Current PSYCHIATRY

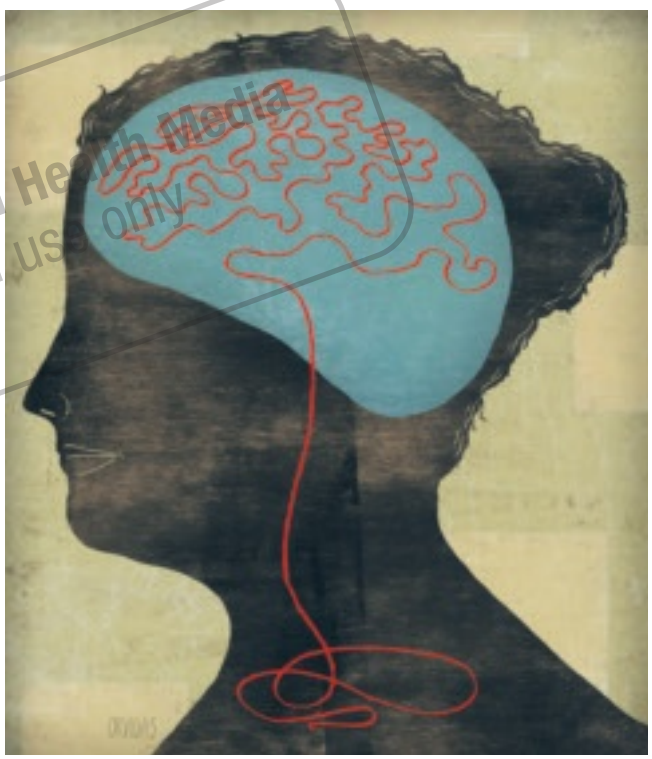
Is it Alzheimer's? How to pare down the possibilities

A clinical guide to rule out other dementing diseases and rare reversible causes

Accurate and early diagnosis of Alzheimer's disease (AD) is evolving, and—although not yet definitive—is no longer one of exclusion. With a careful in-office work-up and routine assessment tools, you can accurately identify >90% of patients with late-onset AD.[1]

AD is by far the most common cause of dementia in older patients. To help you make the diagnosis, this state-of-the-art article discusses:

- AD's clinical presentation and course
- the role of neuropsychological tests for assessing cognitive and functional status
- neuropsychiatric and medical findings that differentiate AD from other dementia causes
- indications for structural neuroimaging with CT or MRI.



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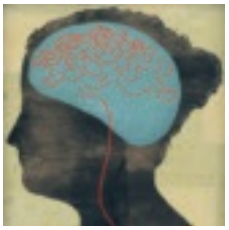
Presentation and course

Variability. AD's gradual onset and progression are characterized by prominent memory loss, anomia, constructional apraxia, anosognosia, and personality changes with affect deregulation, behavioral disturbance, and distorted perception.[1] Amnesia—particularly deficits in anterograde episodic memory—is the most common presentation, but the disease course is heterogeneous and may be affected by:

- patient age at onset
- illness severity at diagnosis
- comorbid medical and neuropsychiatric illnesses
- premorbid cerebral reserves (amount of brain



Alzheimer's diagnosis

Clinical Point

Clinical assessment has low specificity in advanced stages, where all dementia subtypes are similar and comorbidities confuse the picture

damage a person can sustain before reaching a threshold for the clinical expression of dementia).[1-3]

Staging illness severity. AD has 3 clinical stages of cognitive dysfunction:

Mild AD. An individual or close companion may notice increased forgetfulness and word-finding difficulties, a tendency to lose or misplace things, repeated questioning, and some disorientation. Motor skills are intact.

Moderate AD. Cognitive decline continues, memory deteriorates, and self-care ability is markedly impaired. The individual may undergo personality changes, confuse time and place, have trouble communicating and recognizing family members or friends, develop agitation, begin to wander, and experience delusions and hallucinations.

