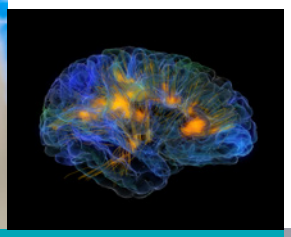


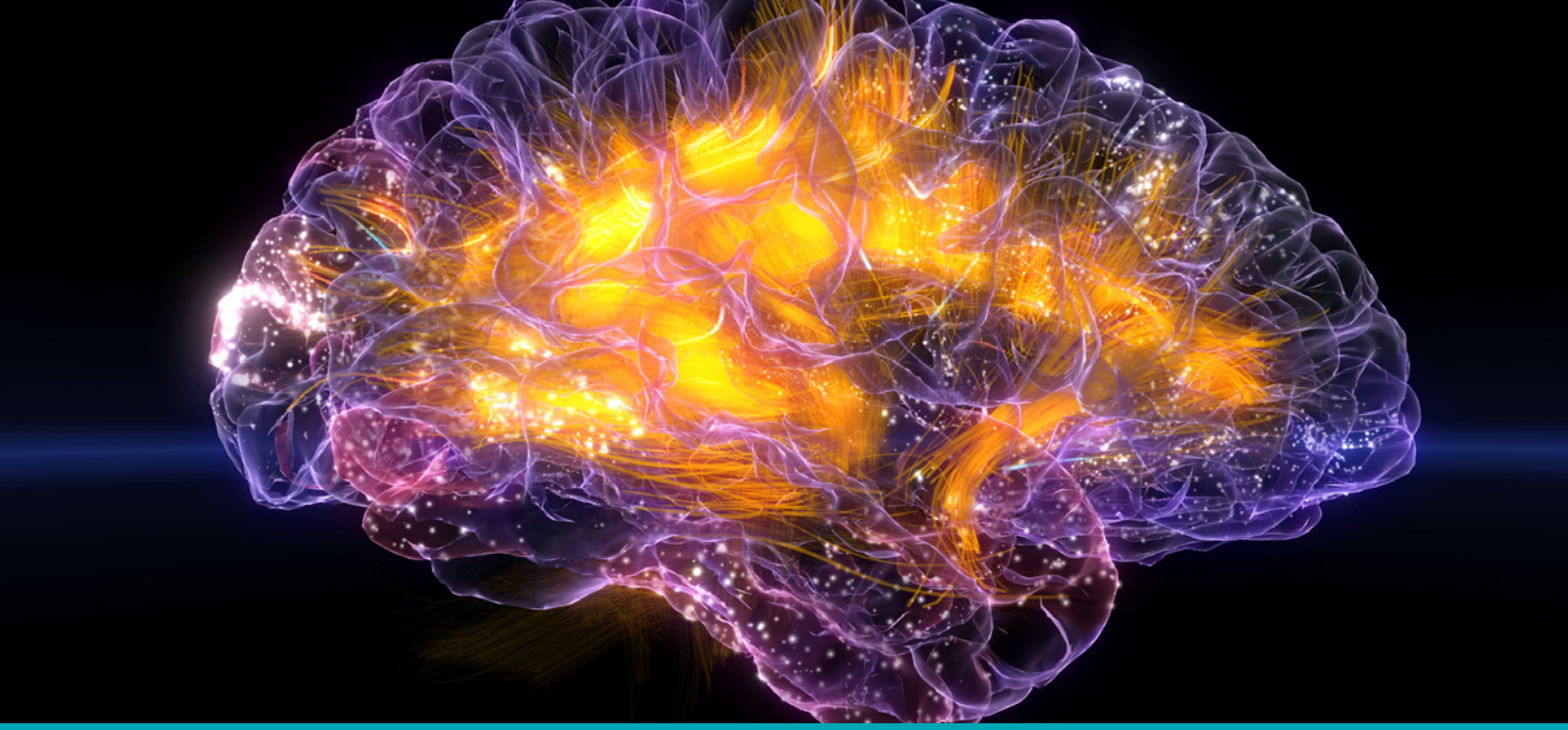
# A Healthcare Provider's Guide To Rapidly Progressive Dementia (RPD):

## Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

This material is provided by UCSF Weill Institute for Neurosciences as an educational resource for health care providers.

