

# Unit 3

## Alzheimer's Dementia

### Alzheimer's Disease

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Alzheimer's disease (AD) is the most common cause of dementia, and the number of affected individuals in the world population is near epidemic proportions,<sup>1</sup> more than 35 million people. Epidemiologists predict a doubling of patients every 20 years, thus by 2050 the number affected will soar to 115 million! AD is the sixth leading cause of death and the only cause among the top 10 that cannot be prevented or cured.<sup>2</sup> Each year there are 7.7 million new cases of dementia, or a new case every 4 seconds.

The cost of AD is staggering. In 2010 the cost worldwide was estimated to be US \$604 billion, a figure that includes direct costs for medical care plus the cost of informal care provided by family and others.<sup>3</sup> If dementia were a country, it would be the world's 18th largest economy; were it a company, it would be the world's largest, with annual revenue exceeding those of Wal-Mart (\$414 billion) and Exxon Mobil (\$311 billion).<sup>3</sup>

Diagnosing AD is challenging and is typically made by excluding other conditions associated with cognitive changes. Computed tomography (CT) and magnetic resonance imaging (MRI) are used to rule out tumor, cerebrovascular disease, and normal pressure hydrocephalus and to detect disease-associated atrophy in the medial temporal lobe and amygdalohippocampal system.<sup>4</sup> Increasingly, physicians are using biomarker data to make the diagnosis, and when paired with behavioral data, accuracy is high.

### Diagnostic Criteria for AD

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In 2011 a collaborative effort between the Alzheimer's Association and the National Institute on Aging resulted in revised diagnostic criteria.<sup>5</sup> The core criteria for *all-cause* dementia are cognitive and behavioral symptoms that: (1) interfere with the ability to function

**Table 3–1.** Overview of the Criteria for Probable Dementia

<b>Probable AD</b>	<p>Impairment in 2 cognitive domains (language, visuospatial, executive or mood or behavioral symptoms)</p> <p>Evidence of progressive worsening of memory and other cognitive functions</p> <p>Insidious onset and clear history of worsening</p> <p>Absence of cerebrovascular disease or other neurological disorders that could affect cognition</p> <p>Symptoms cannot be explained by delirium or other major psychiatric disorder</p> <p>Biomarker evidence from MRI, PET, CSF increases certainty of disease as does evidence of a causative gene</p>
<b>Possible AD</b>	<p>Meets clinical criteria for AD but there is evidence of other systemic or neurological disorder that could affect cognition</p>

at work or at usual activities, (2) represent a decline from previous levels of functioning, (3) are not explained by delirium or major psychiatric disease, and (4) represent cognitive or behavioral impairment involving at least 2 of the following: (a) inability to acquire and remember new information, (b) impaired reasoning and handling of complex tasks, (c) poor judgment impaired, (d) impaired visual spatial abilities, and (e) impaired language functions (changes in personality, behavior, or comporment).<sup>6</sup> Table 3–1 is an overview of the criteria for probable dementia.

### Neuropathology of AD

AD affects the processes that sustain the health of neurons and ultimately destroys interneuronal communication. Historically, it was thought to begin in the cortex; however, recent evidence indicates that its genesis may be in the locus coeruleus,<sup>7</sup> a nucleus in the pons involved with homeostatic mechanisms. In a retrospective study, Braak and Del Tredici<sup>7</sup> observed “pretangle material” in the locus

coeruleus in individuals under the age of 30. Over time the disease proliferates in perirhinal cortex (Figure 3-1), the hippocampal complex in the temporal lobes, and the basal forebrain, areas important to episodic memory.<sup>8,9</sup> Eventually, structural changes occur in the frontal, temporal, and parietal lobes. The brain areas most spared are motor and visual cortices,<sup>10-12</sup> a fact that accounts for the sparing of speech.

Motor symptoms can develop late in the disease, among them change in muscle tone, cogwheel phenomenon, postural instability, and difficulty walking. Collectively, these motor changes are referred to as “extrapyramidal signs,”<sup>13</sup> and their presence is associated with greater dementia severity.<sup>14-18</sup>