Severe AD. An individual with late-stage disease has severe impairment and can be bedridden, incontinent, and unable to understand or speak. Full-time care is required.

Staging informs treatment. In clinical trials, patients with mild-to-moderate AD consistently show small improvements in cognitive and global function when treated with acetylcholinesterase inhibitors (AChEIs) such as donepezil, rivastigmine, and galantamine.[4] Donepezil also is approved for use in severe AD.

Memantine is indicated for symptomatic treatment of moderate-to-severe AD. It differs in mechanism of action from the AChEIs and is thought to inhibit cytotoxic overstimulation of glutamatergic neurons.[4] For moderately advanced AD, memantine appears to be beneficial alone or in combination with AChEIs.

Dementia assessment

Clinical assessment has low sensitivity for early-phase AD and compromised specificity in advanced stages, where all dementia subtypes are similar and comorbidities may confuse the picture. Promising surrogate biomarkers and other diagnostic tools are being developed (***Box 1***),[5-8] but definitive AD diagnosis still requires postmortem histopathologic examination of the cerebral cortex.

Box 1

Biomarkers show promise to improve AD diagnosis

Researchers are investigating surrogates for detecting Alzheimer's disease (AD) and monitoring disease progression.[5]

Serum and CSF markers. AD is viewed as a series of sequential events, beginning with beta-amyloid (β-amyloid) accumulation and progressing through a pathophysiologic cascade to cell death, transmitter deficit, and dementia. A unique biomarker may be associated with each event, either in the primary disease process of β-amyloid production and accumulation or intermediate processes such as tau hyperphosphorylation, oxidation, and inflammation.[5,6]

These biochemical markers are found more consistently in cerebrospinal fluid (CSF) than peripherally. Lower CSF β-amyloid (especially β-amyloid 42) and higher CSF tau and tau-phosphorylated (p-tau) have been found in AD patients compared with normal and disease controls.[7] Some overlap exists, however, among AD and other dementias. Other possible serum, CSF, and urine markers include isoprostanes, sulfatides, oxysterols, homocysteine, apolipoprotein E, alpha 1-antichymotrypsin, 3-nitrotyrosine, and more.[8] No biomarkers are available or recommended for clinical use at this time.

Neuroimaging. Amyloid imaging tracers may increase the capacity of single photon emission computed tomography (SPECT) and positron emission tomography (PET) to detect AD pathology. These tracers have high binding affinity for amyloid and may enable PET/SPECT to detect amyloid deposits in vivo.

Amyloid radioligands are being developed and tested as potential clinical diagnostic tools and surrogate biomarkers of antiamyloid therapies. A radioligand that targets amyloid and neurofibrillary tangles in AD has been developed recently for use as a research tool.

Box 2

Can your AD patient drive or live alone? Consider neuropsychological assessment

Neuropsychological tests disclose a degree of intellectual impairment that correlates with functional impairment and may be particularly useful for assessing:

- mild cognitive impairment when diagnosis is doubtful
- cases where major lifestyle changes may be required, such as driving cessation or assisted-living placement.

These tests can examine performance across different domains of cognitive function, including orientation, memory, attention, naming, comprehension, and praxis.

Limitations. Neuropsychological tests have limitations, including cost and administration time. Some older patients find the tests distressing or tiring, and those with severe dementia are incapable of participating. Patients' anxiety about taking tests, poor test-taking skills, low motivation/effort, and language, cultural, and educational variables limit these tests' usefulness and may influence results.

Interpret a neuropsychological evaluation in the context of other clinical data, such as informant-based history of cognitive decline, evidence of impairment in independent activities of daily living, educational background, depression assessment, sensory impairment, or factors other than dementia that may account for impaired performance.

Source: References 13,14

History and physical exam. Depending on the AD stage at presentation, patients might not be a reliable source of information. For a realistic and unbiased history and evaluation, assess the patient separately and obtain collateral information from reliable informants.

