financial hardship, but both types of caregivers spent the same amount of money per month on caregiving.

Glossary

acetylcholine – a neurotransmitter that transmits impulses between the forebrain and the parts of the brain responsible for memory and information processing

acetylcholinesterase (AChE) – a naturally occurring enzyme that hydrolyzes acetylcholine at the neuron

activities of daily living (ADL) – routine activities required for self-care, such as bathing, grooming, dressing, walking, preparing meals, and household cleanup

agitation – inappropriate vocal or motor activity that is not explained by perceived needs or confusion. Types of agitation include psychosis, delirium, depression, anxiety, anger, and insomnia. Agitation may take the form of aimless wandering, pacing, cursing, screaming, biting, hitting, and scratching.

agnosia – impaired recognition/identification of objects despite intact sensory function

alanine aminotransferase (ALT) – a liver enzyme that indicates liver dysfunction; can be used to monitor potential hepatotoxicity

apathy/vegetation – lack of interest in surroundings, grooming, and social interaction, progressing to staring into space without being aware of people, places, or things in the environment

aphasia – impaired language/speaking

apraxia – impaired movement, despite intact motor function

bradycardia – slow heart rate

Glossary (continued)

cholinesterase inhibitors – drugs that inhibit the enzyme *acetylcholinesterase (AChE)*, which hydrolyzes acetylcholine at the neuron; increases the concentration of acetylcholine at the nerve endings

cognition – the "knowledge" of events that continually occur during consciousness. When cognitive abilities are impaired there is diminished perception, recognition, idea or thought conception, judging, sensing, reasoning, and imagining.

Creutzfeldt-Jakob disease – rapidly progressive disease of the brain caused by a transmissible virus or other type of infection

delusions – incorrect beliefs or judgments that are held with conviction, despite reality to the contrary. Delusions of grandeur: belief of possessing immense wealth, intellect, power; delusions of persecution: belief that people/society are "out to get you"

dementia – a broad clinical syndrome that involves global deterioration of intellectual and cognitive abilities. Pathogenesis is due to impairment of, or damage to, the central nervous system (the brain), but the exact dysfunction is not always easily defined.

disinhibition – a state in which previously held social inhibitions are lost, eg, acts of aggression, not wearing clothes

dystonia – a category of extrapyramidal symptoms that includes facial grimacing, torticollis, oculogyric crisis, and opisthotonos

executive functioning – inability to plan, organize, sequence, think abstractly

extrapyramidal (extra-pyr-RAM-ih-dahl) *effects* – side effects of antipsychotic medications, which include dystonia, parkinsonism, akathisia, and tardive dyskinesia

hallucinations – seeing, hearing, smelling, tasting, or feeling things that are not there; the false perception of sight, sound, smell, taste, or touch, with no basis in reality, eg, seeing people or things that are not present, feeling bugs crawling on skin

Huntington's disease – hereditary neurological disease that causes motor, behavioral, and cognitive deterioration

multi-infarct dementia (MID) – also called vascular dementia; stems from multiple episodes of cerebral ischemia, sometimes referred to as "mini-strokes" or TIAs, which cause the brain damage that leads to dementia

oculogyric (ock-ku-low-JYE-ric) *crisis* – rotation of eyeballs

opisthotonos (oh-pis-THOUGHT-oh-nohs) – backward arching of head

parkinsonism – a combination of neurological signs and symptoms that include akinesia, masked facies, rigidity, and "pin-rolling" hand movements

Pick's disease – a type of frontal lobe dementia that is difficult to diagnose and differentiate from atypical AD. Brain imaging shows atrophy of frontal and/or temporal lobes. Autopsy findings identify Pick inclusion bodies in the brain. Most common between age 50 and 60, but can occur in older population.

primary dementias – those for which no other identifiable disease or condition can be found as the cause of the syndrome

psychosis – distortion/confusion of mental state, emotional response, and overall ability to recognize reality, causing an inability to relate to and communicate with others normally

secondary dementias – those for which a pathological process has been found as the cause, eg, infections, trauma, toxic/metabolic disorders, circulatory disorders, brain tumors, neurological diseases or conditions

suicidal ideation – thinking about death, the act of suicide, and ways to commit suicide

sundowning – agitation, confusion, and disorientation beginning in the late afternoon and becoming more severe at night

syphilis – a sexually transmitted disease that causes dementia in late stages

tardive dyskinesia (TAR-div disk-in-NEE-shah) – involuntary movements of tongue, face, mouth, jaw, extremity muscles, eg, repeated lip-smacking, chewing, protruding of the tongue, and jerky or writhing movements

torticollis (tort-tih-KOHL-is) – spasm of neck muscle that turns the head sideways and to one side

vascular dementia – also called multi-infarct dementia (MID); stems from multiple episodes of cerebral ischemia, sometimes referred to as "mini-strokes," which cause the brain damage that leads to dementia

