

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition: Dementia and Movement Disorders

Variant 1: Probable Alzheimer's disease.

Radiologic Procedure	Rating	Comments	RRL*
MRI head without contrast	8		None
MRI head without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	6		Med
FDG-PET head	6	For problem solving.	High
Tc-99m HMPAO SPECT head	5	For problem solving.	High
CT head without and with contrast	4		Med
MRI spectroscopy head	4		None
MRI functional (fMRI) head	2	For research purposes.	None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 2: Possible Alzheimer's disease.

Radiologic Procedure	Rating	Comments	RRL*
MRI head without contrast	8		None
MRI head without and with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET head	7	For problem solving.	High
CT head without contrast	6		Med
Tc-99m HMPAO SPECT head	6	For problem solving.	High
CT head without and with contrast	5		Med
MRI spectroscopy head	4		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Dementia and Movement Disorders****Variant 3:****Suspected vascular dementia or mixed vascular dementia and Alzheimer's disease.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	6		Med
FDG-PET head	6	For problem solving.	High
MRA head and or neck	6	See statement regarding contrast in text under "Anticipated Exceptions."	None
CTA head and or neck	6		Med
US carotid duplex	6		None
CT head without and with contrast	5		Med
Tc-99m HMPAO SPECT head	5	For problem solving.	High
MRI spectroscopy head	2		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 4:**Frontotemporal dementia.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET head	7	For problem solving.	High
CT head without contrast	6		Med
Tc-99m HMPAO SPECT head	6	For problem solving.	High
CT head without and with contrast	4		Med
MRI spectroscopy head	4		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Dementia and Movement Disorders****Variant 5:****Dementia with Lewy bodies.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
Tc-99m HMPAO SPECT head	7	For problem solving.	High
FDG-PET head	7	For problem solving.	High
CT head without contrast	6		Med
CT head without and with contrast	5		Med
MRI spectroscopy head	3		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 6:**Suspected prion disease (Creutzfeld-Jakob, iatrogenic CJ or variant CJ).**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8	Include diffusion weighted imaging.	None
MRI head without and with contrast	8	Include diffusion weighted imaging. See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	6		Med
MRI spectroscopy head	5		None
CT head without and with contrast	5		Med
Tc-99m HMPAO SPECT head	5	For problem solving.	High
FDG-PET head	5	For problem solving.	High
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Dementia and Movement Disorders****Variant 7:****Suspected normal pressure hydrocephalus.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	6		Med
Cisternography	6	For problem solving.	Med
CT head without and with contrast	5		Med
MRI spectroscopy head	3		None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 8:**Suspected Huntington disease.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	5		Med
Tc-99m HMPAO SPECT head	5	For problem solving.	High
FDG-PET head	5	For problem solving.	High
MRI spectroscopy head	3		None
CT head without and with contrast	3		Med
MRI functional (fMRI) head	2		None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Dementia and Movement Disorders****Variant 9:****Clinical features suggestive of neurodegeneration with brain iron accumulation (NBIA).**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	5		Med
CT head without and with contrast	4		Med
MRI spectroscopy head	3		None
MRI functional (fMRI) head	3		None
Tc-99m HMPAO SPECT head	3	For problem solving.	High
FDG-PET head	3	For problem solving.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 10:**Parkinson's disease: typical clinical features and responds to levodopa.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	7	For problem solving.	None
MRI head without and with contrast	7	For problem solving. See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	6		Med
Tc-99m HMPAO SPECT head	6	For problem solving. Specific ligand.	High
FDG-PET head	6	For problem solving. Dopa PET.	High
CT head without and with contrast	5		Med
MRI spectroscopy head	3		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Dementia and Movement Disorders****Variant 11:****Parkinsonian syndrome: atypical clinical features not responsive to levodopa.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI head without contrast	8		None
MRI head without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	None
Tc-99m HMPAO SPECT head	6	For problem solving.	High
FDG-PET head	6	For problem solving.	High
CT head without contrast	5		Med
CT head without and with contrast	4		Med
MRI spectroscopy head	3		None
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 12:**Motor neuron disease.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI spine without contrast	8	May need multilevel imaging.	None
MRI head without contrast	8		None
MRI spine without and with contrast	7	May need multilevel imaging. See statement regarding contrast in text under "Anticipated Exceptions."	None
MRI head without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT head without contrast	5		Med
CT head without and with contrast	4		Med
MRI spectroscopy head	3		None
Tc-99m HMPAO SPECT head	3	For problem solving.	High
FDG-PET head	3	For problem solving.	High
MRI functional (fMRI) head	2		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