In typical cases, the history guides the physical/neurologic examination. Advancing age and family history are confirmed risk factors for AD; others may include:

- female gender (after age 80)
- cardiovascular disease (such as cerebral infarcts, hypertension, elevated cholesterol/homocysteine, smoking, and diabetes mellitus)
- history of head trauma, especially with loss of consciousness.

Assess premorbid functioning and existing medical conditions. Apraxia, aphasia, and cortical visual impairment may reflect focal signs of atypical AD; consider other neurologic signs in the context of clinical data.

Early and accurate diagnosis of AD is challenging in patients with mixed dementias, comorbid neurologic diseases, or atypical features. Patients with these presentations may require referral to an expert clinician, extensive workup, or longitudinal follow-up before the diagnosis becomes clear.

Neuropsychological testing. Most mental status tests examine orientation, attention/concentration, learning, memory, language, and constructional praxis. The Folstein Mini-Mental State Examination (MMSE)[9] is the most widely used and well-validated mental status test. A score of 10 to 20 on the MMSE is generally considered as moderate AD, and <10 is staged as severe AD.[10] Other mental status testing options include:

- Blessed Information-Memory-Concentration (BIMC)
- Blessed Orientation-Memory-Concentration (BOMC)
- Short Test of Mental Status (STMS)
- Saint Louis University Mental Status (SLUMS).[11,12]

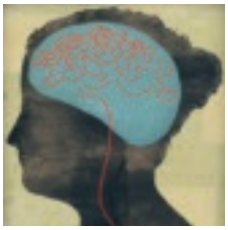
Neuropsychological tests have limitations, but they can supplement clinical cognitive assessment by detecting milder cases and may help answer questions about a patient's ability to drive or live alone (***Box 2***).[13,14]

Reversible causes. If the patient is generally healthy, a core of laboratory tests is recommended in the diagnostic workup (***Table 1, page 56***).[6,15] Other options include:

- CSF examination for atypical presentations, such as unusually rapid symptom

Clinical Point

Apraxia, aphasia, and cortical visual impairment may reflect focal signs of atypical AD



Alzheimer's diagnosis

Clinical Point

Structural neuroimaging with noncontrast CT or MRI is appropriate in the initial evaluation of patients with dementia

Table 1

Recommended lab tests for Alzheimer's disease workup

Test	Rationale
CBC	Anemia and signs of infection
Vitamin B12	Related to reversible dementia, anemia
Folate	Related to reversible dementia, anemia
Homocysteine	More accurate than individual B12/folate tests
C-reactive protein	Ongoing inflammatory reaction
Thyroid function	Hypothyroidism (reversible dementia)
Liver function	Metabolic causes of cognitive impairment
Renal function	Uremia, metabolic causes of cognitive impairment
Electrolytes	Hypo/hypernatremia as a cognitive impairment cause
Glucose	Recurrent hypoglycemia, diabetes mellitus
Lipid panel	Vascular dementia risk factor
Baseline ECG	Cardiac abnormalities as vascular risk factors
STS (optional)	Neurosyphilis

CBC: complete blood count; ECG: electrocardiogram; STS: serologic test for syphilis
Source: Adapted from references 6,15

progression, altered consciousness, or other neurologic manifestations

- EEG to differentiate delirium, seizure disorders, encephalopathies, or a rapidly progressing dementia such as Creutzfeldt-Jakob disease.

Only 1% of dementia causes are considered reversible,[16] but keep them in mind in the AD differential diagnosis (***Table 2, page 61***). Depression, vitamin B12 deficiency, medication side effects, and hypothyroidism are common comorbidities in elderly patients, particularly in those with suspected dementia. Correcting these problems might or might not reverse the dementia.

Because delirium may be the initial presentation of AD or reversible causes, re-evaluate patients for dementia after delirium clears.

