Chapter 10
Alzheimer's Disease and Dementia

Michael Harper and Anne M. Suskind

Description of Disease

Dementia is not a single disease. It is a term that describes a progressive loss of ability in more than one domain of cognition severe enough to result in a decline in an individual's capacity to perform everyday activities. The most common type of dementia is Alzheimer's disease (AD), affecting an estimated 5.7 million Americans [1]. Other common types of dementia are dementia with Lewy bodies, vascular dementia, and frontotemporal dementia. Dementia primarily affects older adults with a prevalence of 10% at age 65 and doubling every 5 years [2, 3]. By the age of 85, it is estimated that 25–50% of individuals will have dementia [4, 5].

Disease Pathophysiology

By definition, dementia is an acquired disorder, the clinical onset of which typically begins after the age of 60. The neuropathologic features that distinguish AD are the deposition of beta amyloid protein in the extracellular regions of the brain and the intracellular neurofibrillary tangles within neurons that are made up of hyperphosphorylated tau protein [6]. Beta amyloid plaques are associated with synaptic

M. Harper
Department of Medicine, Division of Geriatrics, University of California, San Francisco, CA, USA
e-mail: Michale.Harper@ucsf.edu

A. M. Suskind (✉)
Department of Urology, Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, CA, USA
e-mail: Anne.Suskind@ucsf.edu

J. T. Stoffel, E. V. Dray (eds.), *Urological Care for Patients with Progressive Neurological Conditions*, https://doi.org/10.1007/978-3-030-23277-1_10

dysfunction, while the neurofibrillary tangles are linked to axonal loss and ultimately cell death [7]. These changes begin years, if not decades, before symptoms emerge and debate remains as to whether the pathologic changes seen in AD are the cause or result of the disease. Similar to AD, putative proteins have been identified for Lewy body dementia (alpha-synuclein inclusion bodies) and frontotemporal dementia (tau and ubiquitin proteins) [8, 9]. Vascular dementia is caused by any condition that leads to disruption of blood flow to the brain and vascular damage. The most common subtypes of vascular dementia are the result of atherosclerotic, cardioembolic, or small vessel disease.

Organs Affected

In the early stages of dementia, the primary symptom is most often a loss of memory, typically short-term memory, while memories from the remote past are preserved until later stages. Other common symptoms include aphasia (e.g., word finding difficulty), visuospatial dysfunction (e.g., impaired facial recognition and navigation), loss of executive function (e.g., poor judgment and planning), and apraxia or the inability to carry out learned motor tasks despite the presence of an intact motor system (e.g., inability to use a brush to comb one's hair).

A variety of psychological and behavioral symptoms are associated with most dementias and can manifest over the course of the illness. Common symptoms include sleep disturbance, wandering, perseveration, depression, hallucinations and delusions, apathy, irritability, disinhibition, and physical aggressiveness.

Key Testing for Diagnosis

The diagnosis of dementia is based primarily on the clinical presentation, focusing on the history and physical exam. Because of the nature of the illness, the clinician may not be able to rely on the information provided by the patient and therefore gathering information from collateral sources is often necessary. The history should focus on eliciting symptoms of cognitive decline, the onset and progression of the earliest deficits, and the impact on the patient's ability to perform routine daily functions, specifically probing basic and instrumental activities of daily living. The use of a standardized cognitive testing instrument can provide valuable information about the domains of cognition involved and the degree of cognitive impairment. Commonly used instruments include the Mini-Cog [10] and the Montreal Cognitive Assessment (MoCA) [11]. Performance on cognitive testing can be affected by years of education, and when available, cognitive tests should be administered in a patients' native language.

Laboratory and imaging studies are directed at identifying potentially reversible causes of dementia which are in fact rare. The American Academy of Neurology

recommends the following laboratory tests in the routine evaluation of dementia: complete blood count, glucose, serum electrolytes, blood urea nitrogen, creatinine, thyroid stimulating hormone, vitamin B12 level, and liver function tests [12]. Testing for syphilis and HIV is only recommended, if the patient is at high risk for one or both diseases. Neuroimaging looking for evidence of a previous stroke, tumor, hydrocephalus, and subdural hematoma is recommended for all patients being evaluated for cognitive decline. In most cases, a CT scan of the brain is adequate to rule out conspicuous pathology. Functional imaging studies such as functional magnetic resonance imaging (fMRI) and fluorodeoxyglucose positron emission tomography (FDG-PET) have some utility in distinguishing types of dementia but should not be considered a part of routine evaluation.

