# The Jefferson Manual for Neurocritical Care

Jack I. Jallo
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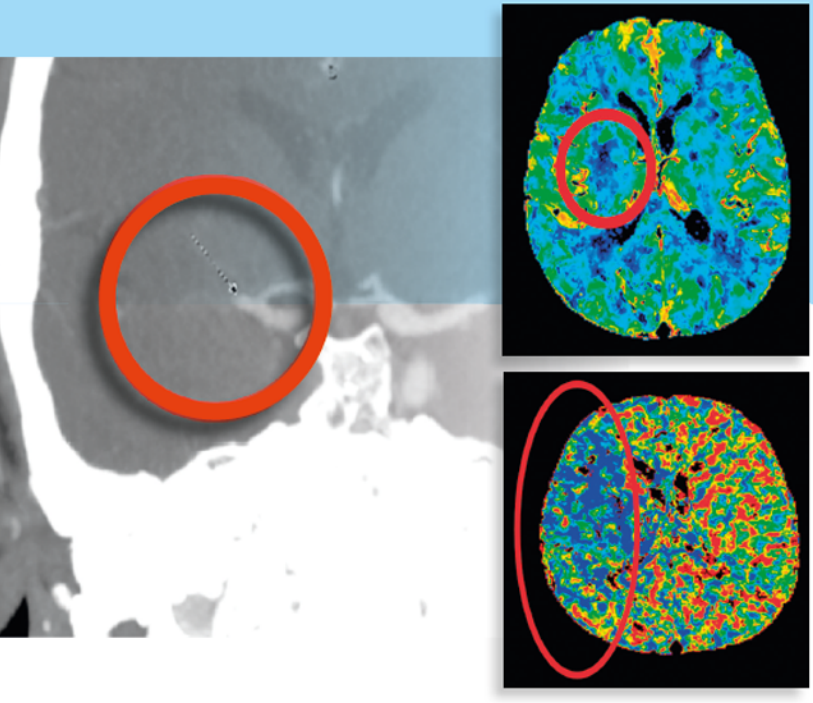

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# The Jefferson Manual for Neurocritical Care

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# Preface

*Everything we do, every thought we've ever had, is produced by the brain. But exactly how it operates remains one of the biggest unsolved mysteries, and it seems the more we probe its secrets, the more surprises we find.*

*Neil deGrasse Tyson*

This book was developed out of a desire to share our knowledge and experience in neurocritical care from Thomas Jefferson University Hospitals. The brain continues to be a "black box" for many practitioners and the need for expertise is greater than ever in this evolving field. As a large quaternary hospital with 40 dedicated neurocritical care beds and 8 board-certified neurointensivists, we have extensive experience with both common and rare neurological and neurosurgical diseases (ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, acute spinal cord injury, traumatic brain injury, encephalitis/meningitis, myasthenia gravis, Guillain-Barré syndrome). Using current guidelines and Thomas Jefferson University protocols, we map out a process for the diagnosis and treatment of the more common diseases managed in the neuro-ICU. We chose a format that would be user-friendly so that any practitioner could use at the bedside. As we continue to discover more of the brain's secrets and advance the field of neurocritical care, we will continue to update this handbook.

We would like to acknowledge and thank all the contributors to this book. Without their dedication and hard work, this book wouldn't have been possible.

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# 1 Encephalopathy and Delirium

*Catriona M. Harrop*

**Abstract**
Encephalopathy is characterized by the National Institute of Neurological Disorders and Stroke as "any diffuse disease of the brain that alters brain function or structure,"[1] and can be classified as acute or chronic. The definition, diagnosis, and treatment of encephalopathy is reviewed here, along with one of its most common symptoms, delirium.

*Keywords*: encephalopathy, delirium, confusion, agitation, arousability, Ramsay score, Riker score

## 1.1 Encephalopathy

### 1.1.1 Definition

The National Institute of Neurological Disorders and Stroke (NINDS) defines encephalopathy as "a term for any diffuse disease of the brain that alters brain function or structure"[1] with the hallmark of encephalopathy being an altered mental state. Encephalopathy can be categorized by chronicity[2]:

- Acute
  - Toxic: due to medications, illicit substances, or toxins
  - Metabolic: due to a metabolic disturbance
  - Toxic-metabolic: due to a combination of both
- Chronic: characterized by a slowly progressive alteration in mental status resulting from permanent structural changes within the brain[2]

### 1.1.2 Causes of Encephalopathy[3]

See ▶ Table 1.1.

### 1.1.3 Diagnosis of Encephalopathy

Diagnosis is guided by the history and physical examination of the patient. It is considered on a case-by-case basis.