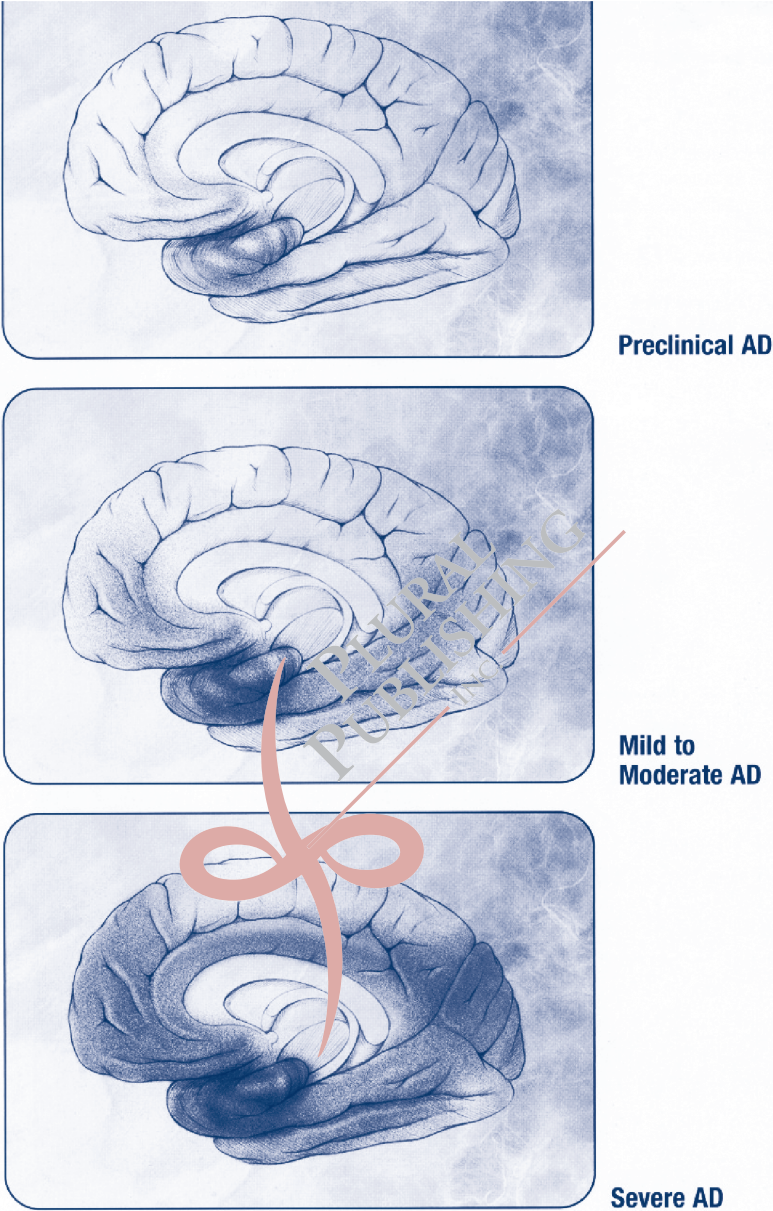
When tissue from the brain of an AD patient is examined microscopically, changes are apparent in the form of neuritic plaques, neurofibrillary tangles, atrophy, and areas of granulovacuolar degeneration. Deposits of amyloid within blood vessels may also be seen.

*Neuritic plaques* (Figure 3-2), called senile plaques in the older literature, are bits and pieces of degenerating neurons that clump together and have an amyloid core. Amyloid-beta is a protein fragment that has been separated from a larger protein called amyloid precursor protein. The disjoined amyloid-beta fragments aggregate and mix with other molecules, neurons, and nonnerve cells. Neuritic plaques are most prevalent in the outer half of the cortex, where the number of neuronal connections is largest.

*Neurofibrillary tangles* (see Figure 3-2) are disintegrating microtubules (microtubules are part of the internal support structure of healthy neurons). Microtubules disintegrate because of changes in tau protein that binds them in healthy brains, giving them supports. Tau is overphosphorylated in AD by enzymes that cause its detachment from the microtubules. As they disintegrate, they become tangled and are a signature morphologic change that confirms the presence of AD.

*Atrophy*, or the shrinking of tissue, is common in AD (Figures 3-3, 3-4, and 3-5), though it may not be visible on CT scan if the patient is in the early stage of the disease. Positron emission tomography (PET) scans show prominent changes in the temporal and parietal lobes and inconsistent changes in frontal lobes. MRI shows substantial atrophy in entorhinal cortex<sup>19,20</sup> and the hippocampal complex.<sup>21,22</sup>

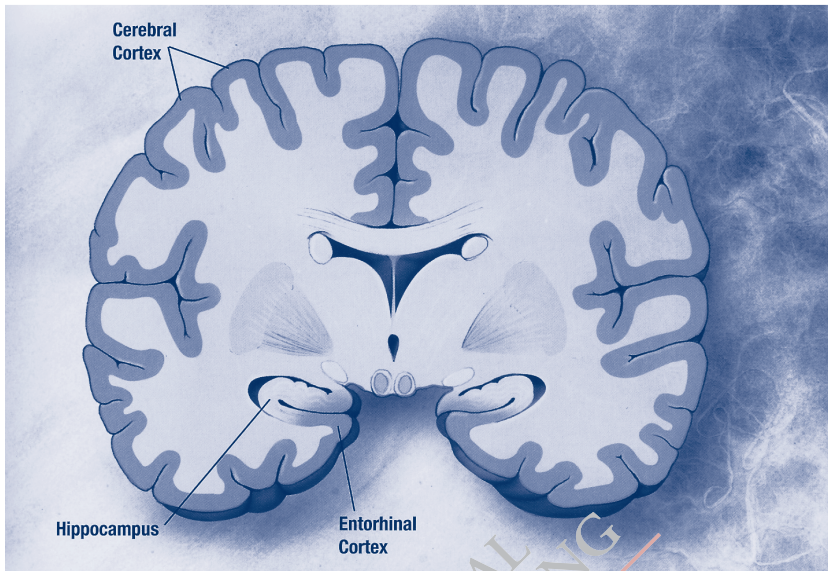
*Granulovacuolar degeneration* refers to fluid-filled spaces within cells that contain granular debris.