Timeline of Progression

Most dementia types begin insidiously and progress slowly; however, there can be wide variability among patients with the same disease. In less common cases, dementia can develop suddenly and progress rapidly with death occurring within months of diagnosis. Patients with AD have a median life expectancy of 4–8 years, but this can vary significantly from as little as 3 years to as long as 20 years [1]. The progression of dementia can be described based on the degree of cognitive loss or based on functional decline. The Global Deterioration Scale (GDS) describes seven stages of dementia using a framework of changes in cognition (see Table 10.1) [13].

Table 10.1 The global deterioration scale

Stages	Clinical characteristics
1: No cognitive decline	No subjective memory complaints
	No evidence of memory deficits with clinical interview
2: Very mild cognitive decline	Subjective memory complaints
	Names
	Placement of objects
	No evidence of memory deficits with clinical interview
	No objective deficits in employment or social situations
3: Mild cognitive decline	Earliest memory deficits can now be objectively identified through clinical interview. Deficits seen include the following:
	Concentration
	Limited memory retention
	Word finding
	Navigation
	Performance issues may arise in work and social situations
	Denial may be present

(continued)

Table 10.1 (continued)

Stages	Clinical characteristics
4: Moderate cognitive decline (mild dementia)	Clear-cut memory deficits are evident on clinical interview. Deficits seen include the following:
	Serial subtractions
	Reduced memory of recent events
	Managing finances
	Orientation and ability to recognize familiar people and faces and travel to familiar places are preserved
	Denial may be more prominent and withdrawal from challenging situations may occur
5: Moderately severe cognitive decline (moderate dementia)	Some assistance with routine activities is needed
	Individuals may no longer be able to:
	Recall their address, phone number, names of close relatives or friends
	Count backward from 40 by 4s or 20 by 2s
	Correctly identify time or place
	Recollection of spouse's and children's names is preserved as is the ability to eat and toilet
6: Severe cognitive decline (moderate dementia)	Deficits may include the following:
	Forgetting name of spouse
	Lack of awareness of recent events and life experiences
	Inability to count backward from 10
	Behavioral and emotional symptoms and personality changes may include the following:
	Delusions and hallucinations
	Anxiety and agitation
	Repetitive behaviors (e.g., phone calls, hand tapping)
	Sleep–wake cycle disturbances
	Assistance is needed with most if not all ADLs[a] and IADLs[b]
	Urinary incontinence episodes are common
7: Very severe cognitive decline (severe dementia)	Dependence for ADLs and IADLs is the rule
	Urinary incontinence predominates
	Walking requires assistance and may be completely lost
	Speech is limited to a few words or perhaps only grunting
	Swallowing and skeletal muscle functions become impaired

Adapted from Reisberg et al. [13]
[a]ADLs basic activities of daily living (bathing, dressing, transfers, toileting, feeding).
[b]IADLs instrumental activities of daily living (telephone, shopping, food preparation, housekeeping, laundry, transportation, medication management, management of finances).

Operative Risk

Patients with dementia may occasionally have an indication to undergo invasive procedures and surgery. It is important to recognize that in the early stages of dementia, many patients will maintain their ability to participate in conversations of informed consent and make independent decisions about their treatment.

For those patients with dementia who proceed with surgery, studies have shown that they are at increased risk for a variety of adverse outcomes including delirium, longer lengths of stay, and greater mortality [14]. Delirium is particularly common with an incidence of 15% after elective noncardiac surgery and can be as high as 35–65% in high-risk operations such as hip fracture repair [15, 16]. While preexisting dementia is considered the strongest predisposing risk factor for postoperative delirium, its presence should be considered in the context of other risk factors including advanced age, limitations in physical function, abnormal serum chemistries, and the type of procedure. While the type and route anesthesia have not been shown to have an impact on the incidence of delirium, using the lowest dose of anesthetic agent possible may reduce the risk [17, 18]. A 2014 best practice statement by the American Geriatrics Society described several recommendations to prevent postoperative delirium that included multifaceted nonpharmacologic interventions (e.g., sensory enhancement, early mobility, cognitive reorientation, sleep enhancement), pain management, avoidance of benzodiazepines, antipsychotics and other high-risk medications (e.g., anticholinergic medications), and assessment and management of other medical contributors to delirium [19].