- Laboratory testing
  - Serum electrolytes
  - Renal function
  - Glucose

- Calcium
- Complete blood count
- Urinalysis
- Hepatic function
- Thyroid function
- Drug levels (if applicable), i.e., phenytoin
- Drugs of abuse screen
- Vitamin levels—B-12, folate
- Arterial blood gas

- Imaging
  - Computed tomography (CT) of brain
  - Magnetic resonance imaging (MRI) of brain

**Table 1.1** Common causes of encephalopathy

| | |
|---|---|
| **Drugs and toxins** | Idiopathic<br>Withdrawal states<br>Medication side effects<br>Poisons |
| **Infections** | Sepsis<br>Systemic infections<br>Fever |
| **Metabolic derangements** | Electrolytes<br>Endocrine disturbance<br>Hypercarbia<br>Hyperglycemia and hypoglycemia<br>Hyperosmolar and hypo-osmolar states<br>Hypoxemia<br>Inborn errors of metabolism<br>Nutritional |
| **Brain disorders** | CNS infection<br>Seizures<br>Head injury<br>Hypertensive encephalopathy<br>Psychiatric disorders |
| **Systemic organ failure** | Cardiac failure<br>Hematologic<br>Hepatic encephalopathy<br>Pulmonary disease<br>Renal failure |

Abbreviation: CNS, central nervous system.

- Evaluation for infections
  - Lumbar puncture
  - Blood cultures
- Seizure evaluation
  - Electroencephalography (EEG)

### 1.1.4 Treatment of Encephalopathy

- Acute encephalopathy
  - Based on treatment of the underlying pathophysiology, i.e., treatment of sepsis and hypothyroidism with the potential for reversal of encephalopathy.
- Chronic encephalopathy
  - Often not amenable to treatment as the inciting insult has caused permanent brain changes, i.e., anoxic encephalopathy.

### 1.1.5 Relationship to Delirium

Delirium can be characterized as the symptom of the underlying abnormal brain function, i.e., encephalopathy.[2]

## 1.2 Delirium

Delirium is a common disorder in hospitalized patients that has significant societal and economic impact.[4] In-hospital mortality rates reportedly associated with delirium range from 22 to 33%.[5,6] Currently patients aged 65 years and older account for more than 48% of hospital care; therefore, the impact of delirium on hospitalized patients will continue to grow as our population ages.[4]

### 1.2.1 Definition

The Diagnostic and Statistical Manual of Mental Disorders (DSM) 5 defines delirium under Neurocognitive Disorders[7] which encompasses "the group of disorders in which the primary clinical deficit is in cognitive function, and that are acquired rather than developmental." The diagnostic criteria are as follows:

- A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
- The disturbance develops over a short period of time (usually from hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
- An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

- The disturbances are not explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or a medication), or exposure to a toxin, or is due to multiple etiologies.

As outlined in the DSM 5, Delirium can be further subdivided into:
- Substance intoxication
- Substance withdrawal
- Medication induced
- Another medical condition
- Multiple etiologies

## 1.2.2 Duration of Symptoms

- **Acute:** Lasting for a few hours or days
- **Persistent:** Lasting for weeks or months

## 1.2.3 Level of Activity (▶ Table 1.2)

- **Hyperactive:** The individual has a hyperactive level of psychomotor activity that may be accompanied by mood lability, agitation, and/or refusal to cooperate with medical care.
- **Hypoactive:** The individual has a hypoactive level of psychomotor activity that may be accompanied by sluggishness and lethargy that approaches stupor.
- **Mixed level of activity:** The individual has a normal level of psychomotor activity even though attention and awareness are disturbed. Also includes individuals whose activity level rapidly fluctuates.

**Table 1.2** Types of delirium

| | Description | RASS score | Prevalence[8] |
|---|---|---|---|
| Hyperactive | Agitation and restlessness | 1 + to 4 + | Rare (1.6%) |
| Hypoactive | Decreased responsiveness, withdrawal, apathy | 0 to 3 | Common in ICU (43.5%) |

Abbreviations: ICU, intensive care unit; RASS, Richmond Agitation Sedation Scale.