Neuroimaging. Structural neuroimaging with a noncontrast CT or MRI is appropriate in the initial evaluation of patients with dementia.[17] More routinely, it is used to exclude rare but potentially correctable dementia causes, such as space-occupying lesions.[18] Hippocampal and entorhinal volume are measured most often in discriminating AD from non-demented aging and other dementias.[19]

Positron emission tomography (PET) using fluorine-18-labeled deoxyglucose (FDG) may help differentiate characteristic patterns of cerebral hypometabolism in the temporoparietal lobes in AD from frontotemporal dementia (FTD) and other less common dementias, particularly during the earliest stages of the disease.[19] Medicare reimbursement for brain PET is limited to differentiating FTD from AD.

Diagnostic criteria

NINCDS-ADRDA. Neuropsychological AD assessment criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) classify AD as probable, possible, or definite:

Possible AD is considered when a patient has an atypical onset, presentation, or course and other secondary illnesses capable of producing dementia are not believed to be the cause.

Probable AD is diagnosed when dementia is established by clinical exam and confirmed with cognitive testing, where ≥2 cognitive domains are progressively affected; includes gradual memory loss not caused by another systemic or brain disease, with age of onset between 40 and 90 years.

Definite AD requires histopathologic evidence of AD in addition to fulfilling criteria for probable AD.[20]

DSM-IV-TR. Similar but broader DSM-IV-TR criteria describe an insidious progressive cognitive decline that affects recent memory and ≥1 other cognitive domain (apraxia, aphasia, agnosia, or executive functioning). This cognitive decline impairs social and occupational function, represents a change

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Table 2

Detecting causes of potentially reversible cognitive impairment

Cause	Examples	Suggested tests
Space-occupying lesions	Subdural hematoma, benign tumors, hydrocephalus	CT/MRI without contrast
Infectious diseases	AIDS dementia complex, syphilis, Lyme disease	Serologic tests
Endocrinopathies/ metabolic/autoimmune disorders	Hypothyroidism, Cushing's disease, uremia, hepatic encephalopathy, Wilson's disease, recurrent hypoglycemia, chronic hypocalcemia, multiple sclerosis, disseminated SLE, sarcoidosis	Thyroid panel, renal and liver function tests, electrolytes, slit lamp test, serum ceruloplasmin
Psychiatric	Depression, alcohol dependence	Geriatric Depression Scale, assess vitamin deficiency states
Nutritional deficiencies	Vitamin B12, thiamine (Wernicke-Korsakoff syndrome), pyridoxine, niacin (pellagra)	Vitamin B12, homocysteine
Medication effects	Benzodiazepines, barbiturates, anticholinergics, opioid analgesics, antihypertensives, antiarrhythmics, antidepressants, anticonvulsants, cardiac drugs such as digitalis and derivatives (among others)	Review patients' medications for drugs that can cause cognitive changes
Others	Autoimmune diseases, heavy metals, illicit drugs, obstructive sleep apnea	Drug screens and specific tests

from a higher level, and is not due to other causes such as delirium.[21]

NINCDS-ADRDA and DSM-IV-TR criteria have comparable sensitivity and specificity for clinical AD diagnosis. Neither requires neuropathologic or genetic assessment (***Box 3, page 62***).[15,17,22-24] Neuroimaging and other tests may be required to rule out other brain diseases that may cause dementia.

Other causes of dementia

Mild cognitive impairment (MCI) may represent a prodromal state for the earliest clinical manifestations of dementia. Symptoms include memory complaints but generally preserved activities of daily living.

Originally introduced to define a progressive, single-symptom amnestic syndrome, MCI has evolved into a classification of amnestic and non-amnestic MCI with single or multiple domains.[25] Amnestic MCI is the most specifically correlated with AD.[26] Neurobiologic similarities between amnestic MCI and clinically diagnosed AD include:

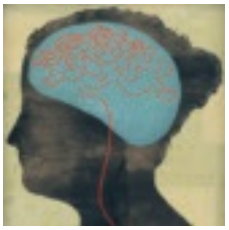
- neuropsychiatric symptoms, such as apathy, mood disturbance, irritability and anxiety
- over-representation of the APOE ε4 allele
- volumetric loss in the entorhinal cortex and hippocampus as measured by MRI
- Glucose hypometabolism in AD-typical regions as measured by FDG-PET
- neuronal loss in vulnerable brain regions.[26]