UCSF Weill Institute for Neurosciences

Memory and Aging Center



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## Diagnosis

### Definition

Dementia is a clinical syndrome defined as a cognitive or behavioral decline that leads to an inability to complete daily tasks independently. Rapidly progressive dementias (RPDs) often develop over weeks to months. Although many RPDs are neurodegenerative in etiology, autoimmune, toxic/metabolic, infectious, neoplastic, and vascular processes can cause similar symptoms. As many of these latter processes are treatable, early and accurate diagnosis is important.[1]

### Etiology

The annual combined incidence of sporadic, genetic, and acquired forms of human prion diseases (hPrD) is estimated at 1–1½ per million per year in most developed countries.[2] hPrDs are rare. Sporadic Creutzfeldt Jakob disease (sCJD) is a type of RPD. hPrDs are caused by the progressive accumulation and spread of abnormally folded proteins known as "prions" in the brain, leading to a unique pattern of neurodegeneration. Other hPrDs include Gerstmann–Sträussler–Scheinker syndrome (GSS) and fatal familial insomnia (FFI). Acquired hPrDs include variant Creutzfeldt Jakob (cCJD) and iatrogenic (iCJD), both of which are very rare today. Many patients referred for hPrD work up are ultimately diagnosed with treatable cell-surface or intracellular neuronal antibodies instead.

Autoimmune encephalitis syndromes, on the other hand, are likely underreported, and are increasingly recognized as a significant cause of idiopathic encephalitis.[3] Cell surface antibody-mediated syndromes are approximately five times more common than intracellular syndromes,[4] are generally more treatable, and are more likely to present with predominantly behavioral symptomatology. Although less common than the cell surface antibody-mediated syndromes, intracellular antibody-associated paraneoplastic syndromes are present in approximately 0.01 to 1% of those diagnosed with cancer[5] and may precede the diagnosis of cancer by years.

### Course

The course of RPD is variable and depends on the cause. The average age of onset of sCJD is 60–70 years. Approximately 90% of patients die within one year of diagnosis and the average disease duration is seven months.[6] Patients may initially present with generalized fatigue, sleep disturbances, and decreased appetite, all of which may occur weeks before the onset of nervous system dysfunction. Behavioral changes can also be an early sign of disease.

Patients with cell surface antibody-mediated or intracellular antibody-associated syndromes may present with limbic encephalitis, psychiatric and behavioral disturbances, sleep disorders, seizures, and neurological signs and symptoms including cerebellar signs, movement disorders, and peripheral nervous system syndromes.

## Differential Diagnosis

The differential diagnosis for RPDs can be broken down into six main categories.[7]

**1. Neurodegenerative**

a. Creutzfeldt Jakob disease (CJD; sporadic, familial, iatrogenic)
b. Alzheimer's disease (AD)
c. Dementia with Lewy bodies (DLB)
d. Frontotemporal dementia (FTD)
e. Corticobasal degeneration (CBD)
f. Progressive supranuclear palsy (PSP)

**2. Infectious**

a. Viral encephalitis, including HSV
b. HIV dementia
c. Progressive multifocal leukoencephalopathy (PML)
d. Subacute sclerosing panencephalitis (SSPE; young adults)
e. Fungal infections (immunosuppression e.g., central nervous system (CNS) aspergillosis,)
f. Syphilis
g. Parasites
h. Lyme disease (rarely encephalopathy)
i. Balamuthia
j. Whipple's disease