Table 1.3 Risk factors for delirium

| Predisposing factors[10] | Precipitating factors[11] | Targeted interventions[12] |
|---|---|---|
| • Cognitive impairment<br>• Severe underlying illness<br>• Advanced age<br>• Functional impairment<br>• Chronic renal insufficiency<br>• Dehydration<br>• Malnutrition<br>• Depression<br>• Substance abuse<br>• Vision or hearing impairment | • Use of physical restraints<br>• Malnutrition<br>• More than three medications<br>• Use of bladder catheter<br>• Psychoactive medication use<br>• Any iatrogenic event<br>• Immobilization<br>• Dehydration | • Noise reduction<br>• Reality orientation program<br>• Early mobilization<br>• Minimize medications<br>• Provision of visual and hearing aids<br>• Volume repletion and proper nutrition<br>• Optimize nonpharmacologic protocols |

A description of a patient in terms of the DSM 5 criteria could look like “acute, hypoactive delirium due to sepsis.”

## 1.2.4 Risk Factors for Delirium

Delirium involves a multifactorial etiology ranging from patient vulnerability to delirium at the time of admission and the occurrence of noxious insults during hospitalization.[9] See ▶ Table 1.3.

## 1.2.5 Clinical Assessment

Assessment begins in the intensive care unit (ICU) setting for the level of arousability, ranging from sedation to agitation, prior to assessing level of consciousness and subsequent delirium.[13]

### Arousability Assessment Tools

- **Richmond Agitation Sedation Scale (RASS):** See ▶ Table 1.4. A 10-point scale ranging from +4 to −5, created to assess sedation and agitation in the adult patient admitted to the ICU. An RASS score of 0 denotes a calm and alert patient. Positive RASS scores indicate positive or aggressive symptoms. Negative RASS scores differentiate between response to verbal commands (−1 to −3) and physical stimulus (−4 to −5).[3]
- **Ramsay score:** See ▶ Table 1.5. It defines the conscious state from a level 1: the patient is anxious, agitated, or restless, through to the continuously sedated level 6: the patient is completely unresponsive.[14]
- **Riker Sedation Agitation Scale (SAS):** See ▶ Table 1.6. It was developed in 1999 with the goal of clearly defining and providing more inclusive levels of sedation and agitation than the Ramsay score.[15]

**Table 1.4** Richmond Agitation Sedation Scale

| Richmond Agitation Sedation Scale | Description |
|---|---|
| +4 Combative | Overtly combative, violent, danger to staff |
| +3 Very agitated | Pulls or removes tubes or catheters; aggressive |
| +3 Agitated | Frequent nonpurposeful movement, fights ventilator |
| +1 Restless | Anxious, but movements not aggressive or vigorous |
| 0 Alert and calm | |
| −1 Drowsy | Not fully alert, but has sustained awakening (eye opening/eye contact) to voice (> 10 s) |
| −2 Light sedation | Briefly awakens with eye contact to voice (< 10 s) |
| −3 Moderate sedation | Movement or eye opening to voice (but no eye contact) |
| −4 Deep sedation | No response to voice, but movement or eye opening to physical stimulation |
| −5 Unable to rouse | No response to voice or physical stimulus |

**Table 1.5** Ramsay Sedation Scale

| Ramsay Sedation Scale | Description |
|---|---|
| 1 | Anxious, agitated, restless |
| 2 | Cooperative, oriented, tranquil |
| 3 | Responsive to commands only |
| 4 | Brisk response to light glabellar tap or loud auditory stimulus |
| 5 | Sluggish response to light glabellar tap or loud auditory stimulus |
| 6 | No response to light glabellar tap or loud auditory stimulus |

## Delirium Assessment

Confusion Assessment Method for the ICU (CAM-ICU): See ▶ Fig. 1.1. Four features assess fluctuation in mental status, inattention, disorganized thinking, and altered level of consciousness.[16]

**Table 1.6** Riker Sedation Scale

| Riker Sedation Agitation Scale | Description |
|---|---|
| 7 Dangerous agitation | Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side to side |
| 6 Very agitated | Requiring restraint and frequent verbal reminding of limits, biting ET tube |
| 5 Agitated | Anxious or physically agitated, calms to verbal instruction |
| 4 Calm and cooperative | Calm, easily arousable, follows commands |
| 3 Sedated | Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again |
| 2 Very sedated | Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously |
| 1 Unarousable | Minimal to no response to noxious stimuli, does not communicate or follow commands |

Abbreviation: ET, endotracheal.