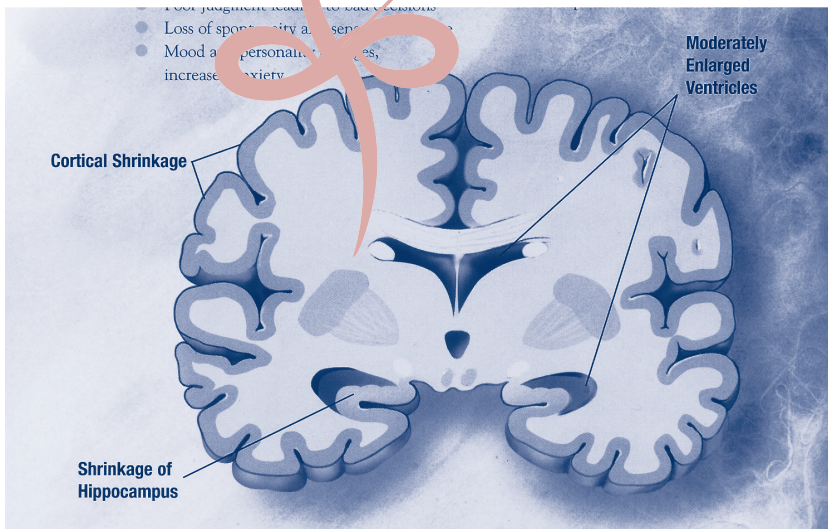
**Figure 3–1.** Brain areas affected by Alzheimer’s disease over the course of the condition. Darker shades indicate areas affected at the various stages of AD. From National Institute on Aging, *Alzheimer’s Disease: Unraveling the Mystery*. Silver Spring, MD: Alzheimer’s Disease Education and Referral (ADEAR) Center; 2002. NIH Publication 02-3782.



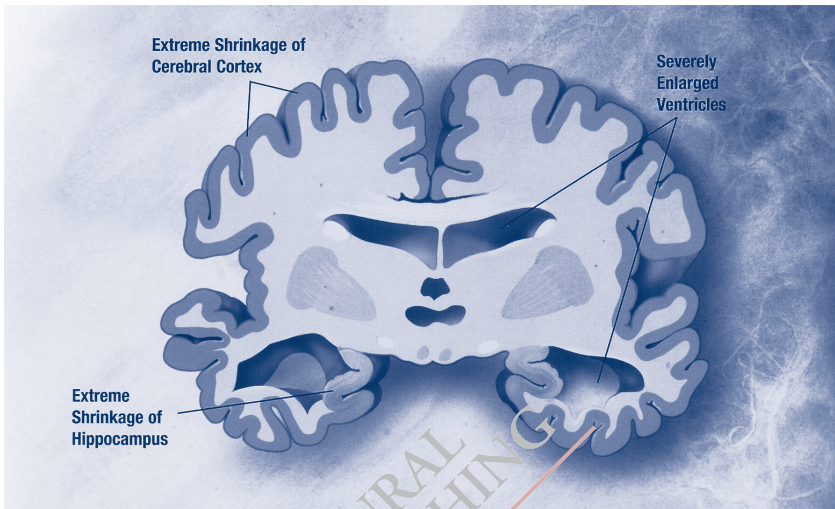
**Figure 3–2.** Neuritic plaques (center clump) and neurofibrillary tangles (Tadpole-shaped bodies). Image courtesy of *Alzheimer's Disease: Unraveling the Mystery*. National Institute on Aging/National Institutes of Health; 2008.



**Figure 3-3.** Schematic showing brain regions affected in the pre-clinical stage of AD. From National Institute on Aging, *Alzheimer's Disease: Unraveling the Mystery*. Silver Spring, MD: Alzheimer's Disease Education and Referral (ADEAR) Center; 2002. NIH Publication 02-3782.



**Figure 3-4.** Schematic showing brain regions affected in mild AD. From National Institute on Aging, *Alzheimer's Disease: Unraveling the Mystery*. Silver Spring, MD: Alzheimer's Disease Education and Referral (ADEAR) Center; 2002. NIH Publication 02-3782.



**Figure 3–5.** Schematic showing brain regions affected in severe AD. From National Institute on Aging, *Alzheimer's Disease: Unraveling the Mystery*. Silver Spring, MD: Alzheimer's Disease Education and Referral (ADEAR) Center; 2002. NIH Publication 02-3782.