Urologic Symptoms/Treatments

Expected Urologic Symptoms

Urinary incontinence among older adults with dementia is common, multifactorial, and may have different origins compared to incontinence among younger healthier adults. One study of patients with established Alzheimer's dementia revealed that urinary incontinence was significantly associated not only with age but also with disinhibition, deficits in attention and orientation, and reduced verbal fluency. These findings suggest that factors other than traditional neural control of continence likely play a role in the development of incontinence in this population [20].

Functional incontinence is a major cause of urinary incontinence among older adults with dementia (Table 10.2). It occurs when the individual has trouble getting to the bathroom due to physical impairment, cognitive impairment, or decreased motivation. Individuals with physical impairment may have physical limitations getting to the bathroom in general or getting to the restroom quickly enough in order to prevent leakage. Individuals with cognitive impairment may not know how to get to the bathroom or even that they need to get to the bathroom, presenting an entirely different set of problems. In more advanced cases of dementia, individuals may be entirely indifferent to continence and may have disturbed consciousness around this, and other self-hygiene issues [21].

Overactive bladder is another major cause of urinary incontinence in older adults with dementia (Table 10.2), which may be present in isolation or in combination

Table 10.2 Urologic symptoms among older adults with dementia

Urologic symptoms	Description of urinary symptoms	Expected urodynamic finding
Functional incontinence	The individual has a difficult time getting to the bathroom due to physical impairment, cognitive impairment or decreased motivation [21]	NA
Overactive bladder	Urinary urgency and frequency may be associated with nocturia and or incontinence [23]	Detrusor overactivity
Underactive bladder	Slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete emptying and dribbling, often with storage symptoms [22]	Detrusor underactivity
Stress incontinence	The symptom of involuntary leakage on effort or exertion, or on sneezing or coughing [23]	Observed leakage from the urethra seen at the exact time of exertion [24]
Nocturnal polyuria	More than 33% of the total daily urine output occurs at night	NA
Drug-induced incontinence and retention	Drugs that affect either the central nervous system or lower urinary tract (i.e., antipsychotic medications, antidepressants, benzodiazepines, sedatives, anticholinergics)	Inability to urinate

with other forms of urinary incontinence such as functional incontinence. For example, if an individual has a strong urge to urinate and has physical limitations or a gait disturbance that makes it difficult to get to the restroom quickly, this may result in leakage that could have otherwise been avoided. Urodynamics, which may be challenging in this patient population, may show associated detrusor overactivity as an objective sign of overactive bladder symptoms.

Other potential urologic problems associated with dementia are outlined in Table 10.2. Underactive bladder, which is defined as a slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete emptying and dribbling, and often with storage symptoms [22], can occur in isolation or in combination with OAB. The latter case results in detrusor hyperactivity with impaired contractile (DHIC) function. Stress incontinence, the symptom of involuntary leakage on effort or exertion, or on sneezing or coughing [23], may also be present in older adults, particularly in older women, with dementia. Nocturnal polyuria, defined as more than 33% of the total daily urine output that occurs at night, is common in the older population and hence may also be present in older adults with dementia. Finally, drug-induced incontinence and retention are important potential causes of urinary symptoms in older adults with dementia, with particular emphasis on antipsychotic medications, antidepressants, benzodiazepines, sedatives, and anticholinergics [21].

Key Goals of Urologic Management

The goals of urologic management should take into account the degree of bother/distress for both the patient and the caregiver, which may be dissimilar at times, making management difficult and nuanced in some cases. In patients with more advanced dementia, the individual may not be particularly bothered by their urologic symptoms; however, the caregiver may be quite distressed, particularly in cases of urinary incontinence. Urinary incontinence among older adults with dementia is a leading cause of institutionalization and therefore, the burdensome effects on the caregiver should be taken seriously.

A literature review of ten studies looking at patients with urinary incontinence living in long-term care facilities revealed that while these individuals value having bladder function, they often believe that urinary incontinence is inevitable and intractable. This attitude is often met with low expectations and many individuals decline further evaluation and treatment. Some express satisfaction with the state of urinary incontinence, even though it is not consistent with their life preferences and those with more severe cognitive impairment often respond with anxiety when caregivers attempt to provide continence care [25].