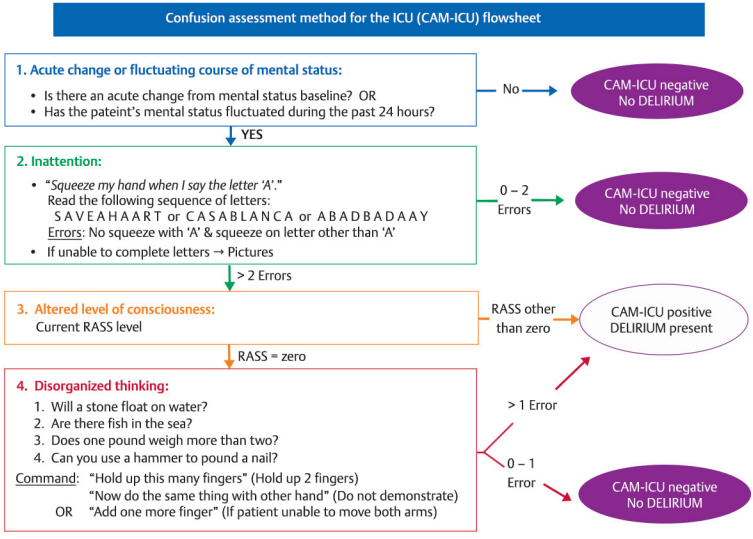


**Fig. 1.1** Confusion assessment method for the intensive care unit (CAM-ICU) flowsheet. 

**Table 1.7** Medications used to treat agitation

| Agent | Mechanism | Advantage | Adverse effects |
|---|---|---|---|
| Midazolam | Increases GABA activity | Rapid onset of action with high metabolic clearance | Respiratory depression, hypotension |
| Lorazepam | Increases GABA activity | Intermediate onset of action with mid-range metabolic clearance | Respiratory depression, hypotension; propylene glycol-related acidosis, nephrotoxicity |
| Diazepam | Increases GABA activity | Rapid onset of action with long half-life (10–20 hours) | Respiratory depression, hypotension, phlebitis |
| Propofol | Increases GABA activity | Rapid onset of action with high metabolic clearance | Pain on injection, hypotension, respiratory depression, hypertriglyceridemia, pancreatitis, allergic reactions, propofol infusion syndrome |
| Dexmedetomidine | Alpha 2 adrenergic receptor agonist | Provides sedation without respiratory depression risk | Bradycardia, hypotension; hypertension with loading dose; loss of airway reflexes |

Abbreviation: GABA, gamma aminobutyric acid.

# 1.3 Treatment

## 1.3.1 Medications for Agitation[3]

See ▶ Table 1.7.

## 1.3.2 Pharmacologic Management of Hyperactive Delirium and Agitation

See ▶ Table 1.8

## 1.3.3 Nonpharmacologic Treatments for Delirium[21]

- Frequent reorientation with signs, clocks, and calendars
- Address dehydration and constipation
- Assess for hypoxia and optimize oxygen saturation
- Assess for underlying infection
- Avoid unnecessary catherization
- Early mobilization

- Address pain
- Review medications
- Nutrition assessment
- Address reversible sensory impairment with glasses and hearing aids
- Promote good sleep hygiene

**Table 1.8** Medications used to treat delirium

| | Mechanism | Advantage | Adverse effects |
|---|---|---|---|
| **Typical antipsychotics**<br>Haloperidol<br>Chlorpromazine<br>Thioridazine | Postsynaptic blockade of dopamine D2 receptors with varying effect on neuronal 5-HT2a, alpha-1, histaminic, and muscarinic receptors[17] | Fewer anticholinergic effects, few active metabolites, minimally sedating, amelioration of hallucinations, delusion, and unstructured thought patterns[18] | Significant risk of extrapyramidal side effects and tardive dyskinesia; cognitive numbness and dysphoria, extrapyramidal side effects, neuroleptic malignant syndrome, dystonic reactions, ventricular arrhythmias, torsades de pointe, cardiac arrest, QT prolongation[17] |
| **Atypical antipsychotics**<br>Olanzapine<br>Risperidone<br>Quetiapine<br>Ziprasidone | Postsynaptic blockade of D2 receptors with varying effect on neuronal 5-HT2a, alpha-1, histaminic, and muscarinic receptors; *serotonin 5-HT2 receptor binding exceeds its loose affinity for dopamine D2* | Generally they have lower risk of extrapyramidal side effects and tardive dyskinesia compared with first-generation antipsychotics[19] | Weight gain and related metabolic effects, hypotension, sedation, anticholinergic symptoms, hyperprolactinemia, extrapyramidal symptoms (EPS), cardiac effects, cardiomyopathies, cataracts, and sexual dysfunction; *anticholinergic effects most prominent with olanzapine, quetiapine, and clozapine* |
| **Benzodiazepines**<br>Midazolam<br>Lorazepam<br>Diazepam | Bind to specific receptors in the gamma aminobutyric acid (GABA) receptor complex, which enhances the binding of this | Anxiolysis is achieved at low doses; rapid effect; duration varies and can be given via continuous infusion for stability | Sedation, respiratory and cardiovascular depression; *paradoxical reaction characterized by agitation, restlessness, and hostility*[20] |

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# 2 Cerebrovascular Emergency: Acute Stroke Diagnosis and Management

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**Abstract**
Stroke is one of the leading causes of disability in the USA. Timely acute interventions in the form of tPA and endovascular therapy have changed the landscape of acute stroke care. Having an organized and efficient system of care is extremely important for delivering acute stroke care. This chapter details the components of acute stroke care from the emergency room to the neurocritical care unit. The chapter covers pre- and post-tPA and endovascular care as well as post stroke complication management in the neurocritical care unit.