Most patients with MCI go on to meet AD criteria within 5 to 10 years, and approximately 80% of those originally diagnosed with MCI prove to have AD at postmortem histopathologic examination.[26,27]

Dementia with Lewy bodies (DLB) is the second most common dementing disorder

Clinical Point

Only 1% of dementia causes are considered reversible, but keep them in mind in the Alzheimer's differential diagnosis



Clinical Point

Vascular dementia was once thought to account for 15% to 20% of dementia illness, but discrete VaD is now viewed as much less common

Box 3

Genetic testing for Alzheimer's?

Genetic testing may become important for high-risk patients or early-stage Alzheimer's disease (AD) when preventive/disease-modifying therapy becomes available. At this time, however, the clinical value and implications of genetic tests remain controversial.[17,22]

Apolipoprotein E (APOE). The APOE ε4 allele is an established risk factor for AD,[23,24] but limitations of APOE testing include:

- inability to predict with sufficient certainty whether or when a person might develop AD
- risk of false alarm or false reassurance
- no established treatment exists for a person with this genetic risk.

Amyloid precursor protein (APP), presenilin 1 (PS1), presenilin 2 (PS2). Age <55 years at onset is characteristic of dominantly inherited, familial AD (early-onset AD) caused by mutations in ≥1 of these 3 genes.[15]

- Mutations are rare (~1% of AD cases).
- Increased APP transcriptional activity is an AD risk factor; onset age correlates inversely with levels of APP expression.
- PS1 mutation testing may benefit patients with early-onset familial AD. If this mutation is found, other presymptomatic at-risk family members may wish to be tested so they can make important life decisions based on the results.[17,22] Careful pre- and post-test counseling is critical.

in late life—after Alzheimer's dementia—and two-thirds of DLB cases overlap with AD. Core DLB clinical features include early recurrent visual hallucinations, fluctuating cognition, spontaneous parkinsonism, and sensitivity to conventional antipsychotics.[15,28]

Parkinson's disease (PD) and DLB may represent a clinicopathologic continuum, and substantial overlap exists among AD, DLB, and PD in underlying disease process and clinical presentation.[15,29] Hallucinations, depression, delusions, and delusional misidentification are seen more often in patients with DLB than AD.[15]

Vascular dementia (VaD) was once thought to account for 15% to 20% of dementing illnesses, but discrete VaD is now viewed as much less common. Whatever the underlying vasculopathy, vascular lesions often coexist with other causes of dementia—usually AD (in 77% of presumed VaD cases).[30]

Compared with AD, patients with VaD have a more subcortical dementia with difficulty retrieving words, organizing and solving complex problems, "absent-mindedness," and psychomotor slowing with relatively preserved language skills. VaD is thought to have a more abrupt onset than AD and "stepladder" deterioration.

Frontotemporal dementia (FTD)—such as Pick's disease—is associated with focal atrophy of the frontal and/or temporal lobes. Mean onset is age 52 to 56, and FTD is less common than AD, VaD, or DLB.

FTD often presents with gradual personality changes (with inappropriate responses or activities) or language changes (with severe naming difficulty and problems with word meaning).[31] Features that may help differentiate FTD from AD include:

- disinhibition/apathy with personality change
- affect disregulation
- behavioral disturbance (frontal type) and expressive/receptive language changes (semantic or primary progressive aphasia) with relatively mild memory loss.[32,33]

Unlike AD, memory usually is unaffected in early FTD, with problems largely secondary to poor concentration and relating to difficulties with working (immediate) memory.