DEMENTIA AND MOVEMENT DISORDERS

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Summary of Literature Review

Dementia

Dementia affects approximately 7% of the general population older than 65 years, and 30% of people older than 80. It is a clinical state characterized by a significant loss of function in multiple cognitive domains that is not due to an impaired level of arousal. Diagnosis of dementia requires either: 1) assessing an individual's current level of cognitive function and documenting a higher level of intellectual function in the past, or 2) documenting a decline in intellectual function by examinations over time. Cognitive defects due to delirium, restricted brain lesions (eg, aphasia), and psychiatric problems (eg, depression) must be excluded [1].

Accurate diagnosis of the specific type of dementia is important given the current availability of therapies such as cholinesterase inhibitors for Alzheimer's disease (AD) [2] that can delay institutionalization. Moreover, there is significant prognostic value in establishing a diagnosis as it enables the clinician to provide anticipatory guidance to the patient and family, to more accurately predict the future course, to facilitate legal and financial planning, and to assist with providing access to community resources [1].

Alzheimer's Disease

Alzheimer's disease is the most frequent type of dementia in the U.S. and most European countries, comprising

about 50%-80% of subjects in various clinicopathological series. The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADDA) have established the criteria for the definite, probable, and possible diagnosis of AD [3]. Criteria for a definite diagnosis are histologic evidence of AD obtained from a biopsy or autopsy in the presence of the clinical criteria for probable AD. Criteria for a diagnosis of probable AD include: 1) the insidious onset and progressive worsening of dementia; 2) prominent difficulty with memory (especially retention and retrieval of new material); 3) onset after age 60; 4) no focal signs or gait difficulties on neurologic examination, especially early in the course; and 5) exclusion of other causes of dementia due to systemic disorders or other intracranial disorders [1,3]. To exclude other intracranial disorders that might cause dementia (including stroke, intra-axial or extra-axial tumors, subdural hematomas, hydrocephalus, and Creutzfeldt-Jakob disease), neuroimaging (magnetic resonance imaging [MRI] or computed tomography [CT]) should be performed. If available, MRI is preferable to CT because of its greater sensitivity in detecting most intracranial pathologies [4]. From 80% to 85% of patients who meet the criteria for probable AD have histologic evidence of AD [1]. However, a prospective neuropathological study has demonstrated that in a population older than 85 years, the prevalence of neuropathologically defined AD was at least two times higher (33%) than the prevalence of clinically diagnosed AD (16%) [5].

Criteria for a diagnosis of possible AD include: 1) variations in the onset, presentation, or clinical course of typical AD, or 2) the presence of a second systemic or intracranial disorder sufficient to produce dementia, but which is not considered to be the cause of the dementia [3]. In either of these scenarios, MRI or (CT, if MRI is unavailable) should be performed to determine whether the patient has other intracranial abnormalities. Patients with possible AD have a greater incidence of other significant intracranial pathologies detected on neuroimaging studies than patients with probable AD [6].

A new clinical entity, mild cognitive impairment (MCI), has been defined more recently. It is a cognitive decline greater than expected for an individual's age and education level but that does not interfere notably with activities of daily life [7,8]. More than half of the patients with MCI progress to dementia within 5 years. The amnesic subtype of MCI may constitute a prodromal stage of AD [7].

The primary role of neuroimaging in the workup of patients with probable or possible AD is to exclude other significant intracranial abnormalities. It is important to evaluate critically the role of imaging in assessing dementias, because the cost of a false positive diagnosis of AD, especially in cases of MCI, are very high. Recent investigations document specific diagnostic neuroimaging features in AD, suggesting an additional direct role of

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neuroimaging. Positron emission tomography (PET) studies with fluorine-18-fluorodeoxyglucose (FDG) show characteristic reductions of regional glucose metabolic rates in patients with probable and definite AD in the parietal, temporal, and posterior cingulate regions [9]. PET accurately discriminates AD patients from normal subjects with a sensitivity of 96% and specificity of 100% [10]. Metabolic neuroimaging studies using FDG paradoxically suggest that hippocampal dysfunction is absent in AD and MCI, but more recently automated FDG-PET analysis has demonstrated reduced hippocampal metabolism in MCI and AD, suggesting that the previous negative results were due to methodological problems [11]. Quantitative FDG-PET measures may improve prediction of the conversion to AD in patients with MCI [12]. A new promising technique for diagnosing AD is the use of molecular imaging with PET to detect in vivo A β amyloid in the brain of patients with AD. This has been achieved using the Pittsburgh compound-B (PIB). This method, however, is not widely available in clinical practice because of the very short half-life of this compound [13]. The American Academy of Neurology (AAN) consensus group did not recommend PET for diagnosing AD [14].