Together these changes (neuritic plaques, neurofibrillary tangles, and granulovacuolar degeneration) in brain cells interrupt intercellular communication and thus information processing.

### Risk Factors for AD

The following factors place an individual at increased risk for developing AD:

- Age
- Family history
- Less education
- Head trauma
- Loneliness
- Gender
- Age of mother at individual's birth

- Having 2 copies of the type 4 allele of apolipoprotein E (ApoE4 allele)
- Having minimal cognitive impairment (MCI).

## Age

Clinically recognizable AD is unusual in individuals younger than 60, but for every decade after the sixth, the number of individuals with AD doubles.<sup>23</sup>

## Family History of AD

People with a first-order relative with AD are 4 times more likely to develop it. However, the majority of cases are sporadic, with only 5% having familial/autosomal dominant inheritance. Familial AD often develops when individuals are in their 40s and is associated with a more fulminating course.<sup>24–26</sup> Results of twin studies indicate that when one twin develops AD, in only 35% to 50% of the cases will the other genetically identical twin be affected.<sup>27</sup>

Three genes are linked to early onset AD: the amyloid precursor protein gene on chromosome 21, the presenilin gene 1 on chromosome 14, and the presenilin gene 2 on chromosome 1. Note that the amyloid precursor protein gene is located on the same chromosome that is affected in Down syndrome, chromosome 21. The presenilin gene 1 on chromosome 14 is suspected of being responsible for the majority of early onset cases.

## Definitions

*Familial*—occurring in more members of a family than would be expected by chance.

*Autosomal*—the gene is located on a chromosome other than the sex chromosome, so the disease is not sex linked; males and females are equally likely to be affected.

*Dominant*—the defective gene dominates its normal partner gene from the unaffected parent.



## Less Education

Individuals with higher levels of education or IQ have been reported less likely to develop AD.<sup>28–31</sup> Uneducated individuals older than 75 have almost twice the risk for dementia compared with elders with 8 or more years of education. A popular explanation for this finding is that educated individuals have a richer network of interneuronal connections (and therefore greater cognitive reserve) that developed from the stimulation provided by more education.<sup>32</sup> Also, individuals with greater cognitive reserve may exhibit less impairment because they are better at mitigating cognitive loss through alternative strategies or compensations.

## History of Head Trauma

Individuals with prior head injury may be at higher risk for AD.<sup>30</sup> Although the specific mechanism underlying the association of AD and head injury is not well understood, scientists theorize that head injury can alter the brain's protective system. Recently, researchers found head injury to be a risk factor for only those individuals with the ApoE4 allele.<sup>33</sup>

## Loneliness

Loneliness is associated with greater risk for AD.<sup>34</sup> In a 4-year longitudinal study of the relation between loneliness/social isolation and presence of dementia, Wilson and colleagues<sup>34</sup> found that cognitive decline more than doubled in lonely persons compared with non-lonely individuals. However, in lonely individuals who died, loneliness was not associated with AD pathology or cerebral infarction, a result that suggests that loneliness may contribute to dementia risk through another mechanism. Wilson and colleagues suggested that the neural systems that support social behavior might be less elaborate in lonely individuals, making them less able to compensate for other neural systems being compromised by age and disease-related neuropathology. In fact, forced social isolation is well known to have a deleterious effect on the brains of animals.

## Gender

Women have higher age-specific prevalence<sup>35,36</sup> and incidence<sup>37,38</sup> of AD than men. The gender effect remains to be explained, though some attribute it to the greater longevity of women.<sup>39</sup>

## Maternal Age

Your mother's age at the time of your birth may influence your risk for developing AD. Both advanced<sup>40</sup> and early<sup>41</sup> maternal age have been reported as influential. The pathogenetic mechanism underlying the association of advanced or early maternal age and AD remains open for speculation.

## Apolipoprotein E4 Allele

A type of cholesterol-carrying protein is a known risk factor for late-onset AD, namely, the ApoE4 allele. ApoE in the body varies in composition across individuals. The specific composition of ApoE is influenced by the presence or absence of 3 major variants of the gene: E2, E3, and E4. An individual inherits one gene that codes for the ApoE protein from each parent. The most common type is ApoE3, and most people inherit 1 or 2 copies. People who develop AD more commonly have the ApoE4 allele, and those with 2 copies of the ApoE4 gene have an 8 times greater risk for developing late-onset AD than individuals with no copies.<sup>42</sup> However, almost half the individuals with AD do not have the ApoE4 genotype, and the presence of an E4 allele accounts for a relatively small percentage of the cases of AD.<sup>43,44</sup>

## Minimal Cognitive Impairment

Although MCI can have many causes, and the cognitive status of a significant percentage of affected individuals does not worsen, MCI can be an early manifestation of AD. Those with amnesic MCI are more likely to evolve to clinically apparent AD than those with the nonamnesic type.