Case Studies

Betty Green

Betty has been brought to Dr. Hager's office by her daughter-in-law, Sue. Dr. Hager is a primary care physician in the small town of Robinson, Indiana. Betty is 76 years old, is widowed, and lives alone in the same neighborhood she has lived in for 40 years. On her last visit to see Betty, Sue noticed several large bruises on Betty's arm and leg. When asked about them, Betty said the "bites," as she called them, were from the cat. Betty's cat died five years earlier and she currently has no pets.

Upon physical examination, Betty is alert and responsive to questions. Betty has lost 8 pounds since Dr. Hager last saw her over a year earlier. He notices additional old bruises on her ribs, but there are no other remarkable signs or symptoms of disease. As Dr. Hager examines Betty, she gives the following answers to his questions:

Dr. Hager: You've lost weight, Betty. How is your appetite?

Betty: Well, Bill (Bill was Betty's husband) just doesn't cook like he used to, and I never was much of a cook.

Dr. Hager: Have you fallen lately, Betty?

Betty: Oh, no. I have good shoes.

Dr. Hager: How are your grandkids? What are their names again? (Sue and Betty's son, Bill, Jr., have a five-year-old boy and a one-year-old girl.)

Betty: Oh, we're all great.

Dr. Hager: What are your grandkids' names?

Betty: Well, uh, fine, fine, fine.

Case Studies (continued)

Dr. Hager asks Betty to sit in the waiting room and asks to see Sue. Betty sits and watches a television game show while Sue goes in to see Dr. Hager. Dr. Hager interviews Sue and learns the following:

Betty's neighbor said that Betty keeps getting lost when she drives them to the new mall outside of town. On their last trip, Betty spilled gasoline all over herself when she tried to fill the gas tank. Betty has stopped asking Sue and Bill about her grandchildren and doesn't seem to recognize them at all when Betty comes to visit. Sometimes she recognizes Sue and sometimes she doesn't. Betty can no longer operate the can opener, and is unable to organize herself enough to cook the holiday meals, which had always been her favorite family events. She can't even prepare any of her favorite dishes. She eats mostly cold cuts and cereal, saying she isn't very hungry. Sue finds the casseroles and soups she brings to Betty untouched in the refrigerator, molding, apparently forgotten. Betty is continually forgetting which day to take the trash out. When asked if there is any history of Alzheimer's or any other type of abnormal behavior in the elderly of the family, Sue relates that Betty's mother had gone "crazy" when she was older and was hospitalized at the age of 82 when she almost burned down her house.

All Betty's lab work comes back normal with the exception of a low hemoglobin, suggesting a low degree of anemia. Dr. Hager suspects early dementia, possibly due to Alzheimer's disease.

Dr. Hager refers Betty to a psychiatrist who does a full diagnostic workup and confirms Dr. Hager's preliminary diagnosis of dementia due to Alzheimer's disease. Betty is given a cholinesterase inhibitor and referred with the family to an Alzheimer's disease support group. Her next-door neighbor is hired to look in on Betty at least four times a day, and Betty is sent to a senior day care center three times a week. Her son and daughter-in-law visit her weekly, and have taken over her grocery and other types of shopping.

Case Discussion

Questions

1) What clues suggested a diagnosis of dementia? Underline the clues.

2) Which of the following symptoms of dementia did Betty exhibit? Give an example of each symptom from Betty's history.

   A. apraxia

   B. aphasia

   C. agnosia

   D. memory impairment, especially recent memory

   E. impaired executive functioning

3) Name the available cholinesterase inhibitors that are prescribed for AD.

4) What stage of dementia do you think Betty is in? Why?

5) As Betty enters the later stages of AD, what symptoms/behavior might cause her to be hospitalized?