MRI-based volumetric measurements of the hippocampal formation are significantly smaller in patients with mild AD compared with controls and compared to patients with other forms of dementia. This finding correlates with a neuropathologic hallmark of AD, which is focal atrophy of the hippocampal formation. MRI volumetric calculations permit differentiation of controls from patients with AD accurately in 85%-100% of cases [15-18]. Although it is not as accurate as MRI, CT also permits detection of hippocampal atrophy in AD patients [19]. Medial temporal lobe atrophy has also been observed in MCI compared to cognitively normal individuals. The presence of this sign has a high predictive value for the progression to dementia [7,20]. The AAN did not recommend quantitative volumetry of the hippocampus [14].

Regional cerebral blood flow determined using single photon emission computed tomography (SPECT) imaging with Tc-99m hexamethyl propylene amine oxime (HMPAO) shows bilateral temporoparietal or hippocampal hypoperfusion in patients with AD [21]. Whether brain SPECT contributes substantially to diagnostic accuracy after a careful clinical examination using current diagnostic criteria is controversial [21,22]. An evidence-based review performed by the AAN concluded that SPECT imaging cannot be recommended for either the initial or the differential diagnosis of suspected dementia because it has not demonstrated superiority to clinical criteria. PET imaging is also not recommended for routine use at this time [14].

Hydrogen-1 MR spectroscopy (MRS) may permit identification of mild to moderate AD with a specificity and sensitivity that suggest the potential for clinical usefulness [23]. Studies of automated MRS for AD diagnosis have reported high sensitivity and moderate specificity. Prospective studies are still lacking to validate

this method for diagnosing AD [24]. Functional MRI, diffusion tensor MRI, and perfusion MRI have been used in AD and MCI patients but are still investigational tools at this time.

Of these neuroimaging tests, MR volumetric analysis of the hippocampal formation and PET assessment of regional glucose metabolism are the most diagnostic of AD. Determining the specific clinical applications of either of these studies in patients with probable or possible AD, MCI, or atypical dementias awaits additional investigation. In patients with a diagnosis of probable AD, either of these neuroimaging studies may permit the accuracy to increase from the 80%-85% range to the 90%-100% range, depending on the prevalence of the disorder in the subject population. In patients with possible AD or other atypical dementias, these neuroimaging studies may also permit a more accurate diagnosis. Volumetric MRI studies, PET studies, and possibly functional MRI likely will play an important role in the evaluation of new therapeutic drug strategies in AD [25].

Frontotemporal Dementia

Frontotemporal dementia (FTD) is a neurodegenerative disorder commonly mistaken for AD. Pathologically, it includes a heterogeneous group of sporadic and familial neuropsychiatric disorders. Pick's disease is one of the neuropathological entities of FTD. Unlike AD, which increases in frequency with age, FTD is rare after the age of 75. The Work Group on Frontotemporal Dementia and Pick's Disease reassessed clinical and neuropathological criteria for FTD in 2001 [26].

The clinical criteria for FTD are:

- The development of behavioral or cognitive deficits manifested by either a) early and progressive change in personality, characterized by difficulty in modulating behavior, often resulting in inappropriate responses or activities, or b) early and progressive change in language, characterized by problems with expression of language or severe naming difficulty and problems with word meaning;
- The deficits outlined in 1a or 1b cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning;
- The course is characterized by a gradual onset and continuing decline in function;
- The deficits outlined in 1a or 1b are not due to other nervous system conditions (eg, cerebrovascular disease), systemic conditions (eg, hypothyroidism), or substance-induced conditions;
- The deficits do not occur exclusively during a delirium;
- The disturbance is not better accounted for by a psychiatric diagnosis.

MRI may show atrophy of the anterior temporal and frontal lobes. PET studies assessing regional glucose metabolism with FDG show the metabolic disturbance most prominent in the frontal and temporal lobes [27].

SPECT studies assessing regional cerebral perfusion with HMPAO show frontal hypoperfusion [28]. Although PET and SPECT could help to make the differential diagnosis between AD and FTD, they are not recommended for routine use at the present time [14].