Other neurodegenerative diseases that might present with dementia include PD, Huntington's disease, progressive supranuclear palsy, corticobasal degeneration, and Creutzfeldt-Jakob disease.[33]

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milk. Therefore, women should not breast-feed during treatment with RISPERDAL® CONSTA® and for at least 12 weeks after the last injection. **Pediatric Use:** RISPERDAL® CONSTA® has not been studied in children younger than 18 years old. **Geriatric Use:** In an open-label study, 57 clinically stable, elderly patients (≥65 years old) with schizophrenia or schizoaffective disorder received RISPERDAL® CONSTA® every 2 weeks for up to 12 months. In general, no differences in the tolerability of RISPERDAL® CONSTA® were observed between otherwise healthy elderly and nonelderly patients. Therefore, dosing recommendations for otherwise healthy elderly patients are the same as for nonelderly patients. Because elderly patients exhibit a greater tendency to orthostatic hypotension than nonelderly patients, elderly patients should be instructed in nonpharmacologic interventions that help to reduce the occurrence of orthostatic hypotension (e.g., sitting on the edge of the bed for several minutes before attempting to stand in the morning and slowly rising from a seated position). In addition, monitoring of orthostatic vital signs should be considered in elderly patients for whom orthostatic hypotension is of concern (see PRECAUTIONS, DOSAGE AND ADMINISTRATION and CLINICAL PHARMACOLOGY in full PI). **Concomitant use with Furosemide in Elderly Patients with Dementia-Related Psychosis:** In placebo-controlled trials in elderly patients with dementia-related psychosis, a higher incidence of mortality was observed in patients treated with furosemide plus oral risperidone when compared to patients treated with oral risperidone alone or with oral placebo plus furosemide. No pathological mechanism has been identified to explain this finding, and no consistent pattern for cause of death was observed. An increase of mortality in elderly patients with dementia-related psychosis was seen with the use of oral risperidone regardless of concomitant use with furosemide. RISPERDAL® CONSTA® is not approved for the treatment of patients with dementia-related psychosis. (See **Boxed WARNING, WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis.**)