Answers

1) Betty has been brought to Dr. Hager's office by her daughter-in-law, Sue. Dr. Hager is a primary care physician in the small town of Robinson, Indiana. Betty is 76 years old, is widowed, and lives alone in the same neighborhood she has lived in for 40 years. On her last visit to see Betty, Sue noticed several large bruises on Betty's arm and leg. When asked about them, Betty said the "bites," as she called them, were from the cat. Betty's cat died five years earlier and she currently has no pets.

Upon physical examination, Betty is alert and responsive to questions. Betty has lost 8 pounds since Dr. Hager last saw her over a year earlier. He notices additional old bruises on her ribs, but there are no other remarkable signs or symptoms of disease. As Dr. Hager examines Betty, she gives the following answers to his questions:

Case Studies (continued)

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Betty: Oh, we're all great.

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Betty: Well, uh, fine, fine, fine.

Dr. Hager asks Betty to sit in the waiting room and asks to see Sue. Betty sits and watches a television game show while Sue goes in to see Dr. Hager. Dr. Hager interviews Sue and learns the following:

Betty's neighbor said that Betty keeps getting lost when she drives them to the new mall outside of town. On their last trip, Betty spilled gasoline all over herself when she tried to fill the gas tank. Betty has stopped asking Sue and Bill about her grandchildren and doesn't seem to recognize them at all when Betty comes to visit. Sometimes she recognizes Sue and sometimes she doesn't. Betty can no longer operate the can opener, and is unable to organize herself enough to cook the holiday meals, which had always been her favorite family events. She can't even prepare any of her favorite dishes. She eats mostly cold cuts and cereal, saying she isn't very hungry. Sue finds the casseroles and soups she brings to Betty untouched in the refrigerator.

molding, apparently forgotten. Betty is continually forgetting which day to take the trash out. When asked if there is any history of Alzheimer's or any other type of abnormal behavior in the elderly of the family, Sue relates that Betty's mother had gone "crazy" when she was older and was hospitalized at the age of 82 when she almost burned down her house.

All Betty's lab work comes back normal with the exception of a low hemoglobin, suggesting a low degree of anemia.

2) A. Apraxia

spilled gasoline

can no longer operate the can opener

B. Aphasia

Betty called bruises "bites"

Oh, no. I have good shoes.

C. Agnosia – Agnosia is impaired recognition/ identification of an object despite intact sensory function. The history did not include any examples of agnosia.

D. Memory impairment, especially recent memory

Bill doesn't cook like he used to and I never was much of a cook.

Betty's cat had died five years earlier and she currently has no pets

Food untouched in the refrigerator

Well, uh, fine, fine, fine.

Getting lost driving to the mall.

Betty had stopped asking about her grandchildren.

Case Studies (continued)

Doesn't seem to recognize them at all

Sometimes she doesn't recognize Sue.

E. Impaired executive functioning

Unable to organize herself enough to cook the holiday meals

Couldn't prepare any of her favorite dishes

Unable to schedule/predict which day to take the trash out

3) Tacrine, donepezil

4) Mild-to-moderate. Impairment is mild, but Betty is still able to perform most activities of daily living and is able to live alone, with supervision.

5) Behavioral/psychiatric problems

Incontinence

Joe Dougherty

Joe and Mary Dougherty are 68 and 72, respectively. Joe has had hypertension since he was in his 50s. At the age of 64, Joe had several TIAs (transient ischemic attacks) during a six-month period, followed by a major stroke that left him with right-sided weakness. He walks with a walker.

In the past two months, Joe has become increasingly forgetful and confused and has experienced aphasia, agnosia, and worsened gait. Mary has awakened several times to find him in another part of the house. When Mary has awakened him to bring him back to bed, he has become angry and belligerent, telling her to go away and let him be. He is no longer able to shower or shave himself.

In the evening, he has started pacing up and down the hall with his walker, and often talks angrily to people who are not there. He has tried to slap Mary on a couple of occasions when she was helping him get ready for bed.

Mary has brought Joe to the neurologist and explained his latest symptoms. A complete physical exam has revealed no apparent physiological cause of the symptoms.

Case Discussion

Questions

1) Based on the history so far, what might the diagnosis be?

2) Underline the major factors that suggest this diagnosis.

3) What stage of this condition is Joe in? State your reasons.