Lewy Body Disease

Dementia with Lewy bodies (DLB) has been recently identified among demented patients. This description has been driven by autopsy studies showing that 15%-25% of elderly demented patients have Lewy bodies in their brainstem and cortex. Among demented elderly, DLB may constitute the most common neurodegenerative pathologic subgroup after pure AD. Antemortem diagnosis of DLB is clinically useful because, 1) DLB is often characterized by a rapidly progressive clinical syndrome, 2) important risks are related to the use of neuroleptic medication, and 3) DLB patients may be particularly responsive to cholinesterase inhibitors.

The DLB consortium [29] has defined criteria for probable and possible DLB disease and has updated them recently [30]. Briefly, the criteria include central features (essential for the diagnosis of DLB), core features (two are necessary for the diagnosis of probable DLB, one for possible), suggestive features, and supportive features. Central features include: dementia; prominent memory impairment not necessarily present in the early stages but usually evident with progression; and deficits on tests of attention, executive function, and visuospatial ability.

Core features include: fluctuating cognition, recurrent visual hallucinations, and spontaneous features of Parkinsonism. Functional imaging of the dopamine transporter (DAT) using SPECT can help to distinguish DLB from AD. DAT striatal activity is normal in AD and low in DLB [31]. Occipital hypoperfusion has been demonstrated using SPECT and occipital hypometabolism using PET. In patients with DLB, MRI shows a preservation of hippocampal and medial temporal lobe volume, no occipital lobe atrophy despite abnormality on functional imaging, and atrophy of the putamen [30].

Many patients with Parkinson's disease (PD) develop dementia (PDD), in most cases at least 10 years after onset of motor symptoms. The only differences between DLB and PDD are age at onset, temporal course, and possibly levodopa responsiveness. DLB should be diagnosed when dementia occurs before or concurrently with PD, and PDD should be diagnosed when dementia occurs in the context of well-established PD [30].

Vascular Dementia

Vascular dementia (VaD) constitutes the second most common type of dementia. The main clinicopathological subtypes are large-vessel VaD and small-vessel VaD. Most patients with a diagnosis of VaD have small-vessel disease. VaD can be prevented or arrested by measures that prevent recurrent infarction (ie, control of hypertension, antiplatelet therapy). Cognition may even improve after these factors are controlled suggesting that at least a portion of dementia is caused by reversible physiologic changes and not infarction. Therefore,

clinical and radiologic tests that aid in distinguishing VaD from less treatable forms of dementia may be beneficial.

A diagnosis of VaD is supported by the following findings: 1) the sudden onset of dysfunction in one or more cognitive domains; 2) a stepwise deteriorating course; 3) focal neurologic signs, including weakness of an extremity, exaggeration of deep tendon reflexes, extensor plantar responses, and gait abnormalities; 4) evidence of stroke risk factors and systemic vascular disease; and 5) evidence of previous strokes [1]. The role of neuroimaging, therefore, is to document the presence or absence of strokes. Reproducibility for the diagnosis of VaD among the different criteria is very low. At present the preferred diagnostic criteria for VaD for research protocols are those developed by the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN). They are probably the most specific, although their sensitivity is probably low. Interestingly, they include imaging criteria for the definition of VaD.

NINDS-AIREN criteria for diagnosing VaD define definite, probable, and possible VaD [32]. The criteria for probable VaD include: dementia; cerebrovascular disease defined by the presence of focal signs and evidence of relevant cerebrovascular disease by brain imaging (CT or MRI); and a relationship between these two disorders. The NINDS-AIREN imaging criteria for VaD include multiple large-vessel infarcts; single strategically placed infarct; multiple basal ganglia; and white matter lacunes or extensive periventricular white matter lesions or combinations of both type of lesions (small-vessel disease). Precise operational definitions of MRI NINDS-AIREN criteria for VaD with interobserver study have been published [33]. Although CT can detect the presence or absence of infarctions in patients with dementia, histopathologically verified cases of VaD with normal CT studies have been reported [9]. Thus MRI is preferable to CT for detecting vascular lesions in patients with dementia.