**3. Toxic/Metabolic**

a. Vitamin B12 (cyanocobalmin) deficiency
b. Vitamin B1 (Thiamine) deficiency
c. Niacin deficiency
d. Folate deficiency (dementia rare)
e. Uremia
f. Wilson's disease
g. Portosystemic encephalopathy
h. Acquired hepatocerebral degeneration
i. Porphyria
j. Bismuth toxicity
k. Lithium toxicity
l. Mercury toxicity
m. Arsenic toxicity
n. Electrolyte abnormalities

**4. Autoimmune**

a. Paraneoplastic (autoimmune) limbic encephalopathy (PLE)
b. Non-paraneoplastic autoimmune (e.g., anti-VGKC mediated)
c. Lupus cerebritis and other rheumatologic encephalitis
d. Other CNS vasculitides
e. Sarcoid

**5. Endocrine Abnormalities**

a. Thyroid disturbances
b. Parathyroid abnormalities
c. Adrenal diseases

**6. Neoplasm-related**

a. Non-autoimmune paraneoplastic conditions
b. Metastases to CNS
c. Primary CNS lymphoma
d. Intravascular lymphoma
e. Lymphomatoid granulomatosis
f. Gliomatosis cerebri

### Diagnostic Approach

Two papers (written in 2007 and 2012) represent a review of 825 patients with RPD. The authors detail a structured approach to diagnosing various types of rapidly progressive dementias with the goal of identifying treatable ones as quickly as possible.[1,7,]

**1.** The initial step is to evaluate for delirium. The recommended diagnostic approach is to first order labs (blood, urine, CSF, imaging, and EEG) to attempt to rule out infections, autoimmune disorder, malignancy, vascular issues, and toxic-metabolic disorders.

**2.** With the results in hand, follow up tests like viral PCRs or CT body scans or serum vitamins B12 and E, can be ordered to pursue likely diagnoses.

**3.** Specific clinical and imaging features (such as movement disorders characteristic of specific cell surface antibody-mediated syndromes or a characteristic pattern of changes seen on diffusion imaging in CJD) can, in some cases, steer the experienced clinician directly to a particular diagnosis.

## Pharmacologic Management

### Medications to Use

Treatments will depend on the type of RPD diagnosed. Syndromes that are related to an underlying medical process, such as endocrine, neoplastic, or vascular disease, may benefit from aggressive treatment of that process, while autoimmune syndromes may respond well to immunotherapy. CJD is not known to have a cure, but some medications may help with symptom relief.

## Other Considerations

### Support Resources

Alzheimer's Association: alz.org

Family Caregiver Alliance: caregiver.org

National Institute of Health/National Institute on Aging: nia.nih.gov/alzheimers

CJD Foundation: cjdfoundation.org

The National Prion Disease Pathology Surveillance Center provides information and free brain autopsy service in the United States: cjdsurveillance.com

### Research and Clinical Trials

The National Institutes of Health maintains an extensive listing of clinical trials at clinicaltrials.gov. Academic medical centers may be engaged in research and clinical trials.

### Safety

If wandering or getting lost is a concern, refer the patient and family to the MedicAlert +Alzheimer's Association Safe Return program (operated by the Alzheimer's Association) alz.org/care/dementia-medic-alert-safe-return.asp.

Other strategies for ensuring safety concerns may include door alarms and increased supervision.

### Driving

Depending on cognitive and motor findings, the patient may be requested to stop driving, complete test of driving abilities through the Department of Motor Vehicles (DMV), or be referred to a driver's safety course that will assess driving ability. Reporting to the department of motor vehicles should be consistent with state laws. Some states have mandatory reporting requirements: the diagnosis is reported to local health departments who then report to the DMV. Individual state requirements can be found at: dmvusa.com.

### Living Situation and Environment

It is important to determine if the patient's residential setting best meets his or her functional and cognitive abilities. Areas of concern may include personal safety (ability to manage medications safely, ability to manage nutritional requirements, ability to manage personal hygiene) and quality of life (activities and engagement that match the person's needs and abilities).

Types of living situations range from living at home alone or living at home with supervision, to board and care, assisted living, or memory care units.

**References**

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