4) Which of Joe's symptoms could be considered "sundowning"?

5) Which of the following medications might the neurologist prescribe for Joe? Explain your rationale for choosing or not choosing each type of drug.

A. hypnotic

B. anticonvulsant

C. cholinesterase inhibitor

D. SSRI

Answers

1) **Multi-infarct dementia, vascular dementia**

2) **Joe and Mary Dougherty are 68 and 72, respectively. Joe has had hypertension since he was in his 50s. At the age of 64, Joe had several TIAs (transient ischemic attacks) during a six-month period, followed by a major stroke that left him with right-sided weakness. He walks with a walker.**

Case Studies (continued)

In the past two months, Joe has become increasingly forgetful and confused and has experienced aphasia, agnosia, and worsened gait. Mary has awakened several times to find him in another part of the house. When Mary has awakened him to bring him back to bed, he has become angry and belligerent, telling her to go away and let him be. He is no longer able to shower or shave himself.

In the evening, he has started pacing up and down the hall with his walker, and often talks angrily to people who are not there. He has tried to slap Mary on a couple of occasions when she was helping him get ready for bed.

Mary has brought Joe to the neurologist and explained his latest symptoms. A complete physical exam has revealed no apparent physiological cause of the symptoms.

3) Severe-to-profound

Joe is having difficulty using the bathroom, and is experiencing sundowning and agitation/ aggression.

4) In the evening, he has started pacing up and down the hall with his walker and often talks angrily to people who are not there. He has tried to slap Mary on a couple of occasions when she was helping him get ready for bed.

Mary has awakened several times to find him in another part of the house. When Mary has awakened him to bring him back to bed, he has become angry and belligerent, telling her to go away and let him be.

5) A. Hypnotic

Short-term use of a hypnotic or benzodiazepine might be indicated to help Joe (and Mary) get a good night's sleep.

B. Anticonvulsant

An anticonvulsant might be indicated for treatment of agitation/aggression.

C. Cholinesterase inhibitor

A cholinesterase inhibitor would probably not be used in this case since it has already advanced to the severe/profound stages.

D. SSRI

Joe does not show any major symptoms of depression for which an SSRI might be indicated.

References

1 Seltzer B. Organic mental disorders. In: Nicholi AM, ed. *The New Harvard Guide to Psychiatry.* Cambridge, Mass: Belknap Press; 1988:358-383.

2 American Psychiatric Association. Practice Guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. *Am J Psychiatry* 1997;154(suppl 5):1-39.

3 Burke JR, Morgenlander JC. Update on Alzheimer's disease. *Postgrad Med* 1999;106(5):86-96.

4 Geldmacher DS, Whitehouse PJ. Evaluation of dementia. *N Engl J Med* 1996;335(5):330-336.

5 Fleming KC, Adams AC, Petersen RC. Dementia: diagnosis and evaluation. *Mayo Clin Proc* 1995;70:1093-1107.

6 Welsh-Bohner KA, Morgenlander JC. Determining the cause of memory loss in the elderly. *Postgrad Med* 1999;106(5):99-119.

7 Daly MP. Diagnosis and management of Alzheimer's disease. *J Am Board Fam Pract* 1999;12(5):375-385.

8 Steffens DC, Morgenlander JC. Initial evaluation of suspected dementia. *Postgrad Med* 1999;106(5):72-83.

9 Berkow R, Fletcher AJ, eds. *The Merck Manual of Diagnosis and Therapy,* 16th ed. Rahway, New Jersey: Merck Research Laboratories; 1992:1635-1644.

10 Tairot PN. Treatment of agitation in dementia. *J Clin Psychiatry* 1999;60(suppl 0):11-20.

11 Cohen-Mansfield J. Agitated behaviors in the elderly. *J Am Geriatr Soc* 1986;34:722-727.

12 Alexopoulos GS, Silver JM, Kahn DA, Frances A, Carpenter D, eds. Treatment of agitation in older persons with dementia: a special report. *Postgrad Med* 1998;April:25.

13 Burke JR, Morgenlander JC. Managing common behavioral problems in dementia. *Postgrad Med* 1999;106(5):131-140.

14 Ory MG, Hoffman RR, Yee JL, Tennstedt S, Schultz R. Prevalence and impact of caregiving: a detailed comparison. *Gerontologist*, April 1999.