Differentiation of VaD from either AD with superimposed cerebrovascular disease or mixed AD and VaD is especially difficult. When VaD is diagnosed, this pathologic diagnosis alone is confirmed in about 25% of cases; more commonly, a mixed disorder with neuropathologic changes of both AD and VaD is found. On neuroimaging studies, extensive infarctions (cortical or lacunar or both) and white-matter changes (hyperintense on T2-weighted MR images or hypodense on CT) in a patient with dementia favor a clinical diagnosis of VaD or mixed VaD and AD over AD. The absence or mild extent of these changes in a patient with dementia argues against a diagnosis of VaD.

FDG-PET in VaD shows multiple focal metabolic defects [27]. Differentiation between AD and VaD is much better achieved by PET than by SPECT. SPECT is of little value in differentiating AD from VaD [34]. Magnetic resonance spectroscopy (MRS) and functional MRI are investigational and, to date, do not appear to clinically help establish a diagnosis of VaD or mixed VaD and AD.

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an autosomal dominant hereditary small-artery vasculopathy caused by mutations in the notch3 gene on chromosome 19. Clinically, the disease is characterized by migraine with aura, strokes and progressive subcortical dementia, and mood disturbances. Usually, the disease begins around the age of 40 with mean disease duration of 20 years followed by death between the ages of 55 and 65. MRI in these patients shows focal lacunar infarcts and leukoariosis. Lesion load increases with age. Besides familial anamnesis and clinical history, structural MRI changes in these patients help to suggest the diagnosis by showing characteristic hyperintense T2 or FLAIR lesions which predominate in the frontal, parietal, and anterior temporal cortexes, and in the external capsule [35]. Diagnosis is confirmed by skin biopsy or detection of a pathogenic notch3 mutation on direct sequencing.

Creutzfeldt-Jakob-Disease

Creutzfeldt-Jakob-Disease (CJD) is a fatal neurodegenerative disorder due to the accumulation of an abnormal form of the human prion protein PrP^{Sc} in the brain. In humans there are three main forms of CJD: 1) sporadic CJD (sCJD) which affects patients between the ages of 50 and 75; 2) iatrogenic CJD; and 3) variant CJD (vCJD) which affect younger patients (average age of onset: 25-30 years). A definite diagnosis of CJD is based on histopathological findings; however, brain biopsy is rarely performed in patients with suspected CJD, and autopsy data are not always available. During life, the diagnosis of probable CJD can be made on the basis of clinical signs, including a rapidly progressive dementia associated with upper motor neuron dysfunction, myoclonus, characteristic EEG (generalized periodic sharp wave complexes), detection of 14-3-3 proteins in the cerebrospinal fluid (CSF) and neuroimaging findings. Although some variability exists, the most common MRI abnormality, other than progressive atrophy, is hyperintense signal on long-TR images in gray-matter structures, usually in the basal ganglia or thalami [36], and less commonly in the cortical gray matter. More recent MRI studies have demonstrated the value of diffusion-weighted imaging (DWI) in diagnosing CJD [37]. Cortical abnormalities were present in 70 of 157 patients (45%) but were visible in 35 of 44 patients (80%) of the available DWI examinations. Basal ganglia were affected in 94 patients (60%), in particular in the caudate nucleus. The most sensitive sequences were DWI (64%) and PD-weighted (63%) [37]. It is suggested that MRI helps to improve the diagnosis of CJD, and incorporation of MRI in the diagnostic criteria has been proposed for sCJD [38].

Marked cerebral hypometabolism on FDG-PET in the early stages of CJD, when no parenchymal abnormalities are present on MRI has been described. Similarly, focal hypoperfusion was detected with SPECT using N-isopropyl-(iodine-123) p-iodoamphetamine (¹²³I-IMP) before CT or MRI showed any abnormalities. Changes in cerebral metabolites using proton MRS have also been described in patients with CJD.

Variant CJD was described in humans for the first time in 1996. Strong evidence indicates transmission to humans of bovine spongiform encephalopathy (BSE) via ingestion of contaminated beef products. As of August 2006 there have been only 2 human cases in the United States, but 162 cases have been observed in the United Kingdom and 20 in France. In contrast to sCJD, vCJD affects younger patients and has a relatively longer duration of illness (median of 14 months as opposed to 4.5 months). In the appropriate clinical context, bilateral hypersignal on a T2-weighted MRI sequence at the level of the pulvinar (pulvinar sign) has been described as a useful noninvasive test for diagnosing vCJD [39]. Histological confirmation of a diagnosis of vCJD can be obtained using tonsil biopsy.