Studies on caregivers emphasize the importance of treating their loved one with dignity, taking them seriously as equal human beings, and making sure that their relational needs are met (i.e., not treating them as an object or task). These findings highlight the importance of understanding a *dignifying caring relationship*, with meaningful interaction between the patient and the physician [26]. These attributes call for a different medical paradigm that incorporates the psychosocial aspects of providing continence care in this population that meet the needs of individuals with complex health conditions who are dependent on another person for assistance [27].

Treatment Options

Treatment of urinary symptoms in adults with dementia should begin with ruling out any underlying reversible/treatable causes. The "DIAPERS" pneumonic for urinary incontinence is a helpful place to start, whereby each letter represents a different potentially treatable cause: delirium, infection, atrophic vaginitis, psychological/behavioral causes, pharmaceuticals, endocrine causes, restricted mobility, and stool impaction.

Once the above factors have been ruled out and or addressed, there are several treatment strategies specific to older adults with urinary incontinence and dementia that can be considered. Toileting regiments/behavioral therapy may be of benefit in the form of prompted voiding, whereby the individual is asked on a regular schedule whether they need toileting assistance, combined with positive reinforcement for using the restroom. This is particularly helpful among individuals with decreased

motivation, cognitive disability, and gait disorders. Additionally, changes to environmental factors such as hallway handrails, canes, walkers, and wheelchairs, easy toilet access and visibility, improvements to bathroom facilities such as lighting, grab bars, toilet seat and height, commodes, and well-designed clothing that can easily be taken off (i.e., Velcro or elastic waistbands instead of buttons or zippers) can help maximize independence and toileting [21]. Discussion of and assistance with continence care products, such as pads and absorbent undergarments, is also important in this population.

For patients with OAB, anticholinergic medications should be used with caution. Alzheimer's dementia is characterized by a central cholinergic deficit. Anticholinergic medications can block cholinergic receptors in the central nervous system (M1-muscarinic receptors in the cerebral cortex and M4 receptors in the basal ganglia), potentially exacerbating declines in cognitive function. Additionally, these medications can interact with acetylcholinesterase inhibitors given to individuals with cognitive impairment to improve cognitive function, further worsening cognition [28]. Studies specifically addressing the efficacy of pharmacotherapy (either anticholinergic or beta3-agonist medications) in individuals with an existing dementia diagnosis are lacking [29].

Treatment Map

Figure 10.1 presents a treatment map for urinary incontinence among older adults with dementia. It emphasizes the importance of addressing both medical and psychosocial issues associated with this problem in this population and is informed by

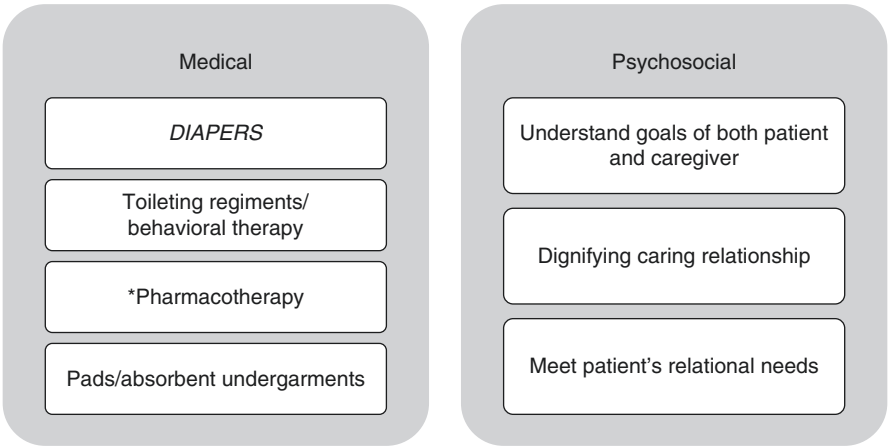

Fig. 10.1 Treatment Map for management of urinary incontinence among older adults with dementia.

Ostaszkeiwicz et al. [27]. Important to the model are the psychosocial aspects of care including: (1) understanding the goals of both the caregiver and the patient; (2) interacting via a dignifying caring relationship, whereby both the patient and the care provider interact and participate in a meaningful, personal and responsible way; and (3) meeting the patient's relational needs meaning that the caregiver treats the patient as more than an object or task [26].