15 Wimo A, Ljunggren G, Winblad B. Costs of dementia and dementia care: a review. *Int J Geriatr Psychiatry* 1992;12:841-856.

16 Diagnostic and Statistical Manual of Mental Disorders: ed 4 (DSM-IV), Washington DC; *American Psychiatric Press* 1994:142-146.

Dementia Backgrounder – Quiz

1. Which of the following statements is not true?

   A. Dementia refers to cognitive and/or psychological deterioration associated with organic brain dysfunction.

   B. Dementia is more prevalent in the elderly, and the prevalence of dementia is increasing in the United States and the world as the "baby-boomers" age.

   C. There is no cure for dementia.

   D. Dementia is referred to as a "functional" brain disease because it has no organic pathogenesis.

2. Mark each statement True or False.

   A. Primary dementias are those for which no other identifiable disease or condition can be found to be responsible for the syndrome. True

   B. Secondary dementias are those for which a pathological process has been found as the cause. True

3. What neurotransmitter is the target of cholinesterase inhibitors?

   A. glycine

   B. acetylcholine

   C. alanine aminotransferase (ALT)

   D. phenothiazine

4. What is known about the pathologic process that occurs in Alzheimer's disease?

A. AD is accompanied by a loss of cholinergic neurons, and acetylcholine is reduced by as much as 90% in patients with AD.

B. The concentration of acetylcholine at the neuron accumulates to toxic levels, eventually causing such symptoms as hyperactivity and aggression.

C. Cholinesterase is absent from the nerve endings in the brain.

D. Cognitive functioning is accelerated by AChE.

5. One of the cholinesterase inhibitors, tacrine, used to treat AD is associated with asymptomatic, reversible _____ in as many as 30% of patients.

A. aggression

B. depression

C. hepatotoxicity

D. bradycardia

6. Which of the following drugs, believed to slow the progression of AD because of neuroprotective effects and antioxidant properties, is used for Parkinson's disease in the United States, and is approved for dementia in Europe?

A. selegiline

B. donepezil

C. trazodone

D. haldol

E. vitamin E

Dementia Backgrounder – Quiz (continued)

7. Antipsychotics:

   A. are also referred to as neuroleptics.

   B. include haloperidol and thioridazine.

   C. are considered "high-potency."

   D. include clozapine, risperidone, olanzapine, and quetiapine.

   E. All of the above

   F. A, B, C

8. "Atypical" antipsychotics:

   A. are also referred to as neuroleptics.

   B. include haloperidol and thioridazine.

   C. are considered "high-potency."

   D. include clozapine, risperidone, olanzapine, and quetiapine.

   E. All of the above

   F. A, B, C

9. True or False?

   Typical antipsychotics are associated with a lower frequency of extrapyramidal side effects than the atypical antipsychotics.

   False

10. In the treatment of dementia, benzodiazepines are effective in the treatment of certain types of agitation and behavioral problems, but they generally are not as effective as antipsychotics. Which of the following is true about the side effects of benzodiazepines?

A. They are dose-related.

B. They include sedation, ataxia, amnesia, confusion and delirium, and paradoxical anxiety.

C. They can lead to worsening of cognition and behavior problems, and/or may be responsible for falling accidents.

D. All of the above

E. B & C

11. What is true about the use of the anticonvulsants, divalproex sodium and carbamazepine, in treating behavioral disturbances in dementia patients?

A. They have been shown effective in preliminary clinical trials.

B. They have been shown effective in many placebo-controlled, double-blind clinical trials.

C. They do not have the same potential for tardive dyskinesia and NMS as antipsychotics.

D. None of the above

E. A & C

F. B & C

Dementia Backgrounder – Quiz (continued)

12. Which of the following statements is true about depression in dementia?

A. Depression occurs in up to 20% of patients with dementia.

B. Patients probably experience depression as a result of their progressive neuron loss.

C. Intensive psychotherapy is useful as an adjunct with a course of antidepressant drug therapy.

D. All of the above

E. A & B

F. A & C

13. Which is **not** true about the treatment of depression associated with dementia?

A. SSRIs may be used, and include desipramine and nortriptyline.

B. SSRIs may be used, and include fluoxetine, paroxetine, and sertraline.

C. SSRIs are first-line therapy for depression in patients with dementia.

D. SSRIs generally are well-tolerated in patients with concomitant dementia and depression.

E. Tricyclic antidepressants have no anticholinergic activity and are not effective in dementia patients.

F. Amitriptyline is associated with an increased risk of worsening cognitive impairment.

G. A & E

H. B & F

14. True or False?

Hypnotics, or benzodiazepines (trazodone and zolpidem), are useful in the short-term treatment of sleep disorders that lead to wandering and behavior disorders during normal sleep hours.