Normal-Pressure Hydrocephalus

Normal-pressure hydrocephalus (NPH) is characterized by the clinical triad of dementia, gait disturbance, and urinary incontinence. Other diagnostic features include normal cerebrospinal fluid (CSF) pressure at lumbar puncture, communicating hydrocephalus documented on MRI or CT, and ventricular influx but no passage of isotope over the convexities on radionuclide cisternography (RC) [40].

Because the dementia and other symptoms can be reversible with shunting, and because patients with NPH who are not shunted may progress symptomatically, distinction between responders and nonresponders is important. Several clinical, laboratory, and imaging signs may improve distinction between responders and nonresponders to shunting. Clinical features that favor shunt responsiveness include predominance of gait disturbance, mild to moderate degree of dementia, and rapid clinical progression of urinary incontinence [40]. MRI or CT findings include at least moderate ventriculomegaly (with rounded frontal horns and marked enlargement of the temporal horns and third ventricle), and absence of or only mild cortical atrophy [40,41]. Increased CSF flow void through the cerebral aqueduct on MRI appears to correlate with a good response to shunt surgery [42]. Cine MRI with inflow technique showing hyperdynamic aqueductal CSF may also help in identifying shunt-responsive NPH patients [43]. SPECT cisternography permits more accurate localization of radionuclide activity than planar cisternography, which partially superimposes different CSF compartments [41]. One study using quantitative RC with SPECT found that a higher relative count value in the lateral and third ventricles was predictive for the patient responding to shunt surgery [41].

Recently, evidence-based guidelines have been developed by the INPH guidelines study group for diagnosing idiopathic normal pressure hydrocephalus (INPH). In these guidelines, the patients are divided into probable INPH, possible INPH, or unlikely INPH. Brain imaging features for diagnosing probable INPH include: ventricular enlargement not entirely attributable to cerebral atrophy or congenital enlargement (Evan's index = maximal width of frontal horns/maximal width of inner skull >0.3); no macroscopic obstruction of CSF flow; and

at least one the following features: enlargement of the temporal horns, callosal angle of 40° or more, evidence of altered brain water content, and aqueductal or fourth ventricle flow void on MRI. Other brain imaging findings, considered as supportive of the diagnosis but not necessary for probable INPH are: brain imaging performed before onset of symptoms showing smaller ventricular size; radionuclide cisternogram showing delayed clearance of radiotracer over the cerebral convexities; cine MRI study showing increased ventricular flow rate; and a SPECT acetazolamide challenge showing decreased periventricular perfusion that is not altered by acetazolamide [44].

In conclusion, dementia is a major cause of disability and death in developed countries. The impact of a demented patient on his or her family is substantial. Neuroimaging studies play a critical role in the evaluation of dementia to rule out structural causes that may be reversible and to contribute to the diagnosis of specific types of dementia with important therapeutic and prognostic implications.

Degenerative Diseases of the Extrapyramidal System

The extrapyramidal centers are large subcortical nuclear structures from which output systems emerge at several points. Since mediation and control of the corticospinal tract are the most prominent functions of these output systems, lesions of the extrapyramidal nuclei typically result in motor dysfunction of various types.

Huntington's Disease

The usual age of onset of Huntington's disease (HD) is in the 4th and 5th decades. It is inherited in an autosomal dominant fashion with complete penetrance. Clinical manifestations are choreoathetosis, rigidity, dementia, and emotional disturbance. The Huntington disease phenotype results from an expanded cytosine, adenine, guanine (CAG) trinucleotide repeat within the *IT15* gene located on chromosome 4 [45]. The discovery of this mutation permits genetic testing to confirm the diagnosis of HD, and also to identify presymptomatic subjects who will develop the disease later in life.

Neuroimaging and pathology studies both show characteristic atrophy of the caudate and/or putamen [46]. MR also shows signal changes of the striatum, either hyperintensity or hypointensity on long-TR or long-TE images [47,48]. Neuronal loss accompanied by loss of myelin and gliosis likely results in the hyperintense signal, while iron accumulation likely accounts for the hypointense signal. Using voxel-based morphometry, it has been shown that patients with HD have significant volume reductions in almost all brain structures, including total cerebrum, total white matter, cerebral cortex, caudate, putamen, globus pallidus, amygdala, hippocampus, brainstem, and cerebellum when compared with healthy age matched controls [49].