References

1. Association; As. Alzheimer's disease facts and figures. Alzheimers Dement. 2016; 2016(14):367–429.
2. Matthews KA, Xu W, Gaglioti AH, et al. Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015–2060) in adults aged >/=65 years. Alzheimers Dement. 2019;15(1):17–24.
3. Corrada MM, Brookmeyer R, Paganini-Hill A, Berlau D, Kawas CH. Dementia incidence continues to increase with age in the oldest old: the 90+ study. Ann Neurol. 2010;67(1):114–21.
4. Koller D, Bynum JP. Dementia in the USA: state variation in prevalence. J Public Health (Oxf). 2015;37(4):597–604.
5. Evans DA, Funkenstein HH, Albert MS, et al. Prevalence of Alzheimer's disease in a community population of older persons. Higher than previously reported. JAMA. 1989;262(18):2551–6.
6. Magalingam KB, Radhakrishnan A, Ping NS, Haleagrahara N. Current concepts of neurodegenerative mechanisms in Alzheimer's disease. Biomed Res Int. 2018;2018:3740461.
7. Theofilas P, Ehrenberg AJ, Nguy A, et al. Probing the correlation of neuronal loss, neurofibrillary tangles, and cell death markers across the Alzheimer's disease Braak stages: a quantitative study in humans. Neurobiol Aging. 2018;61:1–12.
8. Minami A, Nakanishi A, Matsuda S, Kitagishi Y, Ogura Y. Function of alpha-synuclein and PINK1 in Lewy body dementia (Review). Int J Mol Med. 2015;35(1):3–9.
9. Hernandez I, Fernandez MV, Tarraga L, Boada M, Ruiz A. Frontotemporal lobar degeneration (FTLD): review and update for clinical neurologists. Curr Alzheimer Res. 2018;15(6):511–30.
10. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. J Am Geriatr Soc. 2003;51(10):1451–4.
11. Nasreddine ZS, Phillips NA, Bedirian V, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53(4):695–9.
12. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56(9):1143–53.
13. Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry. 1982;139(9):1136–9.
14. Kassahun WT. The effects of pre-existing dementia on surgical outcomes in emergent and nonemergent general surgical procedures: assessing differences in surgical risk with dementia. BMC Geriatr. 2018;18(1):153.
15. Marcantonio ER, Goldman L, Mangione CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA. 1994;271(2):134–9.
16. Rudolph JL, Marcantonio ER. Review articles: postoperative delirium: acute change with long-term implications. Anesth Analg. 2011;112(5):1202–11.
17. Radtke FM, Franck M, Lendner J, Kruger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth. 2013;110(Suppl 1):i98–105.

18. Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clin Proc. 2010;85(1):18–26.
19. American Geriatrics Society Expert Panel on Postoperative Delirium in Older A. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. J Am Coll Surg. 2015;220(2):136–48. e131
20. Alcorn G, Law E, Connelly PJ, Starr JM. Urinary incontinence in people with Alzheimer's disease. Int J Geriatr Psychiatry. 2014;29(1):107–9.
21. Sakakibara R. Dementia and lower urinary tract dysfunction. In: Corcos J, Ginsberg DA, Karsenty G, editors. Textbook of the neurogenic bladder. 3rd ed. Boca Raton, FL: CRC Press; 2016.
22. Uren AD, Drake MJ. Definition and symptoms of underactive bladder. Investig Clin Urol. 2017;58(Suppl 2):S61–7.
23. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003;61(1):37–49.
24. Abrams D, Rutland A, Cameron L. The development of subjective group dynamics: children's judgments of normative and deviant in-group and out-group individuals. Child Dev. 2003;74(6):1840–56.
25. Ostaszkiewicz J, O'Connell B, Dunning T. Residents' perspectives on urinary incontinence: a review of literature. Scand J Caring Sci. 2012;26(4):761–72.
26. Heggestad AK, Nortvedt P, Slettebo A. Dignity and care for people with dementia living in nursing homes. Dementia (London). 2015;14(6):825–41.
27. Ostaszkiewicz J. Reframing continence care in care-dependence. Geriatr Nurs. 2017;38(6):520–6.
28. Winge K. Lower urinary tract dysfunction in patients with Parkinsonism and other neurodegenerative disorders. Handb Clin Neurol. 2015;130:335–56.
29. Orme S, Morris V, Gibson W, Wagg A. Managing urinary incontinence in patients with dementia: pharmacological treatment options and considerations. Drugs Aging. 2015;32(7):559–67.