ADVERSE REACTIONS: Associated with Discontinuation of Treatment: In the 12-week, placebo-controlled trial, the incidence of schizophrenic patients who discontinued treatment due to an adverse event was lower with RISPERDAL® CONSTA® (11%; 22/202 patients) than with placebo (13%; 13/98 patients). **Incidence in Controlled Trials: Commonly Observed Adverse Events in Controlled Clinical Trials:** Spontaneously reported, treatment-emergent adverse events with an incidence of 5% or greater in at least one of the RISPERDAL® CONSTA® groups (25 mg or 50 mg) and at least twice that of placebo were: somnolence, akathisia, parkinsonism, dyspepsia, constipation, dry mouth, fatigue, weight increase. **Dose Dependency of Adverse Events:** ***Extrapyramidal Symptoms:*** The overall incidence of EPS-related adverse events (akathisia, dystonia, parkinsonism, and tremor) in patients treated with 25 mg RISPERDAL® CONSTA® was comparable to that of patients treated with placebo; the incidence of EPS-related adverse events was higher in patients treated with 50 mg RISPERDAL® CONSTA®. **Vital Sign Changes:** RISPERDAL® is associated with orthostatic hypotension and tachycardia (see PRECAUTIONS). In the placebo-controlled trial, orthostatic hypotension was observed in 2% of patients treated with 25 mg or 50 mg RISPERDAL® CONSTA® (see PRECAUTIONS). **Weight Changes:** In the 12-week, placebo-controlled trial, 9% of patients treated with RISPERDAL® CONSTA®, compared with 6% of patients treated with placebo, experienced a weight gain of >7% of body weight at endpoint. **Laboratory Changes:** The percentage of patients treated with RISPERDAL® CONSTA® who experienced potentially important changes in routine serum chemistry, hematology, or urinalysis parameters was similar to or less than that of placebo patients. Additionally, no patients discontinued treatment due to changes in serum chemistry, hematology, or urinalysis parameters. **ECG Changes:** The electrocardiograms of 202 schizophrenic patients treated with 25 mg or 50 mg RISPERDAL® CONSTA® and 98 schizophrenic patients treated with placebo in a 12-week, double-blind, placebo-controlled trial were evaluated. Compared with placebo, there were no statistically significant differences in QTc intervals (using Fridericia's and linear correction factors) during treatment with RISPERDAL® CONSTA®. **Pain Assessment and Local Injection Site Reactions:** The mean intensity of injection pain reported by patients using a visual analog scale (0 = no pain to 100 = unbearably painful) decreased in all treatment groups from the first to the last injection (placebo: 16.7 to 12.6; 25 mg: 12.0 to 9.0; 50 mg: 18.2 to 11.8). After the sixth injection (Week 10), investigator ratings indicated that 1% of patients treated with 25 mg or 50 mg RISPERDAL® CONSTA® experienced redness, swelling, or induration at the injection site. **Other Events Observed During the Premarketing Evaluation of RISPERDAL® CONSTA®:** During its premarketing assessment, RISPERDAL® CONSTA® was administered to 1499 patients in multiple-dose studies. The conditions and duration of exposure to RISPERDAL® CONSTA® varied greatly, and included (in overlapping categories) open-label and double-blind studies, uncontrolled and controlled studies, inpatient and outpatient studies, fixed-dose and titration studies, and short-term and long-term exposure studies. The following reactions were reported: (Note: frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients. It is important to emphasize that, although the reported events occurred during treatment with RISPERDAL® CONSTA®, they were not necessarily caused by it.) **Psychiatric Disorders:** *Frequent:* anxiety, psychosis, depression, agitation, nervousness, paranoid reaction, delusion, apathy. *Infrequent:* anorexia, impaired concentration, impotence, emotional lability, manic reaction, decreased libido, increased appetite, amnesia, confusion, euphoria, depersonalization, paroniria, delirium, psychotic depression. **Central and Peripheral Nervous System Disorders:** *Frequent:* hypertonia, dystonia. *Infrequent:* dyskinesia, vertigo, leg cramps, tardive dyskinesia[a], involuntary muscle contractions, paraesthesia, abnormal gait, bradykinesia, convulsions, hypokinesia, ataxia, fecal incontinence, oculogyric crisis, tetany, apraxia, dementia, migraine. *Rare:* neuroleptic malignant syndrome. [a]In the integrated database of multiple-dose studies (1499 patients with schizophrenia or schizoaffective disorder), 9 patients (0.6%) treated with RISPERDAL® CONSTA® (all dosages combined) experienced an adverse event of tardive dyskinesia. **Body as a Whole/General Disorders:** *Frequent:* back pain, chest pain, asthenia. *Infrequent:* malaise, choking. **Gastrointestinal Disorders:** *Frequent:* nausea, vomiting, abdominal pain. *Infrequent:* gastritis, gastroesophageal reflux, flatulence, hemorrhoids, melena, dysphagia, rectal