Localized 1H nuclear medicine resonance (NMR) spectroscopic studies have found increased lactate concentrations in the occipital cortex of symptomatic HD patients when compared with normal controls [50]. Modification of activation pattern has been demonstrated using functional MRI (fMRI) during a time-

discrimination task in presymptomatic HD compared to control subjects [51]. SPECT studies show hypometabolism of the striatum in HD and in other types of chorea [52]. Progressive striatal and cortical dopamine receptor dysfunction in HD has been shown using (11) C-raclopride PET scans [53].

Neurodegeneration with Brain Iron Accumulation

Neurodegeneration with brain iron accumulation (NBIA) is a heterogeneous group of disorders characterized by neurodegeneration and excessive iron deposition in the basal ganglia [54]. The old name for this syndrome is Hallervorden Spatz disease (HSD). This eponymous term has fallen into disfavor because of the unethical activities of J. Hallervorden, a German neuropathologist, during World War II. There are two types of NBIA: 1) early onset, rapidly progressive (classic) disease and 2) late onset, slowly progressive (atypical) disease. Clinically, the disorder is characterized by relentless progression of gait impairment, rigidity, dystonic posturing, and mental deterioration [55]. The defective gene that causes most cases of NBIA was identified recently. Most patients with NBIA and all of those with the early-onset, rapidly progressive type have mutations in the gene encoding pantothenate kinase 2 (PANK 2) [56]. Moreover, there is a striking correlation between MRI findings in NBIA and the presence or absence of PANK 2 mutations. All patients with the PANK 2 mutation show bilateral areas of hyperintensity within a hypointense zone in the medial globus pallidus on T2-weighted images. This pattern has been described as the "eye of tiger" [56,57].

Parkinsonism

Primary Parkinsonism syndromes include: Parkinson's disease (PD), progressive supranuclear palsy (PSP), and multiple system atrophy (MSA). They include the disorders previously called striatonigral degeneration (SND), sporadic olivopontocerebellar atrophy (OPCA), and the Shy-Drager syndrome. A diagnosis of idiopathic PD is usually based on patient history and physical examination alone. A significant and lasting clinical response to dopaminergic therapy is also a key criterion for diagnosing idiopathic PD. A differentiating between idiopathic PD and MSA can be difficult early in the course of the disease, with up to 30% of MSA patients responding to levodopa in a short period [58]. Imaging data may also be helpful in differentiating MSA from idiopathic PD in difficult cases.

Parkinson's Disease

Idiopathic Parkinson's disease is relatively common [59]. Between 2%-3% of the population may be expected to develop Parkinsonism at some time during life. The age of onset usually ranges between 50 and 60 years.

The neuropathologic hallmarks are loss of neuromelanin-containing neurons, gliosis and Lewy body formation in the substantia nigra (mainly the pars compacta), the locus nucleus, the dorsal nucleus of the vagus, and the substantia innominata. A diminution of the width of the pars compacta on MRI has been described in PD patients compared to controls with overlap between groups [60-62]. This diminished width is thought to reflect selective neuronal loss of the pars compacta. Other authors have

found a normal appearance of the substantia nigra on T2-weighted images in a majority of PD patients [63].

Proton MR spectroscopic studies found an increase in lactate in the occipital lobe in patients with Parkinson's disease compared to controls [64]. ¹⁸F-dopa PET can detect frontal changes in Parkinson's disease and preclinical disease in 30% of asymptomatic adult relatives of familial cases [65]. Single-photon-emission computed tomography (SPECT) with ¹²³I-iodobenzamide predicts dopaminergic responsiveness in patients with Parkinsonism [66]. More recently, it has been demonstrated that FDG-PET performed at the time of initial referral for Parkinsonism accurately predicted the clinical diagnosis of individual patients made at subsequent follow-up [67].

Multiple System Atrophy

The discovery in 1989 of glial cytoplasmic inclusions (GCI) in the brain of patients with multiple system atrophy (MSA) provided a pathological marker for the disorder and confirmed that SND, OPCA, and Shy-Drager syndrome are the same disease with different clinical expression [68]. Criteria for diagnosing MSA have been defined by a multidisciplinary panel [69]. MSA can present with autonomic or motor deficits. The predominant motor deficit can be cerebellar (MSA-C = olivopontocerebellar atrophy) or parkinsonism (MSA-P = striatonigral degeneration) [68]. MSA-P is characterized clinically by Parkinsonian symptoms with prominence of rigidity and with an absent or poor response to anti-Parkinson medication.