15. True or False?

Dementia caregivers and caregivers for other chronic illnesses have a comparable burden in terms of hours per week giving care, employment complications, stress, mental and physical health problems, compromised leisure and family time, and general family conflict.

16. In elderly patients, why should drug therapy be started with lower doses and dosage titration progress more slowly than in a younger population?

A. Because the elderly often have decreased renal clearance of drugs and decreased hepatic metabolism.

B. This population often has multiple medical conditions requiring attention for drug interactions and side effects.

C. Elderly patients are less likely to experience the beneficial extrapyramidal effects of drugs.

D. In elderly patients, some medications make them more susceptible to anticholinergic side effects, and may lead to worsening of cognitive deficits, confusion, and possibly delirium.

E. A, B, C

F. A, B, D

G. B, C, D

Dementia Backgrounder – Quiz (continued)

17. Mark each of the following statements **True** or **False**.

A. Delirium is a type of agitation syndrome in which the consciousness and cognition of the patient change, with fluctuations over minutes to hours. True

B. The cause of delirium may be a medical condition, which requires immediate diagnosis and treatment. True

18. **True** or **False?**

Depression in dementia patients may be mistaken because of its resemblance to medical illness (eg, weight loss, sleep disturbances, fatigue) or dementia (eg, flat affect, loss of interest, poverty of speech).

19. Which of the following is not considered a type of anxiety experienced by patients with agitation?

A. Nervousness, fear, or physical complaints, such as palpitations or stomach disorders

B. Obsessive concern over the safety of their belongings or the whereabouts of their loved ones

C. Observation of angels watering flowers on the windowsill

20. Which of the following is described as the clustering of agitation, confusion, and disorientation beginning in the late afternoon and becoming more severe and at night?

A. hallucinations

B. sundowning

C. psychosis

D. hyperactivity

E. insomnia-induced aggression

21. Anger that is accompanied by physical aggression, such as pushing, slapping, scratching, and extremely loud and extended yelling, is considered:

A. severe

B. mild

C. sundowning

D. paranoid

22. Which of the following is not considered the most common reason for institutionalization in dementia?

A. delusions

B. insomnia

C. agitation

D. sleepwalking

E. apathy

Dementia Backgrounder – Quiz (continued)

23. Which of the following is **not** an extrapyramidal effect of antipsychotic medications?

A. dystonia

B. parkinsonism

C. tardive dyskinesia

D. agitation

For questions 24–28, match the word or phrase with its correct description listed below.

A. facial grimacing, torticollis, oculogyric crisis, opisthotonos

B. akinesia, masked facies, rigidity, "pin-rolling" hand movements

C. dystonia, parkinsonism, akathisia, tardive dyskinesia

D. involuntary movements of tongue, face, mouth, jaw, extremity muscles, eg, repeated lip-smacking, chewing, protruding of the tongue, jerky or writhing movements

E. increased temperature, muscle rigidity, altered mental status, altered pulse and blood pressure, sweating, irregular heart rate

24. Dystonia A
25. Extrapyramidal effects C
26. Parkinsonism B
27. Tardive dyskinesia D
28. Neuroleptic malignant syndrome E

29. Which of the following types of dementia is most likely to have a gradual onset?

A. Alzheimer's disease

B. Vascular dementia

C. Pick's disease

30. **Which of the following types of dementia is most likely to have a sudden onset?**

A. Alzheimer's disease

B. Vascular dementia

C. Pick's disease

D. Parkinson's dementia

Quiz Answers

1. D
2. True, True
3. B
4. A
5. C
6. A
7. F
8. D
9. F
10. D
11. E
12. E
13. G
14. True
15. False
16. F
17. True, True
18. True
19. C
20. B
21. A
22. E
23. D

24. A

25. C

26. B

27. D

28. E

29. A

30. B

Developed by Communications and Training Consultants.

Printed in U.S.A. 00B-733-9552