hemorrhage, stomatitis, colitis, gastric ulcer, gingivitis, irritable bowel syndrome, ulcerative stomatitis. **Respiratory System Disorders:** *Frequent:* dyspnea. *Infrequent:* pneumonia, stridor, hemoptysis. *Rare:* pulmonary edema. **Skin and Appendage Disorders:** *Frequent:* rash. *Infrequent:* eczema, pruritus, erythematous rash, dermatitis, alopecia, seborrhea, photosensitivity reaction, increased sweating. **Metabolic and Nutritional Disorders:** *Infrequent:* hyperuricemia, hyperglycemia, hyperlipemia, hypokalemia, glycosuria, hypercholesterolemia, obesity, dehydration, diabetes mellitus, hyponatremia. **Musculo-Skeletal System Disorders:** *Frequent:* arthralgia, skeletal pain. *Infrequent:* torticollis, arthrosis, muscle weakness, tendinitis, arthritis, arthropathy. **Heart Rate and Rhythm Disorders:** *Frequent:* tachycardia. *Infrequent:* bradycardia, AV block, palpitation, bundle branch block. *Rare:* T-wave inversion. **Cardiovascular Disorders:** *Frequent:* hypotension. *Infrequent:* postural hypotension. **Urinary System Disorders:** *Frequent:* urinary incontinence. *Infrequent:* hematuria, micturition frequency, renal pain, urinary retention. **Vision Disorders:** *Infrequent:* conjunctivitis, eye pain, abnormal accommodation. **Reproductive Disorders, Female:** *Frequent:* amenorrhea. *Infrequent:* nonpuerperal lactation, vaginitis, dysmenorrhea, breast pain, leukorrhea. **Resistance Mechanism Disorders:** *Infrequent:* abscess. **Liver and Biliary System Disorders:** *Frequent:* increased hepatic enzymes. *Infrequent:* hepatomegaly, increased SGPT. *Rare:* bilirubinemia, increased GGT, hepatitis, hepatocellular damage, jaundice, fatty liver, increased SGOT. **Reproductive Disorders, Male:** *Infrequent:* ejaculation failure. **Application Site Disorders:** *Frequent:* injection site pain. *Infrequent:* injection site reaction. **Hearing and Vestibular Disorders:** *Infrequent:* earache, deafness, hearing decreased. **Red Blood Cell Disorders:** *Frequent:* anemia. **White Cell and Resistance Disorders:** *Infrequent:* lymphadenopathy, leucopenia, cervical lymphadenopathy. *Rare:* granulocytopenia, leukocytosis, lymphopenia. **Endocrine Disorders:** *Infrequent:* hyperprolactinemia, gynecomastia, hypothyroidism. **Platelet, Bleeding and Clotting Disorders:** *Infrequent:* purpura, epistaxis. *Rare:* pulmonary embolism, hematoma, thrombocytopenia. **Myo-, Endo-, and Pericardial and Valve Disorders:** *Infrequent:* myocardial ischemia, angina pectoris, myocardial infarction. **Vascular (Extracardiac) Disorders:** *Infrequent:* phlebitis. *Rare:* intermittent claudication, flushing, thrombophlebitis. **Postintroduction Reports:** Adverse events reported since market introduction which were temporally (but not necessarily causally) related to oral RISPERDAL® therapy include the following: anaphylactic reaction, angioedema, apnea, atrial fibrillation, cerebrovascular disorder, including cerebrovascular accident, diabetes mellitus aggravated, including diabetic ketoacidosis, hyperglycemia, intestinal obstruction, jaundice, mania, pancreatitis, Parkinson's disease aggravated, pituitary adenomas, pulmonary embolism, and QT prolongation. There have been rare reports of sudden death and/or cardiopulmonary arrest in patients receiving oral RISPERDAL®. A causal relationship with oral RISPERDAL® has not been established. It is important to note that sudden and unexpected death may occur in psychotic patients whether they remain untreated or whether they are treated with other antipsychotic drugs. Retinal artery occlusion after injection of RISPERDAL® CONSTA® has been reported during postmarketing surveillance. This has been reported in the presence of abnormal arteriovenous anastomosis.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class: RISPERDAL® CONSTA® (risperidone) is not a controlled substance.

For more information on symptoms and treatment of overdosage, see full Prescribing Information.

7519510B - US Patent 4,804,663 Revised September 2007 ©Janssen 2003

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Related Resources

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Drug Brand Names

Donepezil • Aricept
Galantamine • Razadyne
Memantine • Namenda
Rivastigmine • Exelon

Disclosures

Dr. Gebretsadik reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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Bottom Line

To make a clinical diagnosis of Alzheimer's disease, start by eliciting a detailed history from the patient and seeking collateral information from reliable informants. Assess premorbid functioning, existing medical conditions, and neurologic signs. Order routine laboratory tests and neuroimaging to identify non-Alzheimer brain disorders. For early symptoms, consider neuropsychological testing to quantify the patient's intellectual and functional impairment.