*Keywords*: acute stroke, tPA, endovascular therapy, neurocritical care

## 2.1 Epidemiology

- Stroke is the fifth leading cause of death in North America
- It is the leading cause of disability
- 795,000 people/year have a stroke in North America

## 2.2 Etiology

### 2.2.1 Nonmodifiable Risk Factors

- Age
- Sex
- Race
- Family history

### 2.2.2 Modifiable Risk Factors

- Hypertension
- Diabetes mellitus
- Hyperlipidemia
- Smoking
- Excessive alcohol use
- Obstructive sleep apnea

### 2.2.3 Stroke Subtypes

According to TOAST[9] classification there are five subtypes of ischemic stroke:

1. Large artery atherosclerosis
2. Cardioembolism
3. Small vessel occlusion (lacunar stroke)
4. Stroke of other determined etiology
   - Mechanical valves
   - Atrial fibrillation/flutter
   - Left atrial (LA) appendage thrombus
   - Left ventricular (LV) thrombus
   - Recent myocardial infarction (MI)
   - Dilated cardiomyopathy
   - Endocarditis/infection
   - Patent foramen ovale
   - Atrial septal aneurysm
   - Congestive heart failure
   - Vasculopathies
   - Hypercoagulable state
5. Stroke of undetermined etiology/cryptogenic

## 2.3 Common Clinical Presentations

Presentation depends on the vascular territory. See ▶ Table 2.1.

**F.A.S.T.** is the acronym most associated with recognition of early stroke signs:
**F** = Facial weakness
**A** = Arm weakness
**S** = Speech difficulty
**T** = Time to call 9–1-1

Once in the emergency department a more thorough examination using the National Institutes of Health Stroke Scale (NIHSS) is completed (▶ Table 2.2).

## 2.4 Differential Diagnosis for Acute Ischemic Stroke

- Intracerebral hemorrhage (ICH)
- Subarachnoid hemorrhage (SAH)
- Migraine with aura (most auras DO NOT last beyond 60 minutes nor present with loss of function)
- Transient global amnesia
- Postictal Todd's palsy (history of epilepsy or prior Todd's palsy, short duration with improvement)
- Hypoglycemia (rapid improvement with glucose correction)[2]

**Table 2.1** Common clinical presentation by vascular territory

| Vascular territory | Symptoms |
|---|---|
| Middle cerebral artery | Contralateral facial droop, weakness and sensory loss (arm > leg), aphasia, neglect, contralateral homonymous hemianopia, ipsilateral gaze deviation |
| Anterior cerebral artery | Contralateral hemiplegia (leg >> face and arm), abulia, rigidity, gait apraxia, urinary incontinence |
| Posterior cerebral artery | Contralateral homonymous hemianopia, alexia, contralateral sensory loss, cortical blindness, visual hallucinations, optic ataxia, gaze apraxia |
| Subcortical | Contralateral hemiplegia or hemisensory loss (usually face = arm = leg), no cortical features (aphasia, neglect), thalamic strokes may have aphasia, delirium, other cortical features |
| Basilar artery | Cranial nerve palsy, crossed sensory deficits, dizziness, diplopia, dysarthria, dysphagia, vertigo, nausea/vomiting, hiccups, contralateral weakness, ataxia, nystagmus, coma |

# 2.5 Acute Stroke Diagnosis, Treatment, and Management[4]

## 2.5.1 Stroke Activation (▶ Fig. 2.1)

- **ABC**: airway, breathing, circulation
  - $O_2$ saturation > 94% (supplemental oxygen is not recommended if the patient is not hypoxic)
  - Finger-stick glucose should be > 50
- Intravenous (IV) access
- **History:** Past medical, surgical, and medication (ask about antiplatelet and anticoagulant agents)
- Check electrocardiogram (ECG)—rule out acute ST-elevation myocardial infarction (STEMI)
- **Send STAT labs:** Coagulation panel and platelet
- Perform focal stroke examination using NIHSS (▶ Table 2.2 *shows the pictures and sentences used for questions 9 and 10 on the scale.*)