## Predictors of Disease Progression

The average duration of Alzheimer's disease is 8 years, though many victims suffer for 12 or more years. More rapid decline in AD is linked to:

- Early age at onset
- Presence of delusions or hallucinations
- Presence of extrapyramidal signs.

## Protective Factors

Besides a higher level of education, a socially and cognitively active lifestyle later in life reduces the risk for AD.<sup>45</sup> So does regular physical exercise, which appears to have a neuroprotective effect.<sup>46,47</sup> A meta-analysis of 15 prospective studies of 33,816 individuals without dementia revealed that moderate and intense exercise reduced the risk for developing MCI by 35%.<sup>48</sup>

## Effect of AD on Cognitive and Communicative Functions

As stated in the unit on MCI, the onset of AD is insidious, occurring many years before a clinical diagnosis is typically made.<sup>49-52</sup> Early neuropsychological deficits have been demonstrated by investigators using a variety of neuropsychological measures: psychomotor speed,<sup>53</sup> perceptual speed,<sup>54</sup> abstract reasoning,<sup>55</sup> visuospatial performance,<sup>56</sup> verbal ability,<sup>57</sup> and episodic memory.<sup>50-52</sup> Elias and colleagues<sup>58</sup> reported that lower scores on measures of memory and abstract reasoning were particularly strong predictors of probable AD.

The ever-present features of AD are impairment of episodic and working memory, especially executive functions. Other symptoms are more variable and reflect differences in the distribution of neuropathology.<sup>59,60</sup> Some patients have greater visuospatial than language deficits; for others, the reverse is true.<sup>61,62</sup> Those individuals with early-onset AD typically have less hippocampal involvement and greater atrophy in occipital and parietal cortices that

results in poorer performance on visuospatial tests than memory tests.<sup>63,64</sup>

Results of longitudinal studies, using the Mini-Mental State Examination (MMSE), indicate that the average amount of cognitive decline per year is 2 to 4 points.<sup>65</sup> On the Alzheimer's Disease Assessment Scale–Cognitive (ADAS-COG), the average decline is 8 points per year.<sup>16</sup>

## **Early Stage**

As previously stated, the pathophysiologic changes associated with AD begin years before behavioral and cognitive deficits are apparent. Thus, specifying the duration of the early stage is problematic. What is known, however, is the median age of survival after medical diagnosis of individuals in their 80s and 90s. Investigators in England followed more than 13 000 men and women, aged 65 and older, for 14 years.<sup>66</sup> In that period, 438 were diagnosed with dementia, most of whom died. Study results revealed that the men did not live as long as women: 4.1 years for men, 4.6 years for women. Frail individuals died earlier than those more physically fit. The investigators concluded that once an individual is medically diagnosed, life expectancy is approximately half that of a healthy individual of the same age.

When caregivers were asked to specify behavioral changes they observed before the diagnosis of AD was made,<sup>67</sup> they reported:

1. Difficulty handling finances
2. Memory problems
3. Concentration problems
4. Difficulty with complex tasks
5. Forgetting the location of objects
6. Decreased awareness of recent events.

## **Mental Status**

In early-stage AD, the affected individual is disoriented for time but not place or person. Table 3–2 shows the average score, or range of scores, of early-stage AD patients on commonly used mental status tests.

**Table 3–2.** Average Score, or Range of Scores, of Early-Stage Alzheimer's Disease Patients on Commonly Used Mental Status Tests

ABCD Mental Status Test	7.3–12.5
Mini-Mental State Examination	16–24
Clinical Dementia Rating Scale	1
Global Deterioration Scale	3

### ***Motor Function***

Motor function is good and the patient is ambulatory.

### ***Memory Function***

The typical first symptom of AD is a problem with episodic memory: forgetting where the car is parked, getting lost, being repetitious, not remembering having taken medication, and the like. Working memory is also affected early and is manifested by decreased efficiency of encoding and retrieval of information. Individuals have difficulty sustaining attention,<sup>68–71</sup> and span memory is modestly attenuated in some individuals, though not all.

### ***Basic Activities of Daily Living***

Individuals in early-stage AD are generally able to carry out activities of daily living (ADLs), such as bathing, dressing, and feeding themselves and going to the bathroom independently.

### ***Linguistic Communication***

Speech is fluent in early AD, with no evidence of dysarthria or articulation errors.<sup>72</sup> Spoken language is grammatical, though errors of grammar and spelling are common in written language.<sup>73,74</sup> Content of language is noticeably affected and characterized by tangentiality and an increase in the number of “empty words” such as “thing” and “it.” Because AD patients often forget what they just heard or thought, their oral discourse contains more sentence fragments and repetitiousness and is less cohesive than the discourse of healthy peers.<sup>75–77</sup> Then too, AD patients pause more frequently and have a

slower speech rate.<sup>78</sup> Mild dysnomia is common, and when a naming error occurs, it is usually semantically related to the target word (eg, “lime” for “lemon,” “sharp” for “saw”).<sup>79</sup> Performances on tests of receptive vocabulary reveal that vocabulary is shrinking. Performance on tests of verbal fluency show significant deficits compared with healthy elders that worsen as the disease progresses.<sup>71,80</sup>