Neuroimaging and gross pathology show atrophy of the striatum due to neuronal loss, with the putamen more involved than the caudate [70]. At 1.5T, long-TR, long-TE images show putaminal hypointensity, particularly along its posterolateral margin, equal to or more evident than pallidal hypointensity. The degree of hypointense signal correlates significantly with the severity of rigidity [71]. The hypointense signal is due to the paramagnetic effect of iron [70]. PET with ¹⁸F-dopa is useful in differentiating between PD and MSA [72].

More recently, hypointense putaminal signal changes on T2* sequences have been described in MSA more often than in PD but not on T2-weighted images [73]. These discrepancies between the results of recent studies and previous results are probably due to the evolution of MRI sequences currently employed. Fast spin-echo (SE) sequences are far less sensitive to magnetic susceptibility than SE T2-weighted sequences used in 1986 [70]. In a recent study of 230 Japanese patients with MSA, a hyperintense rim at the lateral edge of the dorsolateral putamen was seen on MRI in 34.5% of cases, and a "hot cross bun" sign in the pontine basis (PB) in 63.3% [74]. These putaminal and pontine abnormalities became more prominent as MSA-P and MSA-C features advanced.

Progressive Supranuclear Palsy

Progressive supranuclear palsy (PSP), also called Steele-Richardson-Olszewski syndrome, is one of the most common atypical Parkinsonian syndromes. To improve the specificity and sensitivity of the clinical diagnosis of

PSP, the NINDS and the Society for PSP have developed a set of diagnostic criteria for this disorder. There are three degrees of diagnostic certainty: possible, probable, and definite. Possible PSP requires a gradually progressive disorder with onset at age 40 or later, either vertical supranuclear gaze palsy or both slowing of vertical saccades and prominent postural instability with falls in the first year of onset. Probable PSP requires vertical supranuclear gaze palsy, prominent postural instability, and falls in the first year of onset [75].

Putaminal hypointensity has been described in PSP patients at 1.5T, using long-TR and long-TE sequences [76]. The periaqueductal region of the midbrain is also implicated in the pathology of PSP. Some patients show slight hyperintense signal on the long-TR sequences of the periaqueductal gray matter. It has been shown that anteroposterior diameters of the suprapontine midbrain measured on axial T2-weighted MRI in patients with PSP were significantly lower than those of patients with PD and in control subjects without any overlap between these two groups [77]. Other authors have demonstrated that the average midbrain area of patients with PSP measured on midsagittal MRI was significantly smaller than that of the patients with PD and MSA-P and that of an age-matched control group [78].

Degenerative Diseases of the Motor System

Motor neuron diseases are a heterogeneous group of syndromes in which the upper and/or lower motor neurons degenerate [79]. Amyotrophic lateral sclerosis (ALS) is the most frequent type of motor neuron disease, with an annual incidence rate of 0.4 to 1.76 per 100,000 people. Most patients are 50 years of age or older at the onset of symptoms. The disorder progresses relentlessly; about half the patients are dead within 3 years and 90% within 6 years.

ALS is characterized predominantly by degeneration of the corticospinal tract and lower motor neurons. The extent of corticospinal tract degeneration varies along the neuraxis. It can usually be traced from the lower portion of the spinal cord up through the medulla. Occasionally, degeneration of motor fibers proceeds farther cephalad sequentially through the pyramidal tracts of the brainstem and cerebral peduncles, the posterior part of the posterior limb of the internal capsule, and corona radiata, to the motor cortex. On MRI, atrophy and hyperintense foci of the corticospinal tract is seen on long-TR sequences [80]. This high signal likely reflects characteristic histologic changes of myelin loss and gliosis. Hypointense signal on long-TR and long-TE sequences may also be found in ALS, due to iron deposition [47]. The anterior and lateral portions of the cord may be atrophic and flattened due to loss of motor neurons in the anterior horns and corticospinal tracts. Magnetization transfer measurements are useful for detecting abnormalities associated with degeneration of the pyramidal tract in patients with ALS [81].

Proton magnetic resonance spectroscopy reveals decreased N-acetyl aspartate values in the sensorimotor cortex and brainstem of patients with ALS, consistent

with neuronal dysfunction or loss [82]. Involvement of the corticospinal tract in patients with ALS has been demonstrated using diffusion tensor imaging even at an early stage [83].

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m²), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m². For more information, please see the [ACR Manual on Contrast Media](#) [84].

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria[®] [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

Supporting Document(s)

- [ACR Appropriateness Criteria[®] Overview](#)
- Evidence table under review

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.