### **Language Use**

Writing is more affected than oral language, and written discourse contains intrusions, perseverations, and more spatial-mechanical disturbances than that of healthy peers.<sup>81–85</sup> Although individuals in early-stage AD generally comprehend what they hear and read, they quickly forget it.<sup>86</sup> Mild AD patients often miss the point of a joke and may be confused by sarcasm. Some individuals exhibit logorrhea,<sup>87,88</sup> perhaps from disinhibition associated with frontal lobe damage. Early-stage patients are able to answer most questions and define words.<sup>89</sup>

Table 3–3 presents early linguistic communication symptoms,<sup>90</sup> listed in order of prevalence, from most to least frequent, as reported by 99 primary caregivers of AD patients. The most commonly reported symptom was word-finding difficulty. The least prevalent was an increase in talkativeness.

### **Discourse Sample of Mild AD Patient**

The following discourse sample is typical of early-stage AD patients. The individual who produced this sample was instructed to explain what is happening in the Norman Rockwell painting *Easter Morning*. Rockwell portrays a man sitting in the family living room clad in pajamas and looking sheepish because he is not going to church with his wife and 3 children on Easter Sunday. Rather, he is staying home to read the newspaper, drink coffee, and smoke cigarettes. His wife and children are lined up behind him ready to go out the door.

It's evidently snowing outside of the window. And it's the mother I guess and the two girls and the boy, they are dressed like going to church. Because they each have Bibles in their hands. And this lazy goof. He sits in the chair and he's got his slipper this way and his eyes go over there. His hair looks like

**Table 3–3.** Linguistic Communication Symptoms Listed in Order of Prevalence from Most to Least Frequent (Bayles & Tomoeda<sup>89</sup>)

<b>Most Frequent</b>
Word-finding problems
Difficulty naming objects
Difficulty writing a letter
Impaired comprehension of instructions
Difficulty sustaining a conversation
Problem completing sentences
Tendency to repeat ideas
Reading comprehension problems
Production of meaningless sentences
Decrease in talkativeness
Inappropriate topics
Inappropriate to whom said
Tendency to interpret literally
Failure to recognize humor
Increase in talkativeness
<b>Least Frequent</b>

hell. Pardon me. And whatever he's got on, it's ridiculous. And he, he, he is a good person to do that because he can do it. You know. Get his eyes over. And so, eh, he wants to stay home and see the funny papers and the newspapers and I love that Norman Rockwell anyway. And, eh, he's got his eyes almost out of sight. You know. But yet you can get him, he's a terrific guy. And so all these little darlings get to go to church. That's the way I see it because they each have a Bible their hand and, eh, he's looking to see what he can see. And it looks like he's saying, thank God I don't have to go. Eh, so that's about it.

Notice that the utterances are generally grammatical; however, compared with neurologically normal adults, this mild AD patient is a less efficient communicator. Also, she did not express the gist

of the picture, namely that the wife is angry with her husband for staying home and he is feeling sheepish and guilty. The volume of discourse produced is not necessarily less than a healthy elder would produce but contains fewer ideas. Early-stage AD patients tend to repeat ideas, as did this woman, who repeated mention of the father's eyes, going to church, and holding Bibles. This phenomenon of *ideational perseveration* occurs more in mild and moderate patients than in severe because by the severe stage, individuals with AD have many fewer ideas.

## Middle Stage

Many physicians and neuropsychologists define the middle stage by mental status. When individuals score below 16 on the MMSE, they are recognized as being in the middle stage of the disease. However, no hard and fast rule exists for defining the difference between early and middle stage.

### Mental Status

In midstage AD, the patient changes most dramatically, becoming increasingly dependent on others for survival. Disorientation worsens and includes confusion about place as well as time, although orientation to self is intact. Table 3-4 shows the average scores of midstage individuals on widely used mental status tests.

### Motor Function

Motor function in midstage AD patients remains good, but restlessness is common.

**Table 3-4.** Average Score or Range of Scores of Individuals on Commonly Used Mental Status Tests

ABCD Mental Status Test	1.3–7.7
Mini-Mental State Examination	8–15
Clinical Dementia Rating Scale	2
Global Deterioration Scale	4–6



## **Memory**

Many changes occur in memory in midstage AD, including worsening of episodic memory, attenuation of span memory, encoding and retrieval deficits, and degradation of semantic memory. Midstage patients have difficulty focusing attention, are easily distracted, and can be difficult to engage in activities. Visual-perceptual and visual-constructive deficits are apparent, and in fact AD patients perform inferiorly to healthy peers on virtually all executive function and cognitive-communicative tests.

## **Continence**

During the later portion of midstage AD, incontinence of bladder becomes a problem.

## **Basic Activities of Daily Living**

With supervision and environmental support, most midstage AD patients can carry out basic ADLs. In contrast, instrumental ADLs such as taking messages and managing finances are problematic. It is in this stage that driving becomes an issue. Although the midstage AD patient can manipulate the controls and mechanically drive a car, problems with attention, judgment, and memory make them dangerous to themselves and others.

## **Definitions**

*Activities of daily living*—activities routinely performed in the course of an average day, such as feeding, bathing, dressing, and grooming.

*Instrumental activities of daily living*—activities related to independent living, such as preparing meals, managing finances, shopping, doing housework, and using the telephone.

## **Linguistic Communication**

**Speech.** Speech is fluent, though often slower and halting and filled with more silent pauses that occur outside syntactic boundaries<sup>78</sup> and on more frequently occurring words.

**Form of Language.** The form of language remains generally intact but content is prominently affected.<sup>86</sup> Oral discourse contains fewer nouns relative to verbs,<sup>73,91,92</sup> is less cohesive,<sup>93</sup> and can be described as “empty.” Performance on vocabulary tests indicates loss of vocabulary and greater degradation of conceptual knowledge.<sup>77,86,94</sup> Midstage AD patients are significantly impaired relative to healthy peers in generating exemplars of a category<sup>95–98</sup> and naming on confrontation.<sup>86</sup> Written language is replete with errors. Midstage patients exhibit diminished comprehension of written and spoken language,<sup>99–104</sup> although most do well at the word and phrase level. The mechanics of reading are spared but comprehension is impaired, and that which is comprehended is rapidly forgotten.

**Language Use.** Word-finding difficulties are now more obvious in spontaneous speech and on confrontation and generative naming tests.<sup>72,95,105–107</sup> Ideational repetition<sup>76</sup> is frequent in conversation and when individuals are asked to describe a picture or object. Midstage patients have poor sensitivity to context<sup>108</sup> and may miss the point of jokes. Also, they have a tendency to interpret nonliteral language literally. Although able to perform the mechanics of reading aloud, comprehend written language at the word level, and follow simple commands, midstage patients have serious difficulty defining words and repeating phrases.<sup>89</sup> In terms of writing, midstage patients make many spelling errors and mechanical distortions,<sup>109</sup> and their narratives are less complex.

### ***Discourse Samples of Moderately Demented AD Patients***

Sample 1: Task: Description of the *Easter Morning* picture

Yeah, well, this man is, knows that he is, is in the wrong place here. So, but he's hiding away and, and these other people, I don't know whether this boy is ready to do it or not but this man is doing it from someplace over here, but it won't do it. And, ah, these, these, two children are evidently are just very excellent that they are both the same person. And, this man I don't know, would rather . . . He gets his too. And uh, oh, he's got this thing, worried because it's going to have a . . . going up there, you can see it. [Subject points to the cigarette smoke in the picture.] And all this stuff is just a mess.

Darn fools got anybody. Darn fools got them walking in it. They want to, I don't think they do. I don't want to go in this place. I don't know what he's for. He's looks like he's getting a ten paper. Here's some more paper. Here's some more, my god! Look at it. He has to be worn down before he can do anything, cause these people don't want to work, work anything with him. Don't you think that's about right?

Sample 2: Task: Individual is describing a marble.

*Examiner:* Tell me about this (marble).

*Patient:* Literally speaking, a marble. And the white is uh, is, uh, is the harder part. Well, it's a, I'd say cassium. The colored part, I don't know. Associated rocks. This is, uh, this is of the granitic nature. The whole thing. When you say cassium you're, you're talking about the hardest part of a, of a, of a rock. Well, there's some design to it. Some reason how it took that shape. But, uh, that doesn't mean a whole lot, exactly, the way someone de-, designed it.

As is apparent from these language samples, moderately demented AD patients produce discourse that expresses significantly fewer ideas than that of people with mild dementia. They are increasingly less concise and more repetitious. Intentions are often forgotten, resulting in many sentence fragments. As did the mildly demented patient, the individual who produced this discourse failed to state the gist of the Rockwell picture. The intention to describe remains, but word sequences often have little apparent meaning. Furthermore, there is a lack of self-monitoring and correction.

## Late-Stage AD

During the late stage, AD patients often become disoriented for person as well as place and time. Their MMSE scores range from 0 to 9<sup>110</sup>; on the Clinical Dementia Rating Scale, they score 3.<sup>111</sup> Intellect is devastated by a global failure of working and declarative memory systems, and individuals are unable to carry out basic ADLs. There is incontinence of bladder and bowel. Motor impairment may be present, and in the very late stage, many are nonambulatory.

### **Linguistic Communication**

Speech is typically fluent but generally slower and more halting. In many patients, the form of language remains intact,<sup>112,113</sup> although meaningful output is greatly reduced.<sup>81</sup> Some individuals are mute, others exhibit palilalia (repetition of phrases, words, or syllables that tend to increase in speed at the end of an utterance),<sup>81</sup> echolalia,<sup>74</sup> or jargon.<sup>114</sup> And yet, other advanced patients can contribute to a conversation, state their name, and retain aspects of social language.<sup>115</sup> Reading comprehension is severely impaired, although some can read single words aloud.<sup>112,116</sup> Virtually all late-stage patients are unable to express themselves in writing.

### **Communicative Abilities of Late-Stage AD Patients**

The verbal communication abilities of 49 late-stage AD patients were evaluated in relation to other markers of late-stage AD (incontinence and ambulatory ability). The authors of 2 widely used tools, the Global Deterioration Scale<sup>117</sup> and the Functional Assessment Stages,<sup>118</sup> reported the *virtual loss of all verbal abilities in late-stage AD patients*. As part of a National Institutes of Health–supported longitudinal study of individuals with AD, Bayles and Tomoeda<sup>116</sup> were able to evaluate language in 49 late-stage patients. The Functional Linguistic Communication Inventory (FLCI)<sup>116</sup> was administered to these individuals. The FLCI evaluates greeting and naming, question answering, writing, sign comprehension and object-to-picture matching, word reading and comprehension, ability to reminisce, following of commands, pantomime, gesture, and conversation. Study results revealed that AD patients, who were *incontinent only for bladder*, had more communication skills than individuals who were *bladder and bowel incontinent*. They were able to respond appropriately to a greeting and to a closing comment and compliment. Several could recognize the written form of their name, state their spouse's name, recognize a common object from a line drawing, follow a 1-step command, and even correct misinformation about themselves.

None of the individuals who were incontinent for both bladder and bowel were able to contribute to a conversation. Neither could they state their spouse's name, follow a 2-step command, or provide relevant information about a common object. The most limited language was observed in individuals who were bowel and bladder incontinent and bedridden. However, contrary to what was expected, given previous characterizations of the verbal ability of late-stage

patients,<sup>118</sup> 82% of the study participants produced language during the evaluation.

The incontinent but ambulatory patients produced more words than those who were incontinent and nonambulatory. Of the 10 individuals who were incontinent but ambulatory, 1 AD participant produced 252 words and another produced a single word. Of the 17 individuals who were incontinent and nonambulatory, 3 individuals were nonverbal, 2 produced a single word, and 1 produced 131 words, of which 82 were different words.

The following are examples of answers provided by severely demented study participants to questions such as, "Where would you like to go on a trip?" and "What is your favorite food?"

"Right now I think I'd like to see Hawaii."

"Fruit of all kind is all right with me, I love fruit."

"I don't think I ought to go anywhere cause I'm in bad shape."

"I eat a lot of things now."

### **Discourse Samples of Severely Demented AD Patient**

Sample 1: Task: Description of a button

*Examiner:* Tell me all about this [button].

*Patient:* Well, it's a button, with two holes in it for . . . for sewing on thread. That's the only . . .

*Examiner:* Can you tell me anything else?

*Patient:* Uh, that the only thing I can see.

Sample 2: Task: Description of a nail

*Examiner:* Tell me about this [nail].

*Patient:* That's a shingle nail. That's for tack on shingles and tack on roofing, and to tack on, uh, uh, its, er, a plasterboard.

*Examiner:* Can you describe it to me?

*Patient:* You mean this nail? Yeah, its long, short, small. That's uh, that about all . . .

As you can see, meaningful verbal output has diminished dramatically. However, grammar is generally intact. Without a context, listeners often have difficulty understanding what the AD patient is saying.

## Summary of Important Points

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- AD is the most common cause of dementia.
- The key diagnostic criterion for diagnosis is the presence of multiple cognitive deficits sufficient to interfere with social and occupational functioning that are gradual in onset and progressive in nature.
- AD begins in brain areas important to episodic memory and spreads to areas important to working and declarative memory. Procedural memory is spared until late in the disease course.
- The characteristic morphologic changes in the brain are neuritic plaques and neurofibrillary tangles, with areas of granulovacuolar degeneration and atrophy.
- AD rarely affects individuals younger than 60, but for every decade after the sixth, the number of individuals with AD doubles.
- A small number of individuals develop familial AD in their 40s, an autosomal dominant form of the disease.
- A type of cholesterol carrying protein has been found to be a major risk factor for late-onset AD, namely, the type 4 allele of apolipoprotein E.
- A diagnosis of AD reduces life expectancy to one half that for healthy age-mates.
- Communicative ability gradually deteriorates over the disease course. In the early stages, individuals are verbally fluent and able to comprehend most of what they read and hear but rapidly forget recently acquired information. By end-stage disease, individuals are intellectually devastated, and language output is greatly diminished and often nonsensical.
- Semantics and pragmatics are affected early; phonology and syntax are generally preserved well into the disease course.
- Considerable variability exists in the ability of late-stage AD patients to communicate. Some are mute, others produce some meaningful language.

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